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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF PREVENTION, PESTICIDES AND TOXIC SUBSTANCES

OPP OFFICIAL RECORD
HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

MEMORANDUM

Date: 2/20/08

Subject: Metconazole. Petition for Establishment of Tolerances for Use on Small Grains, Stone Fruits, Tree Nuts, Peanuts, Soybeans, and Sugar Beets. Summary of Analytical Chemistry and Residue Data. PP#6F7094 and PP#6F7095.

DP#s:	348168, 348206	Decision Number:	369859
PC Code:	125619	MRID Nos.:	46665405, 46665407, 46901704-46901712, 46901717, 46901902-46901909, 46901912-46901915, 46902216-46902232, and 46902301-46902305
40 CFR 180.	617		
Chemical Class:	Triazole fungicide (Group 3)		

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This document was originally prepared under contract by Dynamac Corporation (2275 Research Blvd, Suite 300; Rockville, MD 20850; submitted 9/27/2007). The document has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

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Executive Summary

Metconazole (5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol) is a broad-spectrum triazole fungicide (sterol biosynthesis inhibitor). Metconazole is a systemic fungicide which acts primarily as an inhibitor of ergosterol biosynthesis, thereby interfering with synthesis of fungal cell membranes. A tolerance has been established on banana and a Section 18 emergency exemption and supporting time-limited tolerances have been granted for use on soybean (40 CFR §180.617). BASF Corporation is proposing use on barley, oats, rye, triticale, wheat, soybean, and sugar beet (PP#6F7094). Valent U.S.A. Corporation, as the agent for Kureha Corporation, is proposing use on stone fruit, tree nuts, and peanuts (PP#6F7095).

BASF Corporation is proposing the establishment of tolerances for residues of the fungicide metconazole in/on the following raw agricultural and processed commodities:

Barley grain	2.0 ppm
Barley hay	7.0 ppm
Barley straw	7.0 ppm
Beet, Sugar, root	0.1 ppm
Beet, Sugar, tops	2.0 ppm
Beet, Sugar, pulp, dry	1.9 ppm
Beet, Sugar, molasses	0.2 ppm
Beet, Sugar, raw	0.25 ppm
Oat, grain	0.1 ppm
Oat, straw	6.0 ppm
Oat, hay	17.0 ppm
Rye, grain	0.25 ppm
Rye, straw	14.0 ppm
Soybean, forage	3.0 ppm
Soybean, hay	6.0 ppm
Soybean, seed	0.1 ppm
Soybean, aspirated grain fraction	1.0 ppm
Soybean, hulls	0.2 ppm
Soybean, meal	0.1 ppm
Wheat, grain	0.15 ppm
Wheat, hay	16.0 ppm
Wheat, straw	18.0 ppm
Wheat, aspirated grain fraction	10.0 ppm
Wheat, milled byproducts (BP)	1.0 ppm

In conjunction with PP#6F7094, BASF has submitted a FIFRA Section 3 request to register two end-use products, a 0.75 lb/gal soluble concentrate/liquid (SC/L) formulation (Caramba™ Fungicide, EPA File Symbol No. 7969-EUA), and a 0.67 lb/gal SC/L formulation (BAS 556 01F Fungicide, EPA File Symbol No. 7969-EUT) which also contains the active ingredient pyraclostrobin at 0.83 lb/gal. The products are proposed for up to two foliar applications to barley, oats, rye, soybeans, sugar beets, triticale, and wheat at 0.048-0.10 lb ai/A/application for total application rates of 0.113-0.20 lb ai/A for the 0.75 lb/gal SC/L formulation, and at 0.036-

residues are cleaned up by an acetonitrile/hexane partition. The acetonitrile is then removed by rotary evaporation, and the residues are cleaned up using a C18 SPE cartridge. The column eluant is rotary evaporated and the residues are dissolved in toluene. Analysis of the extracts is performed using a gas chromatograph with a nitrogen-phosphorous detector (GC/NPD).

C. RESULTS AND DISCUSSION

Sample storage conditions and intervals are summarized in Table C.2. Samples were stored frozen (~-20 °C) from harvest to analysis for 44 days (1.4 months) for fresh plums and 42 days (1.4 months) for prunes; samples were analyzed within 2 days of extraction. Storage stability of *cis*- and *trans*-metconazole in stone fruit was determined by reanalysis of the fortified control cherry samples documented in *Magnitude of the Residues of Metconazole on Cherries* (MRID 46901707), in which selected samples were re-extracted, in duplicate, 159 days after the initial analysis of all of the crop field trial samples. Reanalysis indicated that both *cis*- and *trans*-metconazole were stable in frozen macerated cherries, with average recoveries of 101 and 103% of the original residues, respectively. Cherries and plums are listed in the same crop group (Fruit, Stone, Group 12) and the storage conditions for cherries were the same as those used in this study; therefore, the storage stability of *cis*- and *trans*-metconazole in frozen storage for 159 days was adequate based on the storage stability recovery results. The storage stability data for cherries may be translated to support the storage conditions and durations of samples from the plum processing study. Field sample residues were not corrected for in-storage dissipation.

The analytical method (Method RM-41C-1) was validated on plum RAC samples prior to treated sample analysis. Method validation was conducted using control peach samples fortified with *cis*- and *trans*-metconazole at two levels (0.02 and 0.1 ppm). The mean recoveries were 90.3 and 95.6% for *cis*-metconazole and the mean recoveries for *trans*-metconazole were 91.7 and 97.1%. The efficiency of the analytical method used in this study is adequate for data collection based on acceptable concurrent method recovery data (see Table C.1).

For each matrix, one control and two fortified control samples were analyzed. For the RAC and processed commodity samples (dried plums), controls were fortified with *cis*- and *trans*-metconazole at 0.02 and 0.10 ppm. For the RAC fortified controls, *cis*-metconazole averaged 96.2% (n=2) and *trans*-metconazole averaged 97.2% (n=2). For the dried plum fortified controls, *cis*-metconazole averaged 94.9% (n=2) and *trans*-metconazole averaged 95.5% (n=2). Residues were not detected at or above the LOD in/on the control samples. The fortification levels encompassed the expected residues in/on plums. The method was adequate for data collection based on acceptable method validation and concurrent method recoveries.

Residue data from the plum study with the metconazole isomers are reported in Table C.3. The results from the trial conducted at an exaggerated total application rate of 2.04 lb ai/A (5.4x the maximum seasonal application rate) and a 14-day PHI show that RAC residues of *cis*-metconazole averaged 0.11 ppm while *trans*-metconazole residues averaged 0.023 ppm. Total metconazole was calculated by taking the sum of *cis*- and *trans*-metconazole residues. The RAC total metconazole residues averaged 0.13 ppm (n=2). The processed fractions (dried plums) were

0.058 lb ai/A/application for total application rates of 0.115-0.157 lb ai/A for the 0.67 lb/gal SC/L formulation. Preharvest intervals (PHIs) of 14 days for sugar beets and 30 days for soybeans and small grains are proposed.

Valent is proposing the establishment of tolerances for residues of the fungicidal chemical metconazole in/on the following raw agricultural commodities:

Fruit, Stone – Crop Group 12	0.20 ppm
Nuts, tree – Crop Group 14	0.02 ppm
Pistachio	0.02 ppm
Almond hulls	5.00 ppm
Peanut	0.02 ppm

HED notes that the petitioner proposed separate tolerances for each of the crops in the stone fruit and tree nut groups (see Table 15 for a full list of crops).

In conjunction with PP#6F7095, Valent has submitted a FIFRA Section 3 request to register a 50% water dispersible granule (WDG) formulation (Metconazole 50 WDG Fungicide, EPA File Symbol 59639-RUT) for use on peanut, stone fruits, and tree nuts as three to four foliar applications at up to 0.125 lb ai/A/application with a maximum seasonal rate of 0.375 lb ai/A for stone fruits and 0.500 lb ai/A for peanuts and tree nuts. PHIs of 14 days (stone fruits and peanuts) and 25 days (tree nuts) are proposed.

Tolerances for metconazole are currently established under 40 CFR §180.617 and are expressed in terms of the fungicide metconazole. There are currently no Codex, Canadian, or Mexican MRLs/tolerances established for metconazole.

The nature of the residue in plants is adequately understood for purposes of these petitions. HED had previously determined, based on a banana metabolism study, that the residue of concern for the tolerance expression and risk assessment was metconazole *per se*. Metabolism studies on canola, mandarin, pea, and wheat were submitted under the current petitions, reflecting labeling in the chlorophenyl or cyclopentyl ring and the triazole ring of metconazole. HED has determined that the residue of concern for the tolerance expression in small grains, soybean, stone fruits, sugar beet, tree nuts, and peanut is metconazole *per* se. HED has also determined that the residue of concern for the risk assessment in soybean, stone fruits, sugar beet, tree nuts, and peanut is metconazole *per se*; the residues of concern for the risk assessment in small grains is metconazole *per se* and the metabolite M11.

The metabolism of metconazole in rotational crops appears to be similar to that observed in primary crops and has been adequately delineated for the purpose of these petitions. HED has determined that the residue of concern for the tolerance expression in rotational crops is metconazole *per* se. HED has also determined that the residue of concern for the risk assessment in rotational crops except for small grains is metconazole *per se*; the residues of concern for the risk assessment in small grains as rotational crops is metconazole *per se* and the metabolite M11.

Adequate ruminant and poultry metabolism data have been provided. Based on the submitted studies, the metabolism of metconazole in ruminants and poultry was generally similar. The

major routes of metabolism involved oxidation and/or oxidative hydroxylation of the methyl group at position 2 of the cyclopentyl ring and oxidative hydroxylation of the phenyl ring. Glucuronic acid conjugates were observed in the goat metabolism studies, and sulfate ester conjugates were observed in the hen metabolism study. In addition, in the hen metabolism study with triazole-labeled metconazole, C-N bond cleavage releasing 1,2,4-T was observed. Based on the available data, HED has determined that the residue of concern for the tolerance expression in livestock commodities is metconazole *per* se. HED also determined that the residues of concern for the risk assessment in livestock commodities are metconazole *per se*, M1 and its glucuronic acid conjugate, M12, and M31 and its glucuronic acid conjugate.

HED has concern for residues of free triazole and its conjugates, triazolylalanine and triazolylacetic acid, in plants and animals as a result of the use of metconazole. However, since separate endpoints for these compounds have been established, exposure and risks from free triazole and its conjugates will be addressed separately.

Data collection methods used to generate field trial, processing and storage stability data have all been adequately validated.

Both BASF and Valent have proposed enforcement methods. ACB/BEAD has reviewed BASF's plant method D0508, Valent's plant method RM-41C-1-1, and BASF's livestock method based on German multiresidue method DFG S19. The petitioner should modify the plant method D0508 to incorporate the recommendations of the ILV laboratory in an official enforcement method document reviewed by the petitioner's quality assurance unit. The petitioner must modify the plant method D0508 to provide information for a second MS/MS ion transition to provide a confirmation of analyte identity. If two ion transitions are not available, the Agency recommends that the petitioner provide an alternate chromatographic column and/or mobile-phase combination. HED concludes that method D0508, with multiresidue methods serving as the confirmatory method until the requested revisions are made, is adequate for enforcing tolerances for residues of metconazole *per se* in/on small grains, soybeans, and sugar beets. HED concludes that Valent's plant method RM-41C-1-1 is adequate for enforcing tolerances on peanuts, stone fruit, and tree nuts. HED also concludes that BASF's livestock method based on German multiresidue method DFG S19 is adequate for enforcing tolerances for residues of metconazole per se in/on livestock commodities.

Multiresidue methods testing data remain outstanding at this time.

Most of the submitted field trial and processing studies are supported by acceptable storage stability data for *cis*- and *trans*-metconazole. For rotational crops, additional storage stability data are required for cis- and *trans*-metconazole reflecting storage for up to 18 months for wheat grain and straw, 19 months for lettuce and wheat hay, and 21 months for radish roots and tops and wheat forage.

A ruminant feeding study has been submitted in which samples of milk, skim milk, cream, and tissues were analyzed for *cis*- and *trans*-metconazole, and samples of liver and kidney were also analyzed for the metabolites M1 and M12. Samples in the feeding study were not analyzed for the triazole metabolites, which were not identified in the triazole-labeled goat metabolism study (in which residues >0.01 ppm or >10% TRR were analyzed). The available data indicate that

tolerances are needed for the meat byproducts of cattle, goat, horse, and sheep at 0.04 ppm. No tolerances for swine commodities are needed. Valent has submitted a waiver request for the requirement for a poultry feeding study. HED has concluded that, based on the relatively high dietary burden (2.03 ppm) for poultry and the residue levels calculated for 1,2,4-T in liver by extrapolation from the hen metabolism study, a poultry feeding study is required.

Adequate field trial data have been submitted to support the proposed uses on barley, rye, soybean, sugar beet, and peanut. The available data on stone fruit and tree nuts will support conditional registration of the WDG formulation and tolerances of 0.20 ppm on stone fruit, 0.04 ppm on tree nuts and pistachio, and 4.0 ppm on almond hulls. The available data for oats and wheat are sufficient to support establishment of tolerances and conditional registration of the BASF 0.75 lb/gal SC/L and 0.67 lb/gal SC/L formulations. The available data will support the proposed tolerances for barley hay and straw; rye grain and straw, and soybean forage and hay. The available field trial data for oats and wheat will support conditional registration and tolerances at the proposed levels for oat hay and straw, and wheat hay, straw, and grain; an increased tolerance is needed for oat grain at 1.0 ppm. The available field trial data for barley grain and peanut indicate that the proposed tolerances of 2.0 ppm for barley grain and 0.02 ppm for peanut are too low; tolerances of 2.5 ppm for barley grain and 0.04 ppm for peanut are recommended. The available field trial data for soybean seed and sugar beet root indicate that the proposed tolerances of 0.1 ppm for each are too high; tolerances of 0.05 ppm for soybean seed and 0.07 ppm for sugar beet root are recommended. The proposed tolerance for sugar beet tops is not required because this commodity is no longer considered a significant livestock feed item. The tolerance calculations for barley hay, straw, and grain; oat hay, straw, and grain; rye straw and grain; soybean forage and hay; sugar beet root; wheat hay, straw, and grain; stone fruit (cherry and peach); and almond hulls are presented in Appendix II. The tolerance spreadsheet could not be used to determine tolerance levels for soybean seed, peanut, almond nutmeat, and pecan nutmeat because >60% of the field trial results for these commodities were below the LOQ.

Adequate processing data have been submitted for peanut, plum, soybean, sugar beet, and wheat to support the proposed uses. The available processing data indicate that residues are not likely to concentrate in peanut meal; soybean meal and refined oil; sugar beet refined sugar; and wheat flour and germ. Because metconazole residues do not concentrate in soybean meal, the proposed tolerance for soybean meal is not required. Because sugar beet raw sugar is not considered a significant food/feed item, a tolerance for this commodity is not required. Metconazole residues were found to concentrate in peanut refined oil; prune; soybean hulls; sugar beet dried pulp and molasses; and wheat bran, middlings, and shorts. Separate tolerances for peanut refined oil and prune are not needed as residues are not likely to concentrate above the recommended tolerances for peanut and plum. The processing data indicate that the proposed tolerances of 0.2 ppm for soybean hulls; 1.9 ppm and 0.2 ppm for sugar beet dried pulp and molasses; and 1.0 ppm for wheat milled byproducts are too high. Tolerances of 0.08 ppm for soybean hulls, 0.70 ppm and 0.08 ppm for sugar beet dried pulp and molasses, and 0.20 ppm for wheat milled byproducts are recommended. The available data for soybean and wheat aspirated grain fractions (AGF) indicate that metconazole residues concentrate in both. Individual tolerances for soybean and wheat AGF are not required. The available data indicate that the maximum expected metconazole residues are >2.5 ppm for soybean AGF and 6.2 ppm for wheat AGF; thus, a tolerance of 7.0 ppm is recommended for aspirated grain fractions.

Pending submission of additional storage stability data, the submitted field rotational crop data are adequate to fulfill data requirements. The available data will support a 30-day PBI for leafy vegetables and *Brassica* leafy vegetables; for all remaining crops other than those listed on the labels, a 120-day PBI must be established. If the petitioner wishes to support reduced plantback intervals for any crops, extensive field rotational crop field trials will be required, and rotational crop tolerances may be needed.

HED notes that one of the proposed new products, the 0.67 lb/gal SC/L formulation (BAS 556 01F Fungicide, EPA File Symbol No. 7969-EUT), contains the active ingredient pyraclostrobin at 0.83 lb/gal. The proposed uses of pyraclostrobin on small grains, soybeans, and sugar beets are not evaluated in this document. Tolerances do exist for residues of pyraclostrobin in/on barley, rye, soybean, sugar beet, and wheat commodities, but not in/on oat commodities [40 CFR §180.582(a)]. The adequacy of the proposed use directions for pyraclostrobin and the availability of adequate supporting residue data will be addressed in a separate review.

HED notes that residue data for the triazole metabolites (1,2,4-triazole, triazolylalanine, and triazolylacetic acid) are not being requested for these two petitions; however, for future submissions, triazole data will be required with plant and livestock metabolism studies, livestock feeding studies, crop field trial studies, and crop processing studies.

Regulatory Recommendations and Residue Chemistry Deficiencies

Provided revised Sections B (label) and F are received, there are no residue chemistry deficiencies that would preclude the registration and establishment of tolerances for residues of metconazole on small grains, sugar beets, soybeans, tree nuts, stone fruit or peanuts provided the remaining deficiencies cited below are satisfied as a condition of registration. Pending the favorable outcome of the 1,2,4-triazole, triazolylalanine, and triazolylacetic acid aggregate risk assessment, and provided the forthcoming Human Health Risk Assessment does not identify any risks of concern, HED recommends for establishment of the following tolerances:

Almond, hulls	4.0 ppm
Barley, grain	2.5 ppm
Barley, hay	7.0 ppm
Barley, straw	7.0 ppm
Beet, sugar, dried pulp	0.70 ppm
Beet, sugar, molasses	0.08 ppm
Beet, sugar, roots	0.07 ppm
Cattle, meat byproducts	0.04 ppm
Fruit, stone, group 12	0.20 ppm
Goat, meat byproducts	0.04 ppm
Grain, aspirated grain fractions	7.0 ppm
Horse, meat byproducts	0.04 ppm
Nut, tree, group 14	0.04 ppm
Oat, grain	1.0 ppm
Oat, hay	17 ppm
Oat, straw	6.0 ppm

Peanut	0.04 ppm
Peanut, refined oil	0.05 ppm
Pistachio	0.04 ppm
Rye, grain	0.25 ppm
Rye, straw	14 ppm
Sheep, meat byproducts	0.04 ppm
Soybean, forage	3.0 ppm
Soybean, hay	6.0 ppm
Soybean, hulls	0.08 ppm
Soybean, seed	0.05 ppm
Wheat, grain	0.15 ppm
Wheat, hay	16 ppm
Wheat, milled byproducts	0.20 ppm
Wheat, straw	18 ppm

Note to PM: Once permanent tolerances have been established as noted above, the time-limited tolerances for aspirated grain fractions, soybean hulls, meal, soybean refined oil, and soybean seed should be revoked. The time-limited tolerances for livestock commodities may be revoked at this time as well.

860.1200 Directions for Use

- The proposed SCL formulation labels should be amended to specify a minimum retreatment interval (RTI) of 6-8 days for small grains. In addition, the label restriction pertaining to green-chopped barley should be removed.

- The proposed labels must be amended to include the following rotational crop restrictions: a 30-day PBI for leafy vegetables and *Brassica* leafy vegetables; and a 120-day PBI for all remaining crops other than those listed on the label.

- The livestock grazing or feeding restrictions listed for the 50% WDG formulation under stone fruits and tree nuts should be removed. This restriction is unnecessary for the stone fruit use, and, in the case of almond hulls, is not permitted because this commodity is not under grower control.

- Since no spray adjuvants were used in the residue field trials on stone fruit and tree nuts, the 50% WDG label should state that no spray adjuvant should be used for stone fruit or tree nuts.

860.1300 Nature of the Residue – Plants

- Additional storage stability information and data are required for the wheat metabolism study. The petitioner must provide the actual dates of initial profiling for the studies to confirm that this step was completed within 6 months of harvest for all samples of grain and straw.

860.1340 Residue Analytical Methods – Crop Commodities

- The petitioner should modify the plant method D0508 to incorporate the recommendations of the ILV laboratory in an official enforcement method document reviewed by the petitioner's quality assurance unit.

- The petitioner must modify the plant method D0508 to provide information for a second MS/MS ion transition to provide a confirmation of analyte identity. If two ion transitions are not available, the Agency recommends that the petitioner provide an alternate chromatographic column and/or mobile-phase combination. Until this revision can be made, multiresidue methods will serve as the confirmatory method.

860.1340 Residue Analytical Methods – Livestock Commodities

- Radiovalidation data are required in support of data collection method M-41M-1.

860.1360 Multiresidue Methods

- HED has previously identified the need for metconazole to be tested through the appropriate FDA multiresidue method protocols. This deficiency remains outstanding.

860.1380 Storage Stability

- For rotational crop commodities, additional storage stability data are required for *cis*- and *trans*-metconazole reflecting storage for up to 18 months for wheat grain and straw, 19 months for lettuce and wheat hay, and 21 months for radish roots and tops and wheat forage.

860.1480 Meat, Milk, Poultry, and Eggs

- A poultry feeding study conducted at 1x, 3x, and 10x the theoretical dietary burden, and reflecting analysis for metconazole, M1, M12, M31, and the triazole metabolites (1,2,4-triazole, TA, and TAA) is required.

860.1550 Proposed Tolerances

- The available field trial data for oats and wheat will support conditional registration and tolerances at the proposed levels for oat hay and straw, and wheat hay, straw, and grain. An increased tolerance is needed for oat grain.

- The proposed tolerance for sugar beet tops is not required because this commodity is no longer considered a significant livestock feed item.

- The proposed tolerance for soybean meal is not required.

- Because sugar beet raw sugar is not considered a significant food/feed item, a tolerance for this commodity is not required.

- Individual tolerances for soybean and wheat AGF are not required; a separate tolerance for "grain, aspirated grain fractions" must be proposed at 7.0 ppm.

- Tolerances must be proposed for the meat byproducts of cattle, goat, horse, and sheep at 0.04 ppm.

- For all remaining commodities, the proposed tolerances must be revised to reflect the recommended tolerance levels and correct commodity definitions as specified in Table 15. Individual tolerances are not required for members of the stone fruit and tree nut crop groups.

Background

Valent has submitted a petition for permanent tolerances (PP#6F7095) and requested registration of a 50% WDG formulation (Metconazole 50 WDG Fungicide, EPA File Symbol 59639-RUT) for use on peanut, stone fruits, and tree nuts. Under a separate petition (PP#6F7094), BASF has proposed permanent tolerances and requested registration of a 0.75 lb/gal SC/L formulation (Caramba™ Fungicide, EPA File Symbol No. 7969-EUA), and a 0.67 lb/gal SC/L formulation

(BAS 556 01F Fungicide, EPA File Symbol No. 7969-EUT) which also contains the active ingredient pyraclostrobin at 0.83 lb/gal for use on barley, oats, rye, soybeans, sugar beets, triticale, and wheat. Permanent tolerances have been established for metconazole (40 CFR §180.617) on banana (for imported bananas) and time-limited tolerances have been established on soybean and livestock commodities (for a Section 18 on soybean).

While one of the BASF formulations contains the additional active ingredient, pyraclostrobin, this residue chemistry memorandum addresses chemistry data requirements for the active ingredient, metconazole, only. Pyraclostrobin residue chemistry data requirements will be addressed in a separate memorandum.

The nomenclature of metconazole is summarized in Table 1, and the physicochemical properties of metconazole are summarized in Table 2. The chemical names and structures of metconazole and its transformation products are presented in Appendix 1.

Table 1. Metconazole Nomenclature.

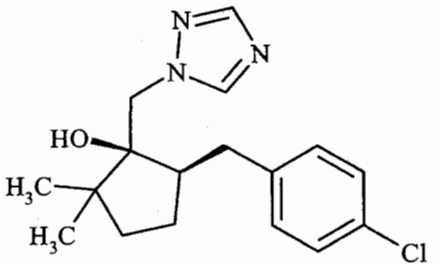
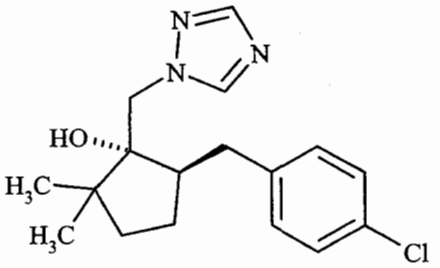
Chemical structure	 *cis*-isomer	 *trans*-isomer
Common name	Metconazole	
Company experimental name	KNF-S-474m (Kureha); BAS 555 F (BASF); V-10116 (Valent)	
IUPAC name	(1RS,5RS:1RS,5SR)-5-(4-chlorobenzyl)-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	
CAS name	5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	
CAS registry number	125116-23-6 (*cis*- and *trans*-isomers) 115850-27-6 (*cis*-isomer) 115850-28-7 (*trans*-isomer)	
End-use products (EP)	50% WDG (Metconazole 50 WDG Fungicide, EPA File Symbol 59639-RUT) 0.75 lb/gal SC/L (Caramba™ Fungicide, EPA File Symbol No. 7969-EUA) 0.67 lb/gal SC/L formulation (BAS 556 01F Fungicide, EPA File Symbol No. 7969-EUT; also contains the active ingredient pyraclostrobin at 0.83 lb/gal)	

Table 2. Physicochemical Properties of Metconazole

Parameter	Value	References* (MRID)
Melting point/range	100.0-108.4°C (using Electrothermal Digital Melting Point Apparatus) (AC900,768 technical grade)	44721505
pH	5.81 at 25°C (1% aqueous suspension)	46808402
Relative density (20°C)	1.14 (relative density to water at 4°C, using capillary-stoppered, density-specific gravity bottle) (Lot No. AC 8879-140B)	44721505
Water solubility (20°C)	Using shake-flask method: 18.7 ± 1.0 mg/L (*cis*-isomer, WL148271, KNF-S-474m) 13.6 ± 1.7 mg/L (*trans*-isomer, WL148271, KNF-S-474m)	44721505

Solvent solubility (g/L) at 20°C — 44721505

Solvent	Metconazole	*cis*	*trans*
acetone	363	251	117
methanol	403	294	117
dichloromethane	481	343	141
ethyl acetate	260	173	90.0
propanol	132	86.6	46.7
toluene	103	66.2	38.0
Hexane	1.40	0.929	0.483

Vapor pressure (20°C)	Using gas-saturation method: $< 1.23 \times 10^{-5}$ Pa or 9.23×10^{-8} mm Hg (metconazole) $< 1.04 \times 10^{-5}$ Pa or 7.80×10^{-8} mm Hg (*cis*-isomer) $< 1.96 \times 10^{-6}$ Pa or 1.47×10^{-8} mm Hg (*trans*-isomer)	44721505
Dissociation constant (pK_a)	11.38±0.03 and 1.06±0.03 (in water at 29.1°C using spectrophotometric method; Lot No. AC 8879-140B)	44721505
Octanol/water partition coefficient, Log(K_{OW})	At 20 °C (using flask shaking method): K_{ow} (log K_{ow}) = 7090±989 (3.85) (Lot No. AC 8879-140B) (TGAI) K_{ow} (log K_{ow}) = 7150±803 (3.85) (*cis*-isomer, CL 354,801) K_{ow} (log K_{ow}) = 6800±1700 (3.8) (*trans*-isomer, CL 354,802)	44721505

UV/visible absorption spectrum — 46808403

pH	λ	A	log ε
cis-isomer			
2.0	221.4	0.828	4.03
6.8		0.8452	4.04
7.0		0.9126	4.08
10.3		0.7226	3.98
trans-isomer			
2.0	221.4	0.9053	4.07
7.0		0.9547	4.10
10.1		0.9893	4.11

* Product Chemistry Reviews: DP #256877, Shyam Mathur, Ph.D., 9/12/2000 and DP #329168, Shyam Mathur, Ph.D., 7/13/07.

860.1200 Directions for Use

The petitioners have submitted draft labels for the BASF 0.75 lb/gal SC/L formulation (Caramba™ Fungicide, EPA File Symbol No. 7969-EUA) and 0.67 lb/gal SC/L formulation (BAS 556 01F Fungicide, EPA File Symbol No. 7969-EUT), and the Valent 50% WDG formulation (Metconazole 50 WDG Fungicide, EPA File Symbol 59639-RUT). The target crops and pests of the proposed end-use products are summarized in Table 3, and the proposed use directions for the three products are presented in Table 4.

Table 3. Summary of Proposed End-Use Products.

Trade Name	Reg. No.	ai Content	Formulation Type	Target Crops	Target Pests
Caramba™	7969-EUA	0.75 lb/gal	SC/L	Barley, oats, rye, triticale, and wheat	Black point, spot blotch, black point (*Cochliobolus* spp., *Alternaria* spp.), head scab, (*Fusarium* spp.), leaf, stem, and stripe rust (*Puccinia* spp.), net blotch, leaf spot and leaf blotch (*Pyrenophora* spp.), Powdery mildew (*Erysiphe graminis*), Scald (*Rhynchosporium secalis*), Septoria leaf and glume blotch (*Septoria* spp., *Stagonospora* spp.), tan spot (*Pyrenophora trichostoma*), spikelet blight (*Alternaria* spp., *Helminthosporium* spp.)
				Soybean	Alternaria leaf spot (*Alternaria* spp.), Anthracnose (*Colletotrichum truncatum*), Asian soybean rust and soybean rust (*Phakopsora pachyrhizi*), brown spot (*Septoria glycines*), Cercospora blight and frogeye leaf spot (*Cercospora kikuchii and C. sojina*), pod & stem blight (*Diaporthe phaseolorum*), Rhizoctonia aerial blight (*Rhizoctonial solani*)
				Sugar beets	Cercospora leaf spot (*Cercospora beticola*) and powdery mildew (*Erysiphe betae*)
BAS 556 01F Fungicide	7969-EUT	0.67 lb/gal metconazole/ 0.83 lb/gal pyraclostrobin	SC/L	Barley, rye, triticale, and wheat	See above
				Soybean	See above
				Sugar beet	See above

Table 3. Summary of Proposed End-Use Products.

Trade Name	Reg. No.	ai Content	Formulation Type	Target Crops	Target Pests
Metconazole 50 WDG Fungicide	59639-RUT	50%	WDG	Peanut	Leaf spot (*Cercospora arachidicola and C. personatum*); Rust (*Puccinia arachidis)*; Sclerotinia blight and white mold/stem rot (*Sclerotinia minor* and *S. rolfsii*)
				Stone fruit	Brown rot blossom blight and fruit brown rot (*Monilinia* spp.), powdery mildew (*Podosphaera leucotricha*), scab (*Cladosporium carpophilum*)
				Tree nuts	Brown rot blossom blight (*Monilinia laxa*), shot hole (*Wilsonomyces carpophilus*), scab (*Cerspora effuse*), panicle and shoot blight (*Botryosphaeria dothidea*)

Table 4. Summary of Directions for Use of Metconazole

Applic. Timing, Type, and Equip.	Formulation [EPA Reg. No.]	Applic. Rate (lb ai/A)	Max. No. Applic. per Season	Max. Seasonal Applic. Rate (lb ai/A)	PHI (days)	Use Directions and Limitations
Barley, Oats, Rye, Wheat, and Triticale						
Foliar, Broadcast, Ground (≥15 gal/A) or aerial (except NY; ≥5 gal/A)	0.75 lb/gal SC/L	0.056-0.10	2	0.20	30 [1]	Begin application immediately after flag leaf emergence or at beginning of anthesis.
	0.67 lb/gal SC/L	0.058		0.115		
Soybean						
Foliar, Broadcast, Ground (≥15 gal/A) or aerial (except NY; ≥5 gal/A)	0.75 lb/gal SC/L	0.048-0.056	2	0.113	30	May be applied from vegetative through full seed (R6) stage. Begin application between early flowering and pod set (R1-R3) or between full flower and full pod set stage (R2-R4). A 10- to 21-day RTI is specified. A nonionic surfactant may be used. The 0.75 lb/gal SC/L may be tank mixed at a maximum application rate of 0.035 lb ai/A with pyraclostrobin.
Foliar, Broadcast, Ground (≥15 gal/A) or aerial (except NY; ≥2 gal/A) [2]	0.67 lb/gal SC/L	0.036-0.045	3	0.135	30 14 (forage) 21 (hay)	

Table 4. Summary of Directions for Use of Metconazole

Applic. Timing, Type, and Equip.	Formulation [EPA Reg. No.]	Applic. Rate (lb ai/A)	Max. No. Applic. per Season	Max. Seasonal Applic. Rate (lb ai/A)	PHI (days)	Use Directions and Limitations
Sugar beet						
Foliar, Broadcast, Ground (≥15 gal/A) or aerial (except NY; ≥5 gal/A)	0.75 lb/gal SC/L	0.08-0.10	2	0.20	14	Begin application prior to disease development. A 14-day RTI is specified. For the 0.67 lb/gal SC/L, use of silicone-containing adjuvants is prohibited.
	0.67 lb/gal SC/L	0.037-0.052	3	0.157		
Peanut						
Foliar, Broadcast, Ground (≥20 gal/A) or aerial (≥5 gal/A)	50% WDG	0.054-0.125	4	0.500	14	Apply on a seven-application schedule with a non-Group 3 fungicide either as applications 1, 2, 6, and 7 for metconazole alone, or as applications 3, 4, 5, and 6 for metconazole in a tank mixture with pyraclostrobin. A 14-day RTI is specified. Use of a nonionic surfactant is recommended for control of certain diseases. A livestock grazing or feeding restriction is specified.
Stone Fruit: Apricot, Cherry (Sweet and Tart), Nectarine, Peach, Plum						
Foliar, Broadcast, Ground or aerial (≥20 gal/A for both)	50% WDG	0.08-0.125	3 (max. of 2 sequential apps.)[3]	0.375	14	Begin applications at green tip (cherry, plum) or early pink bud or pink, white, or red bud stage (apricot, nectarine peach), with additional applications at full bloom or petal fall and, for cherry and plum, subsequently at a 10- to 14-day RTI. No more than 2 applications are to be made after petal fall. A livestock grazing or feeding restriction is specified.

Table 4. Summary of Directions for Use of Metconazole						
Applic. Timing, Type, and Equip.	Formulation [EPA Reg. No.]	Applic. Rate (lb ai/A)	Max. No. Applic. per Season	Max. Seasonal Applic. Rate (lb ai/A)	PHI (days)	Use Directions and Limitations
Tree Nuts: Almond, Filbert, Pecan, Pistachio, Walnut						
Foliar, Broadcast, Ground or aerial (≥20 gal/A for both)	50% WDG	0.08-0.11 for almond, filbert, walnut, and pecan 0.125 for pistachio	4 (max. of 2 sequential apps.)[3]	0.44 for almond, filbert, walnut, and pecan 0.500 for pistachio	25	Almond, filbert, walnut: begin applications at pink bud (~5% bloom) with additional applications at full bloom or petal fall, and subsequently at a 10- to 14-day RTI. Pecan: begin applications when leaves reach ½ mature size. Pistachio: apply at 2- to 3-week intervals beginning late May to early June. No more than 2 applications may be made after petal fall. A livestock grazing or feeding restriction is specified.

[1] For barley, the 0.67 lb/gal SC/L formulation specifies a 30-day PHI but includes the following statement: Do not harvest barley hay or feed green-chopped barley within 14 days of last application.

[2] For aerial applications of the 0.67 lb/gal SC/L formulation to soybeans in 2-5 gal/A, the spray solution must contain crop oil with emulsifier properties at a rate of 0.5-1.0 pt/A. For aerial applications to soybeans at ≥5 gal/A, an approved adjuvant (e.g., NIS) at standard rates may be used.

[3] To avoid development of fungal resistance, alternate after two sequential applications with another fungicide which has a different target site of action.

A 12-hour reentry interval is specified for all three products, and no rotational crop restrictions are listed. The 0.75 lb/gal SC/L formulation may be applied through sprinkler irrigation systems; application through any type of irrigation system is prohibited for the 50% WDG and 0.67 lb/gal SC/L formulations.

No specific tank mix partners are specified for any of the listed products except peanuts and soybeans, for which tank mixing with pyraclostrobin (Headline®) is specified (see above). The labels state that if the products are used in tank mixtures with fungicides from different target site of action groups that are registered for the same use, at least the minimum labeled rates of each fungicide should be used. The label for the 50% WDG recommends use of a jar test to determine compatibility of adjuvants and tank mix partners; the labels for the 0.75 and 0.67 lb/gal SC/L formulations recommend testing tank mixes on a small portion of the crop to be treated to ensure that no phytotoxic response occurs.

Conclusions. The submitted use directions are sufficient to allow evaluation of the submitted residue data relative to the proposed use.

The proposed use directions are supported by the available field trial data pending the following label/Section B revisions:

- The proposed SCL formulation labels should be amended to specify a minimum retreatment interval (RTI) of 6-8 days for small grains. In addition, the label restriction pertaining to green-chopped barley should be removed.

- The proposed labels must be amended to include the following rotational crop restrictions: a 30-day PBI for leafy vegetables and *Brassica* leafy vegetables; and a 120-day PBI for all remaining crops other than those listed on the label.

- The livestock grazing or feeding restrictions listed for the 50% WDG formulation under stone fruits and tree nuts should be removed. This restriction is unnecessary for the stone fruit use, and, in the case of almond hulls, is not permitted because this commodity is not under grower control.

- Since no spray adjuvants were used in the residue field trials on stone fruit and tree nuts, the 50% WDG label should state that no spray adjuvant should be used for stone fruit or tree nuts.

860.1300 Nature of the Residue - Plants

DER Reference: 46901904.der.doc (Canola; includes review of MRID 46901905)
46901907.der.doc (Mandarin)
46901906.der.doc (Pea)
46901902.der.doc (Wheat; includes review of MRID 46901903)
Residue Chemistry Memo DP# 324541, 12/14/05, N. Dodd (PP# 9E05052)

Banana

A banana metabolism study with [^{14}C]metconazole, radiolabeled at the 3,5-triazole position or uniformly in the chlorophenyl ring, was submitted in conjunction with the banana import tolerance petition. In the study, the distribution of parent and metabolites was similar between banana whole fruit, peel, and pulp, and between the two ^{14}C-labels. A total of 90-95% of the total radioactive residues (TRR) was identified in whole fruit, peel and pulp samples. Metconazole was the major residue identified in all banana matrices, accounting for 86-89% of the TRR. A total of five metabolites were also identified, with each one accounting for <4% of the TRR (#0.040 ppm). These metabolites included three hydroxylated metabolites (CL 359451 [M1], CL 382390 [M11], and an unspecified monohydroxy metabolite), a glucose conjugate of hydroxy-metconazole, and TA. No reference standards of 1,2,4-T or TAA were included in the study; detection of these metabolites was not reported.

In banana, metconazole was metabolized primarily through oxidative hydroxylation of the benzylic methylene and the methyl groups on the cyclopentyl ring, followed by conjugation with glucose.

Based on the results of the banana metabolism study, HED determined that the residue of concern for tolerance expression and risk assessment in banana is metconazole *per se.*

Canola

Valent has submitted studies investigating the metabolism of [chlorophenyl-U-^{14}C]metconazole (specific activity 10 μCi/mg) and [triazole-3,5-^{14}C]metconazole (specific activity 9.58 μCi/mg) in canola. Details of the studies are contained in the Data Evaluation Records (DERs) cited above. In brief, radiolabeled test substances were applied as two broadcast foliar applications with a 14-day RTI to canola grown in outdoor plots at the early flowering stage at 0.235 lb ai/A/application (263.5 g ai/ha/application) for the chlorophenyl label and 0.238 lb ai/A/application (264.5 g/ai/ha/application) for the triazole label, for total application rates of 0.470 lb ai/A (527 g ai/ha) and 0.476 lb ai/A (529 g ai/ha), respectively. The total application rates correspond to ~3.5x the maximum proposed seasonal application rate to soybean (the oil-bearing crop proposed for registration). Samples of canola foliage were harvested immediately following the first and second applications, and 14 and 28 days after the second application. Samples of canola pod (pod shell and foliage combined) and seed were harvested at maturity (28 days after the second application), and allowed to dry in the field for 16-22 days.

In the chlorophenyl study, metconazole was the primary residue identified in all canola matrices, accounting for 96.0% and 85.3% TRR (10.36 and 12.75 ppm) in 0-DAT1 and 0-DAT2 foliage, respectively, 67.8% and 60.8% TRR (3.80 and 3.60 ppm) in 14- and 28-DAT2 foliage, respectively, 40.3% TRR (8.32 ppm) in pod, and 39.0% TRR (0.72 ppm) in seed. The only other identified metabolite was M11, which accounted for 0.05-1.4% TRR in foliage, 1.5% TRR in pod, and 7.3% TRR in seed. No other metabolites were characterized in 0-DAT1 foliage, and no single metabolite accounted for >4% TRR in any other foliage sample. OH-metconazoles, including CC-8, accounted for 2.1-6.5% TRR (0.32-0.46 ppm) in 0-2-, 14-, and 28-DAT2 foliage, and GOH-metconazoles accounted for 3.4-14.6% TRR (0.51-0.86 ppm); levels of both types of metabolites increased with increasing sampling interval. In pod and seed, OH-metconazoles, including CC-8, accounted for 20.1% and 26.4% TRR (4.17 and 0.49 ppm), respectively, with individual metabolites present at ≤9.5% TRR (CC-7) in pod and ≤8.3% TRR (CC-10) in seed. GOH-metconazoles accounted for 23.2% and 13.6% TRR (4.79 and 0.25 ppm), respectively, in pod and seed, with individual metabolites present at ≤7.6% TRR (CC-6) in pod and 4.0% TRR (CC-6) in seed. Remaining residues in all matrices consisted of minor components characterized as an extremely polar metabolite (CC-1; ≤3.3% TRR), an extremely nonpolar metabolite (CC-13; ≤2.3% TRR in 14- and 28-day foliage, and pod only), and multicomponent unknowns, accounting for up to 7.1% TRR in foliage, 2.5% TRR in pod, and 4.2% TRR in seed.

In the triazole study, metconazole was the primary residue identified in canola foliage and pod, accounting for 92.9% and 72.8% TRR (8.13 and 7.20 ppm) in 0-DAT1 and 0-DAT2 foliage, respectively, 55.3% and 56.7% TRR (4.77 and 11.53 ppm) in 14- and 28-DAT2 foliage, respectively, and 16.4% TRR (3.32 ppm) in pod; metconazole accounted for 24.1% TRR (0.57 ppm) in seed. The major identified residue in seed was TA, which accounted for 40.2% TRR (0.96 ppm). TA was not found in 0-DAT1 and 0-DAT2 foliage, but was found in 14- and 28-DAT2 foliage at 5.2% and 5.6% TRR (0.45 and 1.15 ppm), respectively, and in pod at 6.7% TRR (1.31 ppm). The only other identified metabolite was M11, which accounted for 1.3-2.0% TRR in 14- and 28-DAT2 foliage, 1.7% TRR in pod, and 4.3% TRR in seed. As in the chlorophenyl study, the majority of the remaining components were characterized as OH-metconazoles or GOH-metconazoles. No single metabolite accounted for >6.4% TRR in any foliage sample.

OH-metconazoles, including CC-4 accounted for 1.1-15.3% TRR (0.1-2.79 ppm) in foliage from all sampling intervals; GOH-metconazoles were not identified in 0-DAT1 foliage, but accounted for 1.9-10.4% TRR (0.18-2.13 ppm) in remaining foliage samples; levels of both types of metabolites increased with increasing sampling interval. In pod and seed, OH-metconazole metabolites, including CC-4, accounted for 39.7% and 13.4% TRR (7.8 and 0.32 ppm), respectively, with individual metabolites present at ≤15.2% TRR (CT-6) in pod and ≤5.4% TRR (CC-10) in seed. GOH-metconazoles accounted for 25.0% and 6.6% TRR (4.93 and 0.15 ppm), respectively, in pod and seed, with individual metabolites present at ≤11.6% TRR (CC-6) in pod and 3.5% TRR (CC-6) in seed. Remaining residues in all matrices consisted of minor components characterized as a relatively polar metabolite (CT-2; ≤2.2% TRR), an extremely nonpolar metabolite (CT-14; ≤2.2% TRR in foliage and pod), and multicomponent unknowns, accounting for up to 17.6% TRR in foliage, 1.1% TRR in pod, and 4.6% TRR in seed.

Based on the submitted canola metabolism studies, the petitioner proposed that the main metabolic route of metconazole in canola is via oxidative hydroxylation of the methylene groups, the methyl groups on the cyclopentyl ring, and possibly of the cyclopentyl ring. The detection of TA as a major seed metabolite in the triazole study indicates that the methylene group between the triazole and cyclopentyl rings is susceptible to oxidative hydroxylation. The large number of OH-metconazole metabolites and glucose conjugates of OH-metconazole suggests monohydroxylation at the various pro-chiral carbons of metconazole, giving rise to chromatographically distinguishable stereoisomeric structures.

Mandarin

Valent has submitted a study investigating the metabolism of [cyclopentyl-^{14}C]metconazole (specific activity 343307.4 dpm/µg) and [triazole-3,5-^{14}C]metconazole (specific activity 388331.3 dpm/µg) in mandarin. Details of the study are contained in the DER cited above. In summary, radiolabeled test substances were applied as single broadcast foliar applications to mandarin trees grown in greenhouses at the fruit-growing stage at 0.178 lb ai/A (200 g ai/ha; ~0.5x the maximum proposed seasonal rate for stone fruits). Samples of mandarin fruits and leaves were harvested 0, 28, and 56 days after treatment (DAT).

Metconazole was the primary residue identified in mandarin peel and leaves from both labels at all sampling intervals, accounting for 92.12-94.71% TRR (0.0972-0.1158 ppm for peel and 3.9240-4.5814 ppm for leaves) in 0-DAT samples; 54.06-56.90% TRR (0.0530-0.0537 ppm in peel and 1.9895-1.9949 ppm in leaves) in 28-DAT samples; and 45.22-48.93% TRR (0.0339-0.0553 ppm in peel and 1.4801-1.4958 ppm in leaves) in 56-DAT samples. Metabolite M21 was the only other identified residue, accounting for 0.22-0.57% TRR, 1.74-2.38% TRR, and 1.64-2.68% TRR, respectively, in 0-, 28-, and 56-DAT peel and leaves. Residues characterized as glucose conjugates (fractions 5-7) accounted for ≤2.55% TRR in 0-DAT peel and leaf samples; 23.72-26.38% TRR (0.0235-0.0255 ppm) and 28.62-29.79% TRR (0.0206-0.0335 ppm) in 28- and 56-DAT peel, respectively; and 17.70-18.48% TRR (0.6452-0.6475 ppm) and 20.97-22.25% TRR (0.6885 and 0.6930 ppm) in 28- and 56-DAT leaves. Portions of these residues were tentatively characterized/identified in 56-DAT samples as glucose conjugates of metconazole metabolites, including: (1) mono- or di-hydroxylated metconazole, aglycones 1 and 3, respectively, at 7.95-8.58% and 2.96-3.37% TRR in peel, and 3.35-3.89% and 0.92-0.98% TRR in leaves; (2) metabolite M2, aglycone 2, at 1.82-1.94% TRR in peel and 0.69-0.82% TRR in

leaves; and (3) metabolite M1, aglycone 4, at 2.96-2.98% TRR in peel and 1.36-1.39% TRR in leaves. Fraction 6, which represented up to 21% TRR in peel and 12% TRR in leaves, was shown to be comprised of multiple components, none exceeding 8.16% TRR in peel extracts or 3.61% TRR in leaves. Two fractions characterized as free metabolites (fractions 8 and 9) together accounted for up to 6.41% TRR in peel and up to 10.25% TRR in leaves. Remaining residues consisted of polar and nonpolar unknowns, which represented ≤2.14% TRR in peel and ≤2.68% TRR in leaves.

Based on the submitted mandarin metabolism study, the petitioner proposed that the main metabolic route of metconazole in mandarin is via hydroxylation to form several metabolites including M1 and M2. These metabolites are further metabolized to form glucose conjugates and/or bound residues. Hydroxylation in the 4-chlorobenzyl position to form M21 was also observed as a minor metabolic pathway.

Pea

Valent has submitted a study investigating the metabolism of [chlorophenyl-U-^{14}C]metconazole (specific activity 9.99 μCi/mg) and [triazole-3,5-^{14}C]metconazole (specific activity 10 μCi/mg) in peas. Details of the study are contained in the document cited above. In summary, the radiolabeled test substances were applied as two or three broadcast foliar applications to pea plants at ~0.193 lb ai/A/application (~216 g ai/ha/application; 1.4x the maximum proposed seasonal application rate for soybean, the legume crop proposed for registration) beginning at the early crop cover stage. Two applications were made to pea plants grown in one pot for each label to simulate applications to green or canned peas, and three applications were made to pea plants grown in a second pot for each label to simulate application to dry peas. Applications were made at 13- and 14-day RTIs; samples of immature pea foliage were harvested immediately following each application [0 days after treatment 1 (0-DAT1), 0-DAT2, and 0-DAT3], and samples of pea seed and straw were collected 13-DAT2 (green pea) and 15-DAT3 (dry pea). The total application rates for the chlorophenyl and triazole labels were 0.188 lb ai/A (211.2-210.9 g ai/ha) following one application, 0.371-0.373 lb ai/A (415.8-418.1 g ai/ha) following two applications, and 0.557-0.559 lb ai/A (623.8-626.1 g ai/ha) following three applications.

The metabolic profile was similar in pea foliage and straw from both labels. Metconazole was the primary residue identified in all samples of foliage and straw. Metconazole accounted for 94.1% and 95.9% TRR (8.251 and 10.201 ppm) in 0-DAT1 foliage, 78.7% and 78.8% TRR (4.796 and 6.858 ppm) in 0-DAT2 foliage, and 79.3% and 66.7% TRR (6.675 and 7.401 ppm) in 0-DAT3 foliage from chlorophenyl- and triazole-label samples, respectively. The majority of the remaining residues were characterized as more polar than metconazole, accounting for 5.3%, 16.4%, and 15.6% TRR (0.461, 1.008, and 1.311 ppm) in 0-DAT1, 0-DAT2, and 0-DAT3 chlorophenyl-label foliage, and for 3.45%, 16.8%, and 29.5% TRR (0.362, 1.453, and 3.279 ppm) in 0-DAT1, 0-DAT2, and 0-DAT3 triazole-label foliage. Residues characterized as less polar than metconazole accounted for ≤3.4% TRR in chlorophenyl-label foliage and ≤1.0% TRR in triazole-label foliage.

Metconazole was generally identified at lower levels in straw, accounting for 58.7% and 54.1% TRR (4.603 and 32.585 ppm), respectively, in 13-DAT2 and 15-DAT3 chlorophenyl-label straw, and for 64.9% and 67.6% TRR (7.804 and 33.219 ppm), respectively, in 13-DAT2 and 15-DAT3

triazole-label straw. Residues characterized as more polar than metconazole accounted for 30.2% and 31.0% TRR (2.370 and 18.679 ppm), respectively, in 13-DAT2 and 15-DAT3 chlorophenyl-label straw, and for 27.3% and 22.9% TRR (3.298 and 11.203 ppm), respectively, in 13-DAT2 and 15-DAT3 triazole-label straw. Residues characterized as less polar than metconazole accounted for ≤7.0% TRR in chlorophenyl-label straw and for ≤2.1% TRR in triazole-label straw. On further examination of the nonextractable residues of 15-DAT3 straw, only minor amounts of radioactivity were found to have been incorporated into cell wall components (≤3.24% TRR in lignin, pectin, cellulose or polysaccharides).

The metabolic profile in pea seed was significantly different in chlorophenyl- and triazole-label samples. Metconazole was the primary residue identified in chlorophenyl-label pea seed, accounting for 35.7% TRR (0.016 ppm) in 13-DAT2 seed and 21.1% TRR (0.043 ppm) in 15-DAT3 seed. In triazole-label seed, the primary identified residue was TA, accounting for 75.9% TRR (1.188 ppm) in 13-DAT2 seed and 89.1% TRR (3.303 ppm) in 15-DAT3 seed; metconazole was a minor residue, accounting for 3.4% and 2.2% TRR, respectively, in 13-DAT2 and 15-DAT3 seed. In chlorophenyl-label seed, residues characterized as more polar than metconazole accounted for 33.6% TRR (0.015 ppm) in 13-DAT2 seed and 53.4% TRR (0.108 ppm) in 15-DAT3 seed, with discrete components present at up to 11.5% TRR (0.005 ppm) and 26.6% TRR (0.054 ppm) at the respective sampling intervals; residues characterized as less polar than metconazole accounted for ≤5.7% TRR. In triazole-label seed, residues characterized as more polar than metconazole accounted for 19.9% TRR (0.311 ppm) in 13-DAT2 seed and 2.7% TRR (0.101 ppm) in 15-DAT3 seed, and residues characterized as less polar than metconazole accounted for ≤0.7% TRR.

Based on the submitted pea metabolism studies, the petitioner proposed that the main metabolic route of metconazole in pea involves oxidative hydroxylation of the methylene groups, the methyl groups on the cyclopentyl ring, and possibly of the cyclopentyl ring itself. The detection of TA as a major metabolite indicates that the methylene group between the triazole and cyclopentyl rings is susceptible to oxidative hydroxylation. The multiple monohydroxylated metabolites and their conjugates represent the various chromatographically distinguishable stereoisomeric structures due to monohydroxylation at the various prochiral carbons of metconazole. Further oxidation of the hydroxylated metabolites to form dihydroxylated or carboxylated derivatives was not evident in pea. However, it appeared that the monohydroxylated metabolites were at least partly conjugated with glucose to form glucosides as terminal residues in the pea foliage, straw and seed.

Wheat

Valent has submitted studies investigating the metabolism of [cyclopentyl-^{14}C]metconazole (specific activity 17.5 µCi/mg) and [triazole-3,5-^{14}C]metconazole (specific activity 23.2 µCi/mg) in winter wheat. Details of the studies are provided in the DERs cited above. The radiolabeled test substances were applied as a single foliar broadcast application to wheat at 0.330 lb ai/A (360 g ai/ha) for the cyclopentyl label and 0.347 lb ai/A (370 g ai/ha) for the triazole label. The total application rates correspond to ~1.7x the maximum proposed seasonal application rate to wheat. Wheat plants were grown in outdoor plots and application was made at Zadoks growth stage 57-60. Samples of wheat grain and straw were harvested 61 days after application for the cyclopentyl label and 73 days after application for the triazole label; samples of forage and hay

were not collected. HED notes that application of the test substance was made to wheat after the stages that forage and hay are normally collected.

Metconazole was the primary identified residue in straw from both labels, accounting for 34.1% TRR (2.01 ppm) in cyclopentyl-label straw and for 22.0% TRR (1.39 ppm) in triazole-label straw. In cyclopentyl-label straw, metabolites M11 and M21 were major residues, accounting for 9.7-9.8% TRR (0.57-0.58 ppm), while in triazole-label straw, M11 was identified at 1.8% TRR (0.11 ppm), and M21 was not identified. Metabolite M30 was identified in straw from both labels, at 1.0% TRR in cyclopentyl-label straw and 5.4% TRR in triazole-label straw. Metabolite M1 was identified at 3.4% TRR in cyclopentyl-label straw, and metabolite M2 was identified at 1.8% TRR in triazole-label straw. Metabolites A2-5 (4191) and TAA were identified in triazole-label straw only, at 3.3% and 0.3% TRR, respectively. Remaining residues in straw were characterized as monohydroxy-metconazole metabolites (1.4% TRR in cyclopentyl-label straw and 11.5% TRR in triazole-label straw) or on the basis of organo- or aqueous solubility. The only metabolites identified in triazole-label grain were TA, at 69.7% TRR (0.46 ppm), and TAA, at 24.2% TRR (0.16 ppm).

Based on the submitted wheat metabolism studies, the petitioner proposed that the main metabolic transformations of metconazole in wheat were oxidation at the benzylic methylene to give the two monohydroxylated stereoisomers (M11 and M21) and the corresponding ketone (M30), and oxidation at the methyl groups of the cyclopentyl ring. Oxidation at the methylene group next to the triazole ring was also indicated due to the presence of triazole conjugates in wheat grain.

Conclusions. Metabolism data have been provided for banana, canola, mandarin, pea, and wheat. The submitted canola and pea metabolism studies are adequate. The wheat metabolism study may be considered adequate to delineate the nature of the residue in wheat grain and straw provided additional storage information is submitted. The petitioner must provide the actual dates of initial profiling for the studies to confirm that this step was completed within 6 months of harvest for all samples of grain and straw.

Provided that the outstanding data for the wheat metabolism study are submitted, HED concludes that, for purposes of these petitions, the nature of the residue in plants is adequately understood. For the subject action, the available data for canola and pea foliage may be translated to support use on wheat hay. The metabolism of metconazole was found to be similar in all crops investigated.

HED has determined that the residue of concern for the tolerance expression in small grains, soybean, stone fruits, sugar beet, tree nuts, and peanut is metconazole *per* se. HED has also determined that the residue of concern for the risk assessment in soybean, stone fruits, sugar beet, tree nuts, and peanut is metconazole *per se*; the residues of concern for the risk assessment in small grains is metconazole *per se* and the metabolite M11. M11 was found at levels exceeding 1 ppm in oat and wheat straw in field trial studies at the proposed application rate, and at higher relative amounts than observed in the nature of the residue studies (ROCKS meeting, DP #348234, 10-JAN-2008 and 16-JAN-2008).

HED generally includes 1,2,4-T, TA, and TAA as residues of concern for risk assessment purposes for most triazole-containing pesticides. 1,2,4-T was a major residue found in some livestock commodities, and TA and TAA were significant residues in some plant metabolism studies. However, since separate endpoints for these compounds have been established, exposure and risks from free triazole and its conjugates will be addressed separately.

860.1300 Nature of the Residue - Livestock

DER Reference: 46901908 (Goat; cyclopentyl label)
46901909 (Goat; triazole label)
46901912 (Hen)

HED notes that two additional hen metabolism studies (MRIDs 46901910 and 46901911) were submitted by Valent. These studies, which were conducted in 1992-1993, are superseded by MRID 46901912; therefore, DERs were not prepared.

Goat (cyclopentyl label)

Valent has submitted a study investigating the metabolism of [cyclopentyl-^{14}C]metconazole (specific activity 10.33 µCi/mg) in goats. Two goats were orally dosed with the radiolabeled test substance at a target dose of 25 mg per day. Goat 1 was dosed for three consecutive days, and Goat 2 was dosed for four consecutive days; a third goat was dosed with a capsule containing ethanol only as a control. Based on the daily feed consumption, average dosing levels were equivalent to 14 and 25 ppm in the diet for Goat 1 and Goat 2, respectively. The dose rates correspond to1.6x and 2.8x the current dietary burden to dairy cattle and 3.8x and 6.8x the dietary burden to beef cattle based on the existing and proposed new uses. Milk was collected twice daily, and selected samples were separated into cream, curds, and whey. Goats were sacrificed 18 hours following the last dosing, and tissue samples of muscle (fore and hind leg), fat (renal and deep body), liver, and kidney were collected.

The in-life and initial analytical phases of the study were conducted by Inveresk Research International (IRI; Tranent, Scotland). Characterization and identification of metabolites in tissues were further investigated at Sittingbourne Research Center (SRC; Sittingbourne, England); these results were used to delineate the nature of the residue in goat matrices.

TRR in goat milk and tissues were determined at IRI. TRR were highest in liver (0.456 ppm, Goat 1; 0.559 ppm, Goat 2), then kidney (0.145 ppm, Goat 1; 0.276 ppm, Goat 2), and were very low in fat (ND-0.015 ppm), muscle (0.001-0.005 ppm) and milk (0.001-0.004 ppm). Fractionation of whole milk samples into cream, curds, and whey yielded average proportions of 4:23:73 (cream:curds:whey). The majority (55-69%) of the radioactivity was excreted, with relatively similar amounts in the urine and feces.

Only kidney and liver had TRR >0.015 ppm; therefore, extractions for metabolite identifications were focused mainly on the kidney and liver samples from Goat 2 (which bore higher residues than Goat 1). Initially at IRI, ~96-98% of the TRR in kidney and liver was extracted using ACN and ACN/water; nonextractable residues were 2.5-3.7% TRR. Kidney and liver samples were re-extracted for further residue characterization at SRC; ~88-89% of the TRR in kidney and liver was extracted using ACN/water; nonextractable residues were calculated by difference (11-12% TRR). The extracted radioactivity from SRC with the nonextractable radioactivity from IRI represented 92% of the TRR by combustion/LSC of kidney and liver. HED notes that samples of renal fat and muscle were also extracted at SRC, but because of very low radioactivity, these data are presented in the distribution table only for informational purposes and are not discussed below.

The extraction procedures and analytical methods used are adequate. The methods for identification and confirmation of residues included reverse and normal phase HPLC and TLC with fraction collection or co-chromatography with reference compounds. Adequate storage stability data demonstrate that the metabolic profile was relatively stable in kidney and liver for the study duration.

Approximately 40-42% TRR was identified in kidney and liver. The parent compound, metconazole, was the major compound identified in liver, accounting for 42.2% TRR (0.236 ppm); the parent only accounted for 2% TRR (0.006 ppm) in kidney. The metabolite M12 (with low levels of closely eluting M13) was identified as the major residue in kidney at 21% TRR (0.058 ppm). Following acid hydrolysis of the polar residues, at least 12 metabolites accounting for 50.5% TRR were characterized in liver (each present at ≤0.09 ppm). Insufficient kidney sample was available following acid hydrolysis for metabolite identification, but the metabolic profiles were essentially the same for kidney and urine; therefore, a urine extract was acid hydrolyzed and partitioned, and the data were converted to kidney equivalents. Based on the urine data, metabolite M1 accounted for 13.7% TRR (0.038 ppm), and co-eluting metabolites M2 and M15 accounted for 3.6% TRR (0.010 ppm) in kidney following acid hydrolysis. The petitioner reported that at least 14 metabolites were characterized in kidney (based on urine data) following acid hydrolysis (each present at ≤0.028 ppm). In general, the unknown metabolites in kidney and liver could only be characterized as monhydroxylated metabolites of metaconazole.

Goat (triazole label)

Valent has submitted a study investigating the metabolism of [triazole-^{14}C]metconazole (specific activity 2.07 GBq/mmole) in goats. A single goat was orally dosed with the radiolabeled test substance at a target dose of 10 mg/kg feed for four consecutive days; a second goat was dosed with a capsule containing corn meal and trace ethanol as a control. Based on the daily feed consumption, the average dosing level was equivalent to 10.36 ppm in the diet. The dose rate corresponds to 1.2x the dietary burden to dairy cattle and 2.8x the dietary burden to beef cattle; see Table 7. Milk samples were collected twice daily, starting the morning prior to the first dosing and continuing until the morning of sacrifice. Goats were sacrificed 17 hours following the last dosing, and tissue samples of muscle (composite of loin, flank, and round), fat (composite of omental, renal, and subcutaneous), liver, and kidney were collected.

The in-life phase of the study was conducted by Genesis Midwest Laboratories (Neillsville, WI), and the analytical phase of the study was conducted by Valent Technical Center (Dublin, CA) and Acorn NMR Inc. (Livermore, CA; NMR analyses).

TRR were highest in liver (0.223 ppm), then kidney (0.110 ppm), and were very low in fat (0.003 ppm), muscle (0.004 ppm), and milk (0.003-0.005 ppm). The majority of the radioactivity was rapidly excreted from the treated goat via urine and feces, with higher levels in the feces. Although residues in milk were low, it appears that residues may have reached a plateau following 3 days of dosing.

Only kidney and liver had TRR >0.01 ppm; therefore, extractions for metabolite identifications were focused mainly on the kidney and liver. Milk Day 4 was also extracted for metabolite characterizations, but TRR levels were extremely low (0.005 ppm); therefore, chromatographic analyses were difficult and inconclusive. Approximately 94-96% of the TRR in kidney and liver was extracted using ACN and ethanol/water; nonextractable residues were 3.7-6.4% TRR (0.004-0.015 ppm).

The ACN and ethanol/water extracts were fractionated into organic and aqueous fractions for analysis; isolated peaks from the organic and aqueous fractions were also combined for chromatographic analysis. The analytical methods used for identification and confirmation of residues are adequate. These included HPLC and TLC with fraction collection and/or co-chromatography with reference compounds. Identification of selected metabolites was confirmed by LC/MS, LC/MS/MS, and/or NMR analysis of tissue metabolites isolated from goat urine. Adequate storage stability data demonstrate that the metabolic profile was relatively stable in kidney and liver for the study duration.

Approximately 65-70% TRR was identified in kidney and liver. The parent compound, metconazole, was the major compound identified in liver, accounting for 37.6% TRR (0.091 ppm); the parent only accounted for 2.3% TRR (0.003 ppm) in kidney. The metabolite M12 was identified as a major residue in kidney at 20.6% TRR (0.024 ppm) and was a minor residue in liver at 1.7% TRR (0.004 ppm). The glucuronic acid conjugate of M31 was also identified as a major residue in kidney at 24.2% TRR (0.028 ppm) and in liver at 13.5% TRR (0.033 ppm). The glucuronic acid conjugate of M1 accounted for 11.7% TRR (0.014 ppm) in kidney and 4.4% TRR (0.011 ppm) in liver. Other minor metabolites identified in kidney and liver, each accounting for ≤6% TRR (≤0.015 ppm) included M1, M31 (liver only; co-eluting with M1), *trans*-M31 (liver only), M32 (liver only), the glucuronic acid conjugate of *trans*-M31 (liver only), and the glucuronic acid conjugate of M32. Additional multicomponent unknowns accounting for 20.9-29.4% TRR were characterized in kidney and liver, each present at ≤0.01 ppm. The petitioner proposed that these unidentified components were likely structural isomers of M1, M31 and monohydroxylated analogues of metconazole based on their polarity and chromatographic similarities with the glucuronic acid conjugates of M1, M31 and M32.

The petitioner used reference standards for the triazole metabolites to analyze the residues in any extract containing >0.01 ppm or >10% TRR. (The reference standards M-20, M-34, and M-35 are 1,2,4-T, TAA, and TA, respectively.) No triazole metabolites were identified in such extracts. Unidentified residues in liver and kidney extracts which corresponded to the HPLC retention times of the triazole metabolites (2.3, 2.3, and 1.9 minutes for 1,2,4-T, TAA, and TA,

respectively) totaled 1.2% TRR (0.003 ppm) in liver extracts and 2.4% TRR (0.003 ppm) in kidney extracts. The data are adequate to conclude that residues of 1,2,4-T, TAA, and TA, if present, are each <10% TRR (<0.01 ppm) in milk, meat, liver and kidney of the goat.

Based on the results of the cyclopentyl and triazole goat metabolism studies, the metabolic pathways of metconazole in goats include oxidative hydroxylation of the methyl group to yield monohydroxylated compounds M1 and M2, oxidative hydroxylation of the phenyl ring to yield monohydroxylated compounds M15 and/or M19, or oxidative hydroxylation of the cyclopentyl ring to yield monohydroxylated compounds M31 and M32. Further oxidation of the hydroxymethyl group to a carboxylic acid yields M12 and likely M13. Glucuronic acid conjugates of metconazole and the primary metabolites were also observed. The *cis:trans* isomer ratios determined in the liver extract (34:66 in cyclopentyl label study and 59:41 in the triazole label study) were very different from the *cis:trans* isomer ratio for the metconazole reference standard (80:20), indicating that the *cis* isomer of metconazole was preferentially metabolized in the goat.

Hen

Valent has submitted a study investigating the metabolism of [cyclopentyl-^{14}C]metconazole (specific activity 0.909 GBq/mmole) and [triazole-^{14}C]metconazole (specific activity 0.907 GBq/mmole) in laying hens. Two groups of five hens were orally dosed with the radiolabeled test substance at a target dose of 10 mg/kg feed for 4.5 consecutive days; a third group of hens (n=3) was dosed with a capsule containing corn meal and trace ethanol as a control. Based on the daily feed consumption, the average dosing level was equivalent to 14.0 ppm [cyclopentyl-^{14}C]metconazole or 12.6 ppm [triazole-^{14}C]metconazole in the diet. The dose rates correspond to 6.9x and 6.2x the dietary burden to poultry; see Table 7. Eggs were collected twice daily and separated into yolks and whites. Hens were sacrificed 4.5 hours following the last dosing, and tissue samples of muscle (thigh and breast), liver, skin with fat, and abdominal fat were collected.

The in-life phase of the study was conducted by Genesis Midwest Laboratories (Neillsville, WI), and the analytical phase of the study was conducted by Valent Technical Center (Dublin, CA) and Acorn NMR Inc. (Livermore, CA; NMR analyses).

TRR, determined by summing extractable and nonextractable radioactivity, were highest in liver (0.790-0.972 ppm), followed by fat (0.091-0.141 ppm), skin with fat (0.075-0.137 ppm), thigh muscle (0.049-0.152 ppm), and breast muscle (0.031-0.145 ppm). TRR in egg whites were <0.001-0.049 ppm and 0.017-0.174 ppm from hens treated with cyclopentyl- and triazole-labeled metconazole, respectively. TRR in egg yolks were <0.001-0.096 ppm and 0.005-0.163 ppm from hens treated with cyclopentyl- or triazole-labeled metconazole, respectively. Residues in egg whites appear to have reached a plateau following 3 or 4 days of dosing with cyclopentyl- and triazole-labeled metconazole, respectively. Maximum residues were observed in egg yolk (both labels) on Day 5. Egg whites from Day 4 and egg yolks from Day 5 were used for extraction; TRR, determined by summing extractable and nonextractable radioactivity were 0.047-0.186 ppm in Day 4 egg whites and 0.088-0.156 ppm in Day 5 egg yolks. Radioactivity was generally higher in the eggs and tissues from the triazole-treated hens. The majority of the radioactivity was rapidly excreted from the treated hens.

The majority of the radioactivity (78-98% TRR) was extracted from hen matrices with ACN. Additional radioactivity (2-10% TRR) was released with water extraction, and small amounts of the TRR (<1-9% TRR) present as oil droplets in fat, skin with fat, egg yolks, and liver were hexane soluble. Nonextractable residues in egg yolk (cyclopentyl label) and liver (both labels) after solvent extraction were acid hydrolyzed which further released ~6-10% TRR. Nonextractable residues in egg whites and yolks and hen tissues were 1.6-7.1% TRR. Accountabilities based on combustion/LSC TRR were 97-109%; the petitioner normalized the TRR for the distribution of metabolites.

The ACN and aqueous extracts of eggs and tissues were analyzed by HPLC and/or TLC. The combined extracts of liver were also acid hydrolyzed to release any conjugated metabolites, and the hydrolysates were analyzed by HPLC; metabolites quantitated following acid hydrolysis in liver are discussed herein because the majority of the unhydrolyzed liver extract consisted of conjugated metabolites. The analytical methods used for identification and confirmation of residues are adequate. These included HPLC and TLC with fraction collection and/or co-chromatography with reference compounds. Identification of selected metabolites was confirmed by LC/MS and/or NMR analysis of tissue metabolites isolated from hen excreta. Approximately 68-93% TRR was identified in eggs and hen tissues (muscle, fat, skin with fat, and liver). Adequate storage stability data demonstrate that the metabolic profile was relatively stable in eggs and hen tissues for the study duration.

The parent metconazole was a major compound identified in fat and skin with fat from both labels, accounting for 35.3-36.7% TRR (0.033-0.050 ppm) in fat and 19.7-27.8% TRR (0.021-0.027 ppm) in skin. The parent was identified as a minor residue in all other hen matrices at 2.5-7.3% TRR (0.003-0.005 ppm) in egg whites, 6.6-11.4% TRR (0.010 ppm) in egg yolks, 3.3-9.8% TRR (0.005 ppm) in thigh muscle, 0.8-5.4% TRR (0.001-0.002 ppm) in breast muscle, and 1.7-4.1% TRR (0.017-0.033 ppm) in liver. Lower levels of the parent were observed in the triazole-label hen matrices, with 1,2,4-T as the major residue (except in fat); other metabolites were similar between the cyclopentyl and triazole labels in hen matrices.

In the cyclopentyl-label hen matrices, the metabolite M1 (co-eluting with small amounts of M31) was identified as a major residue in egg whites at 15.7% TRR (0.007 ppm), egg yolks at 18.2% TRR (0.016 ppm), muscle at 15.7-19.9% TRR (0.006-0.008 ppm), fat at 27.7% TRR (0.025 ppm), skin at 24.1% TRR (0.018 ppm), and liver at 16.2% TRR (0.128 ppm). The metabolite M31 was also identified as a single peak in liver, accounting for 8.1% TRR (0.064 ppm). The carboxylic acid metabolite, CM-2, was identified as a major residue in egg whites at 17.1% TRR (0.008 ppm) and at lower levels in muscle (8.5-10.2% TRR), fat and skin (9.6% TRR), and egg yolk (6.6% TRR); CM-2 was not detected in liver. Metabolite M12 (with co-eluting CM-2/3) was only detected in liver, at 11.5% TRR (0.091 ppm).

The sulfate conjugates of dihydroxy-metconazole (DHM), mono-hydroxy-metconazole (MHM) and M32 were identified in cyclopentyl-label hen matrices at varying levels. The MHM sulfate was a major residue in egg whites (16.3% TRR, 0.008 ppm), egg yolk (13.1% TRR, 0.012 ppm), and muscle (12.9-18.0% TRR, 0.006 ppm), but was a minor residue (≤6% TRR) in fat and skin. The DHM sulfate was a major residue in muscle (9.9-16.8% TRR, 0.003-0.008 ppm), but was a minor residue (<3% TRR) in skin and egg yolk. The sulfate of M32 was a major residue in egg

whites (16.7% TRR, 0.008 ppm), but was present at lower levels in egg yolk (7.9% TRR), muscle (7.9-10.3% TRR), fat (1.6% TRR) and skin (3.7% TRR). The sulfates were not detected in acid-hydrolyzed liver, but various isomers of free DHM, MHM, and M32 (with co-eluting CM-1), and the carboxylic acid metabolite of monohydroxy-metconazole (CHM) and dicarboxylic acid metabolite of metconazole (DCM) were identified at 2.1%, 13.2%, 4.1%, 5.6%, and 9.3% TRR, respectively. The MHM-4 isomer was also detected at ≤8% TRR in egg whites, egg yolks, muscle, fat, and skin.

In the triazole-label hen matrices, 1,2,4-T was the major metabolite identified, at 64.8% TRR (0.120 ppm) in egg whites, 42.9% TRR (0.067 ppm) in egg yolk, 75.2-77.2% TRR (0.112-0.114 ppm) in muscle, 46.7% TRR (0.064 ppm) in skin, 13.3% TRR (0.019 ppm) in fat, and 27.3% TRR (0.265 ppm) in liver. The metabolite M1 (co-eluting with small amounts of M31) was also identified as a significant residue, in egg yolk at 12.8% TRR (0.020 ppm), fat at 13.4% TRR (0.019 ppm), and skin at 10.6% TRR (0.015 ppm), but was a minor residue (≤6% TRR) in egg whites and muscle. M1 and M31 (as individual peaks) were identified in liver at 9.7% TRR (0.094 ppm) and 5.1% TRR (0.049 ppm), respectively. M12, with co-eluting CM-2/3, was only identified in liver (8.3% TRR, 0.081 ppm).

The remaining minor metabolites (each ≤9.7% TRR) identified in triazole-label hen matrices included CM-2 (all matrices but liver), DHM sulfate (all matrices but skin, egg whites, and liver), M32 sulfate (all matrices but liver), and MHM sulfate (all matrices but liver). As for cyclopentyl-label liver, the sulfates were not detected in triazole-label acid hydrolyzed liver, but various isomers of free DHM, MHM, M32 (with co-eluting CM-1), CHM, DCM, and an oxo-metconazole metabolite (OCM) were identified, each at 0.5-9.7% TRR. The MHM-4 isomer was also detected at ≤5% TRR in egg whites, egg yolks, muscle, fat, and skin.

Additional unknown components accounting for 0.5-17.4% TRR were characterized in eggs and hen tissues (both labels), each present at ≤0.01 ppm.

Based on the metabolism study results, metconazole is extensively metabolized in hens through several major pathways involving: (i) oxidation of the methyl group at position 2 of the cyclopentyl ring to form either the carboxylic acid derivative, M12, and its isomers (M13, CM-1 to -3), or the hydroxymethyl derivative, M1, and its isomers (one or more MHM-1 to -6); (ii) oxidation of the methylene group at position 3 of the cyclopentyl ring to form M31 and M32 and their isomers (one or more MHM-1 to -6); (iii) oxidation of M1, M12, M31, M32 and their isomers to DHM, CHM, and DCM; (iv) sulfate ester formation of the hydroxylated metconazole derivatives; and (v) C-N bond cleavage releasing 1,2,4-T from the parent and likely from its metabolites. The metconazole metabolites are more water-soluble than the parent compound and are rapidly eliminated via excreta. In addition, the *cis* and *trans* isomers of metconazole were present approximately in equal portions in the fat and skin extracts, which differed significantly from the *cis*:*trans* isomer ratio for the parent test substance (~85:15), indicating that the *cis* isomer of metconazole was preferentially metabolized in the hen.

Conclusions. The nature of the residue in livestock is fully understood. Based on the submitted studies, the metabolism of metconazole in ruminants and poultry was generally similar. The major routes of metabolism involved oxidation and/or oxidative hydroxylation of the methyl group at position 2 of the cyclopentyl ring and oxidation oxidative hydroxylation of the phenyl

ring. Glucuronic acid conjugates were observed in the goat metabolism studies and sulfate ester conjugates were observed in the hen metabolism study. No triazole metabolites were identified in the goat; however, in the hen metabolism study with triazole-labeled metconazole, C-N bond cleavage releasing 1,2,4-T was observed.

In the goat metabolism study using triazole-labeled metconazole, the petitioner used reference standards for the triazole metabolites (M-20, M34, and M-35 are 1,2,4-T, TAA, and TA, respectively) to analyze the residues in any extract containing >0.01 ppm or >10% TRR. No triazole metabolites were identified in such extracts. Unidentified residues in liver and kidney extracts which corresponded to the HPLC retention times of the triazole metabolites (2.3, 2.3, and 1.9 minutes for 1,2,4-T, TAA, and TA, respectively) totaled 1.2% TRR (0.003 ppm) in liver extracts and 2.4% (0.003 ppm) in kidney extracts. The data are adequate to conclude that residues of 1,2,4-T, TAA, and TA, if present, are each <10% (<0.01 ppm) in milk, meat, liver and kidney of the goat.

HED has concluded that the available livestock metabolism data are adequate to support registration of the proposed new uses. Based on the available data, HED has determined that the residue of concern for the tolerance expression in livestock commodities is metconazole *per* se. HED also determined that the residues of concern for the risk assessment in livestock commodities are metconazole *per se*, M1 and its glucuronic acid conjugate, M12, and M31 and its glucuronic acid conjugate. The major residues observed in the ruminant and poultry metabolism studies were metconazole, M1, M12, and the glucuronic acid conjugates of M1 and M31 (ROCKS meetings, DP #348234, 10-JAN-2008 and 16-JAN-2008).

HED generally includes 1,2,4-T, TA, and TAA as residues of concern for risk assessment purposes for most triazole-containing pesticides. 1,2,4-T was a major residue found in some livestock commodities, and TA and TAA were significant residues in some plant metabolism studies. However, since separate endpoints for these compounds have been established, exposure and risks from free triazoles will be addressed separately.

860.1340 Residue Analytical Methods

DER Reference: 46902216.der.doc (includes review of MRID 46902217; BASF enforcement for crops)
46901704.der.doc (includes review of MRID 46901706; Valent enforcement for crops)
46665405.der.doc (includes review of MRID 46665407; BASF enforcement for livestock)
46901705.der.doc (Valent data collection for livestock)
Residue Chemistry Memo DP# 324541, 12/14/05, N. Dodd (PP# 9E05052)

Plant commodities

Enforcement methods:

American Cyanamid Method M2722
A gas chromatography/nitrogen phosphorous detection (GC/NPD) method (American Cyanamid Method M 2722), including a GC/MS confirmatory method, was previously proposed for enforcing tolerances for residues of the *cis* and *trans* isomers (CL 354801 and CL 354802) of metconazole (CL 900768) in bananas. A successful ILV trial was conducted for this method using samples of whole bananas and banana pulp. In a separate test, the ILV laboratory also

verified the extraction efficiency and accountability of Method M 2722 using samples of whole fruit and pulp from the banana metabolism study. The levels of metconazole determined in whole fruit and pulp were comparable to results from the metabolism study for the same whole fruit and pulp samples. ACB/BEAD has reviewed the method and found it adequate without revision as an enforcement method for bananas.

BASF Method D0508

BASF has submitted LC/MS/MS method D0508 for the determination of residues of metconazole (*cis* and *trans* isomers), and metabolites M21, M11, M30, 1,2,4-T, TA, and TAA in/on wheat grain, wheat straw, soybean seed, soybean hay, sugar beet root, sugar beet tops, wheat flour, soybean oil, sugar beet juice, and sugar beet molasses. Method D0508 was used for data collection in samples from the storage stability study, the small grain, soybean, and sugar beet crop field trials and processing studies, and the field rotational crop studies submitted by BASF and reviewed under PP#6F7094. BASF is proposing method D0508 as an enforcement method and has submitted supporting method validation data and an ILV for method D0508.

Briefly, samples of wheat grain, straw, and flour, sugar beet roots and tops, and soybean seed and hay are extracted with ACN:water (70:30, v:v), and the extract is diluted with MeOH/water, and filtered for analysis of metconazole and metabolites M21, M11, and M30, or evaporated to dryness and redissolved in 0.1% formic acid for analysis of triazole metabolites. Samples of soybean seed are extracted as above for analysis of all analytes except TA; for TA, the ACN/water extract is combined with water, concentrated, and hydrolyzed with 6 N HCl, and the hydrolysate is evaporated to dryness and redissolved in 0.1% formic acid. Samples of soybean oil are combined with ACN/0.1% formic acid, and partitioned with hexane. The aqueous layer is evaporated to dryness and redissolved in MeOH/water for analysis of metconazole, M21, M11, and M30, or redissolved in 0.1% formic acid for analysis of triazole metabolites. Samples of sugar beet molasses, sugar, and juice are extracted with ACN:water (50:50, v:v) and centrifuged. The extract is evaporated to dryness, and redissolved in MeOH/water for analysis of metconazole, M21, M11, and M30, or mixed with water, concentrated, and diluted with 0.1% formic acid for analysis of TAA and TA. The following optional clean-up steps are included: partitioning with hexane/ethyl acetate for soybean forage and hay; and SPE column cleanup (residues eluted with NH_4OH in MeOH) for sugar beet roots and tops (for analysis of TA) and sugar beet processed fractions (for analysis of 1,2,4-T and TA). The method uses three different LC/MS/MS systems (Methods I-III) and monitors a single ion transition for each analyte.

The method LOQs, determined as the lower limit of method validation (LLMV), are 0.01 ppm for metconazole (0.005 ppm for *cis* and *trans* isomers), 0.01 ppm for M21, M11, and M30, and 0.05 ppm for 1,2,4-T, TAA and TA.

Acceptable method validation recoveries (in the acceptable range of 70-120%) were obtained for *cis*- and *trans*-metconazole, M11, M21, 1,2,4-T, TAA, and TA from samples of wheat grain, wheat straw, soybean seed, soybean hay, sugar beet root, sugar beet tops, wheat flour, soybean oil, sugar beet juice, and molasses fortified at the LOQ and 10x LOQ with *cis*- and *trans*-metconazole (0.005 and 0.05 ppm); M11 and M21 (0.01 and 0.1 ppm); and 1,2,4-T, TAA, and TA (0.05 and 0.5 ppm).

Concurrent recovery data were generated in conjunction with the storage stability, crop field trial, processing, and field rotational crop studies submitted by BASF. Maximum fortification levels for the concurrent recovery investigations were generally 0.5 ppm for *cis*- and *trans*-metconazole, 1 ppm for metabolites M11, M21, and M30, and 5 ppm for the triazole metabolites.

No confirmatory analysis procedures were included in the method.

No radiovalidation data were submitted for method D0508; however, HED has concluded that because the extraction solvents used for the data collection method are similar to the aqueous organic solvent mixtures used in the plant metabolism studies, radiovalidation of the method is not required.

Method D0508 has undergone a successful ILV with wheat grain, wheat straw, soybean seed, soybean hay, and sugar beet root, fortified at 0.005 and 0.5 ppm for *cis*- and *trans*-metconazole, 0.01 and 1.0 ppm for metabolites M21, M11 and M30, and 0.05 and 0.5 ppm for metabolites 1,2,4-T, TAA and TA. Generally, adequate recoveries within the acceptable 70-120% range were obtained for all analytes in all commodities. The ILV laboratory noted that the retention times listed for LC/MS/MS Method III (for determination of TA if matrix suppression is observed) appeared to be incorrect and should be corrected. The laboratory also recommended that a comment be added to Section 3.2.6.ii of the method (optional MCS SPE cleanup for sugar beet matrices) indicating that, for sugar beet roots, the extract should be transferred from Section 3.2.4. The laboratory further recommended that the method be revised to include a statement that duplicate injection of each standard level should be performed when generating the calibration curves to confirm instrument stability during the run.

Valent Method RM-41C-1-1

Valent has submitted GC/NPD method RM-41C-1-1 for the determination of residues of *cis* and *trans*-metconazole in/on crops. The method is a revision of method RM-41C-1, which was used for data collection in the peanut, stone fruit, and tree nut crop field trials and peanut and plum processing studies submitted by Valent and reviewed under PP#6F7095. According to the petitioner, method RM-41C-1-1 reflects minor revisions to the original method to correct the nomenclature for *cis*- and *trans*-metconazole and to correct minor typographical errors. Valent is proposing method RM-41C-1-1 as a tolerance enforcement method, and has submitted supporting method validation data on peach as well as an ILV of the method. A confirmatory LC/MS/MS method, method RM-41C-4, was also submitted.

In method RM-41C-1-1, homogenized samples are extracted with ACN:water (70:30, v:v) and filtered. The extract is concentrated to remove ACN and partitioned with hexane (2x). The resulting hexane phases are combined and partitioned with ACN (2x), and the ACN phases are combined with ethyl acetate, concentrated to dryness, and redissolved in MeOH:water (1:1, v:v). The reconstituted extract is applied to a C18 SPE cartridge, and residues are eluted with MeOH:water (5:1, v:v). The eluate is evaporated to aqueous, combined with ethyl acetate, and evaporated to dryness, then redissolved in toluene for GC/NPD analysis. The reported LOQ is 0.02 ppm for each isomer.

In the confirmatory method RM-41C-4, homogenized samples are extracted with ACN/water, filtered, and concentrated to aqueous as above, then partitioned with hexane:ethyl acetate (9:1, v:v; 2x). The resulting hexane/ethyl acetate phase is partitioned with ACN (2x) and the combined ACN phases are concentrated, mixed with ethyl acetate, and evaporated to dryness. The residues are dissolved in MeOH/water (1:1, v:v) and subjected to C18 SPE cleanup as described above. The resulting eluate is diluted with aqueous formic acid for LC/MS/MS analysis. The LOQ, based on the submitted method validation data, is 0.02 ppm for metconazole (total of *cis* and *trans*-isomers).

The methods were adequately validated using samples of peach fruit fortified at 0.02 and 0.1 ppm for method RM-41C-1-1, and samples of wheat straw fortified at 0.02 and 0.1 ppm for method RM-41C-4. Using method RM-41C-1-1, recoveries of *cis*-metconazole ranged from 86.8 to 98.4% (average of 93.8%, standard deviation of 3.5%), and recoveries of *trans*-metconazole ranged from 88.3 to 102.8% (average of 95.3%, standard deviation of 5.0%) from samples of fortified peach fruit. Using method RM-41C-4, recoveries ranged from 81.6 to 97.4% (average of 89.5%, standard deviation of 5.2%) from samples of fortified wheat straw.

The fortification levels used in the method validation and concurrent method validation are adequate to bracket expected residue levels in stone fruit, tree nut, and peanut commodities. The concurrent method validation data in combination with the method validation data are sufficiently representative of the expected residue levels for the commodities included in PP#6F7095.

Method RM-41C-1-1 has undergone an acceptable ILV with almond nutmeat fortified at 0.02-0.2 ppm. Adequate recoveries were obtained for almond nutmeat, ranging from 93.5 to 111% for *cis*-metconazole and from 88.6 to 112% for *trans*-metconazole. No radiovalidation data were submitted for method RM-41C-1-1; however, HED has concluded that because the extraction solvent used for the proposed enforcement method is similar to the aqueous organic solvent mixtures used in the plant metabolism studies, radiovalidation of the method is not required.

Data collection methods: Samples of barley, lettuce, oat, radish, rye, soybean (2005 field trials, processing study), spinach, sugar beet, and wheat commodities from the crop field trial, processing studies, and field rotational crop studies conducted by BASF were analyzed for residues of metconazole (*cis* and *trans* isomers), and metabolites M21, M11, M30, 1,2,4-T, TA, and TAA using the proposed enforcement method, Method D0508.

Samples from the cherry, peach, plum, almond, pecan, and peanut commodities from the crop field trial and field rotational crop studies conducted by Valent were analyzed for residues of metconazole (*cis* and *trans* isomers) using an earlier version of the proposed enforcement method, Method RM-41C-1.

Samples from the soybean field trials conducted in 2004 and samples from the soybean AGF study were analyzed for residues of *cis*- and *trans*-metconazole using an LC/MS/MS method, BASF Method 550/0. The validated LOQ was 0.01 ppm for the parent metconazole (sum of *cis* and *trans* isomers at 0.005 ppm each). The method was adequate for data collection for soybean seed based on acceptable concurrent method recoveries. HED notes that no concurrent recovery or method validation data were included for soybean AGF.

Briefly, residues of metconazole were extracted with MeOH:water:2N HCl (70:25:5 v:v:v), isolated via centrifugation, diluted with water, and partitioned with dichloromethane. The dichloromethane phase was collected, evaporated to dryness, and redissolved in MeOH:water (80:20, v:v) for LC/MS/MS analysis. The validated LOQ was 0.01 ppm for the parent metconazole (sum of *cis* and *trans* isomers at 0.005 ppm each). The limit of detection (LOD) was 0.001 ppm.

Samples of crop commodities from one of the storage stability studies were analyzed for residues of *cis*- and *trans*-metconazole using GC/NPD methods FAMS 050-01 for rye forage, wheat straw, and wheat grain, FAMS 057-01 for carrots and lettuce, and FAMS 059-01 and FAMS 059-02 for rapeseed and rapeseed oil. Methods FAMS 050-01 and FAMS 057-01 are essentially identical; FAMS 059-02 reflects a slight a modification of the extraction procedures of FAMS 059-01 for rapeseed. The validated LOQs were 0.01 ppm for each analyte in carrot, lettuce, rapeseed, rapeseed oil, and wheat grain, and 0.03 ppm for each analyte in rye forage and wheat straw.

For methods FAMS 050-01 and 057-01, samples were extracted with acetone:hexane (1:1, v:v) and centrifuged. Water and NaCl were added, and the extracts were partitioned 2x with ethyl acetate. The ethyl acetate phases were combined, evaporated to near dryness, redissolved in MeOH, and cleaned up by gel permeation chromatography (GPC) for GC/NPD analysis.

For methods FAMS 059-01 and FAMS 059-02, samples of rapeseed were extracted 2x with ACN and centrifuged; samples of rapeseed oil were diluted with hexane and extracted 3x with ACN. The respective extracts were combined, water was added, and the extracts were partitioned 2x with ethyl acetate. The ethyl acetate phases were combined, evaporated to near dryness, redissolved in MeOH, and cleaned up by GPC for GC/NPD analysis.

Samples of wheat grain from the storage stability study for TA were analyzed using a GC/MS method. The method was adequate for data collection based on acceptable concurrent method recoveries. The validated LOQ was 0.10 ppm for TA. Briefly, residues of TA were extracted with water:MeOH (2:1, v:v, followed by 1:1, v:v) and vacuum filtered, then diluted with water and centrifuged. The resulting supernatant was acidified with concentrated HCl and purified on a cation exchange column; residues were eluted with 2 M ammonia solution, and the eluate was concentrated to dryness. The purified extract was esterified with isobutanol/acetyl chloride at reflux, then derivatized with heptafluorobutyric acid anhydride (HFBA) at reflux. The resulting oily residue was sequentially purified on a silica gel column followed by an aluminum oxide column. Residues were eluted from the silica gel column with hexane:acetone (1:1, v:v) and from the aluminum oxide column with cyclohexane:ethyl acetate (1:1, v:v). The resulting eluate was evaporated to dryness and redissolved in ethyl acetate for GC/MS analysis.

Note: The fortification levels used in method validation are not adequate to bracket expected residue levels of residues of concern in all crop commodities in PP#6F7094; while this information will not be required for PP#6F7094, the petitioner should note that this type of information for residues of concern should be provided for future petitions.

Conclusions. Acceptable methods were used for data collection for the crop field trial, processing, and field rotational crop studies submitted in conjunction with PP#s 6F7094 and 6F7095.

BASF method D0508 is adequate for data collection for residues of *cis*- and *trans*-metconazole, metabolites M11 and M21, and the triazole metabolites1,2,4-T, TA, and TAA. Method D0508 was forwarded to ACB/BEAD, along with the ILV recommendations, for petition method review (DP #339992, N. Dodd, 5/29/07). ACB/BEAD (Paul Golden, ACB Project #B07-18, 2/8/08) has determined that the petitioner must modify the plant method D0508 to provide information for a second MS/MS ion transition to provide a confirmation of analyte identity. If two ion transitions are not available, the Agency recommends that the petitioner provide an alternate chromatographic column and/or mobile-phase combination. Until this revision can be made, multiresidue methods will serve as the confirmatory method. The petitioner should modify the plant method D0508 to incorporate the recommendations of the ILV laboratory in an official enforcement method document reviewed by the petitioner's quality assurance unit. HED concludes that method D0508, with multiresidue methods serving as the confirmatory method until the requested revisions are made, is adequate for enforcing tolerances for residues of metconazole *per se* in/on small grains, soybeans, and sugar beets.

Valent method RM-41C-1-1, which determines *cis*- and *trans*- metconazole, is adequate as a data collection method. Method RM-41C-1-1 was forwarded to ACB/BEAD for petition method review (DP #339994, N. Dodd, 5/29/07). ACB/BEAD (DP# 339995, Paul Golden, ACB Project #B07-19, 2/15/08) has reviewed the method and found it adequate as an enforcement method. HED concludes that method RM-41C-1-1 is adequate for enforcing tolerances for residues of metconazole *per se* in/on peanuts, stone fruit, and tree nuts.

Livestock Commodities

Enforcement methods: BASF has submitted a modified version of the German multiresidue method, DFG S19 (referred to as method DFG S19 with modified extraction), for the determination of residues of metconazole (*cis* and *trans* isomers) in/on crop and livestock commodities. BASF is proposing method DFG S19 as an enforcement method for livestock commodities and has submitted supporting method validation data on grapes, peas, wheat grain, rapeseed, milk, bovine muscle, eggs, and bovine fat, and an ILV for method DFG S19. This method was not used for data collection for any of the studies associated with DP#s 348168 and 348206.

For grape, pea, wheat grain, milk, bovine muscle, and egg, samples are homogenized with water:acetone (1:2, v:v), then combined with ethyl acetate:cyclohexane (1:1, v:v), and sodium chloride. An aliquot of the resulting organic phase is filtered through sodium sulfate and concentrated by evaporation, then reconstituted in ethyl acetate. Sodium sulfate:sodium chloride (1:1, w:w) and cyclohexane are added, and the salts are allowed to precipitate. For fat or rapeseed, samples are blended with ACN:acetone (9:1, v:v) and Calflo E and Celite as adsorbents, filtered, and combined with isooctane. The extract is concentrated and redissolved in ethyl acetate:cyclohexane (1:1, v:v) as above. For all matrices, the resulting ethyl acetate/cyclohexane fractions are subjected to sequential cleanup on a GPC column (residues eluted with ethyl acetate/cyclohexane) and a silica gel mini-column (residues eluted with

acetone). The resulting eluate is concentrated by rotary evaporation and reconstituted in ethyl acetate for GC/NPD or GC/MS (confirmatory procedure) analysis. The method LOQ is 0.01 ppm for each isomer.

Acceptable method validation recoveries were obtained for *cis*- and *trans*-metconazole from samples of grape, pea, wheat grain, rapeseed, milk, bovine muscle, egg, and bovine fat fortified with each isomer at 0.01 ppm (LOQ) and 0.10 ppm. Recoveries were generally in the acceptable range of 70-120% for both analytes in all matrices. The fortification levels used in method validation are adequate to bracket expected residue levels of *cis*- and *trans*-metconazole in livestock matrices.

An acceptable confirmatory procedure (GC/MS) was included for the method. No radiovalidation data were submitted; however, because DFG S19 is an established multiresidue method, these data are not required.

Method DFG S19 with modified extraction has undergone an acceptable ILV with grape, pea, wheat grain, rapeseed, milk, bovine muscle, egg, and bovine fat fortified with each isomer at 0.01 and 0.10 ppm. Adequate recoveries, generally within the acceptable range of 70-120%, were obtained for all matrices at both fortification levels.

Method DFG S19 was forwarded to ACB/BEAD for a petition method review (DP #339992, N. Dodd, 5/29/07).

Data collection methods: Valent has submitted the following methods for the determination of metconazole residues in livestock commodities: GC/NPD method RM-41M-1 for the determination of *cis*- and *trans*-metconazole in milk; LC/MS/MS method RM-41M-2 for the determination of *cis*- and *trans*-metconazole in tissues; and LC/MS/MS method RM-41-M3 for the determination of metabolites M1 (free and conjugated) and M12 in liver and kidney. These methods were used for data collection in the cattle feeding study submitted by Valent under PP #6F7095. In support of the methods, Valent has submitted method validation and radiovalidation data.

In method RM-41M-1, samples are extracted with ethyl acetate:MeOH (2:1, v:v; 2x) and filtered. The extracts are combined and concentrated by rotary evaporation. The residue is mixed with 10% NaCl and partitioned with methylene chloride (3x). The methylene chloride layer is drained through sodium sulfate and concentrated to an oily residue. The resulting residue is dissolved in hexane and partitioned with ACN. The ACN phase is concentrated by evaporation, rinsed with ethyl acetate, and evaporated to dryness. Residues are redissolved in toluene for determination by GC/NPD, or dissolved in MeOH for determination by LC/MS/MS (confirmatory method). The reported LOQ is 0.02 ppm for each isomer, based on the LLMV.

In method RM-41M-2, samples are extracted with ACN (3x) and filtered, and the extracts are combined. The ACN extract is partitioned with hexane, and the ACN layer is concentrated to an oily residue, then partitioned with hexane:ethyl acetate (9:1, v:v) using a 10% NaCl rinse. The hexane/ethyl acetate layer is drained through sodium sulfate and partitioned with ACN, and the ACN layer is evaporated to dryness. The residue is dissolved in MeOH and applied to a C18 SPE cartridge; residues are eluted with MeOH:water (5:1, v:v). The eluate is combined with

ethyl acetate, evaporated to dryness, and redissolved in MeOH:water (2:1, v:v) for LC/MS/MS analysis. The method monitors a single ion transition for both *cis*- and *trans*-metconazole. The method LOQ is 0.02 ppm for each isomer, based on the LLMV.

In method RM-41M-3, samples are extracted with MeOH followed by MeOH:water (9:1, v:v) and filtered. The extracts are combined and concentrated by rotary evaporation to remove MeOH. The residue is redissolved in MeOH and mixed with ACN and hexane. The ACN/MeOH layer is adjusted to volume with ACN and divided into two fractions for separate determination of M12 and M1. For M12, the fraction is concentrated, combined with ethyl acetate, and evaporated to dryness, then redissolved in MeOH and water and applied to a C18 SPE cartridge. For M1, the fraction is concentrated, combined with ethyl acetate, and evaporated to dryness, then redissolved in methylene chloride and evaporated to dryness. The residue is redissolved in 3 N HCl and hydrolyzed at 80-85 °C for 1.5 hr to release conjugated residues. The hydrolysate is diluted with water and applied to a C18 cartridge. For both analytes, residues are eluted from the SPE cartridge with MeOH:water (5:1, v:v). The resulting eluates are combined with ethyl acetate, evaporated to dryness, and redissolved in MeOH:water (2:1, v:v) for LC/MS/MS analysis. The method monitors a single ion transition for each analyte. The method LOQ is 0.02 ppm for each analyte, based on the LLMV.

Methods RM-41M-1 and RM-41M-2 were adequately validated using samples of milk and liver fortified at 0.02 ppm and 0.10 ppm with both *cis*- and *trans*-metconazole. Using method RM-41M-1 (both GC/NPD and LC/MS/MS analyses) for milk and RM-41M-2 for liver, method validation recoveries of *cis*- and *trans*-metconazole were within the acceptable range of 70-120% for all samples. Method validation recoveries of metabolites M1 and M12 using method RM-41M-3 were acceptable for samples of kidney fortified with M1 at 0.02 ppm and with M12 at 0.02 and 0.10 ppm; recoveries of M1 ranged from 68.8 to 87.1% (average of 76.6%, standard deviation of 7.7%), and recoveries of M12 ranged from 68.9 to 81.2% (average of 76.2%, standard deviation of 3.9%). Marginally acceptable recoveries were obtained for metabolite M1 in kidney fortified at 0.10 ppm; recoveries ranged from 68.1 to 72.0% (average of 69.5%, standard deviation of 1.6%).

The fortification levels and samples used in method validation for methods RM-41M-1 and R-41M-2 are adequate to bracket expected residue levels of *cis*- and *trans*-metconazole in milk and tissues. Although the fortification levels used for method RM-41M-3 in kidney are adequate to bracket expected residues of M1 and M12, HED notes that low concurrent recoveries were obtained for method RM-41M-3 in the cattle feeding study for liver fortified with M1 at 0.02 and 0.10 ppm (57.4-61.6%), liver fortified with M12 at 0.02 and 0.10 ppm (67.4% and 66.2%, respectively), and kidney fortified with M12 at 0.02 ppm (67.6-68.3%); acceptable recoveries were obtained for M1 in kidney fortified at 0.02 ppm and for M12 in kidney fortified at 0.10 ppm.

Acceptable LC/MS/MS confirmatory procedures were included for GC/NPD method RM-41M-1; however, no confirmatory analysis procedures were included for methods RM-41M-2 and RM-41M-3. No ILV studies were included for the methods. Because the petitioner is not proposing the methods for enforcement purposes, no confirmatory procedures or ILV studies are required.

Acceptable radiovalidation data were submitted for method RM-41M-3. HED has concluded that because the extraction solvent used for method RM-41M-2 is the same as that used in the goat metabolism studies, radiovalidation of this method is not required. Radiovalidation data for method RM-41M-1 are needed.

Conclusions. BASF proposed a method based on the German multiresidue method DFG S19 as an enforcement method for parent metconazole (*cis*- and *trans*-metconazole) in livestock commodities. The method was forwarded to ACB/BEAD for a petition method review (DP #339992, N. Dodd, 5/29/07). ACB/BEAD (Paul Golden, ACB Project #B07-18, 2/8/08) has conducted a successful petition method review. HED concludes that the method is adequate for enforcing tolerances for residues of metconazole *per se* in/on livestock commodities.

Valent methods RM-41M-1, RM-41M-2 and RM-41M-3 are adequate for data collection for residues of *cis*- and *trans*-metconazole and metabolites M1 and M12 except that radiovalidation data are required in support of RM-41M-1.

860.1360 Multiresidue Methods

DER Reference: None
Residue Chemistry Memo DP# 324541, 12/14/05, N. Dodd (PP# 9E05052; MRID 44721509)

The Agency previously reviewed multiresidue methods data for metconazole. Based on its chemical structure, metconazole was not tested using FDA Multiresidue Method Protocols A, B, and G. An acceptable GC response was obtained under Level I conditions using Module DG5, although the test was not conducted in accordance with Protocol C. Metconazole was also not tested through Protocols D, E or F. Based on the available information from related triazole compounds (cyproconazole, dichlobutrazol, hexaconazole, paclobutrazol, and propiconazole), the petitioner concluded that metconazole would be completely recovered through Protocol D (Section 302 E-1) but would not be eluted from a Florisil column.

Conclusions. Metconazole must be tested through the appropriate FDA multiresidue method protocols. This deficiency remains outstanding.

860.1380 Storage Stability

Plant commodities

DER Reference: 46902218.der.doc (includes review of MRIDs 46902219, 46902220, and 46902222)
46902223.der.doc
46902221.der.doc
Residue Chemistry Memo DP# 324541, 12/14/05, N. Dodd (PP# 9E05052)

Storage stability data are available from the previous petition (PP#9E05052). The data indicate that residues of *cis*- and *trans*-metconazole are stable in/on banana whole fruit and banana pulp for at least 6 months.

Storage stability studies

MRIDs 46902218, 46902219, 46902220, and 46902222: BASF has submitted the results of storage stability studies with *cis*- and *trans*-metconazole in carrots, lettuce, rapeseed and rapeseed oil, rye green plant (forage), and wheat grain and straw. Samples of untreated carrots, lettuce, rapeseed, rapeseed oil, and wheat grain were fortified with *cis*- and *trans*-metconazole at 0.10 ppm; samples of rye forage and wheat straw bearing incurred residues of metconazole were obtained from crop field trials. All samples were stored frozen (≤-18 °C) and analyzed at intervals of 0, 1 and/or 3, 6, 9, and 12 months.

Samples were analyzed for residues of *cis*- and *trans*-metconazole by GC/NPD methods FAMS 050-01 for rye forage, wheat straw, and wheat grain, FAMS 057-01 for carrots and lettuce, and FAMS 059-01 and FAMS 059-02 for rapeseed and rapeseed oil. Methods FAMS 050-01 and FAMS 057-01 are essentially identical; FAMS 059-02 reflects a slight a modification of the extraction procedures of FAMS 059-01 for rapeseed. The methods were adequate for data collection based on acceptable concurrent method recoveries. The validated LOQs were 0.01 ppm for each analyte in carrot, lettuce, rapeseed, rapeseed oil, and wheat grain, and 0.03 ppm for each analyte in rye forage and wheat straw.

The results indicate that residues of *cis*- and *trans*-metconazole are relatively stable in/on fortified samples of carrot, lettuce, rapeseed, rapeseed oil, and wheat grain, and weathered residues of *cis*- and *trans*-metconazole are relatively stable in/on rye forage and wheat straw stored frozen for up to 12 months.

MRID 46902223: BASF has submitted the interim results of storage stability studies with *cis*- and *trans*-metconazole, the metabolites M11, M21, and M30, and the triazole metabolites (1,2,4-T, TA, and TAA) in radish root and tops, soybean seed, sugar beet root, and wheat hay, straw, and grain. Samples of untreated crop commodities were fortified with selected analytes at 0.10 ppm for each analyte as follows: (1) radish root with *cis*- and *trans*-metconazole and the triazole metabolites; (2) radish tops and wheat grain with M11, M21, M30, and the triazole metabolites; (3) soybean seed with all analytes; (4) sugar beet root and wheat straw with M11, M21, and M30; and (5) wheat hay with *cis*- and *trans*-metconazole, M11, M21, and M30. All fortified samples were stored frozen (≤-5 °C) and analyzed at intervals of 0, 1, 3, and 6 months. The petitioner noted that further samples are to be analyzed at the 9- and 12-month storage intervals.

Samples were analyzed for residues of *cis*- and *trans*-metconazole, M11, M21, and M30, and the triazole metabolites using an LC/MS/MS method (BASF Method D0508). The method was adequate for data collection based on acceptable concurrent method recoveries. The validated LOQs were 0.01 ppm for the parent metconazole (sum of *cis* and *trans* isomers at 0.005 ppm each) and the metabolites M11, M21, and M30 in/on all plant samples. The validated LOQ was 0.05 ppm for 1,2,4-T, TA, and TAA.

The results of the study are summarized in Table 5.

Table 5.	**Stability of Residues of Metconazole, Metabolites M11, M21, and M30, and Triazole Metabolites 1,2,4-T, TA, and TAA in/on Radish, Soybean, Sugar Beet, and Wheat Commodities Following Storage for up to 6 months at ≤- 5 °C.**							
Commodity	% Corrected Recovery Following Storage for 6 Months							
	Metconazole		M11	M21	M30	1,2,4-T	TAA	TA
	cis	*trans*						
Radish root	83	98	--	--	--	105	102	104
Radish top	--	--	111	88	114	106	81	101
Soybean seed	85	91	117	110	89	78	108	99
Sugar beet root	--	--	110	97	94	--	--	--
Wheat hay	95	95	108	107	98	--	--	--
Wheat straw	--	--	113	96	108	--	--	--
Wheat grain	--	--	86	96	111	85	70	70

* The petitioner indicated an intent to analyze samples at the 9- and 12-month storage intervals.

The results indicate that, following frozen storage for 6 months, residues of *cis*- and *trans*-metconazole are stable in/on radish root, soybean seed, and wheat hay; residues of M11, M21, and M30 are stable in/on radish top, soybean seed, sugar beet root, and wheat hay, straw, and grain; and residues of the triazole metabolites are stable/relatively stable in/on radish root, radish top, soybean seed, and wheat grain.

MRID 46902221: BASF has submitted the results of a storage stability study with the triazole metabolite TA in wheat grain. Samples of untreated wheat grain were fortified with TA at 5.0 ppm, stored frozen (≤-20°C), and analyzed at intervals of 0, 6, and 12 months.

Samples were analyzed for residues of TA using a GC/MS method. The method was adequate for data collection based on acceptable concurrent method recoveries. The validated LOQ was 0.10 ppm for TA.

The results indicate that residues of TA are stable in/on wheat grain for up to 12 months at ≤-20°C.

Concurrent storage stability studies: In addition, the petitioner conducted concurrent storage stability studies with the cherry, almond, and peanut field trials, and the soybean processing study. The results indicated that residues of *cis*- and *trans*-metconazole were stable in/on: (1) cherry for 159 days (5.2 months); (2) almond nutmeats for 664 days (21.8 months) and almond hulls for 784 days (25.8 months); (3) peanut nutmeat for 133 days (4.4 months); and (4) soybean hulls, meal, and oil for 63-66 days (2.1-2.2 months).

Sample storage intervals and conditions

The storage durations and conditions of samples from the crop field trial, processing, and field rotational crop studies submitted in support of this petition are presented in Table 6.

Table 6. Summary of Storage Conditions and Durations of Samples from Crop Field Trial, Processing, and Field Rotational Crop Studies.

Matrix	Storage Temperature (°C)	Actual Storage Duration in Days (Months)	Interval of Demonstrated Storage Stability[1] (Months)		
			Metconazole	M11, M21, M30	Triazole metabolites
Crop field trial studies					
Almond nutmeat	~-20	81-288 (2.7-9.5)	22		
Almond hulls		81-618 (2.7-20.3)	26		
Barley hay	<-10	160-241 (5.3-7.9)	12	6	6
Barley grain		131-228 (4.3-7.5)	12	6	6 (12 for TA)
Barley straw		137-225 (4.5-7.4)	12	6	6
Cherry	~-20	≤123 (4.0)	5		
Oat hay	<-10	230-372 (7.6-12.2)	12	6	6
Oat grain		221-364 (7.3-12.0)	12	6	6 (12 for TA)
Oat straw		213-355 (7.0-11.7)	12	6	6
Peach	~-20	≤131 (4.3)	5		
Peanut	<-22	110-138 (3.6 - 4.5)	4.4		
Pecan	~-20	107-129 (3.5-4.2)	22		
Plum	~-20	63-203 (2.1-6.7)	5		
Prune	~-20	42 (1.4)	5		
Rye grain	<-10	231-350 (7.6-11.5)	12	6	6 (12 for TA)
Rye straw		237-353 (7.8-11.6)	12	6	6
Soybean forage	<-10	61-195 (2.0-6.4)	12	6	6
Soybean hay		68-179 (2.2-5.9)	12	6	6
Soybean seed		40-161 (1.3-5.3)	6	6	6
Sugar beet root	<-10	161-191 (5.3-6.3)	12	6	6
Sugar beet tops		168-197 (5.5-6.5)	12	6	6
Wheat grain	≤-10	122-237 (4.0-7.8)	12	6	6 (12 for TA)
Wheat hay		122-249 (4.0-8.2)	12	6	6
Wheat straw		82-192 (2.7-6.3)	12	6	6
Processing studies					
Peanut	≤-12	139 (4.6)	4.4		
Peanut meal	≤-12	7 days	NA/NR		
Peanut oil	≤-12	7 days	NA/NR		
Soybean seed	<-10	76-91 (2.5-3.0)	6	6	6
Soybean AGF		30 days	NA/NR		
Soybean hulls		85-86 (2.8)	2	2	2
Soybean meal		76-77 (2.5)	2	2	2
Soybean crude oil		62 (2.0)	2	2	2
Soybean refined oil		58-59 (1.9)	2	2	2
Sugar beet root	<-10	161-202 (5.3-6.6)	12	6	6
Sugar beet molasses		21-39 (0.7-1.3)	NA/NR	NA/NR	NA/NR
Sugar beet refined sugar		21-39 (0.7-1.3)	NA/NR	NA/NR	NA/NR

Table 6. Summary of Storage Conditions and Durations of Samples from Crop Field Trial, Processing, and Field Rotational Crop Studies.					
Matrix	Storage Temperature (°C)	Actual Storage Duration in Days (Months)	Interval of Demonstrated Storage Stability[1] (Months)		
			Metconazole	M11, M21, M30	Triazole metabolites
Wheat grain	≤-10	272-328 (9.0-10.8)	12	6	6 (12 for TA)
Wheat AGF (MRID 46902231)		34 (1.0)	12	6	6 (12 for TA)
Wheat AGF (MRID 46902232)		683 (22.5)	12	6	6 (12 for TA)
Wheat bran		43-51 (1.4-1.7)	12	6	6 (12 for TA)
Wheat flour		22-23 (<1)	12	6	6 (12 for TA)
Wheat germ		65-71 (2.1-2.3)	12	6	6 (12 for TA)
Wheat middlings		59-67 (1.9-2.3)	12	6	6 (12 for TA)
Wheat shorts		45-53 (1.4-1.7)	12	6	6 (12 for TA)
Field rotational crop studies					
Lettuce	≤-10	238-585 (7.8-19.2)	12	6	6
Radish root		225-631 (7.4-20.7)	12	6	6
Radish tops		225-631 (7.4-20.7)	12	6	6
Spinach		79-406 (2.6-13.4)	12	6	6
Wheat forage		252-629 (8.3-20.7)	12	6	6
Wheat grain		182-559 (6.0-18.4)	12	6	6 (12 for TA)
Wheat hay		227-577 (7.5-19.0)	12	6	6
Wheat straw		174-551 (5.7-18.2)	12	6	6

[1] Shading indicates that storage stability data are not needed because samples were not analyzed for these metabolites. NA = Not available; NR = Not required.

Conclusions. The available storage stability data for *cis*- and *trans*-metconazole are adequate to support the storage conditions and durations of samples of raw agricultural and processed commodities from the submitted crop field trials and processing studies. Although adequate storage stability data are not available to support the storage conditions and durations of wheat AGF samples reported in MRID 46902232 (which were stored 22.5 months), additional data will not be required, as HED has determined that the wheat AGF data reported in MRID 46902232 are not needed to fulfill data requirements.

For rotational crop commodities, storage stability data were not submitted for all analytes (*cis*- and *trans*-metconazole, metabolites M11, M21, and M30, and the triazole metabolites 1,2,4-T, TA, and TAA) reflecting storage for up to 18 months for wheat grain and straw, 19 months for lettuce and wheat hay, and 21 months for radish roots and tops and wheat forage.

The available storage stability data for the metconazole metabolites M11, M21, and M30 and the triazole metabolites 1,2,4-T, TA, and TAA reflect storage for up to 6 months, with the exception of TA in wheat grain; the available data for TA in wheat grain reflect storage for up to 12 months.

Additional storage stability data are required for *cis*- and *trans*-metconazole reflecting storage for up to 18 months for wheat grain and straw, 19 months for lettuce and wheat hay, and 21 months for radish roots and tops and wheat forage.

Livestock commodities

Milk and tissue samples from the submitted ruminant feeding study were stored frozen at -20 °C prior to analysis. Maximum storage durations were 32 days (1.1 months) for milk and cream samples, 54 days (1.8 months) for tissues analyzed for *cis*- and *trans*-metconazole, and 182 days (6.0 months) for liver and kidney analyzed for M1 and M12. No storage stability data are required to support the storage conditions and durations of whole milk, skim milk or cream because samples were stored for ~30 days. To support the sample storage durations for *cis*- and *trans*-metconazole residues in tissues, a concurrent storage stability study was conducted which indicated that residues were relatively stable in liver, fat, and muscle stored frozen for 108-112 days (~3.6 months). Acceptable storage stability data are available from the goat metabolism studies to support the storage durations for liver and kidney analyzed for metabolites M1 and M12.

Conclusions. The available storage stability data are adequate to support the storage conditions and durations of samples from the cattle feeding study.

860.1400 Water, Fish, and Irrigated Crops

There are no proposed uses that are relevant to this guideline topic.

860.1460 Food Handling

There are no proposed uses that are relevant to this guideline topic.

860.1480 Meat, Milk, Poultry, and Eggs

DER Reference: 46901914.der.doc

There are livestock feedstuffs associated with the proposed uses of metconazole on small grains, soybean, sugar beet, almonds, and peanut. The dietary burdens of metconazole to livestock, based on reasonably balanced diets, are presented in Table 7 (provided by Jerry Stokes and Bernard Schneider, HED). The dietary burdens are 3.70 ppm for beef cattle, 8.78 ppm for dairy cattle, 2.03 ppm for poultry, and 0.69 ppm for swine.

Table 7. Calculation of Dietary Burdens of Metconazole Residues to Livestock.					
Feedstuff	Type[1]	% Dry Matter[2]	% Diet[2]	Recommended Tolerance (ppm)	Dietary Contribution (ppm)[3]
Beef Cattle					
Wheat hay	R	88	10	16.0	1.82
Aspirated grain fractions	CC	85	5	7.0	0.41
Barley grain	CC	88	50	2.5	1.42
Wheat, milled bypdts	CC	88	20	0.20	0.045
Soybean meal	PC	92	15	0.05	0.008
TOTAL BURDEN	--	--	100	--	**3.70**
Dairy Cattle					
Wheat hay	R	88	40	16.0	7.27
Almond hulls	R	90	5	4.0	0.22
Barley grain	CC	88	45	2.5	1.28
Soybean meal	PC	92	10	0.05	0.005
TOTAL BURDEN	--	--	100	--	**8.78**
Poultry					
Barley grain	CC	88	70	2.5	1.99
Rye grain	CC	88	10	0.25	0.028
Soybean meal	PC	92	20	0.05	0.011
TOTAL BURDEN	--	--	100	--	**2.03**
Swine					
Barley grain	CC	88	20	2.5	0.57
Wheat, milled bypdts	CC	88	50	0.20	0.11
Soybean meal	PC	92	20	0.05	0.011
TOTAL BURDEN	--	--	90[4]	--	**0.69**

[1] R: Roughage; CC: Carbohydrate concentrate; PC: Protein concentrate.
[2] OPPTS 860.1000 Table 1 Feedstuffs (October 2006).
[3] Contribution = ([tolerance /% DM] X % diet) for beef and dairy cattle; contribution = ([tolerance] X % diet) for poultry and swine.
[4] The remainder of the diet will consist of feedstuffs on which metconazole is not used.

Ruminants

Valent has submitted a cattle feeding study with metconazole. Three treatment groups of three dairy cows each were dosed orally with gelatin capsules containing metconazole at dose rates of 4.73, 14.6, and 45.7 ppm (low, mid, and high dose) in the diet (dry-weight basis) for 28 consecutive days. The dosing levels correspond to 1.3x, 3.9x, and 12x, respectively, the current dietary burden for beef cattle and 0.54x, 1.7x, and 5.2x, respectively, the dietary burden to dairy cattle. Cows were milked twice daily, and samples were composited daily for each cow. One cow from the low dose group was severely injured and euthanized on dosing day 11. On Day 29 of the study, two of the control cows and all remaining dosed cows were sacrificed within 24 hours of the last dose. Samples of liver, kidney, muscle (hindquarter, pectoral, and abductor), and fat (perirenal, abdominal, and subcutaneous) were collected from each cow. Samples of milk collected on study days 1, 2, 4, 7, 10, 14, 17, 21, 24, and 28 from the high dose cattle were analyzed. In addition, milk from Day 24 was centrifuged to form cream and skim milk samples; samples from the high dose group were analyzed.

Whole milk, skim milk, and cream samples were analyzed for residues of *cis*- and *trans*-metconazole using GC/NPD method RM-41M-1. Tissue samples were analyzed for residues of *cis*- and *trans*-metconazole using LC/MS/MS method RM-41M-2. These methods were adequate for data collection based on acceptable method recoveries. The validated LOQs for RM-41M-1 were 0.02 ppm for each analyte in milk and 0.04 ppm for each analyte in cream. The validated LOQ for RM-41M-2 was 0.02 ppm for each analyte in tissues.

Liver and kidney samples were also analyzed for residues of metabolites M1 (free and conjugated) and M12 using LC/MS/MS method RM-41M-3. The method was adequate for data collection; however, recoveries were generally low, ranging from 57.4 to 61.6% for M1 in liver, 66.2-67.4% for M12 in liver, 69.7-78.5% for M1 in kidney, and 67.6-73.9% for M12 in kidney. The LOQs for method RM-41M-3 were 0.02 ppm for each analyte in liver and kidney.

The LOD for all methods, analytes, and matrices except cream was 0.01 ppm. The LOD for *cis*- and *trans*-metconazole in cream was 0.02 ppm.

Milk and tissue samples were stored frozen at -20 °C prior to analysis. Maximum storage durations were 32 days (1.1 months) for milk and cream samples, 54 days (1.8 months) for tissues analyzed for *cis*- and *trans*-metconazole, and 182 days (6.0 months) for liver and kidney analyzed for M1 and M12. No storage stability data are required to support the storage conditions and durations of whole milk, skim milk, or cream because samples were stored for ~30 days. Adequate storage stability data are available for *cis*- and *trans*-metconazole to support the storage conditions and durations of samples of cattle tissues from the feeding study.

Except as noted below, samples of cattle matrices from the mid- and low-dose groups were not analyzed because residues were low (nondetectable or nonquantifiable) on analysis of samples from the high-dose group. Residues of *cis*- and *trans*-metconazole were below the LOQ (<0.04 ppm for each isomer in cream; <0.02 ppm for each isomer in the remaining matrices) in all samples of whole milk, skim milk, cream, fat, muscle, and kidney from the high-dose group. In liver, residues of *cis*- and *trans*-metconazole were <0.02-0.021 ppm and <0.02 ppm, respectively, in samples from the high-dose group and below the LOQ (both isomers) in samples from the

low- and mid-dose groups. Maximum total metconazole residues (sum of *cis* and *trans* isomers) were 0.041 ppm in liver from the high-dose group; total metconazole residues were <0.04 ppm in all samples of whole and skim milk and tissues from all dosing levels and <0.08 ppm in all samples of cream from all dosing levels.

Residues of metabolites M1 and M12 were below the LOQ (<0.02 ppm) in samples of liver and kidney from the low- and mid-dose groups. Residues of M1 were <0.02-0.049 ppm and <0.02-0.027 ppm in samples of liver and kidney, respectively, from the high-dose group, and residues of M12 were <0.02 ppm and <0.02-0.057 ppm in samples of liver and kidney, respectively, from the high-dose group.

HED notes that samples from the cattle feeding study were not analyzed for the triazole metabolites 1,2,4-T, TA, and TAA.

Residues of metconazole, M1, and M12 were each less than the LOQ except for meat byproducts at the highest dosing level (12x the dietary burden for beef cattle and 5.2x the dietary burden for dairy cattle).

Poultry

Valent has submitted a request to waive the requirements for a poultry feeding study (MRID 46901915). The petitioner calculated a poultry dietary burden of 1.750 ppm based on a diet consisting of 75% barley grain and 25% wheat milled byproducts. The petitioner then normalized the results of the hen metabolism study, in which hens were dosed with [cyclopentyl-^{14}C]metconazole at 14.0 ppm and with [triazole-^{14}C]metconazole at 12.6 ppm, to a 1.750 ppm feeding level. Following normalization, maximum residues of *cis*- and *trans*-metconazole were ≤0.004 ppm in eggs and tissues. Combined residues of the metabolites M1 + M31 were ≤0.003 ppm in all samples except liver, in which normalized residues were observed at the LOQ, 0.0204-0.0244 ppm. Normalized residues of 1,2,4-T were <LOQ in egg white (0.0167 ppm), egg yolk (0.0093 ppm), breast muscle (0.0156 ppm), thigh muscle (0.0158 ppm), fat (0.0026 ppm), and skin (0.0089 ppm), and were 0.0368 ppm in liver. The petitioner concluded that based on the results of the hen metabolism study and the proposed tolerances in poultry feed items, the potential for secondary residues of metconazole in poultry products is negligible; thus, the petitioner concluded that a feeding study and tolerances for poultry commodities are not needed.

HED has calculated a poultry dietary burden of 2.03 ppm (Table 7 above).

Conclusions. The submitted dairy cattle feeding study is acceptable. Samples were analyzed for metconazole (determined as the *cis* and *trans* isomers) and for metabolites M1 and M12 using acceptable methods, and the study is supported by adequate storage stability data.

The petitioner used reference standards for the triazole metabolites to analyze the residues in any extract containing >0.01 ppm or >10% TRR. (The reference standards M-20, M-34, and M-35 are 1,2,4-T, TAA, and TA, respectively.) No triazole metabolites were identified in such extracts. Unidentified residues in liver and kidney extracts which corresponded to the HPLC retention times of the triazole metabolites (2.3, 2.3, and 1.9 minutes for 1,2,4-T, TAA, and TA, respectively) totaled 1.2% TRR (0.003 ppm) in liver extracts and 2.4% TRR (0.003 ppm) in

Table 8.1. Summary of Residue Data from Small Grains Field Trials with Metconazole[1]

Crop matrix	Total Applic. Rate (lb ai/A)	PHI (days)	Analyte	Residue Levels (ppm)						
				n	Min.	Max.	HAFT[2]	Median	Mean	Std. Dev.
BARLEY (proposed use = 0.20 lb ai/A total application rate, 30-day PHI)										
Barley hay	0.20-0.21	6-8	*cis*-Metconazole	24	0.64	3.69	3.69	2.57	2.28	0.99
			trans-Metconazole	24	0.09	0.74	0.68	0.48	0.42	0.20
			Metconazole	**24**	**0.73**	**4.43**	**4.37**	**3.03**	**2.70**	**1.19**
			M11	24	<0.01	0.38	0.36	0.05	0.08	0.10
			M21	24	<0.01	0.20	0.20	0.05	0.06	0.05
			M30	24	<0.01	0.07	0.07	0.01	0.02	0.02
			Total Residues	24	0.80	5.10	5.00	3.15	2.86	1.31
Barley grain	0.20	20-21	*cis*-Metconazole	24	0.09	1.33	1.11	0.40	0.44	0.34
			trans-Metconazole	24	0.02	0.27	0.23	0.07	0.08	0.06
			Metconazole	**24**	**0.11**	**1.60**	**1.34**	**0.48**	**0.52**	**0.40**
			M11	24	<0.01	0.33	0.32	0.03	0.06	0.08
			M21	24	<0.01	0.08	0.07	0.01	0.02	0.02
			M30	24	<0.01	0.05	0.05	0.01	0.02	0.01
			Total Residues	24	0.15	1.83	1.61	0.59	0.62	0.45
Barley straw	0.20	20-21	*cis*-Metconazole	24	0.54	3.94	3.82	2.57	2.35	1.06
			trans-Metconazole	24	0.09	0.82	0.82	0.50	0.46	0.23
			Metconazole	**24**	**0.64**	**4.65**	**4.56**	**3.07**	**2.80**	**1.29**
			M11	24	0.03	1.08	1.02	0.42	0.39	0.32
			M21	24	0.04	0.46	0.43	0.12	0.17	0.14
			M30	24	0.01	0.15	0.15	0.05	0.05	0.04
			Total Residues	24	0.80	5.80	5.65	3.65	3.41	1.45
OAT (proposed use = 0.20 lb ai/A total application rate, 30-day PHI)										
Oat hay	0.20-0.21	6-8	*cis*-Metconazole	24	1.860	10.013	9.584	4.323	5.068	2.363
			trans-Metconazole	24	0.389	1.659	1.659	0.947	0.961	0.406
			Metconazole	**24**	**2.294**	**11.672**	**11.243**	**5.249**	**6.029**	**2.762**
			M11	24	0.01	0.43	0.41	0..05	0.10	0.13
			M21	24	0.03	0.12	0.12	0.10	0.08	0.03
			M30	24	0.01	0.05	0.05	0.02	0.02	0.01
			Total Residues	24	2.57	11.90	11.47	5.68	6.24	2.78
Oat grain	0.20-0.21	20-26	*cis*-Metconazole	24	0.041	0.566	0.477	0.228	0.264	0.145
			trans-Metconazole	24	0.024	0.218	0.134	0.049	0.059	0.041
			Metconazole	**24**	**0.127**	**0.680**	**0.556**	**0.274**	**0.322**	**0.159**
			M11	24	0.01	0.34	0.27	0.09	0.11	0.09
			M21	24	0.02	0.06	0.06	0.03	0.03	0.02
			M30	24	0.01	0.06	0.05	0.01	0.02	0.02
			Total Residues	24	0.17	1.14	0.93	0.46	0.48	0.26

kidney extracts. The data are adequate to conclude that residues of 1,2,4-T, TAA, and TA, if present, are each <10% TRR (<0.01 ppm) in milk, meat, liver and kidney of the goat.

Based on the available data, HED concludes that tolerances are needed for the meat byproducts of cattle, goat, horse, and sheep. No tolerances are needed for milk, fat, or muscle of cattle, goat, horse, and sheep. Residues of *cis*- and *trans*-metconazole were <LOQ in milk, skim milk, cream, muscle, fat, and kidney at the highest dosing level of 45.7 ppm (12x the dietary burden for beef cattle and 5.2x the dietary burden for dairy cattle). Because quantifiable residues of *cis*-metconazole were observed in liver (0.021 ppm) at the highest dosing level, tolerances are needed for meat byproducts at the LOQ. The LOQ for combined residues of *cis*- and *trans*-metconazole is 0.04 ppm. Since metconazole is the sole residue of concern for the tolerance expression in livestock commodities, tolerances are needed for metconazole in the meat byproducts of cattle, goat, horse, and sheep at 0.04 ppm.

The dosing levels used in the study represent 6.9x, 21x, and 66x the dietary burden to swine. Because residues of metconazole were <LOQ in all matrices except liver and kidney from the high-dose group, and were <LOQ in liver and kidney from the mid-dose group, no tolerances are needed for swine commodities.

Based on the poultry metabolism study, residues of cis- and trans-metconazole are not likely to occur in poultry commodities as a result of the proposed and established uses. However, based on the calculated residue levels of 1,2,4-T in liver in the metabolism study at the 1.75 ppm feeding level (which is close to the dietary burden of 2.03 ppm calculated herein), HED believes that a poultry feeding study for analysis of triazole metabolites is warranted. The poultry feeding study must be conducted at 1x, 3x, and 10x the theoretical dietary burden, and reflect analysis for metconazole, M1, M12, M31, and the triazole metabolites 1,2,4-triazole, TA, and TAA. The need for tolerances in poultry commodities will be reassessed when the required feeding study has been received.

860.1500 Crop Field Trials

Small grains

DER Reference: 46902225.der.doc (Barley)
46902226.der.doc (Oats)
46902227.der.doc (Rye)
46902224.der.doc (Wheat)

Table 8.1. Summary of Residue Data from Small Grains Field Trials with Metconazole[1]										
Crop matrix	Total Applic. Rate (lb ai/A)	PHI (days)	Analyte	Residue Levels (ppm)						
				n	Min.	Max.	HAFT[2]	Median	Mean	Std. Dev.
Oat straw	0.20-0.21	20-26	*cis*-Metconazole	24	0.834	5.067	4.821	1.509	1.828	1.062
			trans-Metconazole	24	0.154	0.869	0.828	0.301	0.362	0.205
			Metconazole	**24**	**0.992**	**5.937**	**5.649**	**1.739**	**2.189**	**1.257**
			M11	24	0.02	2.48	2.32	0.35	0.44	0.61
			M21	24	0.02	0.49	0.47	0.06	0.11	0.14
			M30	24	0.01	0.18	0.17	0.04	0.04	0.04
			Total Residues	24	1.18	9.09	8.61	2.31	2.78	1.95
RYE (proposed use = 0.20 lb ai/A total application rate, 30-day PHI)										
Rye grain	0.20-0.21	20-22	*cis*-Metconazole	10	0.032	0.131	0.126	0.062	0.070	0.032
			trans-Metconazole	10	0.008	0.026	0.025	0.013	0.015	0.006
			Metconazole	**10**	**0.040**	**0.157**	**0.150**	**0.075**	**0.085**	**0.039**
			M11	10	<0.01	0.040	0.040	0.025	0.025	0.014
			M21	10	<0.01	0.010	0.010	0.010	0.010	---
			M30	10	<0.01	0.010	0.010	0.010	0.010	---
			Total Residues	10	0.070	0.220	0.210	0.130	0.132	0.046
Rye straw	0.20-0.21	20-22	*cis*-Metconazole	10	1.803	7.358	7.157	3.189	3.623	1.995
			trans-Metconazole	10	0.128	1.426	1.317	0.710	0.642	0.482
			Metconazole	**10**	**1.931**	**8.784**	**8.473**	**3.899**	**4.264**	**2.449**
			M11	10	0.050	0.910	0.755	0.380	0.412	0.310
			M21	10	0.040	0.140	0.125	0.060	0.079	0.041
			M30	10	0.010	0.060	0.050	0.040	0.033	0.016
			Total Residues	10	2.020	9.630	9.070	4.415	4.783	2.586
WHEAT (proposed use = 0.20 lb ai/A total application rate, 30-day PHI)										
Wheat hay	0.18-0.21	6-8]	*cis*-Metconazole	30	1.16	10.98	10.94	5.36	5.55	2.51
			trans-Metconazole	30	0.17	1.72	1.682	0.93	0.95	0.41
			Metconazole	**30**	**1.33**	**12.66**	**12.58**	**6.24**	**6.50**	**2.91**
			M11	30	<0.01	0.48	0.365	0.06	0.10	0.11
			M21	30	0.03	0.19	0.175	0.08	0.09	0.04
			M30	30	<0.01	0.06	0.05	0.02	0.02	0.01
			Total Residues	30	1.60	12.80	12.7	6.55	6.71	2.915
Wheat grain	0.18-0.21	20-22	*cis*-Metconazole	30	0.006	0.097	0.08	0.027	0.033	0.024
			trans-Metconazole	30	<0.005	0.019	0.016	0.006	0.008	0.004
			Metconazole	**30**	**0.011**	**0.116**	**0.0955**	**0.034**	**0.041**	**0.027**
			M11	30	<0.01	0.030	0.03	0.010	0.014	0.006
			M21	30	<0.01	0.010	0.01	0.010	0.010	---
			M30	30	<0.01	<0.010	0.01	0.010	0.010	---
			Total Residues	30	0.040	0.160	0.04	0.070	0.075	0.031

Table 8.1. Summary of Residue Data from Small Grains Field Trials with Metconazole[1]

Crop matrix	Total Applic. Rate (lb ai/A)	PHI (days)	Analyte	Residue Levels (ppm)						
				n	Min.	Max.	HAFT[2]	Median	Mean	Std. Dev.
Wheat straw	0.18-0.21	20-22	*cis*-Metconazole	30	0.153	8.390	8.285	1.335	2.390	2.476
			trans-Metconazole	30	0.048	4.720	4.132	0.908	1.233	1.143
			Metconazole	**30**	**0.266**	**9.842**	**9.729**	**2.751**	**3.623**	**2.565**
			M11	30	0.030	1.290	1.075	0.280	0.383	0.347
			M21	30	0.040	0.450	0.45	0.105	0.151	0.111
			M30	30	0.010	0.140	0.125	0.040	0.055	0.043
			Total Residues	30	0.400	11.300	11.2	3.650	4.210	2.850

[1] Values for "Metconazole" and "Total Residues" are reported on a sample basis and are therefore not summations of tabulated data.
[2] HAFT = Highest average field trial result.

Table 8.2. Summary of Residue Data for the Triazole Metabolites from Small Grain Field Trials with Metconazole.

Crop matrix	Total Applic. Rate (lb ai/A)	PHI (days)	Analyte	Residue Levels (ppm)						
				n	Min.	Max.	HAFT[1]	Median	Mean	Std. Dev.
BARLEY (proposed use = 0.20 lb ai/A total application rate, 30-day PHI)										
Barley grain	0.20	20-21	1,2,4-T	24	<0.05	<0.05	0.05	0.05	0.05	--
			TA	24	<0.05	0.45	0.44	0.07	0.13	0.12
			TAA	24	<0.05	0.18	0.18	0.05	0.07	0.04
OAT (proposed use = 0.20 lb ai/A total application rate, 30-day PHI)										
Oat grain	0.20-0.21	20-26	1,2,4-T	24	<0.05	0.08	0.07	0.05	0.05	0.01
			TA	24	0.06	1.22	1.14	0.16	0.41	0.42
			TAA	24	<0.05	0.40	0.38	0.05	0.14	0.14
RYE (proposed use = 0.20 lb ai/A total application rate, 30-day PHI)										
Rye grain	0.20-0.21	20-22	1,2,4-T	10	<0.05	<0.05	0.05	0.05	0.05	--
			TA	10	<0.05	1.27	1.17	0.05	0.28	0.47
			TAA	10	0.06	1.73	1.65	0.08	0.40	0.66
WHEAT (proposed use = 0.20 lb ai/A total application rate, 30-day PHI)										
Wheat grain	0.18-0.21	20-22	1,2,4-T	30	<0.05	<0.05	0.05	0.05	0.05	--
			TA	30	<0.05	0.691	0.65	0.09	0.17	0.20
			TAA	30	<0.05	0.360	0.34	0.05	0.10	0.09

[1] HAFT = Highest Average Field Trial.

Barley

BASF has submitted field trial data for metconazole on barley. Twelve field trials were conducted in the United States and Canada in Zones 1 (NY, 1 trial), 5 (IL, NE; 2 trials), 7 (ND, NE; 2 trials), 9 (UT; 1 trial), 10 (CA; 1 trial), 11 (ID; 1 trial), and 14 (AB, MB, SK; 4 trials) during the 2004-2005 growing season. Because Canadian Zone 14 is contiguous with the two major U.S. barley-growing regions, Zones 5 and 7, HED has concluded that results from the Canadian trials may be used to address U.S. data requirements for barley.

Each test site included one control plot and two treated plots. The treated plots received two broadcast foliar applications of a 0.75 lb ai/gal SC/L formulation of metconazole at ~0.10 lb ai/A/application, with a 6- to 8-day RTI, for a total seasonal rate of ~0.20 lb ai/A (1x the maximum proposed seasonal application rate for barley). Applications were initiated four weeks prior to the harvest of mature grain (plot 2) or two weeks prior to the cutting of hay (plot 3). Applications were made in 12-30 gal/A spray volumes using ground equipment. A nonionic surfactant was added as a spray adjuvant for all applications.

Barley hay was harvested 7-8 days after the last application and allowed to dry in the field for 0-14 days prior to collection. Barley grain and straw were harvested 20-21 days after the last application. Additional hay samples were collected from one trial 0, 7, and 14 days after the last application, and grain and straw samples were harvested 14, 21, 28, and 35 days after the last application to generate residue decline data.

Samples were analyzed for residues of *cis*- and *trans*-metconazole, metabolites M11, M21, and M30, and the triazole metabolites (barley grain only), 1,2,4-T, TA, and TAA, using an LC/MS/MS method (BASF Method D0508). Residues of metabolites M11, M21, and M30 were converted to parent equivalents using molecular weight conversion factors of 0.95 for M11 and M21 and 0.96 for M30. The validated LOQs were 0.01 ppm for the parent metconazole (sum of *cis* and *trans* isomers at 0.005 ppm each), M11, M21, and M30 in/on barley samples. The validated LOQ was 0.05 ppm for 1,2,4-T, TA, and TAA. The method was adequate for data collection based on acceptable concurrent method recoveries.

Samples were stored frozen (<-10 °C) from harvest to extraction for 160-241 days (5.3-7.9 months) for barley hay, 131-228 days (4.3-7.5 months) for barley grain, and 137-225 days (4.5-7.4 months) for barley straw, and were analyzed within 0-2 days of extraction. Adequate storage stability data are available to support the storage conditions and durations of samples for the barley field trials.

The results of the barley field trials are summarized in Tables 8.1 and 8.2. Maximum residues of *cis*-and *trans*-metconazole in barley hay were 3.69 and 0.74 ppm, respectively; maximum total metconazole residues (sum of *cis* and *trans* isomers) were 4.43 ppm. In barley grain, maximum residues of *cis*- and *trans*-metconazole were 1.33 and 0.27 ppm, respectively, and maximum total metconazole residues were 1.60 ppm. In barley straw, maximum residues of *cis*- and *trans*-metconazole were 3.94 and 0.82 ppm, respectively, and maximum total metconazole residues were 4.65 ppm. Maximum residues of metabolite M11 were 0.38, 0.33, and 1.08 ppm for hay, grain, and straw, respectively; maximum residues of M21 were 0.20, 0.08, and 0.46 ppm for hay,

grain, and straw, respectively; and maximum residues of metabolite M30 were 0.07, 0.05, 0.15 ppm for hay, grain, and straw, respectively.

Residues of 1,2,4-T were below the LOQ (<0.05 ppm) in/on all samples of barley grain; maximum residues of TA and TAA were 0.45 ppm and 0.18 ppm, respectively, in/on barley grain.

The submitted residue decline data indicated that total metconazole residues (sum of *cis* and *trans* isomers) generally declined in barley hay, grain, and straw with increasing preharvest intervals.

Oats

BASF has submitted field trial data for metconazole on oats. Twelve field trials were conducted in the United States and Canada in Zones 1 (NY; 1 trial), 2 (GA, 1 trial), 5 (IL, ND, WI; 3 trials), 5B (QC; 1 trial), 6 (OK; 1 trial), 7 (ND, NE; 2 trials), and 14 (AB, MB, SK; 3 trials) during the 2004-2005 growing season. Because Canadian Zones 5B and 14 are contiguous with the two major U.S. oat-growing regions, Zones 5 and 7, HED has concluded that results from the Canadian trials may be used to address U.S. data requirements for oats.

Each test site included one control plot and two treated plots. The treated plots received two broadcast foliar applications of a 0.75 lb/gal SC/L formulation of metconazole at 0.10-0.11 lb ai/A/application, with a 6- to 8-day RTI, for a total seasonal rate of 0.20-0.21 lb ai/A (1x the maximum proposed seasonal application rate for oats). Applications were initiated four weeks prior to the harvest of mature grain (plot 2) or two weeks prior to the cutting of hay (plot 3). Applications were made in 10-27 gal/A spray volumes. A nonionic surfactant was added as a spray adjuvant for all applications.

Oat hay was harvested 6-8 days after the last application and was allowed to dry in the field for 0-29 days before collection. Oat grain and straw were harvested 20-21 days after the last application, except for one trial in which grain and straw were harvested 26 days after the last application due to adverse weather conditions. Additional hay samples were collected from one trial 0, 7, and 14 days after the last application, and grain and straw samples were harvested 14, 21, 28, and 36 days after the last application to generate residue decline data. Oat forage was not collected from any trial site because applications were initiated at a later growth stage.

Samples were analyzed for residues of *cis*- and *trans*-metconazole, metabolites M11, M21, and M30, and the triazole metabolites (oat grain only), 1,2,4-T, TA, and TAA, using an LC/MS/MS method (BASF Method D0508). Residues of metabolites M11, M21, and M30 were converted to parent equivalents. The validated LOQs were 0.01 ppm for the parent metconazole (sum of *cis* and *trans* isomers at 0.005 ppm each), M11, M21, and M30 in/on oat samples. The validated LOQ was 0.05 ppm for 1,2,4-T, TA, and TAA. The method was adequate for data collection based on acceptable concurrent method recoveries.

Samples were stored frozen (<-10 °C) from harvest to extraction for 230-372 days (7.6-12.2 months) for oat hay, 221-364 days (7.3-12.0 months) for oat grain, and 213-355 days (7.0-11.7 months) for oat straw, and were analyzed within 0-3 days of extraction. Adequate storage

stability data are available to support the storage conditions and durations of samples for the oat field trials.

The results of the oat field trials are summarized in Tables 8.1 and 8.2. Maximum residues of *cis*-and *trans*-metconazole in/on oat hay were 10.01 and 1.66 ppm, respectively; maximum total metconazole residues (sum of *cis* and *trans* isomers) were 11.67 ppm. In oat grain, maximum residues of *cis*- and *trans*-metconazole were 0.57 and 0.22 ppm, respectively, and maximum total metconazole residues were 0.68 ppm. In oat straw, maximum residues of *cis*- and *trans*-metconazole were 5.07 and 0.87 ppm, respectively, and maximum total metconazole residues were 5.94 ppm. Maximum residues of metabolite M11 were 0.43, 0.34, and 2.48 ppm for oat hay, grain, and straw, respectively; maximum residues of M21 were 0.12, 0.06, and 0.49 ppm for oat hay, grain, and straw, respectively; and maximum residues of metabolite M30 were 0.05, 0.06, and 0.18 ppm for oat hay, grain, and straw, respectively.

Maximum residues of 1,2,4-T, TA, and TAA in/on samples of oat grain were 0.08, 1.22, and 0.40 ppm, respectively.

The submitted residue decline data indicated that total metconazole residues (sum of *cis* and *trans* isomers) generally declined in oat hay, grain, and straw with increasing preharvest intervals.

Rye

BASF has submitted field trial data for metconazole on rye. Five field trials were conducted in the United States and Canada in Zones 2 (GA; 1 trial), 5 (NE; 1 trial), 7 (ND; 1 trial), and 14 (MB, SK; 2 trials) during the 2004-2005 growing season. Because Canadian Zone 14 is contiguous with the two major U.S. rye-growing regions, Zones 5 and 7, HED has concluded that results from the Canadian trials may be used to address U.S. data requirements for rye.

Each test site included one control plot and one treated plot. The treated plot received two broadcast foliar applications of a 0.75 lb/gal SC/L formulation of metconazole at 0.10 lb ai/A/application, with a 6- to 8-day RTI, for a total seasonal rate of 0.20-0.21 lb ai/A (1x the maximum proposed seasonal application rate for rye). Applications were initiated four weeks prior to the harvest of mature grain. Applications were made in 14-22 gal/A spray volumes. A nonionic surfactant was added as a spray adjuvant for all applications.

Rye grain and straw were harvested 20-22 days after the last application. Additional grain and straw samples were harvested from one trial 14, 21, 28, and 34 days after the last application to generate residue decline data. Rye forage was not collected from any trial site because applications were initiated at a later growth stage.

Samples were analyzed for residues of *cis*- and *trans*-metconazole, metabolites M11, M21, and M30, and the triazole metabolites (rye grain only), 1,2,4-T, TA, and TAA, using an LC/MS/MS method (BASF Method D0508). Residues of metabolites M11, M21, and M30 were converted to parent equivalents. The validated LOQs were 0.01 ppm for the parent metconazole (sum of *cis* and *trans* isomers at 0.005 ppm each), M11, M21, and M30 in/on rye samples. The validated

LOQ was 0.05 ppm for 1,2,4-T, TA, and TAA. The method was adequate for data collection based on acceptable concurrent method recoveries.

Samples were stored frozen (<-10 °C) from harvest to extraction for 231-350 days (7.6-11.5 months) for rye grain, and 237-353 days (7.8-11.6 months) for rye straw, and were analyzed within 0-6 days of extraction. Adequate storage stability data are available to support the storage conditions and durations of samples for the rye field trials.

The results of the rye field trials are summarized in Tables 8.1 and 8.2. Maximum residues of *cis*-and *trans*-metconazole in/on rye grain were 0.131 and 0.026 ppm, respectively; maximum total metconazole residues (sum of *cis* and *trans* isomers) were 0.157 ppm. In rye straw, maximum residues of *cis*- and *trans*-metconazole were 7.358 and 1.426 ppm, respectively, and maximum total metconazole residues were 8.784 ppm. Maximum residues of metabolite M11 were 0.040 and 0.910 ppm for grain and straw, respectively; maximum residues of M21 were 0.010 and 0.140 ppm for grain and straw, respectively; and maximum residues of metabolite M30 were 0.010 and 0.060 ppm in grain and straw, respectively.

Residues of 1,2,4-T were below the LOQ (<0.05 ppm) in/on all samples of rye grain; maximum residues of TA and TAA were 1.27 ppm and 1.73 ppm, respectively, in/on rye grain.

The submitted residue decline data indicated that total metconazole residues (sum of *cis* and *trans* isomers) generally remained the same or increased slightly in rye grain and straw with increasing preharvest intervals.

Wheat

BASF has submitted field trial data for metconazole on wheat. Fifteen field trials (eight winter wheat and seven spring wheat) were conducted in the United States and Canada in Zones 2 (GA, 1 trial), 4 (AR; 1 trial), 5 (IL, NE; 2 trials), 6 (OK; 1 trial), 7 (ND, NE; 3 trials), 8 (OK, TX; 2 trials), 11 (ID; 1 trial), and 14 (AB, MB, SK; 4 trials) during the 2004-2005 growing season. Because Canadian Zone 14 is contiguous with two major U.S. wheat-growing regions, Zones 5 and 7, HED has concluded that results from the Canadian trials may be used to address U.S. data requirements for wheat.

Each test site included one control plot and two treated plots. The treated plots received two broadcast foliar applications of a 0.75 lb ai/gal SC/L formulation of metconazole at 0.08-0.10 lb ai/A/application, with a 6- to 8-day RTI, for a total seasonal rate of 0.18-0.21 lb ai/A (1x the maximum proposed seasonal application rate for wheat). Applications were initiated four weeks prior to the harvest of mature grain (plot 2) or two weeks prior to the cutting of hay (plot 3). Applications were made in 11-30 gal/A spray volumes using ground equipment. A nonionic surfactant was added as a spray adjuvant for all applications.

Wheat hay was harvested 6-8 days after the last application and allowed to dry in the field or under cover for 0-14 days prior to collection. Wheat grain and straw were harvested 20-22 days after the last application. Additional hay samples were collected from two trials 0, 7-8, and 14 days after the last application, and grain and straw samples were harvested 14, 21-22, 28, and 35-

36 days after the last application to generate residue decline data. Wheat forage was not collected from any trial site because applications were initiated at a later growth stage.

Samples were analyzed for residues of *cis*- and *trans*-metconazole, metabolites M11, M21, and M30, and the triazole metabolites (wheat grain only), 1,2,4-T, TA, and TAA, using an LC/MS/MS method (BASF Method D0508). Residues of metabolites M11, M21, and M30 were converted to parent equivalents. The validated LOQs were 0.01 ppm for the parent metconazole (sum of *cis* and *trans* isomers at 0.005 ppm each), M11, M21, and M30 in/on wheat samples. The validated LOQ was 0.05 ppm for 1,2,4-T, TA, and TAA. The method was adequate for data collection based on acceptable concurrent method recoveries.

Samples were stored frozen (<-10 °C) from harvest to extraction for 122-249 days (4.0-8.2 months) for wheat hay, 122-237 days (4.0-7.8 months) for wheat grain, and 82-192 days (2.7-6.3 months) for wheat straw, and were analyzed within 0-4 days of extraction. Adequate storage stability data are available to support the storage conditions and durations of samples for the wheat field trials.

The results of the wheat field trials are summarized in Tables 8.1 and 8.2. Maximum residues of *cis*-and *trans*-metconazole in/on wheat hay were 10.98 and 1.72 ppm, respectively; maximum total metconazole residues (sum of *cis* and *trans* isomers) were 12.66 ppm. In wheat grain, maximum residues of *cis*- and *trans*-metconazole were 0.097 and 0.019 ppm, respectively, and maximum total metconazole residues were 0.116 ppm. In wheat straw, maximum residues of *cis*- and *trans*-metconazole were 8.39 and 4.720 ppm, respectively, and maximum total metconazole residues were 9.842 ppm. Maximum residues of metabolite M11 were 0.48, 0.03, and 1.29 ppm for hay, grain, and straw, respectively; maximum residues of M21 were 0.19, 0.010, and 0.45 ppm for hay, grain, and straw, respectively; and maximum residues of metabolite M30 were 0.06, <0.01, and 0.14 ppm in hay, grain, and straw.

Residues of 1,2,4-T were below the LOQ (<0.05 ppm) in/on all samples of wheat grain; maximum residues of TA and TAA were 0.691 ppm and 0.360 ppm, respectively, in/on wheat grain.

The submitted residue decline data indicated that total metconazole residues (sum of *cis* and *trans* isomers) generally declined or did not increase in wheat hay, grain, and straw with increasing preharvest intervals.

Conclusions. The submitted small grains field trial data are acceptable in number and geographic representation and reflect the proposed use pattern for barley, oats, rye, wheat, and triticale, except that hay samples were harvested at a 6- to 8-day PHI, and samples of straw and grain were harvested at a 20- to 21-day PHI; the petitioner has proposed a 30-day PHI for uses on small grains. The proposed SCL formulation labels should be amended to specify a minimum retreatment interval (RTI) of 6-8 days for small grains.

Samples were analyzed for the residues of concern using an acceptable method, and the studies are supported by adequate storage stability data.

All samples were analyzed for metconazole (determined as the *cis* and *trans* isomers), as well as three metconazole metabolites, M11, M21, and M30. In addition, samples of grain were analyzed for the triazole metabolites 1,2,4-T, TA, and TAA. Although hay and straw were not analyzed for the triazole metabolites, no additional field trial data will be required for triazoles for these petitions submitted in 2006.

The available field trial data will support tolerances for residues of metconazole in/on barley hay and straw at 7.0 ppm, barley grain at 2.5 ppm, rye straw at 14 ppm, rye grain at 0.25 ppm, oat hay at 17 ppm, oat straw at 6.0 ppm, oat grain at 1.0 ppm, wheat hay at 16 ppm, wheat straw at 18 ppm, and wheat grain at 0.15 ppm. The tolerance calculations for small grains are presented in Appendix II.

Soybean

DER Reference: 46902228.der.doc (includes review of MRID 46902229)

Table 9.1. Summary of Residue Data from Soybean Field Trials with Metconazole[1]

Crop matrix	Total Applic. Rate (lb ai/A)	PHI (days)	Analyte	Residue Levels (ppm)						
				n	Min.	Max.	HAFT[2]	Median	Mean	Std. Dev.
SOYBEAN (proposed use = 0.135 lb ai/A total application rate, 30-day PHI, with a 14-day PHI for forage and 21-day PHI for hay)										
Forage	0.14	6-8	*cis*-Metconazole	42	0.404	2.040	1.800	1.135	1.163	0.423
			trans-Metconazole	42	0.070	0.405	0.371	0.221	0.235	0.087
			Metconazole	**42**	**0.474**	**2.430**	**2.171**	**1.365**	**1.397**	**0.510**
			M11	30	<0.01	0.09	0.09	0.03	0.03	0.02
			M21	30	<0.01	0.03	0.03	0.01	0.02	0.01
			M30	30	<0.01	0.01	0.01	0.01	0.01	---
			Total Residues	30	0.08	2.46	2.29	1.23	1.30	0.55
Hay	0.14	6-8	*cis*-Metconazole	42	0.995	3.930	3.770	2.080	2.116	0.766
			trans-Metconazole	42	0.173	0.808	0.766	0.404	0.427	0.168
			Metconazole	**42**	**1.168**	**4.738**	**4.536**	**2.484**	**2.543**	**0.930**
			M11	30	0.02	0.20	0.20	0.06	0.07	0.04
			M21	30	0.01	0.08	0.08	0.04	0.04	0.02
			M30	30	<0.01	0.04	0.04	0.02	0.02	0.01
			Total Residues	30	1.21	4.89	4.69	2.70	2.72	1.06
Seed	0.14	30	*cis*-Metconazole	42	<0.005	0.036	0.036	0.005	0.008	0.008
			trans-Metconazole	42	<0.005	0.090	0.051	0.005	0.007	0.013
			Metconazole	**42**	**<0.010**	**0.050**	**0.045**	**0.010**	**0.014**	**0.009**
			M11	30	<0.01	<0.01	0.01	0.01	0.01	---
			M21	30	<0.01	<0.01	0.01	0.01	0.01	---
			M30	30	<0.01	<0.01	0.01	0.01	0.01	---
			Total Residues	30	<0.04	0.06	0.06	0.04	0.04	0.01

[1] Values for "Metconazole" and "Total Residues" are reported on a sample basis and are therefore not summations of tabulated data.

[2] HAFT = Highest average field trial result.

Table 9.2. Summary of Residue Data for the Triazole Metabolites from Soybean Field Trials with Metconazole.										
Crop matrix	Total Applic. Rate (lb ai/A)	PHI (days)	Analyte	Residue Levels (ppm)						
				n	Min.	Max.	HAFT[1]	Median	Mean	Std. Dev.
SOYBEAN (proposed use = 0.135 lb ai/A total application rate, 30-day PHI, with a 14-day PHI for forage and 21-day PHI for hay)										
Forage	0.14	6-8	1,2,4-T	30	<0.05	<0.05	0.05	0.05	0.05	--
			TA	30	<0.05	0.23	0.23	0.05	0.06	0.04
			TAA	30	<0.05	<0.05	0.05	0.05	0.05	--
Hay	0.14	6-8	1,2,4-T	30	<0.05	0.08	0.08	0.05	0.06	0.01
			TA	30	<0.05	<0.05	0.05	0.05	0.05	--
			TAA	30	<0.05	0.08	0.08	0.05	0.05	0.01
Seed	0.14	28-32	1,2,4-T	30	<0.05	0.10	0.09	0.05	0.06	0.02
			TA	30	<0.05	0.69	0.67	0.08	0.12	0.15
			TAA	30	<0.05	<0.05	0.05	0.05	0.05	--

[1] HAFT = Highest Average Field Trial.

BASF has submitted field trial data for metconazole on soybean. Twenty-one field trials were conducted in the United States and Canada in Zones 2 (GA, 2 trials), 4 (AR, MS; 3 trials), 5 (IA, IL, MI, MN, NE, WI, and ON; 15 trials), and 5B (QC, 1 trial) during the 2004 and 2005 growing seasons. Because the Canadian trials were conducted in Zones which extend into the U.S. (Zone 5) or are contiguous with the major U.S. soybean-growing zone (Zone 5B), HED has concluded that results from the Canadian trials may be used to address U.S. data requirements for soybean.

Each test site included one control plot and one treated plot. The treated plot received two broadcast foliar applications of a 0.75 lb ai/gal SC/L formulation of metconazole at 0.07-0.08 lb ai/A/application, with a 9- to 11-day RTI, for a total seasonal rate of ~0.14 lb ai/A (~1x the maximum proposed seasonal application rate for soybean). The first applications were made approximately 40 days prior to harvest of mature seed. Applications were made in 10-32 gal/A spray volumes. A nonionic surfactant was added as a spray adjuvant for all applications.

Soybean forage and hay were harvested 6-8 days after the last application and soybean seed were harvested 28-32 days after the last application. Soybean hay was allowed to dry in the field for 0-11 days prior to collection. Additional hay samples were collected from two trials 0, 7, 14, and 20-21 days after the last application, and seed samples were harvested 23, 30, 36-37, and 43-44 days after the last application to generate residue decline data.

Samples from the 15 trials conducted in 2005 were analyzed for residues of *cis*- and *trans*-metconazole, metabolites M11, M21, and M30, and the triazole metabolites 1,2,4-T, TA, and TAA using an LC/MS/MS method (BASF Method D0508). Residues of metabolites M11, M21, and M30 were converted to parent equivalents. Samples from the six trials conducted in 2004 were analyzed for residues of *cis*- and *trans*-metconazole using an LC/MS/MS method, BASF Method 550/0. The validated LOQs were 0.01 ppm for the parent metconazole (sum of *cis* and

trans isomers at 0.005 ppm each for both methods), M11, M21, and M30 in/on soybean samples. The validated LOQ was 0.05 ppm for 1,2,4-T, TA, and TAA. The methods were adequate for data collection based on acceptable concurrent method recoveries.

Samples were stored frozen (<-10 °C) from harvest to extraction for 61-195 days (2.0-6.4 months) for soybean forage, 68-179 days (2.2-5.9 months) for soybean hay, and 40-161 days (1.3-5.3 months) for soybean seed, and were analyzed within 0-5 days of extraction. Adequate storage stability data are available to support the storage conditions and durations of samples for the soybean field trials.

The results of the soybean field trials are summarized in Tables 9.1 and 9.2. Maximum residues of *cis*-and *trans*-metconazole in/on soybean forage were 2.040 and 0.405 ppm, respectively; maximum total metconazole residues (sum of *cis* and *trans* isomers) were 2.430 ppm. In soybean hay, maximum residues of *cis*- and *trans*-metconazole were 3.930 and 0.808 ppm, respectively, and maximum total metconazole residues were 4.738 ppm. In soybean seed, maximum residues of *cis*- and *trans*-metconazole were 0.036 and 0.090 ppm, respectively, and maximum total metconazole residues were 0.050 ppm. Maximum residues of metabolite M11 was 0.09, 0.20, and <0.01 ppm for forage, hay and seed, respectively; maximum residues of M21 were 0.03, 0.08, and <0.01 ppm for forage, hay and seed, respectively; and maximum residues of metabolite M30 were 0.01, 0.04, and <0.01 ppm, respectively, for forage, hay, and seed.

Maximum residues of 1,2,4-T were <0.05, 0.08, and 0.10 ppm in/on soybean forage, hay, and seed, respectively; maximum residues of TA were 0.23, <0.05, and 0.69 ppm for forage, hay, and seed, respectively; and maximum residues of TAA were <0.05, 0.08, and <0.05 ppm for forage, hay, and seed, respectively.

The submitted residue decline data indicated that total metconazole residues (sum of *cis* and *trans* isomers) generally declined in soybean forage, hay, and seed with increasing preharvest intervals.

Conclusions. The submitted soybean field trial data are acceptable and reflect the proposed use pattern for soybeans, except that forage and hay samples were harvested at a 6- to 8-day PHI; the petitioner has proposed a 14-day PHI for forage and a 21-day PHI for hay. The number and locations of field trials are in accordance with OPPTS Guideline 860.1500 requirements for soybean. Samples were analyzed for the residues of concern using an acceptable method, and the studies are supported by adequate storage stability data.

All samples were analyzed for metconazole (determined as the *cis* and *trans* isomers), the residue of concern, as well as three metconazole metabolites, M11, M21, and M30, and the triazole metabolites 1,2,4-T, TA, and TAA.

The available field trial data will support tolerances for residues of metconazole in/on soybean forage at 3.0 ppm, hay at 6.0 ppm, and seed at 0.05 ppm. The tolerance calculations for soybean forage and hay are presented in Appendix II.

Sugar beet

DER Reference: 46902230.der.doc

Table 10. Summary of Residue Data from Sugar Beet Field Trials with Metconazole[1]										
Crop matrix	Total Applic. Rate (lb ai/A)	PHI (days)	Analyte	Residue Levels (ppm)						
				n	Min.	Max.	HAFT[2]	Median	Mean	Std. Dev.
SUGAR BEET (proposed use = 0.20 lb ai/A total application rate, 14-day PHI)										
Treatment 02 - Two foliar applications at a total of 0.20 lb ai/A; PHI = 13-15 days										
Sugar beet root	0.20	13-15	*cis*-Metconazole	24	<0.005	0.039	0.036	0.010	0.013	0.010
			trans-Metconazole	24	<0.005	0.021	0.012	0.005	0.007	0.004
			Metconazole	**24**	**<0.010**	**0.048**	**0.044**	**0.017**	**0.020**	**0.011**
			M11	24	<0.010	<0.010	<0.010	0.010	0.010	--
			M21	24	<0.010	<0.010	<0.010	0.010	0.010	--
			M30	24	<0.010	<0.010	<0.010	0.010	0.010	--
			Total Residues	24	<0.040	0.080	0.075	0.050	0.049	0.011
Sugar beet tops	0.20	13-15	*cis*-Metconazole	24	0.010	1.077	1.037	0.033	0.358	0.429
			trans-Metconazole	24	0.006	0.178	0.173	0.114	0.108	0.049
			Metconazole	**24**	**0.037**	**1.256**	**1.210**	**0.152**	**0.466**	**0.457**
			M11	24	<0.010	0.020	<0.010	0.010	0.010	--
			M21	24	<0.010	0.020	<0.010	0.010	0.010	--
			M30	24	<0.010	<0.010	<0.010	0.010	0.010	--
			Total Residues	24	0.070	1.290	1.240	0.180	0.4990	0.456
Treatment 03 – Two foliar applications at a total of 0.30 lb ai/A; PHI = 13-15 days										
Sugar beet root	0.30	13-15	*cis*-Metconazole	24	<0.005	0.070	0.069	0.014	0.020	0.018
			trans-Metconazole	24	<0.005	0.016	0.015	0.005	0.007	0.003
			Metconazole	**24**	**<0.010**	**0.085**	**0.084**	**0.020**	**0.026**	**0.020**
			M11	24	<0.010	<0.010	<0.010	0.010	0.010	--
			M21	24	<0.010	<0.010	<0.010	0.010	0.010	--
			M30	24	<0.010	<0.010	<0.010	0.010	0.010	--
			Total Residues	24	<0.040	0.110	0.110	0.050	0.056	0.020
Sugar beet tops	0.30	13-15	*cis*-Metconazole	24	0.014	2.067	1.865	0.054	0.605	0.748
			trans-Metconazole	24	0.005	0.426	0.384	0.147	0.154	0.112
			Metconazole	**24**	**0.035**	**2.493**	**2.249**	**0.206**	**0.760**	**0.837**
			M11	24	<0.010	0.030	0.025	0.010	0.014	0.007
			M21	24	<0.010	0.020	0.020	0.020	0.016	0.005
			M30	24	<0.010	<0.010	<0.010	0.010	0.010	--
			Total Residues	24	0.070	2.530	2.285	0.245	0.798	0.838

[1] Values for "Metconazole" and "Total Residues" are reported on a sample basis and are therefore not summations of tabulated data.

[2] HAFT = Highest average field trial result.

Triazole metabolites: Samples of sugar beet roots and tops were also analyzed for the triazole metabolites 1,2,4-T, TA, and TAA. Residues of all three analytes were below the LOQ (<0.05 ppm) in/on all samples of sugar beet roots and tops following both treatments.

BASF has submitted field trial data for metconazole on sugar beets. Twelve field trials, each including two different application rates, were conducted in the United States in Zones 5 (MN, WI; 5 trials), 7 (ND; 1 trial), 8 (TX; 1 trial), 9 (MT; 1 trial), 10 (CA; 2 trials), and 11 (ID; 2 trials) during the 2005 growing season.

Each test site included one control plot and two treated plots. One of the treated plots received two broadcast foliar applications of a 0.75 lb ai/gal SC/L formulation of metconazole at 0.10 lb ai/A/application, with a 13- to 15-day RTI, for a total seasonal rate of 0.20 lb ai/A (Treatment 2; 1x the maximum proposed seasonal application rate for sugar beet). Applications were made in 18-31 gal/A spray volumes. The other treated plot received two broadcast foliar applications of metconazole at ~0.15 lb ai/A, with a 13- to 15-day RTI, for a total rate of ~ 0.30 lb ai/A (Treatment 3; 1.5x the maximum proposed seasonal application rate for sugar beet). Applications were made in 17-30 gal/A spray volumes. A nonionic surfactant was added as a spray adjuvant for all applications.

Sugar beet roots and tops were harvested 13-15 days after the last application. Additional samples were collected from two trials 1, 7, 14-15, 21 and 27-28 days after the last application to generate residue decline data.

Samples were analyzed for residues of *cis*- and *trans*-metconazole, metabolites M11, M21, and M30, and the triazole metabolites 1,2,4-T, TA, and TAA using an LC/MS/MS method (BASF Method D0508). Residues of metabolites M11, M21, and M30 were converted to parent equivalents. The validated LOQs were 0.01 ppm for the parent metconazole (sum of *cis* and *trans* isomers at 0.005 ppm each) and the metabolites M11, M21, and M30 in/on sugar beets. The validated LOQ was 0.05 ppm for 1,2,4-T, TA, and TAA. The method was adequate for data collection based on acceptable concurrent method recoveries.

Samples were stored frozen (<-10 °C) prior to extraction for 161-191 days (5.3-6.3 months) for sugar beet roots and 168-197 days (5.5-6.5 months) for sugar beet tops, and were analyzed within 0-2 days of extraction. Adequate storage stability data are available to support the storage conditions and durations of samples for the sugar beet field trials.

The results of the sugar beet field trials are summarized in Table 10. Following Treatment 2, maximum residues of *cis*-and *trans*-metconazole in sugar beet roots were 0.039 and 0.021 ppm, respectively; maximum total metconazole residues (sum of *cis* and *trans* isomers) were 0.048 ppm. In sugar beet tops, maximum residues of *cis*- and *trans*-metconazole were 1.077 and 0.178 ppm, respectively, and maximum total metconazole residues were 1.256 ppm. Residues of metabolites M11, M21, and M30 in/on roots were each <0.010 ppm, and residues in/on tops were <0.010 ppm for M30 and <0.010-0.020 ppm for M11 and M21.

Following Treatment 3, maximum residues of *cis*- and *trans*-metconazole in roots were 0.070 and 0.016 ppm, respectively, and maximum total metconazole residues were 0.085 ppm. In sugar beet tops, maximum residues of *cis*- and *trans*-metconazole were 2.067 and 0.426 ppm,

respectively, and total metconazole residues were 2.493 ppm. Residues of metabolites M11, M21, and M30 in/on roots were <0.010 ppm, and residues in tops were <0.010-0.030 ppm for M11, <0.010-0.020 ppm for M21, and <0.010 ppm for M30.

Residues of 1,2,4-T, TA, and TAA were below the LOQ (<0.05 ppm) in/on all samples of sugar beet roots and tops following both treatments.

The submitted residue decline data indicated that total metconazole residues generally declined or did not increase in sugar beet roots and tops with increasing preharvest intervals.

Conclusions. The submitted sugar beet field trial data are acceptable. Data from Treatment 2 reflect the proposed use pattern for sugar beets. The number and locations of field trials are in accordance with OPPTS Guideline 860.1500 requirements for sugar beet. Samples were analyzed for the residues of concern using an acceptable method, and the studies are supported by adequate storage stability data.

All samples were analyzed for metconazole (determined as the *cis* and *trans* isomers), the residue of concern, as well as three metconazole metabolites, M11, M21, and M30, and the triazole metabolites 1,2,4-T, TA, and TAA.

The available field trial data will support tolerances for residues of metconazole in/on sugar beet root at 0.07 ppm. A tolerance for sugar beet tops is not required, because this commodity is no longer considered a significant livestock feed item (*Table 1 Feedstuffs*, October 2006). The tolerance calculations for sugar beet root are presented in Appendix II.

Stone fruit group 12

DER Reference: 46901707.der.doc (Cherry)
46901708.der.doc (Peach)
46901709.de1.doc (Plum)

Table 11. Summary of Residue Data from Stone Fruit Crop Field Trials with Metconazole

Crop matrix	Total Applic. Rate (lb ai/A)	PHI (days)	Analyte	Residue Levels (ppm)[1]						
				n	Min.	Max.	HAFT[2]	Median	Mean	Std. Dev.
STONE FRUIT (proposed use = 0.375 lb ai/A total application rate, 14-day PHI)										
1.81 lb/gal FIC formulation										
Cherry	0.405-0.416 0.538 (1 trial)	13-14	*cis*-Metconazole	16	<0.02	0.134	0.119	0.041	0.048	0.032
			trans-Metconazole	16	<0.02	0.028	0.025	0.020	0.021	0.002
			Metconazole	**16**	**<0.04**	**0.162**	**0.143**	**0.061**	**0.068**	**0.033**
Peach	0.403-0.417 0.545 (1 trial)	13-14	*cis*-Metconazole	18	<0.020	0.073	0.066	0.027	0.030	0.015
			trans-Metconazole	18	<0.020	<0.020	0.020	<0.020	<0.020	0.00
			Metconazole	**18**	**<0.040**	**<0.093**	**0.086**	**0.047**	**0.050**	**0.015**
Plum	0.405-0.412 0.538 (1 trial)	13-14	*cis*-Metconazole	12	<0.020	0.04	0.06	0.020	0.024	0.008
			trans-Metconazole	12	<0.020	<0.020	<0.020	<0.020	<0.020	--
			Metconazole	**12**	**<0.040**	**<0.060**	**0.060**	**0.040**	**0.044**	**0.008**

Table 11. Summary of Residue Data from Stone Fruit Crop Field Trials with Metconazole										
Crop matrix	Total Applic. Rate (lb ai/A)	PHI (days)	Analyte	Residue Levels (ppm)[1]						
				n	Min.	Max.	HAFT[2]	Median	Mean	Std. Dev.
50% WDG formulation										
Cherry	0.407-0.410	14	*cis*-Metconazole	4	0.027	0.056	0.052	0.039	0.040	0.014
			trans-Metconazole	4	<0.02	<0.02	0.02	0.020	0.020	0.020
			Metconazole	**4**	**0.049**	**<0.076**	**0.076**	**0.068**	**0.065**	**0.011**
Peach	0.418	14	*cis*-Metconazole	2	<0.02	0.020	0.02	0.02	0.02	--
			trans-Metconazole	2	<0.02	<0.02	0.02	0.02	0.02	--
			Metconazole	**2**	**<0.04**	**<0.040**	**0.04**	**0.04**	**0.04**	--
Plum	0.408	14	*cis*-Metconazole	2	<0.02	0.020	0.02	0.02	0.02	--
			trans-Metconazole	2	<0.02	<0.02	0.02	0.02	0.02	--
			Metconazole	**2**	**<0.04**	**<0.040**	**0.04**	**0.04**	**0.04**	--

[1] Values for "Metconazole" and "Total Residues" are reported on a sample basis and are therefore not summations of tabulated data.
[2] HAFT = Highest average field trial result.

Cherry

Valent has submitted field trial data for metconazole on cherries. Eight field trials were conducted in the United States in Zones 1 (1 trial in NY), 5 (3 trials in MI), 10 (2 trials in CA), and 11 (2 trials in OR) during the 2003, 2004 and 2005 growing seasons.

In a single 2003 trial, a 1.81 lb ai/gal FlC formulation was applied as four broadcast foliar applications, for a total seasonal application rate of 0.538 lb ai/A (1.4x the maximum proposed seasonal rate). In the 2004 and 2005 trials, one treated plot at each site received three broadcast foliar applications of the 1.81 lb/gal FlC at a nominal rate of 0.136 lb ai/A for a total seasonal application rate of 0.405-0.416 lb ai/A (~1.1x the maximum proposed seasonal application rate for stone fruits). In side-by-side trials conducted at the NY site (Trial I) and one MI site (Trial J), a second plot was treated with the 50% WDG formulation according to the same use pattern at a total rate of 0.407-0.410 lb ai/A. For trials reflecting three applications, first applications were made at all sites at full bloom, second applications were made at petal fall (at RTIs of 7-13 days), and third applications were made near fruit maturity (at RTIs of 22-69 days). Applications were made in spray volumes of 104-135 gal/A. No spray adjuvants were added.

At each trial location, one untreated control and two treated mature cherry samples were collected 13 to 14 days following the last test substance application (13- to 14-day PHI). In addition, one control and duplicate treated mature cherry samples were harvested 3, 6 and 10 days after the last application at the 2003 trial and 10, 18 and 22 days after the last application at one OR and one CA trial (Trials E and G) to determine residue decline.

Cherry samples were analyzed for residues of *cis*- and *trans*-metconazole using GC/NPD Method RM-41C-1. The method was adequate for data collection based on acceptable method validation and concurrent method recoveries. The validated LOQ was 0.02 ppm for each isomer.

Samples were stored frozen (at approximately -20°C) prior to analysis; the maximum storage interval from harvest to extraction was 123 days (4.0 months). Samples were analyzed within 1-6 days of extraction. Storage stability of *cis*- and *trans*-metconazole was determined by reanalysis of the fortified control cherry samples from Trial I which were re-extracted, in duplicate, 159 days after the initial analysis of all of the crop field trial samples. Storage stability of *cis*- and *trans*-metconazole in frozen storage for 159 days was acceptable based on the storage stability recovery results.

The results of the cherry field trials are summarized in Table 11. Following three to four applications of the 1.81 lb ai/gal FlC formulation at a total rate of 0.405-0.416 lb ai/A or 0.538 lb ai/A (one trial only) and a PHI of 13-14 days, maximum residues of *cis*- and *trans*-metconazole in/on cherries were 0.134 and 0.028 ppm, respectively, for total metconazole residues of 0.162 ppm. HED notes that, because residues were similar, results for the single trial reflecting four applications were included with the results of the trials reflecting three applications.

In the side-by-side trials conducted with the 1.81 lb/gal FlC and the 50% WDG formulation, total metconazole residues were slightly higher following application of the 50% WDG formulation in each trial. At the NY trial, residues were 0.062-0.069 ppm following application of the FlC formulation and 0.068-0.076 ppm following application of the WDG formulation; at the MI trial residues were <0.04 ppm following application of the FlC formulation and 0.047-0.049 ppm following application of the WDG formulation.

For the three residue decline studies, total metconazole residues declined with increasing PHIs.

Peach

Valent has submitted field trial data for metconazole on peach. Nine field trials were conducted in the United States in Zones 1 (1 trial in PA), 2 (3 trials in GA), 5 (1 trial in MI), 6 (1 trial in TX) and 10 (3 trials in CA) during the 2003, 2004, and 2005 growing seasons.

In a single 2003 trial, a 1.81 lb ai/gal FlC formulation was applied as four broadcast foliar applications, for a total seasonal application rate of 0.545 lb ai/A (1.5x the maximum proposed seasonal rate). In the 2004 and 2005 trials, one treated plot at each site received three broadcast foliar applications of the 1.81 lb/gal FlC at a nominal rate of 0.136 lb ai/A for a total seasonal application rate of 0.403-0.417 lb ai/A (~1.1x the maximum proposed seasonal application rate for stone fruits); in one GA trial, a second plot received three applications at an exaggerated rate of 0.271-0.273 lb ai/A for a total seasonal rate of 0.813 lb ai/A (2.2x). In a side-by-side trial conducted at the PA site (Trial M), a second plot was treated with the 50% WDG formulation according to the same use pattern at a total rate of 0.418 lb ai/A. For trials reflecting three applications, first applications were made at all sites at full bloom, second applications were made at petal fall, at RTIs of 3-15 days, and third applications were made near fruit maturity, at RTIs of 50-117 days. Applications were made in spray volumes of 104-141 gal/A. No spray adjuvants were added to the applications.

At each trial location, one untreated control and two treated mature peach raw agricultural commodity (RAC) samples were collected 13 to 14 days following the last test substance application (13- to 14-day PHI). In addition, one control and duplicate treated mature peach

samples were harvested 3, 7, and 10 days after the last application at the 2003 trial and 10, 18 and 22 days after the last application at one GA trial (Trial K) to determine residue decline.

Peach samples were analyzed for residues of *cis*- and *trans*-metconazole using GC/NPD Method RM-41C-1. The method was adequate for data collection based on acceptable method validation and concurrent method recoveries. The validated LOQ was 0.02 ppm for each isomer.

Samples were stored frozen (at approximately -20°C) prior to analysis; the maximum storage interval from harvest to extraction was 131 days (approximately 4 months). Samples were analyzed within 1-9 days of extraction. The storage stability data for cherries may be translated to support the storage conditions and duration of samples from the peach field trials.

The results of the peach field trials are summarized in Table 11. Following three to four applications of the 1.81 lb/gal FlC formulation at a total rate of 0.403-0.417 lb ai/A or 0.545 lb ai/A (one trial only) and a PHI of 13-14-days, maximum residues of *cis*- and *trans*-metconazole in/on peach were 0.073 and <0.02 ppm, respectively, for total metconazole residues of 0.093 ppm. HED notes that because residues were similar, results for the single trial reflecting four applications were included with the results of the trials reflecting three applications.

In the side-by-side trials conducted with the 1.81 lb/gal FlC and the 50% WDG formulation, total metconazole residues were comparable: <0.040-0.041 ppm following application of the FlC formulation and <0.040 ppm following application of the WDG formulation.

For the two residue decline studies, the total metconazole residues declined with increasing PHIs.

Plum

Valent has submitted field trial data for metconazole on plums and dried plums. Six field trials were conducted in the United States in Zones 5 (1 trial in MI), 10 (4 trials in CA) and 12 (1 trial in OR) during the 2003, 2004, and 2005 growing seasons.

In a single 2003 trial, a 1.81 lb ai/gal FlC formulation was applied as four broadcast foliar applications at a nominal rate of 0.135 lb ai/A, for a total seasonal application rate of 0.538 lb ai/A (1.4x the maximum proposed seasonal rate). In the 2004 and 2005 trials, one treated plot at each site received three broadcast foliar applications of the 1.81 lb/gal FlC at a nominal rate of 0.136 lb ai/A for a total seasonal application rate of 0.405-0.412 lb ai/A (~1.1x the maximum proposed seasonal application rate for stone fruits); in one CA trial, a second plot received three applications at an exaggerated rate of 0.678-0.682 lb ai/A for a total seasonal rate of 2.04 lb ai/A (5.4x). Samples from the exaggerated-rate trial were reserved for the plum processing study (refer to 860.1520). In a side-by-side trial conducted at the OR site (Trial J), a second plot was treated with the 50% WDG formulation according to the same use pattern at a total rate of 0.408 lb ai/A. For trials reflecting three applications, first applications were made at all sites at full bloom, second applications were made at petal fall, at RTIs of 5-17 days, and third applications were made near fruit maturity, at RTIs of 109-133 days. Applications were made in spray volumes of 103-133 gal/A. No spray adjuvants were added to the applications.

At each trial location, one untreated control and two treated mature plum RAC samples were collected 14 days following the last test substance application (14-day PHI). In addition, at the decline study test site (Trial A), one control and duplicate treated mature plum samples were harvested at 3, 7, 10 and 14 days after the last application to determine residue decline.

Plum samples were analyzed for residues of *cis*- and *trans*-metconazole using GC/NPD Method RM-41C-1. The method was adequate for data collection based on acceptable method validation and concurrent method recoveries. The validated LOQ was 0.02 ppm for each isomer.

Samples were stored frozen (at approximately -20°C) prior to analysis. The maximum storage interval from harvest to extraction for samples from the single 2003 trial was 203 days (7 months), and the maximum storage interval from harvest to extraction for samples from the 2004 and 2005 trials was 63 days (2 months); all samples were analyzed within 1-5 days of extraction. The storage stability data for cherries may be translated to support the storage conditions and duration of samples from the peach field trials.

The results of the plum field trials are summarized in Table 11. Following three to four applications of the 1.81 lb/gal FlC formulation at a total rate of 0.405-0.412 lb ai/A or 0.538 lb ai/A (one trial only) and a PHI of 13-14 days, maximum residues of *cis*- and *trans*-metconazole in/on plum were 0.040 and <0.02 ppm, respectively, for total metconazole residues of 0.060 ppm. HED notes that because residues were similar, results for the single trial reflecting four applications were included with the results of the trials reflecting three applications.

In the side-by-side trial conducted with the 1.81 lb/gal FlC and the 50% WDG formulation, total metconazole residues were <0.04 ppm following application of each product.

For the residue decline study, the residue data showed only a very slight decline of metconazole residues between 3 and 14 days after the last of four applications.

Conclusions. HED has determined that the submitted field trial data for the stone fruit group 12 are adequate to support registration of the 50% WDG formulation. All samples were analyzed for metconazole (determined as the *cis* and *trans* isomers) using an acceptable method. A tolerance of 0.20 ppm for the stone fruit group 12 is appropriate. Although samples were not analyzed for the triazole metabolites, field trial data for triazoles are not required for these petitions submitted in 2006.

Tree nut group 14

DER Reference: 46901710.der.doc (includes review of MRID 46901711)

Table 12. Summary of Residue Data from Tree Nut Crop Field Trials with Metconazole[1]										
Crop matrix	Total Applic. Rate (lb ai/A)	PHI (days)	Analyte	Residue Levels (ppm)						
				n	Min.	Max.	HAFT[2]	Median	Mean	Std. Dev.
TREE NUTS (proposed use = 0.500 lb ai/A total application rate, 25-day PHI)										
1.81 lb/gal FlC formulation										
Almond, hulls	0.543-0.570	25	*cis*-Metconazole	10	0.42	3.04	2.49	0.65	1.05	0.84
			trans-Metconazole	10	0.08	0.65	0.50	0.13	0.22	0.19
			Metconazole	**10**	**0.50**	**3.69**	**2.82**	**0.78**	**1.27**	**1.03**
	0.394-0.408	25	*cis*-Metconazole	4	0.30	0.62	0.62	0.48	0.47	0.17
			trans-Metconazole	4	0.07	0.15	0.14	0.11	0.11	0.04
			Metconazole	**4**	**0.37**	**0.76**	**0.76**	**0.59**	**0.58**	**0.21**
Almond, nutmeat	0.543-0.570	25	*cis*-Metconazole	10	<0.02	<0.02	<0.02	0.02	0.02	--
			trans-Metconazole	10	<0.02	<0.02	<0.02	0.02	0.02	--
			Metconazole	**10**	**<0.04**	**<0.04**	**<0.04**	**0.04**	**0.04**	--
	0.394-0.408	25	*cis*-Metconazole	4	<0.02	<0.02	<0.02	0.02	0.02	--
			trans-Metconazole	4	<0.02	<0.02	<0.02	0.02	0.02	--
			Metconazole	**4**	**<0.04**	**<0.04**	**<0.04**	**0.04**	**0.04**	--
Pecan, nutmeat	0.502-0.537	25-32	*cis*-Metconazole	4	<0.02	<0.02	<0.02	0.02	0.02	--
			trans-Metconazole	4	<0.02	<0.02	<0.02	0.02	0.02	--
			Metconazole	**6**	**<0.04**	**<0.04**	**<0.04**	**0.04**	**0.04**	--
50% WDG formulation										
Almond, hulls	0.402-0.407	25	*cis*-Metconazole	4	<0.02	1.69	1.51	0.68	0.77	0.87
			trans-Metconazole	4	<0.02	0.33	0.31	0.15	0.16	0.17
			Metconazole	**4**	**<0.04**	**2.02**	**1.82**	**0.83**	**0.93**	**1.04**
Almond, nutmeat	0.402-0.407	25	*cis*-Metconazole	4	<0.02	<0.02	<0.02	0.02	0.02	--
			trans-Metconazole	4	<0.02	<0.02	<0.02	0.02	0.02	--
			Metconazole	**4**	**<0.04**	**<0.04**	**<0.04**	**0.04**	**0.04**	--
Pecan, nutmeat	0.529	26	*cis*-Metconazole	2	<0.02	<0.02	<0.02	0.02	0.02	--
			trans-Metconazole	2	<0.02	<0.02	<0.02	0.02	0.02	--
			Metconazole	**2**	**<0.04**	**<0.04**	**<0.04**	**0.04**	**0.04**	--

[1] Values for "Metconazole" and "Total Residues" are reported on a sample basis and are therefore not summations of tabulated data.
[2] HAFT = Highest average field trial result.

Valent has submitted field trial data for metconazole on almonds and pecans, the representative commodities of the tree nut group 14. Seven almond field trials were conducted in the United States in Zone 10 (CA) during the 2003 and 2005 growing seasons, and three pecan trials were conducted in Zone 2 (GA; 1 trial), Zone 6 (TX, 1 trial), and Zone 8 (TX; 1 trial) during the 2004 growing season. The petitioner noted that nine pecan field trials were attempted; five trials were lost due to adverse weather conditions, and samples from one trial were lost because shells were not separated from the nutmeats prior to shipment to the analytical laboratory.

In five almond and three pecan field trials, a 1.81 lb ai/gal FlC formulation or a 50% WDG formulation (1 pecan trial only) was applied as two broadcast foliar applications at 0.248-0.273

lb ai/A/application for a total seasonal rate of 0.502-0.570 lb ai/A (1.0-1.1x the maximum proposed seasonal application rate for tree nuts); in one almond trial, a second plot received two applications at an exaggerated rate of 0.540-0.542 lb ai/A/application for a total seasonal rate of 1.082 lb ai/A (2.2x). In the two remaining almond trials, the 1.81 lb/gal FlC formulation and the 50% WDG formulation were applied in side-by-side trials as two broadcast foliar applications at 0.134-0.136 lb ai/A for the first application and 0.260-0.272 lb ai/A for the second application for a total seasonal rate of 0.394-0.408 lb ai/A (0.8x the maximum proposed seasonal application rate). The petitioner noted that the lower rate used in the first application for the side-by-side trials was the result of a protocol error. First applications were made to almonds at full bloom to petal fall and to pecans at late bloom to 7 days after flower drop; second applications were made at hull split for almonds and at hard dough to shuck split for pecans; RTIs ranged from 133 to 178 days. Applications were made in 99.9-149.9 gal/A spray volumes. No spray adjuvants were added to the applications.

Samples of mature almonds and pecans were harvested 25-26 days after the last application, except for one pecan trial in which samples were collected 32 days after the last application due to wet weather conditions. Additional samples of almonds were collected from one trial 15, 20, and 30 days after final application to generate residue decline data.

Samples were analyzed for residues of *cis*- and *trans*-metconazole using GC/NPD method RM-41C-1. The validated LOQ was 0.02 ppm for each isomer, and the reported LOD was 0.01 ppm for each isomer. The method was adequate for data collection based on acceptable concurrent method recoveries. HED notes that samples were not analyzed for residues of the triazole metabolites 1,2,4-T, TA, and TAA.

Samples were stored frozen (~-20 °C) from harvest to analysis for 81-288 days (2.7-9.5 months) for almond hulls, 81-618 days (2.7-20.3 months) for almond nutmeats, and 107-129 days (3.5-4.2 months) for pecan nutmeats. The petitioner conducted a concurrent storage stability study which indicated that residues of *cis*- and *trans*-metconazole are relatively stable under frozen storage conditions in/on samples of almond nutmeats and hulls for up to 664 days (21.8 months) and 784 days (25.8 months), respectively; these data are adequate to support the almond crop field trials.

The results of the tree nut field trials are summarized in Table 12. Residues of *cis*- and *trans*-metconazole were below the LOQ (<0.02 ppm) in/on all samples of almond and pecan nutmeats from the submitted field trials; total metconazole residues (sum of *cis* and *trans* isomers) were <0.04 ppm.

Following two applications of the 1.81 lb ai/gal FlC formulation at a total rate of 0.543-0.570 ppm, maximum residues of *cis*- and *trans*-metconazole in/on almond hulls were 3.04 and 0.65 ppm, respectively, for total metconazole residues of 3.69 ppm.

Results of the side-by-side trials with the 1.81 lb ai/gal FlC and the 50% WDG formulation at total rates of 0.394-0.408 lb ai/A were inconclusive. Following application of the 1.81 FlC formulation, residues of *cis*- and *trans*-metconazole in/on almond hulls were 0.30-0.62 and 0.07-0.15 ppm, respectively, for total metconazole residues of 0.37-0.76 ppm. Following application of the 50% WDG formulation, residues of *cis*- and *trans*-metconazole in/on almond hulls were <0.02-1.69 ppm and <0.02-0.33 ppm, respectively, for total metconazole residues of <0.04-2.02

ppm. The data suggest that use of the 50% WDG formulation may result in higher residues in almond hulls.

The submitted residue decline data indicated that total metconazole residues increased slightly in almond hulls between the 25- and 30-day PHI. Because residues were nondetectable in/on all samples of almond nutmeats at all preharvest intervals, it was not possible to assess residue decline in nutmeats.

Conclusions. HED has determined that the submitted field trial data for the tree nut group 14 are adequate to support registration of the 50% WDG formulation. All samples were analyzed for metconazole (determined as the *cis* and *trans* isomers) using an acceptable method. The submitted crop field trial data reflected the proposed use pattern for tree nuts with respect to maximum seasonal application rate and PHI. A tolerance of 0.04 ppm for the tree nut group 14 is appropriate. Although samples were not analyzed for the triazole metabolites, field trial data for triazoles are not required for these petitions submitted in 2006.

Peanut

DER Reference: 46901712.de1.doc

Table 13. Summary of Residue Data from Peanut Field Trials with Metconazole[1]

Crop matrix	Total Applic. Rate (lb ai/A)	PHI (days)	Analyte	Residue Levels (ppm)						
				n	Min.	Max.	HAFT[2]	Median	Mean	Std. Dev.
PEANUT (proposed use = 0.500 lb ai/A total application rate, 14-day PHI)										
Peanut, nutmeat	0.49-0.51	10-18	*cis*-Metconazole	28	<0.02	<0.02	<0.02	0.02	0.02	--
			trans-Metconazole	28	<0.02	<0.02	<0.02	0.02	0.02	--
			Metconazole	**28**	**<0.04**	**<0.04**	**<0.04**	**0.04**	**0.04**	**--**
Peanut nutmeat	1.00-1.03	14-15	*cis*-Metconazole	6	<0.02	0.04	0.03	0.02	0.02	<0.01
			trans-Metconazole	6	<0.02	<0.02	<0.02	0.02	0.02	--
			Metconazole	**6**	**<0.04**	**<0.06**	**<0.03**	**0.02**	**0.02**	**<0.01**

[1] Values for "Metconazole" and "Total Residues" are reported on a sample basis and are therefore not summations of tabulated data.
[2] HAFT = Highest average field trial result.

Valent has submitted field trial data for metconazole on peanuts. Fourteen field trials were conducted in the United States in Zones 2 (AL, GA, NC, SC, and VA; 9 trials), 3 (FL; 1 trial), 4 (MS; 1 trial), 6 (TX; 2 trials), and 8 (TX, 1 trial) during the 2004 (one trial) and 2005 growing seasons.

At each location, peanut plants received two foliar applications of a 1.81 lb ai/gal FlC or a 50% WDG formulation of metconazole at 0.24-0.26 lb ai/A/application with a 13- to 15-day RTI for a total seasonal rate of 0.49-0.51 lb ai/A (1x the maximum proposed seasonal application rate for peanut). At four of the trial locations, exaggerated-rate applications were made to separate plots at 0.50-0.52 lb ai/A/application for a total seasonal rate of 1.00-1.03 lb ai/A (2x). The 1.81 lb ai/gal FlC formulation was used at the 2004 trial site only, and no adjuvant was used at this site;

a nonionic surfactant was added to the spray mixtures for all remaining sites. Applications were made using ground equipment in spray volumes of 19-23 gal/A.

Peanuts were dug 13-18 days after the last application, and were allowed to dry in the field for 5-9 days or were collected immediately following harvest and moved indoors to dry on tarps. Additional samples were collected from two trials 10, 17-19, and 22 days after the last application to generate residue decline data. Peanut hay was collected from the 2004 trial site only.

Samples of peanut nutmeats were analyzed for residues of *cis*- and *trans*-metconazole using GC/NPD method RM-41C-1. The validated LOQ was 0.02 ppm for each isomer, and the reported LOD was 0.01 ppm for each isomer. The method was adequate for data collection based on acceptable concurrent method recoveries. HED notes that samples were not analyzed for the triazole metabolites 1,2,4-T, TA, and TAA.

Samples were stored frozen (<-22 °C) from harvest to analysis for 110-138 days (3.6-4.5 months). To support sample storage conditions and durations, the petitioner conducted a concurrent storage stability study which indicated that residues of *cis*- and *trans*-metconazole were reasonably stable during frozen storage for up to 133 days in/on peanut nutmeats. These data are adequate to support the peanut field trials.

The results of the peanut field trials are summarized in Table 13. Residues of both *cis*- and *trans*-metconazole were nondetectable (<0.01 ppm) in/on all but two samples of peanut nutmeat harvested 10-18 days after two foliar applications of the 1.81 lb/gal FlC or 50% WDG formulation of metconazole at a total seasonal rate of 0.49-0.51 lb ai/A; residues of *cis*-metconazole at 0.01 ppm (<LOQ) were detected in/on two samples of peanut nutmeats. Combined residues of *cis*- and *trans*-metconazole did not exceed the combined LOQ of 0.04 ppm for total metconazole in/on peanut nutmeats. HED notes that because residues were near or below the LOQ in all trials, results for both formulations were considered together. In samples analyzed from three of the exaggerated-rate trials, quantifiable residues of *cis*-metconazole at 0.02 and 0.04 ppm were detected in two samples from one trial conducted using the 50% WDG formulation for maximum combined residues of <0.06 ppm; remaining residues for both analytes were nondetectable.

Residue decline samples were analyzed from one trial site only. Because residues were nondetectable in/on all samples at all preharvest intervals, it was not possible to assess residue decline.

Conclusions. The submitted peanut field trial data are acceptable and reflect the proposed use pattern for peanut with respect to the maximum seasonal application rate and PHI; the number of applications and the individual application rates used in the field trials differed from the proposed use pattern (two applications at a 2x rate/application vs. the proposed four applications at a 1x rate/application). HED concludes that the submitted data are sufficiently representative of the proposed use pattern for purposes of this petition. Although peanut hay was not collected, the proposed use includes a restriction against the grazing or feeding of peanut hay, which is considered practical (OPPTS 860.1000); therefore, data for peanut hay are not required. The number and locations of field trials are in accordance with OPPTS Guideline 860.1500

requirements for peanut. Samples were analyzed for metconazole (determined as the *cis* and *trans* isomers) using an acceptable method, and the studies are supported by adequate storage stability data.

The submitted data are adequate to support registration of the 50% WDG formulation, which Valent is proposing for use on peanut. The WDG formulation was used in 13 of the 14 field trials. The available field trial data will support tolerances for residues of metconazole in/on peanut nutmeat at the method LOQ (0.04 ppm) for metconazole. Although samples were not analyzed for the triazole metabolites, field trial data for triazoles are not required for these petitions submitted in 2006.

860.1520 Processed Food and Feed

DER Reference: 46901712.de2.doc (Peanut)
46901709.de2.doc (Plum)
46902301.der.doc (Soybean)
46902229.der.doc (Soybean aspirated grain fractions)
46902302.der.doc (Sugar beet)
46902231.der.doc (Wheat)
46902232.der.doc (Wheat aspirated grain fractions)

Table 14. Summary of Processing Factors for Metconazole.

RAC	Processed Commodity	Processing Factor[1]			
		Metconazole	1,2,4-T	TA	TAA
Peanut	Meal	0.9			
	Refined oil	1.3			
Plum	Prune	2.3x			
Soybean	Hulls	1.7x	NC	1.3x	NC
	Meal	0.6x	NC	1.3x	NC
	Refined oil	0.6x	NC	<0.4x	NC
	AGF	>56x			
Sugar beet	Refined sugar	0.8x	NC	NC	NC
	Dried pulp	14x	NC	NC	NC
	Molasses	1.9x	NC	>2.3x	NC
Wheat	Bran	1.9x	NC	2.4x	1.2x
	Flour	0.2x	NC	0.5x	0.9x
	Middlings	2.0x	NC	0.7x	0.9x
	Shorts	2.1x	NC	1.2x	1.0x
	Germ	1.0x	NC	2.5x	1.1x
	AGF	64.3x	NC	<0.6x	1.6x

[1] NC = Not calculated; residues were below the LOQ in the RAC and the processed commodity.

Peanut

Valent has submitted a processing study for metconazole on peanut. In a single trial conducted in MS during the 2005 growing season, the 50% WDG formulation of metconazole was applied to peanut plants as two foliar applications with a 13-day RTI at 1.24-1.26 lb ai/A/application for a total seasonal rate of ~2.5 lb ai/A (~5x the maximum proposed seasonal application rate for peanut). Peanuts were dug 18 days after the final application and were left to dry in the field for 2 days prior to sample collection. Applications were made using ground equipment in spray volumes of ~20 gal/A; a nonionic surfactant was added to the spray mixture. Subsamples of nutmeat were reserved, and the remaining bulk samples were processed into meal and refined oil using simulated commercial processing procedures.

Samples of peanut nutmeats, meal, and refined oil were analyzed for residues of *cis*- and *trans*-metconazole using GC/NPD method RM-41C-1. The validated LOQ was 0.02 ppm for each isomer, and the reported LOD was 0.01 ppm for each isomer. The method was adequate for data collection based on acceptable concurrent method recoveries. HED notes that samples were not analyzed for the triazole metabolites 1,2,4-T, TA, and TAA.

Samples were stored frozen (≤-12 °C) for 139 days (4.6 months) from harvest to analysis for nutmeats and for 7 days from processing to analysis for meal and refined oil. No storage stability data are required for the processed commodities; adequate storage stability data are available to support the storage conditions and duration of peanut nutmeats.

The processing factors for peanut processed commodities are summarized in Table 14. Residues of *cis*- and *trans*-metconazole in peanut nutmeats were 0.04-0.06 and <0.02 ppm, respectively, for total metconazole residues of 0.06-0.08 ppm (average of 0.07 ppm).

Following processing, total metconazole residues were 0.06 ppm in meal and 0.09 ppm in oil. The study results indicate that total metconazole residues do not concentrate in meal (processing factor of 0.9x), but do concentrate slightly in refined oil (processing factor of 1.3x).

The calculated processing factors for peanut meal and oil do not exceed the theoretical concentration factors of 2.2x and 2.8x, respectively (OPPTS 860.1520, Table 3).

Plum

Valent has submitted a study examining the transfer of metconazole into processed plum commodities. The RAC was harvested from a single trial 14 days following the last of three airblast applications of a 1.81 lb ai/gal FlC formulation, made at an exaggerated target application rate of 0.68 lb ai/A/application (0.76 kg ai/ha), with RTIs of 7 and 119 days. The total achieved application rate was 2.04 lb ai/A/season (2.29 kg ai/ha), 5.4x the maximum proposed seasonal application rate for stone fruits. Following harvesting, the fresh plums were processed into dried plums (prunes).

Residues of metconazole in/on plum samples were quantitated using GC/NPD method RM-41C-1. The method was adequate for data collection based on acceptable method validation and concurrent method recoveries. HED notes that samples were not analyzed for the triazole metabolites 1,2,4-T, TA, and TAA.

Samples were stored frozen (~-20 °C) from harvest to analysis for 44 days (1.4 months) for fresh plums and 42 days (1.4 months) for prunes; samples were analyzed within 2 days of extraction. The storage stability data for cherries may be translated to support the storage conditions and durations of samples from the plum processing study.

The processing factors for prunes are summarized in Table 14. The results show that RAC residues of *cis*-metconazole averaged 0.10 ppm while *trans*-metconazole residues average 0.023 ppm. Total metconazole was calculated by taking the sum of *cis*- and *trans*-metconazole residues. The RAC total metconazole residues averaged 0.12 ppm (n=2). The processed fractions (dried plums) were analyzed, and *cis*-metconazole residues averaged 0.24 ppm (n=2), *trans*-metconazole residues averaged 0.052 ppm (n=2) and total metconazole residues averaged 0.28 ppm (n=2). Concentration factors of 2.4x, 2.3x, and 2.3x were calculated for *cis*-, *trans*-, and total metconazole in dried plums using the average residue in the processed sample divided by the average residue in the RAC. The average concentration factors are in agreement with the theoretical concentration factor of 3.5x for plums (OPPTS 860.1520, Table 1).

Soybean

MRID 46902301: BASF has submitted a processing study with soybeans. In four trials conducted in IL, ND, NE, and WI, a 0.75 lb ai/gal SC/L formulation of metconazole was applied as two broadcast foliar sprays to soybeans at 0.35-0.36 lb ai/A, with 8- to 11-day RTIs, for a total rate of 0.70-0.71 lb ai/A (~5x the maximum proposed seasonal application rate for soybean). Applications were made in 15-20 gal/A spray volumes with a nonionic surfactant added as an adjuvant to the spray mixture. Samples of soybean seed were harvested 27-31 days after the last application of metconazole, and were processed into hulls, meal, crude oil, and refined oil using simulated commercial processing procedures.

Samples were analyzed for residues of *cis*- and *trans*-metconazole, metabolites M11, M21, and M30, and the triazole metabolites (1,2,4-T, TA, and TAA) using an LC/MS/MS method (BASF Method D0508). Residues of metabolites M11, M21, and M30 were converted to parent equivalents. The validated LOQs were 0.01 ppm for the parent metconazole (sum of *cis* and *trans* isomers at 0.005 ppm each), M11, M21, and M30 in/on soybean seed and processed samples. The validated LOQ was 0.05 ppm for 1,2,4-T, TA, and TAA. The method was adequate for data collection based on acceptable concurrent method recoveries.

Samples were stored frozen (<-10 °C) prior to extraction for 125-147 days (4.1-4.8 months) for soybean seeds, 85-86 days (2.8 months) for hulls, 76-77 days (2.5 months) for meal, 62 days (2.0 months) for crude oil, and 58-59 days (1.9 months) for refined oil, and were analyzed within 0-2 days of extraction. Adequate storage stability data are available to support the storage conditions and durations of the soybean seed samples. To support sample storage conditions and durations for the processed commodities, the petitioner conducted a concurrent storage stability study which indicated that residues of *cis*- and *trans*-metconazole, M11, M21, M30, 1,2,4-T, TA, and TAA were reasonably stable during frozen storage for 63-66 days in/on soybean hulls, meal, and oil. These data are adequate to support the soybean processing study.

The processing factors for soybean processed commodities are summarized in Table 14. Residues of *cis*-and *trans*-metconazole in soybean seed were <0.005-0.016 and <0.005 ppm,

respectively, for total metconazole residues (sum of *cis* and *trans* isomers) of <0.01-<0.021 ppm. Following processing, respective residues of *cis*-metconazole, *trans*-metconazole, and total metconazole were: 0.013-0.42, <0.005-0.007, and <0.016-0.049 ppm in hulls; <0.005-0.006, <0.005, and <0.01-<0.011 ppm in meal; <0.005-0.011, <0.005, and <0.01-<0.016 ppm in crude oil; and <0.005-0.006, <0.005, and <0.01-0.011 ppm in refined oil. Residues of metabolites M11, M21, and M30 were <0.010 ppm in/on all samples of soybean seed and processed commodities.

The processing data indicate that residues of total metconazole may concentrate in hulls (average processing factor of 1.7x), but do not concentrate in meal, crude oil, or refined oil (respective processing factors of 0.6x, 0.9x, and 0.6x).

The calculated processing factors for hulls do not exceed the maximum theoretical concentration factor of 12x for soybean (OPPTS 860.1520, Table 1).

Residues of 1,2,4-T and TAA were <0.05 ppm in/on all samples of soybean seed and processed commodities. Residues of TA were <0.05-0.16 ppm in soybean seed, <0.05-0.15 ppm in hulls, 0.05-0.21 ppm in meal, and <0.05 ppm in crude and refined oil.

Because residues of 1,2,4-T and TAA were below the LOQ in all soybean samples, processing factors were not calculated. The processing data indicate that residues of TA may concentrate in hulls and meal, with average processing factors of 1.3x. Residues of TA do not concentrate in crude or refined oil (averaging processing factors of <0.4x). The petitioner noted that a reliable estimate of the concentration factor for TA could not be made because apparent residues of TA were found in samples of untreated seed (0.06 ppm), hulls (0.07 ppm) and meal (0.11 ppm) and because triazole-related compounds are naturally abundant in soybean seeds.

HED notes that processing factors were also calculated by the petitioner using total residues of *cis*- and *trans*-metconazole, M11, M21, and M30. When processing factors were calculated using these values, an average processing factor of 1.2x was obtained for hulls, and processing factors of 0.9x, 1.0x, and 0.9x, respectively, were obtained for meal, crude oil, and refined oil.

MRID 46902229: BASF has also submitted data pertaining to AGF for soybeans. In a single field trial conducted in IL in 2004, a 0.75 lb/gal SC/L formulation of metconazole was applied as two broadcast foliar applications to soybeans at 0.07-0.08 lb ai/A/application, with a 9- to 11-day RTI, for a total seasonal rate of ~0.14 lb ai/A (~1x the maximum proposed seasonal application rate for soybean). Applications were made in 10-11 gal/A spray volumes with a nonionic surfactant added as an adjuvant to the spray mixture. Bulk samples of soybean seed were harvested 31 days after the last application of metconazole and were processed into AGF using simulated commercial processing procedures.

Samples of soybean seed and AGF were analyzed for residues of *cis*- and *trans*-metconazole using an LC/MS/MS method, BASF Method 550/0. The validated LOQ was 0.01 ppm for the parent metconazole (sum of *cis* and *trans* isomers at 0.005 ppm each). The method was adequate for data collection for soybean seed based on acceptable concurrent method recoveries. HED notes that no concurrent recovery or method validation data were included for soybean AGF. Samples were not analyzed for the triazole metabolites, 1,2,4-T, TA, and TAA.

Samples were stored frozen (<-10 °C) prior to extraction for 30-91 days (1-3 months) for soybean seed and 30 days (0-1 months) for soybean AGF. Adequate storage stability data are available to support the storage conditions and durations of the soybean seed samples. Because processed samples were stored for 30 days, no data are required to support the storage conditions and durations for soybean AGF commodities. No additional storage stability data are required to support the study.

The processing factor for soybean AGF is presented in Table 14. Residues of *cis*- and *trans*-metconazole in soybean seed were <0.005 ppm each in two samples, for total metconazole residues (sum of *cis* and *trans* isomers) of <0.01 ppm. In two samples of soybean AGF, residues of *cis*-metconazole were 0.33 and 0.58 ppm and residues of *trans*-metconazole were 0.07 and 0.13 ppm, respectively, for total metconazole residues of 0.40 and 0.71 ppm.

The data indicate that total metconazole residues may concentrate in soybean AGF, with an average concentration factor of >56x.

Sugar beet

BASF has submitted a processing study with sugar beets. In four trials conducted in CA, ID, SD, and WI, a 0.75 lb ai/gal SC/L formulation of metconazole was applied as two broadcast foliar sprays to sugar beets at ~0.50 lb ai/A, with ~14 day RTIs, for a total rate of ~1.00 lb ai/A (5x the maximum proposed seasonal application rate for sugar beet). Applications were made in ~25 gal/A spray volumes with a nonionic surfactant added as an adjuvant to the spray mixture. Sugar beet root samples were harvested 14-15 days after the last application of metconazole, and processed into refined sugar, dried pulp, and molasses using simulated commercial processing procedures. In addition, extracted pulp, pressed water, raw juice, lime sludge, thin juice, thick juice, and raw sugar were collected for analysis.

Samples of sugar beet root and processed commodities were analyzed for residues of *cis*- and *trans*-metconazole, metabolites M11, M21, and M30, and the triazole metabolites (1,2,4-T, TA, and TAA) using an LC/MS/MS method (BASF Method D0508). Residues of metabolites M11, M21, and M30 were converted to parent equivalents. The validated LOQ was 0.01 ppm each for parent metconazole (sum of *cis* and *trans* isomers at 0.005 ppm each), M11, M21, and M30 in/on sugar beet root and processed commodities. The LOQ was 0.05 ppm for 1,2,4-T, TA, and TAA. The method was adequate for data collection based on acceptable concurrent method recovery data.

Samples of sugar beet root were stored frozen (<-10 °C) prior to analysis for 161-202 days (5.3-6.6 months); sugar beet processed commodities were stored for 21-45 days (0.7-1.5 months). Adequate storage stability data are available to support the storage conditions and durations of the sugar beet root samples. Because processed samples were stored for just over 1 month, no data are required to support the storage conditions and durations for sugar beet processed commodities. No additional storage stability data are required to support the sugar beet processing study.

The processing factors for sugar beet processed commodities are summarized in Table 14. Residues of *cis*-and *trans*-metconazole in/on sugar beet root were <0.005-0.0128 and <0.005 ppm, respectively, for total metconazole residues (sum of *cis* and *trans* isomers) of <0.01-<0.0232 ppm. Following processing, respective residues of *cis*-metconazole, *trans*-metconazole, and total metconazole were 0.0089-0.7951, <0.005-0.1181, and <0.0139-0.9131 ppm in dried pulp; 0.0101-0.0722, <0.005-0.0110, and <0.0151-0.0832 ppm in molasses; and <0.005-0.0216, <0.005, and <0.01-<0.266 ppm in refined sugar. Residues of metabolites M11, M21, and M30 were <0.010 ppm in/on all samples of sugar beet root and processed commodities, except that residues of M21 were detected in one sample of dried pulp at 0.0137 ppm.

The processing data indicate that residues of total metconazole may concentrate in dried pulp (average processing factor of 14x) and molasses (average processing factor of 1.9x), but do not concentrate in refined sugar (average processing factor of 0.8x). Based on average processing factors for the remaining processed commodities, total metconazole residues do not concentrate in water, raw juice, lime sludge, or thin juice (processing factors 0.6-1x), but may concentrate in pulp, thick juice, and raw sugar (processing factors of 1.3-2.2x).

The calculated processing factors for dried pulp, molasses and sugar do not exceed the maximum theoretical concentration factor of >20x for sugar beets (OPPTS 860.1520, Table 1).

Residues of 1,2,4-T, TA, and TAA were below the LOQ (<0.05 ppm) in/on all samples of sugar beet root and in most processed commodities. Residues of TA were <0.05-0.17 ppm in molasses and <0.05-0.14 ppm in raw sugar.

The processing data indicate that residues of TA may concentrate in molasses and raw sugar (processing factors of >2.3x for both).

HED notes that processing factors were also calculated by the petitioner using total residues of *cis*- and *trans*-metconazole, M11, M21, and M30. When processing factors were calculated using these values, an average processing factor of 6.8x was obtained for dried pulp, and a processing factor of 1.4x was obtained for molasses.

Wheat

MRID 46902231: BASF has submitted a processing study with wheat. (The processing study on wheat satisfies the requirement for studies on barley, oat, and rye.) In four trials conducted in IL, ND, NE, and WI, a 0.75 lb/gal SC/L formulation of metconazole was applied as two broadcast foliar sprays to wheat at 0.50-0.51 lb ai/A, with a 6- to 7-day RTI, for a total rate of 1.00-1.01 lb ai/A (5x the maximum proposed seasonal application rate to small grains). Applications were made in 15-20 gal/A spray volumes with a nonionic surfactant added as an adjuvant to the spray mixture. Wheat grain samples were harvested 20-22 days after the last application of metconazole, and processed into AGF (one site), flour, bran, middlings, shorts, and germ using simulated commercial processing procedures. In addition, cleaned grain, husk, coarse bran, low grade meal, flour type 550, whole meal flour, and whole meal bread samples were collected for analysis.

Samples were analyzed for residues of *cis*- and *trans*-metconazole, metabolites M11, M21, and M30, and the triazole metabolites 1,2,4-T, TA, and TAA using an LC/MS/MS method (BASF Method D0508). Residues of metabolites M11, M21, and M30 were converted to parent equivalents. The validated LOQs were 0.01 ppm for the parent metconazole (sum of *cis* and *trans* isomers at 0.005 ppm each), M11, M21, and M30 in/on wheat samples. The validated LOQ was 0.05 ppm for 1,2,4-T, TA, and TAA. The method was adequate for data collection based on acceptable concurrent method recoveries.

Samples were stored frozen (<-10 °C) prior to extraction for 271-328 days (8.9-10.8 months) for wheat grain, 22-23 days for flour, and 43-71 days for bran, middlings, shorts, and germ; samples were analyzed within 0-6 days of extraction. Adequate storage stability data are available to support the storage conditions and durations of wheat grain samples analyzed for *cis*- and *trans*-metconazole; the data on grain can be translated to support the storage durations and conditions of the processed commodities.

The processing factors for wheat processed commodities are summarized in Table 14. Residues of *cis*-and *trans*-metconazole in/on wheat grain were 0.191-0.348 and 0.047-0.061 ppm, respectively, for total metconazole residues (sum of *cis* and *trans* isomers) of 0.238-0.409 ppm. Following processing, respective residues of *cis*-metconazole, *trans*-metconazole, and total metconazole were 21.190, 4.474, and 25.664 ppm in AGF; 0.046-0.069, 0.010-0.017, and <0.056-0.086 ppm in flour; 0.427-0.730, 0.081-0.137, and 0.508-0.867 ppm in bran; 0.275-1.038, 0.047-0.181, and 0.322-1.219 ppm in middlings; 0.475-0.890, 0.046-0.087, and 0.529-0.977 ppm in shorts; and 0.212-0.318, 0.050-0.074, and 0.262-0.392 ppm in germ. Respective residues of M11, M21, and M30 were 0.04-0.10, 0.01, and 0.01-0.03 ppm in grain; <0.01-0.01, <0.01, and <0.01 ppm in flour; 0.11-0.23, 0.03, and 0.03-0.08 ppm in bran; 0.03-0.15, 0.01-0.04, and <0.01-0.02 ppm in middlings; 0.06-0.12, 0.01-0.02, and 0.01-0.04 ppm in shorts; and 0.03-0.10, <0.01-0.02, and <0.01-0.03 ppm in germ.

The processing data indicate that residues of total metconazole may concentrate in AGF (one sample), bran, middlings, and shorts, with average processing factors of 64.3x, 1.9x, 2.0x, and 2.1x, respectively. Residues of total metconazole do not concentrate in flour or germ (average processing factors of 0.2x and 1.0x, respectively). Based on average processing factors for the remaining processed commodities, total metconazole residues do not concentrate in cleaned grain, low grade meal, flour type 550, whole meal flour, or whole meal bread (processing factors 0.3-1x), but may concentrate in husk (121.4x) and coarse bran (1.9x).

The calculated processing factors for wheat bran, flour, and shorts do not exceed the maximum theoretical concentration factor of 8x for wheat (OPPTS 860.1520, Table 1).

Residues of 1,2,4-T were <0.05 ppm in/on all samples of wheat RAC and processed commodities. Residues of TA were 0.08-0.31, <0.05, <0.05-0.13, 0.15-0.58, <0.05-0.18, 0.11-0.27, and 0.20-0.45 ppm in samples of wheat grain, AGF, flour, bran, middlings, shorts, and germ, respectively. Residues of TAA were 0.05-0.10, 0.08, <0.05-0.09, <0.05-0.12, <0.05-0.09, <0.05-0.10, and 0.06-0.10 ppm in/on samples of wheat grain, AGF, flour, bran, middlings, shorts, and germ, respectively.

The processing data indicate that residues of TA may concentrate in bran, shorts, and germ, with average processing factors of 2.4x, 1.2x, and 2.5x, respectively. Residues of TA do not concentrate in AGF, flour, or middlings (with average processing factors of <0.6x, 0.5x, and 0.7x, respectively). Residues of TAA may concentrate in AGF, bran, and germ, with average processing factors of 1.6x, 1.2x, and 1.1x, respectively; residues do not concentrate in flour, middlings, and shorts (with average processing factors of 0.9x, 0.9x, and 1.0x, respectively).

HED notes that processing factors were also calculated by the petitioner using total residues of *cis*- and *trans*-metconazole, M11, M21, and M30. When processing factors were calculated using these values, average processing factors of 0.2x, 2.0x, 1.7x, 1.8x, and 0.9x were obtained for flour, bran, middlings, shorts, and germ, respectively.

MRID 46902232: BASF has submitted additional data pertaining to AGF for wheat. In a single field trial conducted in TX in 2004, a 1.81 lb/gal FlC formulation was applied to wheat as a single broadcast foliar application at 0.69 lb ai/A (3.4x the maximum proposed seasonal application rate for wheat). The application was made in 21 gal/A, and a nonionic surfactant was added as an adjuvant to the spray mixture. Bulk samples of wheat grain were harvested 30 days after application of metconazole and were processed into AGF using simulated processing procedures. BASF noted that the wheat trial was conducted by Valent, and that wheat grain samples were obtained by BASF for the sole purpose of generating AGF samples for analysis. Samples of wheat grain were not analyzed in the submitted study.

Samples of wheat AGF were analyzed for residues of *cis*- and *trans*-metconazole, metabolites M11, M21, and M30, and the triazole metabolites 1,2,4-T, TA, and TAA using an LC/MS/MS method (BASF Method D0508). Residues of metabolites M11, M21, and M30 were converted to parent equivalents. The validated LOQs were 0.01 ppm for the parent metconazole (sum of *cis* and *trans* isomers at 0.005 ppm each) and the metabolites M11, M21, and M30 in wheat AGF. The validated LOQ was 0.05 ppm for 1,2,4-T, TA, and TAA. The method was adequate for data collection based on acceptable concurrent method recoveries for wheat AGF. The petitioner noted that one of the two treated samples of AGF was too small to be analyzed.

Samples of wheat AGF were generated within 42 days of harvest and were stored frozen (<-8 °C) from sample generation to extraction for 683 days (22.5 months). The available storage stability data for wheat grain are not adequate to support the storage conditions and durations of the AGF samples.

Residues of *cis*- and *trans*-metconazole in/on a single sample of wheat AGF were 3.305 and 0.668 ppm, respectively, and total metconazole residues (sum of *cis* and *trans* isomers) were 3.97 ppm. Residues of metabolites M11, M21, and M30 were 0.03, 0.04, and 0.01 ppm, respectively, and residues of the triazole metabolites were below the LOQ (<0.05 ppm). A processing factor for wheat AGF could not be calculated in this study because residues in the wheat grain RAC were not determined.

Conclusions. The submitted processing data for peanut, plum, soybean, sugar beet, and wheat are acceptable and reflect exaggerated rate applications of metconazole, except for the soybean AGF data which reflect application according to the maximum proposed seasonal application rate. Samples from the peanut and plum processing studies and the soybean AGF study were

analyzed for metconazole (determined as the *cis* and *trans* isomers) using an acceptable method. Samples from the soybean, sugar beet, and wheat processing studies and the wheat AGF study were analyzed for residues of metconazole (determined as the *cis* and *trans* isomers), as well as three metconazole metabolites, M11, M21, and M30, and the triazole metabolites 1,2,4-T, TA, and TAA. All of the studies are supported by adequate storage stability data for *cis*- and *trans*-metconazole.

The wheat AGF data submitted in MRID 46902232 are not adequate to fulfill data requirements, as wheat grain samples were not analyzed and supporting storage stability data for AGF stored for 22.5 months are not available. However, no additional data will be required as the wheat AGF data reported in MRID 46902231 are adequate to satisfy the data requirements.

The processing data for peanut indicate that residues of metconazole do not concentrate in meal but do concentrate in refined oil. Metconazole residues were below the LOQ in/on all samples from the peanut crop field trials; therefore, the expected residues in peanut oil following treatment at 1x are determined by correcting the residues found in the processing study (0.09 ppm) by the degree of exaggeration of the study (5x). Expected residues in peanut oil would be 0.018 ppm. Because this value is less than the recommended 0.04 ppm tolerance for peanut nutmeat, a tolerance is not needed for residues of metconazole in peanut refined oil.

The processing data for plum indicate that residues of metconazole concentrate in prunes. Based on the HAFT residues in plum (0.06 ppm) and the processing factor (2.3x), expected residues in plum would be 0.14 ppm. This value is less than the recommended 0.20 ppm tolerance for the stone fruit group; therefore, a separate tolerance for prune is not required.

The processing data for soybean indicate that residues of metconazole do not concentrate in meal or refined oil, but do concentrate in hulls. Based on the HAFT residues in soybean seed (0.045 ppm) and the processing factor (1.7x), expected residues in hulls would be 0.08 ppm. Because this value is greater than the recommended 0.05 ppm tolerance for soybean, a tolerance is needed for residues of metconazole in soybean hull. A tolerance of 0.08 ppm would be appropriate.

The processing data for sugar beet indicate that residues of metconazole do not concentrate in refined sugar, but do concentrate in dried pulp and molasses. Based on the HAFT residues in sugar beet root (0.044 ppm) and the processing factors for dried pulp (14x) and molasses (1.9x), expected residues would be 0.62 ppm for dried pulp and 0.08 ppm for molasses. Because these values are both greater than the recommended 0.07 ppm tolerance for sugar beet, tolerances are needed for residues of metconazole in dried pulp and molasses. Tolerances of 0.70 ppm and 0.08 ppm would be appropriate for dried pulp and molasses, respectively.

The processing data for wheat indicate that residue of metconazole do not concentrate in flour or germ but do concentrate in bran, middlings, and shorts. Based on the HAFT residues in wheat grain (0.096 ppm) and the processing factors of 1.9x, 2.0x, and 2.1x, respectively, for bran, middlings, and shorts, expected residues would be 0.18, 0.19, and 0.20 ppm for bran, middlings, and shorts, respectively. Because these values are greater than the recommended tolerance of 0.15 ppm, tolerances are needed for these processed commodities. A tolerance of 0.20 ppm would be appropriate for wheat milled byproducts.

The processing study on wheat satisfies the requirement for studies on barley, oat, and rye. Based on the HAFT for barley grain and rye grain and the concentration factor of 1.9x for wheat bran, separate tolerances are not needed for barley bran and rye bran. The barley grain and rye grain tolerances are adequate to cover residues in barley bran and rye bran. Bran is not a processed commodity of oats (OPPTS 860.1520). Residues did not concentrate in wheat flour, so they are not expected to concentrate in barley flour, oat flour, or rye flour.

The submitted data for soybean and wheat AGF indicate that residues of metconazole do concentrate in AGF. Based on the HAFT residues in soybean seed (0.045 ppm) and wheat grain (0.096 ppm) and the processing factors of >56x for soybean AGF and 64.3x for wheat AGF, expected residues would be >2.5 ppm in soybean AGF and 6.2 ppm in wheat AGF. Based on the available data for soybeans and wheat, a tolerance of 7.0 ppm would be appropriate for aspirated grain fractions.

Samples from the submitted processing studies for peanut and plum were not analyzed for the triazole metabolites 1,2,4-T, TA, and TAA. HED will not require additional processing study data for peanut and plum in support of these petitions at this time. When the risk assessment for triazoles was conducted (DP# 322215, 2/7/06, M. Doherty *et al.*), it included use of several triazole fungicides on peanut and plum, and therefore, data are already available demonstrating the potential for concentration of triazole metabolites in the processed commodities of peanut and plum.

860.1650 Submittal of Analytical Reference Standards

An analytical standard for metconazole is currently available in the EPA National Pesticide Standards Repository (personal communication with Theresa Cole, ACB/BEAD, 5/31/07).

860.1850 Confined Accumulation in Rotational Crops

DER Reference: 46901913.der.doc

Valent has submitted a confined rotational crop study with [cyclopentyl-^{14}C]metconazole (specific activity 17.0μCi/mg) and [triazole-3,5-^{14}C]metconazole (specific activity 20.4 μCi/mg). Each radiolabeled test substance was formulated as an emulsifiable concentrate and applied to bare sandy loam soil at a rate equivalent to 0.357 lb ai/A (400 g ai/ha; 0.7x the maximum proposed seasonal rate for any rotatable crop). Rotational crops (radish, lettuce, and wheat) were planted 30 and 120 days after soil treatment, in a greenhouse/controlled chamber environment. Immature whole plants were sampled. Mature crops (radish roots and tops, lettuce, and wheat straw and grain) were harvested. The in-life and analytical phases of the study were conducted by Sittingbourne Research Centre (Sittingbourne, Kent, England).

TRR accumulated at ≥0.01 ppm in all rotational crop matrices planted at the 30- and 120-day PBIs. In immature plants, TRR were comparable for both labels and were higher in 30-day radish, lettuce, and cyclopentyl-label wheat foliage and root than in 120-day samples; in triazole-label wheat foliage and root, TRR were higher or the same in 120-day samples than in 30-day samples. In mature radish roots and tops, lettuce, and wheat grain and straw, TRR were generally higher in triazole-label samples than in cyclopentyl-label samples, except for 120-day

wheat straw, in which TRR were about the same; TRR were generally higher in 120-day samples for both labels than in 30-day samples, except for cyclopentyl-label wheat grain and straw, in which TRR were about the same. Immature crop samples including wheat foliage (forage) were not further analyzed. The following mature crop samples were subjected to extraction procedures and further analysis: 30-day cyclopentyl-label and 30- and 120-day triazole-label radish root and tops; 120-day cyclopentyl-label and 30- and 120-day triazole-label lettuce and wheat straw; and 30- and 120-day triazole-label wheat grain.

The majority of the radioactivity (81.4-88.6% TRR in radish root, 87.8-93.9% in radish tops; 72.7-91.6% in lettuce; 88.6-89.4% in wheat straw; and 83.2-84.7% in wheat grain) was extracted from rotational crop matrices using ACN/water. Further extraction with water released an additional <1.0-6.2% TRR from radish matrices, 10.9-16.7% TRR from lettuce, 1.1-2.1% TRR from wheat straw, and 12.3-14.1% TRR from wheat grain. Nonextractable residues following extraction procedures accounted for 4.6-16.1% TRR (≤0.07 ppm) in radish matrices, 6.0-16.4% (≤0.02 ppm) in lettuce, 9.3-9.6% TRR (≤0.07 ppm) in wheat straw, and 2.7-3.0% TRR (0.01 ppm) in wheat grain. These procedures adequately extracted the majority of the residues from rotational crop matrices. Extraction values were normalized; therefore, accountabilities were 100%.

In general, HPLC was used to generate initial profiles of the organic and aqueous phases following extraction of individual matrices. Identification of metconazole and M30 was confirmed in most matrices by HPLC and/or TLC co-chromatography. TA and TAA were typically identified by TLC co-chromatography and were confirmed by GC/MS following derivatization of the isolated metabolites. In addition, metabolites M12/M13 and a related "ketone metabolite" were tentatively identified in a number of matrices by TLC co-chromatography and/or GC/MS. Glycoside conjugates were characterized on the basis of HPLC retention times and partitioning behavior following hydrolysis.

Metconazole was identified at both PBIs and for both labels in all rotational crop matrices except wheat grain. Metabolite M30 was identified at both PBIs and for both labels in radish root and tops and wheat straw. TA was also identified in triazole-label radish root, radish tops, lettuce, and wheat grain, and TAA was tentatively identified in lettuce and wheat grain. Metabolites M12/M13 and a related ketone metabolite were tentatively identified in radish root and tops and lettuce, and components characterized as glycoside conjugates were characterized in all matrices except wheat grain.

Metconazole was the major identified residue in 30-day radish root (both labels), accounting for 39.2% TRR (0.13 ppm) in cyclopentyl-label root and 28.8% TRR (0.11 ppm) in triazole-label root; metconazole was identified at 15.5% TRR (0.11 ppm) in 120-day radish root. TA was the major identified residue in 120-day triazole-label root, accounting for 45.2% TRR (0.33 ppm), and was identified in 30-day triazole-label root at 19.4% TRR (0.07 ppm). Metabolite M30 was identified as a minor residue in all samples, accounting for 1.4-4.8% TRR. A ketone metabolite was also characterized at 3.1-6.3% TRR in all samples, and M13 and glycoside conjugates were characterized but not quantitated in the aqueous-soluble residues. No remaining individual component accounted for >8% TRR in any radish root sample.

In radish tops, metconazole was identified at 18.4% TRR (0.07 ppm) and 15.5% TRR (0.10 ppm) in 30-day cyclopentyl- and triazole-label tops, respectively, and at 10.8% TRR (0.09 ppm) in 120-day triazole-label tops. TA was identified in 30- and 120-day day triazole-label tops at 30.1% TRR (0.20 ppm) and 33.6% TRR (0.28 ppm; tentative identification), respectively, and metabolite M12 was identified in all samples at 33.6% TRR (0.13 ppm) and 26.8% TRR (0.17 ppm) in 30-day cyclopentyl- and triazole-label tops, respectively, and at 13.3% TRR (0.11 ppm; tentative identification) in 120-day tops. Metabolite M30 was a minor residue in all samples, accounting for 2.3-5.4% TRR. The petitioner additionally characterized glycoside conjugates in the organic and aqueous phases (1.1-11.3% and 2.3-5.3% TRR, respectively) of 30-day radish tops, and the ketone metabolite at 4.7-9.6% TRR in all samples. No remaining individual component accounted for >7% TRR in any radish top sample.

Metconazole was identified at 16.5% TRR (0.02 ppm) in 120-day cyclopentyl-label lettuce, and in triazole-label lettuce (both PBIs) at 1.2-5.0% TRR (0.01 ppm). The petitioner also tentatively identified TA in 30-day triazole-label lettuce (at >18.8%, >0.15 ppm), and TAA in 120-day triazole-label lettuce (at 32.5% TRR, 0.05 ppm). Glycoside conjugates or M12/M13 were characterized but not quantitated in the aqueous-soluble residues.

In wheat straw, metconazole accounted for 3.5-4.0% TRR (0.03 ppm) in 120-day samples (both labels), and for 12.0% TRR (0.07 ppm) in 30-day triazole-label straw. Metabolite M30 was identified at 4.5-5.5% TRR (0.03-0.04 ppm) in all samples. Glycoside conjugates were also characterized at 17.7-18.3% TRR (0.12-0.13 ppm) in 120-day samples (both labels) based on acid hydrolysis and partitioning behavior of aqueous-soluble residues.

Only triazole-label wheat grain samples were subjected to characterization/identification analysis. TA was identified as the major metabolite in 30- and 120-day samples, at 37.0% TRR (0.13 ppm) and 59.4% TRR (0.29 ppm), respectively. TAA was also identified in 120-day samples at 20.6% TRR (0.10 ppm). Remaining residues were characterized as organosoluble (based on partitioning into ethyl acetate (EtOAc), ≤1.3% TRR) or aqueous-soluble. Aqueous-soluble residues were characterized on the basis of TLC distribution in 120-day samples (where no individual component accounted for >11.2% TRR) but were not further investigated in 30-day samples (remaining residues = 58.9% TRR, 0.13 ppm).

The dates of sample combustion, extraction and analysis were not reported; however, a limited number of dated HPLC and TLC chromatograms and GC/MS spectra were included in the study, which indicated that the majority of analyses for characterization/identification of residues were completed within 5-16 months of sample harvest. The petitioner conducted a concurrent storage stability study indicating that the metabolic profile was stable for 7 months in wheat straw. Additional storage stability data are available demonstrating the stability of: (1) metconazole *per se* in carrots, lettuce, and wheat grain and straw for up to 12 months (refer to 46902218.der.doc); (2) metconazole, M30, TA, and TAA in radish roots and tops and wheat grain and straw for up to 6 months (refer to 46902223.der.doc); and (3) TA in wheat grain for up to 12 months (refer to 46902221.der.doc). The available storage stability data are adequate to support the confined rotational crop study.

Based on the submitted confined rotational crop study, the petitioner concluded that the main metabolic transformations were oxidation at the benzylic methylene to form M30, and oxidation

of the methyl groups on the cyclopentane ring to form M12/M13. The presence of TA and TAA in radish tops and roots and wheat grain indicate that oxidative transformation occurs in the plant at the methylene group bearing the triazole ring. The metabolism of metconazole in rotational crops appeared to be extensive; however, detailed characterization and identification of metabolites was limited due to generally low residue levels.

Conclusions. The submitted confined rotational crop data are adequate to satisfy data requirements. The study appears to have adequately delineated the nature of the residue in rotational crops. The metabolism of metconazole appears to proceed in rotational crops via similar mechanisms and to be more extensive than that observed in primary crops (banana, canola, mandarin, pea, and wheat). Two metabolites were identified in rotational crops that were not identified in primary crops, the stereoisomers M12 and M13. HED notes that these metabolites reflect further oxidation of the methyl groups on the cyclopentyl ring of metconazole. HED has determined that the residue of concern for the tolerance expression in rotational crops is metconazole *per* se. HED has also determined that the residue of concern for the risk assessment in rotational crops except for small grains is metconazole *per se*; the residues of concern for the risk assessment in small grains as rotational crops is metconazole *per se* and the metabolite M11 (ROCKS meeting, DP #348234, 10-JAN-2008 and 16-JAN-2008).

The submitted confined study indicates the potential for quantifiable metconazole residues in rotated crop commodities at 30- and 120-day plantback intervals.

860.1900 Field Accumulation in Rotational Crops

DER Reference: 46902303.der.doc (Radish and spinach)
46902305.der.doc (Radish, lettuce, and wheat)
46902304.der.doc (Wheat)

Radish and spinach: BASF has submitted a limited field rotational crop study for metconazole on radish (root and tuber vegetable) and spinach (leafy vegetable). Two limited field rotational crop trials were conducted on radish and spinach (one trial each) during the 2004-2006 growing seasons in the U.S. in Zone 4 (MS).

Each trial consisted of one untreated plot and one treated plot, with soybeans planted as the primary crop. Soybeans received two broadcast foliar applications of a 1.81 lb ai/gal FlC formulation at 0.25 lb ai/A/application with a 13-day RTI, for a total seasonal rate of 0.50 lb ai/A (1x the maximum proposed seasonal application rate for any rotatable crop). The applications were made in spray volumes of ~20 gal/A of water without an adjuvant, using ground equipment.

The primary crop was destroyed and tilled into the soil ~2 weeks after the last application, and the ground was prepared for planting according to area-typical practices. Radish and spinach were planted at PBIs of 35, 129, 157, and 366 days after last application of metconazole to soybean crops. The petitioner noted that the first PBI was 35 days instead of 30 days due to wet weather, and that the second PBI was 129 days instead of 90 days because the first crops were destroyed by cold wet weather, and new crops had to be planted.

Radish tops and roots were harvested at maturity, 33-83 days after planting. Spinach was collected at maturity, 60-177 days after planting.

Samples were analyzed for residues of *cis*- and *trans*-metconazole, metabolites M11, M21, and M30, and the triazole metabolites (1,2,4-T, TA, and TAA) using an LC/MS/MS method (BASF Method D0508). Residues of metconazole metabolites M11, M21, and M30 were converted to parent equivalents. The LOQ was 0.01 ppm for the parent metconazole (sum of *cis* and *trans* isomers at 0.005 ppm each), M11, M21, and M30 in wheat samples. The validated LOQ was 0.05 ppm for 1,2,4-T, TA, and TAA. The reported LOD was 20% of the LOQ. The method was adequate for data collection based on acceptable concurrent method recoveries.

Radish tops and root samples were stored frozen (≤-10 °C) from harvest to extraction for 225-531 days (7.4-17.5 months), and spinach samples were stored for 79-406 days (2.6-13.3 months). All samples were analyzed within 0-7 days of extraction. Adequate storage stability data are available to support the storage conditions and duration of spinach samples analyzed for *cis*- and *trans*-metconazole. Additional data are required reflecting the stability of *cis*- and *trans*-metconazole following frozen storage in/on radish tops and roots for up to 18 months.

At the 35-day PBI, one sample of radish tops bore quantifiable residues of *cis*-metconazole at 0.006 ppm; residues of trans-metconazole were <LOQ for total metconazole residues of <0.011 ppm. Residues of metconazole (*cis* and *trans* isomers), M11, M21, and M30 in remaining samples of radish tops, radish roots, and spinach from the 35-, 129-, 157-, and 366-day PBIs were below the LOQ.

Residues of 1,2,4-T in all samples of radish roots, tops and spinach at all PBIs were below the LOQ. One spinach sample from the 35-day PBI bore residues of TAA at 0.06 ppm; residues were <LOQ in all other samples of radish commodities and spinach. Quantifiable residues of TA were observed in all matrices from PBIs. Residues of TA generally declined from the 35-day PBI to the 366-day PBI in radish tops (from 0.19 ppm to 0.08 ppm) and spinach (from 0.89 ppm to 0.05 ppm), and increased in radish roots (from 0.10 ppm at the 35-day PBI to 0.13 ppm at the 366-day PBI).

Wheat, radish, and lettuce: BASF has submitted a limited field rotational crop study for metconazole in wheat (small grain), radish (root and tuber vegetable), and lettuce (leafy vegetable). Three limited field rotational crop trials were conducted in the U.S. in Zone 10 (CA) during the 2004-2005 growing season on wheat, radish and lettuce (one trial each).

The trials consisted of one untreated plot and one treated plot with tomato planted as the primary crop. Tomatoes received two broadcast foliar applications of metconazole 1.81 lb ai/gal FlC formulation at 0.24-0.25 lb ai/A at a 14-day RTI, for a total seasonal rate of 0.49 lb ai/A (~1x the maximum proposed seasonal application rate for any rotatable crop). Applications were made in spray volumes of 20-21 gal/A of water without an adjuvant, using ground equipment.

The primary crop was destroyed ~2-weeks after the final application of metconazole, tilled into the soil, and the ground was prepared for planting according to area-typical agricultural practices. Wheat, radish, and lettuce were planted at PBIs of 31, 122, 234, and 396 days after the last application of metconazole to the tomato crop.

At each treatment plot, samples of wheat forage, hay, straw and grain, radish tops and roots, and lettuce were collected at the appropriate crop growth stage.

Samples were analyzed for residues of *cis*- and *trans*-metconazole, metabolites M11, M21, and M30, and the triazole metabolites (1,2,4-T, TA, and TAA) using an LC/MS/MS method (BASF Method D0508); samples of wheat hay and straw were not analyzed for the triazole metabolites. Residues of M11, M21, and M30 were converted to parent equivalents. The validated LOQ was 0.01 ppm for the parent metconazole (sum of *cis* and *trans* isomers at 0.005 ppm each), M11, M21, and M30 in wheat samples. The validated LOQ was 0.05 ppm for 1,2,4-T, TA, and TAA. The reported LOD was 20% of the LOQ. The method was adequate for data collection based on generally acceptable concurrent method recoveries.

Wheat samples were stored frozen (~-10 °C) from harvest to extraction for 252-629 days (8.3-20.7 months) for forage, 227-577 days (7.5-19.0 months) for hay, 182-559 days (6.0-18.4 months) for grain, and 174-551 days (5.7-18.1 months) for straw. Radish tops and roots were stored for 267-631 days (8.8-20.7 months), and lettuce was stored for 238-585 days (7.8-19.2 months). Additional storage stability data are required for *cis*- and *trans*-metconazole reflecting storage for up to 18 months for wheat grain and straw, 19 months for lettuce and wheat hay, and 21 months for radish roots and tops and wheat forage.

At the 31-day PBI, quantifiable residues of *cis*-metconazole were found in one sample each of wheat forage and straw (0.005 ppm in each) and two samples of radish tops (0.010-0.011 ppm); residues of *trans*-metconazole in these samples were <0.005 ppm for maximum total metconazole residues of 0.010 ppm in wheat forage and straw and 0.016 ppm in radish tops at the 31-day PBI. In the same radish top samples, quantifiable residues of metabolite M30 were found at 0.014-0.015 ppm. Residues of metconazole (*cis* and *trans* isomers), M11, M21, and M30 in remaining samples of wheat forage, hay, grain, and straw, radish tops and roots, and lettuce from the 31-, 122-, 234-, and 396-day PBIs were below the LOQ.

Residues of 1,2,4-T were below the LOQ in all samples of wheat forage and grain, radish tops and root, and lettuce from all PBIs; residues of TA were below the LOQ in all samples of lettuce from all PBIs; and residues of TAA were below the LOQ in all samples of radish tops and roots and lettuce. Quantifiable residues of TA and TAA were found in wheat forage and grain from all PBIs, and quantifiable residues of TA were found in radish tops and root from all PBIs. TA residues in wheat forage and grain generally declined with increasing PBI, from a maximum of 0.25 ppm in wheat forage at the 122-day PBI to 0.09 ppm at the 396-day PBI and from a maximum of 1.21 ppm in wheat grain at the 31-day PBI to 0.09 ppm at the 396-day PBI. TA residues in radish tops increased slightly in radish tops from 0.13 ppm at the 31-day PBI to 0.19 ppm at the 396-day PBI, and decreased in radish root from 0.23 ppm at the 31-day PBI to 0.15 ppm at the 396-day PBI. Residues of TAA in wheat forage decreased from a maximum of 0.34 ppm at the 31-day PBI to 0.16 ppm at the 396-day PBI, and residues in wheat grain generally decreased from a maximum of 0.77 ppm at the 31-day PBI to 0.45 ppm at the 396-day PBI.

Wheat: BASF has submitted a limited field rotational crop study for metconazole on wheat (a small grain). One rotational crop trial was conducted on wheat during the 2004-2005 growing season in the U.S. in Zone 5 (OH).

The trial consisted of one untreated plot and three treated plots, with wheat planted as the primary crop. The primary wheat crop received two broadcast foliar applications of the 1.81 lb ai/gal FlC formulation of metconazole at 0.25-0.26 lb ai/A/application, at a 14- to 15-day RTI, for a total seasonal rate of 0.50-0.52 lb ai/A (~1x the maximum proposed seasonal rate for any rotated crop). Applications were made using ground equipment in spray volumes of ~15-19 gal/A of water without an adjuvant.

The primary crop was destroyed and tilled into the soil, and the ground was prepared for planting according to area-typical agricultural practices. Rotational wheat was planted at the PBIs of 32, 90, 150, and 365 days after the last application of metconazole to the primary wheat crop.

Samples of wheat forage, hay, straw and grain were collected at the appropriate crop growth stage, 36-203 days after planting for forage, 55-247 days after planting for hay, and 84-266 days after planting for grain and straw.

Samples were analyzed for residues of metconazole (*cis* and *trans* isomers), metabolites M11, M21, and M30, and the triazole metabolites (1,2,4-T, TA, and TAA) using an LC/MS/MS method (BASF Method D0508). Wheat hay and straw were not analyzed for the triazole metabolites. Residues of metabolites M11, M21, and M30 were converted to parent equivalents. The validated LOQ was 0.01 ppm for the parent metconazole (sum of *cis* and *trans* isomers at 0.005 ppm each), M11, M21, and M30 in wheat matrices. The validated LOQ was 0.05 ppm for 1,2,4-T, TA, and TAA. The method was adequate for data collection based on generally acceptable concurrent method recoveries.

Samples were stored frozen (~-10 °C) from harvest to extraction for 336-382 days (11.0-12.6 months) for forage samples, 316-348 days (10.4-11.4 months) for hay samples, 286-328 days (9.4-10.8 months) for grain samples, and 287-329 days (9.4-10.8 months) for straw samples. All samples were analyzed within 0-6 days of extraction. Adequate storage stability data are available to support the storage conditions and duration of wheat commodities analyzed for *cis*- and *trans*-metconazole and of wheat grain analyzed for TA.

Residues of metconazole (*cis* and *trans* isomers), M11, M21, and M30 were below the LOQ (<0.01 ppm) in samples of wheat forage, hay, straw, and grain from the 32-, 90-, 150-, and 365-day PBIs.

Residues of 1,2,4-T were below the LOQ s (<0.05 ppm) in samples of wheat forage and grain from all PBIs. Quantifiable residues of TA and TAA were found in wheat forage and grain from all PBIs, and residues of both analytes generally declined from the 32-day PBI to the 365-day PBI (i.e., from 0.52 to 0.05 ppm for TA and from 0.19 to <0.05 ppm for TAA in wheat forage; and from 0.69 to 0.33 ppm for TA and from 1.00 to 0.22 ppm for TAA in wheat grain).

Conclusions. Pending submission of additional storage stability data, the submitted field rotational crop data are adequate to fulfill data requirements. The studies reflect application of metconazole according to the maximum use pattern proposed for rotatable crops.

All samples were analyzed for metconazole (determined as the *cis* and *trans* isomers), as well as three metconazole metabolites, M11, M21, and M30, and the triazole metabolites 1,2,4-T, TA, and TAA using an acceptable method.

Additional storage stability data are required for *cis*- and *trans*-metconazole reflecting storage for up to 18 months for wheat grain and straw, 19 months for lettuce and wheat hay, and 21 months for radish roots and tops and wheat forage.

The petitioners have not proposed any rotational crop restrictions. The available data will support a 30-day PBI for leafy vegetables and Brassica leafy vegetables; for all remaining crops other than those listed on the labels, a 120-day PBI must be established. If the petitioner wishes to support reduced plantback intervals for any crops, extensive field rotational crop field trials will be required, and rotational crop tolerances may be needed.

860.1550 Proposed Tolerances

Tolerances for metconazole are currently established under 40 CFR §180.617 and are expressed in terms of the fungicide metconazole. There are currently no Codex, Canadian, or Mexican MRLs established for metconazole.

Adequate data are available to support tolerances with conditional registration for all proposed uses. HED has determined that adequate field trial data are available for barley, oat, rye, wheat, soybean, sugar beet, peanut, stone fruit, pistachio, and tree nuts. HED has determined that no additional data for triazoles will be requested for these petitions.

The tolerance spreadsheet in the Agency's *Guidance for Setting Pesticide Tolerances Based on Field Trial Data* was utilized in determining appropriate tolerance levels for barley hay, straw, and grain; oat hay, straw, and grain; rye straw and grain; soybean forage and hay; sugar beet root; and wheat hay, straw, and grain. The tolerance spreadsheet could not be used to determine tolerance levels for soybean seed, peanut, plum, and pecan and almond nutmeats because >60% of the field trial results for these commodities were below the LOQ.

The available field trial data will support the proposed tolerances for barley hay and straw; rye grain and straw; soybean forage and hay; oat hay and straw; and wheat hay, straw, and grain; and stone fruit. An increased tolerance is needed for oat grain at 1.0 ppm. The available field trial data or analytical (LOQ) data for barley grain, peanut, pistachio, and tree nuts indicate that the proposed tolerances of 2.0 ppm for barley grain and 0.02 ppm for peanut, pistachio, and tree nuts are too low; tolerances of 2.5 ppm for barley grain and 0.04 ppm for peanut, pistachio, and tree nuts are recommended. The available field trial data for soybean seed and sugar beet root indicate that the proposed tolerances of 0.1 ppm for each are too high; tolerances of 0.05 ppm for soybean seed and 0.07 ppm for sugar beet root are recommended. The data on almond hulls indicate that the proposed tolerance of 5.0 ppm is too high; a tolerance of 4.0 ppm for almond hulls is recommended. The proposed tolerance for sugar beet tops is not required because this commodity is no longer considered a significant livestock feed item.

Adequate processing data are available for peanut, plum, soybean, and sugar beet; adequate processing data are available for wheat pending submission of additional storage stability data.

The available processing data indicate that metconazole residues are not likely to concentrate in peanut meal; soybean meal and refined oil; sugar beet refined sugar; and wheat flour and germ. Because metconazole residues do not concentrate in soybean meal, the proposed tolerance for soybean meal is not required.

Metconazole residues were found to concentrate in peanut refined oil; prune; soybean hulls; sugar beet dried pulp and molasses; and wheat bran, middlings, and shorts. Separate tolerances for peanut refined oil, sugar beet molasses, and prune are not needed as residues are not likely to concentrate above the recommended tolerances for peanut, sugar beet root, and plum, respectively.

The processing data indicate that the proposed tolerances of 0.2 ppm for soybean hulls, 1.9 ppm for sugar beet dried pulp, and 1.0 ppm for wheat milled byproducts are too high. Tolerances of 0.08 ppm for soybean hulls, 0.70 for sugar beet dried pulp, and 0.20 ppm for wheat milled byproducts are recommended.

The available data for soybean and wheat AGF indicate that metconazole residues concentrate in both. Individual tolerances for soybean and wheat AGF are not required. The available data indicate that the maximum expected metconazole residues are >2.5 ppm for soybean AGF and 6.2 ppm for wheat AGF; thus, a tolerance of 7.0 ppm is recommended for "grain, aspirated grain fractions."

The available cattle feeding study indicates that tolerances are needed for the meat byproducts of cattle, goat, horse, and sheep. No tolerances are needed for milk, fat, or meat of cattle, goat, horse, and sheep, and no tolerances are needed for swine commodities. Tolerances are needed for the meat byproducts of cattle, goat, horse, and sheep at 0.04 ppm. The need for tolerances for poultry commodities will be reassessed when the required poultry feeding study has been submitted.

The proposed tolerances should be revised to reflect the recommended tolerance levels and correct commodity definitions as specified in Table 15. Individual tolerances are not required for members of the stone fruit and tree nut crop groups.

Table15. Tolerance Summary for Metconazole

Commodity	Proposed Tolerance (ppm)	Recommended Tolerance (ppm)	Comments; *Correct Commodity Definition*
Tolerances proposed by BASF			
Barley grain	2.0	2.5	*Barley, grain*
Barley hay	7.0	7.0	*Barley, hay*
Barley straw	7.0	7.0	*Barley, straw*
Beet, Sugar, root	0.1	0.07	*Beet, sugar, roots*
Beet, Sugar, tops	2.0	Not required	This commodity is no longer considered a significant livestock feed item.
Beet, Sugar, pulp, dry	1.9	0.70	*Beet, sugar, dried pulp*
Beet, Sugar, molasses	0.2	0.08	*Beet, sugar, molasses*

Table15. Tolerance Summary for Metconazole			
Commodity	Proposed Tolerance (ppm)	Recommended Tolerance (ppm)	Comments; *Correct Commodity Definition*
Beet, Sugar, raw	0.25	Not required	This commodity is not considered a significant food/feed item.
Oat, grain	0.1	1.0	
Oat, straw	6.0	6.0	
Oat, hay	17.0	17	
Rye, grain	0.25	0.25	
Rye, straw	14.0	14	
Soybean, forage	3.0	3.0	
Soybean, hay	6.0	6.0	
Soybean, seed	0.1	0.05	
Soybean, aspirated grain fraction	1.0	Not required	Residues in soybean AGF will be covered under the grain, aspirated grain fractions tolerance.
Soybean, hulls	0.2	0.08	
Soybean, meal	0.1	Not required	The processing data indicate that residues do not concentrate in soybean meal.
Wheat, grain	0.15	0.15	
Wheat, hay	16.0	16	
Wheat, straw	18.0	18	
Wheat, aspirated grain fraction	10.0	Not required	Residues in wheat AGF will be covered under the grain, aspirated grain fractions tolerance.
Wheat, milled byproducts (BP)	1.0	0.20	*Wheat, milled byproducts*
Grain, aspirated grain fractions	None proposed	7.0	
Cattle, meat byproducts	None proposed	0.04	
Goat, meat byproducts	None proposed	0.04	
Horse, meat byproducts	None proposed	0.04	
Sheep, meat byproducts	None proposed	0.04	

Table15. Tolerance Summary for Metconazole			
Commodity	Proposed Tolerance (ppm)	Recommended Tolerance (ppm)	Comments; *Correct Commodity Definition*
Tolerances proposed by Valent			
Fruit, Stone – Crop Group 12			
Apricot	0.20	0.20	*Fruit, stone, group 12*
Cherry, sweet	0.20		
Cherry, tart	0.20		
Nectarine	0.20		
Peach	0.20		
Plum	0.20		
Plum, Chickasaw	0.20		
Plum, Damson	0.20		
Plum, Japanese	0.20		
Plumcot	0.20		
Prune (fresh)	0.20		
Nuts, tree –Crop Group 14			
Almond	0.02	0.04	*Nut, tree, group 14*
Beech nut	0.02		
Brazil nut	0.02		
Butternut	0.02		
Cashew	0.02		
Chestnut	0.02		
Chinquapin	0.02		
Filbert	0.02		
Hickory nut	0.02		
Macadamia nut (nut bush)	0.02		
Pecan	0.02		
Walnut, black and English (Persian)	0.02		
Pistachio	0.02	0.04	
Almond hulls	5.00	4.0	*Almond, hulls*
Peanut	0.02	0.04	
Peanut, refined oil	None proposed	0.05	

References

DP#: 324541
Subject: Metconazole. Request for a Tolerance on Imported Bananas. Summary of Analytical Chemistry and Residue Data. Petition Number 9E05052.
From: N. Dodd
To: M. Waller
Date: 12/14/05
MRIDs: 44721506, 44721507, 44721508, 44721509, 44721510, and 44721511

DP#:	322215
Subject:	1,2,4-Triazole, Triazole Alanine, Triazole Acetic Acid: Human Health Aggregate Risk Assessment in Support of Reregistration and Registration Actions for Triazole-derivative Fungicide Compounds. Risk Assessment Type: Single Chemical Aggregate; PC Codes: 600074 – 1,2,4-Triazole; 600011 – Triazole Alanine; 600082 – Triazole Acetic Acid
From:	Michael Doherty, Kathleen Raffaele, Kit Farwell, Steve Dapson, Kelly Schumacher, Jack Arthur, David Hrdy, and Iwona Maher
To:	Tamue Gibson/Cynthia Giles-Parker, Michael Goodis, and Susan Lewis
Dated:	2/7/06
MRIDs:	None

Attachments:
International Residue Limit Status sheet
Appendix I - Chemical Names and Structures of Metconazole and Metabolites
Appendix II - Tolerance Assessment Calculations

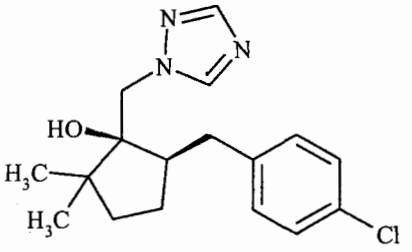
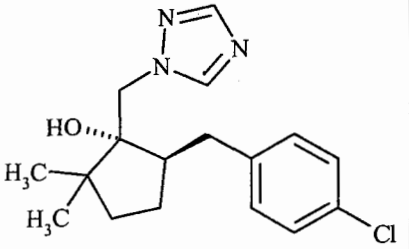
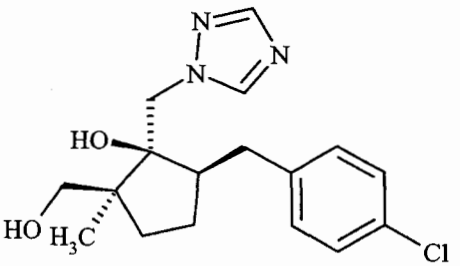
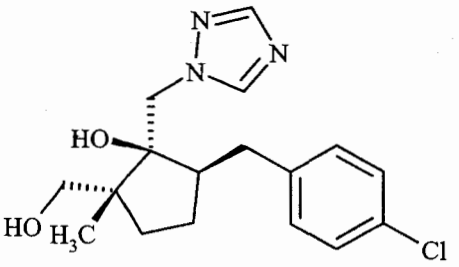
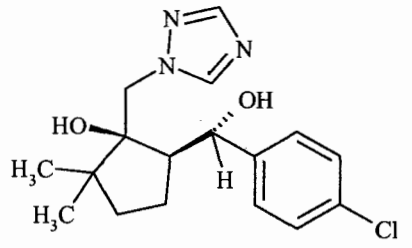
Template Version September 2005

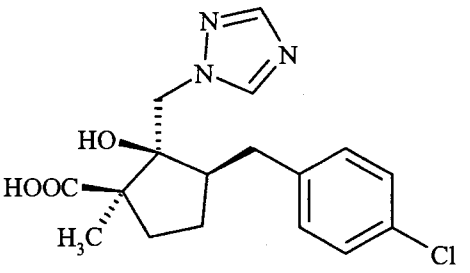
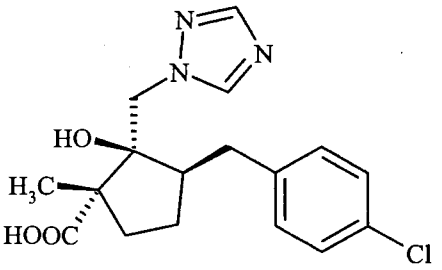
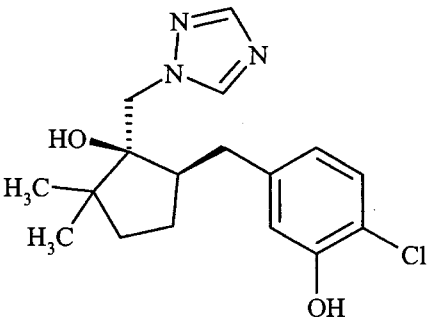
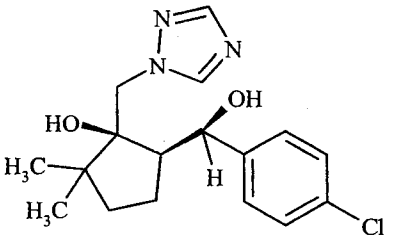
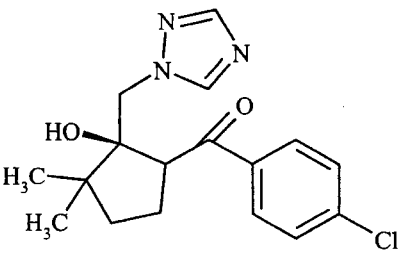
INTERNATIONAL RESIDUE LIMIT STATUS

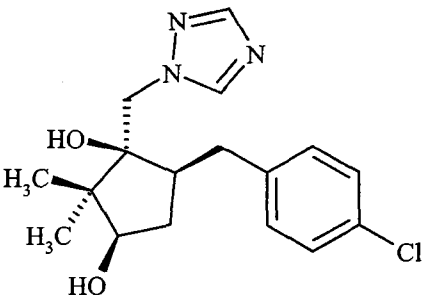
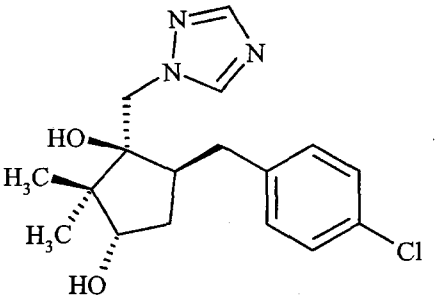
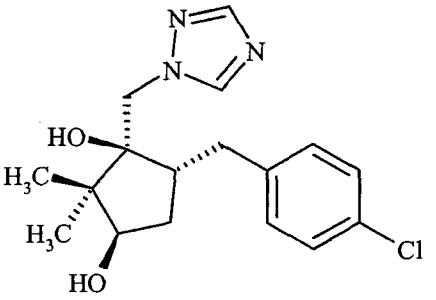
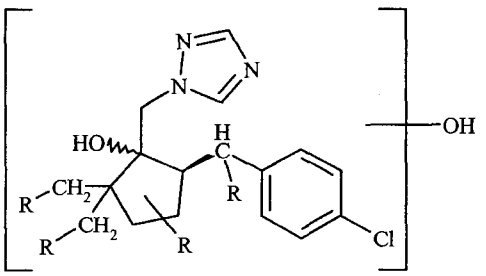
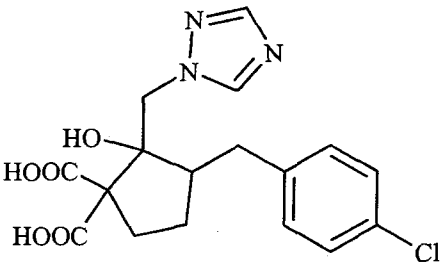
Chemical Name: 5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	Common Name: Metconazole	X Proposed tolerance ☐ Reevaluated tolerance ☐ Other	Date: 5/17/07
Codex Status (Maximum Residue Limits)		U. S. Tolerances	
√ No Codex proposal step 6 or above ☐No Codex proposal step 6 or above for the crops requested		Petition Number: PP#6F7094 and PP#6F7095 DP #s: 348168 and 348206 Other Identifier:	
Residue definition (step 8/CXL): N/A		Reviewer/Branch: N. Dodd/RAB3	
		Residue definition: Metconazole *per se*	

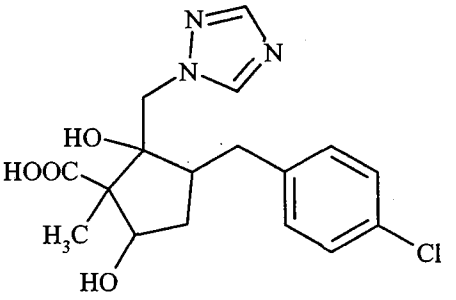
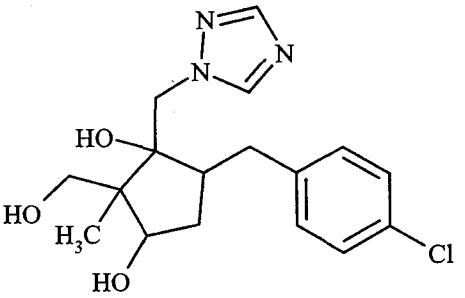
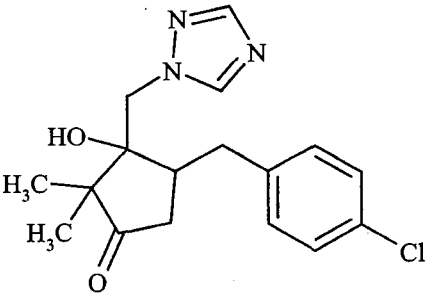
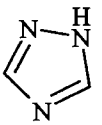
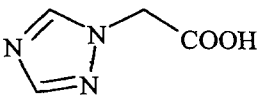
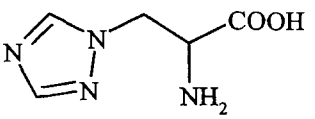
Crop (s)	MRL (mg/kg)	Crop(s)	Tolerance (ppm)
		Fruit, Stone – Crop Group 12	0.20
		Nuts, tree –Crop Group 14	0.02
		Pistachio	0.02
		Almond hulls	5.00
		Peanut	0.02
		Barley grain	2.0
		Barley hay	7.0
		Barley straw	7.0
		Beet, Sugar, root	0.1
		Beet, Sugar, tops	2.0
		Beet, Sugar, pulp, dry	1.9
		Beet, Sugar, molasses	0.2
		Beet, Sugar, raw	0.25
		Oat, grain	0.1
		Oat, straw	6.0
		Oat, hay	17.0
		Rye, grain	0.25
		Rye, straw	14.0
		Soybean, forage	3.0
		Soybean, hay	6.0
		Soybean, seed	0.1
		Soybean, aspirated grain fraction	1.0
		Soybean, hulls	0.2
		Soybean, meal	0.1
		Wheat, grain	0.15
		Wheat, hay	16.0
		Wheat, straw	18.0

		Wheat, aspirated grain fraction	10.0
		Wheat, milled byproducts (BP)	1.0
Limits for Canada		Limits for Mexico	
√ No Limits ☐No Limits for the crops requested		√ No Limits ☐No Limits for the crops requested	
Residue definition: N/A		Residue definition: N/A	
Crop(s)	MRL (mg/kg)	Crop(s)	MRL (mg/kg)
Notes/Special Instructions: S. Funk, 05/21/2007			

APPENDIX I. Chemical Names and Structures of Metconazole and Metabolites.		
Common name; Company code(s)	Chemical name	Chemical structure
Metconazole; M0; KNF-S-474m (Kureha); BAS 555 F (BASF); V-10116 (Valent); AC 900768 and CL 900768 (American Cyanamid); WL148271 (Sittingbourne)	5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	 *cis*-isomer  *trans*-isomer
M1; CL 359451; 2-hydroxymethyl-*cis*-metconazole	5-[(4-chlorophenyl)methyl]-2-methoxyl-2-methyl-1(1*H*-1,2,4-triazol-1-ylmethyl)-1-cyclopentanol or 3-(p-chlorobenzyl)-2-hydroxy-3-methyl-2-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanemethanol	
M2; CL 359452	5-[(4-chlorophenyl)methyl]-2-methoxyl-2-methyl-1(1*H*-1,2,4-triazol-1-yl methyl)-1-cyclopentanol or 3-(p-chlorobenzyl)-2-hydroxy-3-methyl-2-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanemethanol	
M11; CL 382390; CL 197129; KNF-474-M11	5-[(4-chlorophenyl)methoxyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)-1-cyclopentanol or α-(p-chlorophenyl)-2-hydroxy-3,3-dimethyl-2-(1*H*-1,2,4-triazol-1-ylmethyl)-cyclopentanemethanol	

APPENDIX I. Chemical Names and Structures of Metconazole and Metabolites.		
Common name; Company code(s)	Chemical name	Chemical structure
M12; MC 1417; KNF-474-M12; *cis*-metconazole-2-carboxylic acid	5-[(4-chlorophenyl)methyl]-2-carboxyl-2-methyl-1-(1*H*-1,2,4-triazol-1-yl methyl)-1-cyclopentanol	
M13; MC 1417; KNF-474-M13	5-[(4-chlorophenyl)methyl]-2-methyl-2-carboxyl-1-(1*H*-1,2,4-triazol-1-yl methyl)-1-cyclopentanol	
M15	5-[(3-hydroxy-4-chlorophenyl)methyl]-2,2-dimethyl-1-(1-*H*-1,2,4-triazol-1-yl methyl)-1-cyclopentanol	
M21; CL 382391; CL 197130; KNF-474-M21	5-[(4-chlorophenyl)methoxy]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)-1-cyclopentanol or α-(p-chlorophenyl)-2-hydroxy-3,3-dimethyl-2-(1*H*-1,2,4-triazol-1-ylmethyl)-cyclopentanemethanol	
M30; CL 382389; KNF-474-M30	5-[(4-chlorophenyl)keto]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)-1-cyclopentanol or 5-(p-chlorobenzoyl)-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	

APPENDIX I. Chemical Names and Structures of Metconazole and Metabolites.		
Common name; Company code(s)	Chemical name	Chemical structure
M31; [(1S*,3S*,5S*)-3-hydroxy-*cis*-metconazole (and M31 glucuronide)	Not provided	
M32; [(1S*,3R*,5S*)-3-hydroxy-*cis*-metconazole (and M32 glucuronide and M32 sulfate)	Not provided	
trans-M31 (and *trans*-M31 glucuronide	Not provided	
Monohydroxylated metconazole (and glucose conjugates and mono-hydroxy-metconazole sulfate)	Not provided	
Metconazole dicarboxylic acid; DCM	Not provided	

APPENDIX I. Chemical Names and Structures of Metconazole and Metabolites.		
Common name; Company code(s)	Chemical name	Chemical structure
Monohydroxymetconazole carboxylic acid; CHM	Not provided	
Dihydroxy-metconazole; DHM (and DHM sulfate)	Not provided	
Ketone metabolite; oxo-metconazole; OCM (putative structure)	Not provided	
Triazole (1,2,4-T); BF 480-16	1-*H*-1,2,4-triazole	
Triazolylacetic acid (TAA); BF 480-17	1*H*-1,2,4-triazol-1-yl acetic acid	
Triazolylalanine (TA); F3225	2-amino-3-(1*H*-1,2,4-triazol-1-yl)propanoic acid	

Appendix II. Tolerance Assessment Calculations for Small Grains, Soybean, Sugar Beet, Stone Fruit, and Tree Nuts.

Barley Hay, Straw, and Grain

The dataset used to establish tolerances for metconazole on barley hay, straw, and grain consisted of field trial data representing application rates of 0.20 lb ai/A (2 applications at 0.10 lb ai/A/application) with a 7-day PHI for hay and a 21-day PHI for grain and straw. As specified by the *Guidance for Setting Pesticide Tolerances Based on Field Trial Data* SOP, the field trial application rates are within 25% of the maximum label application rate; however, we note that the PHIs are less than the minimum label PHI of 30 days. The residue values used to calculate the tolerance are provided in Table II-1.

All 24 field trial sample results for each commodity were above the LOQ. Since there were no values reported below the LOQ, maximum likelihood estimation (MLE) procedures were not needed to impute censored values.

The dataset for metconazole on barley hay, straw, and grain was entered into the tolerance spreadsheet. For hay and straw, the results from the approximate Shapiro-Francia test statistic (Figures II-2 for hay and II-4 for straw) indicated that the assumption of lognormality should be rejected. Visual inspection of the lognormal probability plots (Figures II-1 for hay and II-3 for straw) provided in the spreadsheet confirmed that the dataset for each commodity is not lognormal. For grain, visual inspection of the lognormal probability plot (Figure II-5) provided in the spreadsheet indicates that the dataset is reasonably lognormal. The result from the approximate Shapiro-Francia test statistic (Figure II-6) confirmed that the assumption of lognormality should not be rejected.

Since the field trial data for metconazole on barley hay and straw are not lognormal, the upper bound on the 89th percentile should be selected as the tolerance value (distribution-free method). Using the rounding procedure as outlined in the *Guidance for Setting Pesticide Tolerances Based on Field Trial Data* SOP, the upper bound on the 89th percentile rounds to the value 7.0 ppm for each. Therefore, 7.0 ppm is the recommended tolerance level for metconazole on barley hay and straw.

Since the field trial data for metconazole on barley grain represent a large dataset (i.e., more than 15 samples) and are reasonably lognormal, the minimum of the 95% upper confidence limit (UCL) on the 95th percentile and the point estimate of the 99th percentile should be selected as the tolerance value. Using the rounding procedure as outlined in the *Guidance for Setting Pesticide Tolerances Based on Field Trial Data* SOP, the 95% UCL on the 95th percentile rounds to the value 2.5 ppm and the point estimate of the 99th percentile also rounds to the value 2.5 ppm (Figure II-6). Because these values are the same, 2.5 ppm is the recommended tolerance level for metconazole on barley grain.

Table II-1. Residue data used to calculate tolerance for metconazole on barley commodities.			
Regulator:	EPA	EPA	EPA
Chemical:	Metconazole	Metconazole	Metconazole
Crop:	Barley hay	Barley grain	Barley straw
PHI:	7 Days	20-21 Days	20-21 Days
App. Rate:	0.20 lb ai/A (2 at 0.10 lb ai/A/application)	0.20 lb ai/A (2 at 0.10 lb ai/A/application)	0.20 lb ai/A (2 at 0.10 lb ai/A/application)
Submitter:	BASF Corporation	BASF Corporation	BASF Corporation
MRID Citation:	MRID 46902225	MRID 46902225	MRID 46902225
	Residues of Metconazole (ppm)[1]		
	2.865	0.225	0.971
	3.180	0.203	0.847
	2.704	1.401	3.312
	2.964	0.955	3.020
	0.857	0.207	1.836
	0.726	0.168	2.131
	0.884	0.162	2.086
	1.497	0.173	1.513
	0.789	0.498	3.184
	0.850	0.460	3.624
	2.243	0.582	4.192
	2.100	0.567	4.208
	3.196	1.082	4.648
	3.272	1.598	4.480
	3.032	0.687	3.328
	3.284	0.634	2.920
	3.836	0.112	0.638
	4.348	0.124	0.697
	3.024	0.311	3.116
	3.248	0.225	3.504
	3.332	0.582	1.945
	3.804	0.563	2.237
	4.428	0.480	4.288
	4.316	0.472	4.536

[1] Total of both *cis* and *trans* isomers.

Figure II-1. Lognormal probability plot of metconazole field trial data for barley hay.

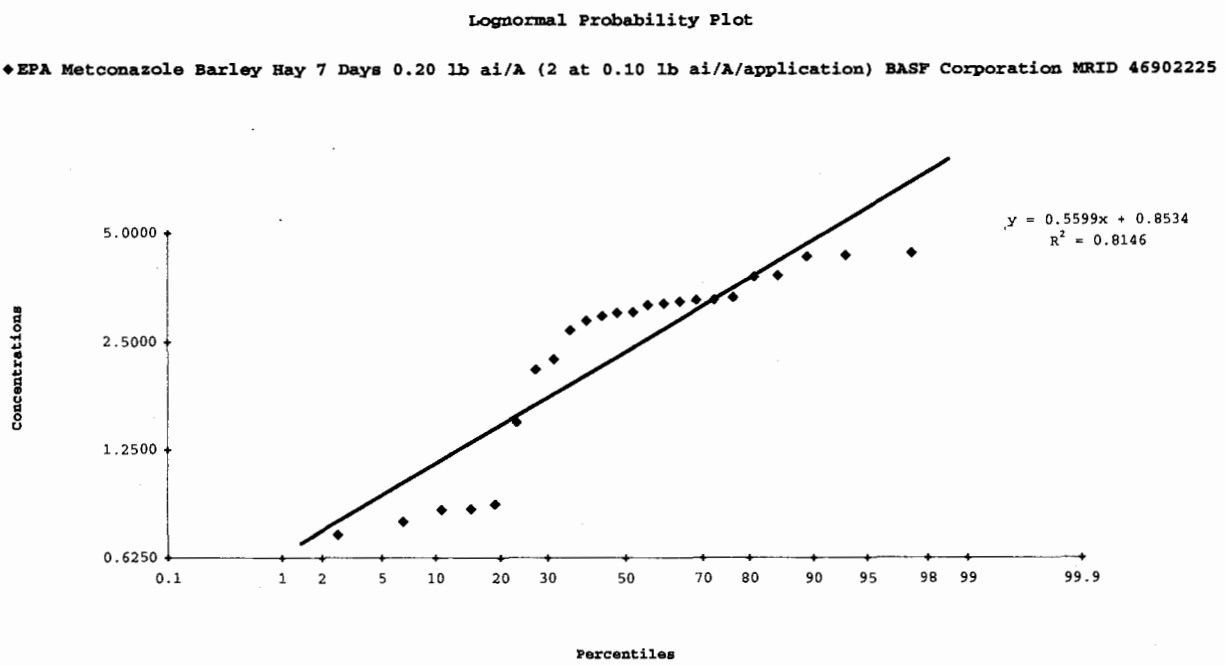


Figure II- 2. Tolerance spreadsheet summary of metconazole field trial data for barley hay.

Regulator:	EPA
Chemical:	Metconazole
Crop:	Barley Hay
PHI:	7 Days
App. Rate:	0.20 lb ai/A (2 at 0.10 lb ai/A/application)
Submitter:	BASF Corporation
MRID Citation:	MRID 46902225
n:	24
min:	0.73
max:	4.43
median;	3.03
average:	2.70

	95th Percentile	99th Percentile	99.9th Percentile
EU Method I Normal	5.0 (6.0)	6.0 (7.0)	7.0 (--)
EU Method I Log Normal	7.0 **(10)**	**10** (16)	16 (--)
EU Method II Distribution-Free	7.0		
California Method μ + 3σ	7.0		
UPLMedian95th	**18**		
Approximate Shapiro-Francia Normality Test	0.8146 p-value <= 0.01: Reject lognormality assumption		

Would you like the above values rounded? (Y or N)==> Y

Figure II- 3. Lognormal probability plot of metconazole field trial data for barley straw.

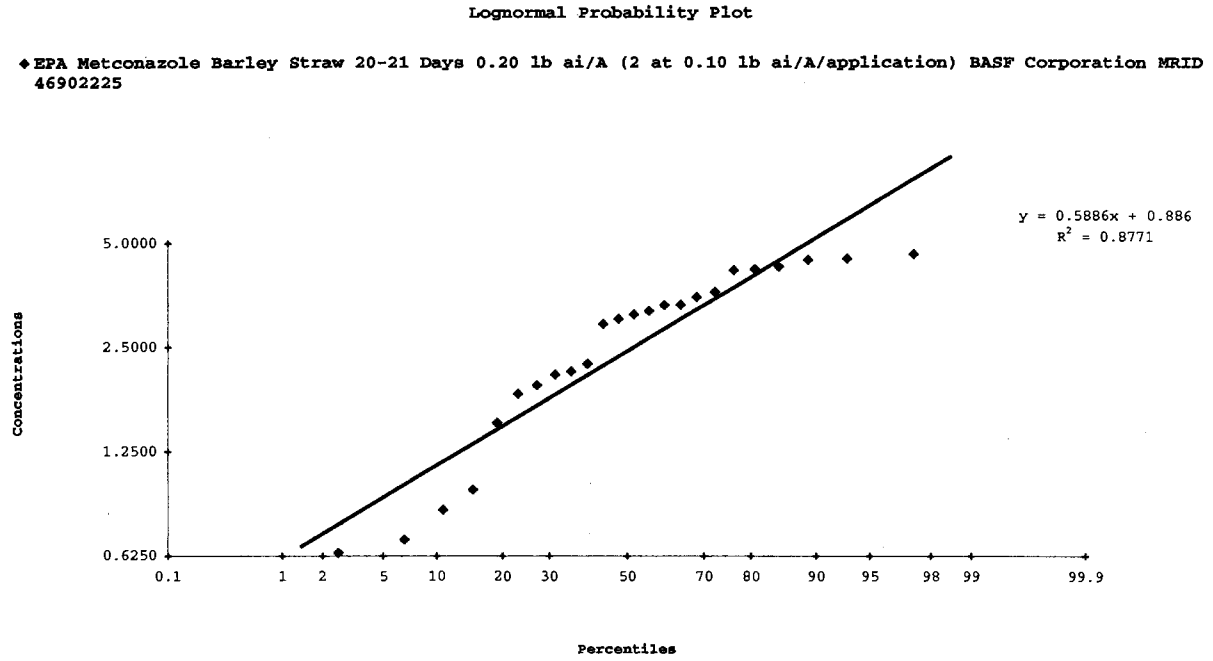


Figure II- 4. Tolerance spreadsheet summary of metconazole field trial data for barley straw.

	Regulator: EPA		
	Chemical: Metconazole		
	Crop: Barley Straw		
	PHI: 20-21 Days		
	App. Rate: 0.20 lb ai/A (2 at 0.10 lb ai/A/application)		
	Submitter: BASF Corporation		
	MRID Citation: MRID 46902225		
	n: 24		
	min: 0.64		
	max: 4.65		
	median: 3.07		
	average: 2.80		
	95th Percentile	**99th Percentile**	**99.9th Percentile**
EU Method I Normal	5.0 (6.0)	6.0 (7.0)	7.0 (--)
EU Method I Log Normal	7.0 **(10)**	**10** (17)	16 (--)
EU Method II Distribution-Free		9.0	
California Method μ + 3σ		7.0	
UPLMedian95th		**19**	
Approximate Shapiro-Francia Normality Test	0.8771 0.05 >= p-value > 0.01 : Reject lognormality assumption		

Would you like the above values rounded? (Y or N)==> Y

Figure II- 5. Lognormal probability plot of metconazole field trial data for barley grain.

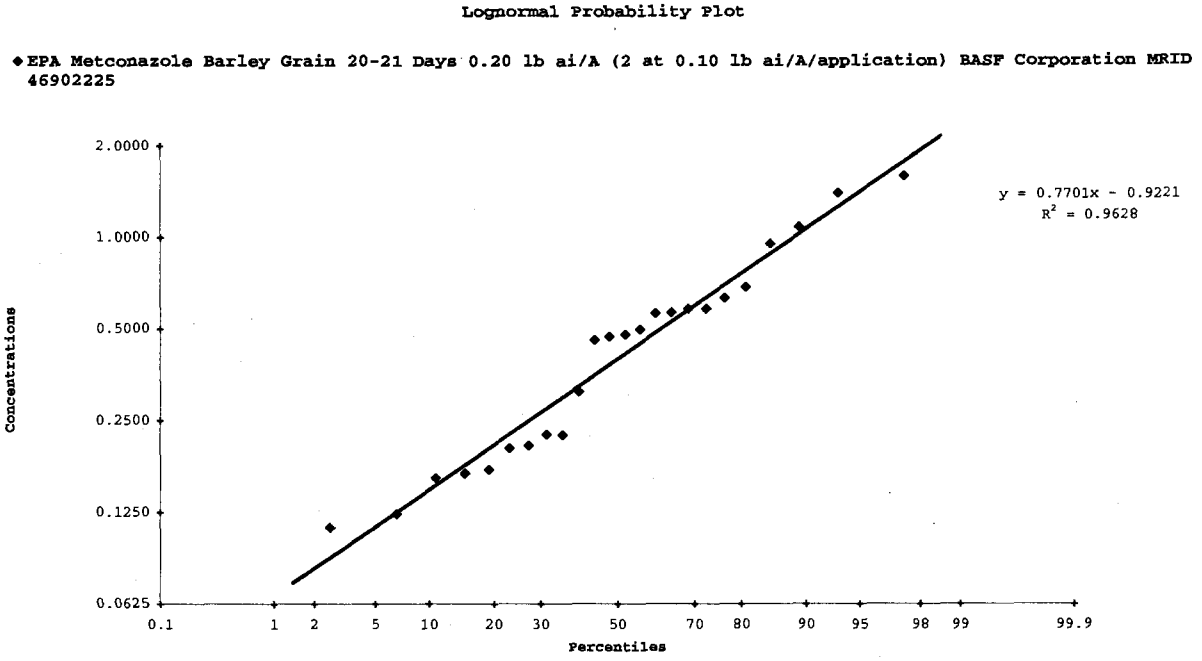


Figure II- 6. Tolerance spreadsheet summary of metconazole field trial data for barley grain.

Regulator:	EPA
Chemical:	Metconazole
Crop:	Barley Grain
PHI:	20-21 Days
App. Rate:	0.20 lb ai/A (2 at 0.10 lb ai/A/application)
Submitter:	BASF Corporation
MRID Citation:	MRID 46902225
n:	24
min:	0.11
max:	1.60
median;	0.48
average:	0.52

	95th Percentile	99th Percentile	99.9th Percentile
EU Method I Normal	1.2 (1.5)	1.5 (1.8)	1.8 (--)
EU Method I Log Normal	1.4 (2.5)	2.5 (4.5)	4.5 (--)
EU Method II Distribution-Free	1.3		
California Method μ + 3σ	**1.8**		
UPLMedian95th	**3.0**		
Approximate Shapiro-Francia Normality Test	0.9628 p-value > 0.05 : Do not reject lognormality assumption		

Would you like the above values rounded? (Y or N)==> Y

Oat Hay, Straw, and Grain

The dataset used to establish tolerances for metconazole on oat hay, straw, and grain consisted of field trial data representing application rates of 0.20 lb ai/A (2 applications at 0.10 lb ai/A/application) with a 7-day PHI for hay, and a 20- to 21-day PHI for straw and grain. As specified by the *Guidance for Setting Pesticide Tolerances Based on Field Trial Data* SOP, the field trial application rates are within 25% of the maximum label application rate; however, we note that the PHIs are less than the minimum label PHI of 30 days. The residue values used to calculate the tolerance are provided in Table II-2.

All 24 field trial sample results for each commodity were above the LOQ. Since there were no values reported below the LOQ, MLE procedures were not needed to impute censored values.

The dataset for metconazole on oat hay, straw, and grain was entered into the tolerance spreadsheet. Visual inspection of the lognormal probability plots (Figures II-7 for hay, II-9 for straw, and II-11 for grain) provided in the spreadsheet indicates that the dataset for each commodity is reasonably lognormal. The results from the approximate Shapiro-Francia test statistic (Figures II-8 for hay, II-10 for straw, and II-12 for grain) confirmed that the assumption of lognormality should not be rejected.

Since the field trial data for metconazole on oat hay, straw, and grain represent a large dataset for each commodity (i.e., more than 15 samples) and are reasonably lognormal, the minimum of the 95% UCL on the 95th percentile and the point estimate of the 99th percentile should be selected as the tolerance value. Using the rounding procedure as outlined in the *Guidance for Setting Pesticide Tolerances Based on Field Trial Data* SOP, the 95% UCL on the 95th percentile rounds to the value 17 ppm for hay, 6.0 ppm for straw, and 1.0 ppm for grain, and the point estimates of the 99th percentile also rounds to the values 17 ppm, 6.0 ppm, and 1.0 ppm (Figures II-8, II-10, and II-12). Because these values are the same, the recommended tolerance levels for metconazole on oat hay, straw, and grain are 17 ppm, 6.0 ppm, and 1.0 ppm.

Table II-2. Residue data used to calculate tolerance for metconazole on oat commodities.

Regulator:	EPA	EPA	EPA
Chemical:	Metconazole	Metconazole	Metconazole
Crop:	Oat Hay	Oat Grain	Oat Straw
PHI:	6-8 Days	20-21 Days	20-21 Days
App. Rate:	0.20 lb ai/A (2 at 0.10 lb ai/A/application)	0.20 lb ai/A (2 at 0.10 lb ai/A/application)	0.20 lb ai/A (2 at 0.10 lb ai/A/application)
Submitter:	BASF Corporation	BASF Corporation	BASF Corporation
MRID Citation:	MRID 46902226	MRID 46902226	MRID 46902226
	Residues of Metconazole (ppm)[1]		
	9.276	0.359	1.526
	9.611	0.345	1.412
	3.794	0.558	2.216
	3.518	0.493	2.223
	4.235	0.574	1.673
	3.365	0.538	1.799

Table II-2. Residue data used to calculate tolerance for metconazole on oat commodities.			
Regulator:	EPA	EPA	EPA
Chemical:	Metconazole	Metconazole	Metconazole
Crop:	Oat Hay	Oat Grain	Oat Straw
PHI:	6-8 Days	20-21 Days	20-21 Days
App. Rate:	0.20 lb ai/A (2 at 0.10 lb ai/A/application)	0.20 lb ai/A (2 at 0.10 lb ai/A/application)	0.20 lb ai/A (2 at 0.10 lb ai/A/application)
Submitter:	BASF Corporation	BASF Corporation	BASF Corporation
MRID Citation:	MRID 46902226	MRID 46902226	MRID 46902226
	Residues of Metconazole (ppm)[1]		
	11.672	0.367	5.361
	10.814	0.430	5.937
	8.071	0.127	1.760
	5.059	0.150	1.102
	2.657	0.183	3.341
	6.969	0.187	2.430
	3.615	0.144	1.222
	4.249	0.141	1.269
	5.964	0.352	0.992
	6.208	0.272	1.006
	5.157	0.430	1.432
	4.622	0.680	1.717
	9.441	0.215	1.430
	9.267	0.167	1.642
	5.341	0.260	2.649
	6.587	0.244	3.290
	2.294	0.276	2.423
	2.911	0.239	2.694

[1] Total of both *cis* and *trans* isomers.

Figure II- 7. Lognormal probability plot of metconazole field trial data for oat hay.

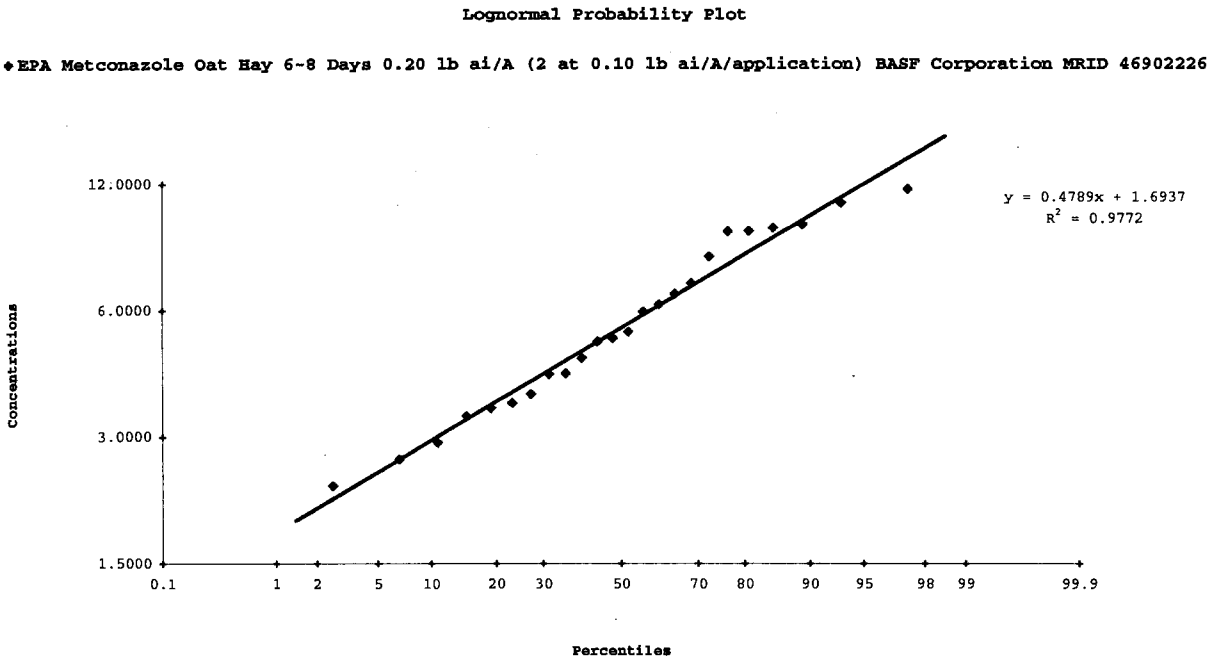


Figure II- 8. Tolerance spreadsheet summary of metconazole field trial data for oat hay.

	Regulator:	EPA	
	Chemical:	Metconazole	
	Crop:	Oat Hay	
	PHI:	6-8 Days	
	App. Rate:	0.20 lb ai/A (2 at 0.10 lb ai/A/application)	
	Submitter:	BASF Corporation	
	MRID Citation:	MRID 46902226	
	n:	24	
	min:	2.29	
	max:	11.67	
	median;	5.25	
	average:	6.03	
	95th Percentile	**99th Percentile**	**99.9th Percentile**
EU Method I Normal	11 (13)	13 (15)	15 (--)
EU Method I Log Normal	12 (17)	17 (25)	25 (--)
EU Method II Distribution-Free		18	
California Method μ + 3σ		**15**	
UPLMedian95th		**35**	
Approximate Shapiro-Francia Normality Test		0.9772 p-value > 0.05 : Do not reject lognormality assumption	

Would you like the above values rounded? (Y or N)==> Y

Figure II- 9. Lognormal probability plot of metconazole field trial data for oat straw.

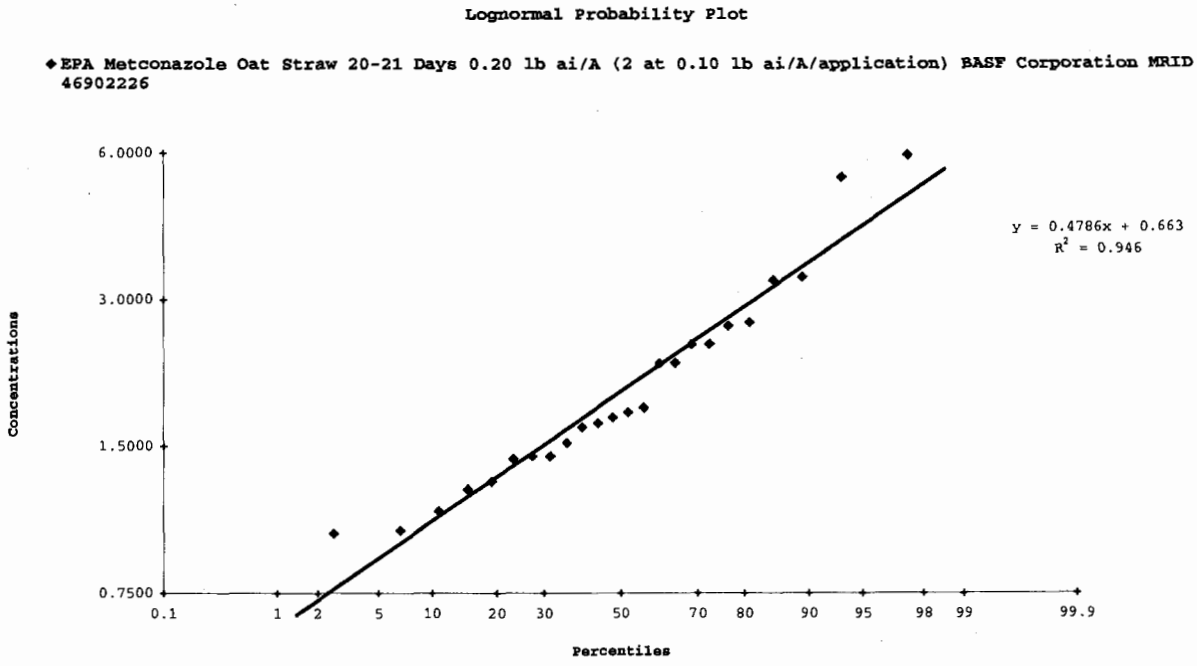


Figure II- 10. Tolerance spreadsheet summary of metconazole field trial data for oat straw.

Regulator:	EPA
Chemical:	Metconazole
Crop:	Oat Straw
PHI:	20-21 Days
App. Rate:	0.20 lb ai/A (2 at 0.10 lb ai/A/application)
Submitter:	BASF Corporation
MRID Citation:	MRID 46902226
n:	24
min:	0.99
max:	5.94
median:	1.74
average:	2.19

	95th Percentile	99th Percentile	99.9th Percentile
EU Method I Normal	4.5 (6.0)	6.0 (7.0)	7.0 (--)
EU Method I Log Normal	4.5 (6.0)	6.0 (9.0)	9.0 (--)
EU Method II Distribution-Free	6.0		
California Method μ + 3σ	**6.0**		
UPLMedian95th	**11**		
Approximate Shapiro-Francia Normality Test	0.9460 p-value > 0.05 : Do not reject lognormality assumption		

Would you like the above values rounded? (Y or N)==> Y

Figure II- 11. Lognormal probability plot of metconazole field trial data for oat grain.

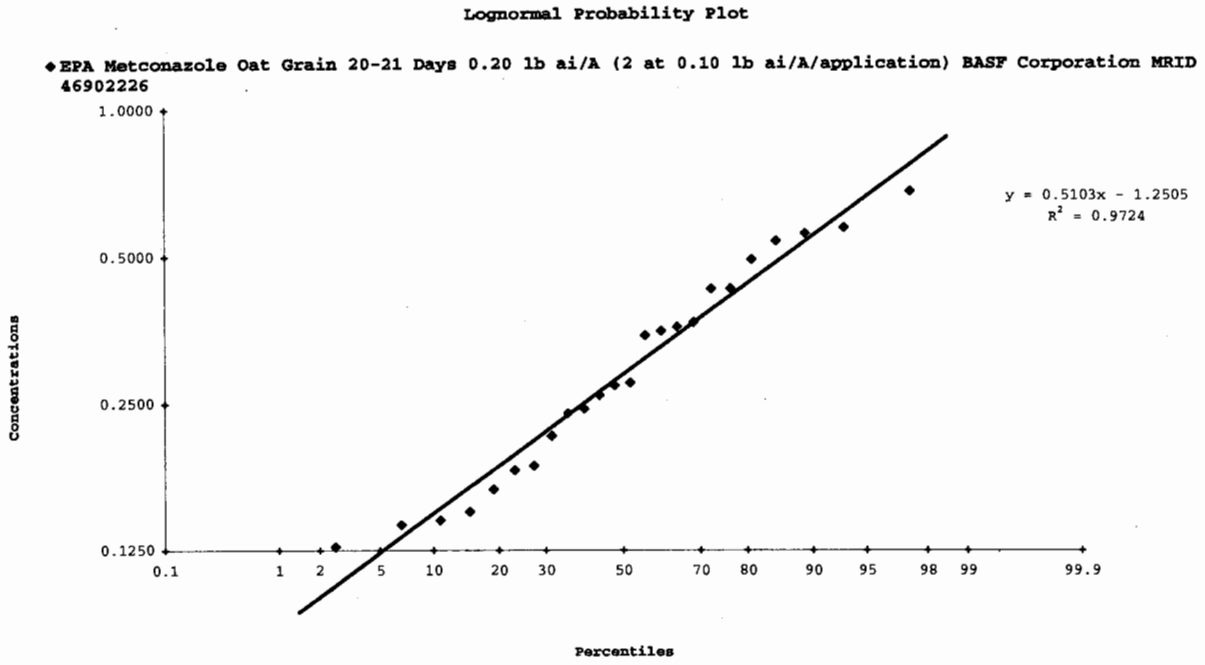


Figure II- 12. Tolerance spreadsheet summary of metconazole field trial data for oat grain.

Regulator:	EPA
Chemical:	Metconazole
Crop:	Oat Grain
PHI:	20-21 Days
App. Rate:	0.20 lb ai/A (2 at 0.10 lb ai/A/application)
Submitter:	BASF Corporation
MRID Citation:	MRID 46902226
n:	24
min:	0.13
max:	0.68
median;	0.27
average:	0.32

	95th Percentile	99th Percentile	99.9th Percentile
EU Method I Normal	0.60 (0.70)	0.70 (0.90)	0.90 (--)
EU Method I Log Normal	0.70 (1.0)	1.0 (1.5)	1.4 (--)
EU Method II Distribution-Free	0.90		
California Method $\mu + 3\sigma$	**0.80**		
UPLMedian95th	**1.7**		
Approximate Shapiro-Francia Normality Test	0.9724 p-value > 0.05 : Do not reject lognormality assumption		

Would you like the above values rounded? (Y or N)==> Y

Rye Straw and Grain

The dataset used to establish a tolerance for metconazole on rye straw and grain consisted of field trial data representing application rates of 0.20 lb ai/A (2 applications at 0.10 lb ai/A/application) with a 20- to 22-day PHI. As specified by the *Guidance for Setting Pesticide Tolerances Based on Field Trial Data* SOP, the field trial application rates are within 25% of the maximum label application rate; however, we note that the PHIs are less than the minimum label PHI of 30 days. The residue values used to calculate the tolerance are provided in Table II-3.

All 10 field trial sample results for each commodity were above the LOQ. Since there were no values reported below the LOQ, MLE procedures were not needed to impute censored values.

The dataset for metconazole on rye straw and grain was entered into the tolerance spreadsheet. Visual inspection of the lognormal probability plots (Figures II-13 for straw and II-15 for grain) provided in the spreadsheet indicates that the dataset is reasonably lognormal for each commodity. The results from the approximate Shapiro-Francia test statistic (Figures II-14 for straw and II-16 for grain) confirmed that the assumption of lognormality should not be rejected.

Since the field trial data for metconazole on rye straw and grain represent a small dataset (i.e., less than 15 samples) and are reasonably lognormal, the upper bound estimate of the 95th percentile based on the median residue value was compared to the minimum of the 95% UCL on the 95th percentile and the point estimate of the 99th percentile, and the minimum value was selected as the tolerance value for each commodity. Using the rounding procedure as outlined in the *Guidance for Setting Pesticide Tolerances Based on Field Trial Data SOP*, the point estimate of the 99th percentile rounds to the value 14 ppm for straw and 0.25 ppm for grain (Figures II-14 and II-16, respectively). Because these values were the minimum values for each commodity, 14 ppm is the recommended tolerance level for metconazole on rye straw, and 0.25 ppm is the recommended tolerance level for metconazole on rye grain.

Table II-3. Residue data used to calculate tolerance for metconazole on rye commodities.

Regulator:	EPA	EPA
Chemical:	Metconazole	Metconazole
Crop:	Rye grain	Rye straw
PHI:	20-22 Days	20-22 Days
App. Rate:	0.20 lb ai/A (2 at 0.10 lb ai/A/application)	0.20 lb ai/A (2 at 0.10 lb ai/A/application)
Submitter:	BASF Corporation	BASF Corporation
MRID Citation:	MRID 46902227	MRID 46902227
	Residues of Metconazole (ppm)[1]	
	0.050	4.446
	0.040	4.348
	0.057	2.181
	0.079	2.437
	0.064	4.716
	0.070	3.449
	0.093	1.931

Table II-3. Residue data used to calculate tolerance for metconazole on rye commodities.		
Regulator:	EPA	EPA
Chemical:	Metconazole	Metconazole
Crop:	Rye grain	Rye straw
PHI:	20-22 Days	20-22 Days
App. Rate:	0.20 lb ai/A (2 at 0.10 lb ai/A/application)	0.20 lb ai/A (2 at 0.10 lb ai/A/application)
Submitter:	BASF Corporation	BASF Corporation
MRID Citation:	MRID 46902227	MRID 46902227
	Residues of Metconazole (ppm)[1]	
	0.092	2.188
	0.157	8.784
	0.144	8.162

[1] Total of both *cis* and *trans* isomers.

Figure II- 13. Lognormal probability plot of metconazole field trial data for rye straw.

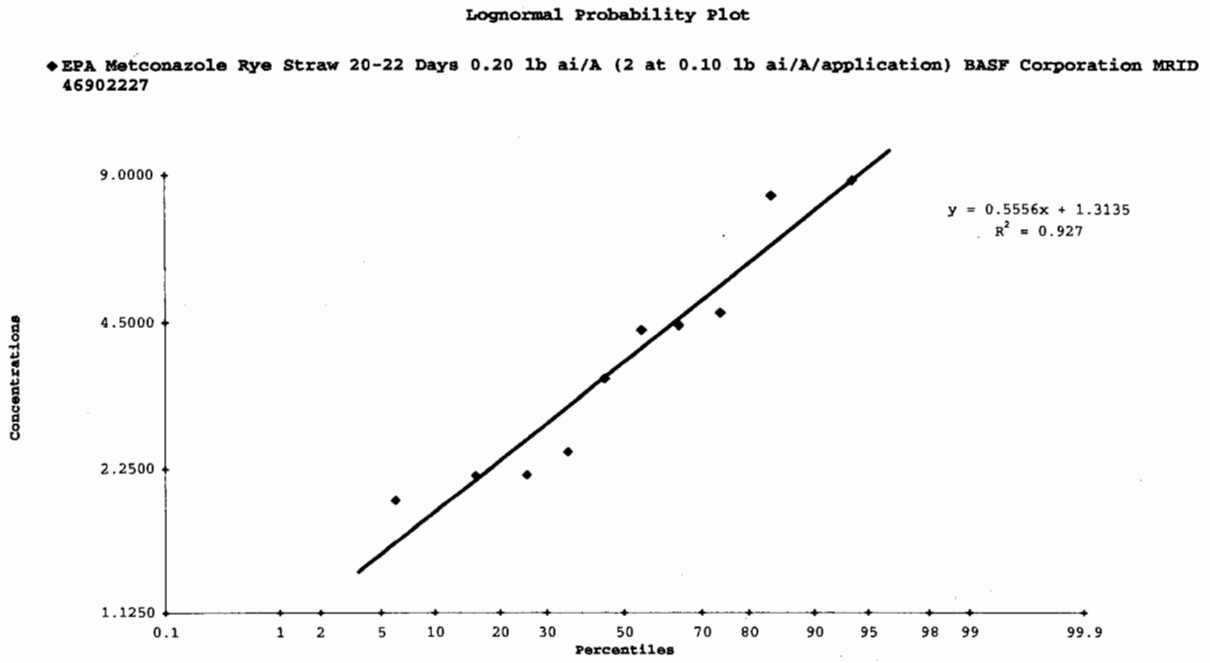


Figure II- 14. Tolerance spreadsheet summary of metconazole field trial data for rye straw.

	Regulator:	EPA	
	Chemical:	Metconazole	
	Crop:	Rye Straw	
	PHI:	20-22 Days	
	App. Rate:	0.20 lb ai/A (2 at 0.10 lb ai/A/application)	
	Submitter:	BASF Corporation	
	MRID Citation:	MRID 46902227	
	n:	10	
	min:	1.93	
	max:	8.78	
	median;	3.90	
	average:	4.26	
	95th Percentile	**99th Percentile**	**99.9th Percentile**
EU Method I Normal	9.0 (12)	10 (15)	12 (--)
EU Method I Log Normal	10 **(19)**	**14** (35)	20 (--)
EU Method II Distribution-Free		12	
California Method $\mu + 3\sigma$		**12**	
UPLMedian95th		**35**	
Approximate Shapiro-Francia Normality Test		0.9270 p-value > 0.05 : Do not reject lognormality assumption	

Would you like the above values rounded? (Y or N)==> Y

Figure II- 15. Lognormal probability plot of metconazole field trial data for rye grain.

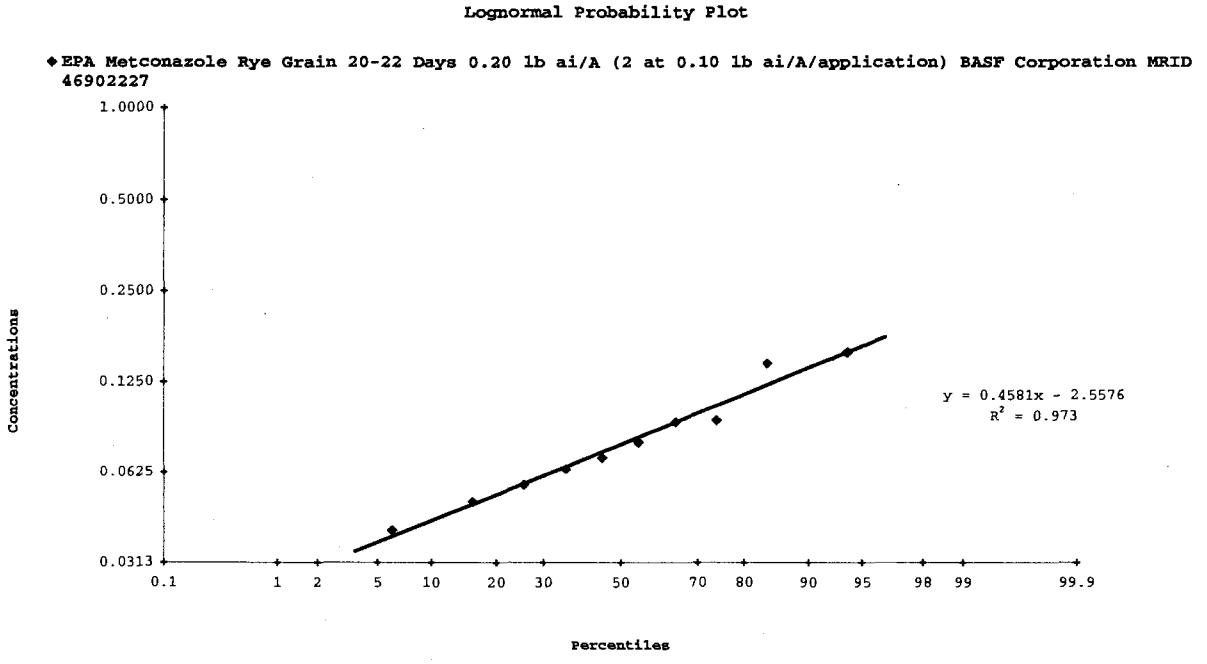


Figure II- 16. Tolerance spreadsheet summary of metconazole field trial data for rye grain.

	Regulator:	EPA	
	Chemical:	Metconazole	
	Crop:	Rye Grain	
	PHI:	20-22 Days	
	App. Rate:	0.20 lb ai/A (2 at 0.10 lb ai/A/application)	
	Submitter:	BASF Corporation	
	MRID Citation:	MRID 46902227	
	n:	10	
	min:	0.04	
	max:	0.16	
	median:	0.07	
	average:	0.08	
	95th Percentile	**99th Percentile**	**99.9th Percentile**
EU Method I Normal	0.15 (0.20)	0.20 (0.25)	0.25 (--)
EU Method I Log Normal	0.20 **(0.30)**	**0.25** (0.45)	0.30 (--)
EU Method II Distribution-Free		0.25	
California Method $\mu + 3\sigma$		**0.25**	
UPLMedian95th		**0.60**	
Approximate Shapiro-Francia Normality Test		0.9730 p-value > 0.05 : Do not reject lognormality assumption	

Would you like the above values rounded? (Y or N)==> Y

Wheat Hay, Straw, and Grain

The dataset used to establish a tolerance for metconazole on wheat hay, straw, and grain consisted of field trial data representing application rates of 0.20 lb ai/A (2 applications at 0.10 lb ai/A/application) with a 6- to 8-day PHI. As specified by the *Guidance for Setting Pesticide Tolerances Based on Field Trial Data* SOP, the field trial application rates are within 25% of the maximum label application rate; however, we note that the PHIs are less than the minimum label PHI of 30 days. The residue values used to calculate the tolerance are provided in Table II-4.

All 30 field trial sample results were above the LOQ for each commodity. Since there were no values reported below the LOQ, MLE procedures were not needed to impute censored values.

The dataset for metconazole on wheat hay, grain, and straw was entered into the tolerance spreadsheet. For hay, the result from the approximate Shapiro-Francia test statistic (Figure II-18) indicated that the assumption of lognormality should be rejected. Visual inspection of the lognormal probability plot (Figure II-17) provided in the spreadsheet confirmed that the dataset is not lognormal. For straw and grain, visual inspection of the lognormal probability plots (Figures II-19 for straw and II-21 for grain) provided in the spreadsheet indicates that the dataset for each commodity is reasonably lognormal. The result from the approximate Shapiro-Francia test statistic (Figures II-20 for straw and II-22 for grain) confirmed that the assumption of lognormality should not be rejected.

Since the field trial data for metconazole on wheat hay are not lognormal, the upper bound on the 89th percentile should be selected as the tolerance value (distribution-free method). Using the rounding procedure as outlined in the *Guidance for Setting Pesticide Tolerances Based on Field*

Trial Data SOP, the upper bound on the 89th percentile rounds to the value 16 ppm. Therefore, 16 ppm is the recommended tolerance level for metconazole on wheat hay.

Since the field trial data for metconazole on wheat straw and grain represent a large dataset for each commodity (i.e., more than 15 samples) and are reasonably lognormal, the minimum of the 95% UCL on the 95th percentile and the point estimate of the 99th percentile should be selected as the tolerance value. Using the rounding procedure as outlined in the *Guidance for Setting Pesticide Tolerances Based on Field Trial Data* SOP, the 95% UCL on the 95th percentile rounds to the value of 18 ppm for straw and 0.15 ppm for grain, and the point estimate of the 99th percentile rounds to the value of 19 ppm for straw and 0.20 ppm for grain (Figures II-20 and II-22, respectively). Because the values 18 ppm and 0.15 ppm were the minimum values for straw and grain, 18 ppm is the recommended tolerance level for metconazole on wheat straw, and 0.15 ppm is the recommended tolerance level for metconazole on wheat grain.

Table II-4. Residue data used to calculate tolerance for metconazole on wheat commodities.			
Regulator:	EPA	EPA	EPA
Chemical:	Metconazole	Metconazole	Metconazole
Crop:	Wheat hay	Wheat grain	Wheat straw
PHI:	6-8 Days	20-22 Days	20-22 Days
App. Rate:	0.20 lb ai/A (2 at 0.10 lb ai/A/application)	0.20 lb ai/A (2 at 0.10 lb ai/A/application)	0.20 lb ai/A (2 at 0.10 lb ai/A/application)
Submitter:	BASF Corporation	BASF Corporation	BASF Corporation
MRID Citation:	MRID 46902224	MRID 46902224	MRID 46902224
	Residues of Metconazole (ppm)[1]		
	3.788	0.037	1.469
	4.536	0.035	1.979
	6.008	0.087	7.630
	6.360	0.100	8.080
	1.332	0.017	3.853
	1.382	0.021	6.749
	7.916	0.077	4.676
	6.652	0.062	4.546
	2.186	0.017	1.715
	1.826	0.013	2.878
	4.820	0.039	2.351
	7.012	0.040	2.624
	5.948	0.014	1.421
	6.120	0.016	1.062
	7.856	0.011	0.266
	6.684	0.011	0.574
	9.940	0.116	9.616
	9.512	0.075	9.842
	10.084	0.032	3.644
	11.220	0.037	4.612
	5.776	0.051	4.176

Table II-4. Residue data used to calculate tolerance for metconazole on wheat commodities.			
Regulator:	EPA	EPA	EPA
Chemical:	Metconazole	Metconazole	Metconazole
Crop:	Wheat hay	Wheat grain	Wheat straw
PHI:	6-8 Days	20-22 Days	20-22 Days
App. Rate:	0.20 lb ai/A (2 at 0.10 lb ai/A/application)	0.20 lb ai/A (2 at 0.10 lb ai/A/application)	0.20 lb ai/A (2 at 0.10 lb ai/A/application)
Submitter:	BASF Corporation	BASF Corporation	BASF Corporation
MRID Citation:	MRID 46902224	MRID 46902224	MRID 46902224
	Residues of Metconazole (ppm)[1]		
	6.040	0.045	5.632
	12.664	0.024	1.197
	12.496	0.022	1.180
	6.476	0.025	2.456
	6.056	0.028	2.554
	5.524	0.028	2.421
	5.496	0.027	2.516
	6.512	0.054	3.364
	6.804	0.054	3.612

[1] Total of both *cis* and *trans* isomers.

Figure II-17. Lognormal probability plot of metconazole field trial data for wheat hay.

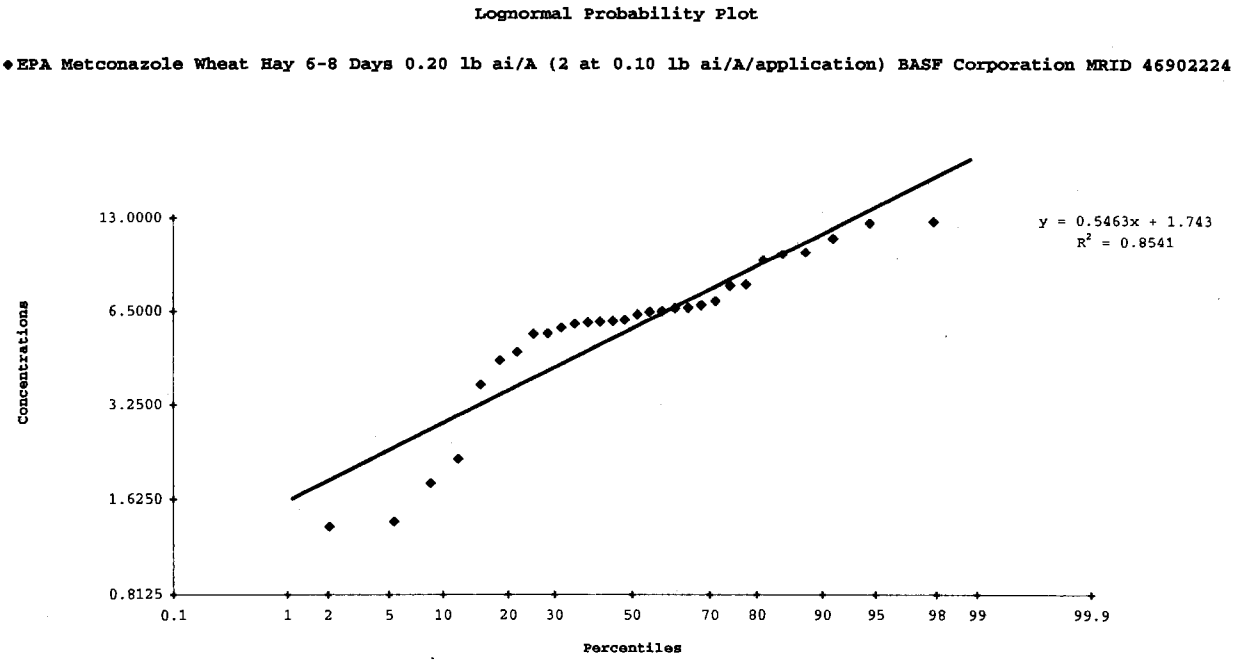


Figure II- 18. Tolerance spreadsheet summary of metconazole field trial data for wheat hay.

	Regulator: EPA		
	Chemical: Metconazole		
	Crop: Wheat Hay		
	PHI: 6-8 Days		
	App. Rate: 0.20 lb ai/A (2 at 0.10 lb ai/A/application)		
	Submitter: BASF Corporation		
	MRID Citation: MRID 46902224		
	n: 30		
	min: 1.33		
	max: 12.66		
	median; 6.24		
	average: 6.50		
	95th Percentile	**99th Percentile**	**99.9th Percentile**
EU Method I Normal	12 (13)	14 (16)	16 (--)
EU Method I Log Normal	15 **(25)**	**25** (35)	35 (--)
EU Method II Distribution-Free		16	
California Method μ + 3σ		16	
UPLMedian95th		**40**	
Approximate Shapiro-Francia Normality Test		0.8541 p-value <= 0.01: Reject lognormality assumption	

Would you like the above values rounded? (Y or N)==> Y

Figure II- 19. Lognormal probability plot of metconazole field trial data for wheat straw.

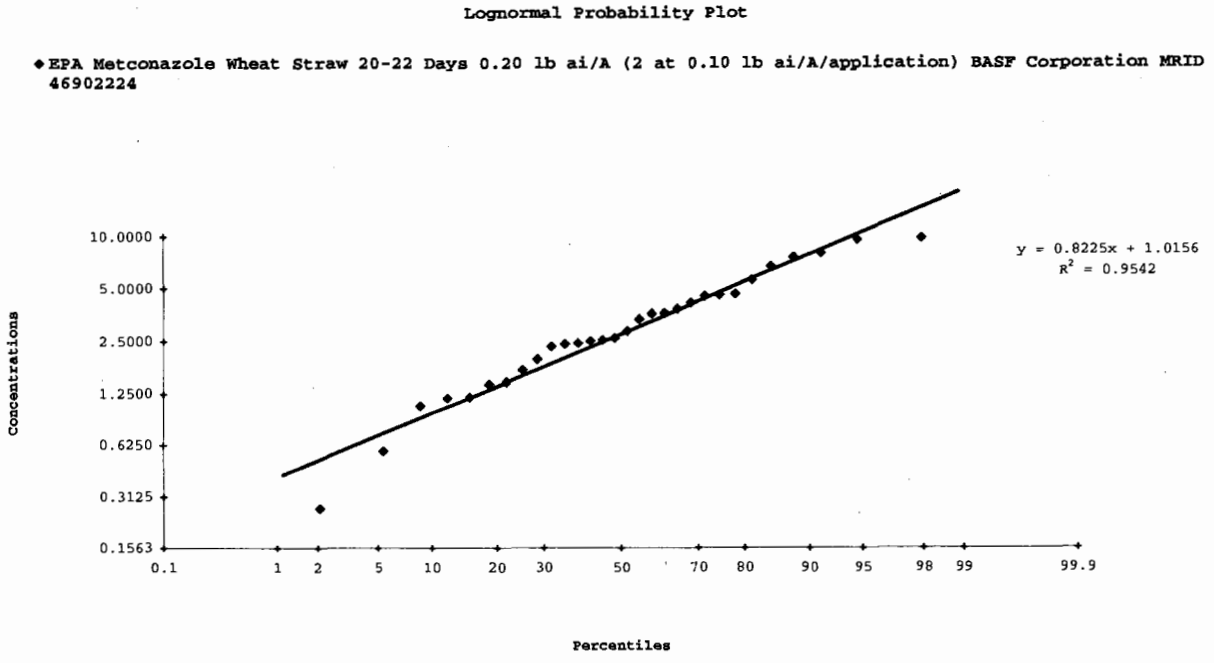


Figure II- 20. Tolerance spreadsheet summary of metconazole field trial data for wheat straw.

Regulator:	EPA
Chemical:	Metconazole
Crop:	Wheat Straw
PHI:	20-22 Days
App. Rate:	0.20 lb ai/A (2 at 0.10 lb ai/A/application)
Submitter:	BASF Corporation
MRID Citation:	MRID 46902224
n:	30
min:	0.27
max:	9.84
median;	2.75
average:	3.62

	95th Percentile	99th Percentile	99.9th Percentile
EU Method I Normal	8.0 (10)	10 (12)	12 (--)
EU Method I Log Normal	11 (18)	**19** (35)	35 (--)
EU Method II Distribution-Free	10		
California Method $\mu + 3\sigma$	**12**		
UPLMedian95th	**16**		
Approximate Shapiro-Francia Normality Test	0.9542 p-value > 0.05 : Do not reject lognormality assumption		

Would you like the above values rounded? (Y or N)==> Y

Figure II- 21. Lognormal probability plot of metconazole field trial data for wheat grain.

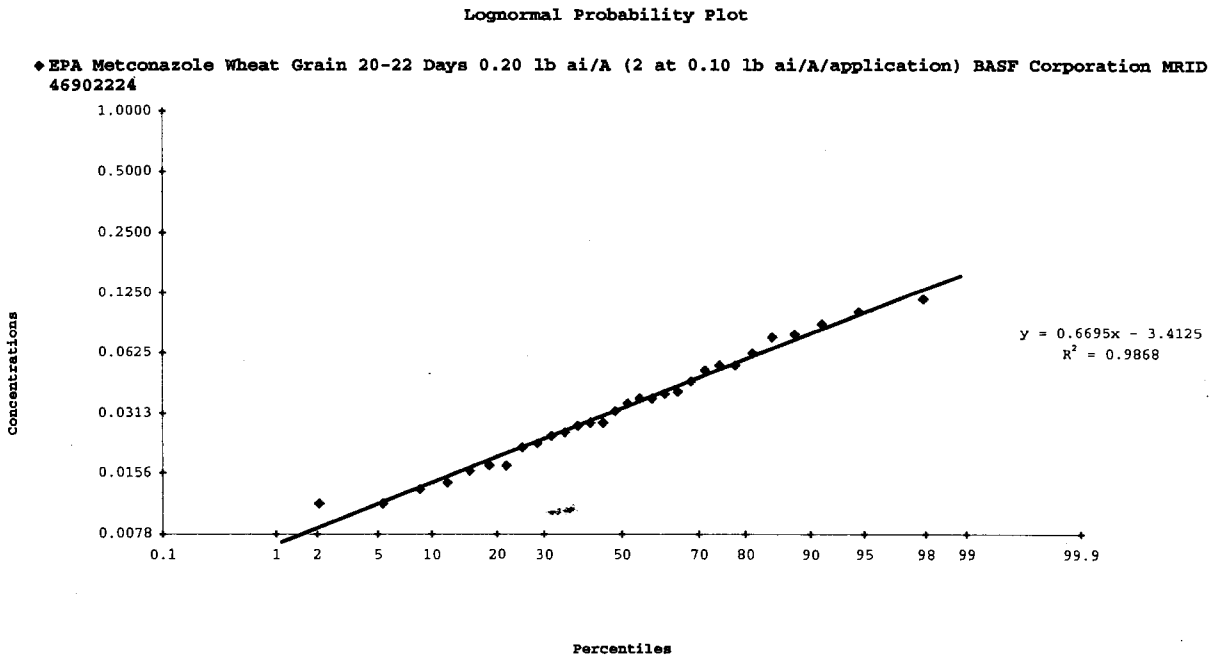


Figure II- 22. Tolerance spreadsheet summary of metconazole field trial data for wheat grain.

	Regulator: EPA		
	Chemical: Metconazole		
	Crop: Wheat Grain		
	PHI: 20-22 Days		
	App. Rate: 0.20 lb ai/A (2 at 0.10 lb ai/A/application)		
	Submitter: BASF Corporation		
	MRID Citation: MRID 46902224		
	n: 30		
	min: 0.01		
	max: 0.12		
	median; 0.03		
	average: 0.04		
	95th Percentile	**99th Percentile**	**99.9th Percentile**
EU Method I Normal	0.09 (0.15)	0.15 (0.15)	0.15 (--)
EU Method I Log Normal	0.10 (0.15)	**0.20** (0.25)	0.25 (--)
EU Method II Distribution-Free		0.15	
California Method $\mu + 3\sigma$		**0.15**	
UPLMedian95th		**0.20**	
Approximate Shapiro-Francia Normality Test		0.9868 p-value > 0.05 : Do not reject lognormality assumption	

Would you like the above values rounded? (Y or N)==> Y

Soybean Forage and Hay

The dataset used to establish a tolerance for metconazole on soybean forage and hay consisted of field trial data representing application rates of 0.14 lb ai/A (2 applications at 0.07 lb ai/A/application) with a 7-day PHI. As specified by the *Guidance for Setting Pesticide Tolerances Based on Field Trial Data* SOP, the field trial application rates are within 25% of the maximum label application rate; however, we note that the PHIs are less than the minimum label PHIs of 14 days for forage and 21 days for hay. The residue values used to calculate the tolerances are provided in Table II-5.

All 42 field trial sample results were above the LOQ for each commodity. Since there were no values reported below the LOQ, MLE procedures were not needed to impute censored values. We note that because >60% of the field trial results for seed were below the LOQ, MLE procedures could not be used for soybean seed.

The dataset for metconazole on soybean forage and hay was entered into the tolerance spreadsheet. Visual inspection of the lognormal probability plots (Figures II-23 for forage and II-25 for hay) provided in the spreadsheet indicates that the dataset is reasonably lognormal. The results from the approximate Shapiro-Francia test statistic (Figures II-24 for forage and II-26 for hay) confirmed that the assumption of lognormality should not be rejected.

Since the field trial data for metconazole on soybean forage and hay represent a large dataset (i.e., more than 15 samples) and are reasonably lognormal, the minimum of the 95% UCL on the 95th percentile and the point estimate of the 99th percentile should be selected as the tolerance value. Using the rounding procedure as outlined in the *Guidance for Setting Pesticide Tolerances Based on Field Trial Data* SOP, the 95% UCL on the 95th percentile rounds to the

value 3.0 ppm for forage and 6.0 ppm for hay, and the point estimate of the 99th percentile rounds to the value 3.5 ppm for forage and 6.0 ppm for hay (Figures II-24 and II-26). Because the 3.0-ppm value was the minimum value for forage, 3.0 ppm is the recommended tolerance level for metconazole on soybean forage. Because these values are the same for hay, 6.0 ppm is the recommended tolerance level for metconazole on soybean hay.

Table II-5. Residue data used to calculate tolerance for metconazole on soybean commodities.		
Regulator:	EPA	EPA
Chemical:	Metconazole	Metconazole
Crop:	Soybean forage	Soybean hay
PHI:	7 Days	7 Days
App. Rate:	0.14 lb ai/A (2 at 0.07 lb ai/A/application)	0.14 lb ai/A (2 at 0.07 lb ai/A/application)
Submitter:	BASF Corporation	BASF Corporation
MRID Citation:	MRID 46902228	MRID 46902228
	Residues of Metconazole (ppm)[1]	
	1.092	2.030
	0.968	1.969
	0.668	3.993
	0.790	2.824
	1.036	3.908
	0.989	3.975
	0.930	1.279
	0.985	1.443
	1.055	1.687
	1.086	2.547
	2.006	2.106
	2.335	2.041
	1.097	1.883
	1.369	2.656
	1.586	4.738
	1.665	4.333
	0.717	1.603
	0.712	1.785
	1.400	3.114
	1.242	3.244
	1.478	2.922
	2.217	2.992
	1.780	3.176
	1.790	3.774
	1.348	2.850
	2.068	3.541
	1.410	1.337
	1.386	1.434
	0.639	1.168

Table II-5. Residue data used to calculate tolerance for metconazole on soybean commodities.		
Regulator:	EPA	EPA
Chemical:	Metconazole	Metconazole
Crop:	Soybean forage	Soybean hay
PHI:	7 Days	7 Days
App. Rate:	0.14 lb ai/A (2 at 0.07 lb ai/A/application)	0.14 lb ai/A (2 at 0.07 lb ai/A/application)
Submitter:	BASF Corporation	BASF Corporation
MRID Citation:	MRID 46902228	MRID 46902228
	Residues of Metconazole (ppm)[1]	
	0.474	1.496
	1.950	3.360
	1.860	3.210
	1.000	1.470
	1.360	1.290
	1.760	2.250
	1.990	1.830
	1.470	2.360
	2.260	2.770
	1.200	2.160
	1.230	3.060
	1.900	2.420
	2.430	2.760

[1] Total of both *cis* and *trans* isomers.

Figure II-23. Lognormal probability plot of metconazole field trial data for soybean forage.

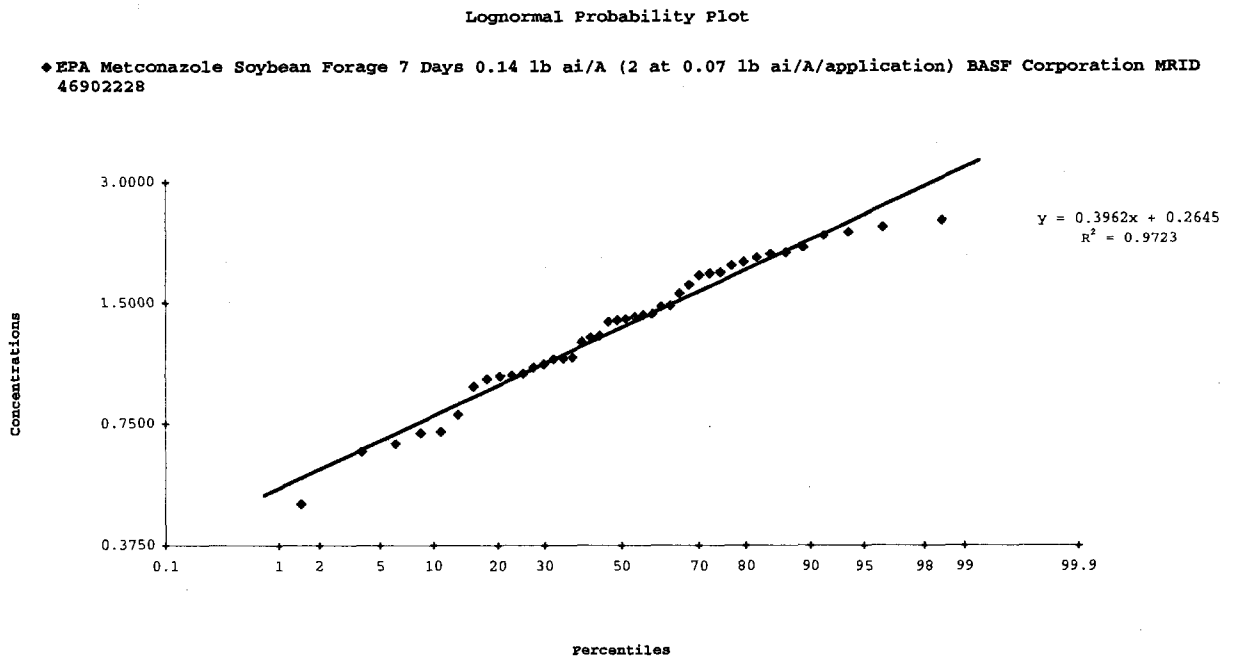


Figure II- 24. Tolerance spreadsheet summary of metconazole field trial data for soybean forage.

Regulator:	EPA
Chemical:	Metconazole
Crop:	Soybean Forage
PHI:	7 Days
App. Rate:	0.14 lb ai/A (2 at 0.07 lb ai/A/application)
Submitter:	BASF Corporation
MRID Citation:	MRID 46902228
n:	42
min:	0.47
max:	2.43
median;	1.36
average:	1.40

	95th Percentile	99th Percentile	99.9th Percentile
EU Method I Normal	2.5 (2.5)	3.0 (3.0)	3.0 (--)
EU Method I Log Normal	2.5 (2.0)	**3.5** (4.5)	4.5 (--)
EU Method II Distribution-Free		4.0	
California Method μ + 3σ		**3.0**	
UPLMedian95th		**8.0**	
Approximate Shapiro-Francia Normality Test		0.9723 p-value > 0.05 : Do not reject lognormality assumption	

Would you like the above values rounded? (Y or N)==> Y

Figure II- 25. Lognormal probability plot of metconazole field trial data for soybean hay.

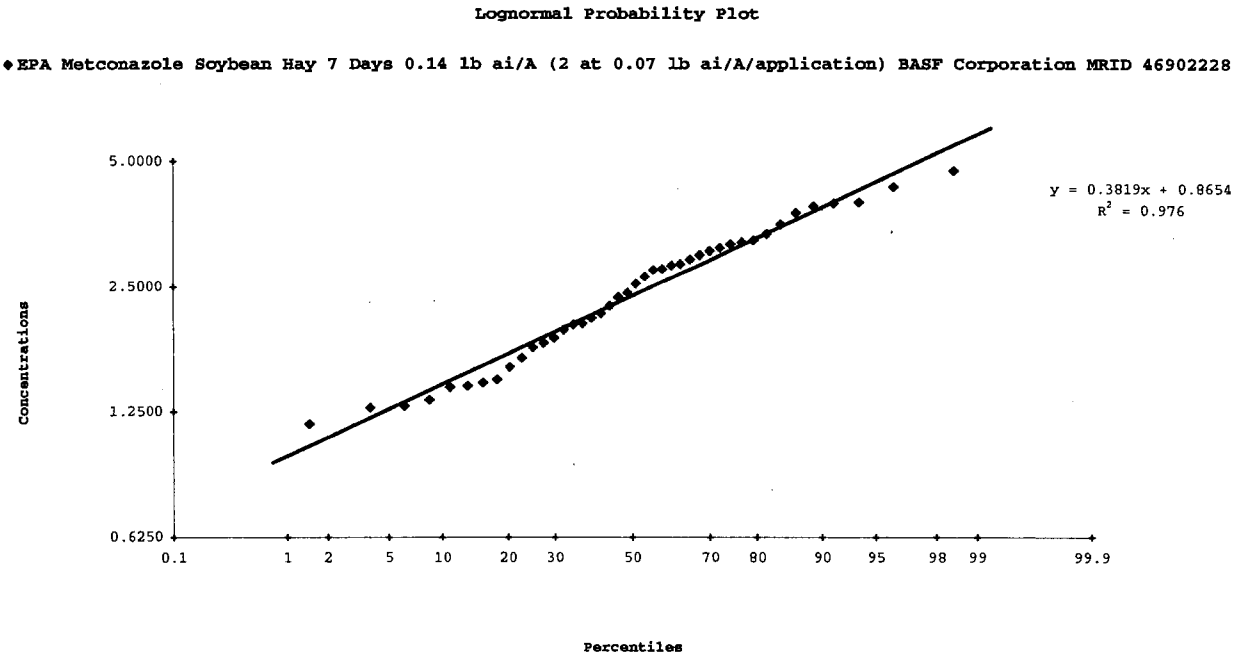


Figure II-26. Tolerance spreadsheet summary of metconazole field trial data for soybean hay.

	Regulator:	EPA	
	Chemical:	Metconazole	
	Crop:	Soybean Hay	
	PHI:	7 Days	
	App. Rate:	0.14 lb ai/A (2 at 0.07 lb ai/A/application)	
	Submitter:	BASF Corporation	
	MRID Citation:	MRID 46902228	
	n:	42	
	min:	1.17	
	max:	4.74	
	median;	2.48	
	average:	2.54	
	95th Percentile	**99th Percentile**	**99.9th Percentile**
EU Method I Normal	4.5 (5.0)	5.0 (6.0)	6.0 (--)
EU Method I Log Normal	4.5 (6.0)	6.0 (8.0)	8.0 (--)
EU Method II Distribution-Free		7.0	
California Method $\mu + 3\sigma$		**6.0**	
UPLMedian95th		**14**	
Approximate Shapiro-Francia Normality Test		0.9760 p-value > 0.05 : Do not reject lognormality assumption	

Would you like the above values rounded? (Y or N)==> Y

Sugar beet

The dataset used to establish a tolerance for metconazole on sugar beet root consisted of field trial data representing application rates of 0.20 lb ai/A (2 applications at 0.10 lb ai/A/application) with a 14-day PHI. As specified by the *Guidance for Setting Pesticide Tolerances Based on Field Trial Data* SOP, the field trial application rates and PHIs are within 25% of the maximum label application rate and minimum label PHI, respectively. The residues values used to calculate the tolerance are provided in Table II-6.

Because 6 of 24 field trial sample results were below LOQ, MLE procedures were needed to impute censored values.

The metconazole-sugar beet root dataset was entered into the tolerance spreadsheet. Visual inspection of the lognormal probability plot (Figure II-27) provided in the spreadsheet indicates that the dataset is reasonably lognormal. The result from the approximate Shapiro-Francia test statistic (Figure II-28) confirmed that the assumption of lognormality should not be rejected.

Since the field trial data for metconazole on sugar beet root represent a large dataset (i.e., more than 15 samples) and are reasonably lognormal, the minimum of the 95% UCL on the 95th percentile and the point estimate of the 99th percentile should be selected as the tolerance value. Using the rounding procedure as outlined in the *Guidance for Setting Pesticide Tolerances Based on Field Trial Data* SOP, the 95% UCL on the 95th percentile rounds to the value 0.07 ppm and the point estimate of the 99th percentile also rounds to the value 0.07 ppm (Figure II-28). Because these values are the same, 0.07 ppm is the recommended tolerance level for metconazole on sugar beet root.

Table II-6. Residue data used to calculate tolerance for metconazole on sugar beet root.	
Regulator:	EPA
Chemical:	Metconazole
Crop:	Sugar beet root (MLE)
PHI:	14 days
App. Rate:	0.20 lb ai/A (2 at 0.10 lb ai/A/application)
Submitter:	BASF
MRID Citation:	MRID 46902230
	Residues of Metconazole (ppm)[1]
	0.011
	0.005
	0.006
	0.007
	0.008
	0.009
	0.039
	0.023
	0.040
	0.048

Table II-6. Residue data used to calculate tolerance for metconazole on sugar beet root.	
Regulator:	EPA
Chemical:	Metconazole
Crop:	Sugar beet root (MLE)
PHI:	14 days
App. Rate:	0.20 lb ai/A (2 at 0.10 lb ai/A/application)
Submitter:	BASF
MRID Citation:	MRID 46902230
	Residues of Metconazole (ppm)[1]
	0.024
	0.015
	0.009
	0.011
	0.023
	0.014
	0.026
	0.012
	0.034
	0.018
	0.019
	0.014
	0.023
	0.020

[1] Total of both *cis* and *trans* isomers.

Figure II- 27. Lognormal probability plot of metconazole field trial data for sugar beet root.

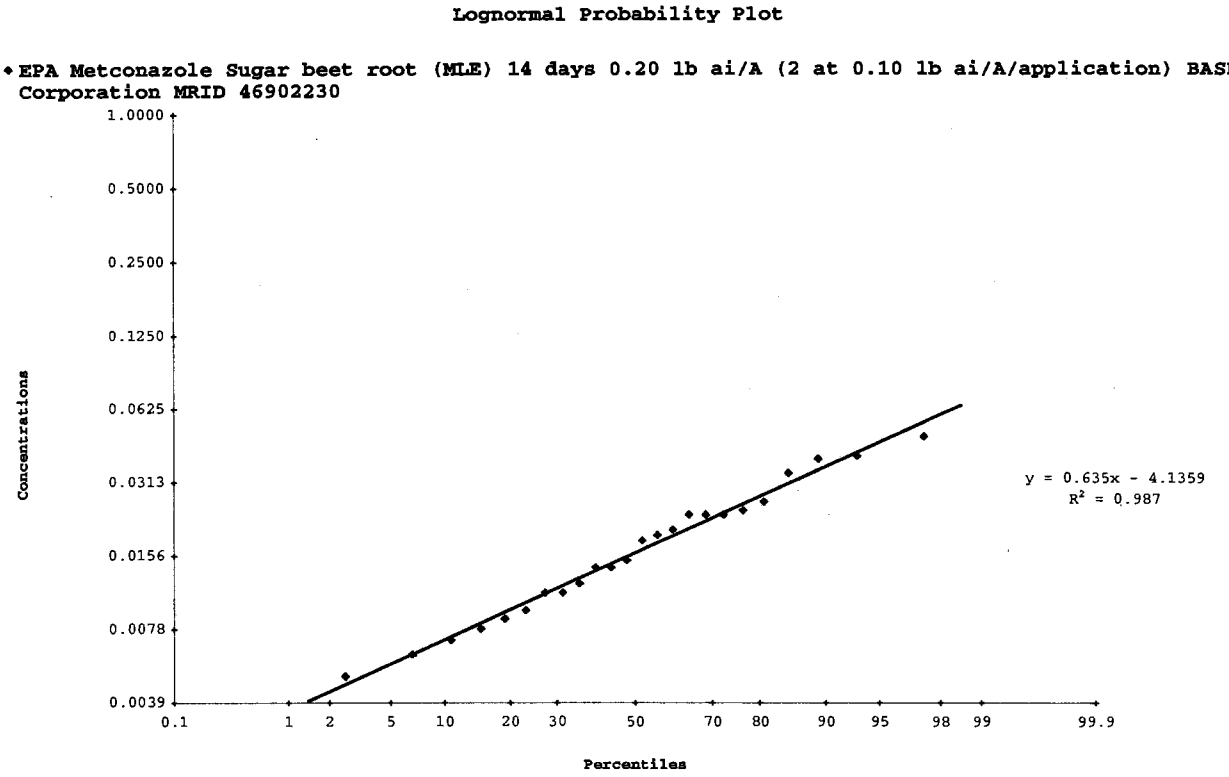


Figure II- 28. Tolerance spreadsheet summary of metconazole field trial data for sugar beet root.

Regulator:	EPA
Chemical:	Metconazole
Crop:	Sugar beet root (MLE)
PHI:	14 days
App. Rate:	0.20 lb ai/A (2 at 0.10 lb ai/A/application)
Submitter:	BASF Corporation
MRID Citation:	MRID 46902230
n:	24
min:	0.01
max:	0.05
median;	0.02
average:	0.02

	95th Percentile	99th Percentile	99.9th Percentile
EU Method I Normal	0.04 (0.05)	0.05 (0.06)	0.06 (--)
EU Method I Log Normal	0.05 (0.07)	0.07 (0.15)	0.15 (--)
EU Method II Distribution-Free	0.05		
California Method $\mu + 3\sigma$	**0.06**		
UPLMedian95th	**0.10**		
Approximate Shapiro-Francia Normality Test	0.9870 p-value > 0.05 : Do not reject lognormality assumption		

Would you like the above values rounded? (Y or N)==> Y

Stone Fruit - Cherry, Peach, Plum

The dataset used to establish tolerances for metconazole on cherry and peach consisted of field trial data representing application rates of 0.40 lb ai/A (3 applications at 0.136 lb ai/A/application) with a 14-day PHI. As specified by the *Guidance for Setting Pesticide Tolerances Based on Field Trial Data* SOP, the field trial application rates and PHIs are within 25% of the maximum label application rate and minimum label PHI proposed for the stone fruit crop group, respectively. HED notes that the 1.81 lb/gal FlC formulation used for the majority of the cherry and peach field trials is not the product proposed for registration. The data from the WDG field trials are included. The residues values used to calculate the tolerances are provided in Table II-7.

Because 4 of 16 field trial results for cherry and 6 of 20 field trial results for peach were below the LOQ, maximum likelihood estimation (MLE) procedures were needed to impute censored values. **HED notes that because >60% of the field trial results for plum were below the LOQ, MLE procedures could not be used.**

The dataset for metconazole on cherry and peach was entered into the tolerance spreadsheet. Visual inspection of the lognormal probability plots (Figures II-29 for cherry and II-31 for peach) provided in the spreadsheet indicates that the dataset is reasonably lognormal for each commodity. The result from the approximate Shapiro-Francia test statistic (Figures II-30 for cherry and II-32 for peach) confirmed that the assumption of lognormality should not be rejected.

Since the field trial data for metconazole on cherry and peach represent a large dataset (i.e., more than 15 samples) and are reasonably lognormal, the minimum of the 95% upper confidence limit (UCL) on the 95th percentile and the point estimate of the 99th percentile should be selected as the tolerance value. Using the rounding procedure as outlined in the *Guidance for Setting Pesticide Tolerances Based on Field Trial Data* SOP, the 95% UCL on the 95th percentile rounds to the values 0.25 ppm and 0.10 ppm for peach, and the point estimate of the 99th percentile rounds to the values 0.20 ppm for cherry and 0.10 ppm for peach (Figures II-30 and II-32). Because 0.20 is the minimum value for cherry, 0.20 ppm is the recommended tolerance level for metconazole on cherry. Because these values are the same, for peach, 0.10 ppm is the recommended tolerance level for metconazole on peach. The stone fruit tolerance should be set at 0.20 ppm.

Table II-7. Residue data used to calculate tolerance for metconazole on cherry and peach.		
Regulator:	EPA	EPA
Chemical:	Metconazole	Metconazole
Crop:	Cherry (MLE)	Peach (MLE)
PHI:	13-14 Days	13-14 Days
App. Rate:	0.407 lb ai/A (3 at 0.136 lb ai/A)	0.407 lb ai/A (3 at 0.136 lb ai/A)
Submitter:	Valent U.S.A.	Valent U.S.A.
MRID Citation:	MRID 46901707	MRID 46901708
	Residues of Metconazole (ppm)	
	0.050	0.027
	0.049	0.030
	0.025	0.033
	0.030	0.035
	0.067	0.037
	0.059	0.038
	0.074	0.043
	0.057	0.047
	0.076	0.047
	0.086	0.052
	0.162	0.093
	0.123	0.079
	0.062	0.043
	0.069	0.047
	0.034	0.049
	0.037	0.066
	0.068	0.052
	0.076	0.042
	0.049	0.046
	0.047	0.041

Figure II- 29. Lognormal probability plot of metconazole field trial data for cherry.

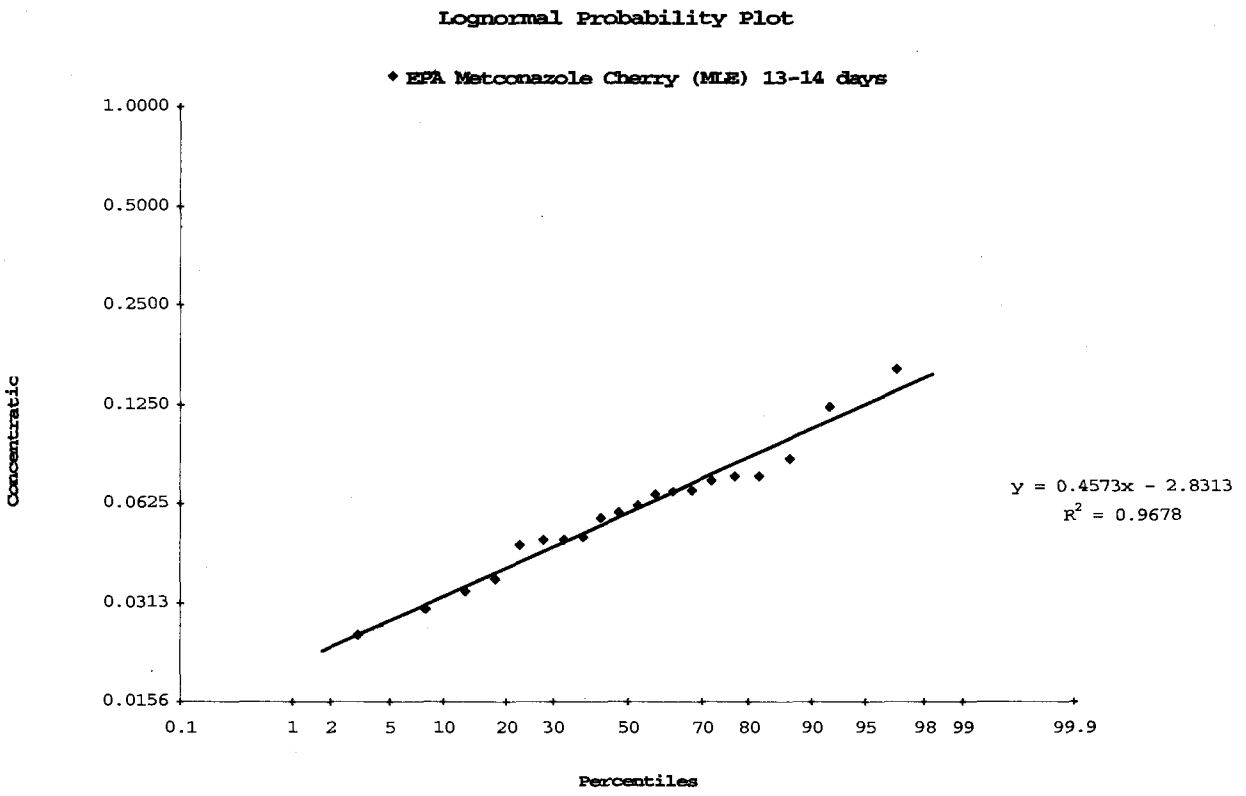


Figure II- 30. Lognormal probability plot of metconazole field trial data for cherry.

	Regulator:	EPA	
	Chemical:	Metconazole	
	Crop:	Cherry (MLE)	
	PHI:	13-14 days	
	App. Rate:	0.407 lb ai/A	
	Submitter:	Valent U.S.A.	
	n:	20	
	min:	0.03	
	max:	0.16	
	median:	0.06	
	average:	0.07	
	95th Percentile	**99th Percentile**	**99.9th Percentile**
EU Method I	0.15	0.15	0.20
Normal	(0.15)	(0.20)	(--)
95/99 Rule	0.15	**0.20**	0.25
	(0.20)	(0.30)	(--)
EU Method II		0.20	
Distribution-Free			
Mean+3SD		**0.20**	
UCLMedian95th		**0.35**	
Approximate		0.9678	
Shapiro-Francia	p-value > 0.05 : Do not reject lognormality assumption		
Normality Test			

Figure II- 31. Lognormal probability plot of metconazole field trial data for peach.

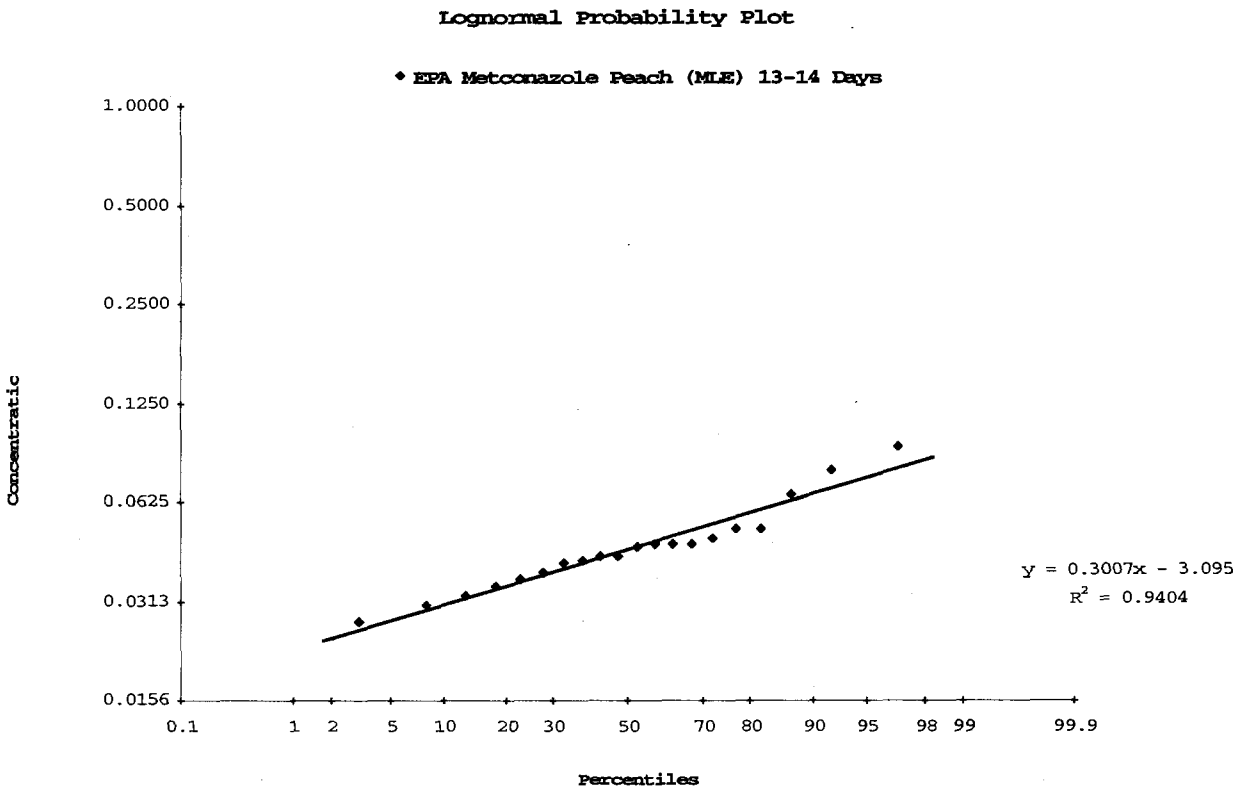


Figure II- 32. Tolerance spreadsheet summary of metconazole field trial data for peach.

	Regulator:	EPA	
	Chemical:	Metconazole	
	Crop:	Peach (MLE)	
	PHI:	13-14 Days	
	App. Rate:	0.407 lb ai/A	
	Submitter:	Valent U.S.A.	
	n:	20	
	min:	0.03	
	max:	0.09	
	median:	0.04	
	average:	0.05	
	95th Percentile	**99th Percentile**	**99.9th Percentile**
EU Method I	0.08	0.09	0.10
Normal	(0.09)	(0.10)	(--)
95/99 Rule	0.08	**0.10**	0.15
	(0.10)	(0.15)	(--)
EU Method II		0.15	
Distribution-Free			
Mean+3SD		**0.10**	
UCLMedian95th		**0.25**	
Approximate		0.9404	
Shapiro-Francia	p-value > 0.05 : Do not reject lognormality assumption		
Normality Test			

Tree Nuts – Almond and Pecan

Because >60% of the field trial results for almond nutmeat and pecan nutmeat were below the LOQ, MLE procedures could not be used for nutmeat.

The dataset used to establish tolerances for metconazole on almond hulls consisted of field trial data representing application rates of 0.394-0.570 ai/A/season with a 25-day PHI. As specified by the *Guidance for Setting Pesticide Tolerances Based on Field Trial Data* SOP, the field trial application rates and PHIs should be within 25% of the maximum label application rate and minimum label PHI proposed for almonds. The proposed rate for almond is 0.44 lb ai/A/season with a 25-day PHI. HED notes that the 1.81 lb/gal FlC formulation used for the majority of the almond field trials is not the product proposed for registration. The data from the WDG field trials are included. The residues values used to calculate the tolerances are provided in Table II-8.

Because 2 of 18 field trial results for almond hulls were below the LOQ, maximum likelihood estimation (MLE) procedures were needed to impute censored values.

The dataset for metconazole on almond hulls were entered into the tolerance spreadsheet. Visual inspection of the lognormal probability plot (Figure II-33) provided in the spreadsheet indicates that the dataset is not lognormal for almond hulls. The result from the approximate Shapiro-Francia test statistic (Figure II-34) confirmed that the assumption of lognormality should be rejected. The almond hull tolerance should be set at 4.0 ppm.

Table II-8. Residue data used to calculate tolerance for metconazole on almond hulls.	
Regulator:	EPA
Chemical:	Metconazole
Crop:	Almond hulls (MLE)
PHI:	25 days
App. Rate:	0.394-0.570 ai/A/season
Submitter:	Valent U.S.A.
MRID Citation:	MRID 46901710
	Residues of Metconazole (ppm) [1]
	0.0235
	0.0326
	1.2000
	1.4800
	0.5000
	0.6100
	0.7200
	0.5500
	2.3800
	3.6900
	0.7700
	0.7800
	0.4300
	0.3700
	0.7600
	0.7500
	1.6100
	2.0200

[1] Total of both *cis* and *trans* isomers.

Figure II- 33. Lognormal probability plot of metconazole field trial data for almond hulls

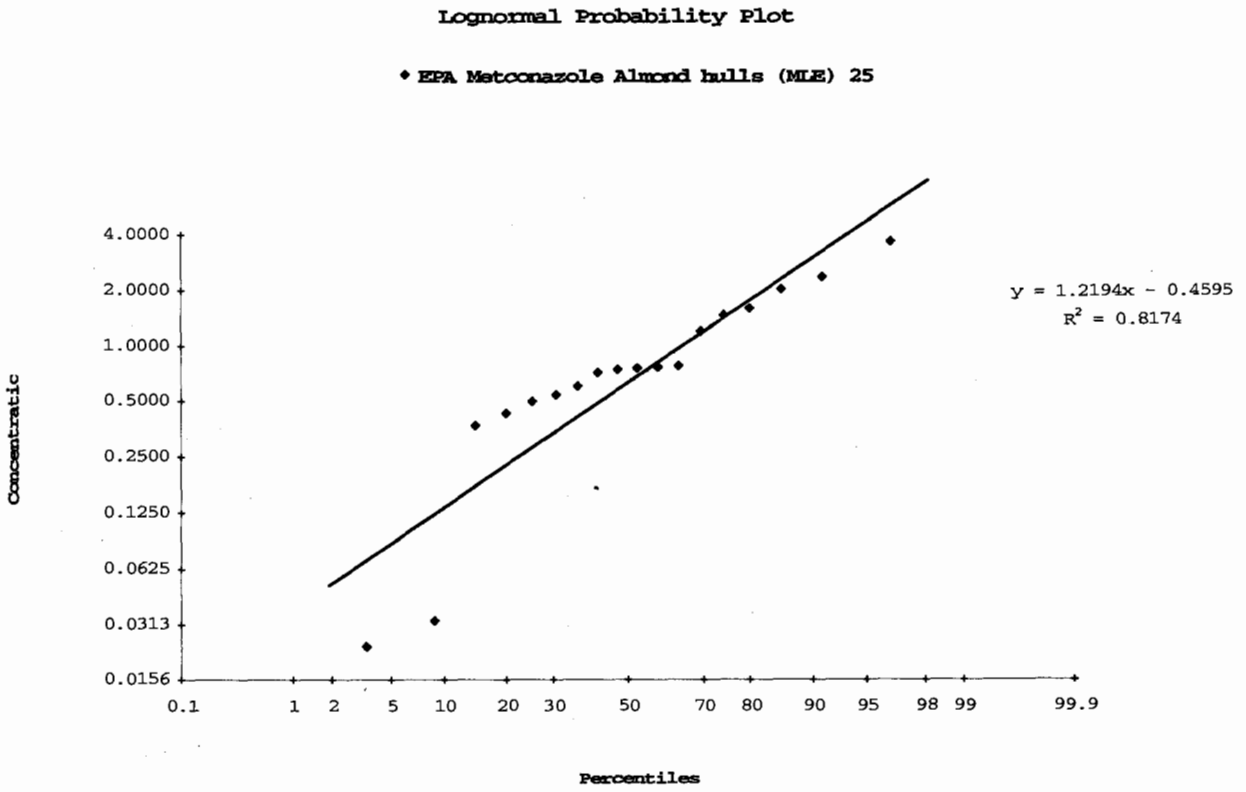


Figure II- 34. Tolerance spreadsheet summary of metconazole field trial data for almond hulls.

	Regulator:	EPA	
	Chemical:	Metconazole	
	Crop:	Almond hulls (MLE)	
	PHI:	25 Days	
	App. Rate:	0.394-0.570 lb	
	Submitter:	Valent U.S.A.	
	n:	18	
	min:	0.02	
	max:	3.69	
	median:	0.76	
	average:	1.04	
	95th Percentile	**99th Percentile**	**99.9th Percentile**
EU Method I	3.0	3.5	4.0
Normal	(3.5)	(4.5)	(--)
95/99 Rule	6.0	**13**	35
	(16)	(50)	(--)
EU Method II		3.5	
Distribution-Free			
Mean+3SD		**4.0**	
UCLMedian95th		**4.5**	
Approximate		0.8174	
Shapiro-Francia	p-value <= 0.01: Reject lognormality assumption		
Normality Test			

Appendix III. ACB/BEAD Reviews of Plant and Livestock Enforcement Methods

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON D.C., 20460
Analytical Chemistry Branch
701 Mapes Road
Ft. Meade, Maryland 20755-5350

OFFICE OF
PREVENTION, PESTICIDES AND TOXIC
SUBSTANCES

February 8, 2008

MEMORANDUM

SUBJECT: Review of Proposed Tolerance Enforcement Methods for Metconazole.
ACB Project # B07-18.

FROM: Paul E.Golden, Chemist
Analytical Chemistry Branch
Biological and Economic Analysis Branch (7503P)

THRU: Bill Chism, Acting Chief
Analytical Chemistry Branch
Biological and Economic Analysis Branch (7503P)

TO: Paula Deschamp, Chief
Registration Action Branch 3 (RAB3)
Health Effects Division (7509P)

INTRODUCTION

The Analytical Chemistry Branch (ACB) was requested by RAB 3 to conduct a tolerance method validation for methods submitted by BASF Corporation to support tolerances for metconazole in several plant and animal commodities. The lab validation was requested in a memo dated May 29, 2007 from N. Dodd (HED) to F. Siegelman (ACB). The ACB has reviewed the proposed enforcement methods data without laboratory validation. Several other metconazole metabolites were included in the analytical methods, but this review focused only on the cis- and trans-isomers of metconazole since the other metabolites are not proposed to be part of the tolerance expression.

ANALYTICAL METHOD(S) AND DOCUMENTATION

PLANT METHODS

MRID# 46902216: Study Title: Method Validation of BASF Analytical Method D0508 Entitled: "The Determination of Residues of Metconazole (BAS 555F) and its Metabolites in Plant Matrices using LC/MS/MS". Authors: M. Saha, R. Gooding. Study Completion Date: June 9, 2006. Performing Laboratory: BASF Agro Research, 26 Davis Drive, Research Triangle Park, NC 27709. Study No. 238522, BASF Registration Document No. 2005/5000141. 221 pages containing the analytical method entitled: Analytical Method No. D0508, The Determination of Residues of Metconazole (BAS 555F) and its Metabolites in Plant Matrices using LC/MS/MS. Authors: M. Saha, R. Gooding. Version: May, 2006. Performing Laboratory: BASF Corporation, BASF Agro Research, 26 Davis Drive, Research Triangle Park, NC 27709. Pages 194-221 of BASF Study No. 238522, Registration Document No. 2005/5000141.

MRID# 46902217: Study Title: Independent Method Validation of BASF Analytical Method D0508: "The Determination of Residues of Metconazole (BAS 555 F) and its Metabolites in Plant Matrices using LC/MS/MS". Authors: R. Perez, A. Ibrahim, R. Hauser, S. Perez. Study Completion Date: June 26, 2006. Performing Laboratory: ADPEN Laboratories, Inc., 11757 Central Parkway, Jacksonville, FL 32224. Laboratory Project ID: BASF Study No. 238582, BASF Registration Document No.'s: 2006/7007032, ADPEN Study Number: 2K6-238582.

ANIMAL METHODS

MRID# 46665405: Study Title: Metconazole (CL 900768): Validation of DFG Method S 19 for the Determination of Residues of Metconazole (CL 900768) as CIS- (CL 354801) and TRANS-Isomer (CL 354802) in Plant Material, Foodstuff of Animal Origin and Soil. Authors: S. Pelz, R. Weeren. Study Completion Date: November 16, 1999. Performing Laboratory: Dr. Specht & Partner, Hamburg, Germany. BASF Registration Document Number: MK-240-003, Report Numbers: CYA-9907V, Az. M8995/99. Sponsor: Cyanamid Forschung GmbH (CFS), Schwabenheim, Germany.

MRID# 46665407: Study Title: Metconazole (CL 900768): Assessment and Validation of the Multi-Residue Enforcement Method DFG S19 with Modified Extraction (and with SDF Cleanup Method 5 for Fatty/Oily Matrices) for the determination of Residues of Metconazole (CL 900768) in Plant Material (Wheat Grain, Grape, Pea and Oilseed Rape Seed) and in Foodstuff of Animal Origin (Milk, Egg, Bovine Muscle and Fat). Author: T. Class. Study Completion Date: September 22, 2003. Performing Laboratory: PTRL Europe, Ulm, Germany. BASF Registration Document Number: 2003/7007238, Report Numbers: P 349 G, CFS 1999-127. Sponsor: Cyanamid Forschung GmbH (CFS), Schwabenheim, Germany.

RECOMMENDATIONS

1. Based on our review of the proposed enforcement methods, without ACB laboratory trial, BASF Corp. plant method D0508 and the animal method based on the German multiresidue method DFG S19 both appear to meet the OPPTS 860.1340 Residue Chemistry Test Guidelines for an acceptable tolerance enforcement method, with the following exception:

- The ACB recommends that the plant method D0508 does not meet the general requirement as a confirmatory method since only one MS/MS ion transition for each analyte is documented. The ACB recommends that the petitioner provide information for a second MS/MS ion transition to provide a confirmation of analyte identity. If two ion transitions are not available, we recommend the petitioner provide an alternate chromatographic column and/or mobile-phase combination to add an additional degree of specificity and further reduce the possibility of false positive residues.

2. The ACB recommends that an Agency laboratory validation is not necessary for the following reasons:

A) The method appears well-written and includes detailed instructions

B) The recovery data are acceptable for all tested commodities.

C) The Independent Laboratory Validation (ILV) data submitted are acceptable and indicate that method performance is reproducible.

3. BASF Corp. has previously submitted analytical reference standards of metconazole (cis- and trans-isomers) to the EPA National Pesticide Standard Repository at our lab for distribution to pesticide enforcement labs.

COMMENTS

1. The plant method only gives one MS/MS ion transition for each analyte. The OPP guidelines require either a confirmatory method or an interference study to eliminate the possibility of false positives while using the primary enforcement method. When mass spectrometry is used for detection in the primary enforcement method, a confirmatory method is waived as long as the detector provides enough selectivity to eliminate false positives. In this plant method, analysis is by LC-MS/MS with quantitation of residues by monitoring one multiple reaction monitoring (MRM) ion transition in the electrospray positive ion mode. While MS/MS provides excellent selectivity, expert opinion has changed over the past several years as mass spectrometrists have gained more experience with the instrumentation. A single MS/MS ion transition was considered sufficient for positive confirmation of analyte residue at one time. However, instances of false positive interferences have led towards consensus that two ion transitions are needed to provide confirmation of residues. References include:

1) Commission Decision 2002/657/EC, Official Journal of the European Communities, August 12, 2002.
2) Guidance for Industry: Mass Spectrometry for Confirmation of the Identity of Animal Drug Residues, US FDA Center for Veterinary Medicine, May 1, 2003.

3) Bethem, et al, Establishing the Fitness for Purpose of Mass Spectrometric Methods, J Am Soc Mass Spectrom 2003, 14, 523-541.

For this reason we now recommend that petitioners provide information for two MS/MS ion transitions. When two transitions are not available, we recommend providing an alternate chromatographic column and/or mobile-phase combination to further reduce the possibility of false positive residues. However, we don't think this should be considered a serious deficiency since metconazole could be confirmed using an existing multiresidue method.

2. The animal method uses an extraction/cleanup following the German multiresidue method DFG S19 with GC-NPD (two alternate GC columns listed) and GC-MSD.

3. Each of the two documents reviewed for the plant method are validation studies of the proposed enforcement method BASF Method D0508. One validation was done by the registrant, BASF, the other by an independent laboratory. The analytical method validated by the registrant in document MRID# 46902216 contains the partial analytical method D0508 (29 pages of procedures only) and is dated May 2006. The analytical method validated by the independent laboratory in document MRID# 46902217 contains the full analytical method D0508 (108 pages) and is dated March 2006. There appeared to be no substantial procedural differences between the May 2006 and March 2006 versions of the analytical method. Both versions (March or May 2006) of the referenced method D0508 specifically state that they were not reviewed by a quality assurance unit (QAU), however. The data collected from both "validation studies of Method D0508" on the other hand was reviewed by a QAU. If BASF Method D0508 is to be distributed as the official enforcement method, ideally there should either be a stand-alone version of D0508 that was QAU reviewed, OR if such a version is not available, a QAU reviewed validation of BASF Method D0508 could be distributed instead (the full 221 pages of MRID # 46902216 for example). The March or May 2006 versions of D0508 (108 pages or 29 pages) should not be distributed as the official enforcement method since they specifically state that they were not QAU reviewed in and of themselves.

4. The ILV data appeared to be acceptable. Both the plant and animal methods were successfully validated by the ILV on the first attempt for the cis- and trans-isomers of metconazole. There were problems reported with Triazoleylacetic acid and Triazoleylalanine in soybean hay, but there was no problem with recovery of the two parent metconazole isomers that are of interest.

5. We didn't have the FDA multiresidue study, but we suspect that the parent metconazole isomers would also be recovered through the method, especially since metconazole is recovered through the German S19 method. FDA is currently monitoring for other triazoles using their multiresidue methods with GC-MS.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON D.C., 20460
Analytical Chemistry Branch
701 Mapes Road
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OFFICE OF
PREVENTION, PESTICIDES AND TOXIC
SUBSTANCES

February 15, 2008

MEMORANDUM

SUBJECT: Review of Proposed Tolerance Enforcement Methods for Metconazole.
ACB Project #: B07-19
DP Number: 339995

FROM: Paul E.Golden, Chemist
Analytical Chemistry Branch
Biological and Economic Analysis Branch (7503P)

THRU: Bill Chism, Acting Chief
Analytical Chemistry Branch
Biological and Economic Analysis Branch (7503P)

TO: Paula Deschamp, Chief
Registration Action Branch 3 (RAB3)
Health Effects Division (7509P)

INTRODUCTION

The Analytical Chemistry Branch (ACB) was requested by RAB 3 to conduct a tolerance method validation for methods submitted by Valent U.S.A. Corporation to support tolerances for metconazole in several plant commodities. The lab validation was requested in a memo dated May 29, 2007 from N. Dodd (HED) to F. Siegelman (ACB). The ACB has reviewed the proposed enforcement method data without laboratory validation.

ANALYTICAL METHOD(S) AND DOCUMENTATION

MRID# 46901704: Study Title: "RM-41C-1-1 Determination of *cis*-Metconazole and *trans*-Metconazole in Crops". Author: G. Fujie. Study Completed: July 10, 2006. Performing Laboratory: Valent U.S.A. Corporation, Valent Technical Center, 6560 Trinity Court, Dublin, CA 94568. Laboratory Project Identification: RM-41C-1-1. 43 pages.

MRID# 46901706: Study Title: Independent Laboratory Validation of the Analytical Method RM-41C-1, Determination of *cis*-Metconazole and *trans*-Metconazole in Crops. Author: P. Noon. Study Completed: May 16, 2006. Performing Laboratory: North Coast Laboratories, Ltd.(NCL), 5680 West End Road, Arcata, CA 95521-9202. Laboratory Project Identification: NCL Study Number 120.010, Valent U.S.A. Project Number VP-29874. 105 pages.

RECOMMENDATIONS

1. Based on our review of the proposed enforcement method, without ACB laboratory trial, Valent method RM-41C-1-1 appears to meet the OPPTS 860.1340 Residue Chemistry Test Guidelines for an acceptable tolerance enforcement method.

2. The ACB recommends that an Agency laboratory validation is not necessary for the following reasons:

A) The method appears well-written and includes detailed instructions

B) The recovery data are acceptable for all tested commodities.

C) The Independent Laboratory Validation (ILV) data submitted are acceptable and indicate that method performance is reproducible.

3. Valent U.S.A. Corp. has previously submitted analytical reference standards of metconazole (*cis*- and *trans*-isomers) to the EPA National Pesticide Standard Repository at our lab for distribution to pesticide enforcement labs.

COMMENTS

1. The OPP guidelines require either a confirmatory method or an interference study to eliminate the possibility of false positives while using the primary enforcement method. Valent U.S.A. has provided a confirmatory method (Valent method RM-41C-4) that may be used to confirm metconazole residues in crops.

2. Valent method RM-41C-1-1 was updated to correct nomenclature and typographical errors found in Valent method RM-41C-1 which was the method validated by the independent laboratory. Both methods appear to have the same procedural content.

3. The ILV data appeared to be acceptable. The method was successfully validated by the ILV

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on the first attempt for the *cis*- and *trans*-isomers of metconazole. The ILV reported a small interfering peak in the vicinity of the *trans*-isomer, but they were able to separate it from the peak of interest using timed event functions in their integration program.

4. We didn't have the FDA multiresidue study, but we suspect that the parent metconazole isomers would also be recovered through the method, especially since metconazole is recovered through the German S19 method (see ACB Project # B07-18 Metconazole Review from Paul Golden dated 2/8/08). FDA is currently monitoring for other triazoles using their multiresidue methods with GC-MS.

Primary Evaluator	This DER was originally prepared under contract by Dynamac Corporation.
Approved by	Nancy Dodd, Chemist *Nancy Dodd* Date: 2/20/08 Registration Action Branch 3 Health Effects Division (7509P)

This DER was originally prepared under contract by Dynamac Corporation (2275 Research Boulevard, Suite 300; Rockville, MD 20850; submitted 09/13/2007). The DER has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

46902305 White, M.; Saha, M. (2006) Field Accumulation of Residues of Metconazole (BAS 555 F) and its Metabolites in Rotational Crops from Limited Field Trials in California: Final Report. Project Number: V/04/27123, 2006/7007128. Unpublished study prepared by BASF Corporation and Excel Research Services, Inc. 228 p.

EXECUTIVE SUMMARY:

BASF Corporation has submitted a limited field rotational crop study for metconazole in wheat (small grain), radish (root and tuber vegetable), and lettuce (leafy vegetable). Three limited field rotational crop trials were conducted in the U.S. in Zone 10 (CA) during the 2004-2005 growing season on wheat, radish and lettuce (one trial each).

The trials consisted of one untreated plot and one treated plot with tomato planted as the primary crop. Tomatoes received two broadcast foliar applications of metconazole 1.81 lb ai/gal flowable concentrate (FlC) formulation at 0.24-0.25 lb ai/A at a 14-day retreatment interval, for a total seasonal rate of 0.49 lb ai/A. Applications were made in spray volumes of 20-21 gal/A of water without an adjuvant, using ground equipment.

The primary crop was destroyed ~2-weeks after the final application of metconazole, tilled into the soil, and the ground was prepared for planting according to area-typical agricultural practices. Wheat, radish, and lettuce were grown at plantback intervals (PBIs) of 31, 122, 234, and 396 days after the last application of metconazole to the tomato crop.

At each treatment plot, samples of wheat forage, hay, straw and grain, radish tops and roots, and lettuce were collected at the appropriate crop growth stage.

Samples were analyzed for residues of *cis*- and *trans*-metconazole, metabolites M11, M21, and M30, and the triazole metabolites [1,2,4-triazole (1,2,4-T), triazolylalanine (TA), and triazolylacetic acid (TAA)] using an LC/MS/MS method (BASF Method D0508); samples of wheat hay and straw were not analyzed for the triazole metabolites. Residues of M11, M21, and

M30 were converted to parent equivalents using molecular weight conversion factors of 0.95 for M11 and M21 and 0.96 for M30. The validated limit of quantitation (LOQ) was 0.01 ppm for the parent metconazole (sum of *cis* and *trans* isomers at 0.005 ppm each), M11, M21, and M30 in wheat samples. The validated LOQ was 0.05 ppm for 1,2,4-T, TA, and TAA. The reported limit of detection was 20% of the LOQ. The method was adequate for data collection based on generally acceptable concurrent method recoveries.

Wheat samples were stored frozen (~-10 °C) from harvest to extraction for 252-629 days (8.3-20.7 months) for forage, 227-577 days (7.5-19.0 months) for hay, 182-559 days (6.0-18.4 months) for grain, and 174-551 days (5.7-18.1 months) for straw. Radish tops and roots were stored for 267-631 days (8.8-20.7 months), and lettuce was stored for 238-585 days (7.8-19.2 months). All samples were analyzed within 0-6 days of extraction. Additional storage stability data are required for *cis*- and *trans*-metconazole reflecting storage for up to 18 months for wheat grain and straw, 19 months for lettuce and wheat hay, and 21 months for radish roots and tops and wheat forage.

At the 31-day PBI, maximum quantifiable residues of *cis*-metconazole were found in one sample each of wheat forage and straw (0.005 ppm in each) and two samples of radish tops (0.010-0.011 ppm); residues of trans-metconazole in these samples were <0.005 ppm for maximum total metconazole residues of 0.010 ppm in wheat forage and straw and 0.016 ppm in radish tops at the 31-day PBI. In the same radish top samples, quantifiable residues of metabolite M30 were found at 0.014-0.015 ppm. Residues of metconazole (*cis* and *trans* isomers), M11, M21, and M30 in remaining samples of wheat forage, hay, grain, and straw, radish tops and roots, and lettuce from the 31-, 122-, 234-, and 396-day PBIs were below the LOQ.

Residues of 1,2,4-T were below the LOQ in all samples of wheat forage and grain, radish tops and root, and lettuce from all PBIs; residues of TA were below the LOQ in all samples of lettuce from all PBIs; and residues of TAA were below the LOQ in all samples of radish tops and roots and lettuce. Quantifiable residues of TA and TAA were found in wheat forage and grain from all PBIs, and quantifiable residues of TA were found in radish tops and root from all PBIs. TA residues in wheat forage and grain generally declined with increasing PBI, from a maximum of 0.25 ppm in wheat forage at the 122-day PBI to 0.09 ppm at the 396-day PBI and from a maximum of 1.21 ppm in wheat grain at the 31-day PBI to 0.09 ppm at the 396-day PBI. TA residues in radish tops increased slightly in radish tops from 0.13 ppm at the 31-day PBI to 0.19 ppm at the 396-day PBI, and decreased in radish root from 0.23 ppm at the 31-day PBI to 0.15 ppm at the 396-day PBI. Residues of TAA in wheat forage decreased from a maximum of 0.34 ppm at the 31-day PBI to 0 0.16 ppm at the 396-day PBI, and residues in wheat grain generally decreased from a maximum of 0.77 ppm at the 31-day PBI to 0.45 ppm at the 396-day PBI.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the data depicting residues in rotational crops are tentatively classified as scientifically acceptable pending submission of storage stability data. For rotational crop commodities, additional storage stability data are required for

cis- and *trans*-metconazole reflecting storage for up to 18 months for wheat grain and straw, 19 months for lettuce and wheat hay, and 21 months for radish roots and tops and wheat forage.

The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP#s 348168 and 348206.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported.

A. BACKGROUND INFORMATION

Metconazole [5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol] is a broad-spectrum triazole Group 3 fungicide (sterol biosynthesis inhibitors). There are currently no registered uses of metconazole in the U.S.; however, a tolerance has been established for banana, and a Section 18 emergency exemption and supporting time-limited tolerances have been granted for use on soybean. BASF Corporation has applied for registration of metconazole in the U.S. for use on barley, oats, rye, soybeans, sugar beets, triticale, and wheat.

The chemical structure and nomenclature of metconazole, and the physicochemical properties of the technical grade of metconazole are presented in Tables A.1 and A.2.

TABLE A.1. Metconazole Nomenclature.

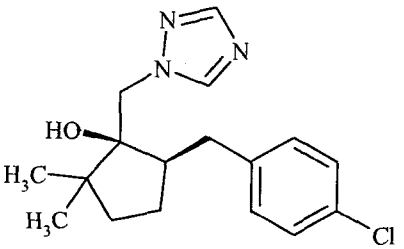
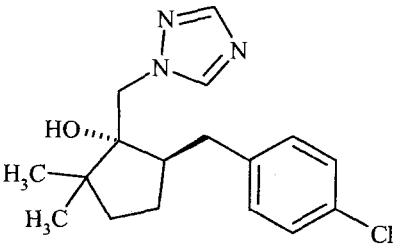
Chemical structure	 *cis*-isomer	 *trans*-isomer
Common name	Metconazole	
Company experimental name	KNF-S-474m (Kureha); BAS 555 F (BASF); V-10116 (Valent)	
IUPAC name	(1RS,5RS:1RS,5SR)-5-(4-chlorobenzyl)-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	
CAS name	5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	
CAS registry number	125116-23-6 (cis- and *trans*-isomers) 115850-27-6 (*cis*-isomer) 115850-28-7 (*trans*-isomer)	
End-use products (EP)	50% WDG (Metconazole 50 WDG Fungicide, EPA File Symbol 59639-RUT) 0.75 lb/gal SC/L (Caramba™ Fungicide, EPA File Symbol No. 7969-EUA) 0.67 lb/gal SC/L formulation (BAS 556 01F Fungicide, EPA File Symbol No. 7969-EUT; also contains the active ingredient pyraclostrobin at 0.83 lb/gal)	

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TABLE A.1. Metconazole Nomenclature.

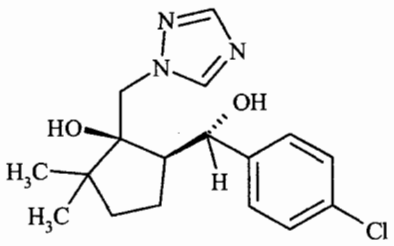
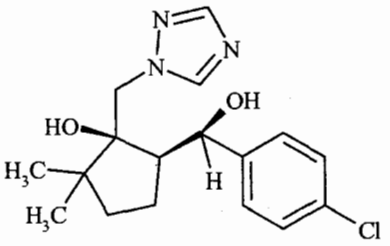
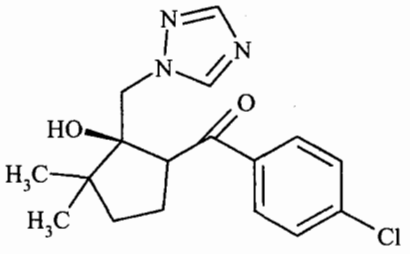
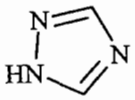
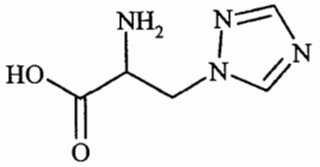
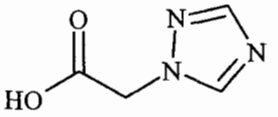
 Metconazole metabolite M11	 Metconazole metabolite M21	 Metconazole metabolite M30
 Triazole metabolite 1,2,4-triazole (1,2,4-T)	 Triazole metabolite triazolylalanine (TA)	 Triazole metabolite triazolylacetic acid (TAA)

Table A.2. Physicochemical Properties of Metconazole

Parameter	Value				References* (MRID)
Melting point/range	100.0-108.4°C (using Electrothermal Digital Melting Point Apparatus) (AC900,768 technical grade)				44721505
pH	5.81 at 25°C (1% aqueous suspension)				46808402
Relative density (20°C)	1.14 (relative density to water at 4°C, using capillary-stoppered, density-specific gravity bottle) (Lot No. AC 8879-140B)				44721505
Water solubility (20°C)	Using shake-flask method: 18.7 ± 1.0 mg/L (*cis*-isomer, WL148271, KNF-S-474m) 13.6 ± 1.7 mg/L (*trans*-isomer, WL148271, KNF-S-474m)				44721505
Solvent solubility (g/L) at 20°C	Solvent	Metconazole	*cis*	*trans*	44721505
	Acetone	363	251	117	
	Methanol	403	294	117	
	dichloromethane	481	343	141	
	ethyl acetate	260	173	90.0	
	Propanol	132	86.6	46.7	
	Toluene	103	66.2	38.0	
	Hexane	1.40	0.929	0.483	
Vapor pressure (20°C)	Using gas-saturation method: $< 1.23 \times 10^{-5}$ Pa or 9.23×10^{-8} mm Hg (metconazole) $< 1.04 \times 10^{-5}$ Pa or 7.80×10^{-8} mm Hg (*cis*-isomer) $< 1.96 \times 10^{-6}$ Pa or 1.47×10^{-8} mm Hg (*trans*-isomer)				44721505
Dissociation constant (pK_a)	11.38±0.03 and 1.06±0.03 (in water at 29.1°C using spectrophotometric method; Lot No. AC 8879-140B)				44721505

Table A.2. Physicochemical Properties of Metconazole

Parameter	Value	References* (MRID)
Octanol/water partition coefficient, Log(K_{OW})	At 20 °C (using flask shaking method): K_{ow} (log K_{ow}) = 7090±989 (3.85) (Lot No. AC 8879-140B) (TGAI) K_{ow} (log K_{ow}) = 7150±803 (3.85) (*cis*-isomer, CL 354,801) K_{ow} (log K_{ow}) = 6800±1700 (3.8) (*trans*-isomer, CL 354,802)	44721505

UV/visible absorption spectrum	pH	Λ	A	log ε	46808403
	cis-isomer				
	2.0	221.4	0.828	4.03	
	6.8		0.8452	4.04	
	7.0		0.9126	4.08	
	10.3		0.7226	3.98	
	trans-isomer				
	2.0	221.4	0.9053	4.07	
	7.0		0.9547	4.10	
	10.1		0.9893	4.11	

* Product Chemistry Reviews: DP #256877, Shyam Mathur, Ph.D., 9/12/2000 and DP #329168, Shyam Mathur, Ph.D., 7/13/07.

B. EXPERIMENTAL DESIGN

B.1. Study Site Information

Three limited field rotational crop trials were conducted in the U.S. in Zone 10 (CA) during the 2004-2005 growing season on wheat, radish and lettuce (one trial each).

The study use pattern is detailed in Table B.1.2. The trials consisted of one untreated plot and one treated plot with tomato planted as the primary crop. Tomatoes received two broadcast foliar applications of metconazole 1.81 lb ai/gal flowable concentrate (FlC) formulation at 0.24-0.25 lb ai/A at a 14-day retreatment interval, for a total seasonal rate of 0.49 lb ai/A. Applications were made in spray volumes of 20-21 gal/A of water without an adjuvant, using ground equipment.

The primary crop was destroyed ~2-weeks after the final application of metconazole, tilled into the soil, and the ground was prepared for planting according to area-typical agricultural practices. The representative crops of wheat, radish, and lettuce were grown at plantback intervals of 31, 122, 234, and 396 days after the last application of metconazole to the tomato crop. Typical agricultural practices were used to grow and maintain the test crops.

Trial site conditions are presented in Table B.1.1. Crop varieties are listed in Table C.3.1. The registrant reported that no maintenance pesticides were applied during the experimental period. The weather conditions at each application and during the field trial duration, along with

historical comparative data were reported for each field trial. Rainfall was supplemented with irrigation as needed. Rainfall and temperatures were reported as being normal, and no variations in weather conditions affected the growth of the crops.

Wheat forage samples were collected 46-73 days after planting by cutting whole, immature green plants 2-3 inches above the soil at the 6-8 inch jointing stage. Hay samples were similarly harvested 73-133 days after planting at early flower to soft dough stage and allowed to dry in the field for up to 3 days prior to collection. Grain and straw were collected 113-205 days after planting, at crop maturity. Grain was separated from the straw by means of a mechanical thresher. Radish RAC samples (roots and tops) were harvested at commercial maturity, 43-73 days after planting. Lettuce samples were collected at commercial maturity, 73-156 days after planting. Decomposed and withered leaves were removed.

TABLE B.1.1 Trial Site Conditions.

Trial Identification: County, State; Year (Trial ID)	Soil characteristics				Meteorological data	
	Type	%OM	pH	CEC meq/g	Rainfall	Temperature
Madera, CA; 2004 (V-27123-04-A)	Loamy sand	0.6	7.4	5.6	Normal	Normal

TABLE B.1.2. Study Use Pattern.

Trial Identification: County, State; Year (Trial ID)	EP[1]	Application					Tank Mix/ Adjuvants
		Method; Timing	Volume GPA[2] [L/ha]	Rate (lb ai/A) [kg ai/ha]	RTI[3] (days)	Total Rate (lb ai/A) [kg ai/ha]	
Madera, CA; 2004 (V-27123-04-A)	1.8 lb ai/gal FIC	1. Broadcast foliar to tomatoes; pre-bloom	21 [196]	0.25 [0.28]	14	0.49	None
		2. Broadcast foliar to tomatoes; bloom to early fruit set	20 [187]	0.24 [0.27]			

[1] EP = End-use Product
[2] GPA = Gallons per acre
[3] RTI = Retreatment Interval

B.2. Sample Handling and Preparation

Samples of each commodity were stored frozen at the field site immediately after harvest. Samples were shipped initially via ACDS freezer truck or overnight courier on dry ice to Valent Technical Center (Dublin, CA) 1-210 days after collection. Samples were stored frozen at Valent for 7-218 days, then shipped by ACDS freezer truck to the analytical laboratory, BASF Agro Research (Research Triangle, NC). At BASF samples were homogenized in the presence of dry ice and stored frozen (~-10 °C) until extraction and analysis.

B.3. Analytical Methodology

Samples of rotational wheat forage, hay, grain and straw, radish tops and roots, and lettuce were analyzed for residues of metconazole, metabolites M11, M21, and M30, and the triazole

metabolites (1,2,4-T, TA, and TAA) using an LC/MS/MS method (BASF Method D0508). Samples of wheat hay and straw were not analyzed for the triazole metabolites. A brief description of the method was included in the MRID.

Briefly, residues of metconazole and its metabolites (M11, M21, and M30) were extracted with acetonitrile (ACN):water (70:30, v:v). The extracts were diluted with methanol:water (80:20, v:v), filtered, and reserved for LC/MS/MS analysis. For determination of residues of 1,2,4-T, TA, and TAA, a separate aliquot of the initial extract was evaporated to dryness, redissolved in 0.1% formic acid in water, filtered, and reserved for LC/MS/MS analysis. Residues of metabolites M11, M21, and M30 were converted to parent equivalents using molecular weight conversion factors of 0.95 for M11 and M21 and 0.96 for M30.

The validated LOQ was 0.01 ppm for the parent metconazole (sum of *cis* and *trans* isomers at 0.005 ppm each), M11, M21, and M30 in wheat samples. The validated LOQ was 0.05 ppm for 1,2,4-T, TA, and TAA. The reported limit of detection was 20% of the LOQ.

The method was validated concurrently with the analysis of field samples using untreated wheat forage, hay, grain, and straw samples, radish root and top samples, and lettuce samples fortified at 0.005 and 0.5 ppm with cis and trans-metconazole; 0.01 and 1.0 ppm with M11, M21, and M30; and at 0.05 and 5.0 ppm with 1,2,4-T, TA, and TAA.

C. RESULTS AND DISCUSSION

Sample storage conditions and durations are summarized in Table C.2. Wheat samples were stored frozen for 252-629 days (8.3-20.7 months) for forage samples, 227-577 days (7.5-19.0 months) for hay samples, 182-559 days (6.0-18.4 months) for grain samples, and 174-551 days (5.7-18.1 months) for straw samples. Radish tops and roots were stored for 267-631 days (8.8-20.7 months), and lettuce samples were stored for 238-585 days (7.8-19.2 months). All samples were analyzed within 0-6 days of extraction. Acceptable storage stability data are available indicating that: (1) residues of *cis*- and *trans*-metconazole are relatively stable under frozen storage conditions in/on wheat grain, rye forage, and wheat straw, lettuce, and carrots for up to 12 months (refer to 46902218.der.doc); (2) residues of M11, M21, and M30 are stable in/on wheat hay, grain, and straw, radish top, and sugar beet root for up to 6 months (refer to 46902223.der.doc); (3) residues of the triazole metabolites are stable/relatively stable in/on wheat grain, radish root, and radish top for up to 6 months (refer to 46902223.der.doc); and (4) residues of TA are stable in/on wheat grain for up to 12 months (refer to 46902221.der.doc). Additional storage stability data are required for *cis*- and *trans*-metconazole reflecting storage for up to 18 months for wheat grain and straw, 19 months for lettuce and wheat hay, and 21 months for radish roots and tops and wheat forage.

Concurrent method recovery data are presented in Table C.1. Samples of rotational crop commodities were analyzed for residues of metconazole (*cis* and *trans* isomers), metabolites M11, M21, and M30, and the triazole metabolites (1,2,4-T, TA, and TAA) using LC/MS/MS Method D0508. Residues of metabolites M11, M21, and M30 were converted to parent equivalents using molecular weight conversion factors of 0.95 for M11 and M21 and 0.96 for

M30. The method was adequate for data collection based on acceptable concurrent method recovery data. Concurrent method recoveries were generally within the acceptable range of 70-120% for wheat commodities (forage, grain, hay, and straw), radish commodities (tops and roots), and lettuce. Low recoveries (61-65%) were obtained for *trans*-metconazole in wheat hay at 0.005 ppm, M11 in radish top at 0.010 ppm and 1,2,4-T in wheat grain at 5.0 ppm.

Apparent residues of *cis*- and *trans*-metconazole, M11, M21, M30 and the triazole metabolites were each below the respective LOQs in two samples each of untreated wheat forage, grain, radish top and root, and lettuce samples from all PBIs. Apparent residues of 1,2,4-T, TA, and TAA were below the LOQ in all wheat forage, grain, radish top and root, and lettuce samples from all PBIs.

Metconazole residue data from the field rotational crop study are presented in Tables C.3.1 (metconazole, M11, M21, and M30) and C.3.2 (triazole metabolites). A summary of residue data for rotated crops is presented in Table C.4. At the 31-day PBI, maximum quantifiable residues of *cis*-metconazole were found in one sample each of wheat forage and straw (0.005 ppm in each) and two samples of radish tops (0.010-0.011 ppm); residues of trans-metconazole in these samples were <0.005 ppm for maximum total metconazole residues of 0.010 ppm in wheat forage and straw and 0.016 ppm in radish tops at the 31-day PBI. In the same radish top samples, quantifiable residues of metabolite M30 were found at 0.014-0.015 ppm. Residues of metconazole (*cis* and *trans* isomers), M11, M21, and M30 in remaining samples of wheat forage, hay, grain, and straw, radish tops and roots, and lettuce from the 31-, 122-, 234-, and 396-day PBIs were below the LOQ.

Residues of 1,2,4-T were below the LOQ in all samples of wheat forage and grain, radish tops and roots, and lettuce from all PBIs; residues of TA were below the LOQ in all samples of lettuce from all PBIs; and residues of TAA were below the LOQ in all samples of radish tops and roots and lettuce. Quantifiable residues of TA and TAA were found in wheat forage and grain from all PBIs, and quantifiable residues of TA were found in radish tops and roots from all PBIs. TA residues in wheat forage and grain generally declined with increasing PBI, from a maximum of 0.25 ppm in wheat forage at the 122-day PBI to 0.09 ppm at the 396-day PBI and from a maximum of 1.21 ppm in wheat grain at the 31-day PBI to 0.09 ppm at the 396-day PBI. TA residues in radish tops increased slightly in radish tops from 0.13 ppm at the 31-day PBI to 0.19 ppm at the 396-day PBI, and decreased in radish root from 0.23 ppm at the 31-day PBI to 0.15 ppm at the 396-day PBI. Residues of TAA in wheat forage decreased from a maximum of 0.34 ppm at the 31-day PBI to 0.16 ppm at the 396-day PBI, and residues in wheat grain generally decreased from a maximum of 0.77 ppm at the 31-day PBI to 0.45 ppm at the 396-day PBI.

TABLE C.1. Summary of Concurrent Recoveries of Metconazole and Metabolites from Rotated Wheat, Radish, and Lettuce Commodities.

Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean (%)
Wheat Forage	*trans*-Metconazole	0.005	1	80	80
		0.500	1	96	96
	cis-Metconazole	0.005	1	76	76
		0.500	1	96	96

TABLE C.1. Summary of Concurrent Recoveries of Metconazole and Metabolites from Rotated Wheat, Radish, and Lettuce Commodities.

Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean (%)
	M11	0.010	1	81	81
		1.000	1	91	91
	M21	0.010	1	97	97
		1.000	1	96	96
	M30	0.010	1	79	79
		1.000	1	97	97
	1,2,4-T	0.050	1	77	77
		5.000	1	73	73
	TA	0.050	1	70	70
		5.000	1	86	86
	TAA	0.050	1	116	116
		5.000	1	107	107
Wheat Grain	*trans*-Metconazole	0.005	1	92	92
		0.500	1	97	97
	cis-Metconazole	0.005	1	83	83
		0.500	1	106	106
	M11	0.010	1	81	81
		1.000	1	116	116
	M21	0.010	1	92	92
		1.000	1	105	105
	M30	0.010	1	76	76
		1.000	1	108	108
	1,2,4-T	0.050	1	77	77
		5.000	1	62	62
	TA	0.050	1	86	86
		5.000	1	75	75
	TAA	0.050	1	98	98
		5.000	1	86	86
Wheat hay	*trans*-Metconazole	0.005	1	61	61
		0.500	1	92	92
	cis-Metconazole	0.005	1	68	68
		0.500	1	92	92
	M11	0.010	1	78	78
		1.000	1	96	96
	M21	0.010	1	94	94
		1.000	1	96	96
	M30	0.010	1	75	75
		1.000	1	95	95
Wheat Straw	*trans*-Metconazole	0.005	1	73	73
		0.500	1	99	99
	cis-Metconazole	0.005	1	81	81
		0.500	1	93	93

TABLE C.1. Summary of Concurrent Recoveries of Metconazole and Metabolites from Rotated Wheat, Radish, and Lettuce Commodities.

Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean (%)
	M11	0.010	1	69	69
		1.000	1	97	97
	M21	0.010	1	77	77
		1.000	1	107	107
	M30	0.010	1	73	73
		1.000	1	113	113
Radish Top	*trans*-Metconazole	0.005	1	79	79
		0.500	1	82	82
	cis-Metconazole	0.005	1	76	76
		0.500	1	74	74
	M11	0.010	1	65	65
		1.000	1	85	85
	M21	0.010	1	83	83
		1.000	1	79	79
	M30	0.010	1	81	81
		1.000	1	81	81
	1,2,4-T	0.050	1	112	112
		5.000	1	83	83
	TA	0.050	1	110	110
		5.000	1	92	92
	TAA	0.050	1	98	98
		5.000	1	104	104
Radish Root	*trans*-Metconazole	0.005	1	76	76
		0.005	1	73	73
	cis-Metconazole	0.010	1	91	91
		0.010	1	75	75
	M30	0.010	1	83	83
	1,2,4-T	0.050	1	72	72
	TA	0.050	1	92	92
	TAA	0.050	1	88	88
Lettuce	*trans*-Metconazole	0.005	1	80	80
		0.500	1	95	95
	cis-Metconazole	0.005	1	75	75
		0.500	1	98	98
	M11	0.010	1	82	82
		1.000	1	91	91
	M21	0.010	1	92	92
		1.000	1	96	96
	M30	0.010	1	88	88
		1.000	1	100	100
	1,2,4-T	0.050	1	94	94
		5.000	1	99	99

TABLE C.1. Summary of Concurrent Recoveries of Metconazole and Metabolites from Rotated Wheat, Radish, and Lettuce Commodities.

Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean (%)
	TA	0.050	1	91	91
		5.000	1	88	88
	TAA	0.050	1	97	97
		5.000	1	98	98

TABLE C.2. Summary of Storage Conditions.

Matrix	Storage Temperature (°C)	Actual Storage Duration[1] Days (Months)	Interval of Demonstrated Storage Stability[2]
Wheat forage	≤-10	252-629 (8.3-20.7)	Acceptable storage stability data are available indicating that residues of *cis*- and *trans*-metconazole are relatively stable in/on wheat grain, rye forage, and wheat straw for up to 12 months; residues of M11, M21, and M30 are stable in/on wheat hay, grain, and straw for up to 6 months; residues of the triazole metabolites are stable/relatively stable in/on wheat grain for up to 6 months; and residues of TA are stable in/on wheat grain stored frozen for up to 12 months.
Wheat hay	≤-10	227-577 (7.5-19.0)	
Wheat grain	≤-10	182-559 (6.0-18.4)	
Wheat straw	≤-10	174-551 (5.7-18.1)	
Radish tops	≤-10	267-631 (8.8-20.7)	Acceptable storage stability data are available indicating that: (1) residues of *cis*- and *trans*-metconazole are relatively stable in/on lettuce and carrots for up to 12 months; residues of M11, M21, and M30 are stable in/on radish top and sugar beet root for up to 6 months; and residues of the triazole metabolites are stable/relatively stable in/on radish root and top for up to 6 months.
Radish roots	≤-10	267-631 (8.8-20.7)	
Lettuce	≤-10	238-585 (7.8-19.2)	Acceptable storage stability data are available indicating that residues of *cis*- and *trans*-metconazole are relatively stable in/on lettuce for up to 12 months; residues of M11, M21, and M30 are stable in/on radish top for up to 6 months; and residues of the triazole metabolites are stable/relatively stable in/on radish top for up to 6 months.

[1] Storage duration from harvest to extraction; samples were analyzed within 1-6 days of extraction.
[2] Refer to 46902218.der.doc, 46902221.der.doc, and 46902223.der.doc.

TABLE C.3.1. Residues of Metconazole, M11, M21, and M30 in Rotational Crops.

Trial ID (County, State; Year)	Crop; Variety	Matrix	Total Rate, (lb ai/A)	Harvest DAP[1]	PBI[2] (days)	Metconazole Residues (ppm parent equivalents)						Total[3]
						Metconazole			Metabolites			
						cis	*trans*	Total	M11	M21	M30	
Madera, CA; 2004 (V-27123-04-A) Zone 10	Winter Wheat; PG507	Forage	0.49	46	31	<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
						0.005	<0.005	0.01	<0.01	<0.01	<0.01	<0.04
				73	122	<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
				67	234	<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
				58	396	<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
Madera, CA; 2004 (V-	Winter Wheat;	Hay	0.49	91	31	<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04

TABLE C.3.1. Residues of Metconazole, M11, M21, and M30 in Rotational Crops.

Trial ID (County, State; Year)	Crop; Variety	Matrix	Total Rate, (lb ai/A)	Harvest DAP[1]	PBI[2] (days)	Metconazole Residues (ppm parent equivalents)						Total[3]
						Metconazole			Metabolites			
						cis	*trans*	Total	M11	M21	M30	
27123-04-A)	PG507			133	122	<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
Zone 10				98	234	<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
				73	396	<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
Madera, CA; 2004 (V-27123-04-A)	Winter Wheat; PG507	Grain	0.49	116	31	<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
Zone 10				205	122	<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
				113	234	<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
				128	396	<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
Madera, CA; 2004 (V-27123-04-A)	Winter Wheat; PG507	Straw	0.49	116	31	0.005	<0.005	0.01	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
Zone 10				205	122	<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
				113	234	<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
				128	396	<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
Madera, CA; 2004 (V-27123-04-A)	Radish, Cherry Belle	Top	0.49	44	31	0.011	<0.005	0.016	<0.01	<0.01	0.015	<0.51
						0.010	<0.005	0.015	<0.01	<0.01	0.014	<0.49
Zone 10				73	122	<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
				57	234	<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
				43	396	<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
Madera, CA; 2004 (V-27123-04-A)	Radish, Cherry Belle	Root	0.49	44	31	<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
Zone 10				73	122	<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
				57	234	<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
				43	396	<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
Madera, CA; 2004 (V-27123-04-A)	Lettuce; Wald-mann's Green	Leaf	0.49	91	31	<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
				156	122	<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04

TABLE C.3.1. Residues of Metconazole, M11, M21, and M30 in Rotational Crops.

Trial ID (County, State; Year)	Crop; Variety	Matrix	Total Rate, (lb ai/A)	Harvest DAP[1]	PBI[2] (days)	Metconazole Residues (ppm parent equivalents)						Total[3]
						Metconazole			Metabolites			
						cis	*trans*	Total	M11	M21	M30	
Zone 10				95	234	<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
				73	396	<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04

[1] DAP = Days After Planting
[2] PBI = Plantback Interval.
[3] Total = total residues; sum of *cis*- and *trans*-metconazole, M11, M21, and M30; values presented as calculated and reported by the petitioner.

TABLE C.3.2. Residues of the Triazole Metabolites in Rotational Crops.

Trial Identification: County, State; Year (Trial ID)	Zone	Crop; Variety	Matrix	Total Rate (lb ai/A)	Harvest DAP[1]	PBI[2]	Triazole Residues (ppm)[3]		
							1,2,4-T	TA	TAA
Madera, CA; 2004 (V-27123-04-A)	10	Winter Wheat; PG507	Forage	0.49	46	31	<0.05	0.15	0.27
							<0.05	0.18	0.34
					73	122	<0.05	0.16	<0.05
							<0.05	0.25	<0.05
					67	234	<0.05	0.11	0.14
							<0.05	0.13	0.13
					58	396	<0.05	0.08	0.14
							<0.05	0.09	0.16
Madera, CA; 2004 (V-27123-04-A)	10	Winter Wheat; PG507	Grain	0.49	116	31	<0.05	1.19	0.77
							<0.05	1.21	0.76
					205	122	<0.05	0.55	0.28
							<0.05	0.65	0.32
					113	234	<0.05	0.80	0.54
							<0.05	0.82	0.58
					128	396	<0.05	0.39	0.45
							<0.05	0.45	0.51
Madera, CA; 2004 (V-27123-04-A)	10	Radish, Cherry Belle	Tops	0.49	44	31	<0.05	0.16	<0.05
							<0.05	0.13	<0.05
					73	122	<0.05	0.10	<0.05
							<0.05	0.10	<0.05
					57	234	<0.05	0.11	<0.05
							<0.05	0.09	<0.05
					43	396	<0.05	0.19	<0.05
							<0.05	0.19	<0.05
Madera, CA; 2004 (V-27123-04-A)	10	Radish, Cherry Belle	Root	0.49	44	31	<0.05	0.19	<0.05
							<0.05	0.23	<0.05
					73	122	<0.05	0.10	<0.05
							<0.05	0.09	<0.05

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TABLE C.3.2. Residues of the Triazole Metabolites in Rotational Crops.

Trial Identification: County, State; Year (Trial ID)	Zone	Crop; Variety	Matrix	Total Rate (lb ai/A)	Harvest DAP [1]	PBI [2]	Triazole Residues (ppm) [3]		
							1,2,4-T	TA	TAA
					57	234	<0.05	0.05	<0.05
							<0.05	0.05	<0.05
					43	396	<0.05	0.15	<0.05
							<0.05	0.15	<0.05
Madera, CA; 2004 (V-27123-04-A)	10	Lettuce; Waldmann's Green	Leaves	0.49	91	31	<0.05	<0.05	<0.05
							<0.05	<0.05	<0.05
					156	122	<0.05	<0.05	<0.05
							<0.05	<0.05	<0.05
					95	234	<0.05	<0.05	<0.05
							<0.05	<0.05	<0.05
					73	396	<0.05	<0.05	<0.05
							<0.05	<0.05	<0.05

[1] DAP = Days After Planting
[2] PBI = Plantback Interval.
[3] NA = Not analyzed

TABLE C.4. Summary of Residue Data in Rotational Crops Following Treatment of a Primary Crop with Metconazole.

Commodity	Total Applic. Rate (lb ai/A)	Analyte	PBI (days)	Residue Levels[1] (ppm)						
				n	Min.	Max.	HAFT[2]	Median (STMdR)	Mean (STMR)	Std. Dev.
Wheat, forage	0.49	*cis*-metconazole	31	2	<0.005	0.005	0.005	0.005	0.005	--
		trans-metconazole		2	<0.005	<0.005	0.005	0.005	0.005	--
		Metconazole		**2**	**<0.01**	**0.01**	**0.01**	**0.01**	**0.01**	--
		M11		2	<0.01	<0.01	0.01	0.01	0.01	--
		M21		2	<0.01	<0.01	0.01	0.01	0.01	--
		M30		2	<0.01	<0.01	0.01	0.01	0.01	--
		Total Residues		2	<0.04	<0.04	0.04	0.04	0.04	--
Wheat, hay	0.49	*cis*-metconazole	31	2	<0.005	<0.005	0.005	0.005	0.005	--
		trans-metconazole		2	<0.005	<0.005	0.005	0.005	0.005	--
		Metconazole		**2**	**<0.01**	**<0.01**	**0.01**	**0.01**	**0.01**	--
		M11		2	<0.01	<0.01	0.01	0.01	0.01	--
		M21		2	<0.01	<0.01	0.01	0.01	0.01	--
		M30		2	<0.01	<0.01	0.01	0.01	0.01	--
		Total Residues		2	<0.04	<0.04	0.04	0.04	0.04	--
Wheat, grain	0.49	*cis*-metconazole	31	2	<0.005	<0.005	0.005	0.005	0.005	--
		trans-metconazole		2	<0.005	<0.005	0.005	0.005	0.005	--
		Metconazole		**2**	**<0.01**	**<0.01**	**0.01**	**0.01**	**0.01**	--
		M11		2	<0.01	<0.01	0.01	0.01	0.01	--
		M21		2	<0.01	<0.01	0.01	0.01	0.01	--

TABLE C.4. Summary of Residue Data in Rotational Crops Following Treatment of a Primary Crop with Metconazole.

Commodity	Total Applic. Rate (lb ai/A)	Analyte	PBI (days)	Residue Levels[1] (ppm)						
				n	Min.	Max.	HAFT[2]	Median (STMdR)	Mean (STMR)	Std. Dev.
		M30		2	<0.01	<0.01	0.01	0.01	0.01	--
		Total Residues		2	<0.04	<0.04	0.04	0.04	0.04	--
Wheat, straw	0.49	*cis*-metconazole	31	2	<0.005	0.005	0.005	0.005	0.005	--
		trans-metconazole		2	<0.005	<0.005	0.005	0.005	0.005	--
		Metconazole		**2**	**<0.01**	**<0.01**	**0.01**	**0.01**	**0.01**	**--**
		M11		2	<0.01	<0.01	0.01	0.01	0.01	--
		M21		2	<0.01	<0.01	0.01	0.01	0.01	--
		M30		2	<0.01	<0.01	0.01	0.01	0.01	--
		Total Residues		2	<0.04	<0.04	0.04	0.04	0.04	--
Radish, tops	0.49	*cis*-Metconazole	31	2	0.010	0.011	0.011	0.011	0.011	--
		trans-Metconazole		2	<0.005	<0.005	0.005	0.005	0.005	--
		Metconazole		**2**	**<0.015**	**0.016**	**0.016**	**0.016**	**0.016**	**--**
		M11		2	<0.01	<0.01	0.01	0.01	0.01	--
		M21		2	<0.01	<0.01	0.01	0.01	0.01	--
		M30		2	0.014	0.015	0.015	0.015	0.015	--
		Total Residues		2	<0.51	<0.49	0.50	0.50	0.50	--
Radish, roots	0.49	*cis*-Metconazole	31	2	<0.005	<0.005	0.005	0.005	0.005	--
		trans-Metconazole		2	<0.005	<0.005	0.005	0.005	0.005	--
		Metconazole		**2**	**<0.01**	**<0.01**	**0.01**	**0.01**	**0.01**	**--**
		M11		2	<0.01	<0.01	0.01	0.01	0.01	--
		M21		2	<0.01	<0.01	0.01	0.01	0.01	--
		M30		2	<0.01	<0.01	0.01	0.01	0.01	--
		Total Residues		2	<0.04	<0.04	0.04	0.04	0.04	--
Lettuce, leaves	0.49	*cis*-Metconazole	31	2	<0.005	<0.005	0.005	0.005	0.005	--
		trans-Metconazole		2	<0.005	<0.005	0.005	0.005	0.005	--
		Metconazole		**2**	**<0.01**	**<0.01**	**0.01**	**0.01**	**0.01**	**--**
		M11		2	<0.01	<0.01	0.01	0.01	0.01	--
		M21		2	<0.01	<0.01	0.01	0.01	0.01	--
		M30		2	<0.01	<0.01	0.01	0.01	0.01	--
		Total residues		2	<0.04	<0.04	0.04	0.04	0.04	--
Wheat, forage	0.49	*cis*-Metconazole	122	2	<0.005	<0.005	0.005	0.005	0.005	--
		trans-Metconazole		2	<0.005	<0.005	0.005	0.005	0.005	--
		Metconazole		**2**	**<0.01**	**<0.01**	**0.01**	**0.01**	**0.01**	**--**
		M11		2	<0.01	<0.01	0.01	0.01	0.01	--
		M21		2	<0.01	<0.01	0.01	0.01	0.01	--

TABLE C.4. Summary of Residue Data in Rotational Crops Following Treatment of a Primary Crop with Metconazole.

Commodity	Total Applic. Rate (lb ai/A)	Analyte	PBI (days)	Residue Levels[1] (ppm)						
				n	Min.	Max.	HAFT[2]	Median (STMdR)	Mean (STMR)	Std. Dev.
		M30		2	<0.01	<0.01	0.01	0.01	0.01	--
		Total residues		2	<0.04	<0.04	0.04	0.04	0.04	--
Wheat, hay	0.49	*cis*-Metconazole	122	2	<0.005	<0.005	0.005	0.005	0.005	--
		trans-Metconazole		2	<0.005	<0.005	0.005	0.005	0.005	--
		Metconazole		**2**	**<0.01**	**<0.01**	**0.01**	**0.01**	**0.01**	--
		M11		2	<0.01	<0.01	0.01	0.01	0.01	--
		M21		2	<0.01	<0.01	0.01	0.01	0.01	--
		M30		2	<0.01	<0.01	0.01	0.01	0.01	--
		Total residues		2	<0.04	<0.04	0.04	0.04	0.04	--
Wheat, grain	0.49	*cis*-Metconazole	122	2	<0.005	<0.005	0.005	0.005	0.005	--
		trans-Metconazole		2	<0.005	<0.005	0.005	0.005	0.005	--
		Metconazole		**2**	**<0.01**	**<0.01**	**0.01**	**0.01**	**0.01**	--
		M11		2	<0.01	<0.01	0.01	0.01	0.01	--
		M21		2	<0.01	<0.01	0.01	0.01	0.01	--
		M30		2	<0.01	<0.01	0.01	0.01	0.01	--
		Total residues		2	<0.04	<0.04	0.04	0.04	0.04	--
Wheat, straw	0.49	*cis*-Metconazole	122	2	<0.005	<0.005	0.005	0.005	0.005	--
		trans-Metconazole		2	<0.005	<0.005	0.005	0.005	0.005	--
		Metconazole		**2**	**<0.01**	**<0.01**	**0.01**	**0.01**	**0.01**	--
		M11		2	<0.01	<0.01	0.01	0.01	0.01	--
		M21		2	<0.01	<0.01	0.01	0.01	0.01	--
		M30		2	<0.01	<0.01	0.01	0.01	0.01	--
		Total residues		2	<0.04	<0.04	0.04	0.04	0.04	--
Radish, tops	0.49	*cis*-Metconazole	122	2	<0.005	<0.005	0.005	0.005	0.005	--
		trans-Metconazole		2	<0.005	<0.005	0.005	0.005	0.005	--
		Metconazole		**2**	**<0.01**	**<0.01**	**0.01**	**0.01**	**0.01**	--
		M11		2	<0.01	<0.01	0.01	0.01	0.01	--
		M21		2	<0.01	<0.01	0.01	0.01	0.01	--
		M30		2	<0.01	<0.01	0.01	0.01	0.01	--
		Total Residues		2	<0.04	<0.04	0.04	0.04	0.04	--

TABLE C.4. Summary of Residue Data in Rotational Crops Following Treatment of a Primary Crop with Metconazole.

Commodity	Total Applic. Rate (lb ai/A)	Analyte	PBI (days)	Residue Levels[1] (ppm)						
				n	Min.	Max.	HAFT[2]	Median (STMdR)	Mean (STMR)	Std. Dev.
Radish, roots	0.49	*cis*-Metconazole	122	2	<0.005	<0.005	0.005	0.005	0.005	--
		trans-Metconazole		2	<0.005	<0.005	0.005	0.005	0.005	--
		Metconazole		**2**	**<0.01**	**<0.01**	**0.01**	**0.01**	**0.01**	**--**
		M11		2	<0.01	<0.01	0.01	0.01	0.01	--
		M21		2	<0.01	<0.01	0.01	0.01	0.01	--
		M30		2	<0.01	<0.01	0.01	0.01	0.01	--
		Total Residues		2	<0.04	<0.04	0.04	0.04	0.04	--
Lettuce, leaves	0.49	*cis*-Metconazole	122	2	<0.005	<0.005	0.005	0.005	0.005	--
		trans-Metconazole		2	<0.005	<0.005	0.005	0.005	0.005	--
		Metconazole		**2**	**<0.01**	**<0.01**	**0.01**	**0.01**	**0.01**	**--**
		M11		2	<0.01	<0.01	0.01	0.01	0.01	--
		M21		2	<0.01	<0.01	0.01	0.01	0.01	--
		M30		2	<0.01	<0.01	0.01	0.01	0.01	--
		Total residues		2	<0.04	<0.04	0.04	0.04	0.04	--
Wheat, forage	0.49	*cis*-Metconazole	234	2	<0.005	<0.005	0.005	0.005	0.005	--
		trans-Metconazole		2	<0.005	<0.005	0.005	0.005	0.005	--
		Metconazole		**2**	**<0.01**	**<0.01**	**0.01**	**0.01**	**0.01**	**--**
		M11		2	<0.01	<0.01	0.01	0.01	0.01	--
		M21		2	<0.01	<0.01	0.01	0.01	0.01	--
		M30		2	<0.01	<0.01	0.01	0.01	0.01	--
		Total residues		2	<0.04	<0.04	0.04	0.04	0.04	--
Wheat, hay	0.49	*cis*-Metconazole	234	2	<0.005	<0.005	0.005	0.005	0.005	--
		trans-Metconazole		2	<0.005	<0.005	0.005	0.005	0.005	--
		Metconazole		**2**	**<0.01**	**<0.01**	**0.01**	**0.01**	**0.01**	**--**
		M11		2	<0.01	<0.01	0.01	0.01	0.01	--
		M21		2	<0.01	<0.01	0.01	0.01	0.01	--
		M30		2	<0.01	<0.01	0.01	0.01	0.01	--
		Total residues		2	<0.04	<0.04	0.04	0.04	0.04	--

TABLE C.4. Summary of Residue Data in Rotational Crops Following Treatment of a Primary Crop with Metconazole.

Commodity	Total Applic. Rate (lb ai/A)	Analyte	PBI (days)	Residue Levels[1] (ppm)						
				n	Min.	Max.	HAFT[2]	Median (STMdR)	Mean (STMR)	Std. Dev.
Wheat, grain	0.49	*cis*-Metconazole	234	2	<0.005	<0.005	0.005	0.005	0.005	--
		trans-Metconazole		2	<0.005	<0.005	0.005	0.005	0.005	--
		Metconazole		**2**	**<0.01**	**<0.01**	**0.01**	**0.01**	**0.01**	**--**
		M11		2	<0.01	<0.01	0.01	0.01	0.01	--
		M21		2	<0.01	<0.01	0.01	0.01	0.01	--
		M30		2	<0.01	<0.01	0.01	0.01	0.01	--
		Total Residues		2	<0.04	<0.04	0.04	0.04	0.04	--
Wheat, straw	0.49	*cis*-Metconazole	234	2	<0.005	<0.005	0.005	0.005	0.005	--
		trans-Metconazole		2	<0.005	<0.005	0.005	0.005	0.005	--
		Metconazole		**2**	**<0.01**	**<0.01**	**0.01**	**0.01**	**0.01**	**--**
		M11		2	<0.01	<0.01	0.01	0.01	0.01	--
		M21		2	<0.01	<0.01	0.01	0.01	0.01	--
		M30		2	<0.01	<0.01	0.01	0.01	0.01	--
		Total Residues		2	<0.04	<0.04	0.04	0.04	0.04	--
Radish, tops	0.49	*cis*-Metconazole	234	2	<0.005	<0.005	0.005	0.005	0.005	--
		trans-Metconazole		2	<0.005	<0.005	0.005	0.005	0.005	--
		Metconazole		**2**	**<0.01**	**<0.01**	**0.01**	**0.01**	**0.01**	**--**
		M11		2	<0.01	<0.01	0.01	0.01	0.01	--
		M21		2	<0.01	<0.01	0.01	0.01	0.01	--
		M30		2	<0.01	<0.01	0.01	0.01	0.01	--
		Total Residues		2	<0.04	<0.04	0.04	0.04	0.04	--
Radish, roots	0.49	*cis*-Metconazole	234	2	<0.005	<0.005	0.005	0.005	0.005	--
		trans-Metconazole		2	<0.005	<0.005	0.005	0.005	0.005	--
		Metconazole		**2**	**<0.01**	**<0.01**	**0.01**	**0.01**	**0.01**	**--**
		M11		2	<0.01	<0.01	0.01	0.01	0.01	--
		M21		2	<0.01	<0.01	0.01	0.01	0.01	--
		M30		2	<0.01	<0.01	0.01	0.01	0.01	--
		Total Residues		2	<0.04	<0.04	0.04	0.04	0.04	--

TABLE C.4. Summary of Residue Data in Rotational Crops Following Treatment of a Primary Crop with Metconazole.

Commodity	Total Applic. Rate (lb ai/A)	Analyte	PBI (days)	Residue Levels[1] (ppm)						
				n	Min.	Max.	HAFT[2]	Median (STMdR)	Mean (STMR)	Std. Dev.
Lettuce, leaves	0.49	*cis*-Metconazole	234	2	<0.005	<0.005	0.005	0.005	0.005	--
		trans-Metconazole		2	<0.005	<0.005	0.005	0.005	0.005	--
		Metconazole		**2**	**<0.01**	**<0.01**	**0.01**	**0.01**	**0.01**	**--**
		M11		2	<0.01	<0.01	0.01	0.01	0.01	--
		M21		2	<0.01	<0.01	0.01	0.01	0.01	--
		M30		2	<0.01	<0.01	0.01	0.01	0.01	--
		Total residues		2	<0.04	<0.04	0.04	0.04	0.04	--
Wheat, forage	0.49	*cis*-Metconazole	396	2	<0.005	<0.005	0.005	0.005	0.005	--
		trans-Metconazole		2	<0.005	<0.005	0.005	0.005	0.005	--
		Metconazole		**2**	**<0.01**	**<0.01**	**0.01**	**0.01**	**0.01**	**--**
		M11		2	<0.01	<0.01	0.01	0.01	0.01	--
		M21		2	<0.01	<0.01	0.01	0.01	0.01	--
		M30		2	<0.01	<0.01	0.01	0.01	0.01	--
		Total Residues		2	<0.04	<0.04	0.04	0.04	0.04	--
Wheat, hay	0.49	*cis*-Metconazole	396	2	<0.005	<0.005	0.005	0.005	0.005	--
		trans-Metconazole		2	<0.005	<0.005	0.005	0.005	0.005	--
		Metconazole		**2**	**<0.01**	**<0.01**	**0.01**	**0.01**	**0.01**	**--**
		M11		2	<0.01	<0.01	0.01	0.01	0.01	--
		M21		2	<0.01	<0.01	0.01	0.01	0.01	--
		M30		2	<0.01	<0.01	0.01	0.01	0.01	--
		Total Residues		2	<0.04	<0.04	0.04	0.04	0.04	--
Wheat, grain	0.49	*cis*-Metconazole	396	2	<0.005	<0.005	0.005	0.005	0.005	--
		trans-Metconazole		2	<0.005	<0.005	0.005	0.005	0.005	--
		Metconazole		**2**	**<0.01**	**<0.01**	**0.01**	**0.01**	**0.01**	**--**
		M11		2	<0.01	<0.01	0.01	0.01	0.01	--
		M21		2	<0.01	<0.01	0.01	0.01	0.01	--
		M30		2	<0.01	<0.01	0.01	0.01	0.01	--
		Total Residues		2	<0.04	<0.04	0.04	0.04	0.04	--

TABLE C.4. Summary of Residue Data in Rotational Crops Following Treatment of a Primary Crop with Metconazole.

Commodity	Total Applic. Rate (lb ai/A)	Analyte	PBI (days)	Residue Levels[1] (ppm)						
				n	Min.	Max.	HAFT[2]	Median (STMdR)	Mean (STMR)	Std. Dev.
Wheat, straw	0.49	*cis*-Metconazole	396	2	<0.005	<0.005	0.005	0.005	0.005	--
		trans-Metconazole		2	<0.005	<0.005	0.005	0.005	0.005	--
		Metconazole		**2**	**<0.01**	**<0.01**	**0.01**	**0.01**	**0.01**	**--**
		M11		2	<0.01	<0.01	0.01	0.01	0.01	--
		M21		2	<0.01	<0.01	0.01	0.01	0.01	--
		M30		2	<0.01	<0.01	0.01	0.01	0.01	--
		Total Residues		2	<0.04	<0.04	0.04	0.04	0.04	--
Radish, tops	0.49	*cis*-Metconazole	396	2	<0.005	<0.005	0.005	0.005	0.005	--
		trans-Metconazole		2	<0.005	<0.005	0.005	0.005	0.005	--
		Metconazole		**2**	**<0.01**	**<0.01**	**0.01**	**0.01**	**0.01**	**--**
		M11		2	<0.01	<0.01	0.01	0.01	0.01	--
		M21		2	<0.01	<0.01	0.01	0.01	0.01	--
		M30		2	<0.01	<0.01	0.01	0.01	0.01	--
		Total Residues		2	<0.04	<0.04	0.04	0.04	0.04	--
Radish, roots	0.49	*cis*-Metconazole	396	2	<0.005	<0.005	0.005	0.005	0.005	--
		trans-Metconazole		2	<0.005	<0.005	0.005	0.005	0.005	--
		Metconazole		**2**	**<0.01**	**<0.01**	**0.01**	**0.01**	**0.01**	**--**
		M11		2	<0.01	<0.01	0.01	0.01	0.01	--
		M21		2	<0.01	<0.01	0.01	0.01	0.01	--
		M30		2	<0.01	<0.01	0.01	0.01	0.01	--
		Total Residues		2	<0.04	<0.04	0.04	0.04	0.04	--
Lettuce, leaves	0.49	*cis*-Metconazole	396	2	<0.005	<0.005	0.005	0.005	0.005	--
		trans-Metconazole		2	<0.005	<0.005	0.005	0.005	0.005	--
		Metconazole		**2**	**<0.01**	**<0.01**	**0.01**	**0.01**	**0.01**	**--**
		M11		2	<0.01	<0.01	0.01	0.01	0.01	--
		M21		2	<0.01	<0.01	0.01	0.01	0.01	--
		M30		2	<0.01	<0.01	0.01	0.01	0.01	--
		Total residues		2	<0.04	<0.04	0.04	0.04	0.04	--

[1] For calculation of the mean and median, the LOQ was used for any results reported as <LOQ in Table C.3.
[2] HAFT = Highest Average Field Trial.

D. CONCLUSION

In limited field rotational crop trials conducted on the representative crops wheat, radish, and lettuce, a primary crop of tomato received two broadcast foliar applications of a 1.81 lb ai/gal FlC formulation of metconazole at a 14-day retreatment interval for a total rate of 0.49 lb ai/A.

The primary crop was destroyed and tilled into the soil ~two weeks after the second application of metconazole, and rotational wheat, radish, and lettuce crops were planted 31, 122, 234, and 396 days after the last application. Samples of wheat matrices (forage, hay, grain, and straw), radish matrices (tops and roots) and lettuce were harvested at the appropriate crop growth stage. An acceptable method was used for quantitation of residues of *cis* and *trans*-metconazole, M11, M21, M30, 1,2,4-T, TA, and TAA in rotational crop matrices. Additional storage stability data are required for *cis*- and *trans*-metconazole reflecting storage for up to 18 months for wheat grain and straw, 19 months for lettuce and wheat hay, and 21 months for radish roots and tops and wheat forage.

E. REFERENCES

DP#:	324541
Subject:	Metconazole. Request for a Tolerance on Imported Bananas. Summary of Analytical Chemistry and Residue Data. Petition Number 9E05052.
From:	N. Dodd
To:	M. Waller
Date:	12/14/05
MRIDs:	44721506, 44721507, 44721508, 44721509, 44721510, and 44721511

F. DOCUMENT TRACKING

RDI: N. Dodd (2/20/08)
Petition Numbers: 6F7094 and 6F7095
DP#s: 348168 and 348206
PC Code: 125619

Template Version June 2005

Primary Evaluator	This DER was originally prepared under contract with Dynamac Corporation.
Approved by	Nancy Dodd, Chemist Nancy Dodd Date: 2/20/08 Registration Action Branch 3 Health Effects Division (7509P)

This DER was originally prepared under contract by Dynamac Corporation (2275 Research Boulevard, Suite 300; Rockville, MD 20850; submitted 09/13/2007). The DER has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORTS:

46665405 Pelz, S.; Weeren, R. (1999) Metconazole (CL 900768): Validation of DFG Method S 19 for the Determination of Residues on Metconazole (CL 900768) as CIS-(CL 354801) and TRANS-Isomer (CL 354802) in Plant Material, Foodstuff of Animal Origin and Soil. Project Number: MK/240/003, CYA/9907V, AZ/M8995/99. Unpublished study prepared by Dr. Specht and Partner, R-VEE-R Distributing Company and Landesuntersuchungsamt fuer das Gesundheitswesen Nordbayern. 127 p.

46665407 Class, T. (2003) Metconazole (CL 900768): Assessment and Validation of the Multi-Residue Enforcement Method DFG S19 with Modified Extraction (and with SDF Cleanup Method 5 for Fatty/Oily Matrices) for the Determination of Metconazole (CL 900768) in Plant Material (Wheat Grain, Grape, Pea and Oilseed Rape Seed) and in Foodstuff of Animal Origin (Milk, Egg, Bovine Muscle and Fat). Project Number: P/349/G, CFS/1999/127, 2003/7007238. Unpublished study prepared by PTRL Europe Gmbh. 180 p.

EXECUTIVE SUMMARY:

BASF has submitted a modified version of the German multiresidue method DFG S19 (referred to as method DFG S19 with modified extraction) for the determination of residues of metconazole (*cis* and *trans* isomers) in/on crop and livestock commodities. BASF is proposing method DFG S19 as an enforcement method for livestock commodities and has submitted supporting method validation data on grapes, peas, wheat grain, rapeseed, milk, bovine muscle, eggs, and bovine fat, and an independent laboratory validation (ILV) for method DFG S19. This method was not used for data collection for any of the studies associated with DP#s 348168 and 348206.

For grape, pea, wheat grain, milk, bovine muscle, and egg, samples are homogenized with water:acetone (1:2, v:v), then combined with ethyl acetate:cyclohexane (1:1, v:v), and sodium chloride. An aliquot of the resulting organic phase is filtered through sodium sulfate and concentrated by evaporation, then reconstituted in ethyl acetate. Sodium sulfate:sodium chloride (1:1, w:w) and cyclohexane are added, and the salts are allowed to precipitate. For fat or

rapeseed, samples are blended with acetonitrile (ACN):acetone (9:1, v:v) and Calflo E and Celite as adsorbents, filtered, and combined with isooctane. The extract is concentrated and redissolved in ethyl acetate:cyclohexane (1:1, v:v) as above. For all matrices, the resulting ethyl acetate/cyclohexane fractions are subjected to sequential cleanup on a gel permeation chromatography (GPC) column (residues eluted with ethyl acetate/cyclohexane) and a silica gel mini-column (residues eluted with acetone). The resulting eluate is concentrated by rotary evaporation and reconstituted in ethyl acetate for GC/NPD or GC/MS (confirmatory procedure) analysis. The method limit of quantitation (LOQ) is 0.01 ppm for each isomer.

Acceptable method validation recoveries were obtained for *cis*- and *trans*-metconazole from samples of grape, pea, wheat grain, rapeseed, milk, bovine muscle, egg, and bovine fat fortified with each isomer at 0.01 ppm (LOQ) and 0.10 ppm. Recoveries were generally in the acceptable range of 70-120% for both analytes in all matrices. The fortification levels used in method validation are adequate to bracket expected residue levels of *cis*- and *trans*-metconazole in livestock matrices.

An acceptable confirmatory procedure (GC/MS) was included for the method. No radiovalidation data were submitted; however, because DFG S19 is an established multiresidue method, these data are not required.

Method DFG S19 with modified extraction has undergone an acceptable ILV with grape, pea, wheat grain, rapeseed, milk, bovine muscle, egg, and bovine fat fortified with each isomer at 0.01 and 0.10 ppm. Adequate recoveries, generally within the acceptable range of 70-120%, were obtained for all matrices at both fortification levels.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the analytical method test data are classified as scientifically acceptable. The proposed enforcement method was forwarded to the Analytical Chemistry Branch (ACB/BEAD) for petition method review (DP #339992, N. Dodd, 5/29/07).

The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP#s 348168 and 348206.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an impact on the validity of the study.

A. BACKGROUND INFORMATION

Metconazole [5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol] is a broad-spectrum triazole Group 3 fungicide (sterol biosynthesis

inhibitors). There are currently no registered uses of metconazole in the U.S.; however, a tolerance has been established for banana, and a Section 18 emergency exemption and supporting time-limited tolerances have been granted for use on soybean. BASF Corporation has applied for registration of metconazole in the U.S. for use on barley, oats, rye, soybeans, sugar beets, triticale, and wheat.

The chemical structure and nomenclature of metconazole, and the physicochemical properties of the technical grade of metconazole are presented in Tables A.1 and A.2.

Table A.1. Metconazole Nomenclature.

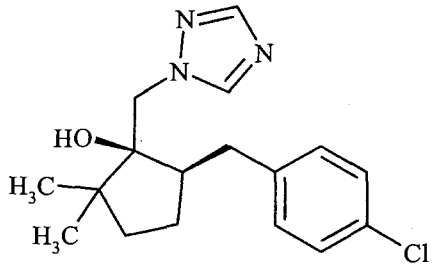
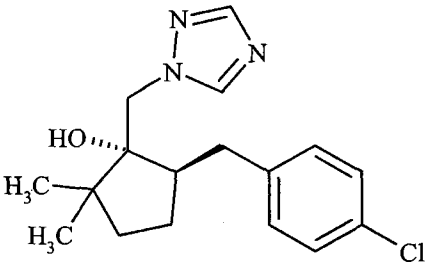
Chemical structure	 *cis*-isomer	 *trans*-isomer
Common name	Metconazole	
Company experimental name	KNF-S-474m (Kureha); BAS 555 F (BASF); V-10116 (Valent)	
IUPAC name	(1RS,5RS:1RS,5SR)-5-(4-chlorobenzyl)-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	
CAS name	5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	
CAS registry number	125116-23-6 (*cis*- and *trans*-isomers) 115850-27-6 (*cis*-isomer) 115850-28-7 (*trans*-isomer)	
End-use products (EP)	50% WDG (Metconazole 50 WDG Fungicide, EPA File Symbol 59639-RUT) 0.75 lb/gal SC/L (Caramba™ Fungicide, EPA File Symbol No. 7969-EUA) 0.67 lb/gal SC/L formulation (BAS 556 01F Fungicide, EPA File Symbol No. 7969-EUT; also contains the active ingredient pyraclostrobin at 0.83 lb/gal)	

Table A.2. Physicochemical Properties of Metconazole

Parameter	Value	References* (MRID)
Melting point/range	100.0-108.4°C (using Electrothermal Digital Melting Point Apparatus) (AC900,768 technical grade)	44721505
pH	5.81 at 25°C (1% aqueous suspension)	46808402
Relative density (20°C)	1.14 (relative density to water at 4°C, using capillary-stoppered, density-specific gravity bottle) (Lot No. AC 8879-140B)	44721505
Water solubility (20°C)	Using shake-flask method: 18.7 ± 1.0 mg/L (*cis*-isomer, WL148271, KNF-S-474m) 13.6 ± 1.7 mg/L (*trans*-isomer, WL148271, KNF-S-474m)	44721505

Table A.2. Physicochemical Properties of Metconazole

Parameter	Value				References* (MRID)
Solvent solubility (g/L) at 20°C	Solvent	Metconazole	*cis*	*trans*	44721505
	acetone	363	251	117	
	methanol	403	294	117	
	dichloromethane	481	343	141	
	ethyl acetate	260	173	90.0	
	propanol	132	86.6	46.7	
	toluene	103	66.2	38.0	
	Hexane	1.40	0.929	0.483	
Vapor pressure (20°C)	Using gas-saturation method: $< 1.23 \times 10^{-5}$ Pa or 9.23×10^{-8} mm Hg (metconazole) $< 1.04 \times 10^{-5}$ Pa or 7.80×10^{-8} mm Hg (*cis*-isomer) $< 1.96 \times 10^{-6}$ Pa or 1.47×10^{-8} mm Hg (*trans*-isomer)				44721505
Dissociation constant (pK_a)	11.38±0.03 and 1.06±0.03 (in water at 29.1°C using spectrophotometric method; Lot No. AC 8879-140B)				44721505
Octanol/water partition coefficient, Log(K_{OW})	At 20 °C (using flask shaking method): K_{ow} (log K_{ow}) = 7090±989 (3.85) (Lot No. AC 8879-140B) (TGAI) K_{ow} (log K_{ow}) = 7150±803 (3.85) (*cis*-isomer, CL 354,801) K_{ow} (log K_{ow}) = 6800±1700 (3.8) (*trans*-isomer, CL 354,802)				44721505
UV/visible absorption spectrum	pH	λ	A	log ε	46808403
	cis-isomer				
	2.0	221.4	0.828	4.03	
	6.8		0.8452	4.04	
	7.0		0.9126	4.08	
	10.3		0.7226	3.98	
	trans-isomer				
	2.0	221.4	0.9053	4.07	
	7.0		0.9547	4.10	
	10.1		0.9893	4.11	

* Product Chemistry Reviews: DP #256877, Shyam Mathur, Ph.D., 9/12/2000 and DP #329168, Shyam Mathur, Ph.D., 7/13/07.

B. MATERIALS AND METHODS

B.1. Data-Gathering Method

Not applicable to this submission.

B.2. Enforcement Method

The petitioner has submitted a description and validation data (MRID 46665405) for German multiresidue method DFG S19 with modified extraction entitled "Gas-Chromatographic Determination of Pesticide Residues after Clean-up by Gel-Chromatography and Mini-Silica Gel-Column Chromatography 6. Communication: Replacement of dichloromethane by ethyl acetate/cyclohexane in liquid-liquid partition and simplified conditions for extraction and liquid-liquid partition." Literature citations for the method and associated clean-up steps and modifications were included in the submission. BASF is proposing the method as a tolerance enforcement method for livestock commodities.

B.2.1. Principle of the Method:

Method DFG S19 is a standard European multiresidue method that was modified for the determination of residues of *cis*- and *trans*-metconazole in a variety of crop and livestock commodities. The method was modified to change the extraction solvent from dichloromethane to ethyl acetate:cyclohexane (1:1, v:v) and to modify the extraction procedure for oily commodities (Cleanup Method 5). The parameters of the method are described in Table B.1.1.

For grape, pea, wheat grain, milk, bovine muscle, and egg, samples are homogenized with water:acetone (1:2, v:v), then combined with ethyl acetate:cyclohexane (1:1, v:v), and sodium chloride. An aliquot of the resulting organic phase is filtered through sodium sulfate and concentrated by evaporation, then reconstituted in ethyl acetate. Sodium sulfate:sodium chloride (1:1, w:w) and cyclohexane are added, and the salts are allowed to precipitate. For fat or rapeseed, samples are blended with ACN:acetone (9:1, v:v) and Calflo E and Celite as adsorbents, filtered, and combined with isooctane. The extract is concentrated and redissolved in ethyl acetate:cyclohexane (1:1, v:v) as above. For all matrices, the resulting ethyl acetate/cyclohexane fractions are subjected to sequential cleanup on a GPC column (residues eluted with ethyl acetate/cyclohexane) and a silica gel mini-column (residues eluted with acetone). The resulting eluate is concentrated by rotary evaporation and reconstituted in ethyl acetate for GC/NPD or GC/MS (confirmatory procedure) analysis. The method LOQ is 0.01 ppm for each isomer.

TABLE B.2.1. Summary Parameters for the Analytical Enforcement Method for the Quantitation of Metconazole Residues in Grape, Pea, Wheat Grain, Rapeseed, Milk, Bovine Muscle, Egg, and Bovine Fat.	
Method ID	Multiresidue method DFG S19 with modified extraction.
Analytes	*cis*-Metconazole and *trans*-metconazole
Extraction solvent/technique	Grape, pea, wheat grain, milk, bovine muscle, and egg: Samples are homogenized with water:acetone (1:2, v:v), then combined with ethyl acetate:cyclohexane (1:1, v:v), and sodium chloride. An aliquot of the resulting organic phase is filtered through sodium sulfate and concentrated by evaporation, then reconstituted in ethyl acetate. Sodium sulfate:sodium chloride (1:1, w:w) and cyclohexane are added, and the salts are allowed to precipitate. Fat or rapeseed (Cleanup Method 5): Samples are blended with ACN:acetone (9:1, v:v) and Calflo E and Celite as adsorbents, filtered, and combined with isooctane. The extract is concentrated under a stream of nitrogen, and redissolved in ethyl acetate:cyclohexane (1:1, v:v) as above.

TABLE B.2.1. Summary Parameters for the Analytical Enforcement Method for the Quantitation of Metconazole Residues in Grape, Pea, Wheat Grain, Rapeseed, Milk, Bovine Muscle, Egg, and Bovine Fat.	
Cleanup strategies	The ethyl acetate/cyclohexane fractions are applied to a GPC column, and residues are eluted with ethyl acetate:cyclohexane (1:1, v:v). Toluene is added, and the eluate is concentrated by evaporation and applied to a silica gel mini-column; residues are eluted with acetone. The eluate is concentrated by rotary evaporation, and the residue is reconstituted in ethyl acetate.
Instrument/Detector	GC using a DB-5 column and a nitrogen/phosphorus detection (NPD) or mass selective detector (MS; confirmatory procedure) with SIM at m/z 319 for quantitation and 125, 250 for verification.
Standardization method	External standardization using a calibration curve for each isomer.
Stability of std solutions	Not addressed.
Retention times	GC/NPD: *cis*-metconazole: ~16.9 min.; *trans*-metconazole: ~17.8 min. GC/MS: *cis*-metconazole: ~11.6 min.; *trans*-metconazole: ~11.9 min.

C. RESULTS AND DISCUSSION

C.1. Data-Gathering Method

Not applicable to this submission.

C.2. Enforcement Method

The method validation data are presented in Table C.1.1. Method validation was conducted by Dr. Specht & Partner (Hamburg, Germany). HED notes that Dr. Specht was also the developer of the method and modifications.

The method validation recoveries of *cis*- and *trans*-metconazole were adequate from samples of grape, pea, wheat grain, rapeseed, milk, bovine muscle, egg, and bovine fat fortified with each isomer at 0.01 ppm (LOQ) and 0.10 ppm. Recoveries were generally in the acceptable range of 70-120% for both analytes in all matrices. The fortification levels used in method validation are adequate to bracket expected residue levels of *cis*- and *trans*-metconazole in livestock matrices.

The performing laboratory reported that the method was run as written without problems and that there were no critical steps. The laboratory did note that for silica gel clean-up, the elution profile of the metconazole isomers must be established with each new batch of gel. Extraction and cleanup time for a set of 12 samples was reported to be ~8 worker hours spread over 2 working days.

The method characteristics for method DFG S19 with modified extraction are presented in Table C.2.2. An acceptable confirmatory procedure (GC/MS) was included for the method. No radiovalidation data were submitted; however, because DFG S19 is an established multiresidue method, these data are not required.

TABLE C.2.1. Recovery Results from Method Validation of Grape, Pea, Wheat Grain, Rapeseed, Milk, Bovine Muscle, Egg, and Bovine Fat using the Enforcement Analytical Method. [1]

Matrix	Spiking Level (ppm)	Recoveries Obtained (%)	Mean Recovery ± Std. Dev. [CV] (%)
***cis*-Metconazole**			
Grape	0.01	76, 79, 81, 85, 87	82 ± 4.4 [5.5]
	0.1	74, 84, 85, 86, 87	83 ± 5.3 [6.3]
Pea	0.01	89, 90, 90, 97, 102	94 ± 5.7 [6.1]
	0.1	79, 84, 86, 87, 88	85 ± 3.6 [4.2]
Wheat grain	0.01	72, 75, 78, 80, 82	77 ± 4.0 [5.1]
	0.1	62, 70, 70, 78, 81	72 ± 7.5 [10]
Rapeseed	0.01	88, 110, 117, 119, 123	111 ± 14 [12]
	0.1	70, 76, 80, 85, 94	81 ± 9.1 [11]
Rapeseed (MSD)[1]	0.01	87, 87, 88, 92, 95	90 ± 3.6 [4.0]
	0.1	78, 81, 81, 85, 86	82 ± 3.3 [4.0]
Milk	0.01	74, 77, 89, 94, 104	88 ± 12 [14]
	0.1	86, 91, 93, 96, 98	93 ± 4.7 [5.0]
Bovine muscle	0.01	73, 80, 81, 89, 102	85 ± 11 [13]
	0.1	90, 90, 98, 100, 101	96 ± 5.4 [5.6]
Egg	0.01	79, 81, 88, 90, 94	86 ± 6.3 [7.3]
	0.1	77, 79, 81, 83, 85	81 ± 3.2 [3.9]
Bovine fat	0.01	63, 72, 73, 80, 82	74 ± 7.5 [10]
	0.1	79, 81, 86, 90, 91	85 ± 5.3[6.2]
Bovine fat (MSD)[2]	0.01	82, 91, 96, 99, 113	96 ± 11 [12]
	0.1	77, 78, 88, 90, 94	85 ± 7.5 [8.8]
***trans*-Metconazole**			
Grape	0.01	73, 81, 86, 87, 99	85 ± 9.5 [11]
	0.1	79, 88, 89, 89, 90	87 ± 4.5 [5.2]
Pea	0.01	89, 90, 100, 100, 102	96 ± 6.2 [6.4]
	0.1	85, 89, 89, 89, 93	89 ± 2.8 [3.2]
Wheat grain	0.01	75, 79, 85, 86, 90	83 ± 6.0 [7.2]
	0.1	76, 78, 83, 85, 87	82 ± 4.66 [5.7]
Rapeseed	0.01	72, 72, 90, 99, 102	87 ± 15 [17]
	0.1	79, 81, 85, 86, 97	86 ± 6.9 [8.2]
Rapeseed (MSD)[1]	0.01	91, 97, 103, 104, 109	101 ± 6.9 [6.9]
	0.1	82, 86, 87, 101, 108	93 ± 11 [12]
Milk	0.01	82, 83, 90, 91, 96	88 ± 5.9 [6.6]
	0.1	93, 97, 98, 98, 101	97 ± 2.9 [3.0]
Bovine muscle	0.01	88, 101, 104, 108, 108	102 ± 8.3 [8.1]
	0.1	92, 101, 104, 105, 110	102 ± 6.7 [6.5]
Egg	0.01	85, 95, 102, 103, 110	99 ± 9.5 [9.6]
	0.1	81, 82, 82, 85, 94	85 ± 5.4 [6.3]
Bovine fat	0.01	71, 72, 80, 80, 86	78 ± 6.3 [8.0]
	0.1	71, 73, 74, 75, 81	75 ± 3.8 [5.0]
Bovine fat (MSD)[2]	0.01	74, 83, 92, 93, 97	88 ± 9.3 [11]
	0.1	67, 71, 72, 85, 89	77 ± 9.6 [13]

[1] Fortification standards were prepared in acetone.
[2] Confirmatory GC/MS analysis conducted due to interferences from the sample matrix at the retention time of *cis*-metconazole in GC/NPD analysis of control samples.

TABLE C.2.2. Characteristics for the Enforcement Analytical Method for the Quantitation of Metconazole Residues in Grape, Pea, Wheat Grain, Rapeseed, Milk, Bovine Muscle, Egg, and Bovine Fat.	
Analytes	*cis*-Metconazole and *trans*-metconazole
Equipment ID	HP 6890 GC system equipped with NPD or MSD, J&W Scientific DB-5 column
Limit of quantitation (LOQ)	0.01 ppm (routine)
Limit of detection (LOD)	0.002 ppm
Accuracy/Precision	Recoveries for both analytes in all commodities were generally within the acceptable range of 70-120%.
Reliability of the Method [ILV]	An independent laboratory method validation [ILV], Study No. P 349 G, CFS 1999-127, was conducted to verify the reliability of the DFG S19 method for the determination of metconazole residues in grape, pea, wheat grain, rapeseed, soil, milk, bovine muscle, eggs and fat. The values obtained are indicative that the method is reliable; see Section C.3.
Linearity	The method/detector response was linear (coefficient of determination, r^2= 0.9999 for *cis*-metconazole and 0.9998 for *trans*-metconazole) within the range of 0.0067-1.0 µg/mL.
Specificity	Some interference was noted at the *cis*-isomer retention time in oily matrices; the performing laboratory recommended that GC/MS analysis be used for these matrices. Peaks were well defined and symmetrical. There appeared to be no carryover to the following chromatograms.

C.3. Independent Laboratory Validation

An ILV (MRID 46665407) for method DFG S19 with modified extraction was conducted by PTRL Europe (Ulm, Germany). HED notes that the study appears to have been originally intended as a method validation study, rather than an ILV; therefore a number of the parameters specified under 860.1340 were not addressed.

Samples of untreated of grape, pea, wheat grain, rapeseed, milk, bovine muscle, egg, and bovine fat (obtained locally by the laboratory, except for rapeseed, which was provided by the study sponsor) were fortified with metconazole at 0.01 (LOQ) and 0.1 ppm. Samples were analyzed according to the method procedures described in Table B.2.1 with the following exceptions: samples were analyzed using a DB-1 (nonpolar) column instead of a DB-5 column; and confirmatory analysis was conducted using a DB-17 (medium polar) column and NPD, rather than GC/MS.

The ILV was successful for all matrices. Recoveries are reported in Table C.3.1.

The independent laboratory evaluated the use of Cleanup Method 5 for eggs and concluded that the modified extraction procedure used for most plant matrices and muscle was preferable for analysis of eggs. The laboratory also assessed full scan GC/MS as a potential confirmatory method. No quantitative results were provided; however, the laboratory concluded that the method may be useful for identification based on mass spectral information.

HED notes that the ILV did not address the following parameters specified under 860.1340: (1) report of contact, if any between the method developer and the performing laboratory; (2) identification of number of sample sets required to achieve acceptable recoveries; (3) description of any problems encountered; (4) identification of any critical steps; and (5) identification of number of work-hours/calendar days required for one set of samples. Although not specifically stated by the laboratory, it does not appear from the report that any difficulties were encountered in performing the method or that there was communication with the method developer. HED has concluded that, in consideration of the extensive nature of the study, the ILV is acceptable for purposes of the subject action.

TABLE C.3.1. Recovery Results Obtained by an Independent Laboratory Validation of the Enforcement Method for the Determination of Metconazole in Grape, Pea, Wheat Grain, Rapeseed, Bovine Muscle, Milk, Egg, and Fat.[1]

Matrix	Spiking Level (ppm)	Recoveries Obtained	Mean Recovery ± Std. Dev. [CV] (%)
		***cis*-Metconazole**	
Grape	0.01	71, 73, 76, 100, 104	85 ± 16 [18]
	0.1	60[2], 89, 91, 92, 92, 106	94 ± 6.8 [7.3]
Grape (DB-17 column)	0.01	101	101
	0.1	88	88
Pea	0.01	72, 73, 83, 89, 109	85 ± 15 [18]
	0.1	67, 73, 75, 76, 80, 87, 87	78 ± 7.4 [9.4]
Pea (DB-17 column)	0.01	106	106
	0.1	100	100
Wheat grain	0.01	74, 80, 91, 92, 94	86 ± 8.7 [10]
	0.1	80, 81, 82, 83, 86	82 ± 2.3 [2.8]
Wheat grain (DB-17 column)	0.01	92	92
	0.1	77	77
Rapeseed	0.01	76, 84, 102, 103, 105	94 ± 13 [14]
	0.1	82, 87, 88, 96, 106	92 ± 9.4 [10]
Rapeseed (DB-17 column)	0.01	77	77
	0.1	102	102
Milk	0.01	73, 74, 79, 87, 95	82 ± 9.3 [11]
	0.1	71, 72, 78, 79, 93	79 ± 8.8 [11]
Milk (DB-17 column)	0.01	77	77
	0.1	96	96
Bovine muscle	0.01	71, 82, 84, 87, 94, 97, 102, 107	91 ± 12 [13]
	0.1	47[2], 61, 68, 70, 79, 81, 85, 87	76 ± 9.7 [13]
Bovine muscle (DB-17 column)	0.01	95	95
	0.1	89	89
Egg	0.01	86, 87, 93, 105, 107, 108, 110, 126	103 ± 13 [13]
	0.1	67, 84, 89, 89, 95, 98, 104, 105	91 ± 12 [13]
Egg (DB-17 column)	0.01	91, 94	93
	0.1	86	86
Bovine fat	0.01	74, 79, 91, 92, 94	86 ± 9 [10]
	0.1	9[2], 75, 81, 81, 92	82 ± 7.1 [8.6]

TABLE C.3.1. Recovery Results Obtained by an Independent Laboratory Validation of the Enforcement Method for the Determination of Metconazole in Grape, Pea, Wheat Grain, Rapeseed, Bovine Muscle, Milk, Egg, and Fat.[1]

Matrix	Spiking Level (ppm)	Recoveries Obtained	Mean Recovery ± Std. Dev. [CV] (%)
Bovine fat (DB-17 column)	0.01	110	110
	0.1	109	109
***trans*-Metconazole**			
Grape	0.01	80, 88, 92, 92, 100	90 ± 7.3 [8.0]
	0.1	59[2], 84, 89, 89, 92, 105	92 ± 7.9 [8.6]
Grape (DB-17 column)	0.01	100	100
	0.1	90	90
Pea	0.01	67, 79, 84, 92, 104	85 ± 13 [16]
	0.1	62, 73, 76, 80, 80, 88, 93	79 ± 10 [13]
Pea (DB-17 column)	0.01	105	105
	0.1	101	101
Wheat grain	0.01	75, 89, 95, 98, 100	91 ± 10 [11]
	0.1	79, 81, 81, 84, 88	83 ± 3.5 [4.2]
Wheat grain (DB-17 column)	0.01	108	108
	0.1	78	78
Rapeseed	0.01	68, 75, 93, 102, 105	89 ± 16 [19]
	0.1	76, 80, 81, 90, 101	86 ± 10 [12]
Rapeseed (DB-17 column)	0.01	80	80
	0.1	109	109
Milk	0.01	74, 74, 83, 85, 86	80 ± 5.9 [7.4]
	0.1	71, 74, 77, 79, 96	79 ± 9.8 [12]
Milk (DB-17 column)	0.01	73	73
	0.1	90	90
Bovine muscle	0.01	60, 67, 68, 74, 80, 83, 83, 91	76 ± 10 [14]
	0.1	50[2], 65, 69, 72, 76, 77, 86, 88	76 ± 8.5 [11]
Bovine muscle (DB-17 column)	0.01	91	91
	0.1	91	91
Egg	0.01	72, 72, 74, 75, 77, 83, 86, 102	80 ± 10 [13]
	0.1	62, 78, 84, 90, 91, 92, 97, 99	87 ± 12 [14]
Egg (DB-17 column)	0.01	86, 89	88
	0.1	85	85
Bovine fat	0.01	68, 77, 81, 82, 88	79 ± 7.4 [9.3]
	0.1	5[2], 68, 70, 79, 86	76 ± 8.3 [11]
Bovine fat (DB-17 column)	0.01	79	79
	0.1	98	98

[1] Except where noted, results reflect analysis using a DB-1 column (30 m for rapeseed, egg, and fat, and 15 m for all other matrices).

[2] The petitioner reported that a portion of this sample may have been lost (low recoveries were observed for both isomers); not included in calculation of mean and standard deviation.

D. CONCLUSION

Adequate method validation data have been submitted for the proposed GC/NPD enforcement method, DFG S19 with modified extraction. Acceptable method validation recoveries were obtained for *cis*- and *trans*-metconazole from samples of grape, pea, wheat grain, rapeseed, milk, bovine muscle, egg and fat fortified with each isomer at 0.01 ppm (LOQ) and 0.10 ppm. Recoveries were generally in the acceptable range of 70-120% for both analytes in all matrices. The fortification levels used in method validation are adequate to bracket expected residue levels of *cis*- and *trans*-metconazole in livestock matrices.

An acceptable confirmatory procedure (GC/MS) was included for the method and the method has undergone a successful ILV. No radiovalidation data were submitted; however, because DFG S19 is an established multiresidue method, these data are not required.

The proposed enforcement method was forwarded to the Analytical Chemistry Branch (ACB/BEAD) for petition method review (DP #339992, N. Dodd, 5/29/07).

E. REFERENCES

DP#:	324541
Subject:	Metconazole. Request for a Tolerance on Imported Bananas. Summary of Analytical Chemistry and Residue Data. Petition Number 9E05052.
From:	N. Dodd
To:	M. Waller
Date:	12/14/05
MRIDs:	44721506, 44721507, 44721508, 44721509, 44721510, and 44721511

F. DOCUMENT TRACKING

RDI: N. Dodd (2/20/08)
Petition Numbers: 6F7094 and 6F7095
DP#s: 348168 and 348206
PC Code: 125619

Template Version June 2005

Primary Evaluator	This DER was originally prepared under contract by Dynamac Corporation.
Approved by	Nancy Dodd, Chemist *Nancy Dodd* Date: 2/20/08 Registration Action Branch 3 Health Effects Division (7509P)

This DER was originally prepared under contract by Dynamac Corporation (2275 Research Boulevard, Suite 300; Rockville, MD 20850; submitted 09/13/2007). The DER has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORTS:

46901704 Fujie, G. (2006) RM-41C-1-1: Determination of cis-Metconazole and trans-Metconazole in Crops. Project Number: RM/41C/1/1, RM/41C/4. Unpublished study prepared by Valent Dublin Laboratory. 43 p.

46901706 Noon, P. (2006) Independent Laboratory Validation of the Analytical Method RM-41C-1, Determination of cis-Metconazole and trans-Metconazole in Crops. Project Number: 200600132, 120/010, VP/29874. Unpublished study prepared by North Coast Laboratories, Inc. 105 p.

EXECUTIVE SUMMARY:

Valent U.S.A. Corporation has submitted GC/NPD method RM-41C-1-1 for the determination of residues of *cis* and *trans*-metconazole in/on crops. The method is a revision of method RM-41C-1, which was used for data collection in the peanut, stone fruit, and tree nut crop field trials and peanut and plum processing studies submitted by Valent and reviewed under DP#s 348168 and 348206. According to the petitioner, method RM-41C-1-1 reflects minor revisions to the original method to correct the nomenclature for *cis*- and *trans*-metconazole and to correct minor typographical errors. Valent is proposing method RM-41C-1-1 as a tolerance enforcement method, and has submitted supporting method validation data on peach and an independent laboratory validation (ILV) of the method. A confirmatory LC/MS/MS method, method RM-41C-4, was also submitted.

In method RM-41C-1-1, homogenized samples are extracted with acetonitrile (ACN):water (70:30, v:v) and filtered. The extract is concentrated to remove ACN and partitioned with hexane (2x). The resulting hexane phases are combined and partitioned with ACN (2x), and the ACN phases are combined with ethyl acetate, concentrated to dryness, and redissolved in methanol:water (1:1, v:v). The reconstituted extract is applied to a C18 SPE cartridge, and residues are eluted with methanol:water (5:1, v:v). The eluate is evaporated to aqueous, combined with ethyl acetate, and evaporated to dryness, then redissolved in toluene for GC/NPD analysis. The reported limit of quantitation (LOQ) is 0.02 ppm for each isomer.

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In method RM-41C-4, homogenized samples are extracted with ACN/water, filtered, and concentrated to aqueous as above, then partitioned with hexane:ethyl acetate (9:1, v:v; 2x). The resulting hexane/ethyl acetate phase is partitioned with ACN (2x) and the combined ACN phases are concentrated, mixed with ethyl acetate, and evaporated to dryness. The residues are dissolved in methanol/water (1:1, v:v), and subjected to C18 SPE cleanup as described above. The resulting eluate is diluted with aqueous formic acid for LC/MS/MS analysis. The LOQ, based on the submitted method validation data, is 0.02 ppm for metconazole (total of *cis* and *trans*-isomers).

The methods were adequately validated using samples of peach fruit fortified at 0.02 and 0.1 ppm for method RM-41C-1-1, and samples of wheat straw fortified at 0.02 and 0.1 ppm for method RM-41C-4. Using method RM-41C-1-1, recoveries of *cis*-metconazole ranged from 86.8 to 98.4% (average of 93.8%, standard deviation of 3.5%), and recoveries of *trans*-metconazole ranged from 88.3 to102.8% (average of 95.3%, standard deviation of 5.0%) from samples of fortified peach fruit. Using method RM-41C-4, recoveries ranged from 81.6 to 97.4% (average of 89.5%, standard deviation of 5.2%) from samples of fortified wheat straw.

For method RM-41C-1-1, the concurrent method validation data in combination with the method validation data are sufficiently representative of the expected residue levels for stone fruit, peanuts, and tree nuts. For peanuts and tree nuts, adequate concurrent method recovery data were included with the peanut and tree nut field trials and peanut and plum processing studies submitted by Valent. The fortification levels used in the method validation and concurrent method validation are adequate to bracket expected residue levels in stone fruit, tree nut, and peanut commodities.

Method RM-41C-1-1 has undergone an acceptable ILV with almond nutmeat fortified at 0.02-0.2 ppm. Adequate recoveries were obtained for almond nutmeat, ranging from 93.5 to 111% for *cis*-metconazole and from 88.6 to112% for *trans*-metconazole. No radiovalidation data were submitted for method RM-41C-1-1; however, HED has concluded that because the extraction solvent used for the proposed enforcement method is similar to the aqueous organic solvent mixtures used in the plant metabolism studies, radiovalidation of the method is not required.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the analytical method test data are classified as scientifically acceptable. The proposed enforcement method was forwarded to the Analytical Chemistry Branch (ACB/BEAD) for petition method review (DP #339994, N. Dodd, 5/29/07).

The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP#s 348168 and 348206.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP) and Data Confidentiality statements were provided for the method submission, but no Quality Assurance statement was provided; the GLP compliance statement noted that the report was not designed to meet FIFRA Good Laboratory Standards because no new data were generated. For the ILV study, signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided; no deviations from regulatory requirements were reported which would have an impact on the validity of the study.

A. BACKGROUND INFORMATION

Metconazole [5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol] is a broad-spectrum triazole Group 3 fungicide (sterol biosynthesis inhibitors). There are currently no registered uses of metconazole in the U.S.; however, a tolerance has been established for banana, and a Section 18 emergency exemption and supporting time-limited tolerances have been granted for use on soybean. Valent U.S.A. Corporation has applied for registration of metconazole in the U.S. for use on peanut, stone fruits, and tree nuts.

The chemical structure and nomenclature of metconazole, and the physicochemical properties of the technical grade of metconazole are presented in Tables A.1 and A.2.

Table A.1. Metconazole Nomenclature.

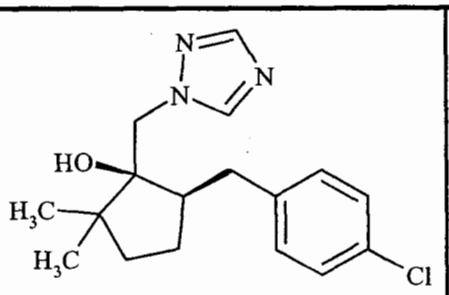
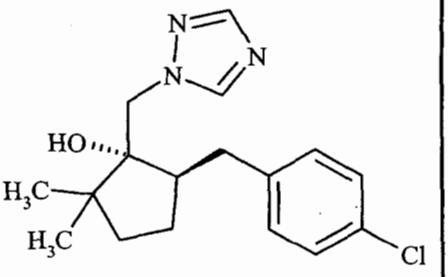
Chemical structure	 *cis*-isomer	 *trans*-isomer
Common name	Metconazole	
Company experimental name	KNF-S-474m (Kureha); BAS 555 F (BASF); V-10116 (Valent)	
IUPAC name	(1RS,5RS:1RS,5SR)-5-(4-chlorobenzyl)-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	
CAS name	5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	
CAS registry number	125116-23-6 (*cis*- and *trans*-isomers) 115850-27-6 (*cis*-isomer) 115850-28-7 (*trans*-isomer)	
End-use products (EP)	50% WDG (Metconazole 50 WDG Fungicide, EPA File Symbol 59639-RUT) 0.75 lb/gal SC/L (Caramba™ Fungicide, EPA File Symbol No. 7969-EUA) 0.67 lb/gal SC/L formulation (BAS 556 01F Fungicide, EPA File Symbol No. 7969-EUT; also contains the active ingredient pyraclostrobin at 0.83 lb/gal)	

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Table A.2. Physicochemical Properties of Metconazole

Parameter	Value	References* (MRID)
Melting point/range	100.0-108.4°C (using Electrothermal Digital Melting Point Apparatus) (AC900,768 technical grade)	44721505
pH	5.81 at 25°C (1% aqueous suspension)	46808402
Relative density (20°C)	1.14 (relative density to water at 4°C, using capillary-stoppered, density-specific gravity bottle) (Lot No. AC 8879-140B)	44721505
Water solubility (20°C)	Using shake-flask method: 18.7 ± 1.0 mg/L (*cis*-isomer, WL148271, KNF-S-474m) 13.6 ± 1.7 mg/L (*trans*-isomer, WL148271, KNF-S-474m)	44721505

Solvent solubility (g/L) at 20°C — 44721505

Solvent	Metconazole	*cis*	*trans*
acetone	363	251	117
methanol	403	294	117
dichloromethane	481	343	141
ethyl acetate	260	173	90.0
propanol	132	86.6	46.7
toluene	103	66.2	38.0
Hexane	1.40	0.929	0.483

Vapor pressure (20°C)	Using gas-saturation method: $< 1.23 \times 10^{-5}$ Pa or 9.23×10^{-8} mm Hg (metconazole) $< 1.04 \times 10^{-5}$ Pa or 7.80×10^{-8} mm Hg (*cis*-isomer) $< 1.96 \times 10^{-6}$ Pa or 1.47×10^{-8} mm Hg (*trans*-isomer)	44721505
Dissociation constant (pK_a)	11.38±0.03 and 1.06±0.03 (in water at 29.1°C using spectrophotometric method; Lot No. AC 8879-140B)	44721505
Octanol/water partition coefficient, Log(K_{OW})	At 20 °C (using flask shaking method): K_{ow} (log K_{ow}) = 7090±989 (3.85) (Lot No. AC 8879-140B) (TGAI) K_{ow} (log K_{ow}) = 7150±803 (3.85) (*cis*-isomer, CL 354,801) K_{ow} (log K_{ow}) = 6800±1700 (3.8) (*trans*-isomer, CL 354,802)	44721505

UV/visible absorption spectrum — 46808403

pH	λ	A	log ε
cis-isomer			
2.0	221.4	0.828	4.03
6.8		0.8452	4.04
7.0		0.9126	4.08
10.3		0.7226	3.98
trans-isomer			
2.0	221.4	0.9053	4.07
7.0		0.9547	4.10
10.1		0.9893	4.11

* Product Chemistry Reviews: DP #256877, Shyam Mathur, Ph.D., 9/12/2000 and DP #329168, Shyam Mathur, Ph.D., 7/13/07.

B. MATERIALS AND METHODS

B.1. Data-Gathering Method

Samples of stone fruits, peanuts and peanut processed commodities, almond nutmeats and hulls, and pecan nutmeats from the submitted field trial and processing studies were analyzed for residues of *cis*- and *trans*-metconazole using GC/NPD method RM-41C-1.

B.2. Enforcement Method

The proposed enforcement method RM-41C-1-1 is a revision of the data-gathering method. The method was revised to correct minor nomenclature and typographical errors, and is entitled "Determination of *cis*-Metconazole and *trans*-Metconazole in Crops." The petitioner has also submitted LC/MS/MS confirmatory method RM-41C-4.

B.2.1. Principle of the Method:

The parameters of method RM-41C-1-1 and confirmatory method RM-41C-4 are described in Table B.2.1.

In method RM-41C-1-1, homogenized samples are extracted with ACN:water (70:30, v:v) and filtered. The extract is concentrated to remove ACN and partitioned with hexane (2x). The resulting hexane phases are combined and partitioned with ACN (2x), and the ACN phases are combined with ethyl acetate, concentrated to dryness, and redissolved in methanol:water (1:1, v:v). The reconstituted extract is applied to a C18 SPE cartridge, and residues are eluted with methanol:water (5:1, v:v). The eluate is evaporated to aqueous, combined with ethyl acetate, and evaporated to dryness, then redissolved in toluene for GC/NPD analysis.

In method RM-41C-4, homogenized samples are extracted with ACN/water, filtered, and concentrated to aqueous as above, then partitioned with hexane:ethyl acetate (9:1, v:v; 2x). The resulting hexane/ethyl acetate phase is partitioned with ACN (2x) and the combined ACN phases are concentrated, mixed with ethyl acetate, and evaporated to dryness. The residues are dissolved in methanol/water (1:1, v:v) and subjected to C18 SPE cleanup as described above. The resulting eluate is diluted with aqueous formic acid for LC/MS/MS analysis.

TABLE B.2.1. Summary Parameters for the Analytical Enforcement Methods Used for the Quantitation of Metconazole Residues in Crop Commodities.		
Method ID	Method RM-41C-1-1	Confirmatory Method RM-41C-4
Analytes	*cis*-Metconazole and *trans*-metconazole	Metconazole (total of *cis* + *trans* isomers)
Extraction solvent/technique	Homogenized samples are blended with ACN:water (70:30, v:v). The extract is vacuum filtered and concentrated to aqueous.	
Cleanup strategies	The aqueous residue is partitioned with hexane (2x), and the hexane phases are combined and partitioned with ACN (2x). The ACN phases are combined with ethyl acetate, evaporated to dryness, and dissolved in methanol:water (1:1, v:v). The reconstituted extract is applied to a C18 SPE cartridge, and residues are eluted with methanol:water (5:1, v:v). The eluate is evaporated to aqueous, combined with ethyl acetate, evaporated to dryness, and then redissolved in toluene for analysis.	The aqueous residue is partitioned with hexane:ethyl acetate (9:1, v:v; 2x), and the hexane/EtOAc phases are combined and partitioned with ACN (2x). The ACN phases are concentrated, combined with ethyl acetate, evaporated to dryness, and dissolved in methanol:water (1:1, v:v). The reconstituted extract is applied to a C18 SPE cartridge, and residues are eluted with methanol:water (5:1, v:v). The eluate is diluted with aqueous formic acid for analysis.
Instrument/Detector	GC/NPD using a DB-5 or DB-17 column and a nitrogen-phosphorus detector (NPD)	LC/MS/MS using a reverse-phase C18 column and a gradient mobile phase of aqueous formic acid/acidified methanol. MS/MS is conducted using electrospray ionization in the positive ion mode monitoring the parent-daughter ion transition 391.9 → 125.2.
Standardization method	External standardization using a calibration curve of at least four standards; response factor calculated for each of four standards by dividing the peak height/area by concentration; coefficient of variation must be ≤10%. Alternatively, a linear fit with a non-zero intercept may be used (linear regression analysis).	External standardization, using a calibration curve of at least four standards; weighted linear fit (1/concentration) for concentration vs. response (linear regression analysis).
Stability of std solutions	Standards stored under refrigeration; duration of stability not addressed.	Standards stored under refrigeration; calibration standards (in methanol/water) to be stored for ≤1 week.
Retention times	DB-5 column: ~7.8 min. for *cis*-metconazole; ~8.15 min for *trans*-metconazole DB-17 column: ~6.9 min. for *cis*-metconazole; ~7.5 min for *trans*-metconazole	~10.3 minutes

C. RESULTS AND DISCUSSION

C.1. Data-Gathering Method

As noted in Section B.2, the data-gathering method, method RM-41C-1, is essentially the same as the proposed enforcement method, method RM-41C-1-1.

C.2. Enforcement Method

The method validation data are presented in Table C.2.1. The method validation recoveries of *cis*- and *trans*-metconazole using method RM-41C-1-1 were adequate from samples of peach fruit fortified at 0.02 ppm (LOQ) and 0.10 ppm (5x LOQ) with *cis*- and *trans*-metconazole.

Recoveries of *cis*-metconazole ranged from 86.8 to 98.4% (average of 93.8%, standard deviation of 3.5%), and recoveries of *trans*-metconazole ranged from 88.3 to 102.8% (average of 95.3%, standard deviation of 5.0%). The method validation recoveries of metconazole using method RM-41C-4 were adequate from samples of wheat straw fortified at the LOQ and 5x the LOQ with metconazole; recoveries ranged from 81.6 to 97.4% (average of 89.5%, standard deviation of 5.2%).

For method RM-41C-1-1, the concurrent method validation data in combination with the method validation data are sufficiently representative of the expected residue levels for stone fruit, peanuts, and tree nuts. Adequate concurrent method recovery data were included with the peanut and tree nut field trials and peanut and plum processing studies submitted by Valent and reviewed under PP #6F7095 (refer to 46901710.de1.doc for tree nuts, 46901712.der.doc for peanut, and 46901710.de2.doc for processed peanut). The fortification levels used in the method validation and concurrent method validation are adequate to bracket expected residue levels in stone fruit, tree nut, and peanut commodities.

The method characteristics for GC/NPD method RM-41C-1-1 and confirmatory LC/MS/MS method RM-41C-4 are presented in Table C.2.2. The extraction and cleanup procedures of the two methods are similar.

The petitioner noted that because the aqueous ACN extraction solvent used in the proposed enforcement method is similar to the aqueous organic solvent mixtures used in the plant metabolism studies, no extraction efficiency method validation study is required. HED concurs that no radiovalidation data are required for the proposed enforcement method.

TABLE C.2.1. Recovery Results from Method Validation of Peach and Wheat Straw using the Enforcement Analytical Methods. [1]

Matrix		Spiking Level (ppm)	Recoveries Obtained (%)	Mean Recovery ± Std. Dev. [CV] (%)
Method RM-41C-1-1				
Peach fruit	*cis*-Metconazole	0.020	86.8, 91.7, 92.4	90.3 ± 3.1 [3.4]
		0.100	93.5, 93.9, 94.8, 94.8, 97.9, 98.4	95.6 ± 2.1 [2.2]
Peach fruit	*trans*-Metconazole	0.020	88.3, 90.7, 96.1	91.7 ± 4.0 [4.4]
		0.100	90.6, 93.9, 95.2, 98.5, 101.8, 102.8	97.1 ± 4.7 [4.9]
Confirmatory Method RM-41C-4				
Wheat straw	Metconazole (sum of *cis* + *trans*)	0.020	81.6, 83.0, 91.2, 91.7	86.9 ± 5.3 [6.1]
		0.100	84.4, 84.4, 86.7, 90.8, 96.2, 97.4	90.0 ± 5.8 [6.4]

[1] Standards were prepared in acetone.

TABLE C.2.2. Characteristics for the Enforcement and Confirmatory Analytical Methods Used for the Quantitation of Metconazole Residues in Crop Commodities.

Method ID	Method RM-41C-1-1	Confirmatory Method RM-41C-4
Analytes	*cis*-Metconazole and *trans*-metconazole	Metconazole (total of *cis* + *trans* isomers)
Equipment ID	Hewlett-Packard Model 5890 GC equipped with a nitrogen-phosphorus detector (NPD); J&W scientific DB-5 or DB-17 column.	Agilent 1100 series HPLC with an Applied Biosystems API 2000 MS system or Finnigan TSQ Quantum LC/MS system, both equipped with a Phenomenex LUNA C18 column.
Limit of quantitation (LOQ)	0.02 ppm for each isomer, based on the lower limit of method validation (LLMV)	Not reported; 0.02 ppm based on LLMV
Method ID	Method RM-41C-1-1	Confirmatory Method RM-41C-4
Limit of detection (LOD)	0.01 ppm; calculated based on a 10-g sample with a 1.0 mL final volume and a 0.1 µg/mL linearity standard in the linearity verification.	
Accuracy/Precision	Percent recoveries and CVs indicate acceptable accuracy/precision for residues of *cis*- and *trans*-metconazole from peaches at the LOQ and 5x the LOQ. Overall recoveries were 86.8-98.4% [average = 93.8%; CV = 3.7%] for *cis*-metconazole and 88.3-102.8% [average = 95.3%; CV = 5.3%] for *trans*-metconazole.	Percent recoveries and CVs indicate acceptable accuracy/precision for residues of metconazole from wheat straw at the LOQ and 10x the LOQ. Recoveries were 81.6-97.4% [average = 89.5%; CV = 5.8%] for metconazole (3:1 *cis*:*trans* ratio).
Reliability of the Method [ILV]	An independent laboratory method validation [ILV], Study No.120.010, was conducted to verify the reliability of method RM-41C-1-1 for the determination of metconazole residues in almond nutmeat. The values obtained are indicative that method RM-41C-1-1 is reliable.	An independent laboratory method validation [ILV] is not required for a confirmatory method.
Linearity	The method/detector response was linear (coefficients of determination, r^2= 0.9992 for *cis*-metconazole and 0.9988 for *trans*-metconazole) within the range of 0.01-0.20 ppm.[1]	No data were provided.
Specificity	Sample chromatograms were included in the submission for method RM-41C-1-1. The control chromatograms generally have no peaks above the chromatographic background, and the spiked sample chromatograms contain only the analyte peak of interest. Peaks were well defined and symmetrical. There appeared to be no carryover to the following chromatograms.	Sample chromatograms were included in the submission for method RM-41C-4. The control chromatogram had no peak above the chromatographic background, and the spiked sample chromatograms contain only the analyte peak of interest. Peaks were well defined and symmetrical. There appeared to be no carryover to the following chromatograms.

[1] from ILV study (MRID No. 46901706)

C.3. Independent Laboratory Validation

An ILV study for method RM-41C-1-1 (version RM-41C-1 was used) was conducted by North Coast Laboratories Ltd. (Arcata, CA). Samples of untreated, macerated almond nutmeat (supplied by the petitioner) were fortified with a mixed standard of *cis*- and *trans*-metconazole,

each at 0.02 ppm (LOQ), 0.04 ppm (2x LOQ) and 0.2 ppm (10x LOQ). Samples were analyzed according to the method procedures described in Table B.2.1.

The laboratory made minor modifications to the method for the ILV trial, including substitution of the proposed DB-5 or DB-17 column (1.5- or 1.0-μ film thickness) with Restek Rtx-5 and a more polar Restek Rtx-35 column (0.25-μ film thickness), and use of a temperature control program instead of packing the column adaptor with glass wool; both modifications were cleared by the sponsor.

The ILV was successful for both analytes on the first trial. Recoveries are reported in Table C.3.1. The laboratory noted that the Rtx-35 column produced sharper peaks which could be more precisely integrated.

The ILV laboratory reported a very slight interfering peak in the control matrix near the *trans*-metconazole retention time; the *trans*-metconazole peak was integrated so that this interference was not included. The reagent control had no peaks in the vicinity of either analyte.

The ILV laboratory reported that the extraction and analysis of 12 samples required 2 calendar days, but noted that the extraction procedure involved rotary evaporation of a fairly large amount of solvent, and that the laboratory had a limited number of rotary evaporators. It was estimated that the procedure could be completed in a single 8-hour day if a sufficient number of rotary evaporators were available.

A record of all communication between the ILV laboratory and the study sponsor was included in the submission. No critical steps or potential problems were identified by the laboratory, and no modifications to the method were recommended.

TABLE C.3.1. Recovery Results Obtained by an Independent Laboratory Validation of the Enforcement Method for the Determination of Metconazole in Almond Nutmeat.

Matrix	Column	Spiking Level (ppm)	Recoveries Obtained (%)	Mean Recovery ± Std. Dev. [CV] (%)
***cis*-Metconazole**				
Almond nutmeat	Rtx-5	0.02	98.6, 98.7, 111	103 ± 7.1 [6.9]
		0.04	105, 105, 106	105 ± 0.59 [0.56]
		0.2	97.2, 99.9, 106	101 ± 4.4 [4.4]
	Rtx-35	0.02	94.7, 99.1, 107	100 ± 6.1 [6.1]
		0.04	100, 100, 101	100 ± 0.64 [0.64]
		0.2	93.5, 95.7, 101	96.9 ± [4.2]
***trans*-Metconazole**				
Almond nutmeat	Rtx-5	0.02	102, 103, 112	106 ±5.1 [4.9]
		0.04	102, 104, 106	104 ±1.8 [1.7]
		0.2	92.3, 95.6, 103	96.9 ±5.2 [5.4]
	Rtx-35	0.02	88.6, 92.0, 104	94.7 ± 7.9 [8.3]
		0.04	99.3, 100, 101	100 ± 0.84 [0.84]
		0.2	94.6, 96.2, 103	97.8 ± 4.3 [4.4]

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D. CONCLUSION

Adequate method validation data have been submitted for the proposed GC/NPD enforcement method, RM-41C-1-1, reflecting analysis of fortified peach samples, and confirmatory method RM-41C-4, reflecting analysis of fortified wheat straw. Based on the available data, the proposed enforcement method is suitable for determination of metconazole *per se* in crop commodities. The method has undergone an acceptable ILV on almond nutmeat. No radiovalidation data were submitted for method RM-41C-1-1; however, since the extraction solvent used for method RM-41C-1-1 is similar to the aqueous organic solvent mixtures used in the plant metabolism studies, radiovalidation of the method is not required. The proposed enforcement method was forwarded to ACB/BEAD for method review (DP #339994, N. Dodd, 5/29/07).

E. REFERENCES

DP#:	324541
Subject:	Metconazole. Request for a Tolerance on Imported Bananas. Summary of Analytical Chemistry and Residue Data. Petition Number 9E05052.
From:	N. Dodd
To:	M. Waller
Date:	12/14/05
MRIDs:	44721506, 44721507, 44721508, 44721509, 44721510, and 44721511

F. DOCUMENT TRACKING

RDI: N. Dodd (2/20/08)
Petition Numbers: 6F7094 and 6F7095
DP#s: 348168 and 348206
PC Code: 125619

Template Version June 2005

Primary Evaluator	This DER was originally prepared under contract by Dynamac Corporation.
Approved by	Nancy Dodd, Chemist Date: 2/20/08 Registration Action Branch 3 Health Effects Division (7509P)

This DER was originally prepared under contract by Dynamac Corporation (2275 Research Boulevard, Suite 300; Rockville, MD 20850; submitted 09/13/2007). The DER has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORTS:

46901705 Gohre, K. (2006) Radiovalidation of Residue Methodology for Metconazole in Animal Tissue. Project Number: VP/30188, 200600145. Unpublished study prepared by Valent Dublin Laboratory. 35 p.

46901914 Green, C. (2006) Magnitude of the Residues of Metconazole in Dairy Cattle Milk and Meat. Project Number: 200600291, 29111, V/05/29111. Unpublished study prepared by Genesis Midwest Laboratories and Valent Dublin Laboratory. 401 p.

EXECUTIVE SUMMARY:

Valent U.S.A. Corporation has submitted the following methods for the determination of metconazole residues in livestock commodities: GC/NPD method RM-41M-1 for the determination of *cis*- and *trans*-metconazole in milk; LC/MS/MS method RM-41M-2 for the determination of *cis*- and *trans*-metconazole in tissues; and LC/MS/MS method RM-41-M3 for the determination of metabolites M1 (free and conjugated) and M12 in liver and kidney. These methods were used for data collection in the cattle feeding study submitted by Valent (46901914.der.doc). In support of the methods, Valent has submitted method validation and radiovalidation data.

In method RM-41M-1, samples are extracted with ethyl acetate:methanol (2:1, v:v; 2x) and filtered. The extracts are combined and concentrated by rotary evaporation. The residue is mixed with 10% NaCl and partitioned with methylene chloride (3x). The methylene chloride layer is drained through sodium sulfate and concentrated to an oily residue. The resulting residue is dissolved in hexane and partitioned with acetonitrile (ACN). The ACN phase is concentrated by evaporation, rinsed with ethyl acetate, and evaporated to dryness. Residues are redissolved in toluene for determination by GC/NPD, or dissolved in methanol for determination by LC/MS/MS (confirmatory method). The reported limit of quantitation (LOQ) is 0.02 ppm for each isomer, based on the lower limit of method validation (LLMV).

In method RM-41M-2, samples are extracted with ACN (3x) and filtered, and the extracts are combined. The ACN extract is partitioned with hexane, and the ACN layer is concentrated to an oily residue, then partitioned with hexane:ethyl acetate (9:1, v:v) using a 10% NaCl rinse. The hexane/ethyl acetate layer is drained through sodium sulfate and partitioned with ACN, and the ACN layer is evaporated to dryness. The residue is dissolved in methanol and applied to a C18 SPE cartridge; residues are eluted with methanol:water (5:1, v:v). The eluate is combined with ethyl acetate, evaporated to dryness, and redissolved in methanol:water (2:1, v:v) for LC/MS/MS analysis. The method monitors a single ion transition for both *cis*- and *trans*-metconazole. The method LOQ is 0.02 ppm for each isomer, based on the LLMV.

In method RM-41M-3, samples are extracted with methanol followed by methanol:water (9:1, v:v) and filtered. The extracts are combined and concentrated by rotary evaporation to remove methanol. The residue is redissolved in methanol and mixed with ACN and hexane. The ACN/methanol layer is adjusted to volume with ACN and divided into two fractions for separate determination of M12 and M1. For M12, the fraction is concentrated, combined with ethyl acetate, and evaporated to dryness, then redissolved in methanol and water and applied to a C18 SPE cartridge. For M1, the fraction is concentrated, combined with ethyl acetate, and evaporated to dryness, then redissolved in methylene chloride and evaporated to dryness. The residue is redissolved in 3 N HCl and hydrolyzed at 80-85 °C for 1.5 hr to release conjugated residues. The hydrolysate is diluted with water and applied to a C18 cartridge. For both analytes, residues are eluted from the SPE cartridge with methanol:water (5:1, v:v). The resulting eluates are combined with ethyl acetate, evaporated to dryness, and redissolved in methanol:water (2:1, v:v) for LC/MS/MS analysis. The method monitors a single ion transition for each analyte. The method LOQ is 0.02 ppm for each analyte, based on the LLMV.

Methods RM-41M-1 and RM-41M-2 were adequately validated using samples of milk and liver fortified at 0.02 ppm and 0.10 ppm with both *cis*- and *trans*- metconazole. Using method RM-41M-1 (both GC/NPD and LC/MS/MS analyses) for milk and RM-41M-2 for liver, method validation recoveries of *cis*- and *trans*-metconazole were within the acceptable range of 70-120% for all samples. Method validation recoveries of metabolites M1 and M12 using method RM-41M-3 were acceptable for samples of kidney fortified with M1 at 0.02 ppm and with M12 at 0.02 and 0.10 ppm; recoveries of M1 ranged from 68.8 to 87.1% (average of 76.6%, standard deviation of 7.7%), and recoveries of M12 ranged from 68.9 to 81.2% (average of 76.2%, standard deviation of 3.9%). Marginally acceptable recoveries were obtained for metabolite M1 in kidney fortified at 0.10 ppm; recoveries ranged from 68.1 to 72.0% (average of 69.5%, standard deviation of 1.6%).

The fortification levels and samples used in method validation for methods RM-41M-1 and R-41M-2 are adequate to bracket expected residue levels of *cis*- and *trans*-metconazole in milk and tissues. Although the fortification levels used for method RM-41M-3 in kidney are adequate to bracket expected residues of M1 and M12, HED notes that low concurrent recoveries were obtained for method RM-41M-3 in the cattle feeding study for liver fortified with M1 at 0.02 and 0.10 ppm (57.4-61.6%), liver fortified with M12 at 0.02 and 0.10 ppm (67.4% and 66.2%, respectively), and kidney fortified with M12 at 0.02 ppm (67.6-68.3%); acceptable recoveries

were obtained for M1 in kidney fortified at 0.02 ppm and for M12 in kidney fortified at 0.10 ppm.

Acceptable LC/MS/MS confirmatory procedures were included for GC/NPD method RM-41M-1; however, no confirmatory analysis procedures were included for methods RM-41M-2 and RM-41M-3. No independent laboratory validation (ILV) studies were included for the methods. Because the petitioner is not proposing the methods for enforcement purposes, no confirmatory procedures or ILV studies are required.

Acceptable radiovalidation data were submitted for method RM-41M-3. HED has concluded that because the extraction solvent used for method RM-41M-2 is the same as that used in the goat metabolism studies, radiovalidation of this method is not required. Radiovalidation data for method RM-41M-1 are needed.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the analytical method test data are classified as scientifically acceptable for method RM-41M-2 and RM-41M-3. Radiovalidation data are required in support of RM-41M-1.

The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP#s 348168 and 348206.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an impact on the validity of the study.

A. BACKGROUND INFORMATION

Metconazole [5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol] is a broad-spectrum triazole Group 3 fungicide (sterol biosynthesis inhibitors). There are currently no registered uses of metconazole in the U.S.; however, a tolerance has been established for banana, and a Section 18 emergency exemption and supporting time-limited tolerances have been granted for use on soybean. Valent U.S.A. Corporation has applied for registration of metconazole in the U.S. for use on peanut, stone fruits, and tree nuts.

The chemical structure and nomenclature of metconazole, and the physicochemical properties of the technical grade of metconazole are presented in Tables A.1 and A.2.

TABLE A.1. Metconazole Nomenclature.

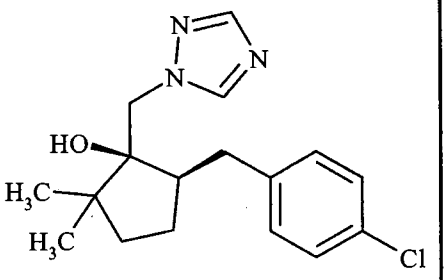
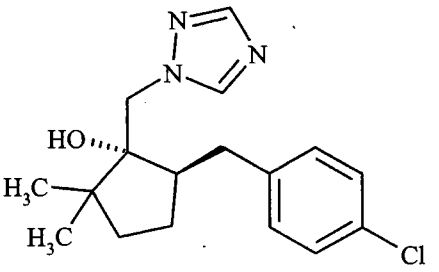
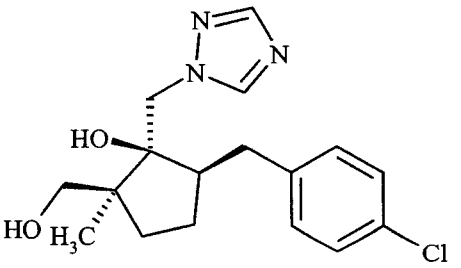
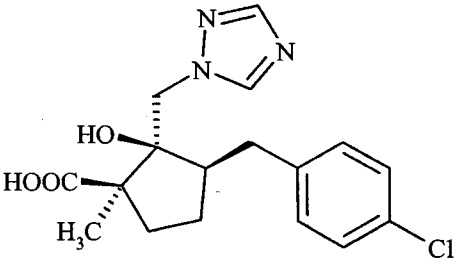
Chemical structure	 *cis*-isomer	 *trans*-isomer
Common name	Metconazole	
Company experimental name	KNF-S-474m (Kureha); BAS 555 F (BASF); V-10116 (Valent)	
IUPAC name	(1RS,5RS:1RS,5SR)-5-(4-chlorobenzyl)-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	
CAS name	5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	
CAS registry number	125116-23-6 (*cis*- and *trans*-isomers) 115850-27-6 (*cis*-isomer) 115850-28-7 (*trans*-isomer)	
End-use products (EP)	50% WDG (Metconazole 50 WDG Fungicide, EPA File Symbol 59639-RUT) 0.75 lb/gal SC/L (Caramba™ Fungicide, EPA File Symbol No. 7969-EUA) 0.67 lb/gal SC/L formulation (BAS 556 01F Fungicide, EPA File Symbol No. 7969-EUT; also contains the active ingredient pyraclostrobin at 0.83 lb/gal)	
Metconazole metabolite M1		
Metconazole metabolite M12		

Table A.2. Physicochemical Properties of Metconazole

Parameter	Value				References* (MRID)
Melting point/range	100.0-108.4°C (using Electrothermal Digital Melting Point Apparatus) (AC900,768 technical grade)				44721505
pH	5.81 at 25°C (1% aqueous suspension)				46808402
Relative density (20°C)	1.14 (relative density to water at 4°C, using capillary-stoppered, density-specific gravity bottle) (Lot No. AC 8879-140B)				44721505
Water solubility (20°C)	Using shake-flask method: 18.7 ± 1.0 mg/L (*cis*-isomer, WL148271, KNF-S-474m) 13.6 ± 1.7 mg/L (*trans*-isomer, WL148271, KNF-S-474m)				44721505
Solvent solubility (g/L) at 20°C	Solvent	Metconazole	*cis*	*trans*	44721505
	acetone	363	251	117	
	methanol	403	294	117	
	dichloromethane	481	343	141	
	ethyl acetate	260	173	90.0	
	propanol	132	86.6	46.7	
	toluene	103	66.2	38.0	
	Hexane	1.40	0.929	0.483	
Vapor pressure (20°C)	Using gas-saturation method: $< 1.23 \times 10^{-5}$ Pa or 9.23×10^{-8} mm Hg (metconazole) $< 1.04 \times 10^{-5}$ Pa or 7.80×10^{-8} mm Hg (*cis*-isomer) $< 1.96 \times 10^{-6}$ Pa or 1.47×10^{-8} mm Hg (*trans*-isomer)				44721505
Dissociation constant (pK_a)	11.38±0.03 and 1.06±0.03 (in water at 29.1°C using spectrophotometric method; Lot No. AC 8879-140B)				44721505
Octanol/water partition coefficient, Log(K_{OW})	At 20 °C (using flask shaking method): K_{ow} (log K_{ow}) = 7090±989 (3.85) (Lot No. AC 8879-140B) (TGAI) K_{ow} (log K_{ow}) = 7150±803 (3.85) (*cis*-isomer, CL 354,801) K_{ow} (log K_{ow}) = 6800±1700 (3.8) (*trans*-isomer, CL 354,802)				44721505
UV/visible absorption spectrum	pH	λ	A	log ε	46808403
	cis-isomer				
	2.0	221.4	0.828	4.03	
	6.8		0.8452	4.04	
	7.0		0.9126	4.08	
	10.3		0.7226	3.98	
	trans-isomer				
	2.0	221.4	0.9053	4.07	
	7.0		0.9547	4.10	
	10.1		0.9893	4.11	

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* Product Chemistry Reviews: DP #256877, Shyam Mathur, Ph.D., 9/12/2000 and DP #329168, Shyam Mathur, Ph.D., 7/13/07.

B. MATERIALS AND METHODS

B.1. Data-Gathering Method

Samples of milk and tissues from the cattle feeding study submitted by Valent were analyzed for residues of *cis*- and *trans*-metconazole using GC/NPD method RM-41M-1 for whole milk, skim milk, and cream, and LC/MS/MS method RM-41M-2 for liver, kidney, muscle, and fat. Samples of liver and kidney were also analyzed for residues of metabolites M1 (free and conjugated) and M12 using LC/MS/MS method RM-41-3. Method RM-41M-1 includes confirmatory analysis by LC/MS/MS. Complete descriptions of the methods and method validation data were included in MRID 46901914.

B.1.1. Principle of the Method:

Valent U.S.A. has submitted complete method descriptions for methods RM-41M-1, RM-41M-2, and RM-41M-3. The parameters of the methods are described in Table B.1.1.

In method RM-41M-1, entitled "Determination of Metconazole in Milk," samples are extracted with ethyl acetate:methanol (2:1, v:v; 2x) and filtered. The extracts are combined and concentrated by rotary evaporation. The residue is mixed with 10% NaCl and partitioned with methylene chloride (3x). The methylene chloride layer is drained through sodium sulfate and concentrated to an oily residue. The resulting residue is dissolved in hexane and partitioned with ACN. The ACN phase is concentrated by evaporation, rinsed with ethyl acetate, and evaporated to dryness. Residues are redissolved in toluene for determination by GC/NPD, or dissolved in methanol for determination by LC/MS/MS (confirmatory method).

In method RM-41M-2, entitled "Determination of Metconazole in Liver," samples are extracted with ACN (3x) and filtered, and the extracts are combined. The ACN extract is partitioned with hexane, and the ACN layer is concentrated to an oily residue, then partitioned with hexane:ethyl acetate (9:1, v:v) using a 10% NaCl rinse. The hexane/ethyl acetate layer is drained through sodium sulfate and partitioned with ACN, and the ACN layer is evaporated to dryness. The residue is dissolved in methanol and applied to a C18 SPE cartridge; residues are eluted with methanol:water (5:1, v:v). The eluate is combined with ethyl acetate, evaporated to dryness, and redissolved in methanol:water (2:1, v:v) for LC/MS/MS analysis. The method monitors a single ion transition for both *cis*- and *trans*-metconazole.

In method RM-41M-3, entitled "Determination of Metconazole in Kidney," samples are extracted with methanol followed by methanol:water (9:1, v:v) and filtered. The extracts are combined and concentrated by rotary evaporation to remove methanol. The residue is redissolved in methanol and mixed with ACN and hexane. The ACN/methanol layer is adjusted to volume with ACN and divided into two fractions for separate determination of M12 and M1. For M12, the fraction is concentrated, combined with ethyl acetate, and evaporated to dryness, then redissolved in methanol and water and applied to a C18 SPE cartridge. For M1, the fraction

is concentrated, combined with ethyl acetate, and evaporated to dryness, then redissolved in methylene chloride and evaporated to dryness. The residue is redissolved in 3 N HCl and hydrolyzed at 80-85 °C for 1.5 hr to release conjugated residues. The hydrolysate is diluted with water and applied to a C18 cartridge. For both analytes, residues are eluted from the SPE cartridge with methanol:water (5:1, v:v). The resulting eluates are combined with ethyl acetate, evaporated to dryness, and redissolved in methanol:water (2:1, v:v) for LC/MS/MS analysis. The method monitors a single ion transition for each analyte.

TABLE B.1.1. Summary Parameters for the Analytical Method Used for the Quantitation of Metconazole, M1, and M12 Residues in Milk and Cattle Tissues.

Method ID	RM-41M-1	RM-41M-2	RM-41M-3
Analytes	*cis*-Metconazole *trans*-Metconazole	*cis*-Metconazole *trans*-Metconazole	M1 (free and conjugated) M12
Matrices	Milk	Tissues	Liver and kidney
Extraction solvent/technique	Samples are extracted 2x with ethyl acetate:methanol (2:1, v:v) and filtered. The extracts are combined, and concentrated by rotary evaporation to remove ethyl acetate/methanol, leaving an aqueous/oily residue.	Samples are extracted 3x with ACN and filtered, and the extracts are combined.	Samples are extracted with methanol followed by methanol:water (9:1, v:v) and filtered. The extracts are combined and concentrated by rotary evaporation to remove methanol, leaving an aqueous residue.
Cleanup strategies	The residue is mixed with 10% NaCl and partitioned 3x with methylene chloride. The methylene chloride layer is drained through sodium sulfate and evaporated to an oily residue. The resulting residue is dissolved in hexane and partitioned with ACN. The ACN phase is concentrated by evaporation, rinsed with ethyl acetate, and evaporated to dryness. Residues are redissolved in toluene for determination by GC/NPD, or dissolved in methanol for determination by LC/MS/MS (confirmatory procedure).	The ACN extract is partitioned with hexane. The ACN layer is evaporated to an oily residue, then partitioned with hexane:ethyl acetate (9:1, v:v) using a 10% NaCl rinse. The hexane/ethyl acetate layer is drained through sodium sulfate and partitioned with ACN, and the ACN layer is evaporated to dryness. The residue is dissolved in methanol and applied to a C18 SPE cartridge; residues are eluted with methanol:water (5:1, v:v). The eluate is combined with ethyl acetate, evaporated to dryness, and redissolved in methanol:water (2:1, v:v).	The residue is redissolved in methanol and partitioned with ACN/hexane. The ACN/methanol layer is adjusted to volume with ACN and divided into two fractions for separate determination of M12 and M1. For M12, the fraction is concentrated, combined with ethyl acetate, and evaporated to dryness, then redissolved in methanol/water and applied to a C18 SPE cartridge. For M1, the fraction is concentrated, combined with ethyl acetate, and evaporated to dryness, then redissolved in methylene chloride and evaporated to dryness. The residue is redissolved in 3 N HCl and hydrolyzed at 80-85 °C for 1.5 hr. The hydrolysate is diluted with water and applied to a C18 cartridge. For both analytes, residues are eluted from the SPE cartridge with methanol:water (5:1, v:v). The resulting eluates are combined with ethyl acetate, evaporated to dryness, and redissolved in methanol:water (2:1, v:v).

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TABLE B.1.1. Summary Parameters for the Analytical Method Used for the Quantitation of Metconazole, M1, and M12 Residues in Milk and Cattle Tissues.

Instrument/Detector	GC/NPD: Using an HP-5 column and a nitrogen-phosphorus detector (NPD). LC/MS/MS: LC/MS/MS using a C8 column and a gradient mobile phase of water/methanol, each containing 0.05% formic acid. MS/MS is conducted using electrospray ionization (ESI) in the positive ion mode monitoring the parent-daughter ion transition 320 → 125.	LC/MS/MS using a C8 column and a gradient mobile phase of water/methanol, each containing 0.05% formic acid. MS/MS is conducted using ESI in the positive ion mode monitoring the parent-daughter ion transition 320 → 125.	LC/MS/MS using a C18 column and a gradient mobile phase of water/methanol, each containing 0.05% formic acid. MS/MS is conducted using ESI in the positive ion mode monitoring the following parent-daughter ion transitions: 336.1 → 125 for M1 and 350.1 → 125 for M12.
Standardization method	GC/NPD and LC/MS/MS: External standardization using a calibration curve of at least four standards; response factor calculated for each of four standards by dividing the peak height/area by concentration; coefficient of variation must be ≤10%. Alternatively, a linear fit with a non-zero intercept may be used (linear regression analysis).	External standardization, using a calibration curve of at least four standards; weighted linear fit (1/concentration) for concentration vs. response (linear regression analysis).	External standardization, using a calibration curve of at least four standards; weighted linear fit (1/concentration) for concentration vs. response (linear regression analysis).
Stability of std solutions	Standards stored under refrigeration. Calibration standards used within 1 week for LC/MS/MS; duration of stability not reported for other standards.	Standards stored under refrigeration. Calibration standards used within 1 week; duration of stability not reported for other standards.	Standards stored under refrigeration. Calibration standards used within 1 week; duration of stability not reported for other standards.
Retention times	GC/NPD: *cis*-metconazole: ~7.3 min. *trans*-metconazole: ~7.7 min. LC/MS/MS: *cis*-metconazole: ~20.2 min. *trans*-metconazole: ~20.7 min.	*cis*-metconazole: ~20.7 min. *trans*-metconazole: ~21.2 min.	M1: ~3.25 min. M12: ~3.87 min.

B.2. Enforcement Method

The petitioner has not proposed the submitted methods for enforcement purposes.

C. RESULTS AND DISCUSSION

C.1. Data-Gathering Method

The method validation data are presented in Table C.1.1. The method validation recoveries of *cis*- and *trans*-metconazole were within the acceptable range of 70-120% for milk fortified at 0.02 and 0.10 ppm with each analyte and analyzed by method RM-41M-1 (using both GC/NPD

and LC/MS/MS analysis) and for liver fortified at 0.02 and 0.10 ppm and analyzed using method RM-41M-2. Method validation recoveries of metabolites M1 and M12 using method RM-41M-3 were acceptable for samples of kidney fortified with M1 at 0.02 ppm and with M12 at 0.02 and 0.10 ppm; recoveries of M1 ranged from 68.8 to 87.1% (average of 76.6%, standard deviation of 7.7%), and recoveries of M12 ranged from 68.9 to 81.2% (average of 76.2%, standard deviation of 3.9%). Marginally acceptable recoveries were obtained for metabolite M1 in kidney fortified at 0.10 ppm; recoveries ranged from 68.1 to 72.0% (average of 69.5%, standard deviation of 1.6%).

The fortification levels and samples used in method validation for methods RM-41M-1 and RM-41M-2 are adequate to bracket expected residue levels of *cis*- and *trans*-metconazole in milk and tissues. Although the fortification levels used for method RM-41M-3 in kidney are adequate to bracket expected residues of M1 and M12, HED notes that low concurrent recoveries were obtained for method RM-41M-3 in the cattle feeding study for liver fortified with M1 at 0.02 and 0.10 ppm (57.4-61.6%), liver fortified with M12 at 0.02 and 0.10 ppm (67.4% and 66.2%, respectively), and kidney fortified with M12 at 0.02 ppm (67.6-68.3%); acceptable recoveries were obtained for M1 in kidney fortified at 0.02 ppm and for M12 in kidney fortified at 0.10 ppm.

The method characteristics for the three methods are presented in Table C.1.2. Acceptable LC/MS/MS confirmatory procedures were included for GC/NPD method RM-41M-1; however, no confirmatory analysis procedures were included for methods RM-41M-2 and RM-41M-3. No ILV studies were included for the methods. Because the petitioner is not proposing the methods for enforcement purposes, no confirmatory procedures or ILV studies are required.

TABLE C.1.1. Recovery Results from Method Validation of Dairy Cattle Matrices using the Data-Gathering Analytical Method. [1]

Matrix	Analyte	Spiking Level (ppm)	Recoveries Obtained (%)	Mean Recovery ± Std. Dev. [CV] (%)
Method RM-41M-1 (GC/NPD determination)				
Whole milk	*cis*-Metconazole	0.02	94.7, 90.5, 92.6	92.6 ± 2.1 [2.3]
		0.10	89.4, 85.9, 90.1, 89.3, 86.1, 86.8	87.9 ± 1.9 [2.1]
	trans-Metconazole	0.02	96.7, 96.0, 93.3	95.3 ± 1.8 [1.9]
		0.10	89.8, 91.0, 92.8, 89.4, 86.8, 88.0	89.6 ± 2.1 [2.4]
Method RM-41M-1 (LC/MS/MS determination)				
Whole milk	*cis*-Metconazole	0.02	84.7, 87.9, 81.7	84.8 ± 3.1 [3.7]
	trans-Metconazole	0.02	83.1, 85.4, 84.3	84.3 ± 1.2 [1.3]
Method RM-41M-2				
Liver	*cis*-Metconazole	0.02	100.6, 102.9, 73.2, 74.0, 78.0	85.7 ± 14.8 [17.2]
		0.10	85.0, 80.8, 79.9, 79.2, 77.6, 76.6	79.9 ± 2.9 [3.7]
	trans-Metconazole	0.02	101.7, 103.6, 74.0, 74.0, 79.9	86.6 ± 14.8 [17.1]
		0.10	86.5, 81.7, 79.5, 81.2, 79.5, 78.4	81.1 ± 2.9 [3.6]

TABLE C.1.1. Recovery Results from Method Validation of Dairy Cattle Matrices using the Data-Gathering Analytical Method. [1]

Matrix	Analyte	Spiking Level (ppm)	Recoveries Obtained (%)	Mean Recovery ± Std. Dev. [CV] (%)
Method RM-41M-3				
Kidney	M1	0.02	87.1, 76.1, 68.8, 74.4	76.6 ± 7.7 [10.0]
		0.10	68.8, 68.8, 72.0, 68.5, 68.1, 71.0	69.5 ± 1.6 [2.3]
	M12	0.02	79.1, 75.6, 68.9, 71.8	73.9 ± 4.4 [6.0]
		0.10	74.3, 77.7, 81.0, 76.5, 75.7, 81.2	77.7 ± 2.8 [3.6]

[1] Fortification standards were prepared in acetone.

TABLE C.1.2. Characteristics for the Data-Gathering Analytical Method Used for the Quantitation of *cis*-Metconazole, *trans*-Metconazole, M1 and M12 Residues in Cattle Matrices.

Method	RM-41M-1	RM-41M-2	RM-41M-3
Analytes	*cis*-Metconazole *trans*-Metconazole	*cis*-Metconazole *trans*-Metconazole	M1 (free and conjugated) M12
Equipment ID	GC/NPD analysis: Hewlett-Packard Model 6890 gas chromatograph with Agilent HP-5 column and NPD. LC/MS/MS analysis: Thermo/Finnigan Quest TSQ LC/MS system with Agilent Zorbax SB-C8 column.	Thermo/Finnigan Quest TSQ LC/MS system with Agilent Zorbax SB-C8 column.	Thermo-Finnigan Quest TSQ LC/MS system with Phenomenex Luna C18(2) column.
Limit of quantitation (LOQ)	0.02 ppm for each isomer; based on LLMV	0.02 ppm for each isomer; based on LLMV	0.02 ppm; based on LLMV
Limit of detection (LOD)	0.01 ppm; based on the lowest linearity standard in the linearity verification.	0.01 ppm; based on the lowest linearity standard in the linearity verification.	0.01 ppm; based on the lowest linearity standard in the linearity verification.
Accuracy/Precision	The percent recoveries and coefficients of variance (CVs) indicate acceptable accuracy/precision for whole milk at the LOQ (0.02 ppm) and at 5x the LOQ. The overall recovery ranges (using both GC/NPD and LC/MS/MS analysis) were 81.7-94.7% (average = 88.3%; CV = 4.0%) for *cis*-metconazole and 83.1-96.7% (average = 89.7%; CV = 4.9%) for *trans*-metconazole.	The percent recoveries and CVs indicate acceptable accuracy/precision for liver at the LOQ (0.02 ppm) and at 5x the LOQ. The overall recovery ranges were 73.2-102.9% (average = 82.5%; CV = 12.2%) for *cis*-metconazole and 74.0-103.6% (average = 83.6%; CV = 12.0%) for *trans*-metconazole.	The percent recoveries and CVs indicate acceptable accuracy/precision for kidney at the LOQ (0.02 ppm) and at 5x the LOQ for M12 and at the LOQ for M1. The recovery ranges were 68.8-87.1% (average= 76.6; CV = 10.0) for M1 at 0.02 ppm and 68.9-81.2% (average = 76.2%; CV = 5.1%) M12 at 0.02 and 0.10 ppm. For M1 fortified at 0.10, recoveries ranged 68.1-72.0 (average = 69.7%; CV = 2.5%)
Reliability of the Method [ILV]	Not conducted.	Not conducted.	Not conducted.

TABLE C.1.2. Characteristics for the Data-Gathering Analytical Method Used for the Quantitation of *cis*-Metconazole, *trans*-Metconazole, M1 and M12 Residues in Cattle Matrices.			
Linearity	The method/detector response was linear (coefficients of $r^2 \geq 0.9992$ for the *cis* and *trans* isomers in milk, skim milk, and cream) within the range of 0.1-2.0 ppm in the cattle feeding study.	The method/detector response was linear (coefficients of $r^2 \geq 0.9953$ for the *cis* and *trans* isomers in liver, kidney, muscle, and fat) within the range of 0.01-0.1 ppm in the cattle feeding study	The method/detector response was linear (coefficients of $r^2 \geq 0.9989$ for M1 and 0.9997 for M12 in liver and kidney) within the range of 0.005-0.100 ppm in the cattle feeding study.
Specificity	The control chromatograms generally have no peaks above the chromatographic background and the spiked sample chromatograms contain only the analyte peak of interest. Peaks were well defined and symmetrical. There appeared to be no carryover to the following chromatograms.		

Valent has submitted radiovalidation data (MRID 46901705) for method RM-41M-3. Samples of goat liver and kidney from the goat metabolism study with [triazole-3,5-^{14}C]metconazole were used (refer to 46901909.der.doc for complete details of the metabolism study).

For the radiovalidation study, samples of homogenized liver and kidney from the metabolism study were extracted with methanol followed by methanol:water (9:1, v:v; 2x) and centrifuged. The methanol extract and the first methanol/water extract were combined for LSC analysis, reflecting the initial extraction procedures of Method RM-41M-3 (Table B.1.1), and the second methanol/water extract was analyzed separately. The remaining nonextractable residues were analyzed by combustion/LSC. Total radioactive residues (TRR) in the samples analyzed by the residue method were determined by summing the radioactivity in the extractable and nonextractable fractions. The results of the study are reported in Table C.1.3.

The TRR determined in the radiovalidation study were slightly higher for all samples than the TRR determined in the metabolism study. TRR for liver were 0.256 and 0.257 ppm in the radiovalidation study and 0.241 in the metabolism study, and TRR for kidney were 0.129 and 0.130 ppm in the radiovalidation study and 0.117 ppm in the metabolism study.

TABLE C.1.3. Extraction Efficiency of Method RM-41M-3 Using Aged Radioactive Residues from a Goat Metabolism Study.

Matrix	Metabolism study [1]		Residue Method				Average Extraction Efficiency [2]
	% TRR	ppm	Sample 1		Sample 2		
			% TRR	Ppm	% TRR	ppm	
Goat liver, treated with [triazole-3,5-^{14}C]metconazole							
TRR	100	0.241	100	0.257	100	0.256	--
MeOH + MeOH/water			94.7	0.243	94.7	0.243	101%
2nd MeOH/water			2.2	0.006	2.1	0.005	--
Total Extractable	93.6	0.226	96.8	0.249	96.8	0.248	110%
Goat kidney, treated with [triazole-3,5-^{14}C]metconazole							
TRR	100	0.117	100	0.129	100	0.130	--
MeOH + MeOH/water			96.8	0.125	97.0	0.126	112%
2nd MeOH/water			2.1	0.003	2.0	0.003	--
Total Extractable	96.3	0.112	98.9	0.128	99.0	0.129	115%

[1] As reported by the petitioner in MRID 46901709.
[2] Extraction efficiency = (ppm determined by the residue method)/ (ppm determined in the metabolism study) x 100

The average extraction efficiencies for method RM-41M-3 were 101% for liver and 112% for kidney. The submitted extraction efficiency data demonstrate that the extraction procedures of Method RM-41M-3 adequately extract aged metconazole-derived residues from goat liver and kidney samples. Although identification of metabolites was not conducted, because recovery of TRR was essentially quantitative, no further radiovalidation is required for Method RM-41M-3.

No radiovalidation data were submitted for methods RM-41M-1 and RM-41M-2. No additional data are required for method RM-41M-2 because the extraction solvent, ACN, is the same as that used in initial extraction of goat kidney and liver in the goat metabolism studies submitted by Valent. Radiovalidation data are required for method RM-41M-1.

C.2. Enforcement Method

The petitioner has not proposed the submitted methods for enforcement purposes.

C.3. Independent Laboratory Validation

An independent laboratory validation study was not submitted.

D. CONCLUSION

The submitted GC/NPD method RM-41M-1 and LC/MS/MS method RM-41M-2 appear to be adequate for determining residues of *cis*- and *trans*-metconazole in milk and tissues. The fortification levels used in method validation are adequate to bracket expected residues in milk and tissues.

LC/MS/MS method RM-41M-3 appears to be marginally adequate for determining residues of and metabolites M1 and M12 in tissues. Method validation recoveries of metabolites M1 and M12 were acceptable for samples of kidney fortified with M1 at 0.02 ppm and with M12 at 0.02 and 0.10 ppm. Marginally acceptable recoveries were obtained for metabolite M1 in kidney fortified at 0.10 ppm. Although the fortification levels used for method RM-41M-3 in kidney are adequate to bracket expected residues of M1 and M12, HED notes that low concurrent recoveries were obtained for method RM-41M-3 in the cattle feeding study for liver fortified with M1 at 0.02 and 0.10 ppm, liver fortified with M12 at 0.02 and 0.10 ppm, and kidney fortified with M12 at 0.02 ppm; acceptable recoveries were obtained for M1 in kidney fortified at 0.02 ppm and for M12 in kidney fortified at 0.10 ppm.

GC/NPD method RM-41M-1 includes confirmatory LC/MS/MS analysis procedures. No confirmatory analysis procedures were included for methods RM-41M-2 and RM-41M-3. In addition, no ILV data were submitted. Because the petitioner is not proposing the methods for enforcement purposes, no confirmatory procedures or ILV studies are required.

Acceptable radiovalidation data were submitted for method RM-41M-3. HED has concluded that because the extraction solvent used for method RM-41M-2 is the same as that used in the goat metabolism studies, radiovalidation of this method is not required. Radiovalidation data for method RM-41M-1 are needed.

E. REFERENCES

DP#:	324541
Subject:	Metconazole. Request for a Tolerance on Imported Bananas. Summary of Analytical Chemistry and Residue Data. Petition Number 9E05052.
From:	N. Dodd
To:	M. Waller
Date:	12/14/05
MRIDs:	44721506, 44721507, 44721508, 44721509, 44721510, and 44721511

F. DOCUMENT TRACKING

RDI: N. Dodd (2/20/08)
Petition Numbers: 6F7094 and 6F7095
DP#s: 348168 and 348206
PC Code: 125619

Template Version June 2005

Metconazole/125619/Valent U.S.A. Corp.
DACO 7.4.1/7.4.2/OPPTS 860.1500/OECD IIA 6.3.1, 6.3.2, 6.3.3 and IIIA 8.3.1, 8.3.2, 8.3.3
Crop Field Trial/ Residue Decline –Sweet and Tart Cherries

Primary Evaluator	This DER was originally prepared under contract by Dynamac Corporation.
Approved by	Nancy Dodd, Chemist Nancy Dodd Date: 2/20/08 Registration Action Branch 3 Health Effects Division (7509P)

Note: This DER was originally prepared under contract by Versar, Inc. (6850 Versar Center, Springfield, VA 22151; submitted 06/29/07). The DER has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORTS:

46901707. Green, C.A. (2006) Magnitude of the Residues of Metconazole on Cherries. Lab Project Number: 25654. Unpublished study prepared by Valent U.S.A. Corporation. 214 pages.

EXECUTIVE SUMMARY:

Valent U.S.A. Corporation has submitted field trial data for metconazole on cherries. Eight field trials were conducted in the United States in Zones 1 (1 trial in NY), 5 (3 trials in MI), 10 (2 trials in CA), and 11 (2 trials in OR) during the 2003, 2004 and 2005 growing seasons. Except for Trial B in Michigan, one treated plot at each site received three airblast foliar applications of Metconazole 1.81 FL, formulated as a 20.5% active ingredient (ai) flowable liquid concentrate (FlC) containing1.81 lb ai/gal. The applications were made at a nominal rate of 0.136 lb ai/A for a total seasonal application rate of ~0.405-0.416 lb ai/A. The treatment plot at Trial B (MI; 2003) received four airblast foliar applications of the test substance, for a total seasonal application rate of 0.538 lb ai/A. In addition to these treatment plots, Trials I in NY and J in MI had a second treatment plot which received treatments using Metconazole 50 WDG, formulated as a 50% water dispersible granule (WDG), according to the same use pattern at a total seasonal application rate of 0.0407-0.410 lb ai/A to provide side- by-side comparison of the two formulations. (Both the FlC and WDG formulations contain a mixture of *cis*- and *trans*-metconazole as the active ingredient in an approximate ratio of 85/15. For trials reflecting three applications, first applications were made at all sites at full bloom, second applications were made at petal fall (at RTIs of 7-13 days), and third applications were made near fruit maturity (at RTIs of 22-69 days). An adjuvant was not added to the spray mixtures for any of the applications.

At each trial location, one untreated control and two treated mature cherry raw agricultural commodity (RAC) samples were collected 13 to 14 days following the last test substance application (13- to 14-day PHI). In addition, one control and duplicate treated mature cherry samples were also harvested 3, 6 and 10 days after the last application at Trial B and at 10, 18 and 22 days after the last application at Trials E and G (OR and CA) to determine residue decline.

Samples were stored frozen (at approximately -20°C) prior to analysis; the maximum storage interval from harvest to extraction was 123 days (4.0 months). Samples were analyzed within 1-6 days of extraction. Storage stability of *cis*- and *trans*-metconazole was determined by reanalysis of the fortified control cherry samples from Trial I which were re-extracted, in duplicate, 159 days after the initial analysis of all of the crop field trial samples. Storage stability of *cis*- and *trans*-metconazole in frozen storage for 159 days was acceptable based on the storage stability recovery results.

Cherry samples were analyzed for residues of *cis*- and *trans*-metconazole using Method RM-41C-1, which uses a gas chromatograph with a nitrogen-phosphorous detector (GC/NPD). The method was adequate for data collection based on acceptable method validation and concurrent method recoveries. The validated LOQ was 0.02 ppm for each isomer.

Following three to four applications of the 1.81 lb/gal FlC formulation at a total rate of 0.405-0.416 lb ai/A or 0.538 lb ai/A (one trial only) and a PHI of 13-14 days, maximum residues of *cis*- and *trans*-metconazole in/on cherries were 0.134 and 0.028 ppm, respectively, for total metconazole residues of 0.162 ppm. HED notes that, because residues were similar, results for the single trial reflecting four applications were included with the results of the trials reflecting three applications.

In the side-by-side trials conducted with the 1.81 lb/gal FlC and the 50% WDG formulation, total metconazole residues were slightly higher following application of the 50% WDG formulation in each trial. At the NY trial, residues were 0.062-0.069 ppm following application of the FlC formulation and 0.068-0.076 ppm following application of the WDG formulation; at the MI trial residues were <0.04 ppm following application of the FlC formulation and 0.047-0.049 ppm following application of the WDG formulation.

For the three residue decline studies, total metconazole residues declined with increasing PHIs.

HED notes that samples were not analyzed for the triazole metabolites (1,2,4-triazole, triazolylalanine, and triazolylacetic acid).

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the field trial residue data are classified as scientifically acceptable.

The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP#s 348168 and 348206.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality

statements were provided. The following deviations from regulatory requirements were reported: soil characterization, weather data, maintenance chemical applications, pesticide history data, irrigation records, cultural practices, and field sample weights for this study were not documented under GLP. Four study protocol deviations were also reported. The Study Director stated that these deviations did not impact the validity of the study.

A. BACKGROUND INFORMATION

Metconazole [5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol] is a broad-spectrum triazole Group 3 fungicide (sterol biosynthesis inhibitors). There are currently no registered uses of metconazole in the U.S.; however, a tolerance has been established for banana, and a Section 18 emergency exemption and supporting time-limited tolerances have been granted for use on soybean. Valent U.S.A. Corporation has applied for registration of metconazole in the U.S. for use on peanut, stone fruits, and tree nuts.

The chemical structure and nomenclature of metconazole, and the physicochemical properties of the technical grade of metconazole are presented in Tables A.1 and A.2.

Table A.1. Metconazole Nomenclature.

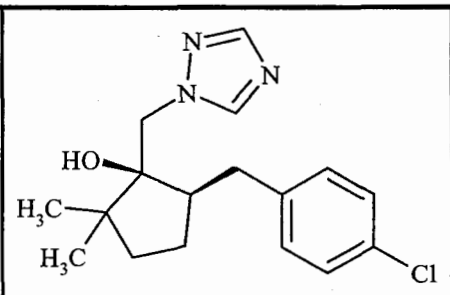
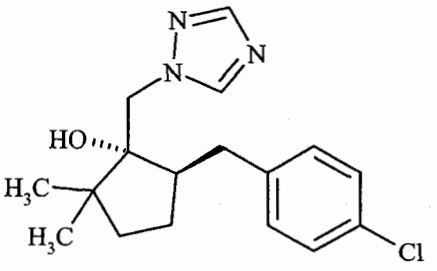
Chemical structure	 *cis*-isomer	 *trans*-isomer
Common name	Metconazole	
Company experimental name	KNF-S-474m (Kureha); BAS 555 F (BASF); V-10116 (Valent)	
IUPAC name	(1RS,5RS:1RS,5SR)-5-(4-chlorobenzyl)-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	
CAS name	5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	
CAS registry number	125116-23-6 (*cis*- and *trans*-isomers) 115850-27-6 (*cis*-isomer) 115850-28-7 (*trans*-isomer)	
End-use products (EP)	50% WDG (Metconazole 50 WDG Fungicide, EPA File Symbol 59639-RUT) 0.75 lb/gal SC/L (Caramba™ Fungicide, EPA File Symbol No. 7969-EUA) 0.67 lb/gal SC/L formulation (BAS 556 01F Fungicide, EPA File Symbol No. 7969-EUT; also contains the active ingredient pyraclostrobin at 0.83 lb/gal)	

Table A.2. Physicochemical Properties of Metconazole

Parameter	Value	References* (MRID)
Melting point/range	100.0-108.4°C (using Electrothermal Digital Melting Point Apparatus) (AC900,768 technical grade)	44721505
pH	5.81 at 25°C (1% aqueous suspension)	46808402
Relative density (20°C)	1.14 (relative density to water at 4°C, using capillary-stoppered, density-specific gravity bottle) (Lot No. AC 8879-140B)	44721505
Water solubility (20°C)	Using shake-flask method: 18.7 ± 1.0 mg/L (*cis*-isomer, WL148271, KNF-S-474m) 13.6 ± 1.7 mg/L (*trans*-isomer, WL148271, KNF-S-474m)	44721505

Solvent solubility (g/L) at 20°C — 44721505

Solvent	Metconazole	*cis*	*trans*
acetone	363	251	117
methanol	403	294	117
dichloromethane	481	343	141
ethyl acetate	260	173	90.0
propanol	132	86.6	46.7
toluene	103	66.2	38.0
Hexane	1.40	0.929	0.483

Vapor pressure (20°C)	Using gas-saturation method: $< 1.23 \times 10^{-5}$ Pa or 9.23×10^{-8} mm Hg (metconazole) $< 1.04 \times 10^{-5}$ Pa or 7.80×10^{-8} mm Hg (*cis*-isomer) $< 1.96 \times 10^{-6}$ Pa or 1.47×10^{-8} mm Hg (*trans*-isomer)	44721505
Dissociation constant (pK_a)	11.38±0.03 and 1.06±0.03 (in water at 29.1°C using spectrophotometric method; Lot No. AC 8879-140B)	44721505
Octanol/water partition coefficient, Log(K_{OW})	At 20 °C (using flask shaking method): K_{ow} (log K_{ow}) = 7090±989 (3.85) (Lot No. AC 8879-140B) (TGAI) K_{ow} (log K_{ow}) = 7150±803 (3.85) (*cis*-isomer, CL 354,801) K_{ow} (log K_{ow}) = 6800±1700 (3.8) (*trans*-isomer, CL 354,802)	44721505

UV/visible absorption spectrum — 46808403

pH	λ	A	log ε
cis-isomer			
2.0	221.4	0.828	4.03
6.8		0.8452	4.04
7.0		0.9126	4.08
10.3		0.7226	3.98
trans-isomer			
2.0	221.4	0.9053	4.07
7.0		0.9547	4.10
10.1		0.9893	4.11

* Product Chemistry Reviews: DP #256877, Shyam Mathur, Ph.D., 9/12/2000 and DP #329168, Shyam Mathur, Ph.D., 7/13/07.

B. EXPERIMENTAL DESIGN

A cherry tree treatment plot at seven of the eight field trial sites received three airblast sprayer applications of the 1.81 Metconazole formulation at a nominal rate of 0.136 lb ai/A, for a total seasonal application rate of 0.405-0.416 lb ai/A. At the eighth trial site (Trial B), the cherry tree treatment plot received four airblast sprayer applications of the 1.81 Metconazole formulation at a nominal rate of 0.136 lb ai/A, for a total seasonal application rate of 0.538 lb ai/A. In addition to these tests, a second cherry tree plot was treated using a 50WDG formulation of metconazole at Trial sites I and J. The re-treatment intervals at the eight sites ranged from 7 to 69 days. Applications were made using airblast sprayers and a spray volume of 104 to 135 gal/A (973 to 1,266 L/ha). An adjuvant was not used for any of the applications.

Single untreated and duplicate treated RAC samples of mature cherries were harvested 13 to 14 days following the last test substance application (13- to 14-day PHI). In addition, one control and duplicate treated mature cherry samples were harvested at 3, 6, and 10 days after the last application at Trial B and at 10, 18 and 22 days after the last application at Trials E and G to determine residue decline. Samples were collected from the control plot first and then from the treated plots. Samples were collected from at least four (4) individual trees in the center of each plot. RAC sample sizes ranged from 2.2 to 4.0 lb (1.0 to 1.8 kg), except for two samples from Trial I which were only 1.0 and 1.2 lbs (0.45 and 0.55 kg) due to bird damage.

Cultivation and trial maintenance methods were conducted in accordance with local agricultural practices; maintenance chemicals used at each trial site during the study were reported. Trifloxystrobin was used as a maintenance chemical at trial sites E and F. This chemical was not on the Approved Pesticide List when these trials were in progress. However, trifloxystrobin was later added to the Approved Pesticide List in 2005. For the growing season, a written description of temperature and precipitation as compared to 10 year historical data was provided, as well as monthly rainfall and irrigation data. The average monthly minimum and maximum temperature measurements were not reported. In general, temperature and rainfall were reported to be within average historical values for the residue study period. Overall precipitation was reported as below normal for Trials E, F, G, H, I, and J and as above normal for Trials B and D. No unusual weather conditions occurred during the study in the majority of the trials, however, it should be noted that rainfall in the month of May 2004 was almost 3X the 10 year average at Trial D and the overall temperatures during the 2005 growing season were the 2nd warmest on record for the past 30 years at Trial I. Irrigation was used as needed for four of the ten trials to supplement when rainfall totals were low.

B.1. Study Site Information

According to the Study Protocol, soil characterization was not required for this study (Table B.1.1). Refer to Table B.1.2 for study use patterns, and Table B.1.3 for geographic locations of submitted and requested trials.

TABLE B.1.1 Trial Site Conditions.

Trial Identification: City, State; NAFTA Region; Year (Trial No.)	Soil characteristics			
	Type	% OM	pH	CEC (meq/g)
Conklin, MI; Region 5; 2003 (V-25654-03-B)	NA*	NA	NA	NA
Conklin, MI; Region 5; 2004 (V-25654-04-D)	NA	NA	NA	NA
Parkdale, OR; Region 11; 2004 (V-25654-04-E)	NA	NA	NA	NA
The Dalles, OR Region 11; 2004 (V-25654-04-F)	NA	NA	NA	NA
Denair, CA; Region 10; 2004 (V-25654-04-G)	NA	NA	NA	NA
Kerman, CA; Region 10; 2004 (V-25654-04-H)	NA	NA	NA	NA
Williamson, NY; Region 1; 2005 (V-25654-05-I)	NA	NA	NA	NA
Conklin, MI; Region 5; 2005 (V-25654-05-J)	NA	NA	NA	NA

*NA – Not Available (data not collected)

TABLE B.1.2. Study Use Pattern.

Trial Identification: City, State; NAFTA Region; Yr (Trial No.)	EP[1]	Application							Tank Mix Adjuvants
		App. No.	Application Method	Growth Stage	Volume[2] GPA [L/ha]	Rate (lb a.i./A) [g a.i./ha]	RTI[3] (days)	Total Rate (lb a.i./A) [g a.i./ha]	
Conklin, MI Region 5; 2003 (V-25654-03-B)	1.81 FL	1	Airblast	Full bloom	117 [1,092]	0.135 [151]	0	0.538 [603]	None
		2	Airblast	Petal fall	112 [1,050]	0.132 [148]	7		
		3	Airblast	25% fruit turning red	119 [1,109]	0.136 [152]	44		
		4	Airblast	90% red fruit	116 [1,088]	0.136 [152]	7		
Conklin, MI Region 5; 2004 (V-25654-04-D)	1.81 FL	1	Airblast	Full bloom	118 [1,106]	0.136 [152]	0	0.407 [457]	None
		2	Airblast	Petal fall	125 [1,169]	0.136 [152]	10		
		3	Airblast	80% red fruit	124 [1,163]	0.136 [152]	44		
Parkdale, OR Region 11; 2004 (V-25654-04-E)	1.81 FL	1	Airblast	Full bloom	130 [1,217]	0.138 [155]	0	0.414 [464]	None
		2	Airblast	Petal fall	132 [1,235]	0.136 [152]	9		
		3	Airblast	Color advancing	131 [1,228]	0.139 [156]	69		
The Dalles, OR Region 11; 2004 (V-25654-04-F)	1.81 FL	1	Airblast	Full bloom	106 [994]	0.138 [154]	0	0.409 [458]	None
		2	Airblast	Petal Fall	104 [972]	0.133 [149]	9		
		3	Airblast	Red fruit	104 [973]	0.138 [155]	50		
Denair, CA Region 10; 2004 (V-25654-04-G)	1.81 FL	1	Airblast	Full bloom	132 [1,233]	0.136 [152]	0	0.405 [453]	None
		2	Airblast	90% Petal fall	135 [1,266]	0.135 [151]	10		
		3	Airblast	Beginning coloring	135 [1,264]	0.134 [150]	29		
Kerman, CA Region 10; 2004 (V-25654-04-H)	1.81 FL	1	Airblast	Full bloom	129 [1,203]	0.135 [151]	0	0.405 [454]	None
		2	Airblast	Petal fall	129 [1,210]	0.136 [152]	10		
		3	Airblast	14 days prior to harvest	129 [1,202]	0.135 [151]	22		

TABLE B.1.2. Study Use Pattern.

Trial Identification: City, State; NAFTA Region; Yr (Trial No.)	EP[1]	Application							Tank Mix Adjuvants
		App. No.	Application Method	Growth Stage	Volume[2] GPA [L/ha]	Rate (lb a.i./A) [g a.i./ha]	RTI[3] (days)	Total Rate (lb a.i./A) [g a.i./ha]	
Williamson, NY Region 1; 2005 (V-25654-05-I)	1.81 FL	1	Airblast	Full bloom	125 [1,171]	0.137 [153]	0	0.416 [466]	None
		2	Airblast	Petal fall	126 [1,175]	0.140 [156]	13		
		3	Airblast	Advanced fruit coloring	125 [1,171]	0.139 [156]	30		
	50 WDG	1	Airblast	Full bloom	125 [1,166]	0.136 [152]	0	0.407 [456]	None
		2	Airblast	Petal fall	120 [1,121]	0.133 [149]	13		
		3	Airblast	Advanced fruit coloring	126 [1,175]	0.139 [156]	30		
Conklin, MI Region 5; 2005 (V-25654-05-J)	1.81 FL	1	Airblast	Full bloom	126 [1,181]	0.136 [153]	0	0.409 [458]	None
		2	Airblast	Petal fall	128 [1,199]	0.137 [153]	13		
		3	Airblast	75% red fruit	124 [1,163]	0.136 [152]	40		
	50 WDG	1	Airblast	Full bloom	126 [1,182]	0.137 [153]	0	0.410 [459]	None
		2	Airblast	Petal fall	128 [1,201]	0.137 [154]	13		
		3	Airblast	75% red fruit	125 [1,164]	0.136 [152]	40		

[1]EP = End-use Product; Metconazole 1.81 FL is a flowable formulation containing 20.5% (nominal) of a mixture of *cis*- and *trans*-metconazole (85/15 ratio) as the active ingredient. Metconazole 50 WDG is a water dispersible granular formulation containing 50% (nominal) of a mixture of *cis*- and *trans*-metconazole (85/15 ratio) as the active ingredient.
[2] GPA = gallons per acre.
[3] Retreatment Interval

TABLE B.1.3. Trial Numbers and Geographical Locations.

NAFTA Growing Zones	Sweet Cherry			Tart Cherry		
	Submitted	Requested as Part of Crop Group 12[1]		Submitted	Requested as Part of Crop Group 12[1]	
		Canada	U.S.		Canada	U.S.
1	1					1
1A						
2						
3						
4						
5			2	3		4
5A						
5B						
6						
7						
7A						
8						
9						1
10	2		2			
11	2		2			
12						
13						
14						
15						
16						
17						
18						
19						
20						
21						
Total	5		6	3		6

[1]The cherry data were submitted with peach and plum data to satisfy EPA Residue Chemistry Test Guidelines in OPPTS 860.1500, Crop Field Trials for Fruit, Stone, Group 12. The guidelines indicate that a total of six sweet or tart cherry trials should be conducted. This requirement was met through the submittal of 5 sweet cherry trials and 3 tart cherry trials.

B.2. Sample Handling and Preparation

After harvesting, all of the samples were transported in ice chests or at ambient temperatures to facilities and stored in a freezer. All of the samples were shipped by freezer truck (ACDS) to the Valent Technical Center in Dublin, CA. Samples were kept under frozen conditions until further preparation (pitting, maceration and sub-sampling), extraction, and analysis.

B.3. Analytical Methodology

Method RM-41C-1 was used to concurrently analyze cherry RAC samples for residues of *cis*- and *trans*-metconazole using a gas chromatograph with a nitrogen-phosphorous detector (GC/NPD). The validated LOQ was 0.02 ppm and the LOD was 0.01 for each *cis*- and *trans*-metconazole.

For Method RM-41C-1, residues of *cis*- and *trans*-metconazole were extracted from each sample with an aqueous acetonitrile mixture (70:30 acetonitrile/water), filtered to remove solids, and the acetonitrile in the filtrate is removed by rotary evaporation to obtain an aqueous residue. The residues are partitioned from the aqueous mixture into hexane, and the residues are cleaned up by an acetonitrile/hexane partition. The acetonitrile is then removed by rotary evaporation, and the residues are cleaned up using a C18 SPE cartridge. The column eluant is rotary evaporated and the residues are dissolved in toluene. Analysis of the extracts is performed using GC/NPD.

C. RESULTS AND DISCUSSION

Sample storage conditions and intervals are summarized in Table C.2. The maximum storage interval of cherry samples, from harvest to extraction, was 123 days (4.0 months). The samples were stored at approximately -20°C. Storage stability of *cis*- and *trans*-metconazole was determined by reanalysis of the fortified control cherry samples from Trial I which were re-extracted, in duplicate, 159 days after the initial analysis of all of the crop field trial samples. Recoveries for the re-extracted fortified control cherry samples averaged 101% for *cis*-metconazole and 103% for *trans*-metconazole. Field sample residues were not corrected for in-storage dissipation.

Cherry samples were analyzed for residues of *cis*- and *trans*-metconazole using Method RM-41C-1. The samples were analyzed within 4 days of extraction. The LOD was 0.01 ppm and the LOQ was 0.02 ppm for each of the two metconazole isomers in cherries. Method validation was conducted using control peach samples fortified with *cis*- and *trans*-metconazole at two levels (0.01 and 0.02 ppm). The mean recoveries were 90.3 and 95.6% for *cis*-metconazole and 91.7 and 97.1% for *trans*-metconazole. Concurrent method recoveries are reported in Table C.1. Controls were fortified with *cis*- and *trans*-metconazole at 0.02, 0.10, 0.50 and 0.75 ppm. Recoveries ranged from 86.7 to 110% for *cis*-metconazole (averaged 97.3% with a standard deviation of 5.63; n=18) and from 90.7 to 116% for *trans*-metconazole (averaged 98.5% with a standard deviation of 6.85; n=18). It should be noted that these values are based on recoveries from the trials reported in this DER. In the summarization of the concurrent recoveries, the study author also included the concurrent recoveries from Trial A. The fortification levels encompassed the expected residues in cherries. The method was adequate for data collection based on acceptable method validation and concurrent method recoveries.

Residue data from the cherry field trials are reported in Table C.3. A summary of the residues in/on cherries from the 14-day PHI trials conducted at the 0.136 lb ai/A application rate (total seasonal rate of 0.405 to 0.538 lb ai/A) using Metconazole 1.81 FL is presented in Table C.4. For these samples, residues of total metconazole (sum of *cis*- and *trans*-metconazole) ranged from <LOQ to 0.162 ppm, residues of *trans*-metconazole ranged from <LOQ (0.02 ppm) to 0.028 ppm and residues of *cis*-metconazole ranged from <LOQ (0.02 ppm) to 0.134 ppm. The average total metconazole residue was 0.068 ppm. These values include the residues detected in Trial B (total average metconazole value of 0.05 ppm), which received four applications of the test product rather than three.

Residues of *cis*- and *trans*-metconazole in/on untreated cherry samples were not detected above the LOD (0.010 ppm).

For the three residue decline studies, total metconazole residues declined with increasing PHIs, although the Day-10 results from Trial G appear low and prevent the estimation of a half-life. For Trials B and E, the reported estimated half-life for metconazole on cherries was 3.3 and 6.2 days, respectively. In calculating these half-lives, the study author did not use values below the LOD and used the LOD value for residues between the LOD and LOQ. Versar also calculated the half-lives for these trials, but used the LOQ value for all residues reported as less than the LOQ. Versar estimated half-life values of 3.69 days (R^2=0.995) for Trial B and 11.78 days (R^2=0.912) for Trial E.

The results from the second treatment plots at Trial sites I and J which received applications of the Metconazole WDG formulation are similar to the results from the treatment plots which received applications of the Metconazole FlC formulation. At Trial site I, the *cis*-metconazole residues averaged 0.052 ppm and the *trans*-metconazole residues were <LOQ. At Trial site J, the *cis*-metconazole residues averaged 0.028 ppm and the *trans*-metconazole residues were <LOQ.

TABLE C.1. Summary of Concurrent Recoveries of Metconazole from Cherry.

Matrix	Spike level (ppm)	Sample size (n)	Recoveries (%)	Mean ± std dev (%)
***cis*-Metconazole**				
Cherry	0.02	9	97.0, 86.7[a], 99.5, 102, 102, 93.0, 94.5, 110, 106	97.3 ± 5.63
	0.1	6	93.9, 90.3[a], 99.1, 102, 94.4, 92.9	
	0.5	2	98.6, 92.6	
	0.75	1	98.1	
***trans*-Metconazole**				
Cherry	0.02	9	108, 96.7[a], 101, 101, 100, 94.5, 95.5, 116, 111	98.5 ± 6.85
	0.1	6	95.0, 93.0[a], 95.0, 97.8, 90.7, 91.8	
	0.5	2	96.8, 91.6	
	0.75	1	98.5	

[a] Recoveries were corrected for residues detected in the control (<0.01 ppm)

TABLE C.2. Summary of Storage Conditions.

Matrix (RAC)	Analyte	Storage Temperature (°C)	Actual Storage Duration (days)	Interval of Demonstrated Storage Stability* (days)
Cherry	*cis*-Metconazole	Approximately -20°C in laboratory	123	159
	trans-Metconazole			

* Storage stability of cis- and trans-metconazole on cherries was determined by reanalysis of treated samples from trial V-25654-05-I after 159 days in frozen storage.

TABLE C.3. Residue Data from Crop Field Trials with Metconazole

Trial Identification: City, State; NAFTA Region; Yr (Trial No.)	Cherry Variety	Commodity	Formulation	Total Rate (lb a.i./A) [g a.i./ha]	PHI (days)	Uncorrected Residue Levels (ppm)*		
						cis-Metconazole	*trans*-Metconazole	Metconazole (total)
Conklin, MI; Region 5; 2003 (V-25654-03-B)	Montmorency (Tart)	fruit	Metconazole 1.81 FL	0.538 [603]	3	0.27	0.065	0.33
						0.25	0.063	0.31
					6	0.17	0.042	0.21
						0.15	0.037	0.19
					10	0.073	0.021	0.094
						0.071	0.021	0.092
					13	0.03	<0.02 (0.01)	0.05
						0.029	<0.02	0.049
Conklin, MI; Region 5; 2004 (V-25654-04-D)	Montmorency (Tart)	fruit	Metconazole 1.81 FL	0.407 [457]	14	<0.02	<0.02	<0.04
						<0.02	<0.02	<0.04
Parkdale, OR; Region 11; 2004 (V-25654-04-E)	Bing (Sweet)	fruit	Metconazole 1.81 FL	0.414 [464]	10	0.052	<0.02 (0.013)	0.072
						0.064	<0.02 (0.016)	0.084
					14	0.047	<0.02 (0.012)	0.067
						0.039	<0.02 (0.01)	0.059
					18	0.027	<0.02	0.047
						0.021	<0.02	0.041
					22	<0.02 (0.015)	<0.02	<0.04
						<0.02 (0.019)	<0.02	<0.04
The Dalles, OR Region 11; 2004 (V-25654-04-F)	Bing (Sweet)	fruit	Metconazole 1.81 FL	0.409 [458]	13	0.054	<0.02 (0.016)	0.074
						0.037	<0.02 (0.011)	0.057
Denair, CA Region 10; 2004 (V-25654-04-G)	Bing (Sweet)	fruit	Metconazole 1.81 FL	0.405 [453]	10	0.050[a]	<0.02[a] (0.013)	0.07
						0.058[a]	<0.02[a] (0.015)	0.078
					14	0.056	<0.02 (0.014)	0.076
						0.066	<0.02 (0.016)	0.086
					18	0.053	<0.02 (0.012)	0.073
						0.050	<0.02 (0.013)	0.070

TABLE C.3. Residue Data from Crop Field Trials with Metconazole

Trial Identification: City, State; NAFTA Region; Yr (Trial No.)	Cherry Variety	Commodity	Formulation	Total Rate (lb a.i./A) [g a.i./ha]	PHI (days)	Uncorrected Residue Levels (ppm)*		
						cis-Metconazole	*trans*-Metconazole	Metconazole (total)
Denair, CA; Region 10; 2004 (V-25654-04-G)	Bing (Sweet)	fruit	Metconazole 1.81 FL	0.405 [453]	22	0.044	<0.02 (0.011)	0.064
						0.04	<0.02 (0.01)	0.060
Kerman, CA; Region 10; 2004 (V-25654-04-H)	Tulare (Sweet)	fruit	Metconazole 1.81 FL	0.405 [454]	14	0.134	0.028	0.162
						0.103	0.021	0.12
Williamson, NY; Region 1; 2005 (V-25654-05-I)	Heartland (Sweet)	fruit	Metconazole 1.81 FL	0.416 [466]	14	0.042	<0.02 (0.016)	0.062
						0.049	<0.02 (0.019)	0.069
			Metconazole 50 WDG	0.407 [456]	14	0.048	<0.02 (0.014)	0.068
						0.056	<0.02 (0.018)	0.076
Conklin, MI; Region 5; 2005 (V-25654-05-J)	Montmorency (Tart)	fruit	Metconazole 1.81 FL	0.409 [458]	14	<0.02 (0.018)	<0.02	<0.04
						<0.02 (0.013)	<0.02	<0.04
			Metconazole 50 WDG	0.410 [459]	14	0.029	<0.02	0.049
						0.027	<0.02	0.047

Notes:
LOQ = 0.02 ppm for each *cis*- and *trans*-metconazole.
LOD = 0.01 ppm for each *cis*- and *trans*-metconazole.
In the calculation of total metconazole, the LOQ value (0.02 ppm) was used when the residue value dropped below the LOQ.
Residues between the LOD and LOQ are reported in parentheses.
[a] Residue is average of two analyses

TABLE C.4.1. Summary of Residue Data from Crop Field Trials with Metconazole (1.81 FL).

Matrix	Total Application Rate (lb a.i./A) [kg a.i./ha]	PHI (days)	Residue Levels* (ppm)						
			n	Min.	Max.	HAFT*	Median (STMdR)	Mean (STMR)	Std. Dev.
Total Metconazole									
Cherry	0.405 to 0.538 [0.453 to 0.603]	13-14	16	<0.040	0.162	0.143	0.061	0.068	0.033
***cis*-Metconazole**									
Cherry	0.405 to 0.538 [0.453 to 0.603]	13-14	16	<0.020	0.134	0.119	0.041	0.048	0.032
***trans*-Metconazole**									
Cherry	0.405 to 0.538 [0.453 to 0.603]	13-14	16	<0.020	0.028	0.025	0.020	0.021	0.002

*Notes:
HAFT = Highest Average Field Trial.
LOQ = 0.02 ppm for each metconazole isomers (*cis*- and *trans*-).
Statistical calculations were performed using a value of LOQ when residues were reported as <LOQ.
Total Metconazole was the sum of both *cis*- and *trans*-metconazole.

D. CONCLUSION

The submitted field trial data are adequate and reflect the use of three foliar applications of the 1.81 FL formulation of metconazole at a nominal rate of 1.36 lb ai/A/application for a total seasonal rate of 0.405-0.416 lb ai/A on cherries grown in the United States with a 14-day PHI. An acceptable method was used for quantitation of residues in/on cherries. Acceptable storage stability data were provided for cherries stored at approximately -20°C for 159 days. The temperature and rainfall recordings were generally within average historical values for the residue study period. No unusual weather conditions occurred during the study in the majority of the trials; however, it should be noted that at Trial D, rainfall in the month of May, 2004 was almost 3X the 10 year average, and it was reported that the overall temperatures during the 2005 growing season at the test site for Trial I were the 2nd warmest on record for the past 30 years. These factors did not appear to have an adverse impact to the results of the studies. Additionally, it does not appear that the agricultural practices used adversely impacted the results of the study.

E. REFERENCES

DP#:	324541
Subject:	Metconazole. Request for a Tolerance on Imported Bananas. Summary of Analytical Chemistry and Residue Data. Petition Number 9E05052.
From:	N. Dodd
To:	M. Waller
Date:	12/14/05
MRIDs:	44721506, 44721507, 44721508, 44721509, 44721510, and 44721511

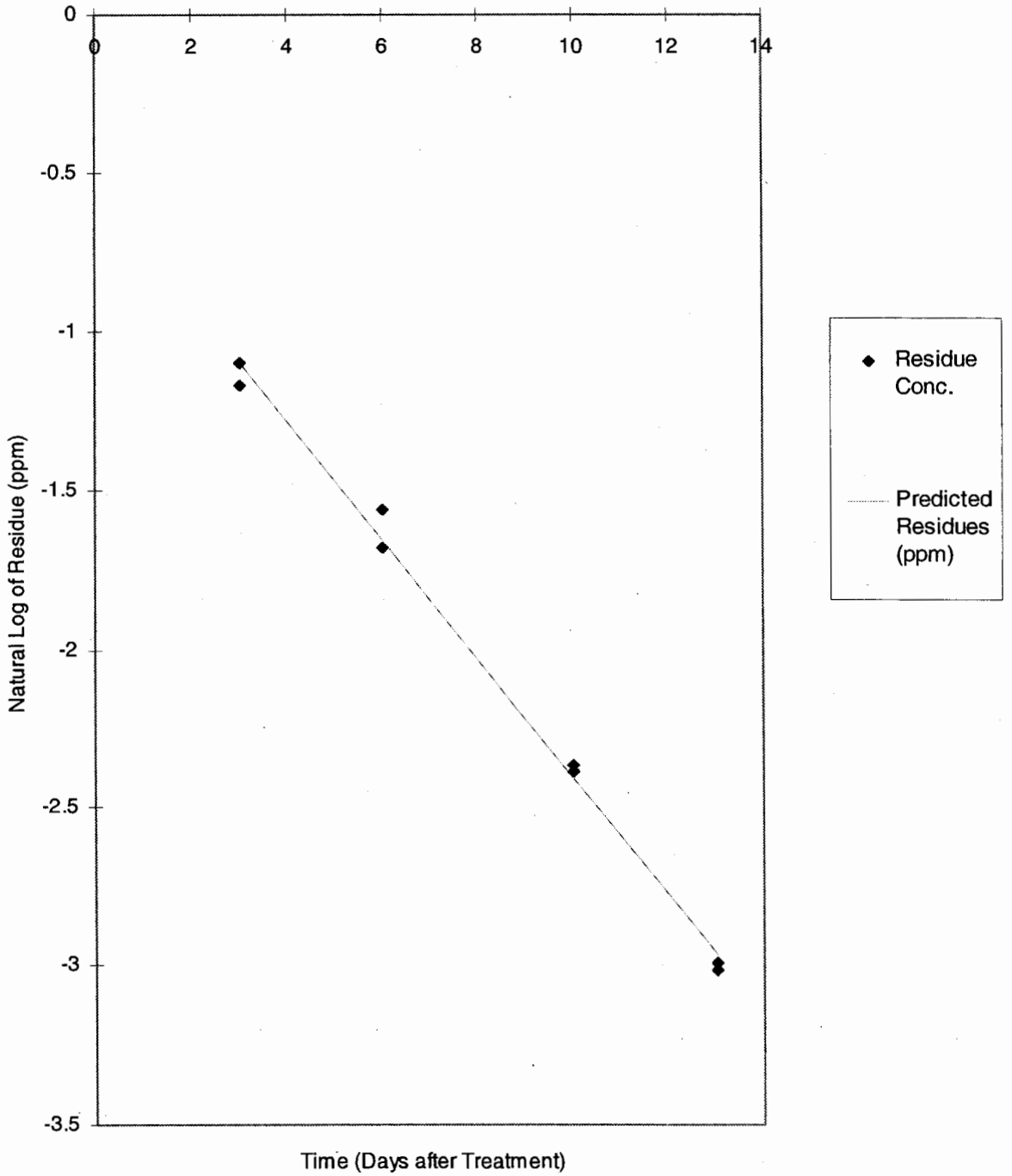
F. DOCUMENT TRACKING

RDI: N. Dodd (2/20/08)
Petition Number: 6F7095
DP#s: 348168 and 348206
PC Code: 125619

Template Version June 2005

APPENDIX 1
(Regression Data for Total Metconazole)

Regression Analysis: Log of Residue vs. Time for Trial B



Regression Analysis: Summary Output for Trial B Total

Regression Statistics	
Multiple R	0.997428
R Square	0.994863
Adjusted R^2	0.994006
Standard Error	0.059302
Observations	8

ANOVA

	df	*SS*	*MS*	*F*	*Signif. F*
Regression	1	4.086086	4.086086	1161.9124	4.24533E-08
Residual	6	0.0211	0.003517		
Total	7	4.107186			

	Coeff.	*Std. Error*	*t Stat*	*P-value*	*Lower 95%*	*Upper 95%*
Intercept	-0.53094	0.048783	-10.8836	3.567E-05	-0.650307429	-0.411569432
Slope	-0.18768	0.005506	-34.0868	4.245E-08	-0.201155694	-0.174210165

Half Life = 3.693182 Days

Predicted Residue Levels

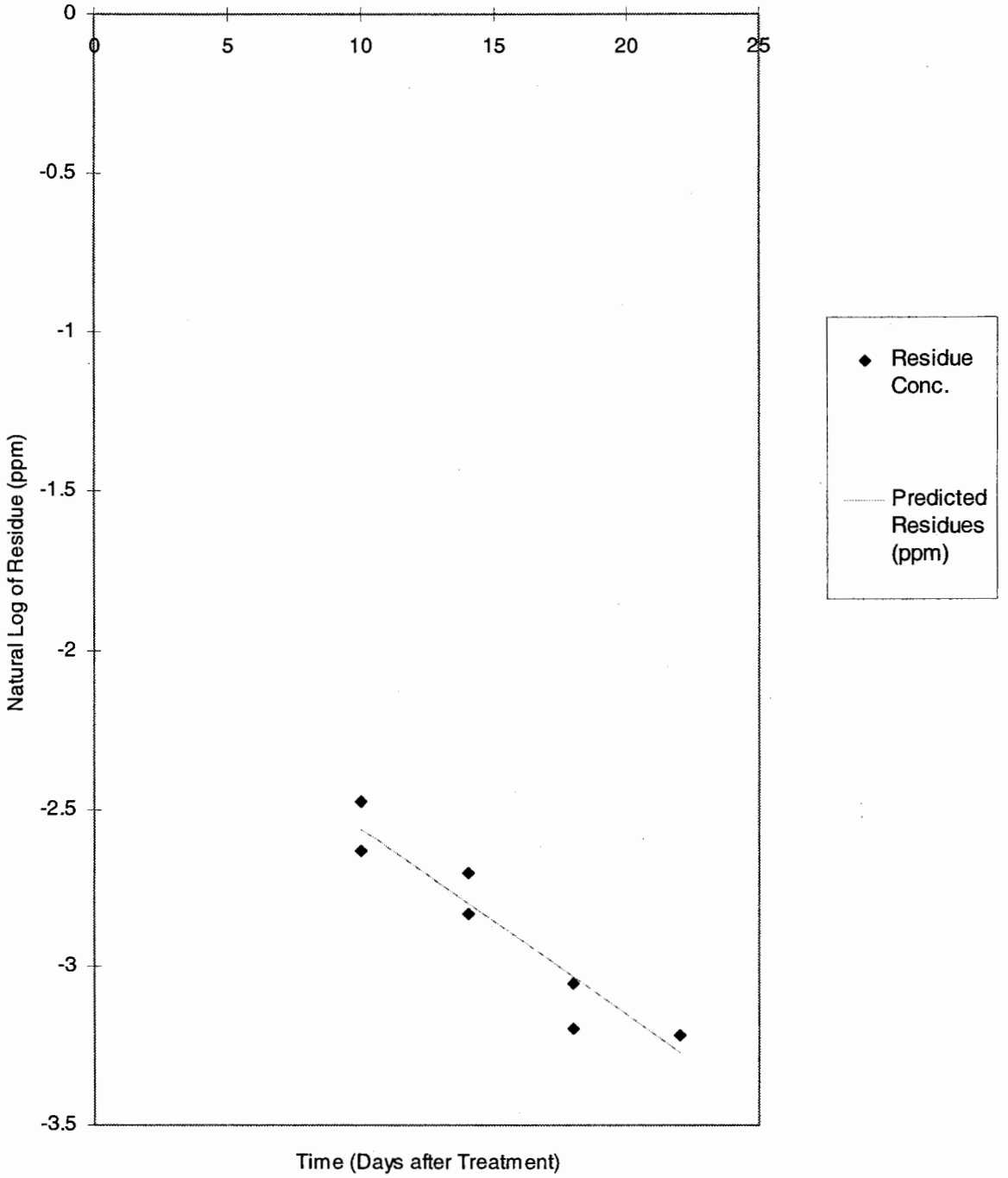
Time (Days)	Residue (ppm)
0	0.588053
1	0.487424
2	0.404015
3	0.334879
4	0.277573
5	0.230074
6	0.190703
7	0.15807
8	0.13102
9	0.1086
10	0.090016
11	0.074612
12	0.061844
13	0.051261
14	0.042489
15	0.035219
16	0.029192
17	0.024196
18	0.020056
19	0.016624
20	0.013779

Time (Days)	Residue (ppm)
21	0.0114212
22	0.0094668
23	0.0078468
24	0.0065041
25	0.0053911
26	0.0044685
27	0.0037039
28	0.0030701
29	0.0025447
30	0.0021092
31	0.0017483
32	0.0014491
33	0.0012012
34	0.0009956
35	0.0008252

Regression Analysis: Means and CVs for Trial B Total

Days after Last Treatment	Residues (ppm)	Mean (ppm)	Standard Deviation (ppm)	Coefficient of Variation (%)
3	0.334	0.323	0.0163	5.04
	0.311			
6	0.211	0.199	0.017	8.53
	0.187			
10	0.094	0.093	0.00141	1.52
	0.092			
13	0.050	0.0495	0.000707	1.43
	0.049			

Regression Analysis: Log of Residue vs. Time for Trial E



Regression Analysis: Summary Output for Trial E Total

Regression Statistics	
Multiple R	0.954958
R Square	0.911945
Adjusted R^2	0.897269
Standard Error	0.094427
Observations	8

ANOVA

	df	*SS*	*MS*	*F*	*Signif. F*
Regression	1	0.554057	0.554057	62.139075	0.000220803
Residual	6	0.053498	0.008916		
Total	7	0.607555			

	Coeff.	*Std. Error*	*t Stat*	*P-value*	*Lower 95%*	*Upper 95%*
Intercept	-1.97482	0.124019	-15.9235	3.894E-06	-2.278284396	-1.671355303
Slope	-0.05885	0.007465	-7.88283	0.0002208	-0.077112449	-0.040579611

Half Life = 11.779 Days

Predicted Residue Levels

Time (Days)	Residue (ppm)
0	0.138786
1	0.130855
2	0.123377
3	0.116326
4	0.109678
5	0.10341
6	0.097501
7	0.091929
8	0.086675
9	0.081722
10	0.077052
11	0.072648
12	0.068497
13	0.064582
14	0.060891
15	0.057412
16	0.054131
17	0.051037
18	0.04812
19	0.04537
20	0.042778

Time (Days)	Residue (ppm)
21	0.040333
22	0.038028
23	0.0358548
24	0.0338057
25	0.0318738
26	0.0300523
27	0.0283349
28	0.0267156
29	0.0251888
30	0.0237493
31	0.0223921
32	0.0211124
33	0.0199059
34	0.0187683
35	0.0176957

Regression Analysis: Means and CVs for Trial E Total

Days after Last Treatment	Residues (ppm)	Mean (ppm)	Standard Deviation (ppm)	Coefficient of Variation (%)
10	0.072	0.078	0.00849	10.9
	0.084			
14	0.067	0.063	0.00566	8.98
	0.059			
18	0.047	0.044	0.00424	9.64
	0.041			
22	0.04	0.04	0	0
	0.04			

Primary Evaluator	This DER was originally prepared under contract by Dynamac Corporation.
Approved by	Nancy Dodd, Chemist *Nancy Dodd* Date: 2/20/08 Registration Action Branch 3 Health Effects Division (7509P)

Note: This DER was originally prepared under contract by Versar, Inc. (6850 Versar Center, Springfield, VA 22151; submitted 06/29/07). The DER has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORTS:

46901708. Green, C.A. (2006) Magnitude of the Residues of Metconazole on Peaches. Lab Project Number: 25662. Unpublished study prepared by Valent U.S.A. Corporation. 224 pages.

EXECUTIVE SUMMARY:

Valent U.S.A. Corporation has submitted field trial data for metconazole on peaches. A total of nine field trials, performed between 2003 and 2005, are presented in this DER. An additional three field trials (Trials A, C and E) were conducted in 2003; however, these three trials were conducted using an additional application and a shorter preharvest interval (PHI) than the other trials and were therefore only presented in the Study Report for supplemental information. The results from these three trials are not presented in this DER.

The nine trials presented in this DER were conducted in the United States encompassing Zones 1 (1 trial in PA), 2 (3 trials in GA), 5 (1 trial in MI), 6 (1 trial in TX) and 10 (3 trials in CA) during the 2003, 2004 and 2005 growing seasons. Except for Trial B in GA, one treated plot at each site received three airblast foliar applications of Metconazole 1.81 FL, formulated as a 20.5% active ingredient (ai) flowable liquid concentrate (FlC). The applications were made at a nominal rate of 0.136 lb ai/A for a total seasonal application rate of 0.403-0.417 lb ai/A/season. The treatment plot at Trial B received four airblast foliar applications of the test substance, for a total seasonal application rate of 0.545 lb ai/A/season. In addition to these treatment plots, Trial G had a second treatment plot which received treatments using Metconazole 1.81 FL at double the application rate (0.272 lb ai/A/application) and Trial M had a second treatment plot which received treatments using Metconazole 50 WDG, formulated as a 50% water dispersible granule (WDG). Both the FL and WDG formulations contain a mixture of *cis*- and *trans*-metconazole as the active ingredient ~~in~~ an approximate ratio of 85/15. Re-treatment intervals at the plots ranged from 7 to 117 days. An adjuvant was not added to the spray mixtures for any of the applications.

At each trial location, one untreated control and two treated mature peach raw agricultural commodity (RAC) samples were collected 13 to 14 days following the last test substance application (13- to 14-day PHI). In addition, one control and duplicate treated mature peach samples were also harvested at 3, 7, and 10 days after the last application at Trial B and 10, 18

and 22 days after the last application at Trial K to determine residue decline.

Samples were stored frozen (at approximately -20°C) prior to analysis; the maximum storage interval from harvest to extraction was 131 days (approximately 4 months). Storage stability of *cis*- and *trans*-metconazole was demonstrated by reanalysis of fortified control cherry samples documented in *Magnitude of the Residues of Metconazole on Cherries* (MRID 46901707), in which selected samples were re-extracted, in duplicate, 159 days after the initial analysis of all of the crop field trial samples. Cherries and peaches are in the same crop group (Fruit, Stone, Group 12) and the storage conditions for cherries were the same as those used in this study; therefore, the cherry storage stability data are adequate.

The summary statistics include all nine trials conducted with Metconazole 1.81 FL at a nominal application rate of 0.136 lb ai/A, which includes Trial B which was performed using 4 applications of the test substance (for a total seasonal application rate of 0.545 lb ai/A) and the remaining trials which were performed using 3 applications of the test substance (for a total seasonal application rate of 0.403-0.417 lb ai/A). The maximum average residues in/on peaches harvested 13 to 14 days after the last application were 0.086 ppm for total metconazole and 0.066 ppm for *cis*-metconazole. All *trans*-metconazole residues were less than the limit of quantitation (LOQ) of 0.02 ppm. The results from the second treatment plot at Trial M which received applications of the Metconazole WDG formulation are similar to the results from the treatment plots which received applications of the Metconazole FL formulation. The *cis*-metconazole residues were <LOQ and 0.020 ppm and the *trans*-metconazole residues were both <LOQ.

For the two residue decline studies, the total metconazole residues declined with increasing PHIs. For Trials B and K, the reported estimated half-lives for total metconazole in/on peaches were 7.7 and 6.6 days, respectively. In calculating these half-lives, the study author did not use values below the limit of detection (LOD) and used the LOD value for residues between the LOD and LOQ. Versar also calculated the half-lives for these trials, but used the LOQ value for all residues reported as less than the LOQ. Versar's estimated half-life values were 12.6 days (R^2=0.942) for Trial B and 9.9 days (R^2=0.843) for Trial K.

HED notes that samples were not analyzed for the triazole metabolites (1,2,4-triazole, triazolylalanine, and triazolylacetic acid).

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the field trial residue data are classified as scientifically acceptable.

The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP#s 348168 and 348206.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. The following deviations from regulatory requirements were reported: real time and historical weather data, pesticide history, cultural practices, the application of maintenance chemicals, irrigation records, the measurement of relative humidity, wind velocity, field sample weights, GPS locations and soil characterization for this study were not documented under GLP. Additionally, original data for the second application at the Trial M site was lost and the pitting of the peaches for Trials H through L was not documented. Numerous study protocol deviations were also reported, including the collection of only 16 peaches at Trial G for the 1X application rate treatment plot. The Study Director stated that these deviations did not impact the validity of the study.

A. BACKGROUND INFORMATION

Metconazole [5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol] is a broad-spectrum triazole Group 3 fungicide (sterol biosynthesis inhibitors). There are currently no registered uses of metconazole in the U.S.; however, a tolerance has been established for banana, and a Section 18 emergency exemption and supporting time-limited tolerances have been granted for use on soybean. Valent U.S.A. Corporation has applied for registration of metconazole in the U.S. for use on peanut, stone fruits, and tree nuts.

The chemical structure and nomenclature of metconazole, and the physicochemical properties of the technical grade of metconazole are presented in Tables A.1 and A.2.

Table A.1. Metconazole Nomenclature.

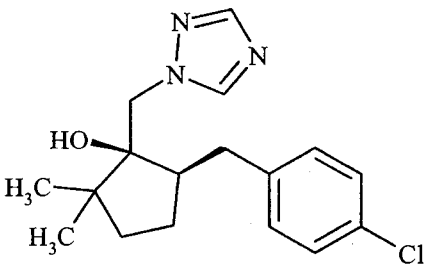
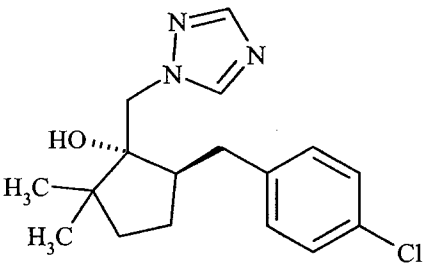
Chemical structure	 *cis*-isomer	 *trans*-isomer
Common name	Metconazole	
Company experimental name	KNF-S-474m (Kureha); BAS 555 F (BASF); V-10116 (Valent)	
IUPAC name	(1RS,5RS:1RS,5SR)-5-(4-chlorobenzyl)-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	
CAS name	5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	
CAS registry number	125116-23-6 (*cis*- and *trans*-isomers) 115850-27-6 (*cis*-isomer) 115850-28-7 (*trans*-isomer)	

Table A.1. Metconazole Nomenclature.	
End-use products (EP)	50% WDG (Metconazole 50 WDG Fungicide, EPA File Symbol 59639-RUT) 0.75 lb/gal SC/L (Caramba™ Fungicide, EPA File Symbol No. 7969-EUA) 0.67 lb/gal SC/L formulation (BAS 556 01F Fungicide, EPA File Symbol No. 7969-EUT; also contains the active ingredient pyraclostrobin at 0.83 lb/gal)

Table A.2. Physicochemical Properties of Metconazole

Parameter	Value				References* (MRID)
Melting point/range	100.0-108.4°C (using Electrothermal Digital Melting Point Apparatus) (AC900,768 technical grade)				44721505
pH	5.81 at 25°C (1% aqueous suspension)				46808402
Relative density (20°C)	1.14 (relative density to water at 4°C, using capillary-stoppered, density-specific gravity bottle) (Lot No. AC 8879-140B)				44721505
Water solubility (20°C)	Using shake-flask method: 18.7 ± 1.0 mg/L (*cis*-isomer, WL148271, KNF-S-474m) 13.6 ± 1.7 mg/L (*trans*-isomer, WL148271, KNF-S-474m)				44721505
Solvent solubility (g/L) at 20°C	Solvent	Metconazole	*cis*	*trans*	44721505
	acetone	363	251	117	
	methanol	403	294	117	
	dichloromethane	481	343	141	
	ethyl acetate	260	173	90.0	
	propanol	132	86.6	46.7	
	toluene	103	66.2	38.0	
	Hexane	1.40	0.929	0.483	
Vapor pressure (20°C)	Using gas-saturation method: $< 1.23 \times 10^{-5}$ Pa or 9.23×10^{-8} mm Hg (metconazole) $< 1.04 \times 10^{-5}$ Pa or 7.80×10^{-8} mm Hg (*cis*-isomer) $< 1.96 \times 10^{-6}$ Pa or 1.47×10^{-8} mm Hg (*trans*-isomer)				44721505
Dissociation constant (pK_a)	11.38±0.03 and 1.06±0.03 (in water at 29.1°C using spectrophotometric method; Lot No. AC 8879-140B)				44721505
Octanol/water partition coefficient, Log(K_{OW})	At 20 °C (using flask shaking method): K_{ow} (log K_{ow}) = 7090±989 (3.85) (Lot No. AC 8879-140B) (TGAI) K_{ow} (log K_{ow}) = 7150±803 (3.85) (*cis*-isomer, CL 354,801) K_{ow} (log K_{ow}) = 6800±1700 (3.8) (*trans*-isomer, CL 354,802)				44721505
UV/visible absorption spectrum	pH	λ	A	log ε	46808403
	cis-isomer				
	2.0	221.4	0.828	4.03	
	6.8		0.8452	4.04	

Table A.2. Physicochemical Properties of Metconazole

Parameter	Value				References* (MRID)
	7.0		0.9126	4.08	
	10.3		0.7226	3.98	
	trans-isomer				
	2.0	221.4	0.9053	4.07	
	7.0		0.9547	4.10	
	10.1		0.9893	4.11	

* Product Chemistry Reviews: DP #256877, Shyam Mathur, Ph.D., 9/12/2000 and DP #329168, Shyam Mathur, Ph.D., 7/13/07.

B. EXPERIMENTAL DESIGN

A peach tree treatment plot at eight of the nine trial sites received three airblast sprayer applications of the 1.81 Metconazole formulation at nominal rates of 0.136 lb ai/A, for a total nominal seasonal application rate of 0.403-0.417 lb ai/A. At the ninth trial site (Trial B), the peach tree treatment plot received four airblast sprayer applications of the 1.81 Metconazole formulation at nominal rates of 0.136 lb ai/A , for a total seasonal application rate of 0.545 lb ai/A. In addition to these tests, a second peach tree plot was treated using a 50WDG formulation of metconazole at Trial site M and a second peach tree plot was treated at double the application rate at Trial site G. The re-treatment intervals at the nine sites ranged from 7 to 117 days. Applications were made using airblast sprayers and a spray volume of 104 to 141 gal/A (973 to 1,319 L/ha). An adjuvant was not used for any of the applications.

Single untreated and duplicate treated RAC samples of mature peach were harvested 13 to 14 days following the last test substance application (13- to 14-day PHI). In addition, at one of the decline study test sites (Trial B), one control and duplicate treated mature peach samples were also harvested at 3, 7, and 10 days after the last application to determine residue decline. At the second decline study test site (Trial K), one control and duplicate treated mature peach samples were also harvested at 10, 18 and 22 days after the last application to determine residue decline. Samples were collected from the control plot first and then from the treated plot. Sample size for the fruit ranged from 4.4 to 19 lb (2.0 to 8.6 kg). For most of the trials, 24 peaches were collected per sample (Trial I had 25 fruit and Trial G had an average of 8 fruit per sample).

Cultivation and trial maintenance methods were conducted in accordance with local agricultural practices; maintenance chemicals used at each trial site during the study were reported. For the growing season, a written description of temperature and precipitation as compared to 10 or 30 year historical data was provided, as well as monthly average rainfall and irrigation data. No unusual weather conditions occurred during the study in the majority of the trials. In general, the precipitation was within the historical averages for the growing season; however, the overall rainfall was reported to be above normal for Trials B, F, and L and below normal for Trials G, H, I, J, and K. In particular, rainfall in the month of May 2004 was almost 3X the 10 year average at Trial F and the spring rainfall amount was greater than the 10 year average at Trial L.

Irrigation was used as needed for four of the nine trials to supplement when rainfall totals were low.

B.1. Study Site Information

According to the Study Protocol, soil characterization was not required for this study (Table B.1.1). Refer to Table B.1.2 for study use patterns and Table B.1.3 for geographic locations of submitted and requested trials.

TABLE B.1.1 Trial Site Conditions.

Trial Identification: City, State; NAFTA Region; Year (Trial No.)	Soil characteristics			
	Type	% OM	pH	CEC (meq/g)
Athens, GA; Region 2; 2003 (V-25662-03-B)	NA*	NA	NA	NA
Conklin, MI; Region 5; 2004 (V-25662-04-F)	NA	NA	NA	NA
Athens, GA; Region 2; 2004 (V-25662-04-G)	NA	NA	NA	NA
Porterville, CA Region 10; 2004 (V-25662-04-H)	NA	NA	NA	NA
Live Oak, CA; Region 10; 2004 (V-25662-04-I)	NA	NA	NA	NA
Marysville, CA; Region 10; 2004 (V-25662-04-J)	NA	NA	NA	NA
Chula, GA; Region 2; 2004 (V-25662-05-K)	NA	NA	NA	NA
Waller, TX; Region 6; 2004 (V-25662-05-L)	NA	NA	NA	NA
Orefield, PA; Region 1; 2005 (V-25662-05-M)	NA	NA	NA	NA

*NA – Not Available (data not collected)

TABLE B.1.2. Study Use Pattern.

Trial Identification: City, State; NAFTA Region; Yr (Trial No.)	EP[1]	Application							Tank Mix Adjuvants
		App. No.	Application Method	Growth Stage	Volume[2] GPA [L/ha]	Rate (lb a.i./A) [g a.i./ha]	RTI[3] (days)	Total Rate (lb a.i./A) [g a.i./ha]	
Athens, GA Region 2; 2003 (V-25662-03-B)	1.81 FL	1	Airblast	Full bloom	111 [1,039]	0.136 [152]	0	0.545 [611]	None
		2	Airblast	Petal fall	109 [1,022]	0.136 [152]	9		
		3	Airblast	Fruit beginning to color	129 [1,210]	0.136 [153]	86		
		4	Airblast	Fruit coloring; beginning to ripen	127 [1,183]	0.137 [154]	7		
Conklin, MI Region 5; 2004	1.81 FL	1	Airblast	Full bloom	118 [1,104]	0.136 [152]	0	0.407 [456]	None

TABLE B.1.2. Study Use Pattern.

Trial Identification: City, State; NAFTA Region; Yr (Trial No.)	EP[1]	Application							Tank Mix Adjuvants
		App. No.	Application Method	Growth Stage	Volume[2] GPA [L/ha]	Rate (lb a.i./A) [g a.i./ha]	RTI[3] (days)	Total Rate (lb a.i./A) [g a.i./ha]	
(V-25662-04-F)		2	Airblast	Petal fall	123 [1,150]	0.135 [151]	10		
		3	Airblast	Immature fruit 2.0 to 2.75" diameter	124 [1,160]	0.136 [153]	71		
Athens, GA Region 2; 2004 (V-25662-04-G)	1.81 FL	1	Airblast	Full bloom	128 [1,197]	0.135 [151]	0	0.408 [457]	None
		2	Airblast	Petal fall	138 [1,291]	0.136 [153]	8		
		3	Airblast	Begin fruit coloring	107 [1,001]	0.137 [153]	117		
	1.81 FL	1	Airblast	Full bloom	129 [1,207]	0.271 [303]	0	0.813 [911]	None
		2	Airblast	Petal fall	136 [1,272]	0.270 [302]	8		
		3	Airblast	Begin fruit coloring	107 [1,001]	0.273 [306]	117		
Porterville, CA Region 10; 2004 (V-25662-04-H)	1.81 FL	1	Airblast	Full bloom	111 [1,038]	0.146 [164]	0	0.417 [467]	None
		2	Airblast	Petal Fall	110 [1,029]	0.134 [150]	13		
		3	Airblast	Fruit coloring approx. 3 inches	141 [1,319]	0.137 [153]	61		
Live Oak, CA Region 10; 2004 (V-25662-04-I)	1.81 FL	1	Airblast	Full bloom	110 [1,029]	0.135 [152]	0	0.407 [456]	None
		2	Airblast	Petal fall	110 [1,029]	0.136 [152]	8		
		3	Airblast	80% Color	109 [1,019]	0.136 [152]	91		
Marysville, CA Region 10; 2004 (V-25662-04-J)	1.81 FL	1	Airblast	Full bloom	111 [1,038]	0.135 [152]	0	0.405 [454]	None
		2	Airblast	Petal fall	111 [1,038]	0.135 [151]	7		
		3	Airblast	14 days prior to harvest	110 [1,029]	0.134 [150]	87		
Chula, GA Region 2; 2004 (V-25662-05-K)	1.81 FL	1	Airblast	Full bloom	137 [1,281]	0.133 [149]	0	0.403 [451]	None
		2	Airblast	Petal fall	109 [1,019]	0.135 [151]	9		
		3	Airblast	1.5 to 2 inch diameter fruit	104 [973]	0.135 [151]	50		
Waller, TX Region 6; 2004 (V-25662-05-L)	1.81 FL	1	Airblast	Full bloom	109 [1,019]	0.136 [152]	0	0.413 [463]	None
		2	Airblast	Petal fall	108 [1,010]	0.137 [154]	15		
		3	Airblast	Beginning of color change	107 [1,001]	0.140 [157]	55		

TABLE B.1.2. Study Use Pattern.

Trial Identification: City, State; NAFTA Region; Yr (Trial No.)	EP[1]	Application							Tank Mix Adjuvants
		App. No.	Application Method	Growth Stage	Volume[2] GPA [L/ha]	Rate (lb a.i./A) [g a.i./ha]	RTI[3] (days)	Total Rate (lb a.i./A) [g a.i./ha]	
Orefield, PA Region 1; 2005 (V-25662-05-M)	1.81 FL	1	Airblast	Full bloom	122 [1,141]	0.140 [157]	0	0.415 [466]	None
		2	Airblast	Petal fall	122 [1,141]	0.140 [157]	3		
		3	Airblast	Firm ripe	110 [1,029]	0.136 [152]	73		
	50 WDG	1	Airblast	Full bloom	127 [1,188]	0.144 [161]	0	0.418 [468]	None
		2	Airblast	Petal fall	121 [1,132]	0.137 [153]	3		
		3	Airblast	Firm ripe	111 [1,038]	0.137 [154]	73		

[1]EP = End-use Product; Metconazole 1.81 FL is a flowable formulation containing 20.5% (nominal) mixture of *cis*- and *trans*-metconazole (85/15 ratio) as the active ingredient. Metconazole 50 WDG is a water dispersible granular formulation containing 50% metconazole as the active ingredient.
[2] GPA = gallons per acre.
[3] Retreatment Interval

TABLE B.1.3. Trial Numbers and Geographical Locations.

NAFTA Growing Zones	Peach		
	Submitted	Requested as Part of Crop Group 12[1]	
		Canada	U.S.
1	1		1
1A			
2	3		3
3			
4			
5	1		1
5A			
5B			
6	1		1
7			
7A			
8			
9			
10	3		3
11			
12			
13			
14			
15			
16			
17			
18			
19			
20			
21			
Total	9		9

[1] Residue data were submitted for cherries and plums to satisfy EPA Residue Chemistry Test Guidelines in OPPTS 860.1500, Crop Field Trials for Fruit, Stone, Group 12.

B.2. Sample Handling and Preparation

After harvesting, all of the samples were transported in ice chests or at ambient temperatures to facilities and stored in a freezer. All of the samples were shipped by freezer truck (ACDS) to the Valent Technical Center in Dublin, CA. Samples were kept under frozen conditions until further preparation (pitting, maceration and sub-sampling), extraction, and analysis.

B.3. Analytical Methodology

Method RM-41C-1 was used to concurrently analyze peach RAC samples for residues of *cis*- and *trans*-metconazole using a gas chromatograph with a nitrogen-phosphorous detector (GC/NPD). The validated limit of quantitation (LOQ) was 0.02 ppm and the limit of detection (LOD) was 0.01 for each *cis*- and *trans*-metconazole; the LOQ for the sum of *cis*- and *trans*-metconazole is 0.04 ppm.

For Method RM-41C-1, residues of *cis*- and *trans*-metconazole were extracted from each sample with an aqueous acetonitrile mixture (70:30 acetonitrile/water), filtered to remove solids, and the acetonitrile in the filtrate is removed by rotary evaporation to obtain an aqueous residue. The residues are partitioned from the aqueous mixture into hexane, and the residues are cleaned up by an acetonitrile/hexane partition. The acetonitrile is then removed by rotary evaporation, and the residues are cleaned up using a C18 SPE cartridge. The column eluant is rotary evaporated and the residues are dissolved in toluene. Analysis of the extracts is performed using GC/NPD.

C. RESULTS AND DISCUSSION

Sample storage conditions and intervals are summarized in Table C.2. The maximum storage interval of peach samples, from harvest to extraction, was 131 days (approximately 4 months). The samples were stored at approximately -20°C. Storage stability of *cis*- and *trans*-metconazole in stone fruit was determined by reanalysis of the fortified control cherry samples documented in *Magnitude of the Residues of Metconazole on Cherries* (MRID 46901707), in which selected samples were re-extracted, in duplicate, 159 days after the initial analysis of all of the crop field trial samples. Reanalysis indicated that both *cis*- and *trans*-metconazole were stable in frozen macerated cherries, with average recoveries of 101 and 103% of the original residues, respectively. Field sample residues were not corrected for in-storage dissipation.

Peach samples were analyzed for residues of *cis*- and *trans*-metconazole using Method RM-41C-1. The samples were analyzed within 10 days of extraction. The limit of detection (LOD) was 0.01 ppm and the limit of quantitation (LOQ) was 0.02 ppm for each of the two metconazole isomers in/on peaches. Method validation was conducted using control peach samples fortified with *cis*- and *trans*-metconazole at two levels (0.01 and 0.02 ppm). The mean recoveries were 90.3% and 95.6% for *cis*-metconazole and 91.7 and 97.1% for *trans*-metconazole. Concurrent method recoveries are reported in Table C.1. Peach control samples were fortified with *cis*- and

trans-metconazole at 0.02, 0.10 and 0.20 ppm. Recoveries ranged from 85.0 to 106% for *cis*-metconazole (average 95.4% with a standard deviation of 5.4; n=20) and from 73.0 to 114% for *trans*-metconazole (average 97.7% with a standard deviation of 8.8; n=20). It should be noted that these values are based on recoveries from the 9 nine trials reported in this DER. In the summarization of the concurrent recoveries, the study author did not use the concurrent recoveries from Trials I and J and included the concurrent recoveries from Trial A. The fortification levels encompassed the expected residues in/on peaches. The method was adequate for data collection based on acceptable method validation and concurrent method recoveries.

Residue data from the peach field trials are reported in Table C.3. A summary of the residue data in/on peaches from the 14-day PHI trials conducted at the 0.136 lb ai/A application rate (total seasonal rate of 0.403 to 0.545 lb ai/A) is presented in Table C.4. For these samples, residues of *trans*-metconazole were not detected above the LOQ and residues of *cis*-metconazole ranged from <LOQ (0.02 ppm) to 0.073 ppm. Residues of total metconazole (sum of *cis*- and *trans*-metconazole) ranged from <LOQ (0.04 ppm) to 0.093 ppm. The average total metconazole residue was 0.050 ppm. These values include the residues detected in Trial B (total metconazole values of 0.043 ppm and 0.047 ppm), which received four applications of the test product rather than three. Residues of *cis*- and *trans*-metconazole in/on untreated peach samples were not detected above the LOD (0.010 ppm).

As shown in the two residue decline studies, total metconazole residues declined with increasing PHIs. The reported estimated half-life for total metconazole on peaches was 7.7 days for Trial B and 6.6 days for Trial K. In calculating these half-lives, the study author did not use values below the LOD and used the LOD value for residues between the LOD and LOQ. Versar also calculated the half-lives for these trials, but used the LOQ value for all residues reported as less than the LOQ. Versar's estimated half-life values were 12.6 days (R^2=0.942) for Trial B and 9.9 days (R^2=0.843) for Trial K.

For the second treatment plot at Trial site G which received treatments at double the application rate (0.272 lb ai/A), the average residues in/on peaches collected after three applications (total of 0.813 lb ai/A) and a 14-day PHI were 0.108 ppm for *cis*-metconazole, 0.022 ppm for *trans*-metconazole, and 0.130 ppm for total metconazole. These values do not appear consistent with the results from the 1X application rate plot. Only 8 peaches were collected per sample from the 1X rate trial instead of 24 peaches per sample and the peaches in the 1X rate trial were 23% heavier than the peaches used in the 2X rate trial. Both the limited number of peaches collected for the 1X rate and the differences in average size of peach may have contributed to this apparent anomaly. The results from the second treatment plot at Trial site M which received applications of the Metconazole WDG formulation are similar to the results from the treatment plots which received applications of the Metconazole FL formulation. The *cis*-metconazole residues were <LOQ and 0.020 ppm and the *trans*-metconazole residues were both <LOQ.

TABLE C.1. Summary of Concurrent Recoveries of Metconazole from Peach.

Matrix	Spike level (ppm)	Sample size (n)	Recoveries (%)	Mean ± std dev (%)
***cis*-Metconazole**				
Peach	0.02	10	90.5, 85.0, 97.0, 101, 101, 106, 103, 95.5, 90.5, 97.0	95.4 ± 5.4
	0.10	9	88.2, 94.0, 97.0, 97.1, 93.5, 96.7, 101, 88.2, 97.0	
	0.20	1	90.0	
***trans*-Metconazole**				
Peach	0.02	10	104, 73.0, 96.5, 107, 108, 107, 105, 114, 104, 96.5	97.7 ± 8.8
	0.10	9	90.6, 94.3, 95.2, 95.5, 93.9, 93.2, 102, 90.6, 95.2	
	0.20	1	91.5	

TABLE C.2. Summary of Storage Conditions.

Matrix (RAC)	Analyte	Storage Temperature (°C)	Actual Storage Duration (days)	Interval of Demonstrated Storage Stability* (days)
Peach	*cis*-Metconazole	Approximately -20°C in laboratory	131	159
	trans-Metconazole			

* Storage stability of cis- and trans-metconazole on stone fruit was determined by reanalysis of treated cherry samples from trial V-25662-05-I after 159 days in frozen storage (MRID 469017-07).

TABLE C.3. Residue Data from Crop Field Trials with Metconazole

Trial Identification: City, State; NAFTA Region; Yr (Trial No.)	Peach Variety	Commodity	Formulation	Total Rate (lb a.i./A) [g a.i./ha]	PHI (days)	Uncorrected Residue Levels (ppm)*		
						cis-Metconazole	*trans*-Metconazole	Metconazole (total)
Athens, GA Region 2; 2003 (V-25662-03-B)	Contender	fruit	Metconazole 1.81 FL	0.545 [611]	3	0.068	<0.02 (0.019)	0.088
						0.059	<0.02 (0.016)	0.079
					7	0.050	<0.02 (0.014)	0.070
						0.049	<0.02 (0.015)	0.069
					10	0.044	<0.02	0.064
						0.040	<0.02	0.060
					14	0.023	<0.02	0.043

TABLE C.3. Residue Data from Crop Field Trials with Metconazole

Trial Identification: City, State; NAFTA Region; Yr (Trial No.)	Peach Variety	Commodity	Formulation	Total Rate (lb a.i./A) [g a.i./ha]	PHI (days)	Uncorrected Residue Levels (ppm)*		
						cis-Metconazole	*trans*-Metconazole	Metconazole (total)
						0.027	<0.02	0.047
Conklin, MI Region 5; 2004 (V-25662-04-F)	Bellaire	fruit	Metconazole 1.81 FL	0.407 [456]	14	<0.02 (0.019)	<0.02	<0.040
						0.027	<0.02	0.047
Athens, GA Region 2; 2004 (V-25662-04-G)	Redskin	fruit	Metconazole 1.81 FL	0.408 [457]	14	<0.02 (0.014)	<0.02	<0.040
						0.032	<0.02	0.052
			Metconazole 1.81 FL	0.813 [911]	14	0.125	0.023	0.148
						0.091	<0.02 (0.017)	0.111
Porterville, CA Region 10; 2004 (V-25662-04-H)	Brittany Lane	fruit	Metconazole 1.81 FL	0.417 [467]	13	0.073	<0.02 (0.015)	0.093
						0.059	<0.02 (0.013)	0.079
Live Oak, CA Region 10; 2004 (V-25662-04-I)	Loadel	fruit	Metconazole 1.81 FL	0.407 [456]	14	<0.02 (0.017)	<0.02	<0.040
						0.023	<0.02	0.043
Marysville, CA Region 10; 2004 (V-25662-04-J)	Stanislaus	fruit	Metconazole 1.81 FL	0.405 [454]	14	0.027	<0.02	0.047
						0.029	<0.02	0.049
Chula, GA Region 2; 2004 (V-25662-05-K)	June Gold	fruit	Metconazole 1.81 FL	0.403 [451]	10	0.083	<0.02 (0.018)	0.103
						0.081	<0.02 (0.018)	0.101
					14	0.046	<0.02 (0.011)	0.066
						0.032	<0.02	0.052
					18	0.034	<0.02	0.054
						0.025	<0.02	0.045
					22	0.025	<0.02	0.045
						<0.02 (0.018)	<0.02	<0.040
Waller, TX Region 6; 2004 (V-25662-05-L)	Texas Royal	fruit	Metconazole 1.81 FL	0.413 [463]	14	0.022	<0.02	0.042
						0.026	<0.02	0.046
Orefield, PA Region 1; 2005 (V-25662-05-M)	Garnet Beauty	fruit	Metconazole 1.81 FL	0.415 [466]	13	<0.02 (0.018)	<0.02	<0.040
						0.021	<0.02	0.041
			Metconazole 50 WDG	0.418 [468]	13	<0.02 (0.015)	<0.02	<0.040
						0.020	<0.02	<0.040

Notes:
LOQ = 0.02 ppm for each *cis*- and *trans*-metconazole.
LOD = 0.01 ppm for each *cis*- and *trans*-metconazole.
The LOQ value (0.02 ppm) was used when the residue value dropped below the LOQ.
If residues were between the LOD and LOQ, these residues are reported in parentheses.

Total metconazole residues were calculated using the LOQ if the *cis*- or *trans*-metconazole residues were reported as <LOQ.

TABLE C.4.1. Summary of Residue Data from Crop Field Trials with Metconazole (1.81 FL).

Matrix	Total Application Rate (lb a.i./A) [kg a.i./ha]	PHI (days)	Residue Levels* (ppm)						
			n	Min.	Max.	HAFT	Median (STMdR)	Mean (STMR)	Std. Dev.
Total Metconazole									
Peach	0.403 to 0.545 [0.451 to 0.611]	13-14	18	<0.040	0.093	0.086	0.047	0.050	0.015
***cis*-Metconazole**									
Peach	0.403 to 0.545 [0.451 to 0.611]	13-14	18	<0.020	0.073	0.066	0.027	0.030	0.015
***trans*-Metconazole**									
Peach	0.403 to 0.545 [0.451 to 0.611]	13-14	18	<0.020	<0.020	<0.020	<0.020	<0.020	0.00

*Notes:
HAFT = Highest Average Field Trial.
LOQ = 0.02 ppm for each of the two metconazole isomers (*cis*- and *trans*-).
Statistical calculations were performed using a value of LOQ when residues were reported as <LOQ.
Total Metconazole is the sum of both *cis*- and *trans*-metconazole.

D. CONCLUSION

The submitted field trial data are adequate and reflect the use of three foliar applications of the 1.81 FL formulation of metconazole at a nominal total rate of 0.407 lb ai/A (0.457 kg ai/ha) on peaches grown in the United States with a 14-day PHI. An acceptable method was used for quantitation of residues in/on peaches. Storage stability data were translated from cherries; acceptable storage stability data were provided for cherries stored at approximately -20°C for 159 days. The temperature and rainfall recordings were generally within average historical values for the residue study period. No unusual weather conditions occurred during the study in the majority of the trials; however, rainfall in the month of May, 2004 was almost 3X the 10 year average at Trial F and it was reported that the spring rainfall amount was greater than the 10 year average at Trial L. Irrigation was used as needed for four of the nine trials to supplement when rainfall totals were low. These factors did not appear to have an adverse impact to the results of the study.

E. REFERENCE

DP#: 324541
Subject: Metconazole. Request for a Tolerance on Imported Bananas. Summary of Analytical Chemistry and Residue Data. Petition Number 9E05052.
From: N. Dodd
To: M. Waller
Date: 12/14/05
MRIDs: 44721506, 44721507, 44721508, 44721509, 44721510, and 44721511

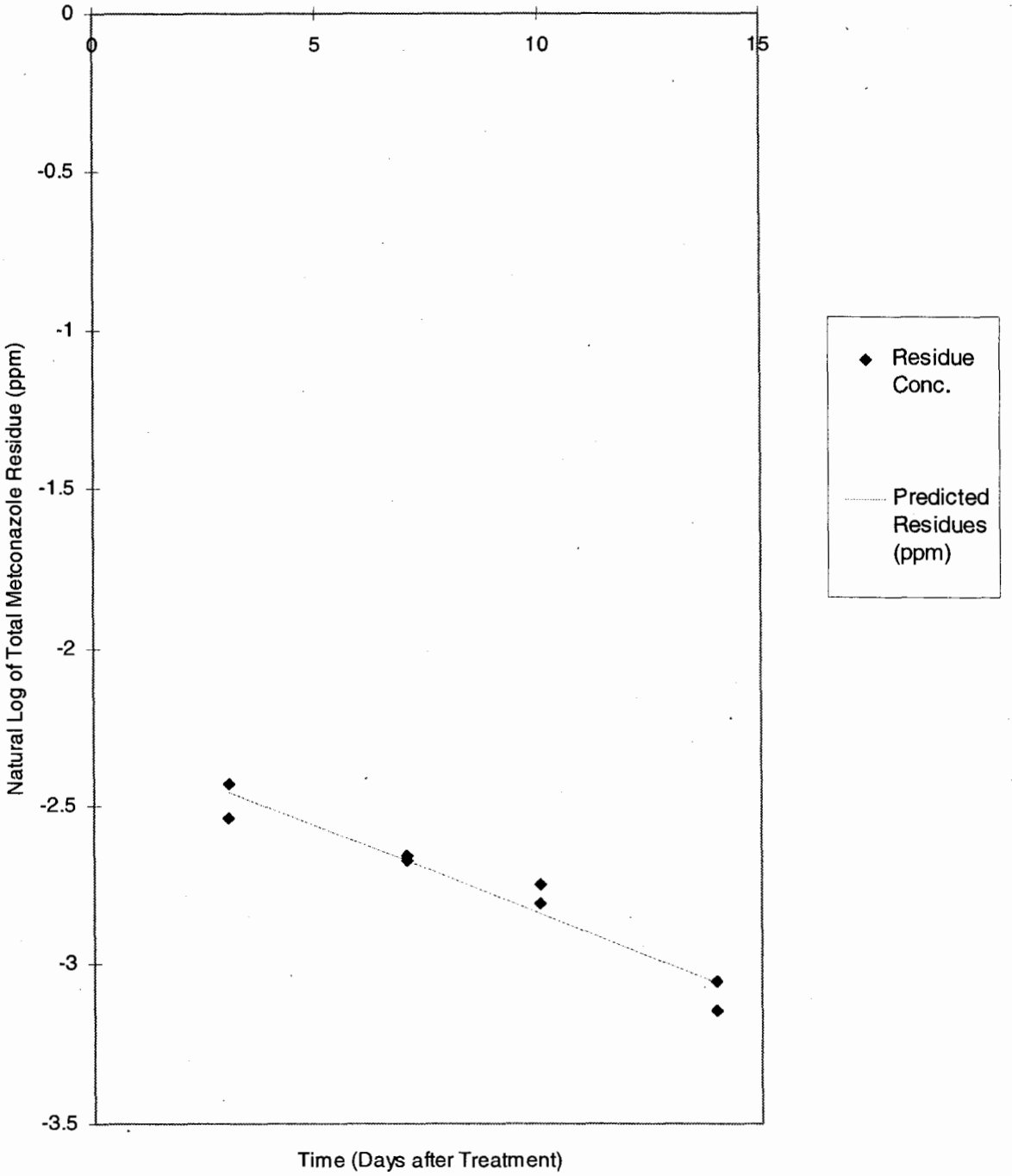
F. DOCUMENT TRACKING

RDI: N. Dodd (2/20/08)
Petition Numbers: 6F7095
DP#s: 348168 and 348206
PC Code: 125619

Template Version June 2005

APPENDIX 1
(Regression Data for Total Metconazole)

Regression Analysis: Log of Total Metconazole Residue vs. Time for Trial B



Regression Analysis: Summary Output for Trial B Total

Regression Statistics	
Multiple R	0.970386
R Square	0.941648
Adjusted R^2	0.931923
Standard Error	0.063631
Observations	8

ANOVA

	df	*SS*	*MS*	*F*	*Signif. F*
Regression	1	0.392037	0.392037	96.824609	6.34969E-05
Residual	6	0.024294	0.004049		
Total	7	0.416331			

	Coeff.	*Std. Error*	*t Stat*	*P-value*	*Lower 95%*	*Upper 95%*
Intercept	-2.29173	0.052501	-43.6509	9.677E-09	-2.420197931	-2.163265303
Slope	-0.05492	0.005581	-9.83995	6.35E-05	-0.068570926	-0.041259295

Half Life = 12.62216 Days

Predicted Residue Levels

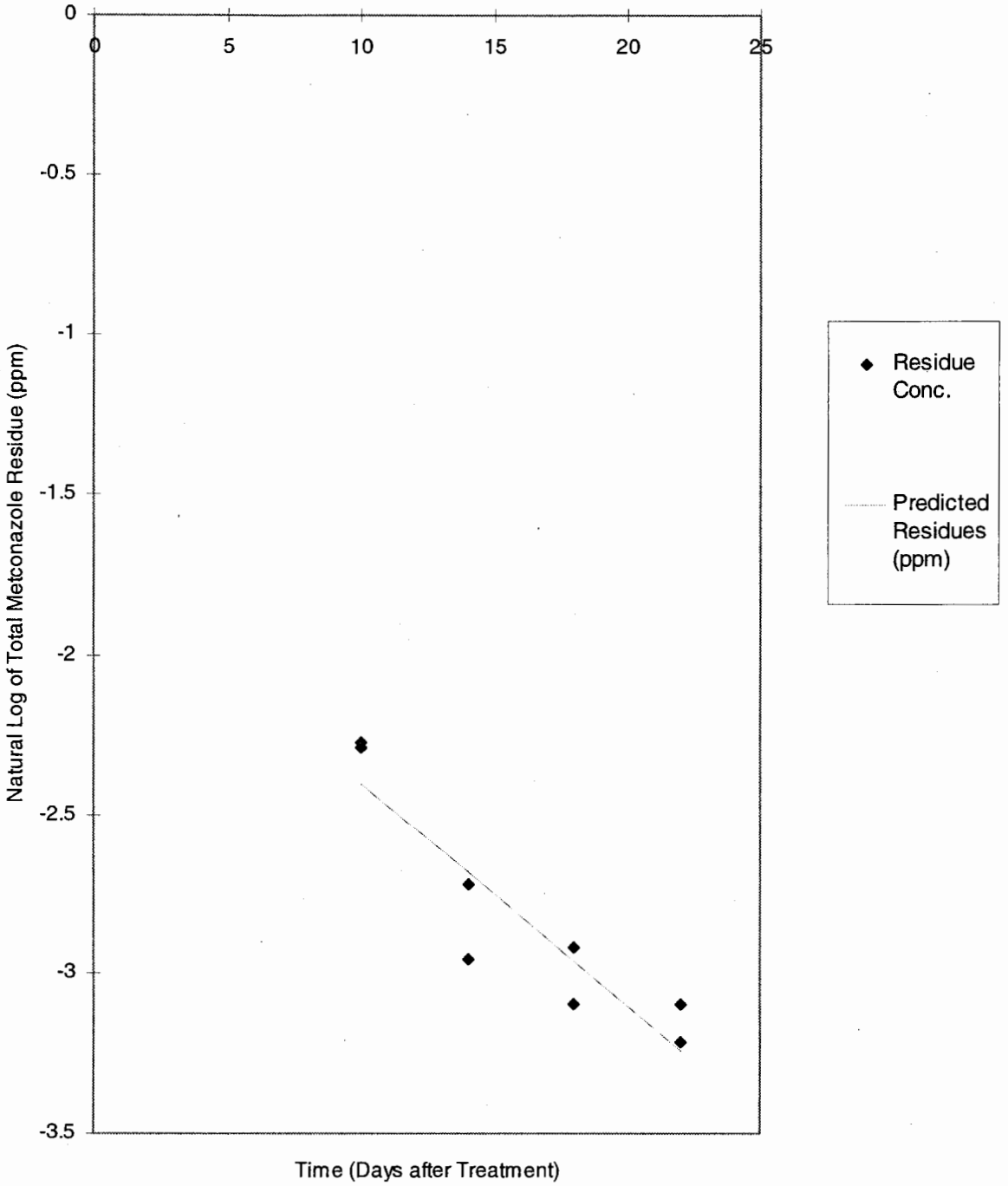
Time (Days)	Residue (ppm)
0	0.101091
1	0.095689
2	0.090576
3	0.085736
4	0.081155
5	0.076819
6	0.072714
7	0.068828
8	0.065151
9	0.061669
10	0.058374
11	0.055255
12	0.052302
13	0.049508
14	0.046862
15	0.044358
16	0.041988
17	0.039744
18	0.037621
19	0.03561
20	0.033708

Time (Days)	Residue (ppm)
21	0.0319064
22	0.0302015
23	0.0285877
24	0.0270601
25	0.0256142
26	0.0242455
27	0.0229499
28	0.0217236
29	0.0205628
30	0.0194641
31	0.018424
32	0.0174395
33	0.0165077
34	0.0156256
35	0.0147906

Regression Analysis: Means and CVs for Trial B Total

Days after Last Treatment	Residues (ppm)	Mean (ppm)	Standard Deviation (ppm)	Coefficient of Variation (%)
3	0.088	0.0835	0.00636	7.62
	0.079			
7	0.070	0.0695	0.000707	1.02
	0.069			
10	0.064	0.062	0.00283	4.56
	0.060			
14	0.043	0.045	0.00283	6.29
	0.047			

Regression Analysis: Log of Total Metconazole Residue vs. Time for Trial K



Regression Analysis: Summary Output for Trial K Total

Regression Statistics	
Multiple R	0.917945
R Square	0.842623
Adjusted R^2	0.816393
Standard Error	0.156448
Observations	8

ANOVA

	df	*SS*	*MS*	*F*	*Signif. F*
Regression	1	0.786291	0.786291	32.124931	0.001297599
Residual	6	0.146856	0.024476		
Total	7	0.933147			

	Coeff.	*Std. Error*	*t Stat*	*P-value*	*Lower 95%*	*Upper 95%*
Intercept	-1.70088	0.205478	-8.27767	0.0001683	-2.203664817	-1.198091786
Slope	-0.0701	0.012368	-5.66789	0.0012976	-0.100366374	-0.039837991

Half Life = 9.887669 Days

Predicted Residue Levels

Time (Days)	Residue (ppm)
0	0.182523
1	0.170166
2	0.158646
3	0.147905
4	0.137892
5	0.128556
6	0.119853
7	0.111739
8	0.104174
9	0.097121
10	0.090546
11	0.084416
12	0.078701
13	0.073372
14	0.068405
15	0.063774
16	0.059456
17	0.055431
18	0.051678
19	0.04818
20	0.044918

Time (Days)	Residue (ppm)
21	0.0418768
22	0.0390416
23	0.0363985
24	0.0339342
25	0.0316368
26	0.029495
27	0.0274981
28	0.0256365
29	0.0239008
30	0.0222827
31	0.0207741
32	0.0193677
33	0.0180565
34	0.016834
35	0.0156943

Regression Analysis: Means and CVs for Trial K Total

Days after Last Treatment	Residues (ppm)	Mean (ppm)	Standard Deviation (ppm)	Coefficient of Variation (%)
10	0.103	0.102	0.00141	1.39
	0.101			
14	0.066	0.059	0.0099	16.8
	0.052			
18	0.054	0.0495	0.00636	12.9
	0.045			
22	0.045	0.0425	0.00354	8.32
	0.040			

Primary Evaluator	This DER was originally prepared under contract by Dynamac Corporation.
Approved by	Nancy Dodd, Chemist *Nancy Dodd* Date: 2/20/08 Registration Action Branch 3 Health Effects Division (7509P)

Note: This DER was originally prepared under contract by Versar, Inc. (6850 Versar Center, Springfield, VA 22151; submitted 06/29/07). The DER has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORTS:

46901709. Green, C.A. (2006) Magnitude of the Residues of Metconazole on Plums and Dried Plums. Lab Project Number: 25671. Unpublished study prepared by Valent U.S.A. Corporation. 195 pages.

EXECUTIVE SUMMARY:

Valent U.S.A. Corporation has submitted field trial data for metconazole on plums and dried plums. A total of six field trials, performed between 2003 and 2005, are presented in this DER. Two additional field trials (Trials B and C) were conducted in 2003; however, these trials used an additional application and a shorter pre-harvest interval (PHI) than the later trials and were only presented in the Study Report for supplemental information. The results from these trials are not presented in this DER.

Five harvest and one decline trial were conducted in the United States encompassing Zones 5 (1 trial in MI), 10 (4 trials in CA) and 12 (1 trial in OR) during the 2003, 2004, and 2005 growing seasons. Except for Trial A in MI, one treated plot at each site received three airblast foliar applications of Metconazole 1.8 FL, formulated as a 20.5% active ingredient (ai) flowable liquid concentrate (FlC). Applications were made at a nominal rate of 0.136 lb ai/A (152 g ai/ha) for a total seasonal rate of 0.405-0.412 lb ai/A/season. The treatment plot at Trial A received four airblast foliar applications of the test substance, for a total seasonal application rate of 0.538 lb ai/A/season. Additionally, a second plot at Trial F received 5X the target rate (0.680 lb ai/A [760 g ai/ha]) and a second plot at Trial J received three airblast foliar applications of Metconazole 50 WDG, formulated as a 50% water dispersible granule ai at a target rate of 0.136 lb ai/A (152 g ai/ha). Both the FL and WDG formulations contain a mixture of *cis*- and *trans*-metconazole as the active ingredient in an approximate ratio of 85/15. Re-treatment intervals at the plots ranged from 5 to 133 days. An adjuvant was not added to the spray mixtures for any of the applications.

At each trial location, one untreated control and two treated mature plum raw agricultural commodity (RAC) samples were collected 14 days following the last test substance application [14-day preharvest interval (PHI)]. In addition, at the decline study test site (Trial A), one control and duplicate treated mature plum samples were also harvested at 3, 7, 10 and 14 days

after the last application to determine residue decline.

Plum samples were analyzed for residues of *cis*- and *trans*-metconazole using a gas chromatograph with a nitrogen-phosphorous detector (GC/NPD) Method RM-41C-1. The method was adequate for data collection based on acceptable method validation and concurrent method recoveries.

Samples were stored frozen (at approximately -20°C) prior to analysis; the maximum storage interval from harvest to extraction was 203 days (7 months), taken from the 2003 trial data. The maximum storage interval of plum samples, from harvest to extraction, for the 2004 and 2005 trials was 63 days (2 months). Storage stability of *cis*- and *trans*-metconazole was demonstrated by reanalysis of the fortified control cherry samples documented in *Magnitude of the Residues of Metconazole on Cherries* (MRID 46901707), in which selected samples were re-extracted, in duplicate, 159 days after the initial analysis of all of the crop field trial samples. Cherries are listed in the same crop group (Fruit, Stone, Group 12) and the storage conditions were the same as those used in this study; therefore, the cherry storage stability are adequate for plums.

Residues of total metconazole (sum of *cis*- and *trans*-metconazole) ranged from <0.04 to 0.060 ppm in/on plums harvested 14 days after the last foliar application at a total rate of 0.405 to 0.538 lb ai/A. Residues of *cis*-metconazole ranged from <LOQ to 0.04 ppm in/on plums, while all residues of *trans*-metconazole were below the LOQ. Residues of *cis*- and *trans*-metconazole from plums harvested at a 14-day PHI were below the LOQ for the one trial where Metconazole 50 WDG was applied.

Residues of *cis*- and *trans*-metconazole in/on untreated plum samples were not detected above the LOD (0.010 ppm).

For the residue decline study, the residue data showed only a very slight decline of metconazole residues between 3 and 14 days after the last of four applications.

Average residues of *cis*- and *trans*-metconazole from plums harvested at a 14-day PHI where the trees were treated at 5X the target application rate (Trial F) were 0.12 and 0.026 ppm, respectively. For *cis*-metconazole, this is very close to the five-fold difference that one would expect given the increased application rate. As concentrations for *trans*-metconazole were below LOQ, no comparison can be made.

HED notes that samples of plums were not analyzed for the triazole metabolites (1,2,4-triazole, triazolylalanine, and triazolylacetic acid).

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the field trial residue data are classified as scientifically acceptable.

The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP#s 348168 and 348206.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. The following deviations from regulatory requirements were reported: weather data, pesticide history, cultural practices, the application of maintenance chemicals, irrigation records, pH measurements, field sample weights, and soil characterization for this study were not collected or recorded under GLP. The Study Director stated that none of these deviations impacted the validity of the study.

A. BACKGROUND INFORMATION

Metconazole [5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol] is a broad-spectrum triazole Group 3 fungicide (sterol biosynthesis inhibitors). There are currently no registered uses of metconazole in the U.S.; however, a tolerance has been established for banana, and a Section 18 emergency exemption and supporting time-limited tolerances have been granted for use on soybean. Valent U.S.A. Corporation has applied for registration of metconazole in the U.S. for use on peanut, stone fruits, and tree nuts.

The chemical structure and nomenclature of metconazole, and the physicochemical properties of the technical grade of metconazole are presented in Tables A.1 and A.2.

Table A.1. Metconazole Nomenclature.

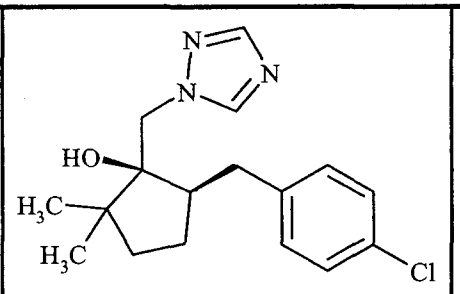
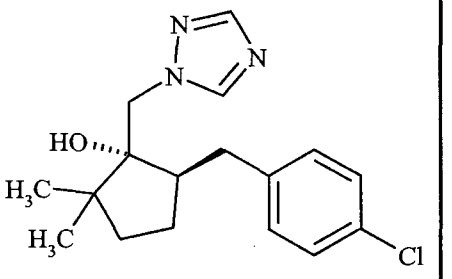
Chemical structure	 *cis*-isomer	 *trans*-isomer
Common name	Metconazole	
Company experimental name	KNF-S-474m (Kureha); BAS 555 F (BASF); V-10116 (Valent)	
IUPAC name	(1RS,5RS:1RS,5SR)-5-(4-chlorobenzyl)-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	

Table A.1. Metconazole Nomenclature.	
CAS name	5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol
CAS registry number	125116-23-6 (*cis*- and *trans*-isomers) 115850-27-6 (*cis*-isomer) 115850-28-7 (*trans*-isomer)
End-use products (EP)	50% WDG (Metconazole 50 WDG Fungicide, EPA File Symbol 59639-RUT) 0.75 lb/gal SC/L (Caramba™ Fungicide, EPA File Symbol No. 7969-EUA) 0.67 lb/gal SC/L formulation (BAS 556 01F Fungicide, EPA File Symbol No. 7969-EUT; also contains the active ingredient pyraclostrobin at 0.83 lb/gal)

Table A.2. Physicochemical Properties of Metconazole

Parameter	Value				References* (MRID)
Melting point/range	100.0-108.4°C (using Electrothermal Digital Melting Point Apparatus) (AC900,768 technical grade)				44721505
pH	5.81 at 25°C (1% aqueous suspension)				46808402
Relative density (20°C)	1.14 (relative density to water at 4°C, using capillary-stoppered, density-specific gravity bottle) (Lot No. AC 8879-140B)				44721505
Water solubility (20°C)	Using shake-flask method: 18.7 ± 1.0 mg/L (*cis*-isomer, WL148271, KNF-S-474m) 13.6 ± 1.7 mg/L (*trans*-isomer, WL148271, KNF-S-474m)				44721505
Solvent solubility (g/L) at 20°C	Solvent	Metconazole	*cis*	*trans*	44721505
	acetone	363	251	117	
	methanol	403	294	117	
	dichloromethane	481	343	141	
	ethyl acetate	260	173	90.0	
	propanol	132	86.6	46.7	
	toluene	103	66.2	38.0	
	Hexane	1.40	0.929	0.483	
Vapor pressure (20°C)	Using gas-saturation method: $< 1.23 \times 10^{-5}$ Pa or 9.23×10^{-8} mm Hg (metconazole) $< 1.04 \times 10^{-5}$ Pa or 7.80×10^{-8} mm Hg (*cis*-isomer) $< 1.96 \times 10^{-6}$ Pa or 1.47×10^{-8} mm Hg (*trans*-isomer)				44721505
Dissociation constant (pK_a)	11.38±0.03 and 1.06±0.03 (in water at 29.1°C using spectrophotometric method; Lot No. AC 8879-140B)				44721505
Octanol/water partition coefficient, Log(K_{OW})	At 20 °C (using flask shaking method): K_{ow} (log K_{ow}) = 7090±989 (3.85) (Lot No. AC 8879-140B) (TGAI) K_{ow} (log K_{ow}) = 7150±803 (3.85) (*cis*-isomer, CL 354,801) K_{ow} (log K_{ow}) = 6800±1700 (3.8) (*trans*-isomer, CL 354,802)				44721505

Table A.2. Physicochemical Properties of Metconazole					
Parameter	Value				References* (MRID)
UV/visible absorption spectrum	pH	λ	A	log ε	46808403
	cis-isomer				
	2.0	221.4	0.828	4.03	
	6.8		0.8452	4.04	
	7.0		0.9126	4.08	
	10.3		0.7226	3.98	
	trans-isomer				
	2.0	221.4	0.9053	4.07	
	7.0		0.9547	4.10	
	10.1		0.9893	4.11	

* Product Chemistry Reviews: DP #256877, Shyam Mathur, Ph.D., 9/12/2000 and DP #329168, Shyam Mathur, Ph.D., 7/13/07.

B. EXPERIMENTAL DESIGN

Treated plots at the six trial sites consisted of six plum trees. Plum trees at five of the six trial sites received three airblast sprayer applications of the 1.81 FL Metconazole formulations at nominal rates of 0.136 lb ai/A (152 g ai/ha), for a total seasonal application rate of 0.405-0.412 lb ai/A. At the sixth trial site (Trial A), plum trees received four airblast sprayer applications of the 1.81 FL Metconazole formulations at nominal rates of 0.136 lb ai/A, for a total seasonal application rate of 0.538 lb ai/A. In addition to these tests, additional plum trees at Trial J were treated using the 50WDG formulation of metconazole and additional plum trees at Trial Site F were treated at 5X the nominal rate (0.680 lb ai/A [760 g ai/ha] for a total seasonal application rate of 2.04 lb ai/A [2280 g ai/ha]). Retreatment intervals at the six sites ranged from 5 to133 days. Applications were made using airblast sprayers and a spray volume of 103 to 133 gal/A (966 to 1,244 L/ha). An adjuvant was not used for any of the applications.

Single untreated and duplicate treated RAC samples of mature plums were harvested 14 days following the last test substance application (14-day PHI). In addition, at the decline study test site (Trial A), one control and duplicate treated mature plum samples were also harvested at 3, 10 and 14 days after the last application to determine residue decline. Samples were collected from the control plot first and then from the treated plot. Sample size for the fruit ranged from 3.2 to 7.3 lb (1.4 to 3.3 kg). In 2003, the plum samples prior to drying each weighed 55 lb. In 2004, the plum samples weighed 55 to 57 lbs. The weight of the 2005 plum samples and the number of plums within each sample for 2004 and 2005 were not reported.

Cultivation and trial maintenance methods were conducted in accordance with local agricultural practices; maintenance chemicals used at each trial site during the study were reported for the trials which took place during the 2004 and 2005 growing seasons. Maintenance and weather data were not provided for the 2003 decline trial (Trial A). Average monthly minimum and maximum temperatures were not reported. Total monthly precipitation and irrigation amounts

were reported for each trial from planting to harvest for the 2004 and 2005 growing seasons. The current test site weather data were compared to 10 or 30 year historical weather data. No unusual weather conditions occurred for the majority of the 2004 and 2005 trials. At Trial G, spring temperatures were higher than normal and rainfall was lower than normal. At Trial J, the months of January through April were drier than normal and the months of May through July were wetter than normal. Irrigation was used as needed for four of the five harvest trials to supplement when rainfall totals were low.

B.1. Study Site Information

According to the Study Protocol, soil characterization was not required for this study (Table B.1.1). Refer to Table B.1.2 for study use patterns, and Table B.1.3 for geographic locations of submitted and requested trials.

TABLE B.1.1 Trial Site Conditions.

Trial Identification: City, State; NAFTA Region; Year (Trial No.)	Soil characteristics			
	Type	% OM	pH	CEC (meq/g)
Ottawa County, MI[1]; Region 5; 2003 (V-25671-03-A)	NA[2]	NA	NA	NA
Selma, CA; Region 10; 2004 (V-25671-04-E)	NA	NA	NA	NA
Kerman, CA; Region 10; 2004 (V-25671-04-F)	NA	NA	NA	NA
Hickman, CA; Region 10; 2004 (V-25671-04-G)	NA	NA	NA	NA
Live Oak, CA Region 10; 2004 (V-25671-04-H)	NA	NA	NA	NA
Dallas, OR; Region 12; 2005 (V-25671-05-M)	NA	NA	NA	NA

1 City location for Trial A was not provided.
2 NA – Not Available (data not collected)

TABLE B.1.2. Study Use Pattern.

Trial Identification: City, State; NAFTA Region; Yr (Trial No.)	EP[1]	Application							Tank Mix Adjuvants
		App. No.	Application Method	BBCH Growth Stage	Volume[2] GPA [L/ha]	Rate (lb a.i./A) [g a.i./ha]	RTI[3] (days)	Total Rate (lb a.i./A) [g a.i./ha]	
Ottawa County, MI[4] Region 5; 2003 (V-25671-03-A)	1.81 FL	1	Airblast	NR[5]	116 - 118[6] [1085 – 1104]	0.135[7] [151]	0	0.538[7] [603]	None
		2	Airblast	NR		0.135 [151]	7		
		3	Airblast	NR		0.135 [151]	104		
		4	Airblast	NR		0.135 [151]	7		
Selma, CA Region 10; 2004 (V-25671-04-E)	1.81 FL	1	Airblast	Full bloom	131 [1,225]	0.137 [153]	0	0.412 [462]	None
		2	Airblast	Petal fall	133 [1,244]	0.138 [155]	7		

TABLE B.1.2. Study Use Pattern.

Trial Identification: City, State; NAFTA Region; Yr (Trial No.)	EP[1]	Application							Tank Mix Adjuvants
		App. No.	Application Method	BBCH Growth Stage	Volume[2] GPA [L/ha]	Rate (lb a.i./A) [g a.i./ha]	RTI[3] (days)	Total Rate (lb a.i./A) [g a.i./ha]	
		3	Airblast	Fruit coloring 2" diameter	132 [1,235]	0.137 [154]	129		
Kerman, CA Region 10; 2004 (V-25671-04-F)	1.81 FL	1	Airblast	Full bloom	131 [1,225]	0.136 [153]	0	0.407 [457]	None
		2	Airblast	Petal fall	129 [1,207]	0.135 [151]	7		
		3	Airblast	Mature fruit	131 [1,225]	0.136 [153]	119		
	1.81 FL	1	Airblast	Full bloom	131 [1,225]	0.682 [764]	0	2.04 [2290]	None
		2	Airblast	Petal fall	130 [1,216]	0.678 [759]	7		
		3	Airblast	Mature fruit	131 [1,225]	0.683 [766]	119		
Hickman, CA Region 10; 2004 (V-25671-04-G)	1.81 FL	1	Airblast	Full bloom	127 [1,188]	0.140 [157]	0	0.415 [466]	None
		2	Airblast	Late petal fall	121 [1,132]	0.139 [156]	6		
		3	Airblast	Fruit Mature, full color, sugar still low	119 [1,113]	0.137 [153]	133		
Live Oak, CA Region 10; 2004 (V-25671-04-H)	1.81 FL	1	Airblast	Full bloom	103 [966]	0.135 [151]	0	0.405 [454]	None
		2	Airblast	Petal Fall	105 [977]	0.136 [152]	5		
		3	Airblast	90% Fruit color	104 [973]	0.135 [151]	109		
Dallas, OR Region 12; 2005 (V-25671-05-J)	1.81 FL	1	Airblast	95-100% Bloom	120 [1,122]	0.136 [152]	0	0.405 [453]	None
		2	Airblast	99% Petal fall	118 [1,104]	0.135 [151]	17		
		3	Airblast	60% Purple	118 [1,104]	0.134 [150]	126		
Dallas, OR Region 12; 2005 (V-25671-05-J)	50 WDG	1	Airblast	95-100% Bloom	120 [1,122]	0.136 [152]	0	0.408 [458]	None
		2	Airblast	99% Petal fall	120 [1,122]	0.136 [152]	17		
		3	Airblast	60% Purple	119 [1,113]	0.137 [153]	126		

[1] EP = End-use Product.
[2] GPA = gallons per acre.
[3] Retreatment Interval
[4] City location in Michigan for Trial A was not reported.
[5] NR=Not Reported
[6] Actual GPA was not reported for each application.
[7] Actual rate was not provided for each application; target rates reported.

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TABLE B.1.3. Trial Numbers and Geographical Locations.

NAFTA Growing Zones	Plum, Stone Fruit Crop Group 12		
	Submitted	Requested[1]	
		Canada	U.S.
1			
1A			
2			
3			
4			
5	1		1
5A			
5B			
6			
7			
7A			
8			
9			
10	4		4
11			
12	1		1
13			
14			
15			
16			
17			
18			
19			
20			
21			
Total	6		6

[1] A 25% reduction was applied to the required number of field trials.

B.2. Sample Handling and Preparation

After harvesting, all of the samples were transported in ice chests or at ambient temperatures to facilities and stored in a freezer. All of the samples were shipped by freezer truck (ACDS) to the Valent Technical Center in Dublin, CA. Samples were kept under frozen conditions (~ -20°C) until further preparation (pitting, maceration and sub-sampling), extraction, and analysis.

B.3. Analytical Methodology

Method RM-41C-1 was used to concurrently analyze plum RAC samples for residues of *cis*- and *trans*-metconazole. The validated limit of quantitation (LOQ) was 0.02 ppm and the limit of detection (LOD) was 0.01 for each *cis*- and *trans*-metconazole.

For Method RM-41C-1, residues of *cis*- and *trans*-metconazole were extracted from each sample with an aqueous acetonitrile mixture (70:30 acetonitrile/water), filtered to remove solids, and the acetonitrile in the filtrate is removed by rotary evaporation to obtain an aqueous residue. The residues are partitioned from the aqueous mixture into hexane, and the residues are cleaned up by

an acetonitrile/hexane partition. The acetonitrile is then removed by rotary evaporation, and the residues are cleaned up using a C18 SPE cartridge. The column eluant is rotary evaporated and the residues are dissolved in toluene. Analysis of the extracts is performed using a gas chromatograph with a nitrogen-phosphorous detector (GC/NPD).

C. RESULTS AND DISCUSSION

Sample storage conditions and intervals are summarized in Table C.2. The maximum storage interval of plum samples, from harvest to extraction, was 203 days (7 months), taken from the 2003 trial data. The maximum storage interval of plum samples, from harvest to extraction, for the 2004 and 2005 trials was 63 days (2 months). The samples were stored at approximately -20°C. Storage stability of *cis*- and *trans*-metconazole in stone fruit was determined by reanalysis of the fortified control cherry samples documented in *Magnitude of the Residues of Metconazole on Cherries* (MRID 46901707), in which selected samples were re-extracted, in duplicate, 159 days after the initial analysis of all of the crop field trial samples. Reanalysis indicated that both *cis*- and *trans*-metconazole were stable in frozen macerated cherries, with average recoveries of 101 and 103% of the original residues, respectively. Cherries and plums are listed in the same crop group (Fruit, Stone, Group 12) and the storage conditions for cherries were the same as those used in this study, therefore, the storage stability of *cis*- and *trans*-metconazole in frozen storage for 159 days was adequate based on the storage stability recovery results. Field sample residues were not corrected for in-storage dissipation.

Plum samples were analyzed for residues of *cis*- and *trans*-metconazole using Method RM-41C-1. The samples were analyzed within 5 days of extraction. The limit of detection (LOD) was 0.01 ppm and the limit of quantitation (LOQ) was 0.02 ppm for both metconazole isomers in/on plums. Method validation was conducted using control peach samples fortified with *cis*- and *trans*-metconazole at two levels (0.02 and 0.1 ppm). The mean recoveries were 90.3 and 95.6% for *cis*-metconazole and the mean recoveries for *trans*-metconazole were 91.7 and 97.1%. Concurrent method recoveries are reported in Table C.1. Concurrent recoveries from plum controls fortified with *cis*- and *trans*-metconazole at 0.02 and 0.10 ppm. Recoveries ranged from 88.0 to 103% for *cis*-metconazole (averaged 95.9% with a standard deviation of 4.31; n=12) and from 89.6 to 111% for *trans*-metconazole (averaged 97.5% with a standard deviation of 6.18; n=12). The fortification levels encompassed the expected residues in/on plums. The method was adequate for data collection based on acceptable method validation and concurrent method recoveries.

Residue data from the plum field trials are reported in Table C.3. A summary of the residue data for plums treated using Metconazole 1.81 FL from the 14-day PHI are presented in Table C.4. Residues of total metconazole (sum of *cis*- and *trans*-metconazole) ranged from <0.04 to 0.060 ppm in/on plums harvested 14 days after the last foliar application at a total rate of 0.405 to 0.538 lb ai/A. Residues of *cis*-metconazole ranged from <LOQ to 0.04 ppm in/on plums, while all residues of *trans*-metconazole were below the LOQ. Residues of *cis*- and *trans*-metconazole from plums harvested at a 14-day PHI were below the LOQ for the one trial where Metconazole 50 WDG was applied.

Residues of *cis*- and *trans*-metconazole in/on untreated plum samples were not detected above the LOD (0.010 ppm).

For the residue decline study, the residue data showed only a very slight decline of metconazole residues between 3 and 14 days after the last of four applications.

Average residues of *cis*- and *trans*-metconazole from plums harvested at a 14-day PHI where the trees were treated at 5X the target application rate (Trial F) were 0.12 and 0.026 ppm, respectively. For *cis*-metconazole, this is very close to the five-fold difference that one would expect given the increased application rate. As concentrations for *trans*-metconazole were below the LOQ, no comparison can be made.

TABLE C.1. Summary of Concurrent Recoveries of Metconazole from Plums.

Matrix	Spike level (ppm)	Sample size (n)	Recoveries (%)	Mean ± std dev (%)
***cis*-Metconazole**				
Plums	0.02	6	89.5, 95.5, 96.0, 98.0, 103, 100	95.1 ± 4.31
	0.10	6	88.0, 93.1, 94.3, 95.5, 98.5, 99.3	
***trans*-Metconazole**				
Plums	0.02	6	94.0, 96.5, 98.0, 103, 105, 111	97.5 ± 6.18
	0.10	6	89.6, 91.3, 93.2, 94.3, 95.0, 99.0	

TABLE C.2. Summary of Storage Conditions.

Matrix (RAC)	Analyte	Storage Temperature (°C)	Actual Storage Duration (days)	Interval of Demonstrated Storage Stability[1] (days)
Plum	*cis*-Metconazole	Approximately -20°C	21-203	159
	trans-Metconazole			

1. Storage stability of cis- and trans-metconazole on cherries (MRID 469017-07).

TABLE C.3. Residue Data from Crop Field Trials with Metconazole

Trial Identification: City, State; NAFTA Region; Yr; (Trial No.)	Plum Variety	Commodity	Formulation	Total Rate (lb a.i./A) [g a.i./ha]	PHI (days)	Uncorrected Residue Levels (ppm)*		
						cis-Metconazole	*trans*-Metconazole	Metconazole (total)
Ottawa County, MI Region 5; 2003 (V-25671-03-A)	Vision	Fruit	Metconazole 1.81 FL	0.538 [603]	3	0.04	<0.02	0.06
						0.04	<0.02	0.06
					7	0.04	<0.02	0.06
						0.04	<0.02 (0.011)	0.06
					10	0.03	<0.02	0.05
						0.04	<0.02	0.06
					14	0.04	<0.02 (0.011)	0.06
						0.04	<0.02	0.06
Selma, CA Region 10; 2004 (V-25671-04-E)	Howard Sun	Fruit	Metconazole 1.81 FL	0.412 [462]	14	<0.02	<0.02	0.040
						<0.02	<0.02	0.040
Kerman, CA	French Prune	Fruit	Metconazole	0.407	14	0.02	<0.02	0.040

TABLE C.3. Residue Data from Crop Field Trials with Metconazole

Trial Identification: City, State; NAFTA Region; Yr; (Trial No.)	Plum Variety	Commodity	Formulation	Total Rate (lb a.i./A) [g a.i./ha]	PHI (days)	Uncorrected Residue Levels (ppm)*		
						cis-Metconazole	*trans*-Metconazole	Metconazole (total)
Region 10; 2004 (V-25671-04-F)			1.81 FL	[457]		0.03	<0.02	0.050
				2.04 [2290]	14	0.12	0.03	0.150
						0.12	0.03	0.150
Hickman, CA Region 10; 2004 (V-25671-04-G)	Grand Rosa	Fruit	Metconazole 1.81 FL	0.415 [466]	14	<0.02	<0.02	0.040
						<0.02 (0.013)	<0.02	0.040
Live Oak, CA Region 10; 2004 (V-25671-04-H)	French Prune	Fruit	Metconazole 1.81 FL	0.405 [454]	14	<0.02 (0.016)	<0.02	0.040
						0.02	<0.02	0.040
Dallas, OR Region 12; 2005 (V-25671-05-J)	Moyer	Fruit	Metconazole 1.81 FL	0.405 [453]	14	<0.02 (0.016)	<0.02	0.040
						<0.02 (0.014)	<0.02	0.040
			Metconazole 50 WDG	0.408 [458]	14	<0.02 (0.013)	<0.02	0.040
						<0.02 (0.012)	<0.02	0.040

Notes:
LOQ = 0.02 ppm for each *cis*- and *trans*-metconazole.
LOD = 0.01 ppm for each *cis*- and *trans*-metconazole.
The LOQ value was used when the residue value dropped below the LOQ. Residues between the LOD and LOQ are reported in parentheses.
The city location for the Michigan test site was not reported. The actual total application rate was not reported for Michigan test site; target rate reported.

TABLE C.4 Summary of Residue Data from Crop Field Trials with Metconazole (1.81 FL)

Matrix	Total Application Rate (lb a.i./A) [kg a.i./ha]	PHI (days)	Residue Levels* (ppm)						
			n	Min.	Max.	HAFT*	Median (STMdR)	Mean (STMR)	Std. Dev.
Total Metconazole									
Plum	0.405 to 0.538 [0.453 to 0.603]	14	14	<0.040	0.060	0.060	0.040	0.044	0.007
***cis*-Metconazole**									
Plum	0.405 to 0.538 [0.453 to 0.603]	14	14	<0.020	0.040	0.040	0.020	0.024	0.007
***trans*-Metconazole**									
Plum	0.405 to 0.538 [0.453 to 0.603]	14	14	<0.020	<0.020	NA	NA	NA	NA

*Notes:
HAFT = Highest Average Field Trial.
LOQ = 0.02 ppm for each of the metconazole isomers (*cis*- and *trans*-).
Statistical calculations were performed using the LOQ when residues were reported as <LOQ.
Total Metconazole was the sum of both *cis*- and *trans*-metconazole.

D. CONCLUSION

The submitted field trial data are adequate and reflect the use of three foliar applications of the 1.81 FL or 50 WDG formulations of metconazole at a total rate of 0.405-0.412 lb ai/A on plums grown in the United States with a 14-day PHI. An acceptable method was used for quantitation of residues in/on plums. Storage stability data were translated from cherries; acceptable storage stability data were provided for cherries stored at approximately -20°C for 159 days. No unusual weather conditions occurred during the study in the majority of the trials. At Trial G, spring temperatures were higher than normal and rainfall was lower than normal. At Trial J, the months of January through April were drier than normal and the months of May through July were wetter than normal. Irrigation was used as needed for four of the five harvest trials to supplement rainfall. These factors did not appear to have an adverse impact to the results of the study.

E. REFERENCES

DP#:	324541
Subject:	Metconazole. Request for a Tolerance on Imported Bananas. Summary of Analytical Chemistry and Residue Data. Petition Number 9E05052.
From:	N. Dodd
To:	M. Waller
Date:	12/14/05
MRIDs:	44721506, 44721507, 44721508, 44721509, 44721510, and 44721511

F. DOCUMENT TRACKING

RDI: N. Dodd (2/20/08)
Petition Number: 6F7095
DP#s: 348168, 348206
PC Code: 125619

Template Version June 2005

Primary Evaluator	This DER was originally prepared under contract by Dynamac Corporation.
Approved by	Nancy Dodd, Chemist *Nancy Dodd* Date: 2/20/08 Registration Action Branch 3 Health Effects Division (7509P)

Note: This DER was originally prepared under contract by Versar, Inc. (6850 Versar Center, Springfield, VA 22151; submitted 06/29/07). The DER has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORTS:

46901709. Green, C.A. (2006) Magnitude of the Residues of Metconazole on Plums and Dried Plums. Lab Project Number: 25671. Unpublished study prepared by Valent U.S.A. Corporation. 195 pages.

EXECUTIVE SUMMARY:

Valent U.S.A. Corporation has submitted a study examining the transfer of metconazole into processed plum commodities. The raw agricultural commodity (RAC) was harvested 14 days following the last of three airblast applications of Metconazole 1.81 FL (a flowable formulation), made at an exaggerated target application rate of 0.68 lb ai/A/application (0.76 kg ai/ha), with re-treatment intervals of 7 and 119 days. The total achieved application rate was 2.04 lb ai/A/season (2.29 kg ai/ha), 5.4x the maximum seasonal application rate according to the Study Report. Following harvesting, the fresh plums were processed into dried plums.

Residues of metconazole in/on plum samples were quantitated using a gas chromatograph with a nitrogen-phosphorous detector (GC/NPD). The method was adequate for data collection based on acceptable method validation and concurrent method recoveries.

Samples were stored frozen (~-20 °C) from harvest to analysis for 44 days (1.4 months) for fresh plums and 42 days (1.4 months) for prunes; samples were analyzed within 2 days of extraction. Storage stability of *cis*- and *trans*-metconazole in stone fruit was determined by reanalysis of the fortified control cherry samples documented in *Magnitude of the Residues of Metconazole on Cherries* (MRID 46901707), in which selected samples were re-extracted, in duplicate, 159 days after the initial analysis of all of the crop field trial samples. The storage stability data for cherries may be translated to support the storage conditions and durations of samples from the plum processing study.

The results from the trial conducted at an exaggerated total application rate of 2.04 lb ai/A (5.4x the maximum seasonal application rate) and a 14-day PHI show that RAC residues of *cis*-metconazole averaged 0.10 ppm while *trans*-metconazole residues averaged 0.023 ppm. Total metconazole was calculated by taking the sum of *cis*- and *trans*-metconazole residues. The RAC

total metconazole residues averaged 0.12 ppm (n=2). The processed fractions (dried plums) were analyzed, and *cis*-metconazole residues averaged 0.24 ppm (n=2), *trans*-metconazole residues averaged 0.052 ppm (n=2) and total metconazole residues averaged 0.28 ppm (n=2). Concentration factors of 2.4x, 2.3x, and 2.3x were calculated for *cis*-, *trans*- and total metconazole in dried plums using the average residue in the processed sample divided by the average residue in the RAC. The average concentration factors are in agreement with the theoretical concentration factor of 3.5x for plums (OPPTS 860.1520, Table 1).

HED notes that samples were not analyzed for the triazole metabolites (1,2,4-triazole, triazolylalanine, and triazolylacetic acid).

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the processed commodity residue data are scientifically acceptable.

The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP#s 348168 and 348206.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. The following deviations from regulatory requirements were reported: weather data, pesticide history, cultural practices, the application of maintenance chemicals, pH measurements, and soil characterization for this study were not collected or recorded under GLP. The processing of the plums at the Sunsweet dehydrator was not documented in compliance with GLP Standards. Sunsweet is a commercial dryer and considers its process proprietary. The Study Director stated that none of these deviations impacted the validity of the study.

A. BACKGROUND INFORMATION

Metconazole [5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol] is a broad-spectrum triazole Group 3 fungicide (sterol biosynthesis inhibitors). There are currently no registered uses of metconazole in the U.S.; however, a tolerance has been established for banana, and a Section 18 emergency exemption and supporting time-limited tolerances have been granted for use on soybean. Valent U.S.A. Corporation has applied for registration of metconazole in the U.S. for use on peanut, stone fruits, and tree nuts.

The chemical structure and nomenclature of metconazole, and the physicochemical properties of the technical grade of metconazole are presented in Tables A.1 and A.2.

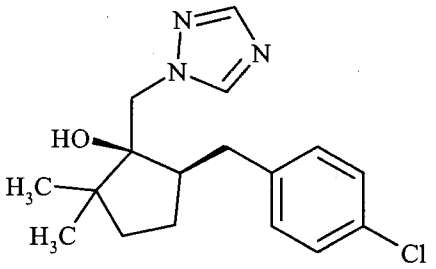
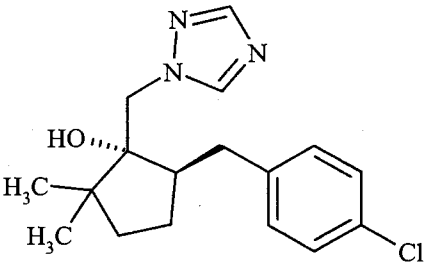
Table A.1. Metconazole Nomenclature.		
Chemical structure	 *cis*-isomer	 *trans*-isomer
Common name	Metconazole	
Company experimental name	KNF-S-474m (Kureha); BAS 555 F (BASF); V-10116 (Valent)	
IUPAC name	(1RS,5RS:1RS,5SR)-5-(4-chlorobenzyl)-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	
CAS name	5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	
CAS registry number	125116-23-6 (*cis*- and *trans*-isomers) 115850-27-6 (*cis*-isomer) 115850-28-7 (*trans*-isomer)	
End-use products (EP)	50% WDG (Metconazole 50 WDG Fungicide, EPA File Symbol 59639-RUT) 0.75 lb/gal SC/L (Caramba™ Fungicide, EPA File Symbol No. 7969-EUA) 0.67 lb/gal SC/L formulation (BAS 556 01F Fungicide, EPA File Symbol No. 7969-EUT; also contains the active ingredient pyraclostrobin at 0.83 lb/gal)	

Table A.2. Physicochemical Properties of Metconazole					
Parameter	Value				References* (MRID)
Melting point/range	100.0-108.4°C (using Electrothermal Digital Melting Point Apparatus) (AC900,768 technical grade)				44721505
pH	5.81 at 25°C (1% aqueous suspension)				46808402
Relative density (20°C)	1.14 (relative density to water at 4°C, using capillary-stoppered, density-specific gravity bottle) (Lot No. AC 8879-140B)				44721505
Water solubility (20°C)	Using shake-flask method: 18.7 ± 1.0 mg/L (*cis*-isomer, WL148271, KNF-S-474m) 13.6 ± 1.7 mg/L (*trans*-isomer, WL148271, KNF-S-474m)				44721505
Solvent solubility (g/L) at 20°C	Solvent	Metconazole	*cis*	*trans*	44721505
	acetone	363	251	117	
	methanol	403	294	117	
	dichloromethane	481	343	141	
	ethyl acetate	260	173	90.0	
	propanol	132	86.6	46.7	
	toluene	103	66.2	38.0	

Table A.2. Physicochemical Properties of Metconazole

Parameter	Value				References* (MRID)
	Hexane	1.40	0.929	0.483	
Vapor pressure (20°C)	Using gas-saturation method: $< 1.23x10^{-5}$ Pa or 9.23×10^{-8} mm Hg (metconazole) $< 1.04x10^{-5}$ Pa or 7.80×10^{-8} mm Hg (*cis*-isomer) $< 1.96x10^{-6}$ Pa or 1.47×10^{-8} mm Hg (*trans*-isomer)				44721505
Dissociation constant (pK_a)	11.38±0.03 and 1.06±0.03 (in water at 29.1°C using spectrophotometric method; Lot No. AC 8879-140B)				44721505
Octanol/water partition coefficient, Log(K_{OW})	At 20 °C (using flask shaking method): K_{ow} (log K_{ow}) = 7090±989 (3.85) (Lot No. AC 8879-140B) (TGAI) K_{ow} (log K_{ow}) = 7150±803 (3.85) (*cis*-isomer, CL 354,801) K_{ow} (log K_{ow}) = 6800±1700 (3.8) (*trans*-isomer, CL 354,802)				44721505
UV/visible absorption spectrum	pH	λ	A	log ε	46808403
	cis-isomer				
	2.0	221.4	0.828	4.03	
	6.8		0.8452	4.04	
	7.0		0.9126	4.08	
	10.3		0.7226	3.98	
	trans-isomer				
	2.0	221.4	0.9053	4.07	
	7.0		0.9547	4.10	
	10.1		0.9893	4.11	

* Product Chemistry Reviews: DP #256877, Shyam Mathur, Ph.D., 9/12/2000 and DP #329168, Shyam Mathur, Ph.D., 7/13/07.

B. EXPERIMENTAL DESIGN

A field trial was conducted in Kerman, CA. A test plot was treated with metconazole 1.8 FL, formulated as a 20.5% active ingredient (ai) flowable liquid (FL). RAC samples of plums were collected 14 days following the last test substance application (14 DALA). Plum trees were treated by three airblast sprays at the target application rate of 0.680 lb a.i./A (total seasonal rate of 2.04 lb a.i./A; 5.4x the maximum seasonal application rate). Applications were made at re-treatment intervals of 7 and 119 days. Following harvesting, the plums were dried. The actual trial use patterns are reported in Table B.1.

B.1. Application and Crop Information

Location City, State; NAFTA Region; Yr (Trial No.)	EP [1]	Application					Tank Mix/ Adjuvants
		Method/Timing	Volume [2] GPA (L/ha)	Rate lb a.i./A (g a.i./ha)	RTI [3] (days)	Total Rate lb a.i./A (g a.i./ha)	
Kerman, CA Region 10; 2004 (V-25671-04-F)	Metconazole 1.81 FL	1. Airblast / Full bloom	131 [1,225]	0.682 [764]	0	2.04 [2290]	None
		2. Airblast / Petal fall	130 [1,216]	0.678 [759]	7		
		3. Airblast / Mature fruit	131 [1,225]	0.683 [766]	119		

[1] EP = End-use Product
[2] Gallons per acre, L/ha
[3] Retreatment Interval

B.2. Sample Handling and Processing Procedures

One untreated control and two treated plum samples were collected at the normal commercial harvest (14-day PHI). The plum samples were harvested from the control plot first and then the treated plot. Over 90% of the fruit was collected due to very light fruit set on the trees in 2004. Normally, less than 50% of the available fruit would be collected to ensure that representative samples are obtained. Bulk fresh prune RAC samples were harvested and delivered to Sunsweet Madera Dehydrator in Madera, California for processing. The harvested untreated fresh prunes weighed 57 lbs and the treated fresh prunes weighed 55 lbs.

Untreated plums were placed in 4 mesh bags containing labels and the treated plums were placed in 3 mesh bags containing labels. The bags of untreated and treated plums were placed on wood drying trays and separated to avoid contamination. The trays were placed in a drying tunnel. The temperature in the drying tunnel was set at 185°F and the samples were dried for approximately 18 hours followed by a cooling period. After drying, the dried plums were placed in coolers and transported to the Excel Research facility where they were pitted by hand and then stored in a freezer. The processing procedure was not documented in the study report because Sunsweet is a commercial dryer and considers its process proprietary. The frozen pitted dried plums were later shipped to the Valent Technical Center in Dublin, California and placed in frozen storage (at approximately -20°C) until maceration, subsampling and analysis.

B.3. Analytical Methodology

Method RM-41C-1 was used to concurrently analyze plum RAC samples for residues of *cis*- and *trans*-metconazole. The validated limit of quantitation (LOQ) was 0.02 ppm and the limit of detection (LOD) was 0.01 for both *cis*- and *trans*-metconazole.

For Method RM-41C-1, residues of *cis*- and *trans*-metconazole were extracted from each sample with an aqueous acetonitrile mixture (70:30 acetonitrile/water). The extract was filtered to remove solids, and the acetonitrile in the filtrate is removed by rotary evaporation to obtain an aqueous residue. The residues are partitioned from the aqueous mixture into hexane, and the

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analyzed and *cis*-metconazole residues averaged 0.24 ppm (n=2), *trans*-metconazole residues averaged 0.052 ppm (n=2) and total metconazole residues averaged 0.29 ppm (n=2). Concentration factors of 2.24, 2.50, and 2.28 were calculated for *cis*-, *trans*- and total metconazole in dried plums using the average residue in the processed sample divided by the average residue in the RAC. The average concentration factors are in agreement with the theoretical concentration factor of 3.5x for plums (OPPTS 860.1520, Table 1).

TABLE C.1. Summary of Concurrent Recoveries of Metconazole from Plum Fractions.

Matrix	Analyte	Spike level (ppm)	Sample size (n)	Recoveries (%)	Mean ± std dev[1] (%)
Plum RAC	*cis*-Metconazole	0.02	1	98.0	96.2
		0.10	1	94.3	
	trans-Metconazole	0.02	1	103	97.2
		0.01	1	91.3	
Dried Plum	*cis*-Metconazole	0.02	1	93.1[2]	94.9
		0.10	1	96.7[2]	
	trans-Metconazole	0.02	1	96.5	95.5
		0.01	1	94.5	

1. Standard deviations for mean values were not calculated because the number of individual values used to calculate the mean was less than three.
2. Residue values were corrected for peak area in control samples.

TABLE C.2. Summary of Storage Conditions.

Matrix (RAC or Extract)	Storage Temperature (°C)	Actual Storage Duration (days)	Interval of Demonstrated Storage Stability (days)
Plum RAC	Approximately -20	203[1]	159[2]
Dried Plum		42	NA[3]

1 The storage duration was based on 2003 trial data. The maximum storage interval of plum samples for 2004 and 2005 trials was 63 days. The storage interval from harvest to analysis for fresh plums in this processing study was 44 days.
2 Storage stability of cis- and trans-metconazole on cherries (MRID 46901707).
3 Not applicable. Study Report stated that storage stability for the dried plums was not required because the 40 day storage interval was not significantly greater than 30 days.

Table C.3. Residue Data from Plum Processing Study with Metconazole.

RAC	Total Rate lb ai/A (g ai/ha)	PHI (days)	Processed Commodity	Residues (ppm)									Processing Factor[2]		
				cis-Metconazole			*trans*-Metconazole			Total Metconazole[1]			*cis*	*trans*	Total
				Rep 1	Rep 2	Avg	Rep 1	Rep 2	Avg	Rep 1	Rep 2	Avg			
Plum	2.04 [2290]	14	RAC	0.11	0.10	0.10	0.024	0.022	0.023	0.13	0.12	0.12	--	--	--
			Dried Plum	0.25	0.22	0.24	0.054	0.049	0.052	0.30	0.27	0.28	2.4	2.3	2.3

Notes: 1. Total metconazole was calculated by taking the sum of cis- and trans-metconazole.
2. Processing factors for dried plum were calculated using the average residue in the processed sample / average residue in the RAC.

D. CONCLUSION

Plum RAC samples were collected from the treatment plot that received a total application of Metconazole 1.81 FL, a flowable formulation, at 5.4x the maximum seasonal application rate. A portion of the RAC samples was processed into dried plums. The average residues for *cis*-, *trans*- and total metconazole in the RAC samples were 0.10, 0.023, and 0.12 ppm, respectively. The average residues for *cis*-, *trans*-, and total metconazole in the processed samples (dried plums) were 0.24, 0.052, and 0.28 ppm, respectively. Concentration factors of 2.4, 2.3 and 2.3 were calculated for *cis*-, *trans*- and total metconazole in dried plums using the average residue in the processed sample divided by the average residue in the RAC. The maximum theoretical concentration factor for the plum group is 3.5x. The submitted processing study is considered adequate to demonstrate the potential for concentration of metconazole residues in the processed commodities of dried plums.

E. REFERENCES

DP#:	324541
Subject:	Metconazole. Request for a Tolerance on Imported Bananas. Summary of Analytical Chemistry and Residue Data. Petition Number 9E05052.
From:	N. Dodd
To:	M. Waller
Date:	12/14/05
MRIDs:	44721506, 44721507, 44721508, 44721509, 44721510, and 44721511

F. DOCUMENT TRACKING

RDI: N. Dodd (2/20/08)
Petition Number: 6F7095
DP#s: 348168 and 348206
PC Code: 125619

Template Version June 2005

Primary Evaluator	This DER was originally prepared under contract by Dynamac Corporation.
Approved by	Nancy Dodd, Chemist *Nancy Dodd* Date: 2/20/08 Registration Action Branch 3 Health Effects Division (7509P)

This DER was originally prepared under contract by Dynamac Corporation (2275 Research Boulevard, Suite 300; Rockville, MD 20850; submitted 09/13/2007). The DER has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORTS:

46901710 Green, C. (2006) Magnitude of the Residues of Metconazole on Almonds. Project Number: 25700, 200600153. Unpublished study prepared by Valent U.S.A. Corporation, Research 2000, Inc. and Excel Research Services, Inc. 214 p.

46901711 Green, C. (2006) Magnitude of the Residues of Metconazole on Pecans. Project Number: 27211, 200600111, V/04/27211. Unpublished study prepared by Agricultural Research Associates, Biological Research Service, Inc. and South Texas Ag Research, Inc. 141 p.

EXECUTIVE SUMMARY:

Valent U.S.A. Corporation has submitted field trial data for metconazole on almonds and pecans, the representative commodities of the tree nut group 14. Seven almond field trials were conducted in the United States in Zone 10 (CA) during the 2003 and 2005 growing seasons, and three pecan trials were conducted in Zone 2 (GA; 1 trial), Zone 6 (TX, 1 trial) and Zone 8 (TX; 1 trial) during the 2004 growing season. The petitioner noted that nine pecan field trials were attempted; five trials were lost due to adverse weather conditions, and samples from one trial were lost because shells were not separated from the nutmeats prior to shipment to the analytical laboratory.

In five almond and three pecan field trials, a 1.81 lb ai/gal flowable concentrate (FlC) formulation or a 50% water-dispersible granule (WDG) formulation (1 pecan trial only) was applied as two broadcast foliar applications at 0.248-0.273 lb ai/A/application for a total seasonal rate of 0.502-0.570 lb ai/A; in one almond trial, a second plot received two applications at an exaggerated rate of 0.540-0.542 lb ai/A/application for a total seasonal rate of 1.082 lb ai/A. In the two remaining almond trials, the 1.81 lb/gal FlC formulation and the 50% WDG formulation were applied in side-by-side trials as two broadcast foliar applications at 0.134-0.136 lb ai/A for the first application and 0.260-0.272 lb ai/A for the second application for a total seasonal rate of 0.394-0.408 lb ai/A. The petitioner noted that the lower rate used in the first application for the side-by-side trials was the result of a protocol error. First applications were made to almonds at full bloom to petal fall and to pecans at late bloom to 7 days after flower drop; second

applications were made at hull split for almonds and at hard dough to shuck split for pecans; retreatment intervals ranged from 133 to 178 days. Applications were made in spray volumes of 99.9-149.9 gal/A. No spray adjuvants were added to the applications.

Samples of mature almonds and pecans were harvested 25-26 days after the last application, except for one pecan trial in which samples were collected 32 days after the last application due to wet weather conditions. Additional samples of almonds were collected from one trial 15, 20, and 30 days after final application to generate residue decline data.

Samples were analyzed for residues of *cis*- and *trans*-metconazole using GC/NPD method RM-41C-1. The validated limit of quantitation (LOQ) was 0.02 ppm for each isomer, and the reported limit of detection (LOD) was 0.01 ppm for each isomer. The method was adequate for data collection based on acceptable concurrent method recoveries.

Samples were stored frozen (~-20 °C) from harvest to analysis for 81-288 days (2.7-9.5 months) for almond hulls, 81-618 days (2.7-20.3 months) for almond nutmeats, and 107-129 days (3.5-4.2 months) for pecan nutmeats. The petitioner conducted a concurrent storage stability study which indicated that residues of *cis*- and *trans*-metconazole are relatively stable under frozen storage conditions in/on fortified samples of almond nutmeats and hulls for up to 664 days (21.8 months) and 784 days (25.8 months), respectively.

Residues of *cis*- and *trans*-metconazole were below the LOQ (<0.02 ppm) in/on all samples of almond and pecan nutmeats from the submitted field trials; total metconazole residues (sum of *cis* and *trans* isomers) were <0.04 ppm.

Following two applications of the 1.81 lb ai/gal FlC formulation at a total rate of 0.543-0.570 ppm, maximum residues of *cis*- and *trans*-metconazole in/on almond hulls were 3.04 and 0.65 ppm, respectively, for total metconazole residues of 3.69 ppm. Side-by-side trials with the 1.81 lb ai/gal FlC and the 50% WDG formulation at total rates of 0.394-0.408 lb ai/A were conducted. Following application of the 1.81 FlC formulation, residues of *cis*- and *trans*-metconazole in/on almond hulls were 0.30-0.62 and 0.07-0.15 ppm, respectively, for total metconazole residues of 0.37-0.76 ppm. Following application of the 50% WDG formulation, residues of *cis*- and *trans*-metconazole in/on almond hulls were <0.02-1.69 ppm and <0.02-0.33 ppm, respectively, for total metconazole residues of <0.04-2.02 ppm.

The submitted residue decline data indicated that total metconazole residues increased slightly in almond hulls between the 25- and 30-day PHI. Because residues were nondetectable in/on all samples of almond nutmeats at all preharvest intervals, it was not possible to assess residue decline in nutmeats.

HED notes that samples were not analyzed for residues of the triazole metabolites [1,2,4-triazole (1,2,4-T), triazolylalanine (TA), and triazolylacetic acid (TAA)].

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the field trial residue data are classified as scientifically acceptable.

The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP#s 348168 and 348206.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an impact on the validity of the study.

A. BACKGROUND INFORMATION

Metconazole [5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cycopentanol] is a broad-spectrum triazole Group 3 fungicide (sterol biosynthesis inhibitors). There are currently no registered uses of metconazole in the U.S.; however, a tolerance has been established for banana, and a Section 18 emergency exemption and supporting time-limited tolerances have been granted for use on soybean. Valent U.S.A. Corporation has applied for registration of metconazole in the U.S. for use on peanut, stone fruits, and tree nuts.

The chemical structure and nomenclature of metconazole, and the physicochemical properties of the technical grade of metconazole are presented in Tables A.1 and A.2.

Table A.1. Metconazole Nomenclature.

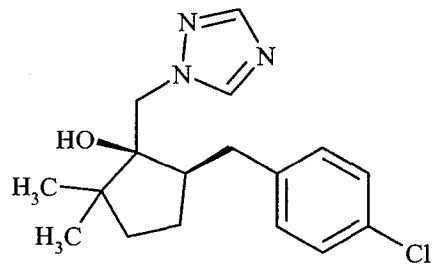
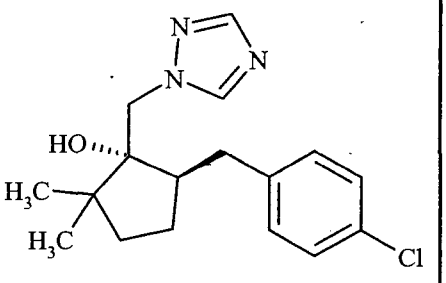
Chemical structure	 *cis*-isomer	 *trans*-isomer
Common name	Metconazole	
Company experimental name	KNF-S-474m (Kureha); BAS 555 F (BASF); V-10116 (Valent)	
IUPAC name	(1RS,5RS:1RS,5SR)-5-(4-chlorobenzyl)-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	
CAS name	5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	
CAS registry number	125116-23-6 (*cis*- and *trans*-isomers) 115850-27-6 (*cis*-isomer) 115850-28-7 (*trans*-isomer)	

Table A.1. Metconazole Nomenclature.	
End-use products (EP)	50% WDG (Metconazole 50 WDG Fungicide, EPA File Symbol 59639-RUT) 0.75 lb/gal SC/L (Caramba™ Fungicide, EPA File Symbol No. 7969-EUA) 0.67 lb/gal SC/L formulation (BAS 556 01F Fungicide, EPA File Symbol No. 7969-EUT; also contains the active ingredient pyraclostrobin at 0.83 lb/gal)

Table A.2. Physicochemical Properties of Metconazole

Parameter	Value	References* (MRID)
Melting point/range	100.0-108.4°C (using Electrothermal Digital Melting Point Apparatus) (AC900,768 technical grade)	44721505
pH	5.81 at 25°C (1% aqueous suspension)	46808402
Relative density (20°C)	1.14 (relative density to water at 4°C, using capillary-stoppered, density-specific gravity bottle) (Lot No. AC 8879-140B)	44721505
Water solubility (20°C)	Using shake-flask method: 18.7 ± 1.0 mg/L (*cis*-isomer, WL148271, KNF-S-474m) 13.6 ± 1.7 mg/L (*trans*-isomer, WL148271, KNF-S-474m)	44721505

Solvent solubility (g/L) at 20°C — 44721505

Solvent	Metconazole	*cis*	*trans*
acetone	363	251	117
methanol	403	294	117
dichloromethane	481	343	141
ethyl acetate	260	173	90.0
propanol	132	86.6	46.7
toluene	103	66.2	38.0
Hexane	1.40	0.929	0.483

Vapor pressure (20°C)	Using gas-saturation method: $< 1.23 \times 10^{-5}$ Pa or 9.23×10^{-8} mm Hg (metconazole) $< 1.04 \times 10^{-5}$ Pa or 7.80×10^{-8} mm Hg (*cis*-isomer) $< 1.96 \times 10^{-6}$ Pa or 1.47×10^{-8} mm Hg (*trans*-isomer)	44721505
Dissociation constant (pK_a)	11.38±0.03 and 1.06±0.03 (in water at 29.1°C using spectrophotometric method; Lot No. AC 8879-140B)	44721505
Octanol/water partition coefficient, Log(K_{OW})	At 20 °C (using flask shaking method): K_{ow} (log K_{ow}) = 7090±989 (3.85) (Lot No. AC 8879-140B) (TGAI) K_{ow} (log K_{ow}) = 7150±803 (3.85) (*cis*-isomer, CL 354,801) K_{ow} (log K_{ow}) = 6800±1700 (3.8) (*trans*-isomer, CL 354,802)	44721505

UV/visible absorption spectrum — 46808403

pH	λ	A	log ε
cis-isomer			
2.0	221.4	0.828	4.03
6.8		0.8452	4.04
7.0		0.9126	4.08

Table A.2. Physicochemical Properties of Metconazole					
Parameter	Value				References* (MRID)
	10.3		0.7226	3.98	
	trans-isomer				
	2.0	221.4	0.9053	4.07	
	7.0		0.9547	4.10	
	10.1		0.9893	4.11	

* Product Chemistry Reviews: DP #256877, Shyam Mathur, Ph.D., 9/12/2000 and DP #329168, Shyam Mathur, Ph.D., 7/13/07.

B. EXPERIMENTAL DESIGN

B.1. Study Site Information

Seven almond field trials were conducted in the United States in Zone 10 (CA) during the 2003 and 2005 growing seasons, and three pecan trials were conducted in Zone 2 (GA; 1 trial), Zone 6 (TX, 1 trial) and Zone 8 (TX; 1 trial) during the 2004 growing season. The petitioner noted that nine pecan field trials were attempted; five trials were lost due to adverse weather conditions, and samples from one trial were lost because shells were not separated from the nutmeats prior to shipment to the analytical laboratory.

In five almond and three pecan field trials, a 1.81 lb ai/gal flowable concentrate (FlC) formulation or a 50% water-dispersible granule (WDG) formulation (1 pecan trial only) was applied as two broadcast foliar applications at 0.248-0.273 lb ai/A/application for a total seasonal rate of 0.502-0.570 lb ai/A; in one almond trial, a second plot received two applications at an exaggerated rate of 0.540-0.542 lb ai/A/application for a total seasonal rate of 1.082 lb ai/A. In the two remaining almond trials, the 1.81 lb/gal FlC formulation and the 50% WDG formulation were applied in side-by-side trials as two broadcast foliar applications at 0.134-0.136 lb ai/A for the first application and 0.260-0.272 lb ai/A for the second application for a total seasonal rate of 0.394-0.408 lb ai/A. The petitioner noted that the lower rate used in the first application for the side-by-side trials was the result of a protocol error. First applications were made to almonds at full bloom to petal fall and to pecans at late bloom to 7 days after flower drop; second applications were made at hull split for almonds and at hard dough to shuck split for pecans; retreatment intervals ranged from133 to 178 days. Applications were made in spray volumes of 99.9-149.9 gal/A. No spray adjuvants were added to the applications.

Samples of mature almonds and pecans were harvested 25-26 days after the last application, except for one pecan trial in which samples were collected 32 days after the last application due to wet weather conditions. Additional samples of almonds were collected from one trial 15, 20, and 30 days after final application to generate residue decline data. Trial site conditions are presented in Table B.1.1, and the study use pattern is presented in Table B.1.2. The crop varieties grown are identified in Table C.3.

The test crops were grown and maintained according to typical agricultural practices for each region; maintenance pesticides and fertilizers were used to produce a commercial quality crop. Rainfall amounts and temperature values were provided; irrigation was used to supplement rainfall as needed. Trial site soil characteristics were not provided. The almond trials experienced normal weather overall. Unusually stormy and wet weather was noted for two pecan trials and one pecan trial experienced drier than average weather.

TABLE B.1.1. Trial Site Conditions.

Trial Identification: County, State; Year (Trial ID)	Soil characteristics			
	Type	%OM	pH	CEC (meq/g)
Almonds				
Glenn, CA; 2003 (V-25700-03-A)	Not provided			
Madera, CA; 2003 (V-25700-03-B)				
Sutter, CA; 2003 (V-25700-03-C)				
Fresno, CA; 2003 (V-25700-03-D)				
Tulare, CA; 2003 (V-25700-03-E)				
Glenn, CA; 2005 (V-25700-05-F)				
Fresno, CA; 2005 (V-25700-05-G)				
Pecans				
Tift, GA; 2004 (V-27211-04-A)	Not provided			
Hockley, TX; 2004 (V-27211-04-D)				
Burleson, TX; 2005 (V-27211-04-I)				

TABLE B.1.2. Study Use Pattern.

Trial Identification: County, State; Year (Trial ID)	EP[1]	Application					Tank Mix/ Adjuvants
		Method; Timing	Volume[2] (GPA)	Rate (lb ai/A)	RTI[3] (days)	Total Rate (lb ai/A)	
Almonds							
Glenn, CA; 2003 (V-25700-03-A)	1.81 lb/gal FlC	1. Airblast; late bloom to early petal fall	110.5	0.274	NA	0.547	None
		2. Airblast; 100% hull split	111	0.273	155		
		1. Airblast; late bloom early petal fall	110.2	0.542	NA	1.082	None
		2. Airblast; 100% hull split	111	0.540	155		
Madera, CA; 2003 (V-25700-03-B)	1.81 lb/gal FlC	1. Airblast; full bloom	140.4	0.275	NA	0.548	None
		2. Airblast; formed almond full size	139.7	0.273	138		
Sutter, CA; 2003 (V-25700-03-C)	1.81 lb/gal FlC	1. Airblast; petal fall	99.9	0.271	NA	0.543	None
		2. Airblast; hull split	100.1	0.272	138		
Fresno, CA; 2003 (V-25700-03-D)	1.81 lb/gal FlC	1. Airblast; bloom, past peak	129.3	0.285	NA	0.570	None
		2. Airblast; hull split 100%	129.1	0.285	144		
Tulare, CA; 2003 (V-25700-03-E)	1.81 lb/gal FlC	1. Airblast; petal fall	149.9	0.275	NA	0.547	None
		2. Airblast; hull split	143	0.272	136		

TABLE B.1.2. Study Use Pattern.

Trial Identification: County, State; Year (Trial ID)	EP[1]	Application					Tank Mix/ Adjuvants
		Method; Timing	Volume[2] (GPA)	Rate (lb ai/A)	RTI[3] (days)	Total Rate (lb ai/A)	
Glenn, CA; 2005 (V-25700-05-F)	1.81 lb/gal FlC	1. Airblast; 20% bloom, 80% fall	110.3	0.136	NA	0.408	None
		2. Airblast; hull split	139.9	0.272	149		
	50% WDG	1. Airblast; 20% bloom, 80% fall	110.2	0.136	NA	0.407	None
		2. Airblast; hull split	140	0.271	149		
Fresno, CA; 2005 (V-25700-05-G)	1.81 lb/gal FlC	1. Airblast; petal fall	118.6	0.134	NA	0.394	None
		2. Airblast; hull split	117.8	0.260	133		
	50% WDG	1. Airblast; petal fall	119.1	0.135	NA	0.402	None
		2. Airblast; hull split	118.2	0.267	133		
Pecans							
Tift, GA; 2004 (V-27211-04-A)	1.81 lb/gal FlC	1. Airblast; petal fall (female bloom)	117	0.254	NA	0.502	None
		2. Airblast; beginning shuck split	108.6	0.248	178		
Hockley, TX; 2004 (V-27211-04-D)	1.81 lb/gal FlC	1. Airblast; 7 days after flower drop	123	0.271	NA	0.537	None
		2. Airblast; beginning shuck split	120.8	0.266	153		
Burleson, TX; 2005 (V-27211-04-I)	50% WDG	1. Airblast; late bloom	128	0.256	NA	0.529	None
		2. Airblast; hard dough	126	0.273	145		

[1] EP = End-use Product
[2] Gallons per acre
[3] RTI = Retreatment Interval

TABLE B.1.3. Trial Numbers and Geographical Locations.

NAFTA Growing Zones	Almond			Pecan		
	Submitted	Requested		Submitted	Requested	
		Canada	U.S.[1]		Canada	U.S.[1]
1						
1A						
2				1		2
3						
4						1
5						
5A						
5B						
6				1		1
7						
7A						
8				1		1
9						
10	7		5			
11						
12						

TABLE B.1.3. Trial Numbers and Geographical Locations.

NAFTA Growing Zones	Almond			Pecan		
	Submitted	Requested		Submitted	Requested	
		Canada	U.S.[1]		Canada	U.S.[1]
13						
14						
15						
16						
17						
18						
19						
20						
21						
Total	7		5	3		5

[1] As specified under OPPTS 860.1500 Tables 2 and 5 for almond and pecan as the representative crops of the tree nut crop group.

B.2. Sample Handling and Preparation

Almond and pecan samples were harvested from trees and then transported to facilities where they were shelled. Almond hull and nutmeat samples and pecan nutmeat samples were stored frozen. Samples were shipped via ACDS freezer truck to the analytical laboratory, Valent Technical Center (Dublin, CA). Once at the laboratory, samples were stored frozen at ~ -20 °C until maceration and subsampling. Macerates were stored frozen until subsequent extraction and analysis.

B.3. Analytical Methodology

Samples of almond hulls and almond and pecan nutmeats were analyzed for residues of *cis*-metconazole and *trans*-metconazole using GC/NPD method RM-41C-1. A detailed description of the method was provided with the MRIDs.

Briefly samples were extracted with acetonitrile (ACN):water (70:30, v:v) and filtered. The extract was concentrated to remove ACN and partitioned with hexane (2x). The resulting hexane phases were combined and partitioned with ACN (2x), and the ACN phases were combined with ethyl acetate, concentrated to dryness, and redissolved in methanol:water (1:1, v:v). The reconstituted extract was applied to a C18 SPE cartridge, and residues were eluted with methanol:water (5:1, v:v). The eluate was evaporated to aqueous, combined with ethyl acetate, and evaporated to dryness, then redissolved in toluene for GC/NPD analysis. The validated LOQ was 0.02 ppm for each isomer, and the LOD was 0.01 ppm for each isomer.

C. RESULTS AND DISCUSSION

Sample storage conditions and intervals are summarized in Table C.2.1. Samples were stored frozen (~-20 °C) from harvest to analysis for 81-288 days (2.7-9.5 months) for almond hulls, 81-618 days (2.7-20.3 months) for almond nutmeats, and 107-129 days (3.5-4.2 months) for pecan nutmeats. To support sample storage conditions and intervals, the petitioner conducted a concurrent storage stability study reflecting analysis of fortified samples of almond nutmeats (Table C.2.2.1) and treated samples of almond hulls bearing weathered residues (C.2.2.2.). These data indicate that residues of *cis*- and *trans*-metconazole are relatively stable under frozen storage conditions in/on samples of almond nutmeats and hulls for up to 664 days (21.8 months) and 784 days (25.8 months), respectively.

Concurrent method recovery data are presented in Table C.1. Samples were analyzed for residues of *cis*-metconazole and *trans*-metconazole using GC/NPD method RM-41C-1. The validated LOQ was 0.02 ppm, and the LOD was 0.01 ppm for each isomer. Concurrent method recoveries were within the acceptable range of 70%-120% for all samples of almond hull fortified at 0.02, 0.10, 0.50, 0.60, 1.5, 2.5, and 4.0 ppm, and all samples of almond and pecan nutmeats fortified at 0.02 and 0.10 ppm. Apparent residues of *cis*- and *trans*-metconazole were below the method LOQ (<0.02 ppm) in/on all untreated samples of almond hulls, almond nutmeat, and pecan nutmeat.

Residue data from the almond and pecan field trials are reported in Table C.3. A summary of the residue data for almonds and pecans is presented in Table C.4. Residues of *cis*- and *trans*-metconazole were below the LOQ (<0.02 ppm) in/on all samples of almond and pecan nutmeats from the submitted field trials; total metconazole residues (sum of *cis* and *trans* isomers) were <0.04 ppm.

Following two applications of the 1.81 lb/gal FlC formulation at a total rate of 0.543-0.570 ppm, residues of *cis*- and *trans*-metconazole in/on almond hulls were 0.42-3.04 and 0.08-0.65 ppm, respectively, for total metconazole residues of 0.50-3.69 ppm; maximum total metconazole residues were 2.40-2.51 ppm, following exaggerated-rate applications of the 1.81 lb/gal FlC formulation at 1.082 lb ai/A in one trial.

Results of the side-by-side trials with the 1.81 lb/gal FlC and the 50% WDG formulation at total rates of 0.394-0.408 lb ai/A were inconclusive. Following application of the 1.81 FlC formulation, residues of *cis*- and *trans*-metconazole in/on almond hulls were 0.30-0.62 and 0.07-0.15 ppm, respectively, for total metconazole residues of 0.37-0.76 ppm. Following application of the 50% WDG formulation, residues of *cis*- and *trans*-metconazole in/on almond hulls were <0.02-1.69 ppm and <0.02-0.33 ppm, respectively, for total metconazole residues of <0.04-2.02 ppm.

The submitted residue decline data indicated that total metconazole residues (sum of *cis* and *trans* isomers) increased slightly in/on almond hulls between the 25- and 30-day PHI, from 0.50-0.61 ppm at the 25-day PHI to 0.79 ppm at the 30-day PHI. Because residues were

nondetectable in/on all samples of almond nutmeats at all harvest intervals, it was not possible to assess residue decline in nutmeats.

TABLE C.1. Summary of Concurrent Recoveries of Metconazole from Tree Nuts.

Matrix	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. (%) [1]
***cis*-Metconazole**				
Almond hulls	0.02	6	78, 87, 91, 96, 104, 105	93 ± 10
	0.10	3	90, 90, 94	91± 2
	0.50	3	90, 97, 99	95 ± 5
	0.60	2	83, 84	84
	1.50	1	97	--
	2.50	1	99	--
	4.00	1	99	--
	Total	**17**	**78-105**	**93 ± 7**
Almond nutmeat	0.02	5	85, 93, 93, 100, 100	94 ± 6
	0.10	10	88, 89, 90, 93, 93, 96, 96, 99, 101, 102	95 ± 5
	Total	**15**	**85-102**	**95 ± 5**
Pecan nutmeat	0.02	2	85, 105	95
	0.10	2	95, 96	96
	Total	**4**	**85-105**	**95 ± 8**
***trans*-Metconazole**				
Almond hulls	0.02	6	85, 86, 97, 100, 100, 103	95 ± 8
	0.10	3	89, 98, 98	95 ± 5
	0.50	3	90, 96, 98	95 ± 4
	0.60	2	87, 88	88
	1.50	1	95	--
	2.50	1	100	--
	4.00	1	92	--
	Total	**17**	**85 - 103**	**94 ± 6**
Almond nutmeat	0.02	5	79, 90, 92, 101, 113	95 ± 13
	0.10	10	86, 93, 94, 94, 94, 95, 98, 99, 107, 108	97 ± 7
	Total	**15**	**79-113**	**96 ± 9**
Pecan nutmeat	0.02	2	87, 105	96
	0.10	2	96, 97	97
	Total	**4**	**87-105**	**96 ± 7**

[1] Standard deviation is only applicable for groups ≥ 3 samples.

TABLE C.2.1. Summary of Storage Conditions.

Matrix	Storage Temperature (°C)	Actual Storage Duration [1]	Interval of Demonstrated Storage Stability
Almond hulls	~-20	81-288 days (2.7-9.5 months)	Residues of *cis*- and *trans*-metconazole residues were relatively stable in/on samples of fortified almond nutmeats for up to 664 days (21.8 months) and treated almond hulls for up to 784 days (25.8 months). Refer to Tables C.2.2.1 and C.2.2.2.
Almond nutmeat		81-618 days (2.7-20.3 months)	
Pecan nutmeat		107-129 days (3.5-4.2 months);	

[1] Actual storage duration from harvest to analysis; samples were analyzed within 1-6 days of extraction.

TABLE C.2.2.1. Stability of Fortified Residues of Metconazole in/on Almond Nutmeats Stored Frozen.

Matrix	Spike Level (ppm)	Storage interval (days)	Fresh Fortification Recovery (%)	Apparent Recovery in Stored Samples (%)	Corrected Recovery (%)[1]
***cis*-Metconazole**					
Almond nutmeats	0.10	0	--	88.4, 89.6	--
	0.10	96	89.4	86.6, 85.2	96.9, 95.3
	0.10	664	95.5	78.0, 78.8	81.7, 82.5
***trans*-Metconazole**					
Almond nutmeats	0.10	0	--	93.8, 94.0	--
	0.10	96	85.5	84.8, 84.1	99.2, 98.4
	0.10	664	95.0	78.4, 79.9	82.5, 84.1

[1] Corrected for concurrent recovery in freshly fortified samples.

TABLE C.2.2.2. Stability of Weathered Residues of Metconazole in/on Almond Hulls Stored Frozen.

Analyte	Spike Level (ppm)[1]	Storage Duration (days)	Fresh Fortification Recovery (%) [Average]	Recovered weathered residues (ppm)	Corrected Recovered residues[2] (ppm)	Corrected Recovery (%)[3]
***cis*-Metconazole**						
Almond hulls	0.10	0	89.6	0.604	0.674	100
	0.50	216	90.1	0.678, 0.689	0.752, 0.765	112, 114
	0.50	784	98.7, 97.4 [98.1]	0.677, 0.588	0.690, 0.599	102, 88.9
***trans*-Metconazole**						
Almond hulls	0.10	0	88.6	0.125	0.141	100
	0.50	216	89.7	0.132, 0.136	0.147, 0.152	104, 108
	0.50	784	97.9, 96.3 [97.1]	0.136, 0.117	0.140, 0.120	99.3, 85.1

[1] Fortified untreated samples were used for fresh fortifications, and treated samples bearing weathered residues were used for stored samples.
[2] Corrected for concurrent recovery in freshly fortified samples.
[3] Calculated using the equation (ppm corrected recovered residues ÷ ppm corrected recovered residues in 0-day samples) * 100.

TABLE C.3. Residue Data from Crop Field Trials with Metconazole.

Trial Identification: County, State; Year (Trial ID)	Zone	Crop; Variety	Commodity or Matrix	Formulation	Total Rate (lb ai/A)	PHI (days)	Metconazole Residues (ppm)[1]		
							cis	*trans*	Combined[2]
Glenn, CA; 2003 (V-25700-03-A)	10	Almond; nonpareil	Hulls	1.81 lb/gal FlC	0.547	25	0.98 1.23	0.22 0.25	1.20 1.48
			Nutmeat				ND ND	ND ND	ND ND
			Hulls	1.81 lb/gal FlC	1.082	25	2.07 1.98	0.44 0.42	2.51 2.40
			Nutmeat				ND ND	ND ND	ND ND
Madera, CA; 2003 (V-25700-03-B)	10	Almond; nonpareil	Hulls	1.81 lb/gal FlC	0.548	15	0.68 0.57	0.14 0.12	0.82 0.69
						20	0.59 0.59	0.11 0.12	0.70 0.71
						25	0.42 0.51	0.08 0.10	0.50 0.61
						30	0.66 0.66	0.13 0.13	0.79 0.79
			Nutmeat			15	ND ND	ND ND	ND ND
						20	ND ND	ND ND	ND ND
						25	ND ND	ND ND	ND ND
						30	ND ND	ND ND	ND ND
Sutter, CA; 2003 (V-25700-03-C)	10	Almond; nonpareil	Hulls	1.81 lb/gal FlC	0.543	25	0.60 0.46	0.12 0.09	0.72 0.55
			Nutmeat				ND ND	ND ND	ND ND
Fresno, CA; 2003 (V-25700-03-D)	10	Almond; nonpareil	Hulls	1.81 lb/gal FlC	0.570	25	1.94[3] 3.04[3]	0.44[3] 0.65[3]	2.38 3.69
			Nutmeat				ND ND	ND ND	ND ND
Tulare, CA; 2003 (V-25700-03-E)	10	Almond; nonpareil	Hulls	1.81 lb/gal FlC	0.547	25	0.65 0.65	0.12 0.13	0.77 0.78
			Almond Nutmeat				ND ND	ND ND	ND ND
Glenn, CA; 2005 (V-25700-05-F)	10	Almond; nonpareil	Hulls	1.81 lb/gal FlC	0.408	25	0.35 0.30	0.08 0.07	0.43 0.37
			Nutmeat				ND ND	ND ND	ND ND
			Hulls	50% WDG	0.407	25	ND ND	ND ND	ND ND
			Nutmeat				ND ND	ND ND	ND ND
Fresno, CA; 2005 (V-25700-05-G)	10	Almond; nonpareil	Hulls	1.81 lb/gal FlC	0.394	25	0.61 0.62	0.15 0.13	0.76 0.75

TABLE C.3. Residue Data from Crop Field Trials with Metconazole.

Trial Identification: County, State; Year (Trial ID)	Zone	Crop; Variety	Commodity or Matrix	Formulation	Total Rate (lb ai/A)	PHI (days)	Metconazole Residues (ppm)[1]		
							cis	*trans*	Combined[2]
			Nutmeat				ND ND	ND ND	ND ND
			Hulls	50% WDG	0.402	25	1.33 1.69	0.28 0.33	1.61 2.02
			Nutmeat				ND ND	ND ND	ND ND
Tift, GA; 2004 (V-27211-04-A)	2	Pecan; Sumners	Nutmeat	1.81 lb/gal FlC	0.502	25	ND ND	ND ND	ND ND
Hockley, TX; 2004 (V-27211-04-D)	8	Pecan; Western Schley	Nutmeat	1.81 lb/gal FlC	0.537	32	ND ND	ND ND	ND ND
Burleson, TX; 2005 (V-27211-05-I)	6	Pecan; Cheyenne	Nutmeat	50% WDG	0.529	26	ND ND	ND ND	ND ND

[1] Residues below the LOD (<0.01 ppm) are reported as ND (nondetectable).
[2] For calculation of the total residues, the LOQ value (0.02 ppm) was used for all residues reported as ND.
[3] The highest value of replicate analyses is reported.

TABLE C.4. Summary of Residue Data from Crop Field Trials with Metconazole.

Commodity	Total Applic. Rate (lb ai/A)	PHI (days)	Analyte	Residue Levels[1] (ppm)						
				n	Min.	Max.	HAFT[2]	Median (STMdR)	Mean (STMR)	Std. Dev.
1.81 lb/gal FlC formulation										
Almond, hulls	0.543-0.570	25	*cis*-Metconazole	10	0.42	3.04	2.49	0.65	1.05	0.84
			trans-Metconazole	10	0.08	0.65	0.50	0.13	0.22	0.19
			Total	10	0.50	3.69	2.82	0.78	1.27	1.03
	0.394-0.408	25	*cis*-Metconazole	4	0.30	0.62	0.62	0.48	0.47	0.17
			trans-Metconazole	4	0.07	0.15	0.14	0.11	0.11	0.04
			Total	4	0.37	0.76	0.76	0.59	0.58	0.21
Almond, nutmeat	0.543-0.570	25	*cis*-Metconazole	10	<0.02	<0.02	<0.02	0.02	0.02	--
			trans-Metconazole	10	<0.02	<0.02	<0.02	0.02	0.02	--
			Total	10	<0.04	<0.04	<0.04	0.04	0.04	--
	0.394-0.408	25	*cis*-Metconazole	4	<0.02	<0.02	<0.02	0.02	0.02	--
			trans-Metconazole	4	<0.02	<0.02	<0.02	0.02	0.02	--
			Total	4	<0.04	<0.04	<0.04	0.04	0.04	--
Pecan, nutmeat	0.502-0.537	25-32	*cis*-metconazole	4	<0.02	<0.02	<0.02	0.02	0.02	--
			trans-metconazole	4	<0.02	<0.02	<0.02	0.02	0.02	--

TABLE C.4. Summary of Residue Data from Crop Field Trials with Metconazole.

Commodity	Total Applic. Rate (lb ai/A)	PHI (days)	Analyte	Residue Levels[1] (ppm)						
				n	Min.	Max.	HAFT[2]	Median (STMdR)	Mean (STMR)	Std. Dev.
			Total	6	<0.04	<0.04	<0.04	0.04	0.04	--
50% WDG formulation										
Almond, hulls	0.402-0.407	25	*cis*-Metconazole	4	<0.02	1.69	1.51	0.68	0.77	0.87
			trans-Metconazole	4	<0.02	0.33	0.31	0.15	0.16	0.17
			Total	4	<0.04	2.02	1.82	0.83	0.93	1.04
Almond, nutmeat	0.402-0.407	25	*cis*-Metconazole	4	<0.02	<0.02	<0.02	0.02	0.02	--
			trans-Metconazole	4	<0.02	<0.02	<0.02	0.02	0.02	--
			Total	4	<0.04	<0.04	<0.04	0.04	0.04	--
Pecan, nutmeat	0.529	26	*cis*-metconazole	2	<0.02	<0.02	<0.02	0.02	0.02	--
			trans-metconazole	2	<0.02	<0.02	<0.02	0.02	0.02	--
			Total	2	<0.04	<0.04	<0.04	0.04	0.04	--

[1] For the calculation of total residues and determination of the HAFT, median, mean, and standard deviation values, the LOQ (0.02 ppm) was used for residues reported as ND in Table C.3.
[2] HAFT = Highest Average Field Trial.

D. CONCLUSION

The submitted field trial data on tree nuts reflect the use of a 1.81 lb ai/gal FlC formulation or a 50% WDG formulation applied as two broadcast foliar applications at 0.248-0.273 lb ai/A/application for a total seasonal rate of 0.502-0.570 lb ai/A to almonds and pecans; at one almond site, almonds in a second plot received two applications at an exaggerated rate of 0.540-0.542 lb ai/A/application for a total seasonal rate of 1.082 lb ai/A. In two additional almond trials, the 1.81 lb ai/gal FlC formulation and the 50% WDG formulation were applied in side-by-side trials as two broadcast foliar applications at 0.134-0.136 lb ai/A for the first application and 0.260-0.272 lb ai/A for the second application for a total seasonal rate of 0.394-0.408 lb ai/A. The trials reflected a 25-day PHI.

An acceptable method was used for the quantitation of residues of *cis*- and *trans*-metconazole. The study is supported by adequate storage stability data.

E. REFERENCES

DP#:	324541
Subject:	Metconazole. Request for a Tolerance on Imported Bananas. Summary of Analytical Chemistry and Residue Data. Petition Number 9E05052.
From:	N. Dodd
To:	M. Waller
Date:	12/14/05
MRIDs:	44721506, 44721507, 44721508, 44721509, 44721510, and 44721511

F. DOCUMENT TRACKING

RDI: N. Dodd (2/20/08)
Petition Numbers: 6F7094 and 6F7095
DP#s: 348168 and 348206
PC Code: 125619

Template Version June 2005

Primary Evaluator	This DER was originally prepared under contract by Dynamac Corporation.
Approved by	Nancy Dodd, Chemist *Nancy Dodd* Date: 2/20/08 Registration Action Branch 3 Health Effects Division (7509P)

This DER was originally prepared under contract by Dynamac Corporation (2275 Research Boulevard, Suite 300; Rockville, MD 20850; submitted 09/13/2007). The DER has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

46901712 Green, C. (2006) Magnitude of the Residues of Metconazole on Peanut Nutmeats and Peanut Processing Fraction. Project Number: 200600181, 25689, V/04/25689. Unpublished study prepared by Ashgrow Crop Management Systems, Inc., Coastal Ag Research, Inc. and Carolina Ag-Research Service, Inc. 367 p.

EXECUTIVE SUMMARY:

Valent U.S.A. Corporation has submitted field trial data for metconazole on peanuts. Fourteen field trials were conducted in the United States in Zones 2 (AL, GA, NC, SC, and VA; 9 trials), 3 (FL; 1 trial), 4 (MS; 1 trial), 6 (TX; 2 trials), and 8 (TX, 1 trial) during the 2004 (one trial) and 2005 growing seasons.

At each location, peanut plants received two foliar applications of a 1.81 lb ai/gal flowable concentrate (FlC) or a 50% water dispersible granule (WDG) formulation of metconazole at 0.24-0.26 lb ai/A/application with a 13- to 15-day retreatment interval for a total seasonal rate of 0.49-0.51 lb ai/A. At four of the trial locations, exaggerated-rate applications were made to separate plots at 0.50-0.52 lb ai/A/application for a total seasonal rate of 1.00-1.03 lb ai/A. The 1.81 lb ai/gal FlC formulation was used at the 2004 trial site only, and no adjuvant was used at this site; a nonionic surfactant was added to the spray mixtures for all remaining sites. Applications were made using ground equipment in spray volumes of 19-23 gal/A.

Peanuts were dug 13-18 days after the last application, and were allowed to dry in the field for 5-9 days or were collected immediately following harvest and moved indoors to dry on tarps. Additional samples were collected from two trials 10, 17-19, and 22 days after the last application to generate residue decline data. Peanut hay was collected from the 2004 trial site only.

Samples of peanut nutmeats were analyzed for residues of *cis*- and *trans*-metconazole using GC/NPD method RM-41C-1. The validated limit of quantitation (LOQ) was 0.02 ppm for each

isomer, and the reported limit of detection (LOD) was 0.01 ppm for each isomer. The method was adequate for data collection based on acceptable concurrent method recoveries.

Samples were stored frozen (<-22 °C) from harvest to analysis for 110-138 days (3.6-4.5 months). To support sample storage conditions and durations, the petitioner conducted a concurrent storage stability study which indicated that residues of *cis*- and *trans*-metconazole were reasonably stable during frozen storage for up to 133 days in/on peanut nutmeats. These data are adequate to support the peanut field trials.

Residues of both *cis*- and *trans*-metconazole were nondetectable (<0.01 ppm) in/on all but two samples of peanut nutmeat harvested 10-18 days after two foliar applications of the 1.81 lb/gal FlC or 50% WDG formulation of metconazole at a total of 0.49-0.51 lb ai/A/season; residues of *cis*-metconazole at 0.01 ppm (<LOQ) were detected in/on two samples of peanut nutmeats. Combined residues of *cis*- and *trans*-metconazole did not exceed the combined LOQ of 0.04 ppm for total metconazole in/on peanut nutmeats. HED notes that because residues were below the LOQ in all trials, results for both formulations were considered together. In samples analyzed from three of the exaggerated-rate trials, quantifiable residues of *cis*-metconazole at 0.02 and 0.04 ppm were detected in two samples from one trial conducted using the 50% WDG formulation for maximum combined residues of <0.06 ppm; remaining residues for both analytes were nondetectable.

Residue decline samples were analyzed from one trial site only. Because residues were nondetectable in/on all samples at all preharvest intervals, it was not possible to assess residue decline.

HED notes that samples were not analyzed for the triazole metabolites [1,2,4-triazole (1,2,4-T), triazolylalanine (TA), and triazolylacetic acid (TAA)].

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the field trial residue data are classified as scientifically acceptable.

Although peanut hay was not sampled, the proposed use includes a restriction against the grazing or feeding of peanut hay; therefore, data for peanut hay are not required.

The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP#s 348168 and 348206.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an impact on the validity of the study.

A. BACKGROUND INFORMATION

Metconazole [5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol] is a broad-spectrum triazole Group 3 fungicide (sterol biosynthesis inhibitors). There are currently no registered uses of metconazole in the U.S.; however, a tolerance has been established for banana, and a Section 18 emergency exemption and supporting time-limited tolerances have been granted for use on soybean. Valent U.S.A. Corporation has applied for registration of fluopicolide in the U.S. for use on peanut, stone fruits, and tree nuts.

The chemical structure and nomenclature of metconazole, and the physicochemical properties of the technical grade of metconazole are presented in Tables A.1 and A.2.

Table A.1. Metconazole Nomenclature.

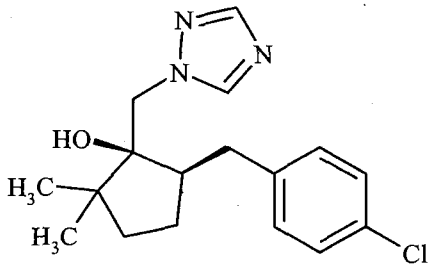
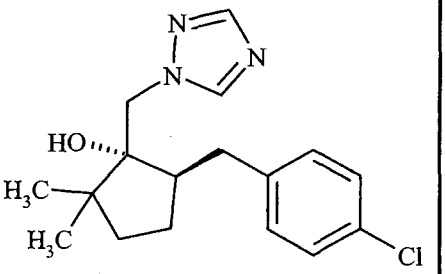
Chemical structure	 *cis*-isomer	 *trans*-isomer
Common name	Metconazole	
Company experimental name	KNF-S-474m (Kureha); BAS 555 F (BASF); V-10116 (Valent)	
IUPAC name	(1RS,5RS:1RS,5SR)-5-(4-chlorobenzyl)-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	
CAS name	5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	
CAS registry number	125116-23-6 (*cis*- and *trans*-isomers) 115850-27-6 (*cis*-isomer) 115850-28-7 (*trans*-isomer)	
End-use products (EP)	50% WDG (Metconazole 50 WDG Fungicide, EPA File Symbol 59639-RUT) 0.75 lb/gal SC/L (Caramba™ Fungicide, EPA File Symbol No. 7969-EUA) 0.67 lb/gal SC/L formulation (BAS 556 01F Fungicide, EPA File Symbol No. 7969-EUT; also contains the active ingredient pyraclostrobin at 0.83 lb/gal)	

Table A.2. Physicochemical Properties of Metconazole

Parameter	Value	References* (MRID)
Melting point/range	100.0-108.4°C (using Electrothermal Digital Melting Point Apparatus) (AC900,768 technical grade)	44721505
pH	5.81 at 25°C (1% aqueous suspension)	46808402
Relative density (20°C)	1.14 (relative density to water at 4°C, using capillary-stoppered, density-specific gravity bottle) (Lot No. AC 8879-140B)	44721505
Water solubility (20°C)	Using shake-flask method: 18.7 ± 1.0 mg/L (*cis*-isomer, WL148271, KNF-S-474m) 13.6 ± 1.7 mg/L (*trans*-isomer, WL148271, KNF-S-474m)	44721505

Solvent solubility (g/L) at 20°C — 44721505

Solvent	Metconazole	*cis*	*trans*
acetone	363	251	117
methanol	403	294	117
dichloromethane	481	343	141
ethyl acetate	260	173	90.0
propanol	132	86.6	46.7
toluene	103	66.2	38.0
Hexane	1.40	0.929	0.483

Vapor pressure (20°C)	Using gas-saturation method: $< 1.23 \times 10^{-5}$ Pa or 9.23×10^{-8} mm Hg (metconazole) $< 1.04 \times 10^{-5}$ Pa or 7.80×10^{-8} mm Hg (*cis*-isomer) $< 1.96 \times 10^{-6}$ Pa or 1.47×10^{-8} mm Hg (*trans*-isomer)	44721505
Dissociation constant (pK_a)	11.38±0.03 and 1.06±0.03 (in water at 29.1°C using spectrophotometric method; Lot No. AC 8879-140B)	44721505
Octanol/water partition coefficient, Log(K_{OW})	At 20 °C (using flask shaking method): K_{ow} (log K_{ow}) = 7090±989 (3.85) (Lot No. AC 8879-140B) (TGAI) K_{ow} (log K_{ow}) = 7150±803 (3.85) (*cis*-isomer, CL 354,801) K_{ow} (log K_{ow}) = 6800±1700 (3.8) (*trans*-isomer, CL 354,802)	44721505

UV/visible absorption spectrum — 46808403

pH	λ	A	log ε
cis-isomer			
2.0	221.4	0.828	4.03
6.8		0.8452	4.04
7.0		0.9126	4.08
10.3		0.7226	3.98
trans-isomer			
2.0	221.4	0.9053	4.07
7.0		0.9547	4.10
10.1		0.9893	4.11

* Product Chemistry Reviews: DP #256877, Shyam Mathur, Ph.D., 9/12/2000 and DP #329168, Shyam Mathur, Ph.D., 7/13/07.

B. EXPERIMENTAL DESIGN

B.1. Study Site Information

Fourteen field trials were conducted in the United States in Zones 2 (AL, GA, NC, SC, and VA; 9 trials), 3 (FL; 1 trial), 4 (MS; 1 trial), 6 (TX; 2 trials), and 8 (TX, 1 trial) during the 2004 (one trial) and 2005 growing seasons.

At each location, peanut plants received two foliar applications of a 1.81 lb ai/gal flowable concentrate (FlC) or a 50% water dispersible granule (WDG) formulation of metconazole at 0.24-0.26 lb ai/A/application with a 13- to 15-day retreatment interval for a total seasonal rate of 0.49-0.51 lb ai/A. At four of the trial locations, exaggerated-rate applications were made to separate plots at 0.50-0.52 lb ai/A/application for a total seasonal rate of 1.00-1.03 lb ai/A. The 1.81 lb ai/gal FlC formulation was used at the 2004 trial site only, and no adjuvant was used at this site; a nonionic surfactant was added to the spray mixtures for all remaining sites. Applications were made using ground equipment in spray volumes of 19-23 gal/A. The study use pattern is detailed in Table B.1.2, and crop varieties are identified in Table C.3.

Peanuts were dug 13-18 days after the last application, and were allowed to dry in the field for 5-9 days or were collected immediately following harvest and moved indoors to dry on tarps. Additional samples were collected from two trials 10, 17-19, and 22 days after the last application to generate residue decline data. Peanut hay was collected from the 2004 trial site only.

The petitioner provided a list of the maintenance pesticides used during the current year for each site as well as a 3-year pesticide history. At two AL sites (trials V-25689-G and H), propiconazole was used as a maintenance chemical during the study. The petitioner noted that no interferences were observed in the chromatograms for samples from these sites.

The total monthly rainfall was reported for each site, along with 10-year historical averages. Although daily temperature information was not provided, the weather conditions for each trial were summarized in comparison to "normal" conditions. Irrigation was used to supplement rainfall as needed. Deviations from normal conditions were reported at nearly every site; however, no impact on the trials was reported except that harvest at the MS site was delayed due to wet conditions. HED notes that information pertaining to soil type was not provided (Table B.1.1). Because the study reflected foliar applications, these data are not required.

TABLE B.1.1. Trial Site Conditions.

Trial Identification (County, State; Year)	Soil characteristics			
	Type	%OM	pH	CEC (meq/g)
Gates, NC; 2004 (V-2569-04-A)	Not provided			
Suffolk, VA; 2005 (V-25689-05-B)				

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TABLE B.1.1. Trial Site Conditions.

Trial Identification (County, State; Year)	Soil characteristics			
	Type	%OM	pH	CEC (meq/g)
Barnwell, SC; 2005 (V-25689-05-C)				
Clarke, GA; 2005 (V-25689-05-D				
Turner, GA; 2005 (V-25689-05-E				
Tift, GA; 2005 (V-25689-05-F)				
Houston, AL; 2005 (V-25689-05-G)				
Henry, AL; 2005 (V-25689-05-H)				
Houston, AL; 2005 (V-25689-05-I)				
Madison, FL; 2005 (V-25689-05-J)				
Wharton, TX; 2005 (V-25689-05-K)				
Erath, TX; 2005 (V-25689-05-L)				
Hockley, TX; 2005(V-25689-05-M)				
Washington, MS; 2005 (V-25689-05-N)				

TABLE B.1.2. Study Use Pattern.

Location (County, State; Year) Trial ID	EP[1]	Application					Tank Mix/ Adjuvants
		Method; Timing	Volume[2] (GPA)	Rate, lb ai/A [g ai/A]	RTI[3] (days)	Total Rate (lb ai/A)	
Gates, NC; 2004 (V-2569-04-A)	1.81 lb/gal FlC	1. Foliar; near maturity	21.9	0.261 [114.8]	NA	0.514	None
		2. Foliar; mature	23.2	0.253 [118.2]	14		
	1.81 lb/gal FlC	1. Foliar; near maturity	22.0	0.523 [237.3]	NA	1.027	
		2. Foliar; mature	23.4	0.504 [228.7]	14		
Suffolk, VA; 2005 (V-25689-05-B)	50% WDG	1. Foliar; nearing maturity	20.7	0.256 [116.3]	NA	0.512	Nonionic surfactant
		2. Foliar; near maturity	20.6	0.255 [115.8]	14		
	50% WDG	1. Foliar; nearing maturity	20.5	0.510 [231.5]	NA	1.018	
		2. Foliar; near maturity	20.4	0.508 [230.4]	14		
Barnwell, SC; 2005 (V-25689-05-C)	50% WDG	1. Foliar; pods filling out	19.7	0.252 [114.2]	NA	0.503	Nonionic surfactant
		2. Foliar; pods mature	19.2	0.251 [114.0]	15		
Clarke, GA; 2005 (V-25689-05-D	50% WDG	1. Foliar; 30% mature pods	20.5	0.249 [113.0]	NA	0.498	Nonionic surfactant
		2. Foliar; 70% mature pods	20.0	0.249 [113.1]	14		
	50% WDG	1. Foliar; 30% mature pods	20.4	0.496 [223.5]	NA	0.997	

TABLE B.1.2. Study Use Pattern.

Location (County, State; Year) Trial ID	EP[1]	Application					Tank Mix/ Adjuvants
		Method; Timing	Volume[2] (GPA)	Rate, lb ai/A [g ai/A]	RTI[3] (days)	Total Rate (lb ai/A)	
		2. Foliar; 70% mature pods	20.0	0.501 [227.1]	14		
Turner, GA; 2005 (V-25689-05-E	50% WDG	1. Foliar; maturing	20.0	0.250 [113.3]	NA	0.502	Nonionic surfactant
		2. Foliar; mature	19.7	0.252 [114.2]	15		
Tift, GA; 2005 (V-25689-05-F)	50% WDG	1. Foliar; pod fill	20.4	0.252 [114.4]	NA	0.505	Nonionic surfactant
		2. Foliar; pod fill	19.7	0.252 [114.5]	13		
Houston, AL; 2005 (V-25689-05-G)	50% WDG	1. Foliar; pod fill	19.5	0.241 [109.1]	NA	0.489	Nonionic surfactant
		2. Foliar; pod fill	19.6	0.248 [112.6]	14		
Henry, AL; 2005 (V-25689-05-H)	50% WDG	1. Foliar; pod fill	19.3	0.247 [112.1]	NA	0.488	Nonionic surfactant
		2. Foliar; pod fill	19.1	0.241 [109.3]	14		
Houston, AL; 2005 (V-25689-05-I)	50% WDG	1. Foliar; late pegging	20.1	0.252 [114.2]	NA	0.504	Nonionic surfactant
		2. Foliar; mature peanut	19.7	0.252 [114.4]	15		
Madison, FL; 2005 (V-25689-05-J)	50% WDG	1. Foliar; late pegging	20.3	0.255 [115.5]	NA	0.507	Nonionic surfactant
		2. Foliar; mature peanut	19.8	0.253 [114.6]	15		
Wharton, TX; 2005 (V-25689-05-K)	50% WDG	1. Foliar; BBCH 73	20.3	0.252 [114.5]	NA	0.501	Nonionic surfactant
		2. Foliar; BBCH 75	19.9	0.248 [112.7]	14		
	50% WDG	1. Foliar; BBCH 73	20.4	0.510 [231.2]	NA	1.008	
		2. Foliar; BBCH 75	19.9	0.498 [225.8]	14		
Erath, TX; 2005 (V-25689-05-L)	50% WDG	1. Foliar; late pegging	20.0	0.249 [112.9]	NA	0.501	Nonionic surfactant
		2. Foliar; late pegging	20.2	0.252 [114.5]	14		
Hockley, TX; 2005 (V-25689-05-M)	50% WDG	1. Foliar; maturing peanuts	20.1	0.250 [113.6]	NA	0.498	Nonionic surfactant
		2. Foliar; maturing peanuts	19.9	0.248 [112.3]	14		
Washington, MS; 2005 (V-25689-05-N)	50% WDG	1. Foliar; flowering, complete row closure	19.8	0.246 [111.7]	NA	0.499	Nonionic surfactant
		2. Foliar; flowering	20.3	0.253 [114.8]	13		

[1] EP = End-use Product

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[2] GPA = Gallons per acre
[3] RTI = Retreatment Interval

TABLE B.1.3. Trial Numbers and Geographical Locations.

NAFTA Growing Zones	Peanut		
	Submitted	Requested	
		Canada	U.S.
1			
1A			
2	9		8
3	1		1
4	1		
5			
5A			
5B			
6	2		2
7			
7A			
8	1		1
9			
10			
11			
12			
13			
14			
15			
16			
17			
18			
19			
20			
21			
Total	14		12

B.2. Sample Handling and Preparation

Samples were shelled and placed in frozen storage at the field sites, after which they were shipped frozen via ACDS freezer truck to the analytical laboratory, Valent Technical Center (Dublin, CA) for residue analysis. At the analytical laboratory, samples were stored frozen (-28 to -22 °C) until maceration and subsampling for extraction and analysis. The analytical laboratory noted that the samples received from one of the TX sites (trial no. V-25689-05-L) were a mixture of shelled and unshelled peanuts, and that the 14-day samples contained some mud and did not appear to have been properly dried. For this trial, which also contained residue decline samples, the 10-day samples were analyzed instead of the 14-day samples; none of the samples from the remaining harvest intervals were analyzed. In addition, samples from the

exaggerated applications at the VA site (V-25689-05-B) and one GA site (V-25689-05-D) were not analyzed.

B.3. Analytical Methodology

Samples of peanut nutmeats were analyzed for residues of *cis*- and *trans*-metconazole using a GC/NPD method (Method RM-41C-1). A complete description of the method was included in the submission.

Briefly, samples were extracted with acetonitrile (ACN):water (70:30, v:v), vacuum filtered, and rotary evaporated to remove ACN. The remaining residue was partitioned into hexane (2x), and the hexane phase was partitioned with ACN (2x). ACN was removed by rotary evaporation, and the residue was dissolved in methanol:water (1:1, v:v), and applied to a C18 SPE cartridge; residues were eluted with methanol:water (5:1, v:v). The eluate was evaporated to dryness and redissolved in toluene for analysis by GC/NPD. The validated LOQ was 0.02 ppm for each isomer, and the reported LOD was 0.01 ppm for each isomer.

C. RESULTS AND DISCUSSION

Sample storage conditions and durations are summarized in Table C.2.1. Samples were stored frozen (<-22 °C) from harvest to analysis for 110-138 days (3.6-4.5 months). To support sample storage conditions and intervals for *cis*- and *trans*-metconazole residues, the petitioner conducted a concurrent storage stability study. Samples of untreated peanut nutmeats were fortified with *cis*- and *trans*-metconazole at 0.10 ppm and stored frozen. Samples were analyzed on day 0 and following storage for 48 and 133 days. Residues of *cis*- and *trans*-metconazole appeared to be relatively stable in/on peanut nutmeats stored frozen; recoveries were 91-100% following 48 days and 82-83% following 133 days of frozen storage. These data are adequate to support the peanut field trials.

Concurrent method recovery data are presented in Table C.1. Samples were analyzed for *cis*- and *trans*-metconazole using GC/NPD method RM-41C-1. The validated LOQ was 0.02 ppm each for *cis*- and *trans*-metconazole. The reported LOD was 0.01 ppm for each analyte. The method was adequate for data collection based on acceptable concurrent method recoveries. Concurrent recoveries were within the acceptable range of 70-120% for peanut nutmeat samples fortified with *cis*- and *trans*-metconazole, each at the LOQ (0.02 ppm) and 0.10 ppm. Apparent residues of *cis*- and *trans*-metconazole were nondetectable (<0.01 ppm each) in/on all samples of untreated peanut nutmeat.

Residue data from the peanut field trials are reported in Table C.3. A summary of the residue data for peanut nutmeats is presented in Table C.4. Residues of both *cis*- and *trans*-metconazole were nondetectable (<0.01 ppm) in/on all but two samples of peanut nutmeat harvested 10-18 days after two foliar applications of the 1.81 lb ai/gal FlC or 50% WDG formulation of metconazole at 0.49-0.51 lb ai/A; residues of *cis*-metconazole at 0.01 ppm (<LOQ) were detected in/on two samples of peanut nutmeats. Combined residues of *cis*- and *trans*-metconazole did not exceed the combined LOQ of 0.04 ppm for total metconazole in/on peanut

nutmeats. HED notes that because residues were below the LOQ in all trials, results for both formulations were considered together. In samples analyzed from three of the exaggerated-rate trials, quantifiable residues of *cis*-metconazole at 0.02 and 0.04 ppm were detected in two samples from one trial conducted using the 50% WDG formulation for maximum combined residues of <0.06 ppm; remaining residues for both analytes were nondetectable.

Residue decline samples were analyzed from one trial site only. Because residues were nondetectable in/on all samples at all harvest intervals, it was not possible to assess residue decline.

TABLE C.1. Summary of Concurrent Recoveries of Metconazole from Peanuts.

Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. (%)
Peanut nutmeat	*cis*-Metconazole	0.02	8	94, 97, 99, 99, 101, 103, 105, 105	100 ± 4
		0.10	12	93, 94, 96, 97, 98, 98, 98, 100, 101, 102, 105, 106	99 ± 4
		Total	**20**	**93-106**	**100 ± 4**
	trans-Metconazole	0.02	8	95, 100, 100, 100, 102, 104, 109, 109	102 ± 5
		0.10	12	86, 91, 92, 96, 97, 98, 98, 98, 100, 104, 105, 107	98 ± 6
		Total	**20**	**86-109**	**100 ± 6**

TABLE C.2.1. Summary of Storage Conditions.

Matrix	Storage Temperature (°C)	Actual Storage Duration[1]	Interval of Demonstrated Storage Stability (days or months)
Peanut nutmeat	<-22	110-138 days (3.6 - 4.5 months)	Residues of *cis*- and *trans*-metconazole were relatively stable in/on peanut nutmeat samples stored frozen for 133 days (see Table C.2.2).

[1] Duration from date dug to date of analysis; samples were analyzed within 1-3 days of extraction.

TABLE C.2.2 Stability of *cis*-Metconazole and *trans*-Metconazole in/on Peanuts Stored Frozen.

Matrix	Spike Level (ppm)	Storage Duration (days)	Fresh Fortification Recovery (%)	Apparent Recovery in Stored Samples (%) [Average]	Average Corrected Recovery in Stored Samples (%)[1]
***cis*-Metconazole**					
Peanut, nutmeats	0.10	0	--	96, 98 [97]	--
		48	93	84, 85 [84]	90
		133	100	81, 83 [82]	82
***trans*-Metconazole**					
Peanut, nutmeats	0.10	0	NA	96, 97 [96]	--
		48	86	85, 86 [86]	100
		133	98	79, 82 [80]	82

[1] Corrected for concurrent recovery in freshly fortified samples.

TABLE C.3. Residue Data from Crop Field Trials with Metonazole.[1]

Trial ID (County, State; Year)	Zone	Crop Variety	Commodity or Matrix	Total Rate (lb ai/A)	PHI (days)	*cis*-metconazole (ppm)	*trans*-metconazole (ppm)	Combined Residues[2] (ppm)
Gates, NC; 2004 [3] V-25689-04-A	2	NC-V11	Nutmeat	0.514	14	ND ND	ND ND	<0.04 <0.04
				1.027		ND ND	ND ND	<0.04 <0.04
Suffolk, VA; 2005 V-25689-05-B	2	Gregory	Nutmeat	0.512	13	ND ND	ND ND	<0.04 <0.04
Barnwell, SC; 2005 V-25689-05-C	2	Georgia Green	Nutmeat	0.503	10	ND ND	ND ND	<0.04 <0.04
					14	ND ND	ND ND	<0.04 <0.04
					19	ND ND	ND ND	<0.04 <0.04
					22	ND ND	ND ND	<0.04 <0.04
Clarke, GA; 2005 V-25689-05-D	2	Georgia Green	Nutmeat	0.498	14	ND ND	ND ND	<0.04 <0.04
Turner, GA; 2005 V-25689-05-E	2	Georgia Green	Nutmeat	0.502	15	ND ND	ND ND	<0.04 <0.04
Tift, GA; 2005 V-25689-05-F	2	Georgia Green	Nutmeat	0.505	14	ND ND	ND ND	<0.04 <0.04
Houston, AL; 2005 V-25689-05-G	2	Georgia Green	Nutmeat	0.489	14	ND ND	ND ND	<0.04 <0.04
Henry, AL; 2005 V-25689-05-H	2	Carver's	Nutmeat	0.488	14	ND ND	ND ND	<0.04 <0.04
Houston, AL; 2005 V-25689-05-I	2	Georgia Green	Nutmeat	0.504	15	ND ND	ND ND	<0.04 <0.04
Madison, FL; 2005 V-25689-05-J	3	Georgia Green	Nutmeat	0.507	15	ND ND	ND ND	<0.04 <0.04
Wharton, TX; 2005 V-25689-05-K	6	Tamspan90	Nutmeat	0.501	15	(0.01) ND	ND ND	<0.04 ND
				1.008		0.02[4] 0.04[4]	ND ND	<0.04 <0.06
Erath, TX; 2005 V-25689-05-L	6	Tamrun 96	Nutmeat	0.501	10	ND ND	ND ND	<0.04 <0.04
Hockley, TX; 2005 V-25689-05-M	8	Spanco	Nutmeat	0.498	13	(0.01) ND	ND ND	<0.04 ND
Washington, MS; 2005 (V-25689-05-N	4	Georgia Green	Nutmeat	0.499	18	ND ND	ND ND	<0.04 <0.04

[1] ND = Not detected (<0.01 ppm); detectable residues less than the LOQ (<0.02 ppm) are reported in parentheses.
[2] Total *cis*-metconazole + *trans*-metconazole; for calculation of the total residues, the LOQ value (0.02 ppm) was used for all residues reported as ND or below the LOQ.
[3] The 1.81 lb ai/gal FlC formulation was used for this trial; for all remaining trials, the 50% WDG formulation was used.
[4] Mean of replicate determinations.

TABLE C.4. Summary of Residue Data from Crop Field Trials with Metconazole.

Commodity	Total Applic. Rate (lb ai/A)	Analyte	PHI (days)	Residue Levels (ppm) [1]						
				n	Min.	Max.	HAFT[2]	Median (STMdR)	Mean (STMR)	Std. Dev.
Peanut, nutmeat[3]	0.49-0.51	cis-Metconazole	10-18	28	<0.02	<0.02	<0.02	0.02	0.02	--
		trans-Metconazole		28	<0.02	<0.02	<0.02	0.02	0.02	--
		Total residues		28	<0.04	<0.04	<0.04	0.04	0.04	--
Peanut nutmeat[3]	1.00-1.03	cis-Metconazole	14-15	6	<0.02	0.04	0.03	0.02	0.02	<0.01
		trans-Metconazole		6	<0.02	<0.02	<0.02	0.02	0.02	--
		Total residues		6	<0.04	<0.06	<0.03	0.02	0.02	<0.01

[1] For calculation of median, mean, and standard deviation, the LOQ was used for any results reported as <LOQ in Table C.3.
[2] HAFT = Highest Average Field Trial.
[3] Including results from one trial conducted with the 1.81 lb ai/gal FlC formulation at each application rate.

D. CONCLUSION

The submitted field trial data are adequate and reflect the use of two foliar applications of the 1.81 lb ai/gal FlC or the 50% WDG formulation of metconazole at a total seasonal rate of 0.49-0.51 lb ai/A. An acceptable method was used for quantitation of residues of *cis*- and *trans*-metconazole, and the study is supported by adequate storage stability data.

E. REFERENCES

DP#: 324541
Subject: Metconazole. Request for a Tolerance on Imported Bananas. Summary of Analytical Chemistry and Residue Data. Petition Number 9E05052.
From: N. Dodd
To: M. Waller
Date: 12/14/05
MRIDs: 44721506-44721511

F. DOCUMENT TRACKING

RDI: N. Dodd (2/20/08)
Petition Numbers: 6F7094 and 6F7095
DP#s: 348168 and 348206
PC Code: 125619

Template Version June 2005

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Primary Evaluator	This DER was originally prepared under contract by Dynamac Corporation.
Approved by	Nancy Dodd, Chemist *Nancy Dodd* Date: 2/20/08 Registration Action Branch 3 Health Effects Division (7509P)

This DER was originally prepared under contract by Dynamac Corporation (2275 Research Boulevard, Suite 300; Rockville, MD 20850; submitted 09/17/2007). The DER has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

46901712 Green, C. (2006) Magnitude of the Residues of Metconazole on Peanut Nutmeats and Peanut Processing Fraction. Project Number: 200600181, 25689, V/04/25689. Unpublished study prepared by Ashgrow Crop Management Systems, Inc., Coastal Ag Research, Inc. and Carolina Ag-Research Service, Inc. 367 p.

EXECUTIVE SUMMARY:

Valent U.S.A. Corporation has submitted a processing study for metconazole on peanut. In a single trial conducted in MS during the 2005 growing season, the 50% water dispersible granule (WDG) formulation of metconazole was applied to peanut plants as two foliar applications with a 13-day retreatment interval at 1.24-1.26 lb ai/A/application for a total seasonal rate of ~2.5 lb ai/A. Peanuts were dug 18 days after the final application and were left to dry in the field for 2 days prior to sample collection. Applications were made using ground equipment in spray volumes of ~20 gal/A; a nonionic surfactant was added to the spray mixture. Subsamples of nutmeat were reserved, and the remaining bulk samples were processed into meal and refined oil using simulated commercial processing procedures.

Samples of peanut nutmeats, meal, and refined oil were analyzed for residues of *cis*- and *trans*-metconazole using GC/NPD method RM-41C-1. The validated limit of quantitation (LOQ) was 0.02 ppm for each isomer, and the reported limit of detection (LOD) was 0.01 ppm for each isomer. The method was adequate for data collection based on acceptable concurrent method recoveries.

Samples were stored frozen (≤-12 °C) for 139 days (4.6 months) from harvest to analysis for nutmeats and for 7 days from processing to analysis for meal and refined oil. No storage stability data are required for the processed commodities; adequate storage stability data are available to support the storage conditions and duration of peanut nutmeats.

Residues of *cis*- and *trans*-metconazole in peanut nutmeats were 0.04-0.06 and <0.02 ppm, respectively for total metconazole residues of 0.06-0.08 ppm (average of 0.07 ppm).

Following processing total metconazole residues were 0.06 ppm in meal and 0.09 ppm in oil. The study results indicate that total metconazole residues do not concentrate in meal (processing factor of 0.9x), but do concentrate slightly in refined oil (processing factors of 1.3x).

The calculated processing factors for peanut meal and oil do not exceed the theoretical concentration factors of 2.2x and 2.8x, respectively (OPPTS 860.1520, Table 3).

HED notes that samples were not analyzed for the triazole metabolites [1,2,4-triazole (1,2,4-T), triazolylalanine (TA), and triazolylacetic acid (TAA)].

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the processed commodity residue data are classified as scientifically acceptable.

The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP#s 348168 and 348206.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an impact on the validity of the study.

A. BACKGROUND INFORMATION

Metconazole [5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol] is a broad-spectrum triazole Group 3 fungicide (sterol biosynthesis inhibitors). There are currently no registered uses of metconazole in the U.S.; however, a tolerance has been established for banana, and a Section 18 emergency exemption and supporting time-limited tolerances have been granted for use on soybean. Valent U.S.A. Corporation has applied for registration of fluopicolide in the U.S. for use on peanut, stone fruits, and tree nuts.

The chemical structure and nomenclature of metconazole, and the physicochemical properties of the technical grade of metconazole are presented in Tables A.1 and A.2.

Table A.1. Metconazole Nomenclature.

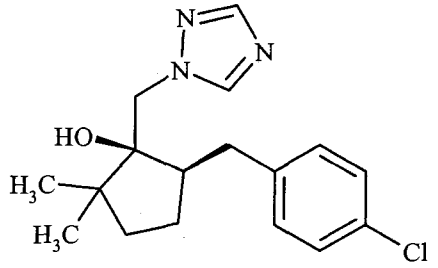
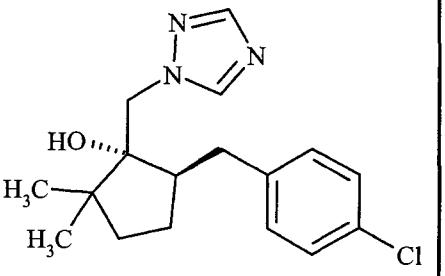
Chemical structure	 *cis*-isomer	 *trans*-isomer
Common name	Metconazole	
Company experimental name	KNF-S-474m (Kureha); BAS 555 F (BASF); V-10116 (Valent)	
IUPAC name	(1RS,5RS:1RS,5SR)-5-(4-chlorobenzyl)-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	
CAS name	5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	
CAS registry number	125116-23-6 (*cis*- and *trans*-isomers) 115850-27-6 (*cis*-isomer) 115850-28-7 (*trans*-isomer)	
End-use products (EP)	50% WDG (Metconazole 50 WDG Fungicide, EPA File Symbol 59639-RUT) 0.75 lb/gal SC/L (Caramba™ Fungicide, EPA File Symbol No. 7969-EUA) 0.67 lb/gal SC/L formulation (BAS 556 01F Fungicide, EPA File Symbol No. 7969-EUT; also contains the active ingredient pyraclostrobin at 0.83 lb/gal)	

Table A.2. Physicochemical Properties of Metconazole

Parameter	Value				References* (MRID)
Melting point/range	100.0-108.4°C (using Electrothermal Digital Melting Point Apparatus) (AC900,768 technical grade)				44721505
pH	5.81 at 25°C (1% aqueous suspension)				46808402
Relative density (20°C)	1.14 (relative density to water at 4°C, using capillary-stoppered, density-specific gravity bottle) (Lot No. AC 8879-140B)				44721505
Water solubility (20°C)	Using shake-flask method: 18.7 ± 1.0 mg/L (*cis*-isomer, WL148271, KNF-S-474m) 13.6 ± 1.7 mg/L (*trans*-isomer, WL148271, KNF-S-474m)				44721505
Solvent solubility (g/L) at 20°C	Solvent	Metconazole	*cis*	*trans*	44721505
	acetone	363	251	117	
	methanol	403	294	117	
	dichloromethane	481	343	141	
	ethyl acetate	260	173	90.0	
	propanol	132	86.6	46.7	
	toluene	103	66.2	38.0	
	Hexane	1.40	0.929	0.483	

Table A.2. Physicochemical Properties of Metconazole

Parameter	Value				References* (MRID)
Vapor pressure (20°C)	Using gas-saturation method: $< 1.23x10^{-5}$ Pa or 9.23×10^{-8} mm Hg (metconazole) $< 1.04x10^{-5}$ Pa or 7.80×10^{-8} mm Hg (*cis*-isomer) $< 1.96x10^{-6}$ Pa or 1.47×10^{-8} mm Hg (*trans*-isomer)				44721505
Dissociation constant (pK_a)	11.38±0.03 and 1.06±0.03 (in water at 29.1°C using spectrophotometric method; Lot No. AC 8879-140B)				44721505
Octanol/water partition coefficient, Log(K_{OW})	At 20 °C (using flask shaking method): K_{ow} (log K_{ow}) = 7090±989 (3.85) (Lot No. AC 8879-140B) (TGAI) K_{ow} (log K_{ow}) = 7150±803 (3.85) (*cis*-isomer, CL 354,801) K_{ow} (log K_{ow}) = 6800±1700 (3.8) (*trans*-isomer, CL 354,802)				44721505
UV/visible absorption spectrum	pH	λ	A	log ε	46808403
	cis-isomer				
	2.0	221.4	0.828	4.03	
	6.8		0.8452	4.04	
	7.0		0.9126	4.08	
	10.3		0.7226	3.98	
	trans-isomer				
	2.0	221.4	0.9053	4.07	
	7.0		0.9547	4.10	
	10.1		0.9893	4.11	

* Product Chemistry Reviews: DP #256877, Shyam Mathur, Ph.D., 9/12/2000 and DP #329168, Shyam Mathur, Ph.D., 7/13/07.

B. EXPERIMENTAL DESIGN

B.1. Application and Crop Information

In a single trial conducted in MS during the 2005 growing season, the 50% WDG formulation of metconazole was applied to peanut plants as two foliar applications with 13-day retreatment interval at 1.24-1.26 lb ai/A/application for a total seasonal rate of ~2.5 lb ai/A.

Peanuts were dug 18 days after the final application and were left to dry in the field for 2 days prior to sample collection. Applications were made using ground equipment in spray volumes of ~20 gal/A; a nonionic surfactant was added to the spray mixture. Subsamples of nutmeat were reserved, and the remaining bulk samples were processed into meal and refined oil.

Peanuts were dug up at maturity 18 days after the last treatment and were left in the field to dry for two days prior to collection of peanut samples. The petitioner noted that the dig date was delayed by 4 days due to wet weather.

The total monthly rainfall was reported, along with 10-year historical averages. Although daily temperature information was not provided, the weather conditions for each trial were summarized in comparison to "normal" conditions. Irrigation was used to supplement rainfall as needed. Weather conditions at the site had no adverse impact on the trial except that harvest was delayed due to wet conditions.

TABLE B.1.1. Study Use Pattern on Peanut.

Location (County, State; Year) Trial ID	EP[1]	Application					Tank Mix/ Adjuvants
		Method; Timing	Volume (GPA)[2]	Rate (lb ai/A)	RTI[3] (days)	Total Rate (lb ai/A)	
Washington, MS; 2005 V-25689-05-N	50% WDG	1. Foliar; flowering with complete canopy closure	19.8-20.1	1.239-1.258	13	2.497	Nonionic surfactant
		2. Foliar; flowering					

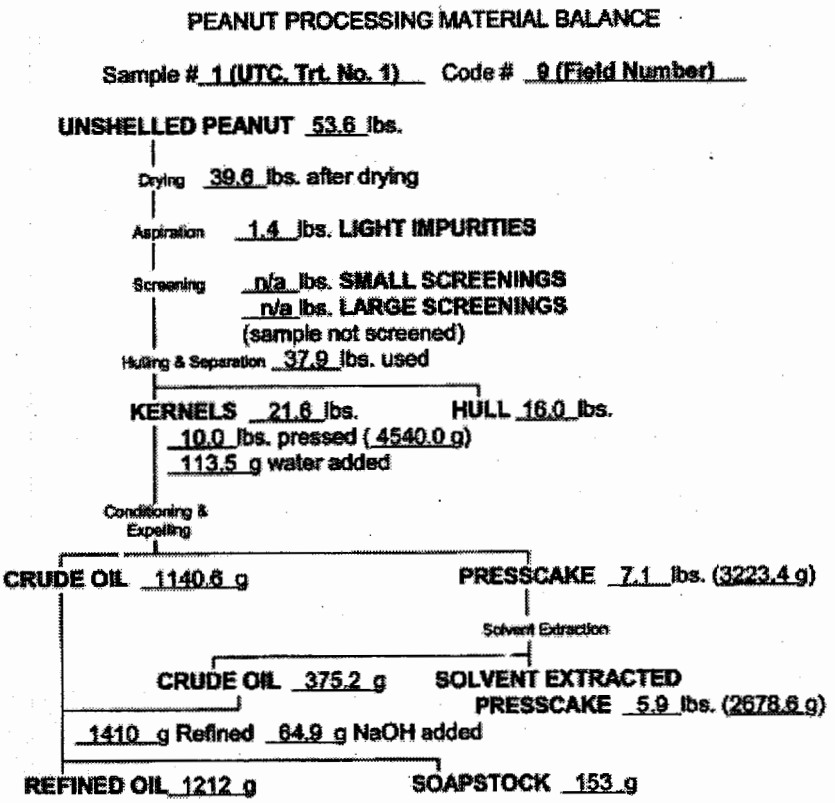
[1] EP = End-use Product
[2] GPA = Gallons per acre
[3] RTI = Retreatment Interval

B.2. Sample Handling and Processing Procedures

After collection, peanut samples were shelled and stored in a freezer on-site. Peanut nutmeats were shipped via ACDS freezer truck to GLP Technologies (Navasota, TX) for processing, where samples were stored frozen (≤-12 °C) until they were processed into meal and refined oil using simulated commercial processing procedures. Processing was initiated within 119 days of harvest. Processed samples were shipped on dry ice to the analytical laboratory, Valent Technical Center (Dublin, CA), where they were stored frozen (≤-23 °C) until maceration (nutmeats only), extraction, and analysis.

The peanut processing procedures are summarized in the flow chart below, which was copied without alteration from MRID 46901712.

FIGURE B.2.1. Processing Flowchart for Peanuts.



B.3. Analytical Methodology

Samples of peanut nutmeats, meal, and refined oil were analyzed for residues of *cis*- and *trans*-metconazole using GC/NPD method RM-41C-1. A detailed description of the method was provided with the MRID.

Briefly, samples were extracted with acetonitrile (ACN):water (70:30, v:v); the extract was isolated by vacuum filtration and concentrated by rotary evaporation to remove ACN. The remaining residue was partitioned into hexane (2x), and the hexane phase was partitioned with ACN (2x). ACN was removed by rotary evaporation, and the residue was dissolved in methanol:water (1:1, v:v), and applied to a C18 SPE cartridge; residues were eluted with methanol:water (5:1, v:v). The eluate was evaporated to dryness and redissolved in toluene for analysis by GC/NPD. The validated LOQ was 0.02 ppm for each isomer, and the reported LOD was 0.01 ppm for each isomer.

C. RESULTS AND DISCUSSION

Sample storage intervals and conditions are summarized in Table C.2. Samples were stored frozen (≤-12 °C) for 139 days (4.6 months) from harvest to analysis for nutmeats and for 7 days from processing to analysis for meal and refined oil. No storage stability data are required for the processed commodities. To support sample storage conditions and durations of peanut nutmeats, the petitioner conducted a concurrent storage stability study in conjunction with the peanut field trials (refer to 46901712.de1.doc). The study results indicate that residues of *cis*- and *trans*-metconazole are relatively stable in/on peanut nutmeats stored frozen for up to 133 days. These data are adequate to support the storage conditions and duration for peanut nutmeats from the processing study.

Concurrent method recovery data are presented in Table C.1. Samples were analyzed for residues of *cis* and *trans*-metconazole using GC/NPD method RM-41C-1. The validated LOQ was 0.02 ppm for each isomer, and the reported LOD was 0.01 ppm for each isomer. The method was adequate for data collection based on acceptable concurrent method recoveries; recoveries were generally within the acceptable range of 70-120% *cis*- and *trans*-metconazole. Apparent residues of cis and trans-metconazole were each below the LOQ in/on untreated nutmeat, meal, and refined oil samples.

Residue data from the peanut processing study are reported in Table C.3. Residues of *cis*- and *trans*-metconazole in peanut nutmeats were 0.04-0.06 and <0.02 ppm, respectively for total metconazole residues of 0.06-0.08 ppm (average of 0.07 ppm).

Following processing, total metconazole residues were 0.06 ppm in meal and 0.09 ppm in oil. The study results indicate that total metconazole residues do not concentrate in meal (processing factor of 0.9x), but do concentrate slightly in refined oil (processing factors of 1.3x).

The calculated processing factors for peanut meal and oil do not exceed the theoretical concentration factors of 2.2x and 2.8x, respectively (OPPTS 860.1520, Table 3).

TABLE C.1. Summary of Concurrent Recoveries of Metconazole from Peanut Nutmeat and Processed Commodities.

Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. (%)
Nutmeats	*cis*-Metconazole	0.02	1	99	--
		0.10	1	102	--
	trans-Metconazole	0.02	1	104	--
		0.10	1	104	--
Meal	*cis*-Metconazole	0.02	3	98, 98, 103	100 ± 3
		0.10	2	95, 102	99
	trans-Metconazole	0.02	3	100, 101, 105	102 ± 3
		0.10	2	94, 103	99

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TABLE C.1. Summary of Concurrent Recoveries of Metconazole from Peanut Nutmeat and Processed Commodities.

Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. (%)
Oil	*cis*-Metconazole	0.02	3	93, 102, 126	107 ± 17
		0.10	1	98	--
	trans-Metconazole	0.02	3	98, 101, 110	103 ± 6
		0.10	1	100	--

TABLE C.2. Summary of Storage Conditions.

Matrix (RAC or Extract)	Storage Temperature (°C)	Actual Storage Duration [1]	Interval of Demonstrated Storage Stability
Peanut nutmeat	≤ -12 °C	139 days (4.6 months)	Residues of *cis*- and *trans*-metconazole were relatively stable in/on peanut nutmeat samples stored frozen for 133 days.[2]
Peanut meal		7 days	None submitted or required
Peanut refined oil		7 days	

[1] Duration from day of harvest/processing to analysis. Extracts were stored frozen for 1-3 days prior to analysis.
[2] Refer to 46901712.der.doc.

TABLE C.3. Residue Data from Peanut Processing Study with Metconazole.

Trial ID (County, State; Year)	Total Rate (lb ai/A)	PHI[1] (days)	Fraction	Residues (ppm)[2]			Processing Factor[4]
				cis-Metconazole	*trans*-Metconazole	Total Metconazole[3]	Total Metconazole
Washington, MS; 2005 (V-25689-05-O)	2.5	18 (2)	Nutmeat (RAC)	0.04	ND	<0.06	--
				0.05	ND	<0.07	
				0.06	ND	<0.08	
			Meal	0.04	ND	<0.06	0.9x
				0.04	ND	<0.06	
				0.04	ND	<0.06	
			Refined oil	0.07	ND	<0.09	1.3x
				0.07	ND	<0.09	
				0.08	ND	<0.10	

[1] Peanut plants were dug up and left in the field to dry; days left in the field prior to collection are reported in parentheses.
[2] ND = Not detected; the LOD was 0.01 ppm for each isomer.
[3] For calculation of total residues, the LOQ (0.02 ppm) was used for any results reported as ND.
[4] Processing factors calculated by dividing the residue in the processed fraction by the average residue in the peanut nutmeat (RAC).

D. CONCLUSION

Total metconazole residues were 0.06 ppm in meal and 0.09 ppm in oil. The study results indicate that total metconazole residues do not concentrate in meal (processing factor of 0.9x), but do concentrate slightly in refined oil (processing factors of 1.3x).

Acceptable methods were used for quantitation of residues in/on peanut nutmeats and processed commodities, and the study is supported by acceptable storage stability data.

E. REFERENCES

DP#: 324541
Subject: Metconazole. Request for a Tolerance on Imported Bananas. Summary of Analytical Chemistry and Residue Data. Petition Number 9E05052.
From: N. Dodd
To: M. Waller
Date: 12/14/05
MRIDs: 44721506-44721511

F. DOCUMENT TRACKING

RDI: N. Dodd (2/20/08)
Petition Numbers: 6F7094 and 6F7095
DP#s: 348168 and 348206
PC Code: 125619

Template Version June 2005

Primary Evaluator	This DER was originally prepared under contract by Dynamac Corporation.
Approved by	Nancy Dodd, Chemist Nancy Dodd Date: 2/20/08 Registration Action Branch 3 Health Effects Division (7509P)

This DER was originally prepared under contract by Dynamac Corporation (2275 Research Boulevard, Suite 300; Rockville, MD 20850; submitted 09/13/2007). The DER has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORTS:

46901902 Edwards, V. (1991) [cyclopentyl-(Carbon 14)]WL148271 (KNF-S-474m): Metabolism in Wheat. Project Number: 200300436, SBGR/91/017. Unpublished study prepared by Sittingbourne Research Center, Biotech. 56 p.

46901903 Edwards, V. (1991) [triazole-14(Carbon)] WL136184 (KNF-S-474c): Metabolism in Wheat. Project Number: 200400092, SBGR/91/016. Unpublished study prepared by Sittingbourne Research Center. 108 p.

EXECUTIVE SUMMARY:

Valent U.S.A. Corporation has submitted studies investigating the metabolism of [cyclopentyl-^{14}C]metconazole (specific activity 17.5 µCi/mg) and [triazole-3,5-^{14}C]metconazole (specific activity 23.2 µCi/mg) in winter wheat. The radiolabeled test substances were formulated as emulsifiable concentrate formulations then applied as a single foliar broadcast application to wheat at 0.330 lb ai/A (360 g ai/ha) for the cyclopentyl label and 0.347 lb ai/A (370 g ai/ha) for the triazole label. Wheat plants were grown in outdoor plots and application was made at Zadoks growth stage 57-60. Samples of wheat grain and straw were harvested 61 days after application for the cyclopentyl label and 73 days after application for the triazole label; samples of forage and hay were not collected. HED notes that application of the test substance was made to wheat at a growth stage after the stages that forage and hay are normally collected. The in-life and analytical phases of the study were conducted by Sittingbourne Research Center (Sittingbourne, Kent, England).

Total radioactive residues (TRR), determined by combustion/LSC, were 0.074 ppm in chlorophenyl-label wheat grain and 5.88 ppm in chlorophenyl-label wheat straw. In triazole-label samples, TRR were 0.66 ppm in grain and 6.33 ppm in straw.

Extraction with acetonitrile (ACN)/water released the majority of radioactivity in samples of cyclopentyl-label wheat grain and in straw from both labels: 75.6% TRR (0.06 ppm) in wheat grain, and 81.7-84.9% TRR (4.99-5.17 ppm) in wheat straw. Because of low TRR, residues in

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cyclopentyl-label grain were not further investigated. In triazole-label grain, extraction with water released the majority of radioactivity: 94.5% TRR (0.62 ppm). Additional residues were released in straw from both labels by mild base hydrolysis at reflux: 9.8-15.7% TRR (0.58-0.99 ppm). Remaining nonextractable residues were ≤10% TRR (≤0.03 ppm) in grain and ≤5% TRR in straw. These procedures adequately extracted the majority of residues from wheat matrices. Accountabilities for grain were 92.4-99.8%; accountabilities for straw could not be calculated because nonextractable residues following hydrolysis procedures were not reported. The studies reflect relatively lengthy storage intervals, particularly for triazole-label straw, and is supported by very limited storage stability data. The petitioner must provide the actual dates of initial profiling for the studies to confirm that this step was completed within 6 months of harvest for all samples.

Residues in cyclopentyl-label straw were initially profiled by HPLC. Metconazole was identified by HPLC co-chromatography, and identification was confirmed by GC/FID. Metabolites M1, M11, M21, and M30 were identified in cyclopentyl-label straw by HPLC co-chromatography and confirmed by GC/FID (M11 and M21), GC/MS (M11, M21, and M30) and LC/MS (M11, M21, and M30). Two monohydroxylated metabolites were tentatively identified in cyclopentyl-label straw by LC/MS. In triazole-label samples, initial profiling was conducted by TLC. Metconazole was identified in straw by TLC and HPLC co-chromatography, and metabolites M2, M11, M30, triazolylacetic acid (TAA), and A2-5 (4191; a mixture of mono- and dihydroxylated carboxylic acid metabolites isolated from the rat metabolism study) were identified by HPLC co-chromatography. Identification of metconazole was confirmed by GC/MS. Monohydroxylated metabolites were characterized in triazole-label straw by LC/MS or by chromatographic behavior. In triazole-label grain, triazolylalanine (TA) and TAA were identified by TLC co-chromatography and confirmed by GC/MS following derivatization of the isolated metabolites.

Metconazole was the primary identified residue in straw from both labels, accounting for 34.1% TRR (2.01 ppm) in cyclopentyl-label straw and for 22.0% TRR (1.39 ppm) in triazole-label straw. In cyclopentyl-label straw, metabolites M11 and M21 were major residues, accounting for 9.7-9.8% TRR (0.57-0.58 ppm), while in triazole-label straw, M11 was identified at 1.8% TRR (0.11 ppm), and M21 was not identified. Metabolite M30 was identified in straw from both labels, at 1.0% TRR in cyclopentyl-label straw and 5.4% TRR in triazole-label straw. Metabolite M1 was identified at 3.4% TRR in cyclopentyl-label straw, and metabolite M2 was identified at 1.8% TRR in triazole-label straw. Metabolites A2-5 (4191) and TAA were identified in triazole-label straw only, at 3.3% and 0.3% TRR, respectively. Remaining residues in straw were characterized as monohydroxy-metconazole metabolites (1.4% TRR in cyclopentyl-label straw and 11.5% TRR in triazole-label straw) or on the basis of organo- or aqueous solubility. The only metabolites identified in triazole-label grain were TA, at 69.7% TRR (0.46 ppm), and TAA, at 24.2% TRR (0.16 ppm).

Based on the submitted wheat metabolism studies, the petitioner proposed that the main metabolic transformations of metconazole in wheat were oxidation at the benzylic methylene to give the two monohydroxylated stereoisomers (M11 and M21) and the corresponding ketone (M30), and oxidation at the methyl groups of the cyclopentyl ring. Oxidation at the methylene

group next to the triazole ring was also indicated due to the presence of triazole conjugates in wheat grain.

HED notes that this study determines the nature of the residue in wheat grain and straw; forage and hay were analyzed.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the studies, the plant metabolism data on wheat grain and straw are classified as scientifically acceptable pending submission of additional storage stability information. The studies may be considered adequate to delineate the nature of the residue in wheat grain and straw provided additional storage stability information/data are submitted. The petitioner must provide the actual dates of initial profiling for the studies to confirm that this step was completed within 6 months of harvest for all samples of grain and straw.

The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP#s 348168 and 348206.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an impact on the validity of the study.

A. BACKGROUND INFORMATION

Metconazole [5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol] is a broad-spectrum triazole Group 3 fungicide (sterol biosynthesis inhibitors). There are currently no registered uses of metconazole in the U.S.; however, a tolerance has been established for banana, and a Section 18 emergency exemption and supporting time-limited tolerances have been granted for use on soybean. Valent U.S.A. Corporation has applied for registration of metconazole in the U.S. for use on peanut, stone fruits, and tree nuts.

The chemical structure and nomenclature of metconazole, and the physicochemical properties of the technical grade of metconazole are presented in Tables A.1 and A.2.

Table A.1. Metconazole Nomenclature.

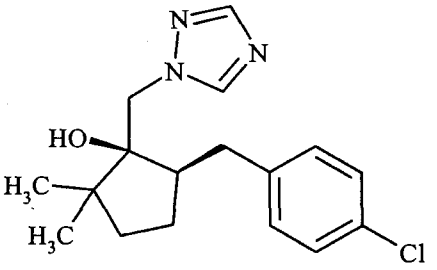
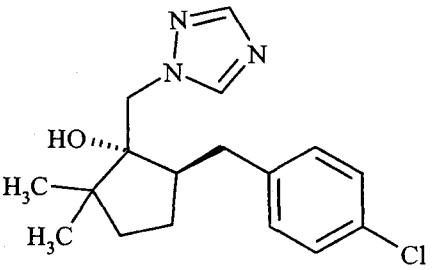
Chemical structure	 *cis*-isomer	 *trans*-isomer
Common name	Metconazole	
Company experimental name	KNF-S-474m (Kureha); BAS 555 F (BASF); V-10116 (Valent)	
IUPAC name	(1RS,5RS:1RS,5SR)-5-(4-chlorobenzyl)-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	
CAS name	5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	
CAS registry number	125116-23-6 (*cis*- and *trans*-isomers) 115850-27-6 (*cis*-isomer) 115850-28-7 (*trans*-isomer)	
End-use products (EP)	50% WDG (Metconazole 50 WDG Fungicide, EPA File Symbol 59639-RUT) 0.75 lb/gal SC/L (Caramba™ Fungicide, EPA File Symbol No. 7969-EUA) 0.67 lb/gal SC/L formulation (BAS 556 01F Fungicide, EPA File Symbol No. 7969-EUT; also contains the active ingredient pyraclostrobin at 0.83 lb/gal)	

Table A.2. Physicochemical Properties of Metconazole

Parameter	Value				References* (MRID)
Melting point/range	100.0-108.4°C (using Electrothermal Digital Melting Point Apparatus) (AC900,768 technical grade)				44721505
pH	5.81 at 25°C (1% aqueous suspension)				46808402
Relative density (20°C)	1.14 (relative density to water at 4°C, using capillary-stoppered, density-specific gravity bottle) (Lot No. AC 8879-140B)				44721505
Water solubility (20°C)	Using shake-flask method: 18.7 ± 1.0 mg/L (*cis*-isomer, WL148271, KNF-S-474m) 13.6 ± 1.7 mg/L (*trans*-isomer, WL148271, KNF-S-474m)				44721505
Solvent solubility (g/L) at 20°C	Solvent	Metconazole	*cis*	*trans*	44721505
	acetone	363	251	117	
	methanol	403	294	117	
	dichloromethane	481	343	141	
	ethyl acetate	260	173	90.0	
	propanol	132	86.6	46.7	
	toluene	103	66.2	38.0	
	Hexane	1.40	0.929	0.483	

Table A.2. Physicochemical Properties of Metconazole					
Parameter	Value				References* (MRID)
Vapor pressure (20°C)	Using gas-saturation method: $< 1.23x10^{-5}$ Pa or 9.23×10^{-8} mm Hg (metconazole) $< 1.04x10^{-5}$ Pa or 7.80×10^{-8} mm Hg (*cis*-isomer) $< 1.96x10^{-6}$ Pa or 1.47×10^{-8} mm Hg (*trans*-isomer)				44721505
Dissociation constant (pK_a)	11.38±0.03 and 1.06±0.03 (in water at 29.1°C using spectrophotometric method; Lot No. AC 8879-140B)				44721505
Octanol/water partition coefficient, Log(K_{OW})	At 20 °C (using flask shaking method): K_{ow} (log K_{ow}) = 7090±989 (3.85) (Lot No. AC 8879-140B) (TGAI) K_{ow} (log K_{ow}) = 7150±803 (3.85) (*cis*-isomer, CL 354,801) K_{ow} (log K_{ow}) = 6800±1700 (3.8) (*trans*-isomer, CL 354,802)				44721505
UV/visible absorption spectrum	pH	λ	A	log ε	46808403
	cis-isomer				
	2.0	221.4	0.828	4.03	
	6.8		0.8452	4.04	
	7.0		0.9126	4.08	
	10.3		0.7226	3.98	
	trans-isomer				
	2.0	221.4	0.9053	4.07	
	7.0		0.9547	4.10	
	10.1		0.9893	4.11	

* Product Chemistry Reviews: DP #256877, Shyam Mathur, Ph.D., 9/12/2000 and DP #329168, Shyam Mathur, Ph.D., 7/13/07.

B. EXPERIMENTAL DESIGN

B.1. Test Site and Crop Information

The field test sites were located at Sittingbourne Research Center (Sittingbourne, Kent, England). A summary of the test site information is provided in Table B.1.1, and a summary of the crop information is provided in Table B.1.2. Wheat plants were grown outdoors in 1-m^2 plots. The plots were maintained following normal agricultural practices, and maintenance pesticides were applied as needed. Daily weather conditions (rainfall and temperature) were reported.

Samples of wheat grain and straw were collected 61 days (cyclopentyl label) and 73 days (triazole label) following application of the test substances. Ears of wheat were cut off using scissors, and straw was cut off just above ground level. Triazole-label samples were allowed to dry on the bench overnight before processing. Forage and hay samples were not collected. HED notes that application of the test substance was made to wheat at a growth stage after the stages that forage and hay are normally collected.

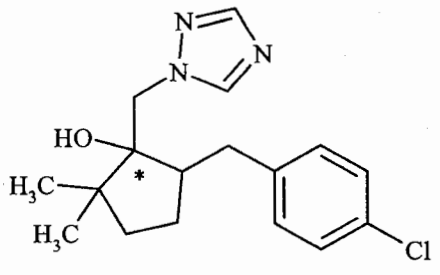
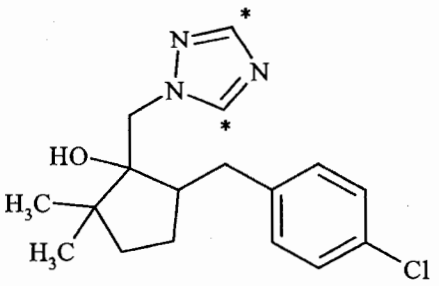
TABLE B.1.1. Test Site Information.					
Type	Method	Soil characteristics[1]			
		Type	%OM	pH	CEC
Foliar Treatment	Single foliar broadcast spray application using a gas-driven spray gun	Not provided			

[1] Only required for studies involving a soil treatment.

TABLE B.1.2. Crop Information.				
Crop; crop group	Variety	Growth stage at application	Growth stage at harvest	Harvested Matrix
Winter wheat; Grain, cereal, group 15, and Grain, cereal, forage, fodder, and straw, group 16	Avalon	Cyclopentyl label: Zadoks 57-60; between ¾ of inflorescence emerged and early anthesis Triazole label: Zadoks 57-59; between ¾ of inflorescence emerged and inflorescence completed	Maturity	Grain and straw

B.2. Test Materials

The radiolabeled test substances were formulated as emulsifiable concentrate formulations by dissolving them in blank formulation containing surfactant. The characteristics of the test substances are presented in Table B.2.1.

TABLE B.2.1. Test Material Characteristics.		
Chemical structure		
Radiolabel position	[cyclopentyl-^{14}C]metconazole	[triazole-3,5-^{14}C]metconazole
Lot No.	1099	1039
Purity	99%	99%
Specific activity	17.5 µCi/mg	23.2 µCi/mg

B.3. Study Use Pattern

The formulated test substances were applied as a single foliar broadcast foliar application to winter wheat (Zadoks growth stage 57-60) at a total application rate of 0.330 lb ai/A for the cyclopentyl label and 0.347 lb ai/A for the triazole label. Applications were made using a gas-

driven spray gun fitted with a fine nozzle. Details of the study use pattern are presented in Table B.3.1.

TABLE B.3.1. Use Pattern Information.

Chemical name	[cyclopentyl-^{14}C]metconazole	[triazole-3,5-^{14}C]metconazole
Application method	The test substances were formulated as emulsifiable concentrate formulations using formulation blank.	
Application rate	0.330 lb ai/A (360 g ai/ha)	0.347 lb ai/A (370 g ai/ha)
Number of applications	One	One
Timing of applications	Zadoks 57-60; between ¾ of inflorescence emerged and early anthesis	Zadoks 57-59; between ¾ of inflorescence emerged and inflorescence completed
PHI	61 days	73 days.

B.4. Identification/Characterization of Residues

B.4.1. Sample Handling and Preparation

The wheat ears were threshed using a single-ear threshing machine, and the grain and chaff were collected separately. The grain samples were ground to a fine powder; straw and chaff were processed together using a rotary knife mill. Following subsampling for combustion analysis, the processed grain and straw samples were stored frozen until processing and analysis.

Cyclopentyl-label grain was extracted using two methods. For method A, the sample was extracted 3x with water; results of this extraction procedure were not reported. For method B, the sample was sequentially extracted with ACN:water (9:1, v:v), ACN:water (1:1, v:v), and water, and the extracts were collected by filtration. The ACN/water extracts were combined and diluted with water, then acidified to pH 2 with concentrated HCl, and partitioned three times with EtOAc. The EtOAc phase was dried over sodium sulfate and concentrated. Because TRR in cyclopentyl-label grain were low, the extracts were not further investigated.

Cyclopentyl-label straw was soaked for 10 minutes in ACN:water (9:1, v:v), then homogenized, and filtered. Remaining residues were extracted with ACN:water (1:1, v:v; 2x), centrifuged, and filtered; the first two extracts, containing the majority of the radioactivity, were combined and subjected to partitioning with EtOAc as described above for grain. The EtOAc phase was reserved for HPLC analysis.

To generate additional material for metabolite identification, a large subsample of straw was extracted and partitioned as described above, except that only the first two EtOAc phases were collected. The combined EtOAc phases were dried over sodium sulfate, concentrated by evaporation, and filtered to remove sediment, then evaporated to dryness and redissolved in ACN for preparative column chromatography on a C18 column. Residues were sequentially eluted with water, ACN, and methanol, and the methanol fractions, containing the major portion of the recovered radioactivity, were combined, concentrated, redissolved in methanol, and subjected to further purification/fractionation by preparative column chromatography.

Triazole-label grain was extracted using three methods. For Method A, the sample was sequentially extracted with acetone, ACN, ACN:water (7:3, v:v), and water (2x), and filtered or centrifuged. For method B, the sample was extracted with water (3x), and centrifuged/filtered, and the extracts were reserved for analysis. Method C was similar to Method B, except that samples were initially soaked in water for 10 minutes prior to homogenization for extraction. The Method C extracts were combined and subjected to a number of characterization procedures including enzyme hydrolysis with cellulase, β-glucuronidase, and sulfatase, followed by partitioning with dichloromethane (DCM), and acid and base hydrolysis with concentrated HCl or 2 M HCl followed by partitioning with DCM. The Method C aqueous extract was also reserved for TLC analysis.

Triazole-label straw was also extracted using three methods. Method A was the same as Method A for grain. A subsample of the combined Method A extracts was diluted with water and subjected to partitioning with DCM (3x), and the resulting organic and aqueous phases were reserved for TLC analysis. For Method B, the sample was extracted 2x with ACN:water (1:1, v:v), followed by water (2x) and filtered or centrifuged. Method E was intended to provide material for direct comparison with the cyclopentyl-label study, and was the same as the extraction procedure described above for cyclopentyl-label straw. The ACN/water extracts following method E extraction were combined, acidified to pH 2 with HCl, and partitioned with EtOAc. The resulting phases were reserved for TLC and/or HPLC analysis.

The nonextractable residues of straw (both labels) were refluxed with either water, 0.1 M HCl, or 0.01 M NaOH for 4 hours. The extracts/hydrolysates were combined with ACN, the water and NaOH extracts were adjusted to pH 2 with concentrated HCl, and all extracts were partitioned with EtOAc; the EtOAc phases following reflux with water and NaOH were reserved for HPLC analysis.

Representative flow charts for wheat grain and straw are presented below; no flow chart was provided for triazole-label grain. The flow charts were copied without alteration from MRIDs 46901902 and 46901903.

Figure B.4.1. Extraction Flowchart for Wheat Grain (Cyclopentyl Label)

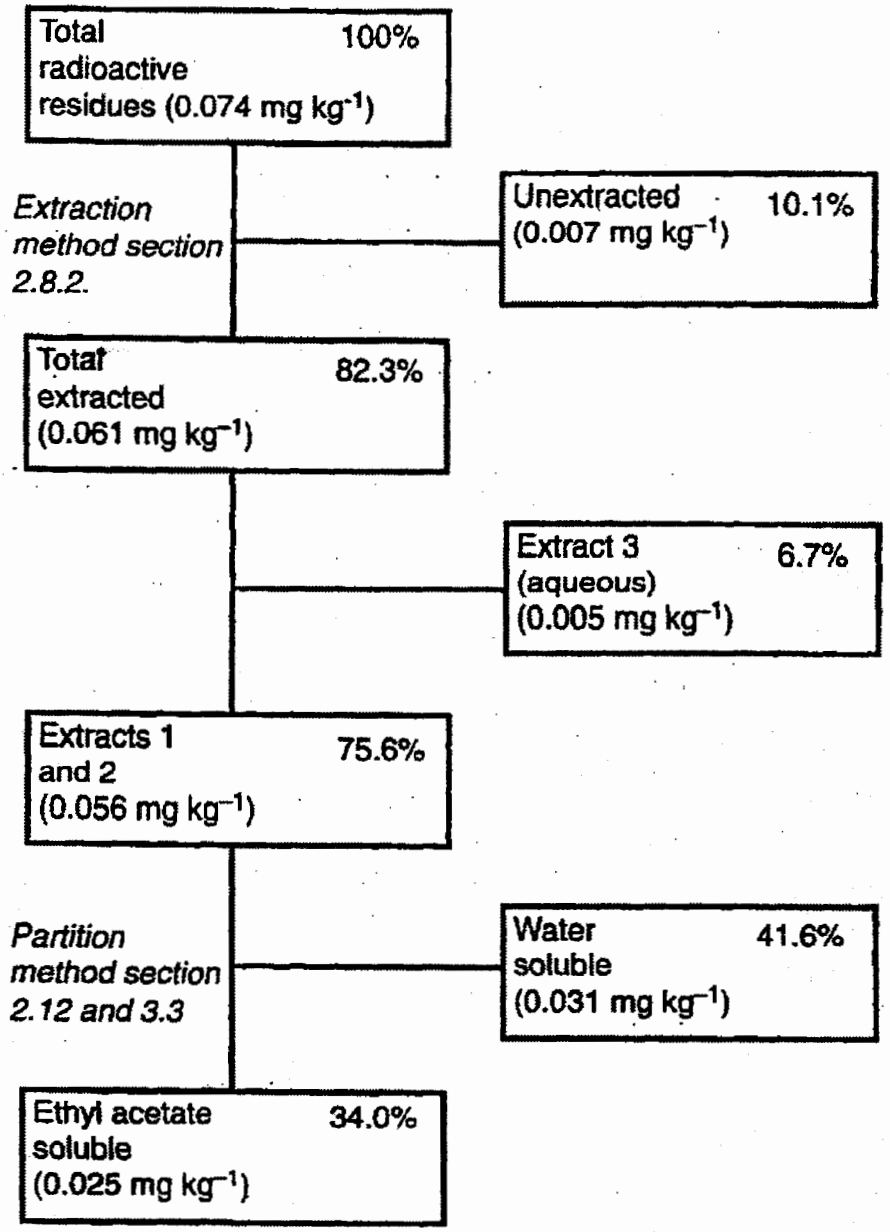


Figure B.4.2. Extraction Flowchart for Wheat Straw (Cyclopentyl Label)

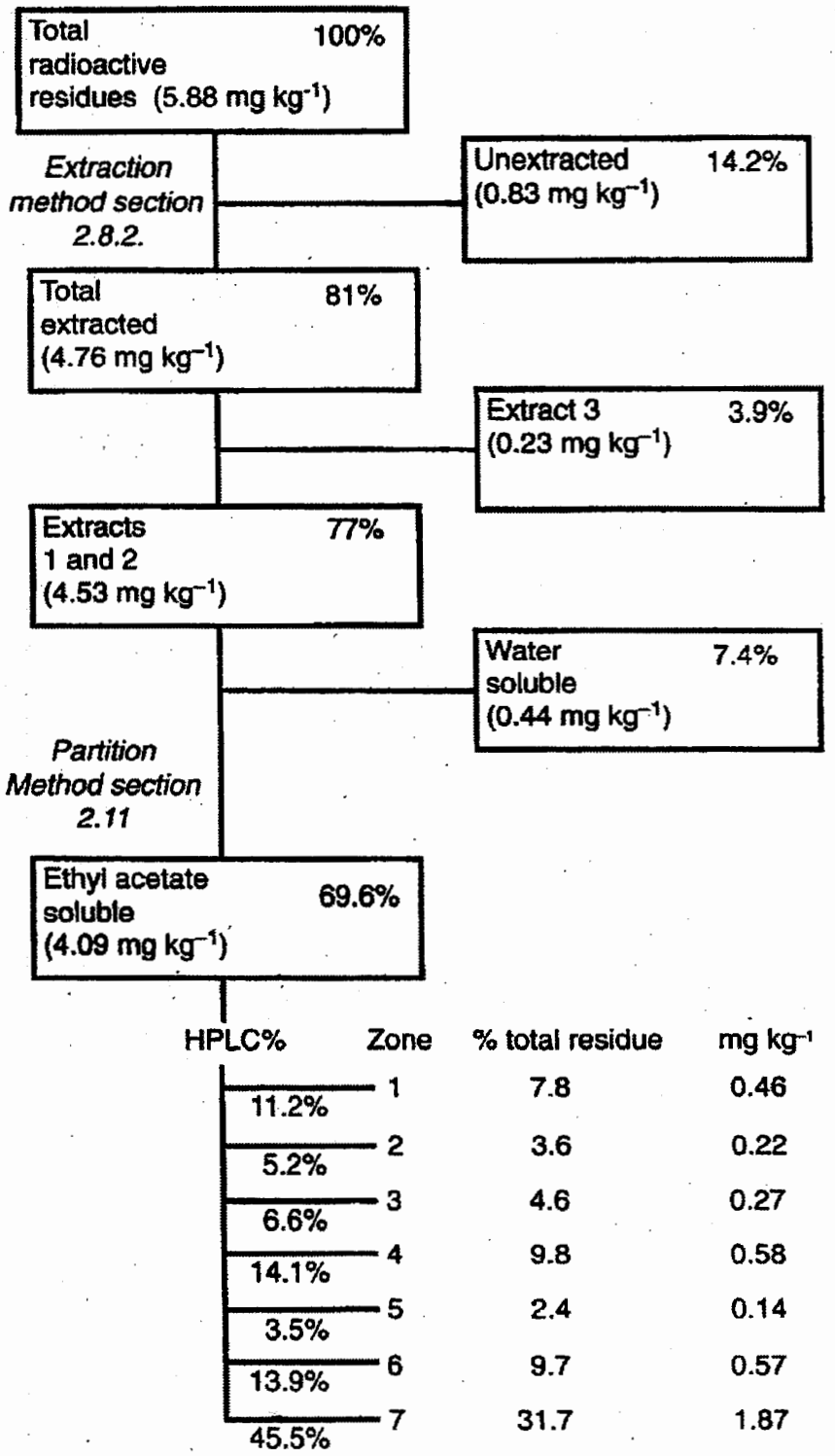
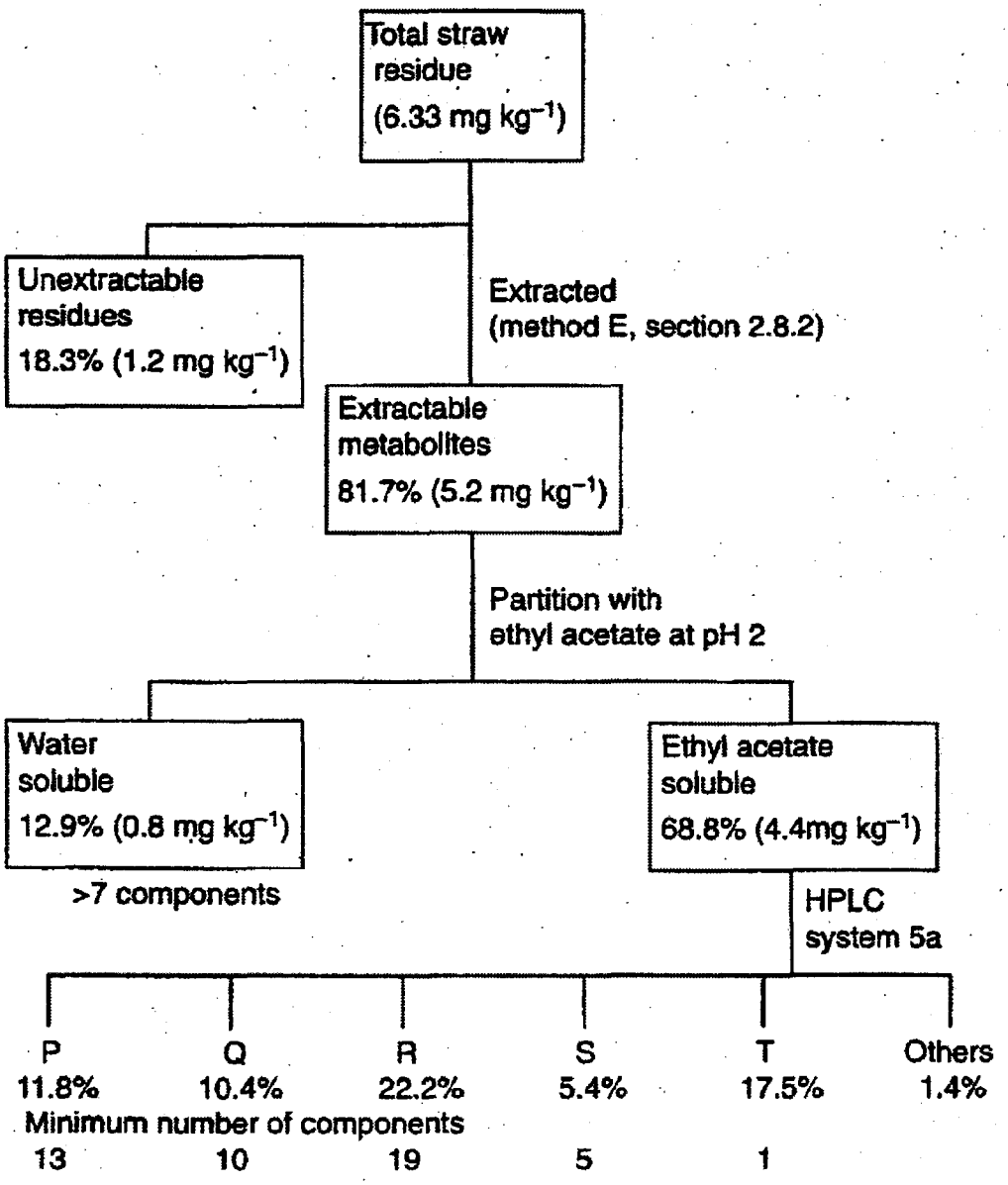


Figure B.4.3. Extraction Flowchart for Straw (Triazole Label)



B.4.2. Analytical Methodology

TRR were determined by combustion in six subsamples each of cyclopentyl-label grain and straw and triazole-label straw, and in triplicate subsamples of triazole-label grain, by combustion/LSC. TRR in extracts were determined by LSC. No limits of detection or quantitation were reported.

Cyclopentyl-label straw extracts and hydrolysates were analyzed by HPLC, with confirmatory analysis by GC/FID, GC/MS or LC/MS. HPLC analyses were conducted on systems equipped with UV detectors and flow-through radiodetectors and/or fraction collectors. Systems **e** and **f** both used reverse-phase C18 columns and gradient mobile phases of water and ACN; system **e** was used for initial profiling, as well as for preparative HPLC and co-chromatography of selected extracts and isolated fractions, and system **f** was used for semi-preparative chromatography. System **d** used a normal-phase amino column and a mobile phase of hexane/tetrahydrofuran and was used purification of isolated metabolites and co-chromatography. System **b** used a silica column and a mobile phase of DCM/hexane/tetrahydrofuran, and was used for determination of the isomer ratio.

GC/FID was conducted using a system equipped with an HP-5 column and a flame ionization detector, and GC/MS was conducted using the same system linked to a mass selective detector and operated under the same conditions. LC/MS was conducted using HPLC system **e** and a mass spectrometer with thermospray ionization.

Triazole-label sample extracts and hydrolysates were analyzed by TLC and/or HPLC, with confirmatory analysis by GC/MS or LC/MS. TLC analyses were conducted using silica gel plates (Merck F254) and a number of solvent systems: solvent system **c**, EtOAc, was used for the analysis of the DCM and aqueous phases of straw; solvent system **e,** EtOAc:formic acid:water (70:2:2, v:v, or 70:8:8, v:v:v), was used for analysis and/or co-chromatography of the ACN/water extract of straw and the organic and aqueous phases of straw following DCM and/or EtOAc partitioning; and solvent systems **j,** propanol:water:ammonia (12:3:1, v:v:v), and **k,** propan-2-ol:water:triethylamine (12:3:0.2, v:v:v), were both used for the analysis of grain extracts and the aqueous extract of straw following EtOAc partitioning. For preparative TLC, solvent system **k** was used with an LK6F silica gel plates. A radioanalyzer was used to locate and quantify radioactive components. HPLC/UV analyses were conducted on systems equipped with a UV detector, a radiodetector, and for some systems, a fraction collector. Systems **5a** and **5b** both used a reverse-phase C18 column and gradient mobile phases of water/ACN (5a) or water/ACN, each containing 0.1% formic acid (5b); both systems were used for profiling, preparative HPLC, and/or co-chromatography. Systems **6** and **7** both used normal-phase amino columns and gradient mobile phases of hexane/tetrahydrofuran; these systems were also used for preparative HPLC and/or co-chromatography.

Selected aqueous-soluble residues from the triazole study were subjected to further cleanup using strong anion exchange (SAX)/strong cation exchange (SCX) on a BondElut cartridge; residues were eluted with HCl (pH 2) in water for SAX and NH_4OH (pH 11) for SCX.

For determination of TA and TAA by GC/MS, residues were derivatized by butylation, with 20% HCl in 1-butanol, and acylation with heptafluorobutyric acid anhydride (HFBA).

GC/MS was used for confirmation of the identification of metconazole, and derivatized residues of TA and TAA in triazole-label straw and/or grain. GC/MS was conducted using both chemical and electron impact ionization. LCMS was used for tentative identification of monohydroxy metabolites in straw, and was conducted using HPLC system **5a** and a mass spectrometer with thermospray ionization.

C. RESULTS AND DISCUSSION

The petitioner provided the sampling dates for both studies; however, analysis dates were not provided. According to the petitioner, characterization analysis of cyclopentyl-label grain was completed within 6 weeks of harvest, and the initial quantitative profile for straw was obtained within 4 months of harvest, while initial TLC profiling in triazole-label grain and straw were completed within 2 months of harvest. The petitioner indicated that initial HPLC profiling of the DCM phase of triazole-label straw was conducted on a sample extracted 6 months after harvest, and the definitive quantitative profile was obtained following storage of the EtOAc phase for 18 months. A limited number of dated chromatograms and spectra were included in the studies which indicated that initial profiling in the cyclopentyl-label straw was completed within 2.5 months of harvest, and that confirmatory GC/FID, GC/MS, and LC/MS analyses for cyclopentyl-label samples were completed ~1 year after harvest. Dated chromatograms and spectra included in the triazole submission indicate that analysis for the triazole study was completed within ~17 months of harvest for grain, with TLC profiling of the Method C aqueous residues conducted ~14 months after harvest, and that analysis was completed within ~31 months of harvest for straw. The petitioner reported that a sample of the EtOAc phase of triazole-label straw was re-analyzed following 1 year of storage, and that the metabolite profile was unchanged; however, no supporting data were included. The petitioner must provide the actual dates of initial profiling for the studies to confirm that this step was completed within 6 months of harvest for all samples.

TRR in wheat matrices, determined by combustion/LSC, are reported in Table C.2.1. Following a single foliar broadcast application of [cyclopentyl-^{14}C]metconazole at 0.330 lb ai/A, TRR were 0.074 ppm in wheat grain and 5.88 ppm in wheat straw harvested 61 days after treatment. Following a single foliar broadcast application of [triazole-3,5-^{14}C]metconazole at 0.347 lb ai/A, TRR were 0.66 ppm in wheat grain and 6.33 ppm in wheat straw harvested 73 days after treatment.

The distribution of radioactivity in wheat matrices is presented in Tables C.2.2.1 (cyclopentyl label) and C.2.2.2 (triazole label). Extraction with ACN/water released the majority of radioactivity in samples of cyclopentyl-label wheat grain and in straw from both labels: 75.6% TRR (0.06 ppm) in wheat grain, and 81.7-84.9% TRR (4.99-5.17 ppm) in wheat straw. Because of low TRR, residues in cyclopentyl-label grain were not further investigated. In triazole-label grain, extraction with water released the majority of radioactivity: 94.5% TRR (0.62 ppm). Additional residues were released in straw from both labels by mild base hydrolysis at reflux:

9.8-15.7% TRR (0.58-0.99 ppm). Remaining nonextractable residues were ≤10% TRR (≤0.03 ppm) in grain and ≤5% TRR in straw. These procedures adequately extracted the majority of residues from pea matrices. Accountabilities for grain were 92.4-99.8%; accountabilities for straw could not be calculated because nonextractable residues following hydrolysis procedures were not reported.

Residues in cyclopentyl-label straw were initially profiled by HPLC. Metconazole was identified by HPLC co-chromatography, and identification was confirmed by GC/FID. Metabolites M1, M11, M21, and M30 were identified in cyclopentyl-label straw by HPLC co-chromatography and confirmed by GC/FID (M11 and M21), GC/MS (M11, M21, and M30) and LC/MS (M11, M21, and M30). Two monohydroxy metabolites were tentatively identified in cyclopentyl-label straw by LC/MS. In triazole-label samples, initial profiling was conducted by TLC. Metconazole was identified in straw by TLC and HPLC co-chromatography, and metabolites M2, M11, M30, TAA, and A2-5 (4191; a mixture of mono- and dihydroxylated carboxylic acid metabolites isolated from the rat metabolism study) were identified by HPLC co-chromatography. Identification of metconazole was confirmed by GC/MS. Monohydroxy metabolites were characterized in triazole-label straw by LC/MS or by chromatographic behavior. In triazole-label grain, TA and TAA were identified by TLC co-chromatography and confirmed by GC/MS following derivatization of the isolated metabolites. A more detailed discussion of the characterization/identification procedures by matrix is provided below.

HED notes that information and data pertaining to the extraction and fractionation procedures and distribution of metabolites appeared variously in the submission in text, tables, and/or flow charts, making it difficult to track results for a given matrix. The study included numerous procedures that appeared to be exploratory and/or did not result in characterization/identification of residues; these procedures are either discussed in brief or are not presented in this DER. In many cases data were provided as % TRR only, and ppm values had to be calculated by the study reviewer.

The characterization and identification of residues in wheat matrices are summarized in Tables C.2.3.1 (cyclopentyl-label grain and straw) and C.2.3.2 (triazole-label grain and straw). Metconazole was the primary identified residue in straw from both labels, accounting for 34.1% TRR (2.01 ppm) in cyclopentyl-label straw and for 22.0% TRR (1.39 ppm) in triazole-label straw. In cyclopentyl-label straw, metabolites M11 and M21 were major residues, accounting for 9.7-9.8% TRR (0.57-0.58 ppm), while in triazole-label straw, M11 was identified at 1.8% TRR (0.11 ppm), and M21 was not identified. Metabolite M30 was identified in straw from both labels, at 1.0% TRR in cyclopentyl-label straw and 5.4% TRR in triazole-label straw. Metabolite M1 was identified at 3.4% TRR in cyclopentyl-label straw, and metabolite M2 was identified at 1.8% TRR in triazole-label straw. Metabolites A2-5 (4191) and TAA were identified in triazole-label straw only, at 3.3% and 0.3% TRR, respectively. Remaining residues in straw were characterized as monohydroxy-metconazole metabolites (1.4% TRR in cyclopentyl-label straw and 11.5% TRR in triazole-label straw) or on the basis of organo- or aqueous solubility. The only metabolites identified in triazole-label grain were TA, at 69.7% TRR (0.46 ppm), and TAA, at 24.2% TRR (0.16 ppm).

Initial HPLC analysis of the EtOAc phase of cyclopentyl-label straw following partitioning with ACN/water yielded give seven zones, designated SEA 1-7. Co-chromatography on reverse and normal phase systems indicated that SEA 4, 6, and 7 consisted of single components corresponding to M11, M21, and metconazole; the remaining zones were found to be composed of multiple components, each <5% TRR. Initial HPLC analysis also indicated the presence of metabolite M30 and monohydroxy metconazole metabolites in SEA 5. Small amounts of M1 were identified in SEA 3 by co-chromatography with M1. Identification of metconazole was confirmed by GC/FID.

Residues in cyclopentyl-label straw were further investigated using the large subsample of cyclopentyl-label straw. Preparative chromatography of this subsample yielded three main fractions, which on HPLC were found to contain SEA 4 and SEA 6 (fractions 2 and 3) and metconazole; the isolated metconazole was analyzed on system b to determine the isomer ratio in the sample (72:28, *cis:trans*). Fractions 2 and 3 were subjected to semi-preparative HPLC on system f to isolate two major metabolites. Normal phase HPLC of the two fractions of interest resulted in two major fractions of interest: X (SEA 6), Y (SEA 4), and three minor fractions, Xa, Ya, and Yb (SEA5). Metabolites X and Y were subjected to normal phase HPLC co-chromatography and analysis by GC/FID, GC/MS following purification by normal-phase HPLC, and LC/MS which confirmed that fraction X was M21 and fraction Y was M11. Metabolite M30 was identified by co-chromatography and confirmed by LC/MS and HPLC analysis, and two monohydroxy metabolites were tentatively identified by LC/MS alone; these metabolites did not correspond to any reference compounds and were not further investigated.

In triazole-label grain, the majority of characterization/identification was conducted on the Method C aqueous extract. Enzyme and chemical hydrolysis procedures following DCM partitioning were not successful in releasing residues. To further investigate the aqueous extract, starches and other macromolecules were removed by concentrating the extract and subjecting it to organic solvent precipitation with methanol followed by centrifugation. Following precipitation of macromolecules, the concentrated extract was purified by SAX and reverse-phase C18 cartridge chromatography; residues were eluted from a series of SAX cartridges with 1% ammonium hydroxide, pH 11, and the purified fractions were applied to the C18 cartridges; residues were again eluted with ammonium hydroxide. The Method C aqueous extract was also subjected to preparative TLC on silica gel plates using a solvent system of propanol:water:triethylamine (12:3:0.2, v:v:v). The bands of interest were scraped from the plates, and residues were eluted with ACN:water (1:4, v:v). TLC analysis of the purified extract resulted in separation of a major and minor component. TLC co-chromatography suggested the presence of TA and TAA. The two components were further separated using SCX cartridge chromatography, and a subsample of the fraction which was collected following preparative TLC was subjected to derivatization with HFBA following esterification with butanol. Identification of TA and TAA was confirmed by TLC co-chromatography with derivatized standards and GC/MS analysis.

In triazole-label straw, the combined Method A extracts were initially profiled by TLC, suggesting a broad range of components. Following partitioning with DCM, metconazole was identified in the organic phase by TLC co-chromatography, and identification was confirmed by

GC/MS; residues in the aqueous phase were characterized by TLC analysis as polar metabolites. A subsample of the Method E ACN/water extract was partitioned with EtOAc. Initial HPLC profiling indicated the presence of metconazole and up to 12 metabolites. The extract was further fractionated with preparative HPLC, yielding five zones designated P, Q, R, S, and T. Zone T corresponded to metconazole; the remaining zones were subjected to further partitioning with DCM followed by EtOAc (zones P and Q) and preparative HPLC to further resolve individual components. Zone P was found to be comprised of three major components, P1, P2, and P3. Component P2 co-chromatographed on HPLC with a standard isolated from the rat metabolism study, A2-5 (4191), which consisted of a mixture of mono- and dihydroxylated carboxylic acid metabolites; further HPLC analysis of the remaining components suggested the presence of up to 13 minor components. Zone Q was further fractionated by preparative HPLC into three components. Fractionation of the first component, Q1, yielded two components, which, on further investigation via LC/MS, were tentatively identified as monohydroxy metabolites. Zone R was resolved by preparative HPLC into four components. HPLC analysis indicated the presence of metabolite M2 in R1, monohydroxylated metabolites in R2, and metabolite M11 in R4, and Zone S was found to correspond to metabolite M30 on HPLC analysis and co-chromatography. The aqueous phase of straw following EtOAc partitioning was subjected to TLC and HPLC analysis and derivatization with HFBA, which indicated the presence of a small amount of TA; acid hydrolysis of the aqueous phase and subsequent HPLC analysis indicated the presence of components corresponding to zones Q and R of the organic phase. Further examination of the nonextractable residues of straw following NaOH hydrolysis indicated the presence of metconazole by HPLC co-chromatography.

C.1. Storage Stability

The petitioner provided the sampling dates for both studies; however, analysis dates were not provided. The petitioner stated that characterization analysis of cyclopentyl-label grain was completed within 6 weeks of harvest, and that the initial quantitative profile for straw was obtained within 4 months of harvest. A limited number of dated chromatograms and spectra were included in the cyclopentyl study which indicate that initial profiling in straw was completed within 76 days (2.5 months of harvest), and that confirmatory GC/FID, GC/MS, and LC/MS analyses were completed ~1 year after harvest. In the triazole study, the petitioner stated that TLC profiling of DCM and aqueous residues in grain and straw were completed within 2 months of harvest. Initial HPLC profiling of the DCM phase of straw was conducted on a sample extracted 6 months after harvest, and the definitive quantitative profile was obtained following storage of the EtOAc phase for 18 months. Dated chromatograms and spectra included in the submission indicate that analysis for the triazole study was completed within ~17 months of harvest for grain, with TLC profiling of the Method C aqueous residues conducted ~14 months after harvest, and within ~31 months of harvest for straw.

To examine the stability of the metabolic profile in the EtOAc phase, a subsample of the extract that had been stored for 1 year in ACN solution at 4 °C was analyzed by HPLC, yielding the same metabolic zones; no supporting chromatograms or quantitative/qualitative data were submitted. The petitioner also noted that the extractability of residues was measured at several time points during the analytical phase, and that consistent results were obtained.

TABLE C.1. Summary of Storage Conditions.			
Matrix	Storage Temperature (°C)	Actual Storage Duration[1]	Interval of Demonstrated Storage Stability
Cyclopentyl label			
Wheat grain	Frozen (temperature unspecified)	Up to 6 weeks (characterization analysis complete)	No data required because initial profiling was completed within 6 months.
Wheat straw		Up to 4 months (initial quantitative profile complete	
Triazole label			
Wheat straw	Frozen (temperature unspecified)	2-17 months (initial TLC profiling completed in 2 months; TLC profiling of Method C aqueous extract completed 14 months after harvest)	None submitted.
		2-31 months (initial TLC profiling completed in 2 months; initial HPLC profiling conducted on sample extracted following storage for 6 months)	Petitioner stated that metabolic profile was unchanged in EtOAc phase analyzed by HPLC 18 months after initial analysis.

[1] Based on statement made by the petitioner and/or dated chromatograms/spectra. Analysis dates for individual matrices were not provided.

C.2. Identification, Characterization, and Distribution of Residues

TABLE C.2.1. Total Radioactive Residues (TRR) in Wheat.				
Matrix	PHI (days)	Application rate (lb ai/A)	Cyclopentyl label	Triazole label
			ppm	ppm
Wheat grain	Cyclopentyl label: 61 Triazole label: 73	Cyclopentyl label: 0.330 Triazole label: 0.347	0.074	0.66
Wheat straw			5.88	6.33

TABLE C.2.2.1 Distribution of the Parent and the Metabolites in Wheat Matrices Following Application of [cyclopentyl-^{14}C]Metconazole at 0.330 lb ai/A.[1]				
Metabolite Fraction	Wheat Grain		Wheat Straw	
	TRR = 0.074 ppm		TRR = 5.88 ppm	
	%TRR	ppm	%TRR	ppm
ACN:water (9:1, v:v)	18.7	0.014	65.6	3.86
ACN:water (1:1, v:v)	56.9	0.042	11.4	0.67
Combined ACN/water	75.6	0.061	81.0	4.76
Aqueous	41.6	0.031	7.4	0.44
EtOAc	34.0	0.025	69.6	4.09
SEA 1			7.8	0.46
SEA 2			3.6	0.22
SEA 3			4.6	0.27
M1			3.4	<0.2
SEA 4; **M11**			9.8	0.58
SEA 5;			2.4	0.14
X_a; **M30**			1.0	0.06
Y_a; monohydroxy metabolite			0.9	0.05

TABLE C.2.2.1 Distribution of the Parent and the Metabolites in Wheat Matrices Following Application of [cyclopentyl-^{14}C]Metconazole at 0.330 lb ai/A.[1]

Metabolite Fraction	Wheat Grain		Wheat Straw	
	TRR = 0.074 ppm		TRR = 5.88 ppm	
	%TRR	ppm	%TRR	ppm
Y_b; monohydroxy metabolite			0.5	0.03
SEA 6; **M21**			9.7	0.57
SEA 7; **Metconazole**			31.7	1.87
ACN:water (1:1, v:v)			3.9	0.23
Water	6.7	0.005		
Unextractable	10.1	0.007	14.2	0.83
Base hydrolysis			9.8	0.58
EtOAc			7.5	0.44
Metconazole			2.4	0.14
Unknowns (≥12 components)			5.1	0.30
Aqueous			NR[2]	NR
Unextractable			NR	NR

[1] Shading indicates that the extraction step and/or characterization analysis was not conducted for the matrix in question.
[2] NR = Not reported.

TABLE C.2.2.2 Distribution of the Parent and the Metabolites in Wheat Matrices Following Application of [triazole-3,5-^{14}C]Metconazole at 0.347 lb ai/A.[1]

Metabolite Fraction	Wheat grain		Wheat straw	
	TRR = 0.66 ppm		TRR = 6.33 ppm	
	%TRR	ppm	%TRR	ppm
Method A				
Acetone	0.8	0.005	39.7	2.51
CAN	<0.1	<0.001	7.6	0.48
ACN/water	18.5	0.12	17.6	1.11
Water	65.5	0.43	7.0	0.44
Water	7.5	0.05	1.7	0.11
Combined acetone, ACN, ACN/water, and water			73.6	4.66
DCM			52.8	3.3
Metconazole			19.5	1.2
Metabolites			33.3	2.1
Aqueous (polar metabolites)			20.8	1.3
Unextractable	4.3	0.03	15.6	0.99
Method B (straw)				
ACN:water (1:1, v:v)			71.9	4.55
ACN:water (1:1, v:v)			4.6	0.29
Water			2.3	0.15
Water			1.6	0.10
Unextractable			16.6	1.05
Method C (grain)				
Water	75.1	0.50		
Water	16.0	0.11		
Water	3.4	0.02		

TABLE C.2.2.2 Distribution of the Parent and the Metabolites in Wheat Matrices Following Application of [triazole-3,5-^{14}C]Metconazole at 0.347 lb ai/A.[1]

Metabolite Fraction	Wheat grain		Wheat straw	
	TRR = 0.66 ppm		TRR = 6.33 ppm	
	%TRR	ppm	%TRR	ppm
Total extracted	94.5	0.62		
Triazolylalanine	69.7	0.46		
Triazolylacetic acid	24.2	0.16		
Unextractable	5.3	0.03		
Method E (Straw)				
ACN:water (9:1, v:v)			57.5	3.64
ACN:water (1:1, v:v)			18.5	1.17
ACN:water (1:1, v:v)			5.7	0.36
Combined ACN/water			81.7	5.17
EtOAc (subsample 1; SS1)			68.8	4.36
Metconazole			18.2	1.15
Metabolites			50.6	3.20
Aqueous (SS1)			NR	NR
EtOAc (SS2)			68.8	4.36
Zone P (Rt 15-25 min.)			11.8	0.75
P1 (≥2 components)			3.4	0.22
P2 (≥3 components); **A2-5 (4191)**			3.3	0.21
P3 (≥2 components)			1.0	0.06
Others			0.2	0.01
Zone Q (Rt 26-31 min.)			10.4	0.66
Q1			7.2	0.46
Q1a; **monohydroxylated metabolite** (tentative)			2.1	0.13
Q1b; **monohydroxylated metabolite** (tentative)			3.7	0.23
Others (3 components)			1.4	0.09
Q2			1.3	0.08
Q3			0.5	0.03
Others (2 components)			1.2	0.08
Zone R (Rt 36-47 min.)			22.2	1.41
R1			2.0	0.13
R1a; **M2**			1.8	0.11
Others (2 components)			0.2	0.01
R2; **monohydroxylated metabolite**			5.7	0.36
R3			5.3	0.34
R3a			0.3	0.02
R3b			1.0	0.06
R3d			3.8	0.24
Others (2 components)			0.2	0.01
R4			5.2	0.33
R4c; **M11**			1.8	0.11
Others (6 components)			3.5	0.22
Others (3)			3.5	0.22

TABLE C.2.2.2 Distribution of the Parent and the Metabolites in Wheat Matrices Following Application of [triazole-3,5-^{14}C]Metconazole at 0.347 lb ai/A.[1]

Metabolite Fraction	Wheat grain		Wheat straw	
	TRR = 0.66 ppm		TRR = 6.33 ppm	
	%TRR	ppm	%TRR	ppm
Zone S (Rt 48-52 min.); **M30**			5.4	0.34
Zone T; **Metconazole**			17.5	1.11
Aqueous SS2			12.9	0.82
Preparative TLC A			3.6	0.23
HPLC Rt 24.2 min.			1.0	0.06
HPLC Rt 26 min			0.1	0.01
Preparative TLC B			3.5	0.22
HPLC Rt 21.7 min; **Triazolylacetic Acid**			0.3	0.02
Preparative TLC C (calculated by subtraction)			5.8	0.37
Unextractable			18.3	1.16
Base hydrolysis			15.7	0.99
EtOAc			10.2	0.65
Metconazole			4.5	0.28
Aqueous			NR[2]	NR
Unextractable			NR	NR

[1] Shading indicates that the extraction step and/or characterization analysis was not conducted for the matrix in question.
[2] NR = Not reported.

TABLE C.2.3.1. Summary of Characterization and Identification of Radioactive Residues in Wheat Matrices Following Application of [cyclopentyl-^{14}C]Metconazole at 0.330 lb ai/A.

Compound	Wheat Grain		Wheat Straw	
	TRR = 0.074 ppm		TRR = 5.88 ppm	
	% TRR	ppm	% TRR	ppm
Metconazole			34.1	2.01
M1			3.4	0.2
M11			9.8	0.58
M21			9.7	0.57
M30			1.0	0.06
Monohydroxy metabolites			1.4	0.08
Multicomponent unknowns			5.1	0.30
ACN/water soluble	75.6	0.06	3.9	0.23
EtOAc soluble	--	--	11.4	0.68
Water soluble	6.7	0.005	7.4	0.44
Total identified	--	--	58.0	3.42
Total characterized	82.3	0.060	29.2	1.79
Total extractable	82.3	0.060	88.4	5.20
Unextractable (PES)[1]	10.1	0.01	NR[2]	NR
Accountability[3]	92.4		NC[4]	

[1] Residues remaining after exhaustive extractions.
[2] NR = Not reported.
[3] Accountability = (Total extractable + Total unextractable)/(TRR from combustion analysis; see TABLE C.2.1) * 100.
[4] NC = Not calculated.

TABLE C.2.3.2. Summary of Characterization and Identification of Radioactive Residues in Wheat Matrices Following Application of [triazole-3,5-^{14}C]Metconazole at 0.347 lb ai/A.

Compound	Wheat Grain		Wheat Straw	
	TRR = 0.66 ppm		TRR = 6.33 ppm	
	% TRR	ppm	% TRR	ppm
Metconazole	--	--	22.0	1.39
M2	--	--	1.8	0.11
M11	--	--	1.8	0.11
M30	--	--	5.4	0.34
TA	69.7	0.46	--	--
TAA	24.2	0.16	0.3	0.02
A2-5 (4191)	--	--	3.3	0.21
Monohydroxylated metabolites	--	--	11.5	0.72
Organosoluble unknowns	--	--	21.5	1.35
Polar unknowns (aqueous soluble)	--	--	9.4	0.60
Total identified	93.9	0.62	34.6	2.18
Total characterized	--	--	42.4	2.67
Total extractable	94.5	0.62	97.4	6.16
Unextractable (PES)[1]	5.3	0.03	NR[2]	NR
Accountability[3]	99.8%		NC[4]	

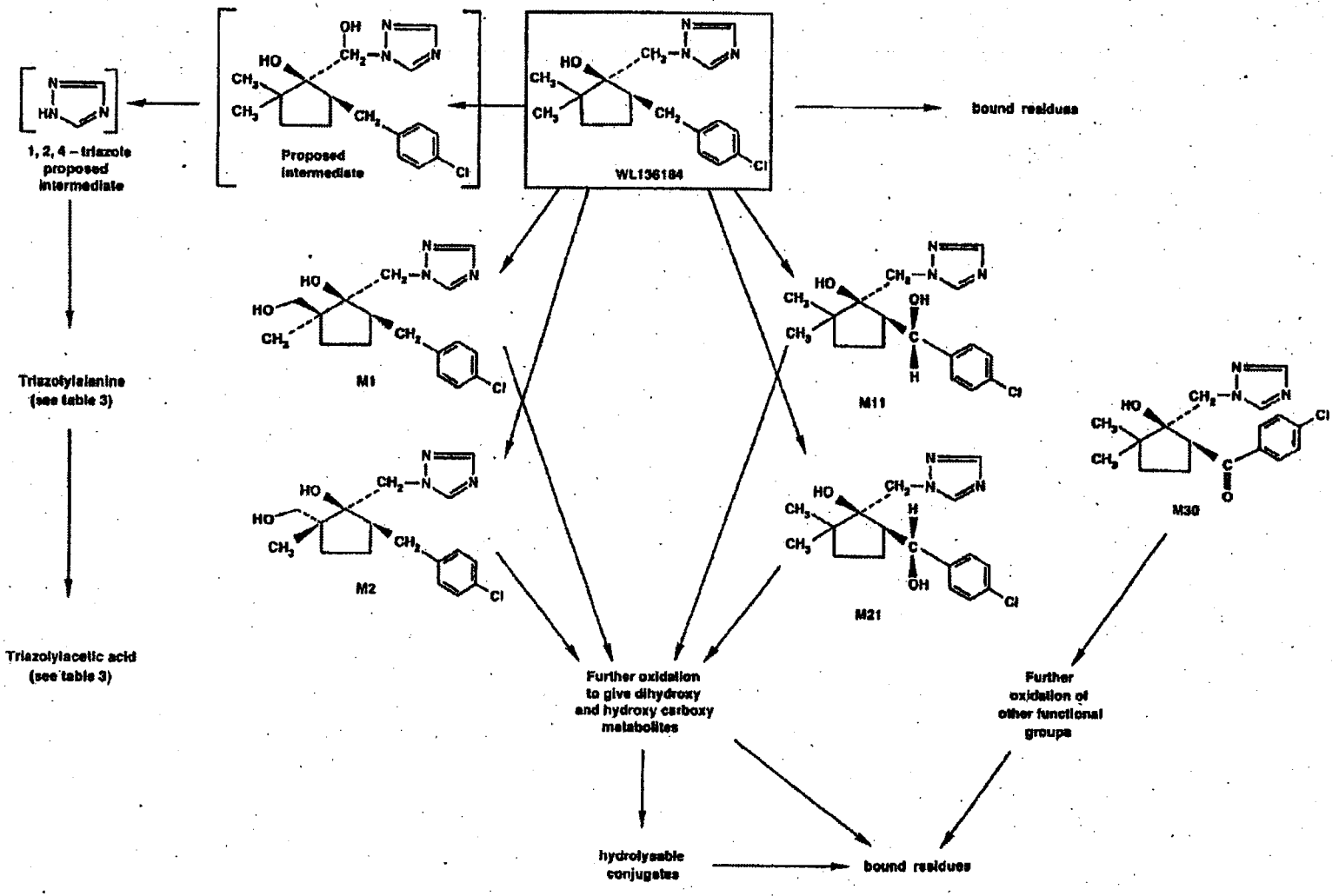
[1] Residues remaining after exhaustive extractions.
[2] NR = Not reported.
[3] Accountability = (Total extractable + Total unextractable)/(TRR from combustion analysis; see TABLE C.2.1) * 100.
[4] NC = Not calculated.
[4] NC = Not calculated.

C.3. Proposed Metabolic Profile

Based on the submitted wheat metabolism studies, the petitioner proposed that the main metabolic transformations of metconazole in wheat were oxidation at the benzylic methylene to give the two monohydroxylated stereoisomers (M11 and M21) and the corresponding ketone (M30), and oxidation at the methyl groups of the cyclopentyl ring. Oxidation at the methylene group next to the triazole ring was also indicated due to the presence of triazole conjugates in wheat grain.

The figure below was copied without alteration from MRID 46901903.

FIGURE C.3.1. Proposed Metabolic Profile of Metconazole in Wheat



EPA's Records Disposition Schedule PEST 361 Scientific Data Reviews HED Records Center - File R157862 - Page 312 of 792

TABLE C.3.1. Identification of Compounds from Metabolism Study

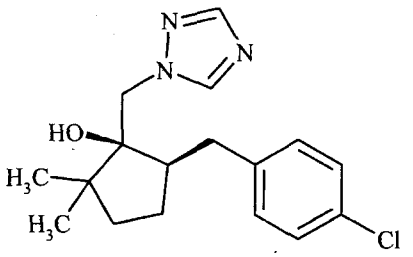
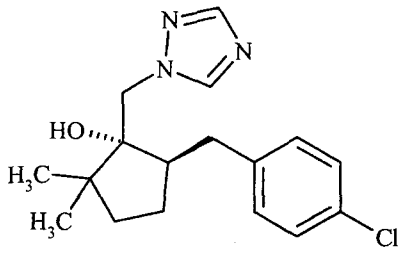
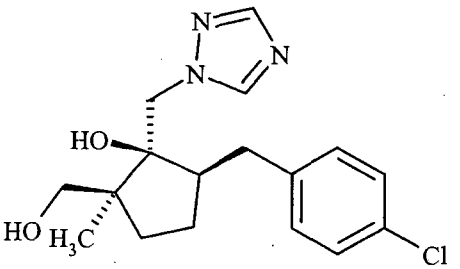
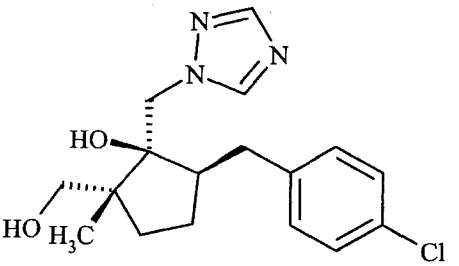
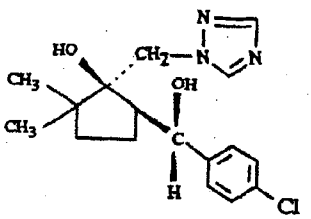
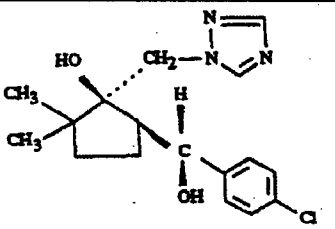
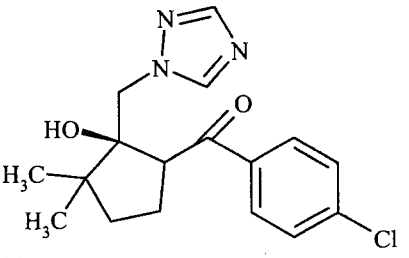
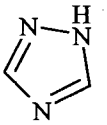
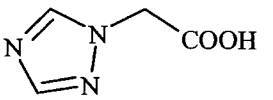
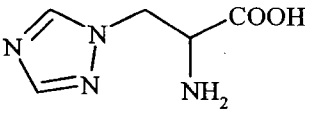
Common name/code Figure C.3.1 ID No.	Chemical name	Chemical structure
Metconazole; WL148271	5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	 *cis*-isomer  *trans*-isomer
M1	5-[(4-chlorophenyl)methyl]-2-methoxyl-2-methyl-1(1*H*-1,2,4-triazol-1-ylmethyl)-1-cyclopentanol	
M2	5-[(4-chlorophenyl)methyl]-2-methoxyl-2-methyl-1(1*H*-1,2,4-triazol-1-ylmethyl)-1-cyclopentanol	
M11	5-[(4-chlorophenyl)methoxyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)-1-cyclopentanol	

TABLE C.3.1. Identification of Compounds from Metabolism Study		
Common name/code Figure C.3.1 ID No.	Chemical name	Chemical structure
M21	5-[(4-chlorophenyl)methoxyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)-1-cyclopentanol	
M30	5-[(4-chlorophenyl)keto]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)-1-cyclopentanol	
A2-5 (419.1); mixture of mono- and dihydroxylated carboxylic acid metabolites from rat metabolism study	Not provided	Not provided
Triazole (1,2,4-T)	1*H*-1,2,4-triazole	
Triazolylacetic acid (TAA)	1*H*-1,2,4-triazol-1-yl acetic acid	
Triazolylalanine (TA)	2-amino-3-(1*H*-1,2,4-triazol-1-yl)propanoic acid	

D. CONCLUSION

Following a single foliar broadcast application of [cyclopentyl-^{14}C]metconazole at 0.330 lb ai/A, TRR were 0.074 ppm in wheat grain and 5.88 ppm in wheat straw harvested 61 days following application. Following a single foliar broadcast application of [triazole-3,5-^{14}C]metconazole at 0.347 lb ai/A, TRR were 0.66 ppm in wheat grain and 6.33 ppm in wheat straw harvested 71 days following application. Samples of wheat forage and hay were not analyzed.

Metconazole was the primary identified residue in straw from both labels, accounting for 34.1% TRR in cyclopentyl-label straw and for 22.0% TRR in triazole-label straw. In cyclopentyl-label straw, metabolites M11 and M21 were major residues, accounting for 9.7-9.8% TRR, while in triazole-label straw, M11 was identified at 1.8% TRR (0.11 ppm), and M21 was not identified. Metabolite M30 was identified in straw from both labels, at 1.0% TRR in cyclopentyl-label straw

and 5.4% TRR in triazole-label straw. Metabolite M1 was identified at 3.4% TRR in cyclopentyl-label straw, and metabolite M2 was identified at 1.8% TRR in triazole-label straw. Metabolites A2-5 (4191) and TAA were identified in triazole-label straw only, at 3.3% and 0.3% TRR, respectively. Remaining residues in straw were characterized as monohydroxy-metconazole metabolites (1.4% TRR in cyclopentyl-label straw and 11.5% TRR in triazole-label straw) or on the basis of organo- or aqueous solubility. The only metabolites identified in triazole-label grain were TA, at 69.7% TRR, and TAA, at 24.2% TRR. Residues in cyclopentyl-label grain were not subjected to analysis for characterization/identification of residues

Acceptable methods were used for extraction and characterization/identification of residues; however, residues were not investigated in two of the raw agricultural commodities of wheat, forage and hay. In addition, the study reflects relatively lengthy storage intervals, particularly for triazole-label straw, and is supported by very limited storage stability data. The petitioner must provide the actual dates of initial profiling for the studies to confirm that this step was completed within 6 months of harvest for all samples.

Based on the submitted wheat metabolism studies, the petitioner proposed that the main metabolic transformations of metconazole in wheat were oxidation at the benzylic methylene to give the two monohydroxylated stereoisomers (M11 and M21) and the corresponding ketone (M30), and oxidation at the methyl groups of the cyclopentyl ring. Oxidation at the methylene group next to the triazole ring was also indicated due to the presence of triazole conjugates in wheat grain.

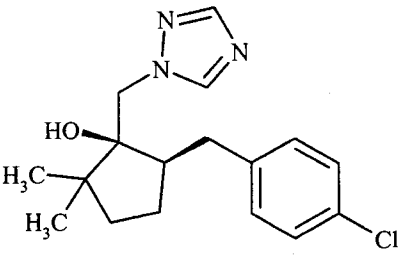
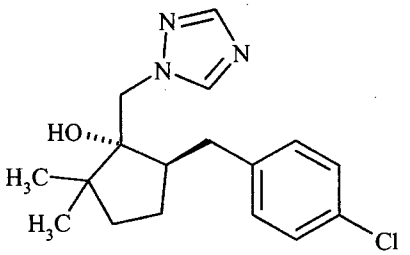
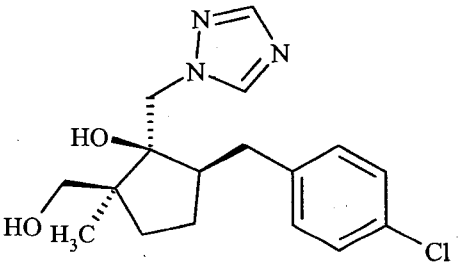
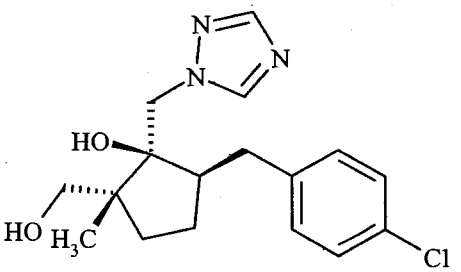
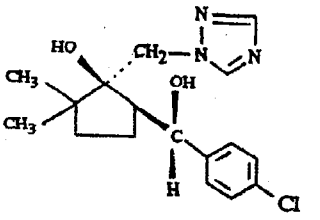
E. REFERENCES

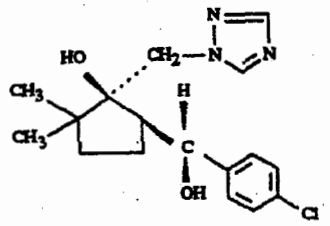
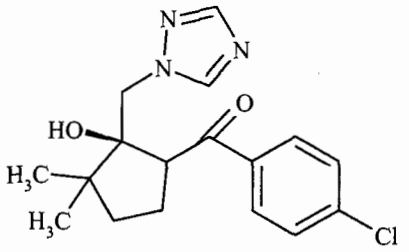
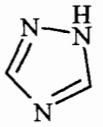
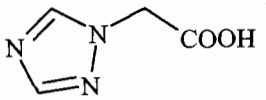
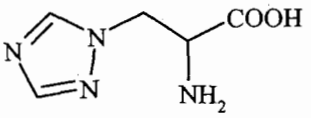
DP#:	324541
Subject:	Metconazole. Request for a Tolerance on Imported Bananas. Summary of Analytical Chemistry and Residue Data. Petition Number 9E05052.
From:	N. Dodd
To:	M. Waller
Date:	12/14/05
MRIDs:	44721506, 44721507, 44721508, 44721509, 44721510, and 44721511

F. DOCUMENT TRACKING

RDI: N. Dodd (2/20/08)
Petition Numbers: 6F7094 and 6F7095
DP#s: 348168 and 348206
PC Code: 125619

Template Version June 2005

APPENDIX I. Chemical Names and Structures of Reference Standards Used in Wheat Metabolism Study.		
Common name; Company code	Chemical name	Chemical structure
Metconazole; WL148271	5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	 *cis*-isomer  *trans*-isomer
M1	5-[(4-chlorophenyl)methyl]-2-methoxyl-2-methyl-1(1*H*-1,2,4-triazol-1-ylmethyl)-1-cyclopentanol	
M2	5-[(4-chlorophenyl)methyl]-2-methoxyl-2-methyl-1(1*H*-1,2,4-triazol-1-ylmethyl)-1-cyclopentanol	
M11	5-[(4-chlorophenyl)methoxyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)-1-cyclopentanol	

APPENDIX I. Chemical Names and Structures of Reference Standards Used in Wheat Metabolism Study.		
Common name; Company code	Chemical name	Chemical structure
M21	5-[(4-chlorophenyl)methoxyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)-1-cyclopentanol	
M30	5-[(4-chlorophenyl)keto]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)-1-cyclopentanol	
A2-5 (4191)	Not provided	Not provided
Triazole (1,2,4-T)	1*H*-1,2,4-triazole	
Triazolylacetic acid (TAA)	1*H*-1,2,4-triazol-1-yl acetic acid	
Triazolylalanine (TA)	2-amino-3-(1*H*-1,2,4-triazol-1-yl)propanoic acid	

Primary Evaluator	This DER was originally prepared under contract by Dynamac Corporation.
Approved by	Nancy Dodd, Chemist Nancy Dodd Date: 2/20/08 Registration Action Branch 3 Health Effects Division (7509P)

This DER was originally prepared under contract by Dynamac Corporation (2275 Research Boulevard, Suite 300; Rockville, MD 20850; submitted 09/13/2007). The DER has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORTS:

46901904 Kao, L. (1997) CL 900768 (Metconazole): Metabolism of [Triazole-3,5-(Carbon 14)] CL 900768 in Canola Under Field Conditions. Project Number: 200600109, MET/97/015, M96P768MPB1. Unpublished study prepared by Excel Research Services, Inc., American Cyanamid Co. and Enviro-Quest. 314 p.

46901905 Kao, M. (1997) CL 900768 (Metconazole): Metabolism of [p-Chlorophenyl-U-(Carbon 14)] CL 900768 in Canola Under Field Conditions. Project Number: 200600107, MET/97/016, M96P768MB2. Unpublished study prepared by Excel Research Services, Inc., Ag-Quest Inc. and American Cyanamid Co. 350 p.

EXECUTIVE SUMMARY:

Valent U.S.A. Corporation has submitted studies investigating the metabolism of [chlorophenyl-U-^{14}C]metconazole (specific activity 10 µCi/mg) and [triazole-3,5-^{14}C]metconazole (specific activity 9.58 µCi/mg) in canola. The radiolabeled test substances were dissolved in n-amyl alcohol and formulated in mineral spirits/surfactant (Shellsol/Dobanol, 2:1, v:v), then applied as two broadcast foliar applications with a 14-day retreatment interval to canola grown in outdoor plots at the early flowering stage at 0.235 lb ai/A/application (263.5 g ai/ha/application) for the chlorophenyl label and 0.238 lb ai/A/application (264.5 g/ai/ha/application) for the triazole label, for total application rates of 0.470 lb ai/A (527 g ai/ha) and 0.476 lb ai/A (529 g ai/ha), respectively. Samples of canola foliage were harvested immediately following the first and second applications (0 days after treatment one (0-DAT1) and 0-DAT2, respectively), and 14, and 28 days after the second application (14- and 28-DAT2), and samples of canola pod (pod shell and foliage combined) and seed were harvested at maturity, 28-DAT2, and allowed to dry in the field for 16-22 days. The in-life phase of the study was conducted by Excel Research Services at Ag-Quest Laboratory (Minto, MB), and the analytical phase of the study was conducted by American Cyanamid Company (Princeton, NJ).

Total radioactive residues (TRR) in chlorophenyl-label canola matrices, determined by combustion/LSC, were 10.79 ppm in 0-DAT1 foliage, 14.95 ppm in 0-DAT2 foliage, 5.60 and

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5.92 ppm in 14- and 28-DAT2 foliage, and 20.67 and 1.85 ppm in pod and seed. The petitioner noted that the high TRR in pod was likely the result of moisture loss on drying. In triazole-label canola matrices, TRR were 8.76 and 9.89 ppm in 0-DAT1 and 0-DAT2 foliage, 8.63 ppm in 14-DAT2 foliage, 20.35 ppm in 28-DAT2 foliage, 19.62 ppm in pod, and 2.39 ppm in seed. The petitioner attributed the higher residues in 28-DAT2 foliage to moisture loss in the mature plant, and higher residues in pod to loss on drying in the field.

Extraction with methanol (MeOH) or MeOH and water released the majority of the radioactivity from all samples of canola foliage and pod from both labels: 93.38-97.73% TRR (8.56-14.24 ppm) from 0-DAT1 and 0-DAT2 foliage, 61.28-75.51% TRR (4.10-12.47 ppm) from 14- and 28-DAT2 foliage, and 60.28-74.19% TRR (12.46-14.56 ppm) from pod. In 14- and 28-DAT2 foliage from the chlorophenyl study, additional residues were released by sequential hydrolysis/extraction with 2% HCl (3.80-5.29% TRR), pepsin (0.78-1.03% TRR), cellulase (1.11-1.79% TRR), 6 N HCl (10.20-11.04% TRR), and MeOH (3.05-5.47% TRR). In the triazole study, additional residues were released from 0-DAT1 through 28-DAT2 foliage by sequential extraction/hydrolysis with 1% acetic acid or HCl (1.36-2.02% TRR in samples from the first three intervals and 19.69% TRR in 28-DAT2 foliage), 2% HCl (0.44-2.12% TRR), and pepsin (0.33-0.83% TRR). In 14- and 28-DAT2 foliage from the triazole study, further hydrolysis with cellulase and 6 N HCl released 1.22-2.44% TRR, and 8.10-8.53% TRR, respectively. In chlorophenyl-label pod, additional residues were released by sequential extraction/hydrolysis with water and acetone (4.63% TRR), 2% HCl (2.05% TRR), pepsin and cellulase (2.34% TRR), 6 N HCl (3.83% TRR), and MeOH (17.38% TRR), while in triazole-label pod, additional residues were released by sequential extraction/hydrolysis with 2% HCl (4.32% TRR), pepsin (2.00% TRR), water (0.28% TRR), cellulase (0.38% TRR), 6 N HCl (1.39% TRR), and MeOH (10.68% TRR). Extraction with detergent (Triton X-100) released ≤0.6% TRR from 14- and 28-DAT2 chlorophenyl-label foliage and pod, and ≤0.4% TRR from triazole-label foliage and pod.

In seed from both labels, initial extraction with hexane released 12.12-14.42% TRR (0.27-0.29 ppm). Sequential extraction/hydrolysis with MeOH, water, 2% HCl, and water released 34.70-35.97% TRR (0.64-0.86 ppm), 22.60-31.71% TRR (0.42-0.76 ppm), 7.68-16.43% TRR (0.18-0.30 ppm), and 1.76-1.80% TRR (0.03-0.04 ppm), respectively; pepsin hydrolysis released 3.26-4.29% TRR. Remaining nonextractable residues in chlorophenyl and triazole-label samples, respectively, were ≤4.90% TRR (≤0.71 ppm) and ≤8.75% TRR (≤1.24 ppm) in foliage, 9.29% TRR (1.92 ppm) and 6.36% TRR (1.25 ppm) in pod, and 6.8% TRR (0.13 ppm) and 6.5% TRR (0.15 ppm) in seed. These procedures adequately extracted the majority of residues from canola matrices. Because extraction results were normalized, accountabilities for all matrices were 100%. Both studies are supported by adequate storage stability data.

Residues were identified and confirmed by HPLC with additional characterization/confirmatory analysis by LC/MS. HPLC analysis yielded up to14 distinct metabolite components, CC-1 through CC-13 in the chlorophenyl study and CT-1 through CT-14 in the triazole study Metconazole (CC/CT-12), metabolite M11 (CC/CT-11), and triazolylalanine (TAA; CT-1) were identified by retention time comparisons with reference standards. Metabolites CC-1, CC-13, CT-2, and CT-14 were characterized as extremely or relatively polar (CC-1 and CT-2) or

extremely nonpolar (CC-13 and CT-14) based on their respective retention times. Remaining metabolites where characterized on the basis of LC/MS analysis and/or β-glucosidase hydrolysis: CC-2 through CC-6 and CT-5 and CT-7 were characterized as glucose conjugates of monohydroxylated metconazole (GOH-metconazoles); and CC-7, CC-9, and CC-10, and CT-8, CT-9, CT-10, and CT-13 were characterized as monohydroxylated metconazole metabolites (OH-metconazoles). The following metabolites were found to consist of multiple components: CC-8 (one OH-metconazole and three GOH-metconazoles), CT-3 (two GOH-metconazoles), CT-4 (one OH- and one GOH-metconazole), and CT-6 (two OH-metconazoles).

In the chlorophenyl study, metconazole was the primary residue identified in all canola matrices, accounting for 96.0% and 85.3% TRR (10.36 and 12.75 ppm) in 0-DAT1 and 0-DAT2 foliage, respectively, 67.8% and 60.8% TRR (3.80 and 3.60 ppm) in 14- and 28-DAT2 foliage, respectively, 40.3% TRR (8.32 ppm) in pod, and 39.0% TRR (0.72 ppm) in seed. The only other identified metabolite was M11, which accounted for 0.05-1.4% TRR in foliage, 1.5% TRR in pod, and 7.3% TRR in seed. No other metabolites were characterized in 0-DAT1 foliage, and no single metabolite accounted for >4% TRR in any other foliage sample. OH-metconazoles, including CC-8, accounted for 2.1-6.5% TRR (0.32-0.46 ppm) in 0-2-, 14-, and 28-DAT2 foliage, and GOH-metconazoles accounted for 3.4-14.6% TRR (0.51-0.86 ppm); levels of both types of metabolites increased with increasing sampling interval. In pod and seed, OH-metconazoles, including CC-8, accounted for 20.1% and 26.4% TRR (4.17 and 0.49 ppm), respectively, with individual metabolites present at ≤9.5% TRR (CC-7) in pod and ≤8.3% TRR (CC-10) in seed. GOH-metconazoles accounted for 23.2% and 13.6% TRR (4.79 and 0.25 ppm), respectively, in pod and seed, with individual metabolites present at ≤7.6% TRR (CC-6) in pod and 4.0% TRR (CC-6) in seed. Remaining residues in all matrices consisted of minor components characterized as an extremely polar metabolite (CC-1; ≤3.3% TRR), an extremely nonpolar metabolite (CC-13; ≤2.3% TRR in 14- and 28-day foliage, and pod only), and multicomponent unknowns, accounting for up to 7.1% TRR in foliage, 2.5% TRR in pod, and 4.2% TRR in seed.

In the triazole study, metconazole was the primary residue identified in canola foliage and pod, accounting for 92.9% and 72.8% TRR (8.13 and 7.20 ppm) in 0-DAT1 and 0-DAT2 foliage, respectively, 55.3% and 56.7% TRR (4.77 and 11.53 ppm) in 14- and 28-DAT2 foliage, respectively, and 16.4% TRR (3.32 ppm) in pod; metconazole accounted for 24.1% TRR (0.57 ppm) in seed. The major identified residue in seed was TAA, which accounted for 40.2% TRR (0.96 ppm). TAA was not found in 0-DAT1 and 0-DAT2 foliage, but was found in 14- and 28-DAT2 foliage at 5.2% and 5.6% TRR (0.45 and 1.15 ppm), respectively, and in pod at 6.7% TRR (1.31 ppm). The only other identified metabolite was M11, which accounted for 1.3-2.0% TRR in 14- and 28-DAT2 foliage, 1.7% TRR in pod, and 4.3% TRR in seed. As in the chlorophenyl study, the majority of the remaining components were characterized as OH-metconazoles or GOH-metconazoles. No single metabolite accounted for >6.4% TRR in any foliage sample. OH-metconazoles, including CC-4, accounted for 1.1-15.3% TRR (0.1-2.79 ppm) in foliage from all sampling intervals; GOH-metconazoles were not identified in 0-DAT1 foliage, but accounted for 1.9-10.4% TRR (0.18-2.13 ppm) in remaining foliage samples; levels of both types of metabolites increased with increasing sampling interval. In pod and seed, OH-metconazole metabolites, including CC-4, accounted for 39.7% and 13.4% TRR (7.8 and 0.32

ppm), respectively, with individual metabolites present at ≤15.2% TRR (CT-6) in pod and ≤5.4% TRR (CC-10) in seed. GOH-metconazoles accounted for 25.0% and 6.6% TRR (4.93 and 0.15 ppm), respectively, in pod and seed, with individual metabolites present at ≤11.6% TRR (CC-6) in pod and 3.5% TRR (CC-6) in seed. Remaining residues in all matrices consisted of minor components characterized as a relatively polar metabolite (CT-2; ≤2.2% TRR), an extremely nonpolar metabolite (CT-14; ≤2.2% TRR in foliage and pod), and multicomponent unknowns, accounting for up to 17.6% TRR in foliage, 1.1% TRR in pod, and 4.6% TRR in seed.

Based on the submitted canola metabolism studies, the petitioner proposed that the main metabolic route of metconazole in canola is via oxidative hydroxylation of the methylene groups, the methyl groups on the cyclopentyl ring, and possibly of the cyclopentyl ring. The detection of triazolylalanine as a major seed metabolite in the triazole study indicates that the methylene group between the triazole and cyclopentyl rings is susceptible to oxidative hydroxylation. The large number of OH-metconazole metabolites and glucose conjugates of OH-metconazole suggests monohydroxylation at the various pro-chiral carbons of metconazole, giving rise to chromatographically distinguishable stereoisomeric structures.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the plant metabolism data are classified as scientifically acceptable. The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP#s 348168 and 348206.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an impact on the validity of the study.

A. BACKGROUND INFORMATION

Metconazole [5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol] is a broad-spectrum triazole Group 3 fungicide (sterol biosynthesis inhibitors). There are currently no registered uses of metconazole in the U.S.; however, a tolerance has been established for banana, and a Section 18 emergency exemption and supporting time-limited tolerances have been granted for use on soybean. Valent U.S.A. Corporation has applied for registration of metconazole in the U.S. for use on peanut, stone fruits, and tree nuts.

The chemical structure and nomenclature of metconazole, and the physicochemical properties of the technical grade of metconazole are presented in Tables A.1 and A.2.

Table A.1. Metconazole Nomenclature.

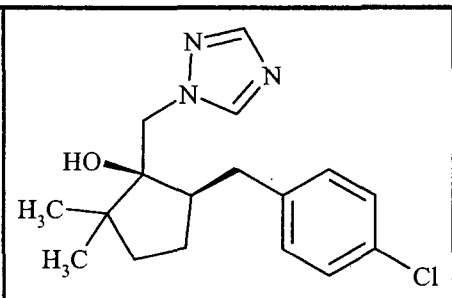
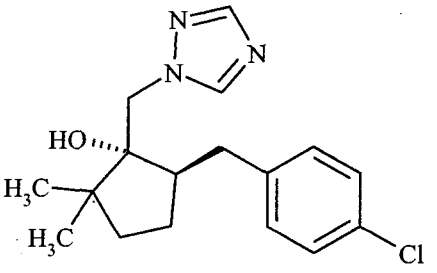
Chemical structure	 *cis*-isomer	 *trans*-isomer
Common name	Metconazole	
Company experimental name	KNF-S-474m (Kureha); BAS 555 F (BASF); V-10116 (Valent)	
IUPAC name	(1RS,5RS:1RS,5SR)-5-(4-chlorobenzyl)-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	
CAS name	5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	
CAS registry number	125116-23-6 (*cis*- and *trans*-isomers) 115850-27-6 (*cis*-isomer) 115850-28-7 (*trans*-isomer)	
End-use products (EP)	50% WDG (Metconazole 50 WDG Fungicide, EPA File Symbol 59639-RUT) 0.75 lb/gal SC/L (Caramba™ Fungicide, EPA File Symbol No. 7969-EUA) 0.67 lb/gal SC/L formulation (BAS 556 01F Fungicide, EPA File Symbol No. 7969-EUT; also contains the active ingredient pyraclostrobin at 0.83 lb/gal)	

Table A.2. Physicochemical Properties of Metconazole

Parameter	Value				References* (MRID)
Melting point/range	100.0-108.4°C (using Electrothermal Digital Melting Point Apparatus) (AC900,768 technical grade)				44721505
pH	5.81 at 25°C (1% aqueous suspension)				46808402
Relative density (20°C)	1.14 (relative density to water at 4°C, using capillary-stoppered, density-specific gravity bottle) (Lot No. AC 8879-140B)				44721505
Water solubility (20°C)	Using shake-flask method: 18.7 ± 1.0 mg/L (*cis*-isomer, WL148271, KNF-S-474m) 13.6 ± 1.7 mg/L (*trans*-isomer, WL148271, KNF-S-474m)				44721505
Solvent solubility (g/L) at 20°C	Solvent	Metconazole	*cis*	*trans*	44721505
	acetone	363	251	117	
	methanol	403	294	117	
	dichloromethane	481	343	141	
	ethyl acetate	260	173	90.0	
	propanol	132	86.6	46.7	
	toluene	103	66.2	38.0	
	Hexane	1.40	0.929	0.483	

Table A.2. Physicochemical Properties of Metconazole

Parameter	Value	References* (MRID)
Vapor pressure (20°C)	Using gas-saturation method: $< 1.23x10^{-5}$ Pa or 9.23×10^{-8} mm Hg (metconazole) $< 1.04x10^{-5}$ Pa or 7.80×10^{-8} mm Hg (*cis*-isomer) $< 1.96x10^{-6}$ Pa or 1.47×10^{-8} mm Hg (*trans*-isomer)	44721505
Dissociation constant (pK_a)	11.38±0.03 and 1.06±0.03 (in water at 29.1°C using spectrophotometric method; Lot No. AC 8879-140B)	44721505
Octanol/water partition coefficient, Log(K_{OW})	At 20 °C (using flask shaking method): K_{ow} (log K_{ow}) = 7090±989 (3.85) (Lot No. AC 8879-140B) (TGAI) K_{ow} (log K_{ow}) = 7150±803 (3.85) (*cis*-isomer, CL 354,801) K_{ow} (log K_{ow}) = 6800±1700 (3.8) (*trans*-isomer, CL 354,802)	44721505

UV/visible absorption spectrum	pH	λ	A	log ε	46808403
	cis-isomer				
	2.0	221.4	0.828	4.03	
	6.8		0.8452	4.04	
	7.0		0.9126	4.08	
	10.3		0.7226	3.98	
	trans-isomer				
	2.0	221.4	0.9053	4.07	
	7.0		0.9547	4.10	
	10.1		0.9893	4.11	

* Product Chemistry Reviews: DP #256877, Shyam Mathur, Ph.D., 9/12/2000 and DP #329168, Shyam Mathur, Ph.D., 7/13/07.

B. EXPERIMENTAL DESIGN

B.1. Test Site and Crop Information

The field test sites were located at the Enviro-Quest facilities in Minto, MB. A summary of the test site information is provided in Table B.1.1, and a summary of the crop information is provided in Table B.1.2. Canola plants were grown outdoors in field plots surrounded by plastic barriers to control spray drift. The plots were maintained following normal agricultural practices, and maintenance pesticides and fertilizers were applied as needed. Daily weather conditions (rainfall and temperature) were reported; irrigation was used in the triazole study only. The petitioner stated that weather conditions during the trial were typical for the area.

Samples of canola foliage were harvested immediately following the first and second applications (0-DAT1 and 0-DAT2, respectively), and 14 and 28 days after the second application. Remaining canola plants were cut at the 28-DAT2 interval and were left to dry in the field for 22 days (chlorophenyl label) or 16 days (triazole label) prior to collection of pods

and seed. At pod and seed collection, the dried canola plants were mashed to separate the seed from the pod.

TABLE B.1.1. Test Site Information.

Label	Type	Method	Soil characteristics			
			Type	%OM	pH	CEC
Chlorophenyl	Foliar Treatment	Two broadcast foliar spray applications using a CO_2 sprayer	Loam	2.5	8.3	31.7 meq/100 g
Triazole				4.9	8.1	41.2 meq/100 g

TABLE B.1.2. Crop Information.

Crop; crop group	Variety	Growth stage at application	Growth stage at harvest [1]	Harvested Matrix
Canola; Oilseed group 20 [proposed]	Chlorophenyl label: 45A71 Triazole label: Legend	Chlorophenyl label: 1: 30% bloom (petal fall) 2: 90% bloom Triazole label: 1: 50% bloom (petal fall) 2: 90% bloom	0-DAT1; immature	Foliage; whole above-ground portion of plant
			0-DAT2; immature	
			14-DAT2; immature	
			28-DAT2; mature	Foliage
				Pods (pods + straw) and seed; plants cut and left to dry in the field for 16-22 days

[1] 0-DAT1 = immediately following the first application; 0-DAT2 = immediately following the second application; remaining intervals reflect days after second applications.

B.2. Test Materials

The radiolabeled test substances were isotopically diluted with [triazole-3,5-^{13}C]metconazole and nonlabeled metconazole, then dissolved in n-amyl alcohol and formulated in mineral spirits/surfactant (Shellsol/Dobanol, 2:1, v:v). The characteristics of the test substances are presented in Table B.2.1.

TABLE B.2.1. Test Material Characteristics.

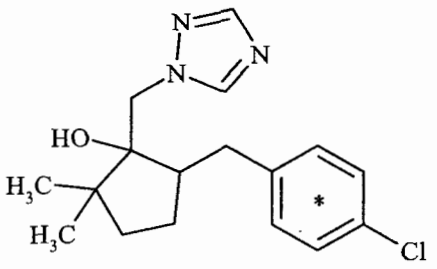
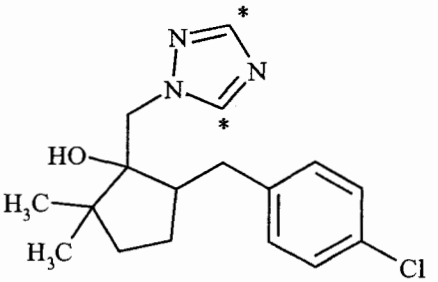
Chemical structure		
Radiolabel position	[chlorophenyl-U-^{14}C]metconazole	[triazole-3,5-^{14}C]metconazole
Lot No.	RPR/C16/159/1 and RPR/C16/165/1	AC 10011-137
cis/trans Ratio	79.3:20.7	81.5:18.5
Purity	99.6%	99.8%
Specific activity – test substance	161.9 µCi/mg	30.86 µCi/mg

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TABLE B.2.1. Test Material Characteristics.		
Specific activity – application solution	10 µCi/mg (22,200 dpm/µg)	9.58 µCi/mg (21,268 dpm/µg)

B.3. Study Use Pattern

The formulated test substances were applied as two broadcast foliar applications with a 14-day retreatment interval to canola at the early flowering stage in spray volumes of 45 gal/A at 0.235 lb ai/A/application (263.5 g ai/ha/application) for the chlorophenyl label and 0.238 lb ai/A/application (264.5 g/ai/ha/application) for the triazole label, for total application rates of 0.470 lb ai/A (527 g ai/ha) and 0.476 lb ai/A (529 g ai/ha), respectively. Applications were made using a CO_2 sprayer. Details of the study use pattern are presented in Table B.3.1.

TABLE B.3.1. Use Pattern Information.		
Chemical name	[chlorophenyl-U-^{14}C]metconazole	[triazole-3,5-^{14}C]metconazole
Application method	The isotopically diluted test substance was formulated in mineral spirits/surfactant and applied as two broadcast foliar applications using a CO_2 sprayer	
Application rate	0.235 lb ai/A/application (263.5 g ai/ha/ application) for a total application rate of 0.470 lb ai/A (527 g ai/ha)	0.238 lb ai/A/application (264.5 g/ai/ha/application) for a total application rate of 0.476 lb ai/A (529 g ai/ha)
Number of applications	2	2
Timing of applications	Application 1: 49 days after planting Application 2: 14 days after first application	Application 1: 55 days after planting Application 2: 14 days after first application
PHI	Foliage: immediately following the first and second applications (0-DAT1 and 0-DAT2, respectively), and 14 and 28 days after the second application (14- and 28-DAT2) Canola pod (pod shell and foliage combined) and seed: 28-DAT2 (cut samples dried in the field for 16-22 days).	

B.4. Identification/Characterization of Residues

B.4.1. Sample Handling and Preparation

Harvested samples were placed in coolers immediately following collection and were placed in freezers (-33 to -11 °C) at the field site within 80 minutes of completion of sampling. Samples were shipped from the field sites on dry ice via overnight carrier to the analytical laboratory, American Cyanamid (Princeton, NJ) within 3-20 days of harvest for foliage samples and within 29-48 days of harvest for pod and seed samples. At American Cyanamid, samples were stored at -40 to 0 °C prior to preparation for analysis.

Samples of canola foliage, pod, and seed were prepared for extraction by grinding in the presence of dry ice. The prepared samples were stored frozen prior to analysis.

Foliage samples were extracted 3x with MeOH and centrifuged. The resulting supernatants were combined. The nonextractable residues of 14- and 28-DAT2 foliage from the chlorophenyl study were subjected to sequential extraction/hydrolysis with: (1) 2% HCl (at room temperature, overnight); (2) pepsin (at 37 °C, overnight), (3) cellulase (at 37 °C, overnight); (4) 0.5% Triton X-100 for 6 hours; (5) 6 N HCl (at reflux, overnight); and (6) MeOH, 1-3x. The nonextractable

residues of foliage from the triazole study (all sampling intervals) were subjected to sequential hydrolysis with 1% acetic acid or HCl (no details provided) followed by 2% HCl and pepsin as described above. Remaining nonextractable residues of 14- and 28-DAT2 foliage were sequentially extracted/hydrolyzed with cellulase, 0.5% Triton X-100, and 6 N HCl as described above. Resulting extracts/hydrolysates containing high radioactivity were reserved for individual analysis by HPLC; extracts/hydrolysates containing low radioactivity were combined for HPLC analysis.

Pod samples were soaked in water overnight, then extracted 1x with MeOH. Nonextractable residues were extracted 5x with MeOH, and centrifuged. The resulting supernatants were combined, and the nonextractable residues were subjected to sequential extraction/hydrolysis with: (1) water, 4x (chlorophenyl label only); (2) acetone, 2x (chlorophenyl label only); (3) 2% HCl; (4) pepsin; (5) water (triazole label only; no details provided); (6) cellulase; (7) 0.5% Triton X-100; (8) 6 N HCl at reflux; and (9) MeOH, 3x. Details of the sequential extraction/hydrolysis procedures were not provided for the chlorophenyl label except as noted; for the triazole study, the petitioner stated that nonextractable residues were extracted as described for foliage.

The seed sample was extracted with hexane (2-3x), and the hexane phases were combined, concentrated, and redissolved in hexane, then partitioned 2x with acetonitrile (ACN). Nonextractable residues were extracted 3x with MeOH and centrifuged. The resulting supernatants were combined, and the remaining nonextractable residues were subjected to sequential extraction/hydrolysis with: (1) water, 4x; (2) 2% HCl (at room temperature, overnight); (3) water; and (4) pepsin (as described above for foliage). The hexane fraction and remaining extracts/hydrolysates were reserved for HPLC analysis.

Representative flow charts for foliage, pod, and seed are presented below. The flow charts were copied without alteration from MRID 46901905.

Figure B.4.1. Extraction Flowchart for 28-DAT2 Canola Foliage (Chlorophenyl label)

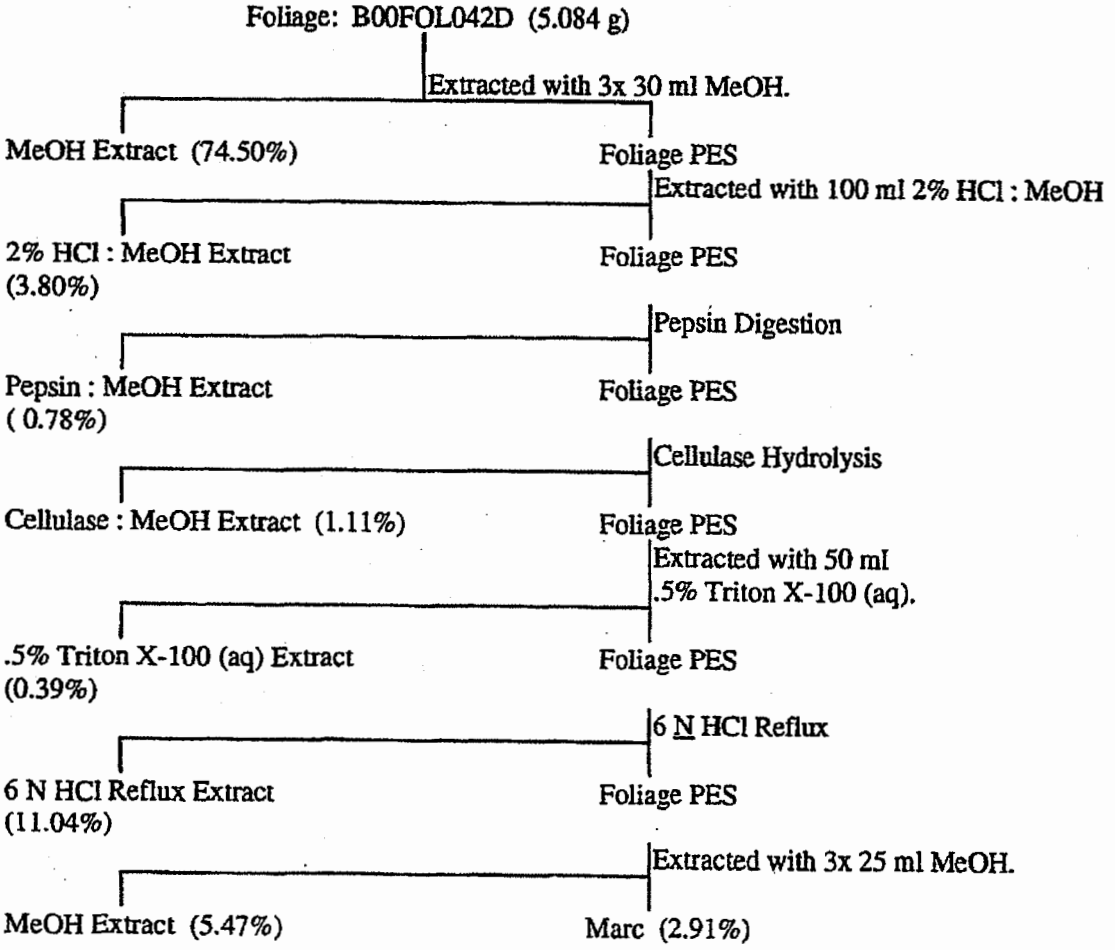


Figure B.4.2 Extraction Flowchart for Canola Pod (Chlorophenyl label)

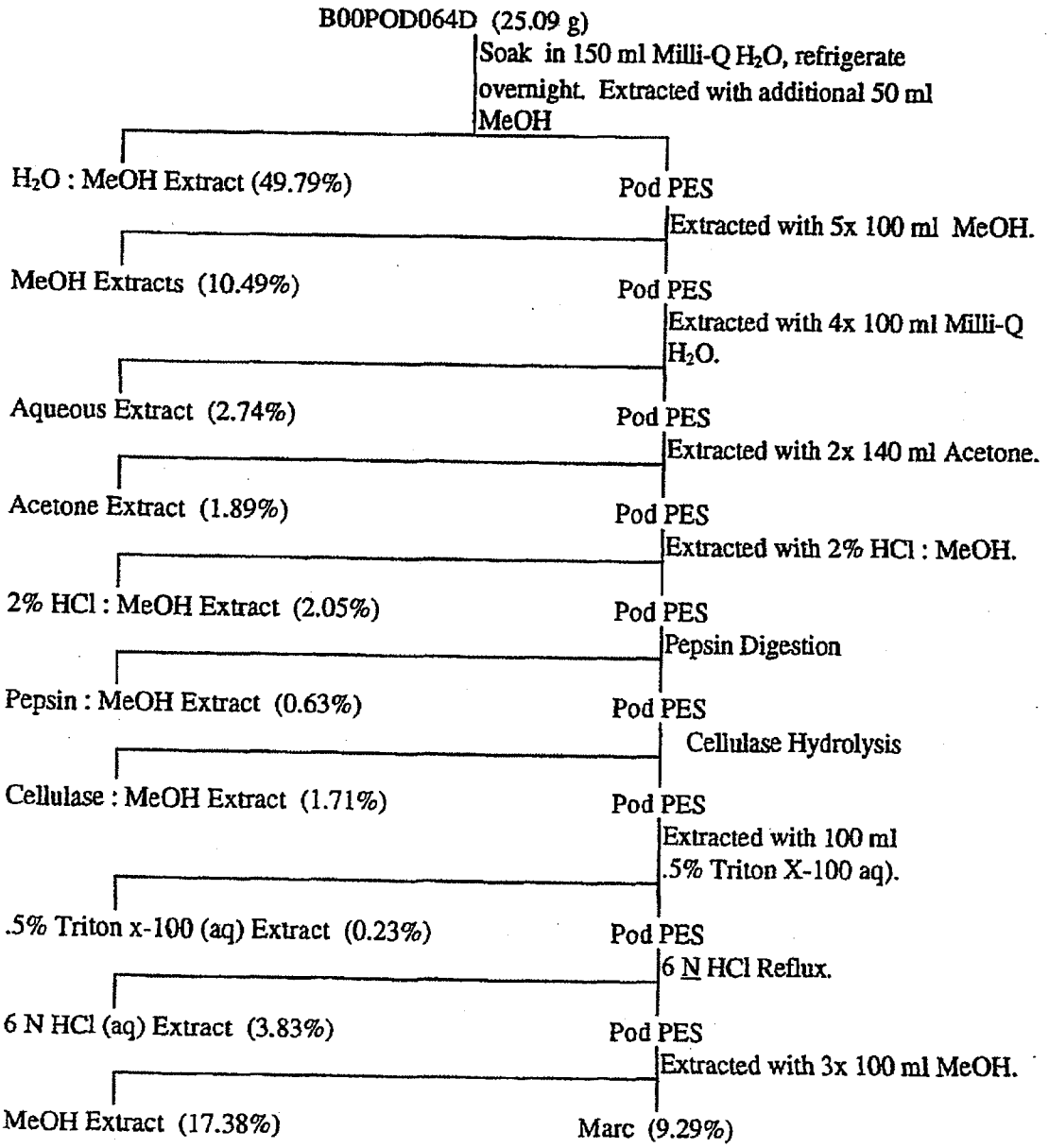
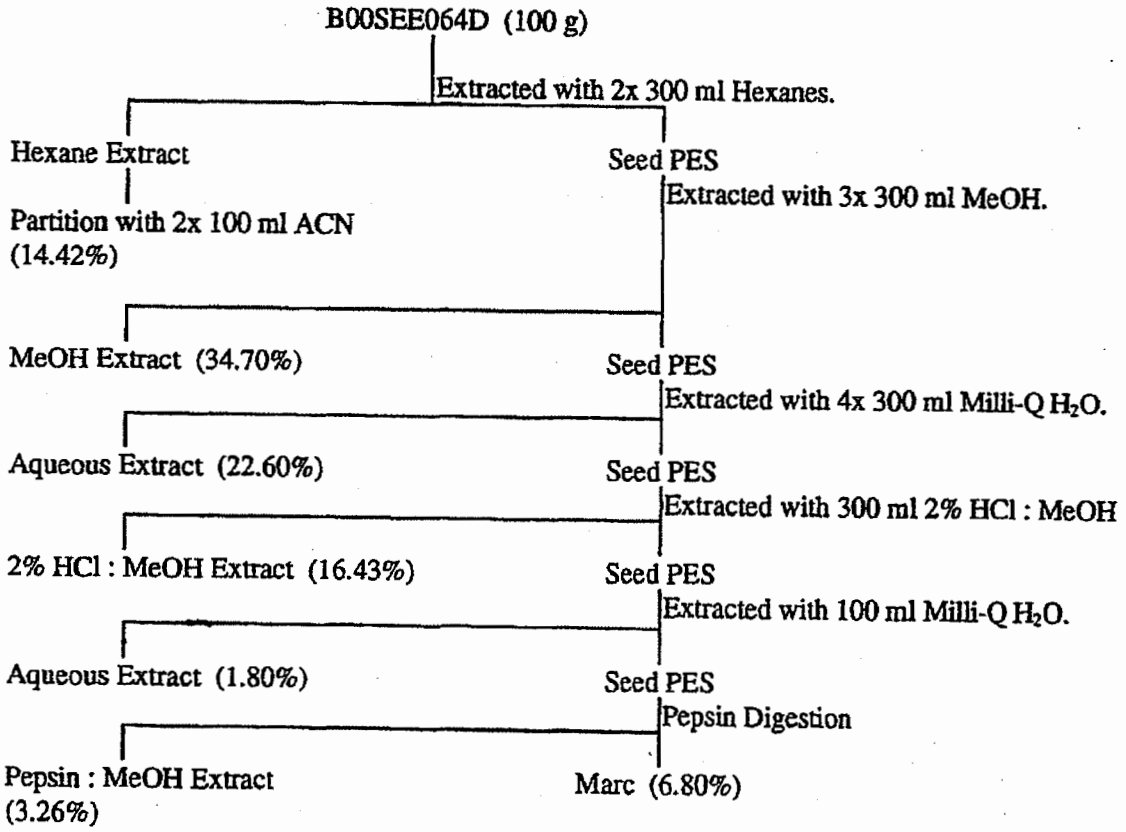


Figure B.4.3 Extraction Flowchart for Canola Seed (Chlorophenyl Label)



B.4.2. Analytical Methodology

TRR were determined in triplicate aliquots of canola foliage, seed, and pod and in nonextractable residues by combustion/liquid scintillation counting (LSC). TRR in extracts were determined by LSC. The reported limits of detection for TRR determinations were 0.004 ppm for foliage and pod samples from both labels, 0.004 ppm for chlorophenyl-label seed, and 0.005 ppm for triazole-label seed.

Sample extracts and hydrolysates were analyzed by HPLC on systems equipped with a UV detector (232 or 254 nm), an in-line radioactivity detector, and a fraction collector. Initial profiling was conducted on foliage extracts using a C18 column and a gradient mobile phase of 0.05% ammonium hydroxide and 0.0125% formic acid in water/ACN (System III for chlorophenyl study; System VI for triazole study). The distribution of metabolites in extracts and hydrolysates was determined using a reverse phase amino column and a gradient mobile phase of ACN/1% formic acid in water (System I, both studies). Identification of metabolites was confirmed in the chlorophenyl study using a graphite column and a gradient mobile phase of MeOH/isopropanol/50% THF in water (System II) and in the triazole study using the same column and a gradient mobile phase of MeOH/1% formic acid in water (System V). Metabolites were identified by retention time comparisons with known reference standards on HPLC System I; the reference standards used in the study are listed in Appendix I.

In addition, five additional HPLC systems (Systems IV-IX) were used for isolation/purification of metabolites in the chlorophenyl study. The columns and mobile phases were: (1) amino column and gradient mobile phase of MeOH/1% formic acid in water for System IV; (2) amino column and gradient mobile phase of ACN/1% formic acid in water for Systems V, VI, and IX; (3) graphite column and gradient mobile phase of MeOH/isopropanol/1% formic acid in water for System VII; and (4) graphite column and gradient mobile phase of MeOH/isopropanol/50% THF in water for System VIII. Metabolites in the triazole study were isolated/purified using Systems III through V; Systems III and IV used an amino column and gradient mobile phases of ACN/1% formic acid in water, and System V is described above.

The metconazole-derived residues in pod and seed were isolated for metabolite characterization and identification using HPLC System I. Unknowns CC-1 and CT-1 were isolated from the aqueous extract of seed using HPLC Systems III and V. Each isolated component was individually composited from several HPLC runs and further purified on HPLC System I or IV prior to LC/MS analysis. The predominant metconazole-derived residues in the ACN extracts of seed and the 6 N HCl hydrolysates and/or MeOH extracts of pod were also isolated for analysis.

Isolated unknowns characterized as glucose conjugates (CC-2, CC-3, CC-4, CC-5, and CC-6, and CT-3, CT-4, CT-5, and CT-7) were also subjected to enzyme hydrolysis with β-glucosidase (in 0.2 M sodium acetate buffer, pH 5.0) at 37 °C for ~18 hours. The hydrolysates were separated by centrifugation and analyzed by HPLC on Systems I and/or II.

Isolated and purified metabolites were also analyzed by LC/MS with electrospray ionization. The LC system included a C18 column and a gradient mobile phase of water/MeOH, each containing 1% acetic acid.

C. RESULTS AND DISCUSSION

The storage conditions and intervals for canola are presented in Table C.1. The petitioner provided the dates of sampling and initial and final analysis for all samples, and stated that the initial metabolic profiles for foliage, seed, and pod were determined following 1-91 days of freezer storage for chlorophenyl-label samples and following 8-58 days of storage for triazole-label samples. Storage stability data were submitted which indicated that the metabolic profiles for canola seed and pod were relatively stable in the MeOH/water extracts following frozen storage for ~7.3-7.5 months. Because initial profiling was completed within ~3 months for both studies, and the majority of samples (14- and 28-DAT2 foliage, seed, and pod from the chlorophenyl study; all samples from the triazole study) were analyzed within 7.2 months of harvest, no additional storage stability data are required to support the study.

TRR in canola matrices, determined by combustion/LSC, are reported in Table C.2.1. Following one or two broadcast foliar applications of [chlorophenyl-U-^{14}C]metconazole at 0.235 lb ai/A/application, TRR were 10.79 ppm in canola foliage harvested immediately following the first application (0-DAT1 foliage), 14.95 ppm in foliage harvested immediately following the second application (0-DAT2 foliage), 5.60 and 5.92 ppm in foliage harvested 14 and 28 days after the second application, and 20.67 and 1.85 ppm in pod and seed harvested 28 days after the

second application and allowed to dry in the field for 22 days. The petitioner noted that the high TRR in pod was likely the result of moisture loss on drying. Following one or two broadcast foliar applications of [triazole-3,5-^{14}C]metconazole at 0.238 lb ai/A/application, TRR were 8.76 and 9.89 ppm in 0-DAT1 and 0-DAT2 foliage, 8.63 ppm in 14-DAT2 foliage, 20.35 ppm in 28-DAT2 foliage, 19.62 ppm in pod, and 2.39 ppm in seed. The petitioner attributed the higher residues in 28-DAT2 foliage to moisture loss in the mature plant, and higher residues in pod to loss on drying in the field.

The distribution of radioactivity in canola matrices is presented in Tables C.2.2.1 (chlorophenyl-label foliage), C.2.2.2 (chlorophenyl-label pod and seed), C.2.2.3 (triazole-label foliage) and C.2.2.4 (triazole-label pod and seed). Extraction with MeOH or MeOH and water released the majority of the radioactivity from all samples of canola foliage and pod from both labels: 93.38-97.73% TRR (8.56-14.24 ppm) from 0-DAT1 and 0-DAT2 foliage, 61.28-75.51% TRR (4.10-12.47 ppm) from 14- and 28-DAT2 foliage, and 60.28-74.19% TRR (12.46-14.56 ppm) from pod. In 14- and 28-DAT2 foliage from the chlorophenyl study, additional residues were released by sequential hydrolysis/extraction with 2% HCl (3.80-5.29% TRR), pepsin (0.78-1.03% TRR), cellulase (1.11-1.79% TRR), 6 N HCl (10.20-11.04% TRR), and MeOH (3.05-5.47% TRR). In the triazole study, additional residues were released from 0-DAT1 through 28-DAT2 foliage by sequential extraction/hydrolysis with 1% acetic acid or HCl (1.36-2.02% TRR in samples from the first three intervals and 19.69% TRR in 28-DAT2 foliage), 2% HCl (0.44-2.12% TRR), and pepsin (0.33-0.83% TRR). In 14- and 28-DAT2 foliage from the triazole study, further hydrolysis with cellulase and 6 N HCl released 1.22-2.44% TRR, and 8.10-8.53% TRR, respectively. In chlorophenyl-label pod, additional residues were released by sequential extraction/hydrolysis with water and acetone (4.63% TRR), 2% HCl (2.05% TRR), pepsin and cellulase (2.34% TRR), 6 N HCl (3.83% TRR), and MeOH (17.38% TRR), while in triazole-label pod, additional residues were released by sequential extraction/hydrolysis with 2% HCl (4.32% TRR), pepsin (2.00% TRR), water (0.28% TRR), cellulase (0.38% TRR), 6 N HCl (1.39% TRR), and MeOH (10.68% TRR). Extraction with detergent (Triton X-100) released ≤0.6% TRR from 14- and 28-DAT2 chlorophenyl-label foliage and pod, and ≤0.4% TRR from triazole-label foliage and pod.

In seed from both labels, initial extraction with hexane released 12.12-14.42% TRR (0.27-0.29 ppm). Sequential extraction/hydrolysis with MeOH, water, 2% HCl, and water released 34.70-35.97% TRR (0.64-0.86 ppm), 22.60-31.71% TRR (0.42-0.76 ppm), 7.68-16.43% TRR (0.18-0.30 ppm), and 1.76-1.80% TRR (0.03-0.04 ppm), respectively; pepsin hydrolysis released 3.26-4.29% TRR. Remaining nonextractable residues in chlorophenyl and triazole-label samples, respectively, were ≤4.90% TRR (≤0.71 ppm) and ≤8.75% TRR (≤1.24 ppm) in foliage, 9.29% TRR (1.92 ppm) and 6.36% TRR (1.25 ppm) in pod, and 6.8% TRR (0.13 ppm) and 6.5% TRR (0.15 ppm) in seed. These procedures adequately extracted the majority of residues from canola matrices. Because extraction results were normalized, accountabilities for all matrices were 100%.

Residues were identified and confirmed by HPLC with additional characterization/confirmatory analysis by LC/MS. The characterization and identification of residues in canola matrices are summarized in Tables C.2.3.1 (chlorophenyl-label foliage), C.2.3.2 (chlorophenyl-label pod and

seed), C.2.3.1 (triazole-label foliage) and C.2.3.2 (triazole-label pod and seed). HPLC analysis yielded 13 distinct metabolite components, CC-1 through CC-13, in the chlorophenyl study, and 14 distinct components, CT-1 through CT-14, in the triazole study. Metconazole (CC/CT-12), metabolite M11 (CC/CT-11), and TAA (CT-1) were identified by retention time comparisons with reference standards, and identification was confirmed by LC/MS. Metabolites CC-1, CC-13, CT-2, and CT-14 were characterized as extremely or relatively polar (CC-1 and CT-2) or extremely nonpolar (CC-13 and CT-14) based on their respective retention times on HPLC System I; the petitioner noted that CT-14 may also have been an impurity of the treatment solution. The remaining metabolites (CC-2 through CC-10, CT-3 through CT-10, and CT-13) were further characterized by LC/MS analysis and/or β-glucosidase hydrolysis as OH-metconazoles and/or GOH-metconazoles. Metabolites, CC-7, CC-9, CC-10, and CT-8, CT-9, CT-10, and CT-13 were characterized as OH-metconazoles, and metabolites CC-2 through CC-6 and CT-5 and CT-7 were characterized as GOH-metconazoles. The following metabolites were found to consist of multiple components: CC-8 (one OH-metconazole and three GOH-metconazoles), CT-3 (two GOH-metconazoles), CT-4 (one OH- and one GOH-metconazole), and CT-6 (two OH-metconazoles). Further characterization of the glucose conjugates with β-glucosidase indicated released aglycones, some of which corresponded to characterized OH-metconazole metabolites, and some of which did not match any of the metabolites found in the study. The petitioner concluded that the aglycones of the glucose conjugates CC-2 through CC-6 were most likely the products of hydroxylation at two of the four pro-chiral carbon atoms.

In the chlorophenyl study, metconazole was the primary residue identified in all canola matrices, accounting for 96.0% and 85.3% TRR (10.36 and 12.75 ppm) in 0-DAT1 and 0-DAT2 foliage, respectively, 67.8% and 60.8% TRR (3.80 and 3.60 ppm) in 14- and 28-DAT2 foliage, respectively, 40.3% TRR (8.32 ppm) in pod, and 39.0% TRR (0.72 ppm) in seed. The only other identified metabolite was M11, which accounted for 0.05-1.4% TRR in foliage, 1.5% TRR in pod, and 7.3% TRR in seed. No other metabolites were characterized in 0-DAT1 foliage, and no single metabolite accounted for >4% TRR in any other foliage sample. OH-metconazoles, including CC-8, accounted for 2.1-6.5% TRR (0.32-0.46 ppm) in 0-2-, 14-, and 28-DAT2 foliage, and GOH-metconazoles accounted for 3.4-14.6% TRR (0.51-0.86 ppm); levels of both types of metabolites increased with increasing sampling interval. In pod and seed, OH-metconazoles, including CC-8, accounted for 20.1% and 26.4% TRR (4.17 and 0.49 ppm), respectively, with individual metabolites present at ≤9.5% TRR (CC-7) in pod and ≤8.3% TRR (CC-10) in seed. GOH-metconazoles accounted for 23.2% and 13.6% TRR (4.79 and 0.25 ppm), respectively, in pod and seed, with individual metabolites present at ≤7.6% TRR (CC-6) in pod and 4.0% TRR (CC-6) in seed. Remaining residues in all matrices consisted of minor components characterized as an extremely polar metabolite (CC-1; ≤3.3% TRR), an extremely nonpolar metabolite (CC-13; ≤2.3% TRR in 14- and 28-day foliage, and pod only), and multicomponent unknowns, accounting for up to 7.1% TRR in foliage, 2.5% TRR in pod, and 4.2% TRR in seed.

In the triazole study, metconazole was the primary residue identified in canola foliage and pod, accounting for 92.9% and 72.8% TRR (8.13 and 7.20 ppm) in 0-DAT1 and 0-DAT2 foliage, respectively, 55.3% and 56.7% TRR (4.77 and 11.53 ppm) in 14- and 28-DAT2 foliage, respectively, and 16.4% TRR (3.32 ppm) in pod; metconazole accounted for 24.1% TRR (0.57

ppm) in seed. The major identified residue in seed was TAA, which accounted for 40.2% TRR (0.96 ppm). TAA was not found in 0-DAT1 and 0-DAT2 foliage, but was found in 14- and 28-DAT2 foliage at 5.2% and 5.6% TRR (0.45 and 1.15 ppm), respectively, and in pod at 6.7% TRR (1.31 ppm). The only other identified metabolite was M11, which accounted for 1.3-2.0% TRR in 14- and 28-DAT2 foliage, 1.7% TRR in pod, and 4.3% TRR in seed. As in the chlorophenyl study, the majority of the remaining components were characterized as OH-metconazoles or GOH-metconazoles. No single metabolite accounted for >6.4% TRR in any foliage sample. OH-metconazoles, including CC-4, accounted for 1.1-15.3% TRR (0.1-2.79 ppm) in foliage from all sampling intervals; GOH-metconazoles were not identified in 0-DAT1 foliage, but accounted for 1.9-10.4% TRR (0.18-2.13 ppm) in remaining foliage samples; levels of both types of metabolites increased with increasing sampling interval. In pod and seed, OH-metconazoles, including CC-4, accounted for 39.7% and 13.4% TRR (7.8 and 0.32 ppm), respectively, with individual metabolites present at ≤15.2% TRR (CT-6) in pod and ≤5.4% TRR (CC-10) in seed. GOH-metconazoles accounted for 25.0% and 6.6% TRR (4.93 and 0.15 ppm), respectively, in pod and seed, with individual metabolites present at ≤11.6% TRR (CC-6) in pod and 3.5% TRR (CC-6) in seed. Remaining residues in all matrices consisted of minor components characterized as a relatively polar metabolite (CT-2; ≤2.2% TRR), an extremely nonpolar metabolite (CT-14; ≤2.2% TRR in foliage and pod), and multicomponent unknowns, accounting for up to 17.6% TRR in foliage, 1.1% TRR in pod, and 4.6% TRR in seed.

C.1. Storage Stability

The petitioner provided the dates of sampling and initial and final analysis for all samples, and stated that the initial metabolic profiles for foliage, seed, and pod were determined following 1-91 days of freezer storage for the chlorophenyl study and 8-58 days of storage for the triazole study. To demonstrate storage stability, a subsample of the MeOH/water extract of seed from the chlorophenyl study was analyzed by HPLC 139 days after sample harvest and re-analyzed following storage for ~7.3 months, and a subsample of the MeOH/water extract of pod from the triazole study was analyzed by HPLC 113 days after sample harvest and re-analyzed following storage for ~7.5 months. Comparison of the chromatographic results indicates that there were no significant changes in the metabolic profiles over the storage interval.

TABLE C.1. Summary of Storage Conditions.

Matrix	Storage Temperature (°C)	Actual Storage Duration[1]		Interval of Demonstrated Storage Stability
		Chlorophenyl	Triazole	
0-DAT1 Foliage	≤0	10-397 days (0.3-13.1 months)	22-204 days (0.7-6.7 months)	None submitted
0-DAT2 Foliage		4-383 days (0.1-12.6 months)	8-190 days (0.3-6.2 months)	
14-DAT2 Foliage		7-220 days (0.2-7.2 months)	8-83 days (0.3-2.7 months)	
28-DAT2 Foliage		10-206 days (0.3-6.8 months)	8-69 days (0.3-2.3 months)	
Pod		113-173 days (3.7-5.7 months)	74-201 days (2.4-6.6 months)	~7.5 months for residues in the MeOH extract of pod (triazole study)

TABLE C.1. Summary of Storage Conditions.

Matrix	Storage Temperature (°C)	Actual Storage Duration[1]		Interval of Demonstrated Storage Stability
		Chlorophenyl	Triazole	
Seed		113-206 days (3.7-6.8 months)	66-169 days (2.2-5.6 months)	~7.3 months for residues in the MeOH/water extract of seed (chlorophenyl study)

[1] Interval from harvest to analysis; interval from harvest to extraction was not reported.

C.2. Identification, Characterization, and Distribution of Residues

TABLE C.2.1. Total Radioactive Residues (TRR) in Canola Foliage, Pod, and Seed.

Matrix	No. of Applications	PHI[1] (days)	Application rate (lb ai/A)	Chlorophenyl label (ppm)	Triazole label (ppm)
0-DAT1 Foliage	1	0	0.243	10.79	8.76
0-DAT2 Foliage	2	0	0.486	14.95	9.89
14-DAT2 Foliage		14		5.60	8.63
28-DAT2 Foliage		28		5.92	20.35
Pod		28 [16-22]		20.67	19.62
Seed		28 [16-22]		1.85	2.39

[1] Days samples were allowed to dry in the field are presented in brackets; samples from the chlorophenyl study were dried for 22 days, and samples from the triazole study were dried for 16 days.

TABLE C.2.2.1. Distribution of the Parent and the Metabolites in Canola Foliage Following Application of [chlorophenyl-U-^{14}C]Metconazole at 0.235 (0-DAT1 Foliage) or 0.470 lb ai/A (remaining samples).[1]

Metabolite Fraction[2]	0-DAT1 Foliage		0-DAT2 Foliage		14-DAT2 Foliage		28-DAT2 Foliage	
	TRR = 10.79 ppm		TRR = 14.95 ppm		TRR = 5.60 ppm		TRR = 5.92 ppm	
	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm
MeOH	97.73	10.55	95.27	14.24	73.13	4.10	74.50	4.41
Metconazole	96.0	10.36	85.3	12.75	49.4	2.77	44.5	2.63
M11 (CL 382390; CC-11)	0.5	0.05	1.1	0.16	0.8	0.05	1.1	0.06
CC-1 (polar unknown)	--	--	1.3	0.19	0.3	0.02	3.2	0.19
CC-2 (G-OH)	--	--	1.0	0.15	2.1	0.12	2.1	0.12
CC-3 (G-OH)	--	--	0.3	0.04	2.4	0.13	2.5	0.15
CC-4 (G-OH)	--	--	1.2	0.18	3.1	0.17	2.6	0.15
CC-5 (G-OH)	--	--	--	--	2.6	0.14	3.3	0.19
CC-6 (G-OH)	--	--	0.9	0.14	3.5	0.20	3.9	0.23
CC-7 (OH)	--	--	--	--	2.5	0.14	3.4	0.20
CC-8 (OH + G-OH)	--	--	0.9	0.14	0.3	0.02	1.3	0.08
CC-9 (OH)	--	--	1.0	0.15	1.9	0.11	2.1	0.12
CC-10 (OH)	--	--	1.1	0.16	0.7	0.04	0.7	0.04
Others	1.3	0.13	1.3	0.19	3.6	0.20	3.8	0.22
2% HCl					5.29	0.30	3.80	0.22
Metconazole					3.7	0.21	2.2	0.13
M11 (CL 382390; CC-11)					0.1	<0.01	<0.1	<0.01
CC-1 (polar unknown)					--	--	0.1	<0.01

TABLE C.2.2.1. Distribution of the Parent and the Metabolites in Canola Foliage Following Application of [chlorophenyl-U-^{14}C]Metconazole at 0.235 (0-DAT1 Foliage) or 0.470 lb ai/A (remaining samples).[1]

Metabolite Fraction[2]	0-DAT1 Foliage		0-DAT2 Foliage		14-DAT2 Foliage		28-DAT2 Foliage	
	TRR = 10.79 ppm		TRR = 14.95 ppm		TRR = 5.60 ppm		TRR = 5.92 ppm	
	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm
CC-5 (G-OH)					--	--	0.1	<0.01
CC-6 (G-OH)					--	--	<0.1	<0.01
CC-7 (OH)					0.1	<0.01	0.2	0.01
CC-9 (OH)					--	--	0.1	<0.01
CC-10 (OH)					--	--	<0.1	<0.01
Others					1.4	0.08	1.1	0.06
Pepsin (comb. with cellulase)					1.03	0.06	0.78	0.05
Cellulase (comb. with pepsin)					1.79	0.10	1.11	0.07
Combined pepsin/cellulase					2.83	0.17	1.9	0.11
Metconazole					2.1	0.11	1.3	0.08
M11 (CL 382390; CC-11)					--	--	<0.1	<0.01
CC-1 (polar unknown)					--	--	<0.1	<0.01
CC-5 (G-OH)					--	--	<0.1	<0.01
CC-6 (G-OH)					--	--	0.1	<0.01
CC-9 (OH)					0.2	<0.01	<0.1	<0.01
Others					0.5	0.03	0.5	0.03
0.5% Triton X-100					0.60	0.03	0.39	0.02
6 N HCl (comb. with MeOH)					10.20	0.57	11.04	0.65
MeOH (comb. with 6 N HCl)					3.05	0.17	5.47	0.33
Combined 6 N HCl/MeOH					13.25	0.74	16.5	0.98
Metconazole					12.7	0.70	12.8	0.76
M11 (CL 382390; CC-11)					--	--	0.2	0.01
CC-1 (polar unknown)					<0.1	<0.01	--	--
CC-7 (OH)					0.1	<0.01	--	--
CC-8 (OH + G-OH)					<0.1	<0.01	--	--
CC-9 (OH)					<0.1	<0.01	--	--
CC-10 (OH)					<0.1	<0.01	--	--
CC-13 (nonpolar unknown)					0.2	<0.01	1.6	0.10
Others					0.2	0.01	1.8	0.11
Unextractable	2.27	0.24	4.73	0.71	4.90	0.27	2.91	0.17

[1] Shading indicates that the extraction step and/or characterization analysis was not conducted for the matrix in question.
[2] G-OH = glucoside of OH-metconazole; OH = OH-metconazole.

TABLE C.2.2.2. Distribution of the Parent and the Metabolites in Canola Pod and Seed Following Application of [chlorophenyl-U-^{14}C]Metconazole at 0.470 lb ai/A.[1]

Metabolite Fraction[2]	Canola pod		Canola seed	
	TRR = 20.67 ppm		TRR = 1.85 ppm	
	%TRR	ppm	%TRR	ppm
Hexane			14.42	0.27
Metconazole			12.6	0.23
M11 (CL 382390; CC-11)			1.0	0.02

TABLE C.2.2.2. Distribution of the Parent and the Metabolites in Canola Pod and Seed Following Application of [chlorophenyl-U-^{14}C]Metconazole at 0.470 lb ai/A.[1]

Metabolite Fraction[2]	Canola pod		Canola seed	
	TRR = 20.67 ppm		TRR = 1.85 ppm	
	%TRR	ppm	%TRR	ppm
CC-10 (OH)			0.6	0.01
Others			0.2	<0.01
Water/MeOH (comb. with MeOH)	49.79	10.29		
MeOH (comb. with water/MeOH for pod)	10.49	2.17	34.70	0.64
Combined water/MeOH + MeOH	60.28	12.46		
Metconazole	20.3	4.19	14.6	0.27
M11 (CL 382390; CC-11)	1.2	0.24	2.6	0.05
CC-1 (polar unknown)	0.4	0.08	1.6	0.03
CC-2 (G-OH)	1.3	0.26	0.4	<0.01
CC-3 (G-OH)	2.4	0.49	1.0	0.02
CC-4 (G-OH)	5.9	1.22	2.2	0.04
CC-5 (G-OH)	4.5	0.92	2.1	0.04
CC-6 (G-OH)	6.8	1.40	1.8	0.03
CC-7 (OH)	8.6	1.78	2.1	0.04
CC-8 (OH + G-OH)	3.3	0.68	0.7	0.01
CC-9 (OH)	2.5	0.53	0.9	0.02
CC-10 (OH)	2.5	0.51	3.1	0.06
Others	0.8	0.16	1.7	0.03
Aqueous (combined with acetone for pod)	2.74	0.57	22.60	0.42
Acetone (combined with aq. for pod)	1.89	0.39		
Combined aqueous/acetone	4.63	0.96		
Metconazole	0.8	0.17	1.8	0.03
M11 (CL 382390; CC-11)	<0.1	<0.01	1.3	0.02
CC-1 (polar unknown)	0.1	0.03	0.1	<0.01
CC-2 (G-OH)	0.1	0.03	0.7	0.01
CC-3 (G-OH)	0.2	0.04	0.5	<0.01
CC-4 (G-OH)	0.4	0.08	0.8	0.01
CC-5 (G-OH)	0.5	0.10	1.7	0.03
CC-6 (G-OH)	0.6	0.12	1.9	0.03
CC-7 (OH)	0.6	0.13	4.6	0.08
CC-8 (OH + G-OH)	0.5	0.10	2.2	0.04
CC-9 (OH)	0.5	0.09	4.2	0.08
CC-10 (OH)	0.2	0.04	1.9	0.04
Others	0.1	0.02	1.0	0.02
2% HCl (comb. with aq. for seed)	2.05	0.42	16.43	0.30
Aqueous (comb. with 2% HCl for seed)			1.80	0.03
Comb. 2% HCl + Aqueous			18.2	0.34
Metconazole	0.8	0.17	9.3	0.17
M11 (CL 382390; CC-11)	0.2	0.03	2.2	0.04
CC-1 (polar unknown)	<0.1	<0.01	<0.1	<0.01
CC-2 (G-OH)	--	--	<0.1	<0.01

TABLE C.2.2.2. Distribution of the Parent and the Metabolites in Canola Pod and Seed Following Application of [chlorophenyl-U-^{14}C]Metconazole at 0.470 lb ai/A.[1]

Metabolite Fraction[2]	Canola pod		Canola seed	
	TRR = 20.67 ppm		TRR = 1.85 ppm	
	%TRR	ppm	%TRR	ppm
CC-3 (G-OH)	--	--	0.1	<0.01
CC-4 (G-OH)	<0.1	<0.01	0.1	<0.01
CC-5 (G-OH)	0.1	0.01	0.1	<0.01
CC-6 (G-OH)	0.1	0.02	0.2	<0.01
CC-7 (OH)	--	--	0.5	<0.01
CC-8 (OH + G-OH)	<0.1	<0.01	0.2	<0.01
CC-9 (OH)	<0.1	<0.01	2.2	0.04
CC-10 (OH)	0.1	0.3	2.8	0.05
CC-13 (nonpolar unknown)	0.6	0.13	--	--
Others	0.1	0.01	0.5	<0.01
Pepsin (comb. with cellulase for pod)	0.63	0.13	3.26	0.06
Cellulase (comb. with pepsin for pod)	1.71	0.35		
Combined pepsin/cellulase	2.34	0.48		
Metconazole	0.5	0.11	0.8	0.01
M11 (CL 382390; CC-11)	<0.1	<0.01	0.3	<0.01
CC-1 (polar unknown)	0.1	0.01	0.9	0.02
CC-3 (G-OH)	<0.1	<0.01	--	--
CC-4 (G-OH)	0.1	0.03	--	--
CC-5 (G-OH)	0.1	0.02	--	--
CC-6 (G-OH)	0.1	0.02	--	--
CC-7 (OH)	0.3	0.05	--	--
CC-8 (OH + G-OH)	0.1	0.02	<0.1	<0.01
CC-9 (OH)	0.1	0.02	0.5	<0.01
CC-10 (OH)	0.1	0.01	--	--
CC-13 (nonpolar unknown)	0.1	0.02	--	--
Others	0.8	0.16	0.8	0.01
0.5% Triton X0199	0.23	0.05		
6 N HCl (comb. with MeOH)	3.83	0.79		
MeOH (comb. with 6 N HCl)	17.38	3.59		
Combined 6 N HCl and MeOH	21.21	4.38		
Metconazole	17.8	3.68		
M11 (CL 382390; CC-11)	0.2	0.03		
CC-1 (polar unknown)	<0.1	<0.01		
CC-3 (G-OH)	<0.1	<0.01		
CC-4 (G-OH)	0.1	<0.01		
CC-7 (OH)	<0.1	<0.01		
CC-8 (OH + G-OH)	0.1	0.02		
CC-9 (OH)	0.4	0.09		
CC-10 (OH)	0.2	0.04		
CC-13 (nonpolar unknown)	1.6	0.33		
Others	0.7	0.15		

TABLE C.2.2.2. Distribution of the Parent and the Metabolites in Canola Pod and Seed Following Application of [chlorophenyl-U-^{14}C]Metconazole at 0.470 lb ai/A.[1]

Metabolite Fraction[2]	Canola pod		Canola seed	
	TRR = 20.67 ppm		TRR = 1.85 ppm	
	%TRR	ppm	%TRR	ppm
Unextractable	9.29	1.92	6.80	0.13

[1] Shading indicates that the extraction step and/or characterization analysis was not conducted for the matrix in question.
[2] G-OH = glucoside of OH-metconazole; OH = OH-metconazole.

TABLE C.2.2.3. Distribution of the Parent and the Metabolites in Canola Foliage Following Application of [triazole-3,5-^{14}C]Metconazole at 0.238 (0-DAT1 Foliage) or 0.476 lb ai/A (remaining samples).[1]

Metabolite Fraction[2]	0-DAT1 Foliage		0-DAT2 Foliage		14-DAT2 Foliage		28-DAT2 Foliage	
	TRR = 8.76 ppm		TRR = 9.89 ppm		TRR = 8.63 ppm		TRR = 20.35 ppm	
	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm
MeOH	97.67	8.56	93.38	9.24	75.51	6.52	61.28	12.47
Metconazole	92.9	8.13	72.8	7.20	50.9	4.39	39.5	8.03
M11 (CL 382390; CC-11)	--	--	--	--	1.3	0.11	1.4	0.29
Triazolylalanine	--	--	--	--	2.3	0.19	1.5	0.31
CT-2 (polar unknown)	--	--	--	--	0.5	0.04	1.2	0.24
CT-3 (G-OH)	--	--	1.8	0.18	4.5	0.39	2.4	0.49
CT-4 (OH + G-OH)	--	--	1.1	0.11	2.8	0.24	2.4	0.49
CT-5 (G-OH)	--	--	--	--	1.9	0.17	1.8	0.36
CT-6 (OH)	--	--	--	--	3.0	0.26	1.2	0.24
CT-7 (G-OH)	--	--	--	--	--	--	2.1	0.44
CT-8 (OH)	--	--	--	--	3.6	0.31	2.5	0.51
CT-9 (OH)	--	--	--	--	0.6	0.05	0.7	0.15
CT-10 (OH)	--	--	--	--	1.3	0.12	1.7	0.35
CT-13 (OH)	1.2	0.10	--	--	0.7	0.06	1.3	0.27
CT-14 (nonpolar unknown)	2.2	0.19	--	--	1.2	0.10	1.3	0.27
Others	1.4	0.12	17.6	1.74	0.8	0.07	0.1	0.02
1% Ac. acid or 1% HCl (comb. with cellulase or Triton)	1.36	0.12	1.87	0.18	2.02	0.17	19.69	4.01
2% HCl (comb. with cellulase or Triton)	0.44	0.04	0.80	0.08	2.07	0.18	2.12	0.43
Pepsin (comb. with cellulase or Triton)	0.33	0.03	0.44	0.04	0.67	0.06	0.83	0.17
Cellulase (comb. with acid/pepsin for 14-DAT2 or Triton for 28-DAT2)					2.44	0.21	1.22	0.25
Comb. acid/enzyme					7.20	0.62		
Metconazole					4.4	0.38		
Triazolylalanine					0.9	0.07		
Others					2.0	0.17		
0.5% Triton X-100 (comb. with acid/enzyme for 28-DAT2)					0.43	0.04	0.27	0.05
Comb. acid/enzyme/Triton							24.13	4.91
Metconazole							11.6	2.36
M11 (CL 382390; CC-11)							0.6	0.12
Triazolylalanine							3.4	0.68

TABLE C.2.2.3. Distribution of the Parent and the Metabolites in Canola Foliage Following Application of [triazole-3,5-^{14}C]Metconazole at 0.238 (0-DAT1 Foliage) or 0.476 lb ai/A (remaining samples).[1]

Metabolite Fraction[2]	0-DAT1 Foliage		0-DAT2 Foliage		14-DAT2 Foliage		28-DAT2 Foliage	
	TRR = 8.76 ppm		TRR = 9.89 ppm		TRR = 8.63 ppm		TRR = 20.35 ppm	
	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm
CT-2 (polar unknown)							0.1	0.02
CT-3 (G-OH)							1.9	0.38
CT-4 (OH + G-OH)							1.2	0.24
CT-5 (G-OH)							1.0	0.19
CT-6 (OH)							0.6	0.13
CT-7 (G-OH)							1.3	0.26
CT-8 (OH)							0.6	0.12
CT-9 (OH)							0.1	0.02
CT-10 (OH)							0.6	0.12
Others							1.3	0.27
6 N HCl					8.10	0.70	8.53	1.74
Metconazole					--	--	5.6	1.14
Triazolylalanine					2.1	0.18	0.7	0.15
CT-3 (G-OH; 2 components)					0.4	0.03	--	--
CT-8 (OH)					2.7	0.24	--	--
CT-10 (OH)					0.4	0.03	--	--
CT-13 (OH)					--	--	0.8	0.16
CT-14 (nonpolar unknown)					--	--	0.1	0.01
Others					2.5	0.22	1.3	0.27
Unextractable	0.20	0.02	3.50	0.35	8.75	0.76	6.07	1.24

[1] Shading indicates that the extraction step and/or characterization analysis was not conducted for the matrix in question.
[2] G-OH = glucoside of OH-metconazole; OH = OH-metconazole.

TABLE C.2.2.4. Distribution of the Parent and the Metabolites in Canola Pod and Seed Following Application of [triazole-3,5-^{14}C]Metconazole at 0.476 lb ai/A.[1]

Metabolite Fraction[2]	Canola pod		Canola seed	
	TRR = 19.62 ppm		TRR = 2.39 ppm	
	%TRR	ppm	%TRR	ppm
Hexane			12.12	0.29
Metconazole			10.5	0.25
M11 (CL 382390; CC-11)			0.8	0.02
CT-10 (OH)			0.4	<0.01
Others			0.5	0.01
Water/MeOH (comb. with MeOH)	12.37	2.43		
MeOH (comb. with water/MeOH for pod)	61.82	12.13	35.97	0.86
Combined water/MeOH + MeOH	74.19	14.56		
Metconazole	3.7	0.73	8.4	0.20
M11 (CL 382390; CC-11)	1.3	0.26	1.6	0.04
Triazolylalanine	6.0	1.18	16.0	0.38
CT-2 (polar unknown)	2.2	0.42	0.4	<0.01
CT-3 (G-OH)	11.6	2.27	0.5	0.01

TABLE C.2.2.4. Distribution of the Parent and the Metabolites in Canola Pod and Seed Following Application of [triazole-3,5-^{14}C]Metconazole at 0.476 lb ai/A.[1]

Metabolite Fraction[2]	Canola pod		Canola seed	
	TRR = 19.62 ppm		TRR = 2.39 ppm	
	%TRR	ppm	%TRR	ppm
CT-4 (OH + G-OH)	11.3	2.21	0.8	0.02
CT-5 (G-OH)	8.4	1.65	1.5	0.03
CT-6 (OH)	15.0	2.94	1.4	0.03
CT-7 (G-OH)	4.4	0.87	0.8	0.02
CT-8 (OH)	5.9	1.15	0.2	<0.01
CT-9 (OH)	1.1	0.22	0.7	0.02
CT-10 (OH)	2.9	0.58	2.4	0.06
Others	0.3	0.07	1.2	0.03
Aqueous			31.71	0.76
Metconazole			0.7	0.02
M11 (CL 382390; CC-11)			0.4	0.01
Triazolylalanine			22.7	0.54
CT-2 (polar unknown)			0.2	<0.01
CT-3 (G-OH)			0.3	<0.01
CT-4 (OH + G-OH)			0.4	<0.01
CT-5 (G-OH)			0.5	0.01
CT-6 (OH)			0.8	0.02
CT-7 (G-OH)			2.1	0.05
CT-8 (OH)			1.4	0.03
CT-9 (OH)			0.3	<0.01
CT-10 (OH)			0.7	0.02
Others			1.3	0.03
2% HCl (comb. with aqueous for seed)	4.32	0.85	7.68	0.18
Metconazole	2.3	0.46		
M11 (CL 382390; CC-11)	0.2	0.03		
Triazolylalanine	0.2	0.03		
CT-4 (OH + G-OH)	0.1	0.03		
CT-5 (G-OH)	0.1	0.02		
CT-6 (OH)	0.1	0.02		
CT-7 (G-OH)	0.3	0.05		
CT-8 (OH)	0.1	0.03		
CT-9 (OH)	0.2	0.05		
CT-10 (OH)	0.2	0.04		
CT-13 (OH)	0.2	0.03		
Others	0.4	0.09		
Aqueous (comb. with 2% HCl)			1.76	0.04
Combined 2% HCl/Aq			9.44	0.23
Metconazole			3.2	0.08
M11 (CL 382390; CC-11)			1.0	0.02
Triazolylalanine			1.1	0.03
CT-5 (G-OH)			0.1	<0.01

TABLE C.2.2.4. Distribution of the Parent and the Metabolites in Canola Pod and Seed Following Application of [triazole-3,5-^{14}C]Metconazole at 0.476 lb ai/A.[1]

Metabolite Fraction[2]	Canola pod		Canola seed	
	TRR = 19.62 ppm		TRR = 2.39 ppm	
	%TRR	ppm	%TRR	ppm
CT-6 (OH)			0.1	<0.01
CT-7 (G-OH)			0.5	0.01
CT-8 (OH)			0.5	0.01
CT-9 (OH)			0.8	0.02
CT-10 (OH)			1.4	0.03
Others			0.9	0.02
Pepsin	2.00	0.39	4.29	0.10
Metconazole	0.8	0.15	1.3	0.03
M11 (CL 382390; CC-11)	0.1	0.03	0.4	<0.01
Triazolylalanine	0.1	0.02	0.4	<0.01
CT-4 (OH + G-OH)	<0.1	<0.01	0.2	<0.01
CT-5 (G-OH)	0.1	0.02	0.3	<0.01
CT-6 (OH)	0.1	0.02	0.1	<0.01
CT-7 (G-OH)	0.1	0.02	0.2	<0.01
CT-8 (OH)	0.1	0.03	0.2	<0.01
CT-9 (OH)	0.3	0.05	0.1	<0.01
CT-10 (OH)	0.1	0.03	0.5	0.01
Others	0.2	0.04	0.7	0.02
Aqueous	0.28	0.05		
Metconazole	0.1	0.02		
Triazolylalanine	<0.1	<0.01		
CT-3 (G-OH)	<0.1	<0.01		
CT-4 (OH + G-OH)	<0.1	<0.01		
CT-5 (G-OH)	<0.1	<0.01		
CT-7 (G-OH)	<0.1	<0.01		
CT-10 (OH)	<0.1	<0.01		
Others	0.1	0.02		
Cellulase	0.38	0.07		
Metconazole	0.2	0.03		
M11 (CL 382390; CC-11)	<0.1	<0.01		
Triazolylalanine	<0.1	<0.01		
CT-4 (OH + G-OH)	<0.1	<0.01		
CT-5 (G-OH)	<0.1	<0.01		
CT-6 (OH)	<0.1	<0.01		
CT-7 (G-OH)	<0.1	<0.01		
CT-8 (OH)	<0.1	<0.01		
CT-9 (OH)	<0.1	<0.01		
CT-10 (OH)	<0.1	<0.01		
Others	0.1	0.01		
0.5% Triton X-100	0.40	0.08		
Metconazole	0.2	0.04		

TABLE C.2.2.4. Distribution of the Parent and the Metabolites in Canola Pod and Seed Following Application of [triazole-3,5-^{14}C]Metconazole at 0.476 lb ai/A.[1]

Metabolite Fraction[2]	Canola pod		Canola seed	
	TRR = 19.62 ppm		TRR = 2.39 ppm	
	%TRR	ppm	%TRR	ppm
M11 (CL 382390; CC-11)	<0.1	<0.01		
Triazolylalanine	<0.1	<0.01		
CT-8 (OH)	<0.1	<0.01		
CT-9 (OH)	<0.1	<0.01		
CT-10 (OH)	<0.1	<0.01		
Others	0.1	0.02		
6 N HCl (comb. with MeOH)	1.39	0.27		
MeOH (comb. with 6 N HCl)	10.68	2.10		
Combined 6 N HCl and MeOH	12.07	2.37		
Metconazole	9.1	1.79		
M11 (CL 382390; CC-11)	0.1	0.02		
Triazolylalanine	0.3	0.06		
CT-4 (OH + G-OH)	0.1	0.02		
CT-6 (OH)	<0.1	<0.01		
CT-7 (G-OH)	<0.1	<0.01		
CT-8 (OH)	0.4	0.08		
CT-9 (OH)	0.1	0.02		
CT-10 (OH)	0.1	0.02		
CT-13 (OH)	1.2	0.24		
CT-14 (nonpolar unknown)	0.1	0.01		
Others	0.5	0.10		
Unextractable	6.36	1.25	6.47	0.15

[1] Shading indicates that the extraction step and/or characterization analysis was not conducted for the matrix in question.
[2] G-OH = glucoside of OH-metconazole; OH = OH-metconazole.

TABLE C.2.3.1. Summary of Characterization and Identification of Radioactive Residues in Canola Foliage Following Application of [chlorophenyl-U-^{14}C]Metconazole at 0.235 (0-DAT1 Foliage) or 0.470 lb ai/A (remaining samples).

Compound	0-DAT1 Foliage		0-DAT2 Foliage		14-DAT2 Foliage		28-DAT2 Foliage	
	TRR = 10.79 ppm		TRR = 14.95 ppm		TRR = 5.60 ppm		TRR = 5.92 ppm	
	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm
Metconazole	96.0	10.36	85.3	12.75	67.8	3.80	60.8	3.60
M11 (CL 382390; CC-11)	0.5	0.05	1.1	0.16	0.8	0.05	1.4	0.08
CC-1 (polar unknown)	--	--	1.3	0.19	0.5	0.03	3.3	0.20
CC-2 (G-OH)	--	--	1.0	0.15	2.1	0.11	2.1	0.12
CC-3 (G-OH)	--	--	0.3	0.04	2.4	0.13	2.5	0.15
CC-4 (G-OH)	--	--	1.2	0.18	3.1	0.17	2.6	0.15
CC-5 (G-OH)	--	--	--	--	2.6	0.14	3.4	0.20
CC-6 (G-OH)	--	--	0.9	0.14	3.5	0.19	4.0	0.24
CC-7 (OH)	--	--	--	--	2.6	0.14	3.6	0.21
CC-8 (OH + G-OH)	--	--	0.9	0.14	0.3	0.02	1.3	0.08
CC-9 (OH)	--	--	1.0	0.15	2.1	0.12	2.2	0.13

TABLE C.2.3.1. Summary of Characterization and Identification of Radioactive Residues in Canola Foliage Following Application of [chlorophenyl-U-^{14}C]Metconazole at 0.235 (0-DAT1 Foliage) or 0.470 lb ai/A (remaining samples).

Compound	0-DAT1 Foliage		0-DAT2 Foliage		14-DAT2 Foliage		28-DAT2 Foliage	
	TRR = 10.79 ppm		TRR = 14.95 ppm		TRR = 5.60 ppm		TRR = 5.92 ppm	
	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm
CC-10 (OH)	--	--	1.1	0.16	0.7	0.04	0.7	0.04
CC-13 (nonpolar unknown)	--	--	--	--	0.2	<0.01	1.6	0.10
Others	1.3	0.13	1.3	0.19	5.8	0.32	7.1	0.42
Aqueous (Triton X-100)	--	--	--	--	0.6	0.03	0.4	0.02
Total identified	96.5	10.41	86.4	12.91	68.6	3.85	62.2	3.68
Total characterized	1.3	0.13	9.0	1.334	26.5	1.44	34.8	2.06
Total extractable	97.73	10.55	95.27	14.24	95.09	5.33	97.09	5.75
Unextractable (PES)[1]	2.27	0.24	4.73	0.71	4.90	0.27	2.91	0.17
Accountability[2]	100		100		100		100	

[1] Residues remaining after exhaustive extractions.
[2] Accountability = (Total extractable + Total unextractable)/(TRR from combustion analysis; see TABLE C.2.1) * 100; extraction results were normalized.

TABLE C.2.3.2 Summary of Characterization and Identification of Radioactive Residues in Canola Pod and Seed Following Application of [chlorophenyl-U-^{14}C]Metconazole at 0.470 lb ai/A.

Compound	Canola pod		Canola seed	
	TRR = 20.67 ppm		TRR = 1.85 ppm	
	% TRR	ppm	% TRR	ppm
Metconazole	40.3	8.32	39.0	0.72
M11 (CL 382390; CC-11)	1.5	0.32	7.3	0.14
CC-1 (polar unknown)	0.6	0.13	2.7	0.05
CC-2 (G-OH)	1.4	0.29	1.1	0.02
CC-3 (G-OH)	2.6	0.54	1.5	0.03
CC-4 (G-OH)	6.5	1.35	3.1	0.06
CC-5 (G-OH)	5.1	1.05	3.9	0.07
CC-6 (G-OH)	7.6	1.56	4.0	0.07
CC-7 (OH)	9.5	1.97	7.2	0.13
CC-8 (OH + G-OH)	4.0	0.83	3.1	0.06
CC-9 (OH)	3.6	0.74	7.8	0.15
CC-10 (OH)	3.0	0.63	8.3	0.15
CC-13 (nonpolar unknown)	2.3	0.48	--	--
Others	2.5	0.51	4.2	0.08
Aqueous (Triton X-100)	0.2	0.05	--	--
Total identified	41.8	8.64	46.3	0.86
Total characterized	48.9	10.13	46.9	0.87
Total extractable	90.74	18.75	93.21	1.72
Unextractable (PES)[1]	9.29	1.92	6.8	0.13
Accountability[2]	100		100	

[1] Residues remaining after exhaustive extractions.
[2] Accountability = (Total extractable + Total unextractable)/(TRR from combustion analysis; see TABLE C.2.1) * 100; extraction results were normalized.

TABLE C.2.3.3. Summary of Characterization and Identification of Radioactive Residues in Canola Foliage Following Application of [triazole-3,5-^{14}C]Metconazole at 0.238 (0-DAT1 Foliage) or 0.476 lb ai/A (remaining samples).

Compound	0-DAT1 Foliage		0-DAT2 Foliage		14-DAT2 Foliage		28-DAT2 Foliage	
	TRR = 8.76 ppm		TRR = 9.89 ppm		TRR = 8.63 ppm		TRR = 20.35 ppm	
	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm
Metconazole	92.9	8.13	72.8	7.20	55.3	4.77	56.7	11.53
M11 (CL 382390; CC-11)	--	--	--	--	1.3	0.11	2.0	0.41
Triazolylalanine	--	--	--	--	5.2	0.45	5.6	1.15
CT-2 (polar unknown)	--	--	--	--	0.5	0.04	1.3	0.26
CT-3 (G-OH)	--	--	1.9	0.18	4.9	0.43	4.3	0.87
CT-4 (OH + G-OH)	--	--	1.1	0.11	2.8	0.24	3.6	0.72
CT-5 (G-OH)	--	--	--	--	1.9	0.17	2.7	0.56
CT-6 (OH)	--	--	--	--	3.0	0.26	1.8	0.37
CT-7 (G-OH)	--	--	--	--	--	--	3.4	0.70
CT-8 (OH)	--	--	--	--	6.4	0.55	3.1	0.63
CT-9 (OH)	--	--	--	--	0.6	0.05	0.9	0.17
CT-10 (OH)	--	--	--	--	1.7	0.15	2.3	0.47
CT-13 (OH)	1.2	0.10	--	--	0.8	0.06	2.1	0.43
CT-14 (nonpolar unknown)	2.2	0.19	--	--	1.2	0.10	1.4	0.28
Others	1.4	0.12	17.6	1.74	5.3	0.46	2.8	0.57
Mild acid/MeOH-soluble	1.8	0.16	2.67	0.26	--	--	--	--
Pepsin hydrolysate	0.3	0.03	0.4	0.04	--	--	--	--
Aqueous (Triton X-100)	--	--	--	--	0.4	0.04	--	--
Total identified	92.9	8.13	72.8	7.2	61.8	5.33	64.3	13.09
Total characterized	6.9	0.60	23.67	2.33	29.5	2.55	29.7	6.03
Total extractable	99.80	8.75	96.50	9.55	91.24	7.88	93.94	19.12
Unextractable (PES)[1]	0.20	0.02	3.5	0.35	8.75	0.76	6.07	1.24
Accountability[2]	100		100		100		100	

[1] Residues remaining after exhaustive extractions.
[2] Accountability = (Total extractable + Total unextractable)/(TRR from combustion analysis; see TABLE C.2.1) * 100; extraction results were normalized.

TABLE C.2.3.4 Summary of Characterization and Identification of Radioactive Residues in Canola Pod and Seed Following Application of [triazole-3,5-U-^{14}C]Metconazole at 0.476 lb ai/A.

Compound	Canola pod		Canola seed	
	TRR = 19.62 ppm		TRR = 2.39 ppm	
	% TRR	ppm	% TRR	ppm
Metconazole	16.4	3.32	24.1	0.57
M11 (CL 382390; CC-11)	1.7	0.33	4.3	0.10
Triazolylalanine	6.7	1.31	40.2	0.96
CT-2 (polar unknown)	2.2	0.42	0.6	0.01
CT-3 (G-OH)	11.6	2.28	0.8	0.02
CT-4 (OH + G-OH)	11.5	2.26	1.4	0.03
CT-5 (G-OH)	8.6	1.70	2.3	0.05
CT-6 (OH)	15.2	2.99	2.3	0.05
CT-7 (G-OH)	4.8	0.95	3.5	0.08

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TABLE C.2.3.4 Summary of Characterization and Identification of Radioactive Residues in Canola Pod and Seed Following Application of [triazole-3,5-U-^{14}C]Metconazole at 0.476 lb ai/A.

Compound	Canola pod		Canola seed	
	TRR = 19.62 ppm		TRR = 2.39 ppm	
	% TRR	ppm	% TRR	ppm
CT-8 (OH)	6.6	1.30	2.4	0.06
CT-9 (OH)	1.8	0.35	1.9	0.05
CT-10 (OH)	3.4	0.67	5.4	0.13
CT-13 (OH)	1.2	0.23	--	--
CT-14 (nonpolar unknown)	0.1	0.01	--	--
Others	1.1	0.22	4.6	0.11
Total identified	24.8	4.96	68.6	1.63
Total characterized	68.1	13.38	25.2	0.59
Total extractable	93.64	18.37	93.53	2.23
Unextractable (PES)[1]	6.36	1.25	6.47	0.15
Accountability[2]	100		100	

[1] Residues remaining after exhaustive extractions.
[2] Accountability = (Total extractable + Total unextractable)/(TRR from combustion analysis; see TABLE C.2.1) * 100; extraction results were normalized.

C.3. Proposed Metabolic Profile

Based on the submitted canola metabolism studies, the petitioner proposed the following metabolic pathway for metconazole. The main metabolic route of metconazole in canola is via oxidative hydroxylation of the methylene groups, the methyl groups on the cyclopentyl ring, and possibly of the cyclopentyl ring. The detection of triazolylalanine as a major seed metabolite in the triazole study indicates that the methylene group between the triazole and cyclopentyl rings is susceptible to oxidative hydroxylation. The large number of OH-metconazole metabolites and glucose conjugates of OH-metconazole suggests monohydroxylation at the various pro-chiral carbons of metconazole, giving rise to chromatographically distinguishable stereoisomeric structures.

FIGURE C.3.1. Proposed Metabolic Profile of Metconazole in Canola
This figure was copied without alteration from MRID 46901904.

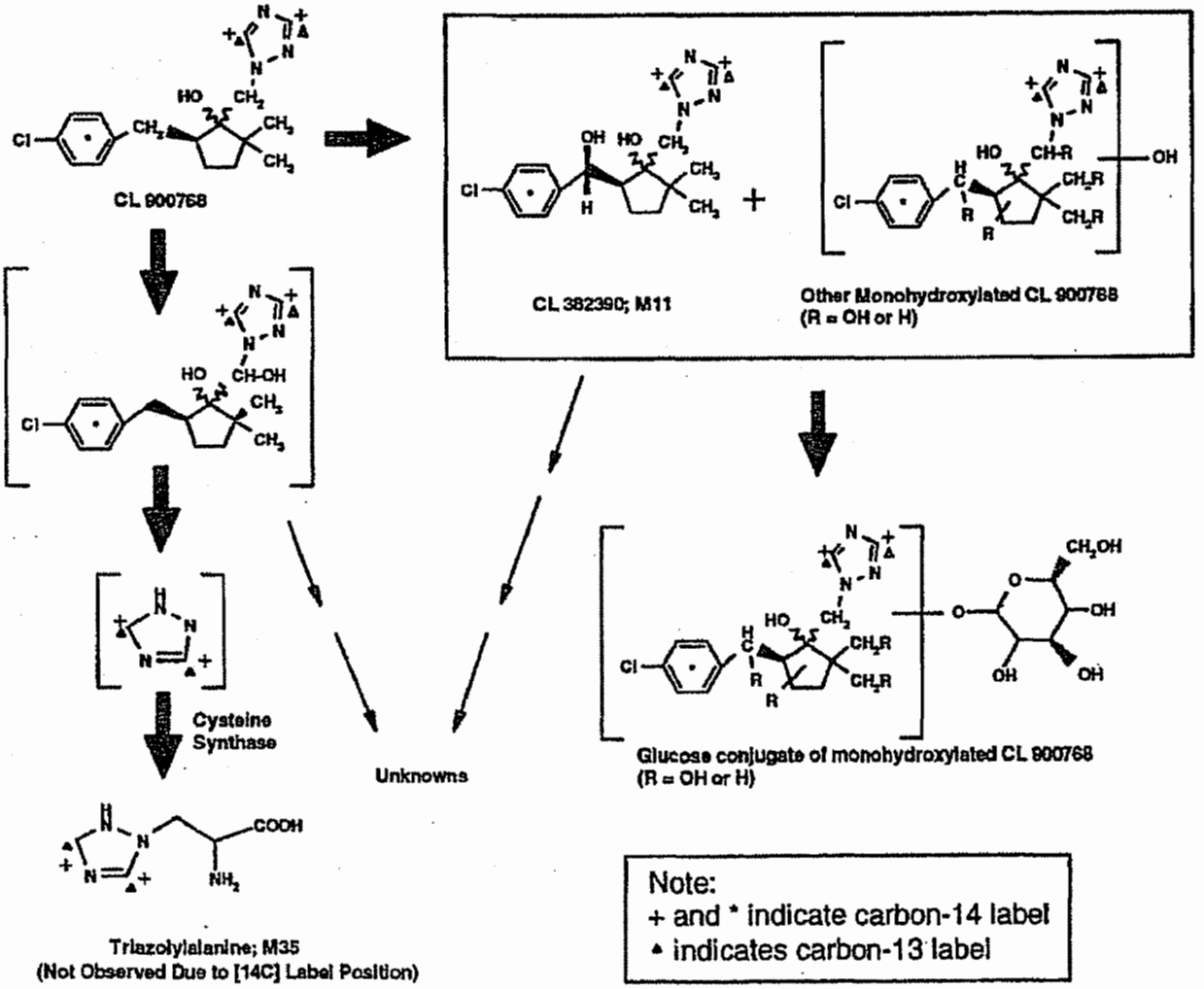
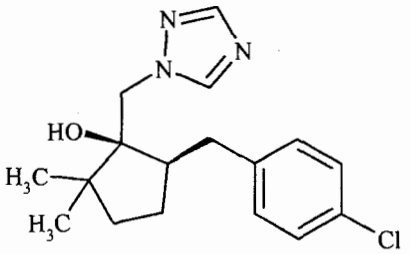
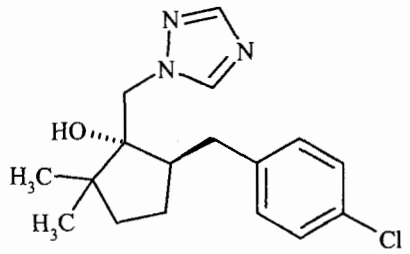
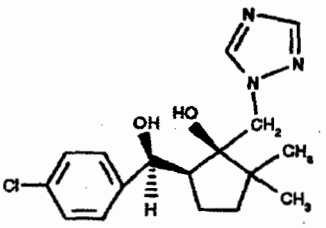
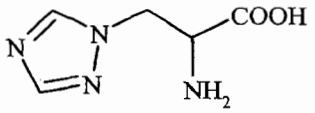
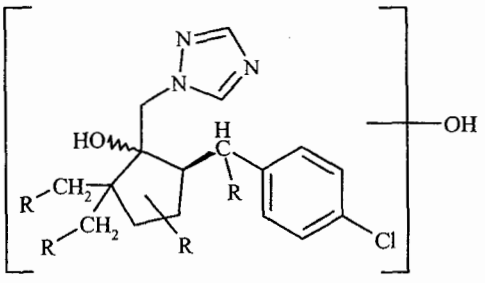
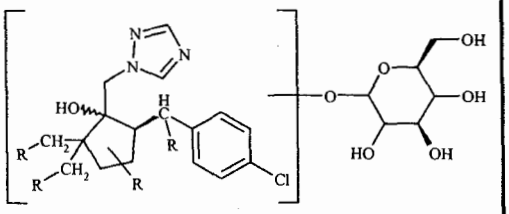


TABLE C.3.1. Identification of Compounds from Metabolism Study

Common name/code Figure C.3.1 ID No.	Chemical name	Chemical structure
Metconazole	5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	 *cis*-isomer  *trans*-isomer
M11	5-[(4-chlorophenyl)methoxy]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl) cyclopentanol	
Triazolylalanine (TA)	2-amino-3-(1*H*-1,2,4-triazol-1-yl)propanoic acid	
Monohydroxylated metconazole		
Glucose conjugate of monohydroxylated metconazole		

D. CONCLUSION

Following one or two broadcast foliar applications of [chlorophenyl-U-^{14}C]metconazole at 0.235 lb ai/A/application, TRR were 10.79 ppm in canola foliage harvested immediately following the first application (0-DAT1 foliage), 14.95 ppm in foliage harvested immediately following the second application (0-DAT2 foliage), 5.60 and 5.92 ppm in foliage harvested 14 and 28 days after the second application (14- and 28-DAT2 foliage), and 20.67 and 1.85 ppm in pod and seed harvested 28 days after the second application and allowed to dry in the field for 22 days. The petitioner noted that the high TRR in pod was likely the result of moisture loss on drying. Following one or two broadcast foliar applications of [triazole-3,5-^{14}C]metconazole at 0.238 lb ai/A/application, TRR were 8.76 and 9.89 ppm in 0-DAT1 and 0-DAT2 foliage, 8.63 ppm in 14-DAT2 foliage, 20.35 ppm in 28-DAT2 foliage, 19.62 ppm in pod, and 2.39 ppm in seed. The petitioner attributed the higher residues in 28-DAT2 foliage to moisture loss in the mature plant, and higher residues in pod to loss on drying in the field.

In the chlorophenyl study, metconazole was the primary residue identified in all canola matrices, accounting for 96.0% and 85.3% TRR in 0-DAT1 and 0-DAT2 foliage, respectively, 67.8% and 60.8% TRR in 14- and 28-DAT2 foliage, respectively, 40.3% TRR in pod, and 39.0% TRR in seed. The only other identified metabolite was M11, which accounted for 0.05-1.4% TRR in foliage, 1.5% TRR in pod, and 7.3% TRR in seed. No other metabolites were characterized in 0-DAT1 foliage, and no single metabolite accounted for >4% TRR in any other foliage sample. OH-metconazoles accounted for 2.1-6.5% TRR in 0-2-, 14-, and 28-DAT2 foliage, and GOH-metconazoles accounted for 3.4-14.6% TRR; levels of both types of metabolites increased with increasing sampling interval. In pod and seed, OH-metconazoles metabolites accounted for 20.16% and 26.4% TRR, respectively, with individual metabolites present at ≤9.5% in pod and ≤8.3% TRR in seed. GOH-metconazoles accounted for 23.2% and 13.6% TRR, respectively, in pod and seed, with individual metabolites present at ≤7.6% TRR in pod and 4.0% TRR in seed. Remaining residues in all matrices consisted of minor components characterized as an extremely polar metabolite, an extremely nonpolar metabolite, and multicomponent unknowns.

In the triazole study, metconazole was the primary residue identified in canola foliage and pod, accounting for 92.9% and 72.8% TRR in 0-DAT1 and 0-DAT2 foliage, respectively, 55.3% and 56.7% TRR in 14- and 28-DAT2 foliage, respectively, and 16.4% TRR in pod; metconazole accounted for 24.1% TRR in seed. The major identified residue in seed was TAA, which accounted for 40.2% TRR. TAA was not found in 0-DAT1 and 0-DAT2 foliage, but was found in 14- and 28-DAT2 foliage at 5.2% and 5.6% TRR, respectively, and in pod at 6.7% TRR. The only other identified metabolite was M11, which accounted for 1.3-2.0% TRR in 14- and 28-DAT2 foliage, 1.7% TRR in pod, and 4.3% TRR in seed. As in the chlorophenyl study, the majority of the remaining components were characterized as OH-metconazoles or GOH-metconazoles. No single metabolite accounted for >6.4% TRR in any foliage sample. OH-metconazoles accounted for 1.1-15.3% TRR in foliage from all sampling intervals; GOH-metconazoles were not identified in 0-DAT1 foliage, but accounted for 1.9-10.4% TRR in remaining foliage samples; levels of both types of metabolites increased with increasing sampling interval. In pod and seed, OH-metconazoles accounted for 39.7% and 13.4% TRR, respectively, with individual metabolites present at ≤15.2% TRR in pod and ≤5.4% TRR in seed.

GOH-metconazoles accounted for 25.0% and 6.6% TRR, respectively, in pod and seed, with individual metabolites present at ≤11.6% TRR in pod and 3.5% TRR in seed. Remaining residues in all matrices consisted of minor components characterized as a relatively polar metabolite, an extremely nonpolar metabolite, and multicomponent unknowns.

The studies are supported by adequate storage stability data, and acceptable methods were used for extraction and characterization/identification of residues.

Based on the submitted canola metabolism studies, the petitioner proposed the following metabolic pathway for metconazole. The main metabolic route of metconazole in canola is via oxidative hydroxylation of the methylene groups, the methyl groups on the cyclopentyl ring, and possibly of the cyclopentyl ring. The detection of triazolylalanine as a major seed metabolite in the triazole study indicates that the methylene group between the triazole and cyclopentyl rings is susceptible to oxidative hydroxylation. The large number of OH-metconazole metabolites and glucose conjugates of OH-metconazole suggests monohydroxylation at the various pro-chiral carbons of metconazole, giving rise to chromatographically distinguishable stereoisomeric structures.

E. REFERENCES

DP#:	324541
Subject:	Metconazole. Request for a Tolerance on Imported Bananas. Summary of Analytical Chemistry and Residue Data. Petition Number 9E05052.
From:	N. Dodd
To:	M. Waller
Date:	12/14/05
MRIDs:	44721506, 44721507, 44721508, 44721509, 44721510, and 44721511

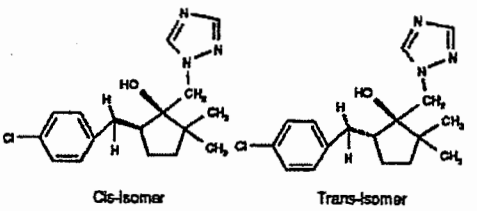
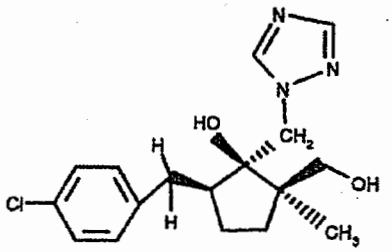
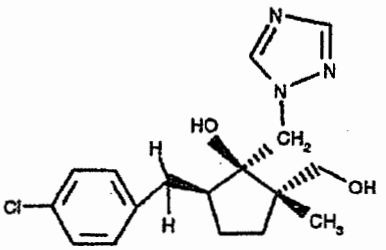
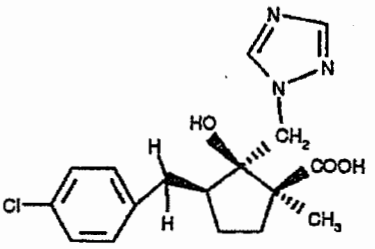
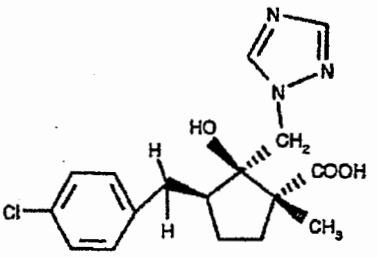
F. DOCUMENT TRACKING

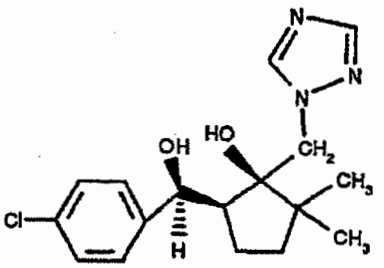
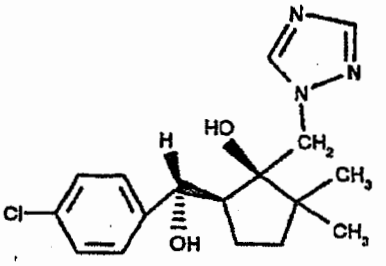
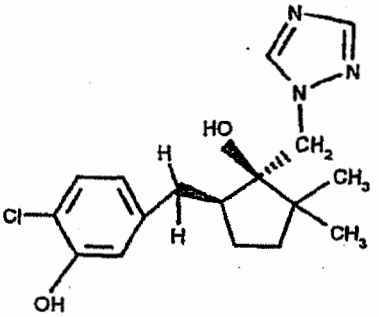
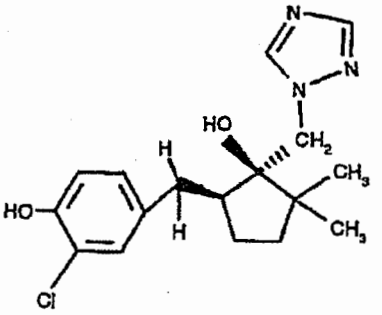
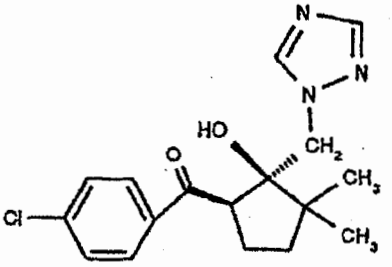
RDI: N. Dodd (2/20/08)
Petition Numbers: 6F7094 and 6F7095
DP#s: 348168 and 348206
PC Code: 125619

Template Version June 2005

APPENDIX I. Chemical Names and Structures of Reference Standards Used in the Canola Metabolism Study. [The following table was copied without alteration from MRID 46901905]

Table of Compounds

Compound Code	Chemical Name	Structures
CL 900768	(5-[(4-chlorophenyl)methyl]-2-,2-dimethyl-1-(1H-1,2,4-triazol-1-yl methyl)-1-cyclopentanol)	 Cis-isomer Trans-isomer
CL 359451 (M1)	(5-[(4-chlorophenyl)methyl]-2-methoxyl,2-methyl-1-(1H-1,2,4-triazol-1-yl methyl)-1-cyclopentanol)	
CL 359452 (M2)	(5-[(4-chlorophenyl)methyl]-2-methoxyl,2-methyl-1-(1H-1,2,4-triazol-1-yl methyl)-1-cyclopentanol)	
CL 359138 (M12)	(5-[(4-chlorophenyl)methyl]-2-carboxyl,2-methyl-1-(1H-1,2,4-triazol-1-yl methyl)-1-cyclopentanol)	
CL 359139 (M13)	(5-[(4-chlorophenyl)methyl]-2-methyl,2-carboxyl-1-(1H-1,2,4-triazol-1-yl methyl)-1-cyclopentanol)	

Compound Code	Chemical Name	Structures
CL 382390 (M11)	(5-[(4-chlorophenyl)methoxyl]-2-,2-dimethyl-1-(1H-1,2,4-triazol-1-yl methyl)-1-cyclopentanol)	
CL 382391 (M21)	(5-[(4-chlorophenyl)methoxyl]-2-,2-dimethyl-1-(1H-1,2,4-triazol-1-yl methyl)-1-cyclopentanol)	
CL 359453 (M15)	(5-[(3-hydroxy-4-chlorophenyl)methyl]-2-,2-dimethyl-1-(1H-1,2,4-triazol-1-yl methyl)-1-cyclopentanol)	
CL 395838 (M19)	(5-[(4-hydroxy-3-chlorophenyl)methyl]-2-,2-dimethyl-1-(1H-1,2,4-triazol-1-yl methyl)-1-cyclopentanol)	
CL 382389 (M30)	(5-[(4-chlorophenyl)keto]-2-,2-dimethyl-1-(1H-1,2,4-triazol-1-yl methyl)-1-cyclopentanol)	

Primary Evaluator	This DER was originally prepared under contract by Dynamac Corporation.
Approved by	Nancy Dodd, Chemist *Nancy Dodd* Date: 2/20/08 Registration Action Branch 3 Health Effects Division (7509P)

This DER was originally prepared under contract by Dynamac Corporation (2275 Research Boulevard, Suite 300; Rockville, MD 20850; submitted 09/13/2007). The DER has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

46901906 Class, T.; Schluter, H. (2002) Metconazole (BAS 55 F; AC 900768): Metabolism of Carbon-14 Labeled AC 900768 in Peas. Project Number: 200600104, MET/02/006. Unpublished study prepared by Cyanamid Forshung Gmbh (CFS) and PTRL Europe Gmbh. 178 p.

EXECUTIVE SUMMARY:

Valent U.S.A. has submitted a study investigating the metabolism of [chlorophenyl-U-^{14}C]metconazole (specific activity 9.99 µCi/mg) and [triazole-3,5-^{14}C]metconazole (specific activity 10 µCi/mg) in peas. The radiolabeled test substances were formulated as soluble concentrate formulations and applied as two or three broadcast foliar applications to pea plants at ~0.193 lb ai/A/application (~216 g ai/ha/application) beginning at the early crop cover stage. Two applications were made to pea plants grown in one pot for each label to simulate applications to green or canned peas, and three applications were made to pea plants grown in a second pot for each label to simulate application to dry peas. Applications were made at 13- and 14-day retreatment intervals; samples of immature pea foliage were harvested immediately following each application [0 days after treatment 1 (0-DAT1), 0-DAT2, and 0-DAT3], and samples of pea seed and straw were collected 13-DAT2 (green pea) and 15-DAT3 (dry pea). The total application rates for the chlorophenyl and triazole labels were 0.188 lb ai/A (211.2-210.9 g ai/ha) following one application, 0.371-0.373 lb ai/A (415.8-418.1 g ai/ha) following two applications, and 0.557-0.559 lb ai/A (623.8-626.1 g ai/ha) following three applications. The in-life phase of the study was conducted by Cyanamid Forschung GmbH (Schwabenheim, Germany), and the analytical phase of the study was conducted by PTRL Europe (Ulm, Germany).

Total radioactive residues (TRR) were calculated by summing radioactivity in extractable and unextractable residues and by combustion/LSC; summed values were used for all further determinations. In chlorophenyl-label samples, summed TRR were 8.77, 6.09, and 8.42 ppm for 0-DAT1, 0-DAT2, and 0-DAT3 foliage, 7.85 ppm and 60.26 ppm for 13-DAT2 and 15-DAT3 straw, and 0.044 ppm and 0.203 ppm for 13-DAT2 and 15-DAT3 seed. In triazole-label samples TRR were 10.63, 8.70, and 11.09 ppm for 0-DAT1, 0-DAT2, and 0-DAT3 foliage, 12.03 and

49.11 ppm for 13-DAT2 and 15-DAT3 straw, and 1.57 and 3.71 ppm for 13-DAT2 and 15-DAT3 seed.

Samples of pea foliage and straw were initially rinsed with acetone, which removed 6.6-40.1% TRR (0.580-3.491 ppm) and 2.7-4.9% TRR (0.213-2.950 ppm) for foliage and straw, respectively. Extraction with acetone released the majority of the radioactivity from all samples of pea foliage and straw: 52.2-92.8% TRR (3.461-9.280 ppm) for 0-DAT1, 0-DAT2, and 0-DAT3 foliage, and 74.7-89.2% TRR (7.003-44.99 ppm) for 13-DAT2 and 15-DAT3 straw. Acetone also released the majority of radioactivity from seed treated with the chlorophenyl label, 47.9-71.5% TRR (0.031-0.097 ppm); extraction with acetone released ≤10.9% TRR from triazole-label seed. The majority of radioactivity in seed treated with the triazole label was released by extraction with methanol (MeOH)/water, 50.9-77.7% TRR (1.218-1.888 ppm); in chlorophenyl-label samples, extraction with MeOH/water released 7.6% TRR from 13-DAT2 seed and 32.4% TRR from 15-DAT3 seed. Remaining residues were released by extraction with acetone/MeOH/water for foliage (up to 8.3% TRR), with MeOH/water and water for straw (up to 10.9% TRR), and with water for seed (up to 39.5% TRR). These procedures adequately extracted the majority of residues from pea matrices. Nonextractable residues following extraction were ≤3.4% TRR (≤0.295 ppm) in foliage, ≤2.8% TRR (≤1.663 ppm) in straw, and ≤15.5% TRR (≤0.198 ppm) in seed. Because TRR were calculated by summation, accountabilities for all matrices were at or near 100%. When TRR determined by summation were compared with TRR determined by combustion/LSC, accountabilities ranged from 40 to 171%. The study is supported by adequate storage stability data.

Metconazole was identified and confirmed by TLC and/or HPLC co-chromatography in pea matrices, and triazolylalanine (TA) was identified in the MeOH/water extracts of triazole-label pea seed by TLC co-chromatography. All remaining components were initially characterized as more or less polar than metconazole based on relative elution by TLC. Radioactivity was separated into regions of interest (ROIs), which consisted of either discrete components or diffuse areas of relatively low radioactivity delineated by discrete components. For further characterization of remaining residues, the petitioner conducted extensive analysis of 15-DAT3 pea straw. The surface rinses and extracts of pea straw were initially investigated by TLC, then aliquots of the surface rinses and extracts were combined for further analysis by HPLC. A less polar metabolite observed in chlorophenyl-label straw from both sampling intervals was determined to be the result of cleavage of the triazole moiety because it did not appear in triazole-label samples. The metabolite did not co-chromatograph with any reference standard, and further investigation via LC/MS/MS was unsuccessful because of its low concentration. Metabolites characterized as more polar than metconazole were further characterized in straw by TLC, HPLC, and LC/MS/MS analysis following acid and β-glucosidase hydrolysis as monohydroxylated metconazole and glucoside conjugates of monohydroxylated metconazole; no quantitative data were provided. Metabolites in pea foliage and seed were characterized as several isomers of monohydroxylated metconazole and corresponding glucose conjugates based on comparison of TLC chromatographic results with those of 15-DAT3 straw. No further attempts were made to characterize/identify residues of metconazole in peas.

The metabolic profile was similar in pea foliage and straw from both labels. Metconazole was the primary residue identified in all samples, accounting for 94.1% and 95.9% TRR (8.251 and 10.201 ppm) in 0-DAT1 foliage, 78.7% and 78.8% TRR (4.796 and 6.858 ppm) in 0-DAT2 foliage, and 79.3% and 66.7% TRR (6.675 and 7.401 ppm) in 0-DAT3 foliage from chlorophenyl- and triazole-label samples, respectively. The majority of remaining residues were characterized as more polar than metconazole, accounting for 5.3%, 16.4%, and 15.6% TRR (0.461, 1.008, and 1.311 ppm) in 0-DAT1, 0-DAT2, and 0-DAT3 chlorophenyl-label foliage, and for 3.45%, 16.8%, and 29.5% TRR (0.362, 1.453, and 3.279 ppm) in triazole-label foliage. Residues characterized as less polar than metconazole accounted for ≤3.4% TRR in chlorophenyl-label foliage and ≤1.0% TRR in triazole-label foliage.

Metconazole was generally identified at lower levels in straw, accounting for 58.7% and 54.1% TRR (4.603 and 32.585 ppm), respectively, in 13-DAT2 and 15-DAT3 chlorophenyl-label straw, and for 64.9% and 67.6% TRR (7.804 and 33.219 ppm), respectively, in 13-DAT2 and 15-DAT3 triazole-label straw. Residues characterized as more polar than metconazole accounted for 30.2% and 31.0% TRR (2.370 and 18.679 ppm), respectively, in 13-DAT2 and 15-DAT3 chlorophenyl-label straw, and for 27.3% and 22.9% TRR (3.298 and 11.203 ppm), respectively, in 13-DAT2 and 15-DAT3 triazole-label straw. Residues characterized as less polar than metconazole accounted for ≤7.0% TRR in chlorophenyl-label straw and for ≤2.1% TRR in triazole-label straw. On further examination of the nonextractable residues of 15-DAT3 straw, only minor amounts of radioactivity were found to have been incorporated into cell wall components (≤3.24% TRR in lignin, pectin, cellulose or polysaccharides).

The metabolic profile in pea seed was significantly different in chlorophenyl- and triazole-label samples. Metconazole was the primary residue identified in chlorophenyl-label pea seed, accounting for 35.7% TRR (0.016 ppm) in 13-DAT2 seed and 21.1% TRR (0.043 ppm) in 15-DAT3 seed. In triazole-label seed, the primary identified residue was TA, accounting for 75.9% TRR (1.188 ppm) in 13-DAT2 seed and 89.1% TRR (3.303 ppm) in 15-DAT3 seed; metconazole was a minor residue, accounting for 3.4% and 2.2% TRR, respectively, in 13-DAT2 and 15-DAT3 seed. In chlorophenyl-label seed, residues characterized as more polar than metconazole accounted for 33.6% TRR (0.015 ppm) in 13-DAT seed and 53.4% TRR (0.108 ppm) in 15-DAT seed, with discrete components present at up to 11.5% TRR (0.005 ppm) and 26.6% TRR (0.054 ppm) at the respective sampling intervals; residues characterized as less polar than metconazole accounted for ≤5.7% TRR. In triazole-label seed, residues characterized as more polar than metconazole accounted for 19.9% TRR (0.311 ppm) in 13-DAT2 seed and 2.7% TRR (0.101 ppm) in 15-DAT3 seed, and residues characterized as less polar than metconazole accounted for ≤0.7% TRR.

Based on the submitted pea metabolism studies, the petitioner proposed that the main metabolic route of metconazole in pea involves oxidative hydroxylation of the methylene groups, the methyl groups on the cyclopentyl ring, and possibly of the cyclopentyl ring itself. The detection of TA as a major metabolite indicates that the methylene group between the triazole and cyclopentyl rings is susceptible to oxidative hydroxylation. The multiple monohydroxylated metabolites and their conjugates represent the various chromatographically distinguishable stereoisomeric structures due to monohydroxylation at the various prochiral carbons of

metconazole. Further oxidation of the hydroxylated metabolites to form dihydroxylated or carboxylated derivatives was not evident in pea. However, it appeared that the monohydroxylated metabolites were at least partly conjugated with glucose to form glucosides as terminal residues in the pea foliage, straw and seed.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the plant metabolism data are classified as scientifically acceptable. The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP#s 348168 and 348206.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an impact on the validity of the study.

A. BACKGROUND INFORMATION

Metconazole [5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1H-1,2,4-triazol-1-ylmethyl)cyclopentanol] is a broad-spectrum triazole Group 3 fungicide (sterol biosynthesis inhibitors). There are currently no registered uses of metconazole in the U.S.; however, a tolerance has been established for banana, and a Section 18 emergency exemption and supporting time-limited tolerances have been granted for use on soybean. Valent U.S.A. Corporation has applied for registration of metconazole in the U.S. for use on peanut, stone fruits, and tree nuts.

The chemical structure and nomenclature of metconazole, and the physicochemical properties of the technical grade of metconazole are presented in Tables A.1 and A.2.

Table A.1. Metconazole Nomenclature.

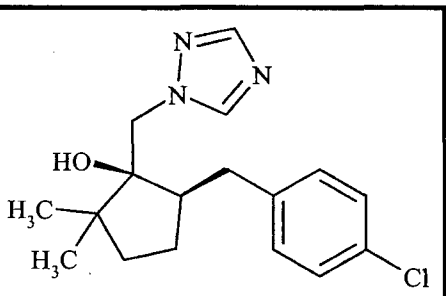
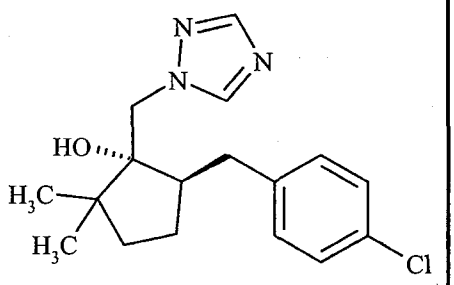
Chemical structure	 *cis*-isomer	 *trans*-isomer
Common name	Metconazole	
Company experimental name	KNF-S-474m (Kureha); BAS 555 F (BASF); V-10116 (Valent)	

Table A.1. Metconazole Nomenclature.	
IUPAC name	(1RS,5RS:1RS,5SR)-5-(4-chlorobenzyl)-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol
CAS name	5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol
CAS registry number	125116-23-6 (*cis*- and *trans*-isomers) 115850-27-6 (*cis*-isomer) 115850-28-7 (*trans*-isomer)
End-use products (EP)	50% WDG (Metconazole 50 WDG Fungicide, EPA File Symbol 59639-RUT) 0.75 lb/gal SC/L (Caramba™ Fungicide, EPA File Symbol No. 7969-EUA) 0.67 lb/gal SC/L formulation (BAS 556 01F Fungicide, EPA File Symbol No. 7969-EUT; also contains the active ingredient pyraclostrobin at 0.83 lb/gal)

Table A.2. Physicochemical Properties of Metconazole					
Parameter	Value				References* (MRID)
Melting point/range	100.0-108.4°C (using Electrothermal Digital Melting Point Apparatus) (AC900,768 technical grade)				44721505
pH	5.81 at 25°C (1% aqueous suspension)				46808402
Relative density (20°C)	1.14 (relative density to water at 4°C, using capillary-stoppered, density-specific gravity bottle) (Lot No. AC 8879-140B)				44721505
Water solubility (20°C)	Using shake-flask method: 18.7 ± 1.0 mg/L (*cis*-isomer, WL148271, KNF-S-474m) 13.6 ± 1.7 mg/L (*trans*-isomer, WL148271, KNF-S-474m)				44721505
Solvent solubility (g/L) at 20°C	Solvent	Metconazole	*cis*	*trans*	44721505
	acetone	363	251	117	
	methanol	403	294	117	
	dichloromethane	481	343	141	
	ethyl acetate	260	173	90.0	
	propanol	132	86.6	46.7	
	toluene	103	66.2	38.0	
	Hexane	1.40	0.929	0.483	
Vapor pressure (20°C)	Using gas-saturation method: $< 1.23 \times 10^{-5}$ Pa or 9.23×10^{-8} mm Hg (metconazole) $< 1.04 \times 10^{-5}$ Pa or 7.80×10^{-8} mm Hg (*cis*-isomer) $< 1.96 \times 10^{-6}$ Pa or 1.47×10^{-8} mm Hg (*trans*-isomer)				44721505
Dissociation constant (pK_a)	11.38±0.03 and 1.06±0.03 (in water at 29.1°C using spectrophotometric method; Lot No. AC 8879-140B)				44721505

Table A.2. Physicochemical Properties of Metconazole

Parameter	Value				References* (MRID)
Octanol/water partition coefficient, Log(K_{OW})	At 20 °C (using flask shaking method): K_{ow} (log K_{ow}) = 7090±989 (3.85) (Lot No. AC 8879-140B) (TGAI) K_{ow} (log K_{ow}) = 7150±803 (3.85) (*cis*-isomer, CL 354,801) K_{ow} (log K_{ow}) = 6800±1700 (3.8) (*trans*-isomer, CL 354,802)				44721505
UV/visible absorption spectrum	pH	λ	A	log ε	46808403
	cis-isomer				
	2.0	221.4	0.828	4.03	
	6.8		0.8452	4.04	
	7.0		0.9126	4.08	
	10.3		0.7226	3.98	
	trans-isomer				
	2.0	221.4	0.9053	4.07	
	7.0		0.9547	4.10	
	10.1		0.9893	4.11	

* Product Chemistry Reviews: DP #256877, Shyam Mathur, Ph.D., 9/12/2000 and DP #329168, Shyam Mathur, Ph.D., 7/13/07.

B. EXPERIMENTAL DESIGN

B.1. Test Site and Crop Information

The field test site was located at Cyanamid Forschung GmbH, in Schwabenheim, Germany. A summary of the test site information is provided in Table B.1.1, and a summary of the crop information is provided in Table B.1.2. Pea plants were grown outdoors in pots placed in surrounding soil to achieve the same soil climatic conditions.

The plots were maintained following normal agricultural practices, and maintenance pesticides and fertilizers were applied as needed. Daily weather conditions (rainfall and temperature) were reported; irrigation was used to supplement rainfall as needed. The petitioner stated that weather conditions during the trial were typical for the area.

Samples of pea foliage were harvested immediately following each application (0 days after treatment 1 (0-DAT1), 0-DAT2, and 0-DAT3), and samples of pea seed and straw were collected 13-DAT2 (green pea) and 15-DAT3 (dry pea). All plants were cut above the ground. After removing the seeds, the empty pods were combined with the straw.

TABLE B.1.1. Test Site Information.

Label	Type	Method	Soil characteristics			
			Type	%OM	pH	CEC
Chlorophenyl Triazole	Foliar Treatment	Two (foliage) or three (seed and straw) broadcast foliar spray applications using a stationary sprayer	Silty Loam	0.88	7.7	21 meq/100 g

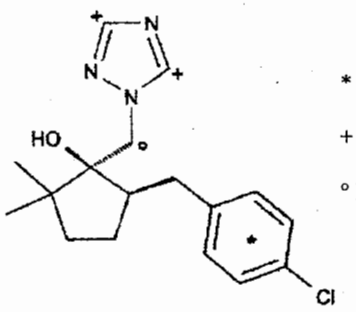
TABLE B.1.2. Crop Information.

Crop; crop group	Variety	Growth stage at application	Growth stage at harvest	Harvested Matrix
Peas	Kleine Rheinlanderin	1: crop cover 2: 13 days following first application 3: 14 days following the second application	Immature	0-DAT1 and 0-DAT2 foliage; whole above ground portion of plant
			BBCH 79	0-DAT3 foliage; whole above-ground portion of plant 13-DAT2 green pea and straw; seeds removed from pods, pods combined with straw
			BBCH 89	15-DAT3 dry pea and straw; seeds removed from pods, pods combined with straw

B.2. Test Materials

The radiolabeled test substances were isotopically diluted with [^{13}C]metconazole and nonlabeled metconazole, then formulated as soluble concentrate formulations and suspended in water. The characteristics of the test substances are presented in Table B.2.1.

TABLE B.2.1. Test Material Characteristics.

Chemical structure	 * Indicates the position of the chlorophenyl ring [^{14}C]-label + Indicates the position of the triazole ring [^{14}C]-label ° Indicates the position of the methylene [^{13}C]-label	
Radiolabel position	[chlorophenyl-U-^{14}C]metconazole	[triazole-3,5-^{14}C]metconazole
Lot No.	AC10727-49	AC10011-137
Purity	98.2%	98.2%
Specific activity – test substance	35.8 µCi/mg	30.86 µCi/mg
Specific activity – application solution	9.99 µCi/mg	10 µCi/mg

B.3. Study Use Pattern

The formulated test substances were applied as two or three broadcast foliar applications to pea plants at ~0.193 lb ai/A/application (~216 g ai/ha/application) beginning at the early crop cover stage. Two applications were made to pea plants grown in one pot for each label to simulate applications to green or canned peas, and three applications were made to pea plants grown in a second pot for each label to simulate application to dry peas. Applications were made at 13- and 14-day retreatment intervals. The total application rates for the chlorophenyl and triazole labels were 0.188 lb ai/A (211.2-210.9 g ai/ha) following one application, 0.371-0.373 lb ai/A (415.8-418.1 g ai/ha) following two applications, and 0.557-0.559 lb ai/A (623.8-626.1 g ai/ha) following three applications. Applications were made using a stationary sprayer. Details of the study use pattern are presented in Table B.3.1.

TABLE B.3.1. Use Pattern Information.

Chemical name	[chlorophenyl-U-^{14}C]metconazole	[triazole-3,5-^{14}C]metconazole
Application method	The isotopically diluted test substance was formulated as a soluble concentrate formulation and applied as two or three broadcast foliar applications using a stationary sprayer.	
Application rate	One application: 0.188 lb ai/A (211.2 g ai/ha) Two applications: 0.371 lb ai/A (415.8 g ai/ha) Three applications: 0.557 lb ai/A (623.8 g ai/ha)	One application: 0.188 lb ai/A (210.9 g ai/ha) Two applications: 0.373 lb ai/A (418.1 g ai/ha) Three applications: 0.559 lb ai/A (626.1 g ai/ha)
Number of applications	Two or three applications	
Timing of applications	Application 1: crop cover Application 2: 13 days following first application Application 3: 14 days following the second application	
PHI	Foliage: 0 days after each application (0-DAT1, 0-DAT2, and 0-DAT3) Green pea and straw: 13 days after second application (13-DAT2) Dry pea and straw: 15 days after third application (15-DAT3)	

B.4. Identification/Characterization of Residues

B.4.1. Sample Handling and Preparation

Harvested samples were placed in freezers (-18 °C) at the field site within 6 hours of completion of sampling, and were shipped frozen to the analytical laboratory, PTRL Europe (Ulm, Germany). At the analytical laboratory, samples were stored at -18 °C prior to preparation for analysis. Samples of pea foliage, straw, and seed were prepared for extraction by grinding following submersion in liquid nitrogen. The prepared samples were stored frozen prior to analysis.

Samples of 0-DAT1 and 0-DAT2 foliage were surface extracted with acetone:water (7:3, v:v). The plant materials were then cut into small pieces and extracted with acetone followed by acetone:MeOH:water (1:1:1, v:v:v). Samples of 0-DAT3 foliage, and straw and pea seed from both sampling intervals were surface extracted (except pea seed) with acetone:water (7:3, v:v), then cut into small pieces and sequentially extracted with acetone (2x), MeOH:water (4:1, v:v; 2x), and water (2x). Like extracts were combined.

The nonextractable residues of straw from both sampling intervals and labels were subjected to sequential extraction/hydrolysis with: (1) 0.1 M HCl (at room temperature for 30 minutes); (2) ACN:1 M HCl at (reflux for 20 hours); and (3) 6 M HCl (at reflux for 20 hours). A separate subsample of the nonextractable residues of 15-DAT3 straw (both labels) was subjected to extraction of cell wall components according to the following sequential procedures: (1) extraction of water-soluble polysaccharides and proteins using water:MeOH (350:2.5, v:v); (2) extraction of pectic substances using a 1% solution of sodium ethylenediaminetetraacetic acid (Na_2EDTA) or treatment with pectinase; (3) extraction of lignin using dimethyl sulfoxide (DMSO; 2x); (4) extraction of noncellulosic polysaccharides using 33% ammonium hydroxide solution; and (5) extraction of cellulose using Schweizer's reagent.

Representative flow charts for foliage, seed, and straw are presented below. The flow charts were copied without alteration from MRID 46901906.

Figure B.4.1.1. Extraction Flowchart for 0-DAT1 Pea Foliage (Chlorophenyl label)

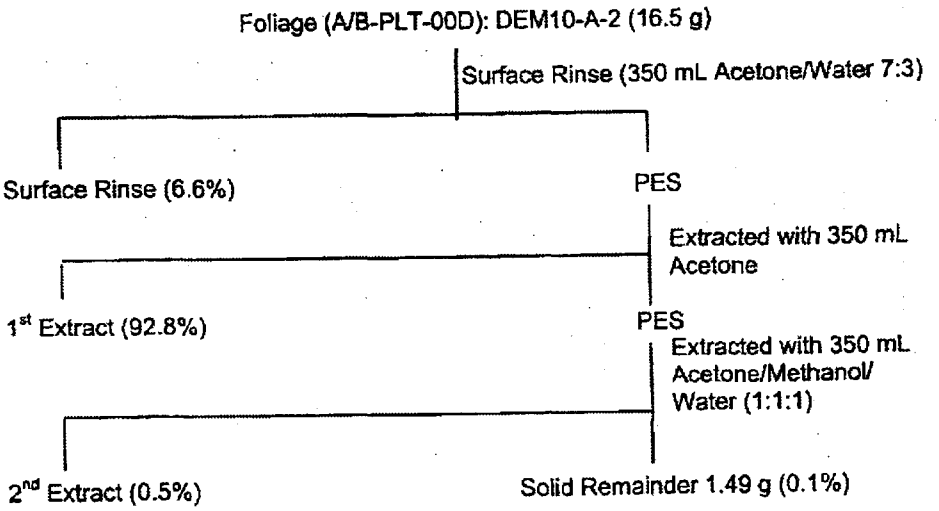


Figure B.4.1.2. Extraction Flowchart for 0-DAT3 Pea Foliage (Chlorophenyl label)

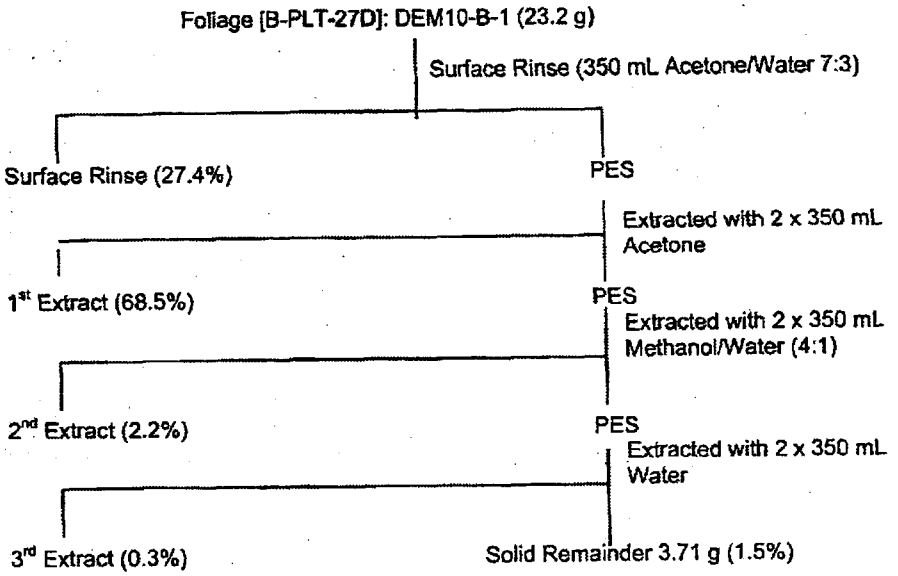


Figure B.4.1.3. Extraction Flowchart for 15-DAT3 Pea Straw (Chlorophenyl label)

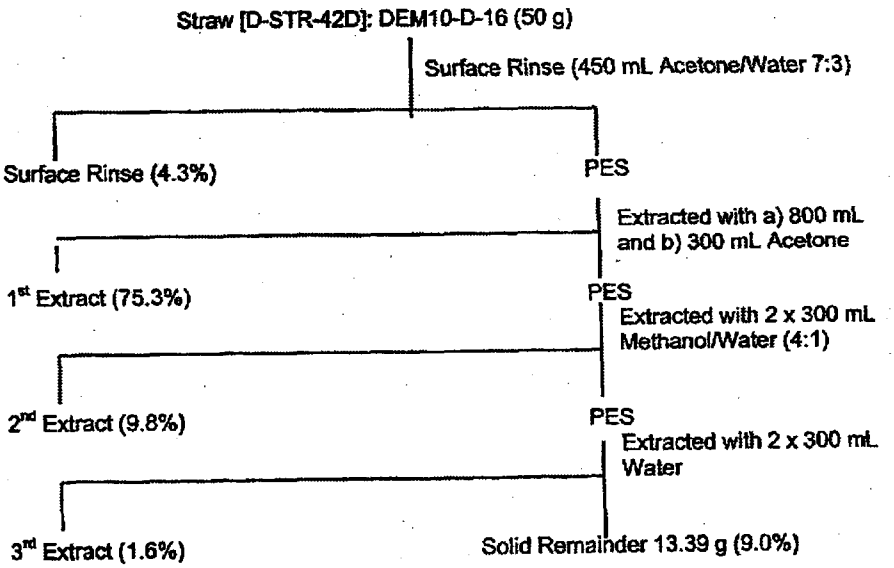


Figure B.4.1.3 (cont'd). Extraction Flowchart for 15-DAT3 Pea Straw (Chlorophenyl label)

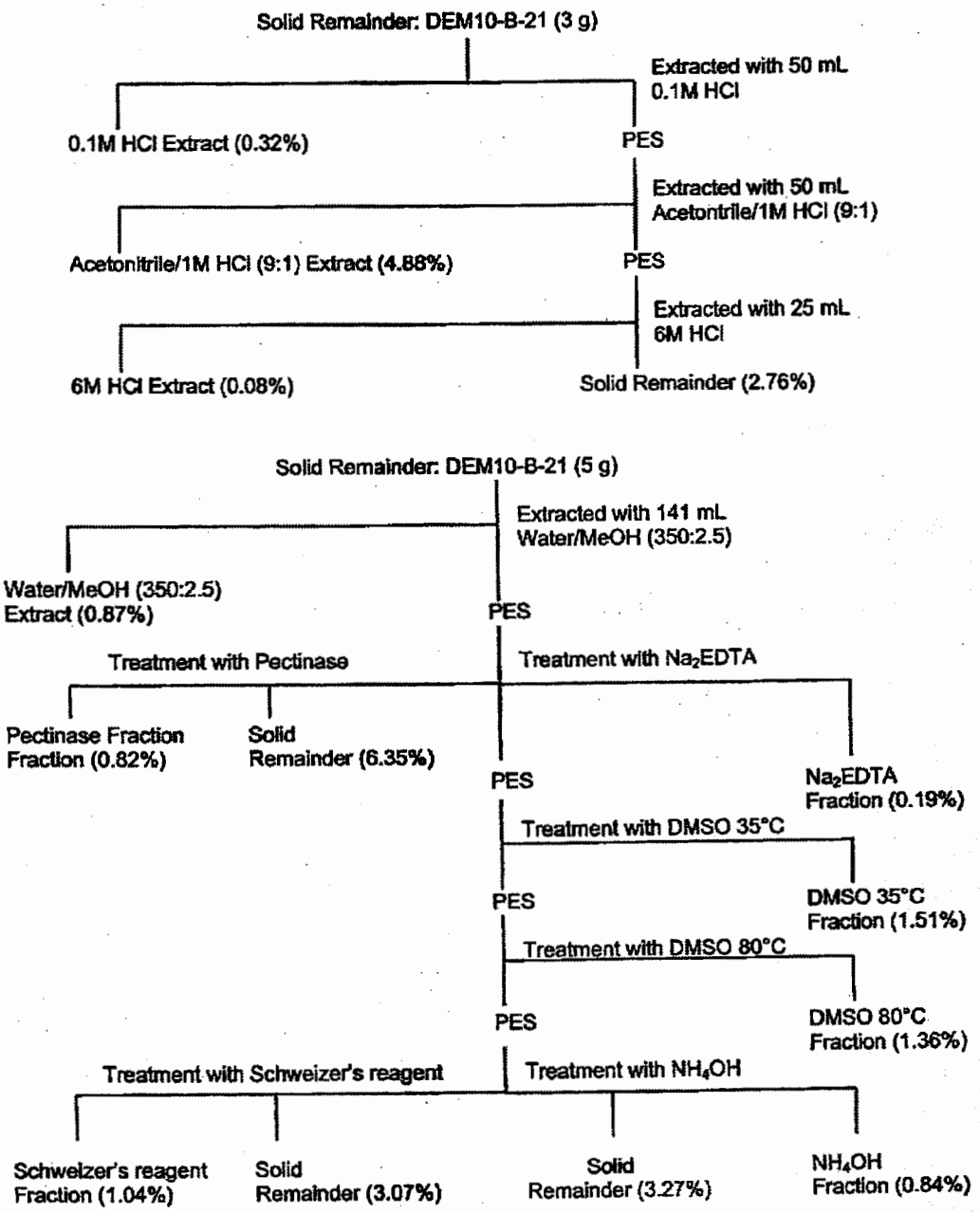
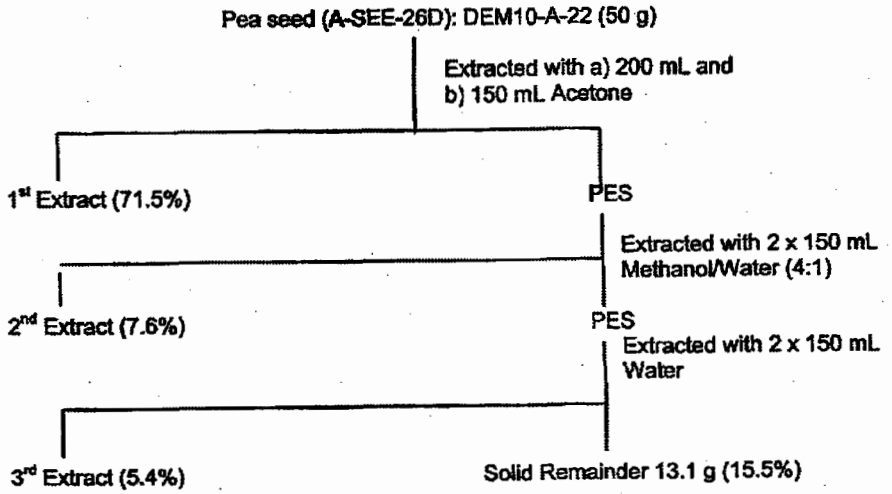


Figure B.4.1.4. Extraction Flowchart for 13-DAT2 Pea Seed (Chlorophenyl label)



B.4.2. Analytical Methodology

TRR were determined in samples and nonextractable residues by combustion/liquid scintillation counting (LSC). TRR in extracts were determined by LSC. The reported limits of detection for TRR determinations were 0.003-0.004 ppm for foliage, straw, and seed.

Extracts containing sufficient radioactivity were subjected to TLC and/or HPLC analysis. TLC analysis was conducted on precoated silica gel plates, using a solvent system of dichloromethane:acetone (1:1; v:v). HPLC analysis was carried out on a system equipped with a reverse phase C18 column, a UV detector, and an in-line radioactivity detector, and using a mobile phase of ACN/MeOH/water/acetic acid. Metconazole was identified by TLC co-chromatography and retention time comparisons with known reference standards on HPLC System I, and TA was identified by TLC co-chromatography; the reference standards used in the study are listed in Appendix I.

Isolated components from straw samples were subjected to LC/MS/MS analysis following further extraction with HCl on a system equipped with a C18 column, using a gradient mobile phase of ACN/MeOH/water/acetic acid in water and electrospray ionization.

To investigate the presence of metconazole conjugates, the MeOH/water extracts of straw were subjected to acid hydrolysis with 1 M HCl (at reflux for 5 hours) or enzyme hydrolysis with β-glucosidase (in acetate buffer, pH 5, at 37 °C for 24 hours) followed by partitioning with ethyl acetate.

C. RESULTS AND DISCUSSION

The storage conditions and intervals for peas are presented in Table C.1. The petitioner provided the dates of sampling, extraction, and initial and final analysis for all samples. Samples of pea foliage and straw were extracted and analyzed within 3 months of harvest; extracts of pea seed were stored for up to 7.6 months prior to analysis. No storage stability data were submitted in support of the study. Because samples of pea foliage and straw were analyzed within 3 months of harvest, no additional data are required. Storage stability data are available from the canola metabolism study indicating that the metabolic profile was stable in the MeOH and MeOH/water extracts of canola pod and seed, respectively, for up to ~7.5 months for pod and ~7.3 months for seed (refer to 46901904.der.doc). These data are acceptable to support the storage intervals for pea seed extracts.

TRR in pea matrices, calculated by summing radioactivity in extractable and unextractable residues and by combustion/LSC, are reported in Table C.2.1. Following two or three broadcast foliar applications of [chlorophenyl-U-^{14}C]metconazole or [triazole-3,5-^{14}C]metconazole, TRR, calculated by summing radioactivity in surface washes and extractable and nonextractable residues in chlorophenyl-label samples were 8.77, 6.09, and 8.42 ppm for 0-DAT1, 0-DAT2, and 0-DAT3 foliage, 7.85 ppm and 60.26 ppm for 13-DAT2 and 15-DAT3 straw, and 0.044 ppm and 0.203 ppm for 13-DAT2 and 15-DAT3 seed. In triazole-label samples TRR were 10.63, 8.70, and 11.09 ppm for 0-DAT1, 0-DAT2, and 0-DAT3 foliage, 12.03 and 49.11 ppm for 13-DAT2 and 15-DAT3 straw, and 1.57 and 3.71 ppm for 13-DAT2 and 15-DAT3 seed.

The distribution of radioactivity in pea matrices is presented in Tables C.2.2.1, C.2.2.2, and C.2.2.3 (chlorophenyl-label foliage, straw, and seed) and C.2.2.4, C.2.2.5, and C.2.2.6 (triazole-label foliage, straw, and seed). Samples of pea foliage and straw were initially rinsed with acetone, which removed 6.6-40.1% TRR (0.580-3.491 ppm) and 2.7-4.9% TRR (0.213-2.95 ppm) for foliage and straw, respectively. Extraction with acetone released the majority of the radioactivity from all samples of pea foliage and straw: 52.2-92.8% TRR (3.461-9.280 ppm) for 0-DAT1, 0-DAT2, and 0-DAT3 foliage, and 74.7-89.2% TRR (7.003-44.99 ppm) for 13-DAT2 and 15-DAT3 straw. Acetone also released the majority of radioactivity from seed treated with the chlorophenyl label, 47.9-71.5% TRR (0.031-0.097 ppm); extraction with acetone released ≤10.9% TRR from triazole-label seed. The majority of radioactivity in seed treated with the triazole label was released by extraction with MeOH/water, 50.9-77.7% TRR (1.218-1.888 ppm); in chlorophenyl-label samples, extraction with MeOH/water released 7.6% TRR from 13-DAT2 seed and 32.4% TRR from 15-DAT3 seed. Remaining residues were released by extraction with acetone/MeOH/water for foliage (up to 8.3% TRR), with MeOH/water and water for straw (up to 10.9% TRR), and with water for seed (up to 39.5% TRR). These procedures adequately extracted the majority of residues from pea matrices. Nonextractable residues following extraction were ≤3.4% TRR (≤0.295 ppm) in foliage, ≤2.8% TRR (≤1.663 ppm) in straw, and ≤15.5% TRR (≤0.198 ppm) in seed. Because TRR were calculated by summation, accountabilities for all matrices were at or near 100%. When TRR determined by summation were compared with TRR determined by combustion/LSC, accountabilities ranged from 40 to 171%.

The characterization and identification of residues in pea matrices are summarized in Tables C.2.3.1, C.2.3.2, and C.2.3.3 (chlorophenyl-label foliage, straw, and seed), and C.2.3.4, C.2.3.5, and C.2.3.6 (triazole-label foliage, straw, and seed). Metconazole was identified and confirmed by TLC and/or HPLC co-chromatography in pea matrices, and TA was identified in the MeOH/water extracts of triazole-label pea seed by TLC co-chromatography. All remaining components were initially characterized as more or less polar than metconazole based on relative elution by TLC. Radioactivity was separated into regions of interest (ROIs), which consisted of either discrete components or diffuse areas of relatively low radioactivity delineated by discrete components. For further characterization of remaining residues, the petitioner conducted extensive analysis of 15-DAT3 pea straw. The surface rinses and extracts of pea straw were initially investigated by TLC, then aliquots of the surface rinses and extracts were combined for further analysis by HPLC. A less polar metabolite observed in chlorophenyl-label straw from both sampling intervals (13-DAT2 and 15-DAT3) was determined to be the result of cleavage of the triazole moiety because it did not appear in triazole-label samples. The metabolite did not co-chromatograph with any reference standard, and further investigation via LC/MS/MS was unsuccessful because of its low concentration. Metabolites characterized as more polar than metconazole were further characterized in straw by TLC, HPLC, and LC/MS/MS analysis following acid and β-glucosidase hydrolysis as monohydroxylated metconazole and glucoside conjugates of monohydroxylated metconazole; no quantitative data were provided. Metabolites in pea foliage and seed were characterized as several isomers of monohydroxylated metconazole and corresponding glucose conjugates based on comparison of TLC chromatographic results with those of 15-DAT3 straw. No further attempts were made to characterize/identify residues of metconazole in peas.

The metabolic profile was similar in pea foliage and straw from both labels. Metconazole was the primary residue identified in all samples of foliage and straw, accounting for 94.1% and 95.9% TRR (8.251 and 10.201 ppm) in 0-DAT1 foliage, 78.7% and 78.8% TRR (4.796 and 6.858 ppm) in 0-DAT2 foliage, and 79.3% and 66.7% TRR (6.675 and 7.401 ppm) in 0-DAT3 foliage from chlorophenyl- and triazole-label samples, respectively. The majority of remaining residues were characterized as more polar than metconazole, accounting for 5.3%, 16.4%, and 15.6% TRR (0.461, 1.008, and 1.311 ppm) in 0-DAT1, 0-DAT2, and 0-DAT3 chlorophenyl-label foliage, and for 3.45%, 16.8%, and 29.5% TRR (0.362, 1.453, and 3.279 ppm) in triazole-label foliage. Residues characterized as less polar than metconazole accounted for ≤3.4% TRR in chlorophenyl-label foliage and ≤1.0% TRR in triazole-label foliage.

Metconazole was generally identified at lower levels in straw, accounting for 58.7% and 54.1% TRR (4.603 and 32.585 ppm), respectively, in 13-DAT2 and 15-DAT3 chlorophenyl-label straw, and for 64.9% and 67.6% TRR (7.804 and 33.219 ppm), respectively, in 13-DAT2 and 15-DAT3 triazole-label straw. Residues characterized as more polar than metconazole accounted for 30.2% and 31.0% TRR (2.370 and 18.679 ppm), respectively, in 13-DAT2 and 15-DAT3 chlorophenyl-label straw, and for 27.3% and 22.9% TRR (3.298 and 11.203 ppm), respectively, in 13-DAT2 and 15-DAT3 triazole-label straw. Residues characterized as less polar than metconazole accounted for ≤7.0% TRR in chlorophenyl-label straw and for ≤2.1% TRR in triazole-label straw. On further examination of the nonextractable residues of 15-DAT3 straw,

only minor amounts of radioactivity were found to have been incorporated into cell wall components (≤3.24% TRR in lignin, pectin, cellulose or polysaccharides).

The metabolic profile in pea seed was significantly different in chlorophenyl- and triazole-label samples. Metconazole was the primary residue identified in chlorophenyl-label pea seed, accounting for 35.7% TRR (0.016 ppm) in 13-DAT2 seed and 21.1% TRR (0.043 ppm) in 15-DAT3 seed. In triazole-label seed, the primary identified residue was TA, accounting for 75.9% TRR (1.188 ppm) in 13-DAT2 seed and 89.1% TRR (3.303 ppm) in 15-DAT3 seed; metconazole was a minor residue, accounting for 3.4% and 2.2% TRR, respectively, in 13-DAT2 and 15-DAT3 seed. In chlorophenyl-label seed, residues characterized as more polar than metconazole accounted for 33.6% TRR (0.015 ppm) in 13-DAT seed and 53.4% TRR (0.108 ppm) in 15-DAT seed, with discrete components present at up to 11.5% TRR (0.005 ppm) and 26.6% TRR (0.054 ppm) at the respective sampling intervals; residues characterized as less polar than metconazole accounted for ≤5.7% TRR. In triazole-label seed, residues characterized as more polar than metconazole accounted for 19.9% TRR (0.311 ppm) in 13-DAT2 seed and 2.7% TRR (0.101 ppm) in 15-DAT3 seed, and residues characterized as less polar than metconazole accounted for ≤0.7% TRR.

C.1. Storage Stability

The petitioner provided the dates of sampling, extraction, and initial and final analysis for all samples. The storage conditions and intervals for pea matrices are presented in Table C.1. Samples were extracted shortly after harvest, and extracts were stored frozen prior to analysis. Samples of pea foliage and straw were extracted and analyzed within 3 months of harvest; extracts of pea seed were stored for up to 7.6 months prior to analysis.

No storage stability data were submitted in support of the study. Because samples of pea foliage and straw were analyzed within 3 months of harvest, no additional data are required. Storage stability data are available from the canola metabolism study indicating that the metabolic profile was stable in the MeOH and MeOH/water extracts of canola pod and seed, respectively, for up to ~7.5 months for pod and ~7.3 months for seed (refer to 46901904.der.doc). These data are acceptable to support the storage intervals for pea seed extracts.

TABLE C.1. Summary of Storage Conditions.

Matrix	Storage Temperature (°C)	Actual Storage Duration[1] Days (Months)		Interval of Demonstrated Storage Stability
		Chlorophenyl	Triazole	
Foliage	< -18	12-71 (0.4-2.3)	12-77 (0.4-2.5)	None submitted
Straw		84-89 (2.8-2.9)	80-89 (2.6-2.9)	
Seed		231-244 (7.6-8.0)	217-232 (7.1-7.6)	The metabolic profile was stable in MeOH and MeOH/water extracts of canola pod and seed, respectively, for up to ~7.5 months for pod and ~7.3 months for seed.[2]

[1] Interval from harvest to analysis; samples were analyzed within 72, 76, and 230 days of extraction for samples of foliage, straw, and seed, respectively.
[2] Refer to 46901904.der.doc.

C.2. Identification, Characterization, and Distribution of Residues

TABLE C.2.1. Total Radioactive Residues (TRR) in Pea Matrices.

Matrix	No. of applications	PHI (days)	Application Rate (lb ai/a)	Chlorophenyl label (ppm)		Triazole label (ppm)	
				Summation[1]	Combustion	Summation	Combustion
0-DAT1 Foliage	1	0	0.188	8.77	5.13	10.63	9.58
0-DAT2 Foliage	2	13	0.371-0.373	6.09	12.85	8.70	5.38
0-DAT3 Foliage	2	13	0.557-0.559	8.42	21.28	11.09	20.76
13-DAT2 Straw	2	13	0.371-0.373	7.85	9.94	12.03	10.20
15-DAT3 Straw	3	15	0.557-0.559	60.26	168.2	49.11	63.38
13-DAT2 Seed	2	13	0.371-0.373	0.044	0.038	1.57	1.62
15-DAT3 Seed	3	15	0.557-0.559	0.203	0.226	3.71	3.92

[1] Calculated by summing residues in the surface rinse and extractable and nonextractable radioactivity; summed TRR values were used for all further determinations.

TABLE C.2.2.1 Distribution of the Parent and the Metabolites in Pea Foliage Following Application of [chlorophenyl-U-^{14}C]Metconazole at ~0.193 lb ai/A/application. [1]

Metabolite Fraction[2]	0-DAT1 Foliage		0-DAT2 Foliage		0-DAT3 Foliage	
	TRR = 8.77 ppm		TRR = 6.09 ppm		TRR = 8.42 ppm	
	%TRR	ppm	%TRR	ppm	%TRR	ppm
Acetone/water surface wash	6.6	0.580	39.2	2.386	27.4	2.310
ROI 1	0.7	0.065	3.6	0.222	1.1	0.097
ROI 2	0.3	0.023	1.7	0.104	0.8	0.064
Metconazole	5.6	0.491	32.7	1.992	25.1	2.113
ROI 4	<0.1	0.001	1.1	0.069	0.4	0.037
Acetone extract	92.8	8.137	56.8	3.461	68.5	5.769
ROI 1	2.7	0.234	8.7	0.533	8.4	0.705
ROI 2	1.6	0.139	1.4	0.085	3.6	0.304
Metconazole	88.5	7.76	45.4	2.766	53.7	4.517
ROI 4	<0.1	0.002	0.3	0.016	0.5	0.038
ROI 5	--	--	0.9	0.052	2.4	0.204
ROI 6	--	--	0.1	0.009	--	--
Acetone/MeOH/water extract	0.5	0.043	1.8	0.111	2.2	0.187
ROI 1			0.8	0.050	1.5	0.127
ROI 2			0.2	0.014	0.2	0.014
Metconazole			0.6	0.038	0.5	0.045
ROI 4			0.2	0.009	<0.1	<0.001
Aqueous extract					0.3	0.029
Unextractable	0.1	0.012	2.2	0.137	1.5	0.123

[1] Shading indicates that the extraction step and/or characterization analysis was not conducted for the matrix in question.
[2] ROIs presented based on polarity relative to metconazole, with ROI 1 more polar than metconazole.

TABLE C.2.2.2 Distribution of the Parent and the Metabolites in Pea Straw Following Application of [chlorophenyl-U-^{14}C]Metconazole at ~0.193 lb ai/A/application. [1]

Metabolite Fraction[2]	13-DAT2 Straw		15-DAT3 Straw	
	TRR = 7.85 ppm		TRR = 60.26 ppm	
	%TRR	ppm	%TRR	ppm
Acetone/water surface wash	2.7	0.213	4.9	2.950
ROI 1	0.5	0.040	1.1	0.680
ROI 2	0.2	0.018	0.4	0.228
ROI 3 (15-DAT3)	--	--	0.3	0.171
Metconazole	1.9	0.146	3.0	1.803
ROI 4 (13-DAT2)/ROI 5 (15-DAT3)	0.1	0.008	<0.1	0.001
ROI 5 (13-DAT2)/ROI 6 (15-DAT3) 1	<0.1	0.002	0.1	0.063
ROI 7	--	--	<0.1	0.004
Acetone extract	89.2	7.003	74.7	44.99
ROI 1	24.1	1.896	9.1	5.480
ROI 2	1.2	0.090	4.1	2.493
ROI 3	2.2	0.173	4.3	2.619
Metconazole	56.3	4.423	50.5	30.43
ROI 5	0.2	0.014	1.2	0.697
ROI 6	5.2	0.407	4.9	2.938
ROI 7	--	--	0.6	0.337
MeOH/water extract	1.9	0.153	10.9	6.574
ROI 1	1.4	0.110	10.1	6.061
ROI 2	0.1	0.008	0.3	0.159
ROI 3 (13-DAT2)	0.1	0.007	--	--
Metconazole	0.4	0.028	0.6	0.352
ROI 5 (13-DAT2)/ROI 4 (15-DAT3)	<0.1	<0.001	<0.1	0.001
Aqueous extract	0.4	0.035	1.5	0.892
ROI 1	0.3	0.022	1.2	0.717
ROI 2	0.1	0.006	0.1	0.071
ROI 3 (15-DAT3)	--	--	0.2	0.093
Metconazole	0.1	0.006	--	--
ROI 4	<0.1	<0.001	<0.1	0.011
Unextractable subsample 1 (SS1)	5.7	0.449	8.0	4.845
0.1 M HCl	0.18	0.014	0.32	0.193
ACN/1 M HCl	4.13	0.324	4.88	2.941
6 M HCl	0.07	0.005	0.08	0.048
Unextractable	1.34	0.105	2.76	1.663
Unextractable subsample 2 (SS2)			8.0	4.845
Water/MeOH (water soluble polysaccharides)			0.87	0.524
Unextractable SS2-1			NR	NR
Pectinase (pectin)			0.82	0.494
Unextractable			6.35	3.827
Unextractable SS2-2			NR	NR
Na_2EDTA (pectin)			0.19	0.114
DMSO (lignin)			2.87	1.730

TABLE C.2.2.2 Distribution of the Parent and the Metabolites in Pea Straw Following Application of [chlorophenyl-U-^{14}C]Metconazole at ~0.193 lb ai/A/application. [1]

Metabolite Fraction[2]	13-DAT2 Straw		15-DAT3 Straw	
	TRR = 7.85 ppm		TRR = 60.26 ppm	
	%TRR	ppm	%TRR	ppm
Unextractable SS2-2a			NR	NR
NH_4OH (noncellulose polysaccharides)			0.84	0.506
Unextractable			3.27	1.971
Unextractable SS2-2b			NR	NR
Schweizer's reagent (cellulose)			1.04	0.627
Unextractable			3.07	1.850

[1] Shading indicates that the extraction step and/or characterization analysis was not conducted for the matrix in question.
[2] ROIs presented based on polarity relative to metconazole, with ROI 1 more polar than metconazole.

TABLE C.2.2.3 Distribution of the Parent and the Metabolites in Pea Seed Following Application of [chlorophenyl-U-^{14}C]Metconazole at ~0.193 lb ai/A/application. [1]

Metabolite Fraction[2]	13-DAT2 Seed		15-DAT3 Seed	
	TRR = 0.044 ppm		TRR = 0.203 ppm	
	%TRR	ppm	%TRR	ppm
Acetone extract	71.5	0.031	47.9	0.097
ROI 1	11.5	0.005	17.1	0.035
ROI 2	22.1	0.010	7.5	0.015
Metconazole	35.7	0.016	21.1	0.043
ROI 4	2.1	0.001	2.1	0.004
MeOH/water extract	7.6	0.003	32.4	0.066
ROI 1			26.6	0.054
ROI 2			2.2	0.004
ROI 3			3.6	0.007
Aqueous extract	5.4	0.002	8.0	0.016
Unextractable	15.5	0.007	11.8	0.024

[1] Shading indicates that the extraction step and/or characterization analysis was not conducted for the matrix in question.
[2] ROIs presented based on polarity relative to metconazole, with ROI 1 more polar than metconazole.

TABLE C.2.2.4 Distribution of the Parent and the Metabolites in Pea Foliage Following Application of [triazole-3,5-^{14}C]Metconazole at ~0.193 lb ai/A/application. [1]

Metabolite Fraction[2]	0-DAT1 Foliage		0-DAT2 Foliage		0-DAT3 Foliage	
	TRR = 10.63 ppm		TRR = 8.70 ppm		TRR = 11.09 ppm	
	%TRR	ppm	%TRR	ppm	%TRR	ppm
Acetone/water surface wash	12.0	1.273	40.1	3.491	15.4	1.705
ROI 1	0.3	0.028	2.5	0.214	5.3	0.590
ROI 2	0.2	0.021	1.3	0.110	0.3	0.032
Metconazole	11.4	1.215	35.7	3.110	9.7	1.078
ROI 4	0.1	0.008	0.6	0.056	0.1	0.006
Acetone extract	87.3	9.281	52.2	4.543	73.1	8.114
ROI 1	1.1	0.116	7.7	0.667	13.9	1.540
ROI 2	1.7	0.181	2.1	0.180	2.3	0.258
Metconazole	84.1	8.94	42.1	3.661	56.5	6.263

TABLE C.2.2.4 Distribution of the Parent and the Metabolites in Pea Foliage Following Application of [triazole-3,5-^{14}C]Metconazole at ~0.193 lb ai/A/application. [1]

Metabolite Fraction[2]	0-DAT1 Foliage		0-DAT2 Foliage		0-DAT3 Foliage	
	TRR = 10.63 ppm		TRR = 8.70 ppm		TRR = 11.09 ppm	
	%TRR	ppm	%TRR	ppm	%TRR	ppm
ROI 4	0.4	0.044	0.4	0.035	0.5	0.052
Acetone/MeOH/water extract	0.6	0.064	4.3	0.373	8.3	0.925
ROI 1	0.1	0.011	3.0	0.264	7.4	0.822
ROI 2	0.05	0.005	0.2	0.018	0.3	0.037
Metconazole	0.4	0.046	1.0	0.087	0.5	0.060
ROI 4	<0.1	0.002	<0.1	0.003	<0.1	0.005
Aqueous extract					0.5	0.059
Unextractable	0.1	0.013	3.4	0.295	2.6	0.291

[1] Shading indicates that the extraction step and/or characterization analysis was not conducted for the matrix in question.
[2] ROIs presented based on polarity relative to metconazole, with ROI 1 more polar than metconazole.

TABLE C.2.2.5 Distribution of the Parent and the Metabolites in Pea Straw Following Application of [[triazole-3,5-^{14}C]Metconazole at ~0.193 lb ai/A/application. [1]

Metabolite Fraction[2]	13-DAT2 Straw		15-DAT3 Straw	
	TRR = 12.03 ppm		TRR = 49.11 ppm	
	%TRR	ppm	%TRR	ppm
Acetone/water surface wash	3.1	0.374	4.3	2.107
ROI 1	0.6	0.068	1.3	0.627
ROI 2	0.2	0.029	0.3	0.139
Metconazole	2.3	0.276	2.7	1.339
ROI 4	<0.1	0.001	<0.1	0.001
Acetone extract	85.5	10.28	75.3	37.00
ROI 1	19.0	2.290	5.9	2.909
ROI 2	1.3	0.155	5.1	2.494
ROI 3	2.9	0.346	--	--
Metconazole	61.9	7.443	64.1	31.50
ROI 5 (13-DAT2)/ROI 4 (15-DAT3)	0.4	0.043	0.2	0.100
MeOH/water extract	3.5	0.422	9.8	4.797
ROI 1	2.4	0.291	8.3	4.075
ROI 2	0.3	0.042	0.6	0.308
Metconazole	0.6	0.072	0.8	0.380
ROI 4	--	--	0.1	0.034
ROI 5	0.1	0.012	--	--
ROI 6	<0.1	0.006	--	--
Aqueous extract	0.8	0.091	1.6	0.769
ROI 1	0.5	0.064	1.2	0.576
ROI 2	0.1	0.013	0.2	0.075
Metconazole	0.1	0.013	--	--
ROI 4 (13-DAT2)/ROI 3 (15-DAT3)	<0.1	0.001	0.2	0.100
ROI 4 (15-DAT3)	--	--	<0.1	0.018
Nonextractable subsample 1 (SS1)	7.2	0.862	9.0	4.434
0.1 M HCl	0.18	0.022	0.31	0.152

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TABLE C.2.2.5 Distribution of the Parent and the Metabolites in Pea Straw Following Application of [[triazole-3,5-^{14}C]Metconazole at ~0.193 lb ai/A/application. [1]

Metabolite Fraction[2]	13-DAT2 Straw		15-DAT3 Straw	
	TRR = 12.03 ppm		TRR = 49.11 ppm	
	%TRR	ppm	%TRR	ppm
ACN/1 M HCl	5.01	0.603	6.32	3.104
6M HCl	0.20	0.024	0.32	0.157
Unextractable	1.78	0.214	2.08	1.021
Nonextractable subsample 2 (SS2)			9.0	4.434
Water/MeOH (water soluble polysaccharides)			0.77	0.378
Unextractable SS2-1			NR[3]	NR
Pectinase (pectin)			0.68	0.334
Unextractable			7.58	3.723
Unextractable SS2-2			NR	NR
Na_2EDTA (pectin)			0.15	0.074
DMSO (lignin)			3.24	1.591
Unextractable SS2-2a			NR	NR
NH_4OH (noncellulose polysaccharides)			1.01	0.496
Unextractable			3.86	1.896
Unextractable SS2-2b			NR	NR
Schweizer's reagent (cellulose)			1.16	0.570
Unextractable			3.71	1.822

[1] Shading indicates that the extraction step and/or characterization analysis was not conducted for the matrix in question.
[2] ROIs presented based on polarity relative to metconazole, with ROI 1 more polar than metconazole.
[3] NR = Not reported

TABLE C.2.2.6 Distribution of the Parent and the Metabolites in Pea Seed Following Application of [triazole-3,5-^{14}C]Metconazole at ~0.193 lb ai/A/application.

Metabolite Fraction[1]	13-DAT2 Seed		15-DAT3 Seed	
	TRR = 1.57 ppm		TRR = 3.71 ppm	
	%TRR	ppm	%TRR	ppm
Acetone extract	10.9	0.171	4.3	0.159
ROI 1	4.3	0.067	1.3	0.048
ROI 2	3.2	0.050	0.3	0.010
ROI 3 (15-DAT3)	--	--	0.4	0.016
Metconazole	3.4	0.053	2.2	0.081
ROI 4 (13-DAT2) ROI 5 (15-DAT3)	<0.1	<0.001	0.1	0.003
MeOH/water extract	77.7	1.218	50.9	1.888
TA	75.9	1.188	50.2	1.861
ROI 2	1.9	0.029	0.7	0.027
Aqueous extract	10.9	0.171	39.5	1.464
ROI 1	10.5	0.165	38.9	1.442
ROI 2	0.4	0.006	0.6	0.021
Unextractable	0.5	0.008	5.3	0.198

[1] ROIs presented based on polarity relative to metconazole, with ROI 1 more polar than metconazole.

TABLE C.2.3.1 Summary of Characterization and Identification of Radioactive Residues in Pea Foliage Matrices Following Application of [chlorophenyl-U-^{14}C]Metconazole at ~0.193 lb ai/A/application.

Compound	0-DAT1 Foliage		0-DAT2 Foliage		0-DAT3 Foliage	
	TRR = 8.77 ppm		TRR = 6.09 ppm		TRR = 8.42 ppm	
	%TRR	ppm	%TRR	ppm	%TRR	ppm
Metconazole	94.1	8.251	78.7	4.796	79.3	6.675
More polar than metconazole	5.3	0.461	16.4	1.008	15.6	1.311
Less polar than metconazole	<0.1	0.003	2.6	0.155	3.4	0.280
Aqueous/organosoluble	0.5	0.043	--	--	0.3	0.029
Total identified	94.1	8.251	78.7	4.796	79.3	6.675
Total characterized	5.8	0.507	19.0	1.163	19.3	1.620
Total extractable	99.9	8.763	97.8	5.958	98.4	8.294
Unextractable (PES)[1]	0.1	0.012	2.2	0.137	1.5	0.123
Accountability[2]	100		100		100	

[1] Residues remaining after exhaustive extractions.
[2] Accountability = Total extractable + Total unextractable.

TABLE C.2.3.2 Summary of Characterization and Identification of Radioactive Residues in Pea Straw Matrices Following Application of [chlorophenyl-U-^{14}C]Metconazole at ~0.193 lb ai/A/application.

Compound	13-DAT2 Straw		15-DAT3 Straw	
	TRR = 7.85 ppm		TRR = 60.26 ppm	
	%TRR	ppm	%TRR	ppm
Metconazole	58.7	4.603	54.1	32.585
More polar than metconazole	30.2	2.370	31.0	18.679
Less polar than metconazole	5.8	0.433	7.0	4.145
Acid hydrolyzed	4.5	0.792	5.3	3.182
Total identified	58.7	4.603	54.1	32.585
Total characterized	40.5	3.595	43.3	26.006
Total extractable	99.9	7.853	100.0	60.251
Unextractable (PES)[1]	1.3	0.105	2.8	1.663
Accountability[2]	101.2		102.8	

[1] Residues remaining after exhaustive extractions.
[2] Accountability = Total extractable + Total unextractable.

TABLE C.2.3.3 Summary of Characterization and Identification of Radioactive Residues in Pea Seed Matrices Following Application of [chlorophenyl-U-^{14}C]Metconazole at ~0.193 lb ai/A/application.

Compound	13-DAT2 Seed		15-DAT3 Seed	
	TRR = 0.044 ppm		TRR = 0.203 ppm	
	%TRR	ppm	%TRR	ppm
Metconazole	35.7	0.016	21.1	0.043
More polar than metconazole	33.6	0.015	53.4	0.108
Less polar than metconazole	2.1	0.001	5.7	0.011
Aqueous/organosoluble	13.0	0.005	8.0	0.016
Total identified	35.7	0.016	21.1	0.043

TABLE C.2.3.3 Summary of Characterization and Identification of Radioactive Residues in Pea Seed Matrices Following Application of [chlorophenyl-U-^{14}C]Metconazole at ~0.193 lb ai/A/application.

Compound	13-DAT2 Seed		15-DAT3 Seed	
	TRR = 0.044 ppm		TRR = 0.203 ppm	
	%TRR	ppm	%TRR	ppm
Total characterized	48.7	0.021	67.1	0.135
Total extractable	84.5	0.036	88.3	0.179
Unextractable (PES)[1]	15.5	0.007	11.8	0.024
Accountability[2]	100		100.1	

[1] Residues remaining after exhaustive extractions.
[2] Accountability = Total extractable + Total unextractable.

TABLE C.2.3.4 Summary of Characterization and Identification of Radioactive Residues in Pea Foliage Matrices Following Application of [triazole-3,5-^{14}C]Metconazole at ~0.193 lb ai/A/application.

Compound	0-DAT1 Foliage		0-DAT2 Foliage		0-DAT3 Foliage	
	TRR = 10.63 ppm		TRR = 8.70 ppm		TRR = 11.09 ppm	
	%TRR	ppm	%TRR	ppm	%TRR	ppm
Metconazole	95.9	10.201	78.8	6.858	66.7	7.401
More polar than metconazole	3.45	0.362	16.8	1.453	29.5	3.279
Less polar than metconazole	0.5	0.054	1.0	0.094	0.6	0.063
Aqueous-soluble	--	--	--	--	0.5	0.059
Total identified	95.9	10.201	78.8	6.858	66.7	7.401
Total characterized	3.95	0.416	17.8	1.547	30.6	3.401
Total extractable	99.9	10.617	96.6	8.407	97.3	10.802
Unextractable (PES)[1]	0.1	0.013	3.4	0.295	2.6	0.291
Accountability[2]	100		100		99.9	

[1] Residues remaining after exhaustive extractions.
[2] Accountability = Total extractable + Total unextractable.

TABLE C.2.3.5 Summary of Characterization and Identification of Radioactive Residues in Pea Straw Matrices Following Application of [triazole-3,5-^{14}C]Metconazole at ~0.193 lb ai/A/application.

Compound	13-DAT2 Straw		15-DAT3 Straw	
	TRR = 12.03 ppm		TRR = 49.11 ppm	
	%TRR	ppm	%TRR	ppm
Metconazole	64.9	7.804	67.6	33.219
More polar than metconazole	27.3	3.298	22.9	11.203
Less polar than metconazole	1.3	0.154	2.1	1.022
Acid hydrolyzable	5.4	0.649	7.0	3.413
Total identified	64.9	7.804	67.6	33.219
Total characterized	34.0	4.101	32.0	15.638
Total extractable	97.5	11.725	96.4	47.317
Unextractable (PES)[1]	1.8	0.214	2.1	1.021
Accountability[2]	99.3		98.5	

[1] Residues remaining after exhaustive extractions.
[2] Accountability = Total extractable + Total unextractable.

TABLE C.2.3.6 Summary of Characterization and Identification of Radioactive Residues in Pea Seed Matrices Following Application of [triazole-3,5-^{14}C]Metconazole at ~216 g ai/ha/application.

Compound	13-DAT2 Seed		15-DAT3 Seed	
	TRR = 1.57 ppm		TRR = 3.71 ppm	
	%TRR	ppm	%TRR	ppm
Metconazole	3.4	0.053	2.2	0.081
TA	75.9	1.188	89.1	3.303
More polar than metconazole	19.9	0.311	2.7	0.101
Less polar than metconazole	0.4	0.006	0.7	0.024
Total identified	79.3	1.241	91.3	3.384
Total characterized	20.3	0.317	3.4	0.125
Total extractable	99.5	1.56	94.7	3.511
Unextractable (PES)[1]	0.5	0.008	5.3	0.198
Accountability[2]	100		100	

[1] Residues remaining after exhaustive extractions.
[2] Accountability = Total extractable + Total unextractable.

C.3. Proposed Metabolic Profile

Based on the submitted pea metabolism studies, the petitioner proposed that the main metabolic route of metconazole in pea involves oxidative hydroxylation of the methylene groups, the methyl groups on the cyclopentyl ring, and possibly of the cyclopentyl ring itself. The detection of TA as a major metabolite indicates that the methylene group between the triazole and cyclopentyl rings is susceptible to oxidative hydroxylation. The multiple monohydroxylated metabolites and their conjugates represent the various chromatographically distinguishable stereoisomeric structures due to monohydroxylation at the various prochiral carbons of metconazole. Further oxidation of the hydroxylated metabolites to form dihydroxylated or carboxylated derivatives was not evident in pea. However, it appeared that the monohydroxylated metabolites were at least partly conjugated with glucose to form glucosides as terminal residues in the pea foliage, straw and seed.

The figure below was copied without alteration from MRID 46901906.

FIGURE C.3.1. Proposed Metabolic Profile of Metconazole in Peas

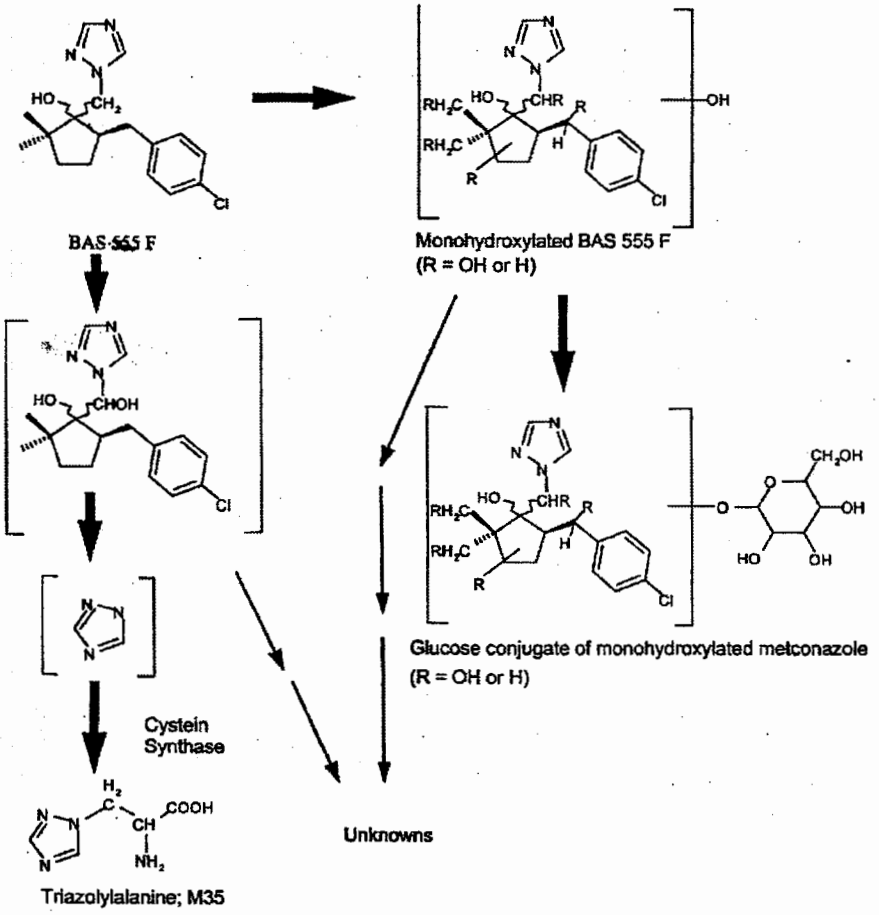
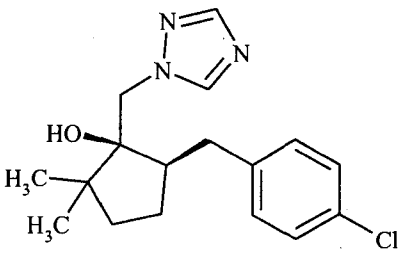
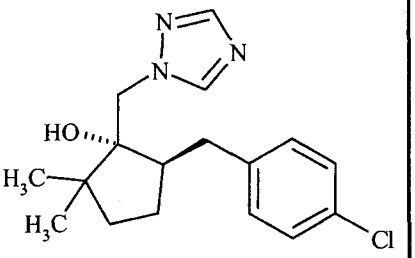
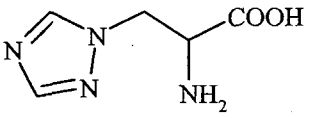


TABLE C.3.1. Identification of Compounds from Metabolism Study

Common name/code Figure C.3.1 ID No.	Chemical name	Chemical structure
Metconazole	5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	 *cis*-isomer  *trans*-isomer
Triazolylalanine (TA); CL 147267	2-amino-3-(1*H*-1,2,4-triazol-1-yl)propanoic acid	

D. CONCLUSION

Following two or three broadcast foliar applications of [chlorophenyl-U-^{14}C]metconazole and [triazole-3,5-^{14}C]metconazole, TRR, calculated by summing radioactivity in surface washes and extractable and nonextractable residues in chlorophenyl-label samples, were 8.77, 6.09, and 8.42 ppm for 0-DAT1, 0-DAT2, and 0-DAT3 foliage, 7.85 ppm and 60.26 ppm for 13-DAT2 and 15-DAT3 straw, and 0.044 ppm and 0.203 ppm for 13-DAT2 and 15-DAT3 seed. In triazole-label samples TRR were 10.63, 8.70, and 11.09 ppm for 0-DAT1, 0-DAT2, and 0-DAT3 foliage, 12.03 and 49.11 ppm for 13-DAT2 and 15-DAT3 straw, and 1.57 and 3.71 ppm for 13-DAT2 and 15-DAT3 seed.

The metabolic profile was similar in pea foliage and straw from both labels. Metconazole was the primary residue identified in all samples of foliage and straw, accounting for 94.1% and 95.9% TRR in 0-DAT1 foliage, 78.7% and 78.8% TRR in 0-DAT2 foliage, and 79.3% and 66.7% TRR in 0-DAT3 foliage from chlorophenyl- and triazole-label samples, respectively. The majority of remaining residues were characterized as more polar than metconazole, accounting for 5.3%, 16.4%, and 15.6% TRR in 0-DAT1, 0-DAT2, and 0-DAT3 chlorophenyl-label foliage, and for 3.45%, 16.8%, and 29.5% TRR in triazole-label foliage. Residues characterized as less polar than metconazole accounted for ≤3.4% TRR in chlorophenyl-label foliage and ≤1.0% TRR in triazole-label foliage.

Metconazole was generally identified at lower levels in straw, accounting for 58.7% and 54.1% TRR, respectively, in 13-DAT2 and 15-DAT3 chlorophenyl-label straw, and for 64.9% and 67.6% TRR, respectively, in 13-DAT2 and 15-DAT3 triazole-label straw. Residues characterized as more polar than metconazole accounted for 30.2% and 31.0% TRR, respectively, in 13-DAT2 and 15-DAT3 chlorophenyl-label straw, and for 27.3% and 22.9% TRR, respectively, in 13-DAT2 and 15-DAT3 triazole-label straw. Residues characterized as less polar than metconazole accounted for ≤7.0% TRR in chlorophenyl-label straw and for ≤2.1% TRR in triazole-label straw. On further examination of the nonextractable residues of 15-DAT3 straw, only minor amounts of radioactivity were found to have been incorporated into cell wall components (≤3.24% TRR in lignin, pectin, cellulose or polysaccharides).

The metabolic profile in pea seed was significantly different in chlorophenyl- and triazole-label samples. Metconazole was the primary residue identified in chlorophenyl-label pea seed, accounting for 35.7% TRR in 13-DAT2 seed and 21.1% TRR in 15-DAT3 seed. In triazole-label seed, the primary identified residue was TA, accounting for 75.9% TRR in 13-DAT2 seed and 89.1% TRR in 15-DAT3 seed; metconazole was a minor residue, accounting for 3.4% and 2.2% TRR, respectively in 13-DAT2 and 15-DAT3 seed. In chlorophenyl-label seed, residues characterized as more polar than metconazole accounted for 33.6% TRR in 13-DAT2 seed and 53.4% TRR in 15-DAT3 seed, with discrete components present at up to 11.5% TRR and 26.6% TRR at the respective sampling intervals; residues characterized as less polar than metconazole accounted for ≤5.7% TRR. In triazole-label seed, residues characterized as more polar than metconazole accounted for 19.9% TRR in 13-DAT2 seed and 2.7% TRR in 15-DAT3 seed, and residues characterized as less polar than metconazole accounted for ≤0.7% TRR.

The study is supported by adequate storage stability data, and acceptable methods were used for extraction and characterization/identification of residues.

Based on the submitted pea metabolism studies, the petitioner proposed that the main metabolic route of metconazole in pea involves oxidative hydroxylation of the methylene groups, the methyl groups on the cyclopentyl ring, and possibly of the cyclopentyl ring itself. The detection of TA as a major metabolite indicates that the methylene group between the triazole and cyclopentyl rings is susceptible to oxidative hydroxylation. The multiple monohydroxylated metabolites and their conjugates represent the various chromatographically distinguishable stereoisomeric structures due to monohydroxylation at the various prochiral carbons of metconazole. Further oxidation of the hydroxylated metabolites to form dihydroxylated or carboxylated derivatives was not evident in pea. However, it appeared that the monohydroxylated metabolites were at least partly conjugated with glucose to form glucosides as terminal residues in the pea foliage, straw and seed.

E. REFERENCES

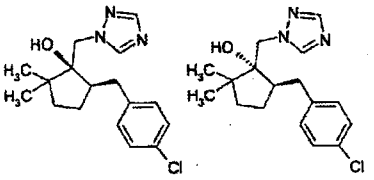
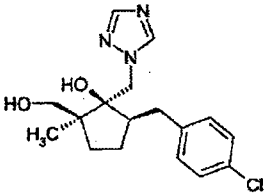
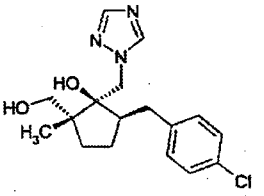
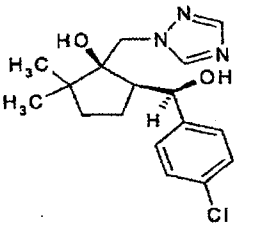
DP#:	324541
Subject:	Metconazole. Request for a Tolerance on Imported Bananas. Summary of Analytical Chemistry and Residue Data. Petition Number 9E05052.
From:	N. Dodd
To:	M. Waller
Date:	12/14/05
MRIDs:	44721506, 44721507, 44721508, 44721509, 44721510, and 44721511

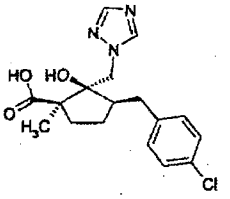
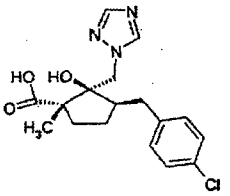
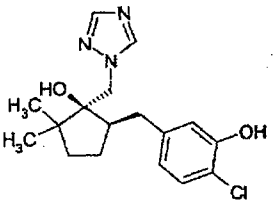
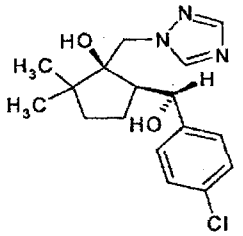
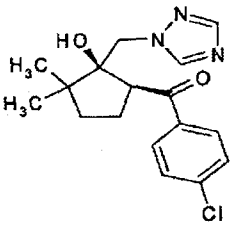
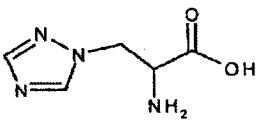
F. DOCUMENT TRACKING

RDI: N. Dodd (2/20/08)
Petition Numbers: 6F7094 and 6F7095
DP#s: 348168 and 348206
PC Code: 125619

Template Version June 2005

APPENDIX I. Chemical Names and Structures of Reference Standards Used in Pea Metabolism Study.

Compound Code	Chemical Name	Structure
Metconazole; BAS 555 F ; AC 900768; CL 900768 (M0) CAS Number: Chemical Formula: Molecular Weight:	5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol 125116-23-6 $C_{17}H_{22}ClN_3O$ 319.83	 Cis-Isomer Trans-Isomer
CL359451 (M1) CAS Number: Chemical Formula: Molecular Weight:	3-(p-chlorobenzyl)-2-hydroxy-3-methyl-2-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentane-methanol Not allocated $C_{17}H_{22}ClN_3O_2$ 335.80	
CL359452 (M2) CAS Number: Chemical Formula: Molecular Weight:	3-(p-chlorobenzyl)-2-hydroxy-3-methyl-2-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentane-methanol Not allocated $C_{17}H_{22}ClN_3O_2$ 335.80	
CL382390 (M21) CAS Number: Chemical Formula: Molecular Weight:	alpha-(p-chlorophenyl)-2-hydroxy-3,3-dimethyl-2-(1*H*-1,2,4-triazol-1-ylmethyl)-cyclopentanemethanol 153322-43-1 $C_{17}H_{22}ClN_3O_2$ 333.50	

CL359138 (M12)	3-(p-chlorobenzyl)-2-hydroxy-3-methyl-2-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentane-carboxylic acid	
CAS Number:	Not allocated	
Chemical Formula:	$C_{17}H_{20}ClN_3O_3$	
Molecular Weight:	349.82	
CL359139 (M13)	3-(p-chlorobenzyl)-2-hydroxy-3-methyl-2-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentane-carboxylic acid	
CAS Number:	Not allocated	
Chemical Formula:	$C_{17}H_{20}ClN_3O_3$	
Molecular Weight:	349.82	
CL359453 (M15)	5-(4-chloro-3-hydroxybenzyl)-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-yl-methyl)-cyclopentanol	
CAS Number:	Not allocated	
Chemical Formula:	$C_{17}H_{22}ClN_3O_2$	
Molecular Weight:	335.80	
CL382391 (M11)	alpha-(p-chlorophenyl)-2-hydroxy-3,3-dimethyl-2-(1*H*-1,2,4-triazol-1-ylmethyl)-cyclopentanemethanol	
CAS Number:	153322-43-1	
Chemical Formula:	$C_{17}H_{22}ClN_3O_2$	
Molecular Weight:	333.50	
CL382389 (M30)	5-(p-chlorobenzoyl)-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	
CAS Number:	153208-73-2	
Chemical Formula:	$C_{17}H_{20}ClN_3O_2$	
Molecular Weight:	333.50	
CL147267 (M35) Triazolylalanine	1*H*-1,2,4-Triazole-1-propionic acid, alpha-amino	
CAS Number:	Not allocated	
Chemical Formula:	$C_5H_8N_4O_2$	
Molecular Weight:	156.15	

Primary Evaluator	This DER was originally prepared under contract by Dynamac Corporation.
Approved by	Nancy Dodd, Chemist Nancy Dodd Date: 2/20/08 Registration Action Branch 3 Health Effects Division (7509P)

This DER was originally prepared under contract by Dynamac Corporation (2275 Research Boulevard, Suite 300; Rockville, MD 20850; submitted 09/13/2007). The DER has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

46901907 Satoh, K. (2002) Metabolic Fate of KNF-474m in Mandarins. Project Number: 200400252, IET/01/8005. Unpublished study prepared by Institute of Environmental Toxicology. 280 p.

EXECUTIVE SUMMARY:

Valent U.S.A. Corporation has submitted a study investigating the metabolism of [cyclopentyl-^{14}C]metconazole (specific activity 343307.4 dpm/µg) and [triazole-3,5-^{14}C]metconazole (specific activity 388331.3 dpm/µg) in mandarin. The radiolabeled test substances were formulated with a surfactant extender formulation blank and water. Each test substance was then applied as a single broadcast foliar application to mandarin trees grown in greenhouses at the fruit-growing stage at 0.178 lb ai/A (200 g ai/ha). Samples of mandarin fruits and leaves were harvested 0, 28, and 56 days after treatment (DAT). Following harvest, samples of whole fruits and leaves were initially rinsed with methanol, after which fruits were separated into peel and flesh prior to extraction and analysis. The in-life and analytical phases of the study were conducted by The Institute of Environmental Toxicology (Ibaraki, Japan).

Total radioactive residues (TRR) in mandarin matrices were determined by summing radioactivity in the surface wash, methanol/water extract, and nonextractable residues. TRR in 0-, 28-, and 56-DAT fruit were 0.1031, 0.0974, and 0.1127 ppm, respectively, following application of the cyclopentyl-labeled test substance and 0.1259, 0.0991, and 0.0716 ppm following application of the triazole-labeled test substance. In leaves harvested 0, 28, and 56 DAT, TRR were 4.2227, 3.4995, and 3.0903 ppm, respectively, following application of the cyclopentyl-labeled test substance, and 4.8372, 3.6605, and 3.3074 ppm, respectively, following application of the triazole-labeled test substance.

The methanol surface wash released the majority of radioactivity, 80.33-83.95% TRR, from all 0-DAT samples. In 28-DAT samples, 18.15-19.85% TRR was released from fruit and 51.80-55.75% TRR was released from leaves. In 56-DAT samples, 11.53-15.24% TRR was released from fruit and 39.10-45.88% TRR was released from leaves. These data indicate that

metconazole migrated rapidly into mandarin fruit tissues following application, and that translocation in leaves was slower than in fruit. Extraction with methanol/water released the majority of the remaining radioactivity from mandarin peel, flesh, and leaves, respectively: 15.74-18.16%, <0.17-0.26%, and 17.12-18.86% TRR, respectively, from 0-DAT samples; 73.83-74.66%, 1.32-1.88%, and 35.95-43.16% TRR, respectively, from 28-DAT samples; and 75.64-80.15%, 1.48-3.01%, and 47.34-51.34% TRR, respectively, from 56-DAT samples. Remaining nonextractable residues for all harvest intervals were ≤6.74% TRR (0.0076 ppm) in peel, ≤0.10% (0.001 ppm) in flesh, and ≤9.55% TRR (0.3163 ppm) in leaves. Residues in mandarin flesh were not further analyzed. These procedures adequately extracted the majority of the residues from mandarin matrices. Because TRR were determined by summing extractable and nonextractable radioactivity, accountabilities for all matrices were 100%. The study is supported by adequate storage stability data.

Metconazole (*cis* and *trans*) and M21 (in Fraction 10) were identified and confirmed by HPLC and TLC co-chromatography; based on TLC results, the petitioner concluded that M21 represented only a portion of HPLC fraction 10. No isomerization between *cis*- and *trans*-isomers of metconazole was observed. Remaining residues were characterized by SPE fractionation and HPLC retention time comparisons; four aglycones were tentatively identified following mild acid hydrolysis of the methanol SPE fraction. HED notes that the petitioner did not include analysis for triazole metabolites (1,2,4-triazole, triazolylalanine, or triazolylacetic acid) in the study.

Metconazole was the primary residue identified in mandarin peel and leaves from both labels at all sampling intervals, accounting for 92.12-94.71% TRR (0.0972-0.1158 ppm for peel and 3.9240-4.5814 ppm for leaves) in 0-DAT samples; 54.06-56.90% TRR (0.0530-0.0537 ppm in peel and 1.9895-1.9949 ppm in leaves) in 28-DAT samples; and 45.22-48.93% TRR (0.0339-0.0553 ppm in peel and 1.4801-1.4958 ppm in leaves) in 56-DAT samples. Metabolite M21 was the only other identified residue, accounting for 0.22-0.57% TRR, 1.74-2.38% TRR, and 1.64-2.68% TRR, respectively, in 0-, 28-, and 56-DAT peel and leaves. Residues characterized as glucose conjugates (fractions 5-7) accounted for ≤2.55% TRR in 0-DAT peel and leaf samples; 23.72-26.38% TRR (0.0235-0.0255 ppm) and 28.62-29.79% TRR (0.0206-0.0335 ppm) in 28- and 56-DAT peel, respectively; and 17.70-18.48% TRR (0.6452-0.6475 ppm) and 20.97-22.25% TRR (0.6885 and 0.6930 ppm) in 28- and 56-DAT leaves. Portions of these residues were tentatively characterized/identified in 56-DAT samples as glucose conjugates of metconazole metabolites, including: (1) mono- or dihydroxylated metconazole, aglycones 1 and 3, respectively, at 7.95-8.58% and 2.96-3.37% TRR in peel, and 3.35-3.89% and 0.92-0.98% TRR in leaves; (2) metabolite M2, aglycone 2, at 1.82-1.94% TRR in peel and 0.69-0.82% TRR in leaves; and (3) metabolite M1, aglycone 4, at 2.96-2.98% TRR in peel and 1.36-1.39% TRR in leaves. Fraction 6, which represented up to 21% TRR in peel and 12% TRR in leaves, was shown to be comprised of multiple components, none exceeding 8.16% TRR in peel extracts or 3.61% TRR in leaves. Two fractions characterized as free metabolites (fractions 8 and 9) together accounted for up to 6.41% TRR in peel and up to 10.25% TRR in leaves. Remaining residues consisted of polar and nonpolar unknowns, which represented ≤2.14% TRR in peel and ≤2.68% TRR in leaves.

Based on the submitted mandarin metabolism study, the petitioner proposed that the main metabolic route of metconazole in mandarin is via hydroxylation to form several metabolites including M1 and M2. These metabolites are further metabolized to form glucose conjugates and/or bound residues. Hydroxylation in the 4-chlorobenzyl position to form M21 was also observed as a minor metabolic pathway.

HED notes that samples were not analyzed for the triazole metabolites (1,2,4-triazole, triazolylalanine, and triazolylacetic acid).

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the plant metabolism data are classified as scientifically acceptable.

The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP#s 348168 and 348206.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an impact on the validity of the study.

A. BACKGROUND INFORMATION

Metconazole [5-[(4-cyclopentyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol] is a broad-spectrum triazole Group 3 fungicide (sterol biosynthesis inhibitors). There are currently no registered uses of metconazole in the U.S.; however, a tolerance has been established for banana, and a Section 18 emergency exemption and supporting time-limited tolerances have been granted for use on soybean. Valent U.S.A. Corporation has applied for registration of metconazole in the U.S. for use on peanut, stone fruits, and tree nuts.

The chemical structure and nomenclature of metconazole, and the physicochemical properties of the technical grade of metconazole are presented in Tables A.1 and A.2.

Table A.1. Metconazole Nomenclature.

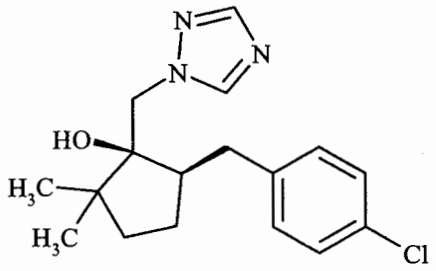
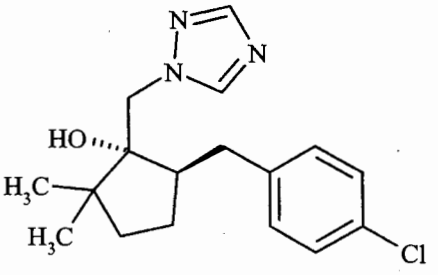
Chemical structure	 *cis*-isomer	 *trans*-isomer
Common name	Metconazole	
Company experimental name	KNF-S-474m (Kureha); BAS 555 F (BASF); V-10116 (Valent)	
IUPAC name	(1RS,5RS:1RS,5SR)-5-(4-chlorobenzyl)-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	
CAS name	5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	
CAS registry number	125116-23-6 (*cis*- and *trans*-isomers) 115850-27-6 (*cis*-isomer) 115850-28-7 (*trans*-isomer)	
End-use products (EP)	50% WDG (Metconazole 50 WDG Fungicide, EPA File Symbol 59639-RUT) 0.75 lb/gal SC/L (Caramba™ Fungicide, EPA File Symbol No. 7969-EUA) 0.67 lb/gal SC/L formulation (BAS 556 01F Fungicide, EPA File Symbol No. 7969-EUT; also contains the active ingredient pyraclostrobin at 0.83 lb/gal)	

Table A.2. Physicochemical Properties of Metconazole

Parameter	Value				References* (MRID)
Melting point/range	100.0-108.4°C (using Electrothermal Digital Melting Point Apparatus) (AC900,768 technical grade)				44721505
pH	5.81 at 25°C (1% aqueous suspension)				46808402
Relative density (20°C)	1.14 (relative density to water at 4°C, using capillary-stoppered, density-specific gravity bottle) (Lot No. AC 8879-140B)				44721505
Water solubility (20°C)	Using shake-flask method: 18.7 ± 1.0 mg/L (*cis*-isomer, WL148271, KNF-S-474m) 13.6 ± 1.7 mg/L (*trans*-isomer, WL148271, KNF-S-474m)				44721505
Solvent solubility (g/L) at 20°C	Solvent	Metconazole	*cis*	*trans*	44721505
	acetone	363	251	117	
	methanol	403	294	117	
	dichloromethane	481	343	141	
	ethyl acetate	260	173	90.0	
	propanol	132	86.6	46.7	
	toluene	103	66.2	38.0	
	Hexane	1.40	0.929	0.483	

Table A.2. Physicochemical Properties of Metconazole

Parameter	Value	References* (MRID)
Vapor pressure (20°C)	Using gas-saturation method: $< 1.23 \times 10^{-5}$ Pa or 9.23×10^{-8} mm Hg (metconazole) $< 1.04 \times 10^{-5}$ Pa or 7.80×10^{-8} mm Hg (*cis*-isomer) $< 1.96 \times 10^{-6}$ Pa or 1.47×10^{-8} mm Hg (*trans*-isomer)	44721505
Dissociation constant (pK_a)	11.38±0.03 and 1.06±0.03 (in water at 29.1°C using spectrophotometric method; Lot No. AC 8879-140B)	44721505
Octanol/water partition coefficient, Log(K_{OW})	At 20 °C (using flask shaking method): K_{ow} (log K_{ow}) = 7090±989 (3.85) (Lot No. AC 8879-140B) (TGAI) K_{ow} (log K_{ow}) = 7150±803 (3.85) (*cis*-isomer, CL 354,801) K_{ow} (log K_{ow}) = 6800±1700 (3.8) (*trans*-isomer, CL 354,802)	44721505

UV/visible absorption spectrum — 46808403

pH	λ	A	log ε
cis-isomer			
2.0	221.4	0.828	4.03
6.8		0.8452	4.04
7.0		0.9126	4.08
10.3		0.7226	3.98
trans-isomer			
2.0	221.4	0.9053	4.07
7.0		0.9547	4.10
10.1		0.9893	4.11

* Product Chemistry Reviews: DP #256877, Shyam Mathur, Ph.D., 9/12/2000 and DP #329168, Shyam Mathur, Ph.D., 7/13/07.

B. EXPERIMENTAL DESIGN

B.1. Test Site and Crop Information

The in-life and analytical phases of the study were conducted by The Institute of Environmental Toxicology (Ibaraki, Japan). The field test sites were located at the Enviro-Quest facilities in Minto, MB. A summary of the test site information is provided in Table B.1.1, and a summary of the crop information is provided in Table B.1.2. Mandarin trees bearing ≥10 fruits were grown in pots and were transferred to greenhouses (4 m^2 floor area/phytotron) 35 days prior to application. Trees were watered once or twice daily and were fertilized with a commercial fertilizer; insect pests were removed by hand. Daytime and nighttime temperatures and relative humidity were reported for the duration of the study.

Samples of mandarin leaves and whole fruits were harvested immediately following application (0 DAT) and 28 and 56 DAT.

3 87

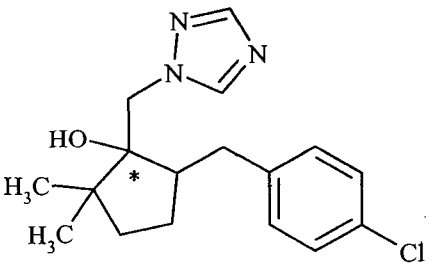
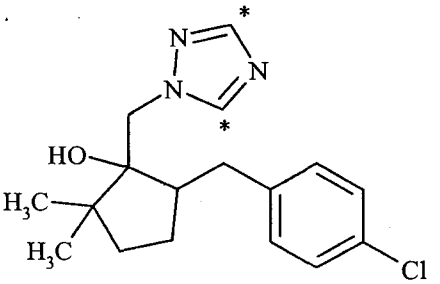
TABLE B.1.1. Test Site Information.						
Label	Type	Method	Soil characteristics			
			Type	%OM	pH	CEC
Cyclopentyl	Foliar Treatment	Two broadcast foliar spray applications using a CO_2 sprayer	Loam	2.5	8.3	31.7 meq/100 g
Triazole				4.9	8.1	41.2 meq/100 g

TABLE B.1.2. Crop Information.				
Crop; crop group	Variety	Growth stage at application	Growth stage at harvest [1]	Harvested Matrix
Mandarin; Fruit, citrus, group 10	Satsuma mandarin; v. Wase Unshu	Fruit-growing stage	0- DAT	Leaves and whole fruits
			28-DAT; immature	
			56-DAT; mature	

[1] DAT = days after treatment.

B.2. Test Materials

The radiolabeled test substances were dissolved in ethyl acetate and diluted with acetonitrile (ACN) to prepare stock solutions. The stock solutions were reduced to dryness and redissolved in methanol, then formulated with a surfactant extender formulation blank and water prior to application. The characteristics of the test substances are presented in Table B.2.1.

TABLE B.2.1. Test Material Characteristics.		
Chemical structure		
Radiolabel position	[cyclopentyl-^{14}C]metconazole	[triazole-3,5-^{14}C]metconazole
Lot No.	CP-2397	CFQ12045
cis/trans Ratio	87:13	83:17
Purity	98.8%	>99.7%
Specific activity – test substance	1.83 GBq/mmol (5.71 MBq/mg)	2.07 GBq/mmol (56 µCi/mmol)
Specific activity – application solution	343307.4 dpm/µg	388331.3 dpg/µg

B.3. Study Use Pattern

Each formulated test substance was applied as a single broadcast foliar application to two mandarin trees for each label at the fruit-growing stage at a nominal application rate of 0.178 lb ai/A (200 g ai/ha). Applications were made using a hand sprayer. The petitioner reported that the actual application rates for the cyclopentyl- and triazole-labeled test substances were 98.3% (~0.175 lb ai/A) and 97.9% (~0.174 lb ai/A) of the target rate. Details of the study use pattern are presented in Table B.3.1.

TABLE B.3.1. Use Pattern Information.

Chemical name	[cyclopentyl-^{14}C]metconazole and [triazole-3,5-^{14}C]metconazole
Application method	The isotopically diluted test substances were formulated with a surfactant extender and applied as a single broadcast foliar application using a hand sprayer.
Application rate	0.178 lb ai/A (200 g ai/ha)
Number of applications	1
Timing of applications	Fruit-growing stage (~2 months before harvest)
PHI	0, 28, and 56 days

B.4. Identification/Characterization of Residues

B.4.1. Sample Handling and Preparation

Harvested samples were placed in frozen storage (~20 °C) following collection. Samples of whole fruits and leaves were surface-rinsed with methanol. The surface rinses were concentrated by rotary evaporation and dried under a stream of nitrogen, then redissolved in methanol and reserved for HPLC analysis. The rinsed fruit samples were prepared for extraction by separating the samples into peel and flesh. The peel and flesh samples were frozen and then homogenized in the presence of dry ice. Leaf samples were cut into small pieces prior to homogenization.

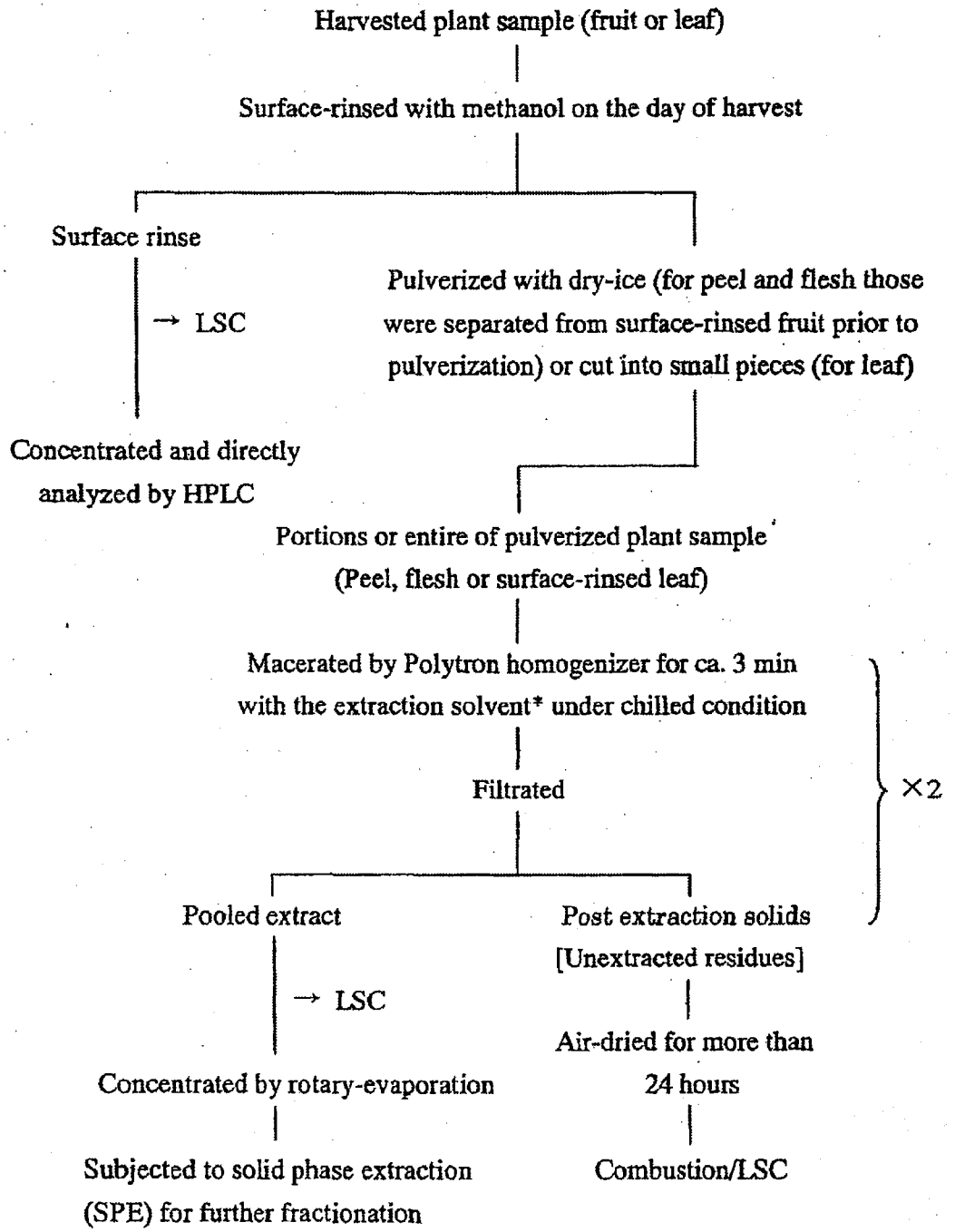
Homogenized samples of peel, flesh, and leaves were extracted 2x with methanol:water (7:3, v:v for peel and flesh, and 1:1, v:v for leaves) and filtered. The resulting methanol/water extracts for each matrix were combined, concentrated to remove organic solvent, and subjected to solid phase extraction (SPE, except 0-DAT flesh) on a reverse phase C18 mini column. Following collection of the initial aqueous eluate containing high-polar residues, the remaining residues were fractionated into low-polar and polar components by sequential elution with hexane:ethyl acetate (1:1, v:v) and methanol, respectively. The resulting hexane/ethyl acetate and methanol eluates were combined (designated "SPE organic fraction"), concentrated to dryness, and then redissolved in methanol or ACN and reserved for HPLC analysis.

Separate subsamples of the SPE methanol fractions of 56-DAT peel and leaf for both labels were further subjected to acid hydrolysis with 0.1 M HCl (at 100 °C for 1 day) and/or enzyme hydrolysis with cellulase (at 37 °C for 1 day). The resulting hydrolysates were subjected to SPE as described above.

The extracts of mandarin flesh samples were not subjected to further analysis due to low radioactivity.

Representative flow charts are presented below in Figures B.4.1.1 (extraction for fruit and leaf), B.4.1.2 (SPE for fruit and leaf), and B.4.1.3 (hydrolysis for 56-DAT peel and leaf). The flow charts were copied without alteration from MRID 46901907.

Figure B.4.1.1. Extraction Flowchart for Mandarin Fruit and Leaf



* Methanol:water (7:3, v/v) for peel and flesh samples, and methanol:water (1:1, v/v) for leaf sample.

Figure B.4.1.2. Solid Phase Extraction Flowchart for Mandarin Fruit and Leaf

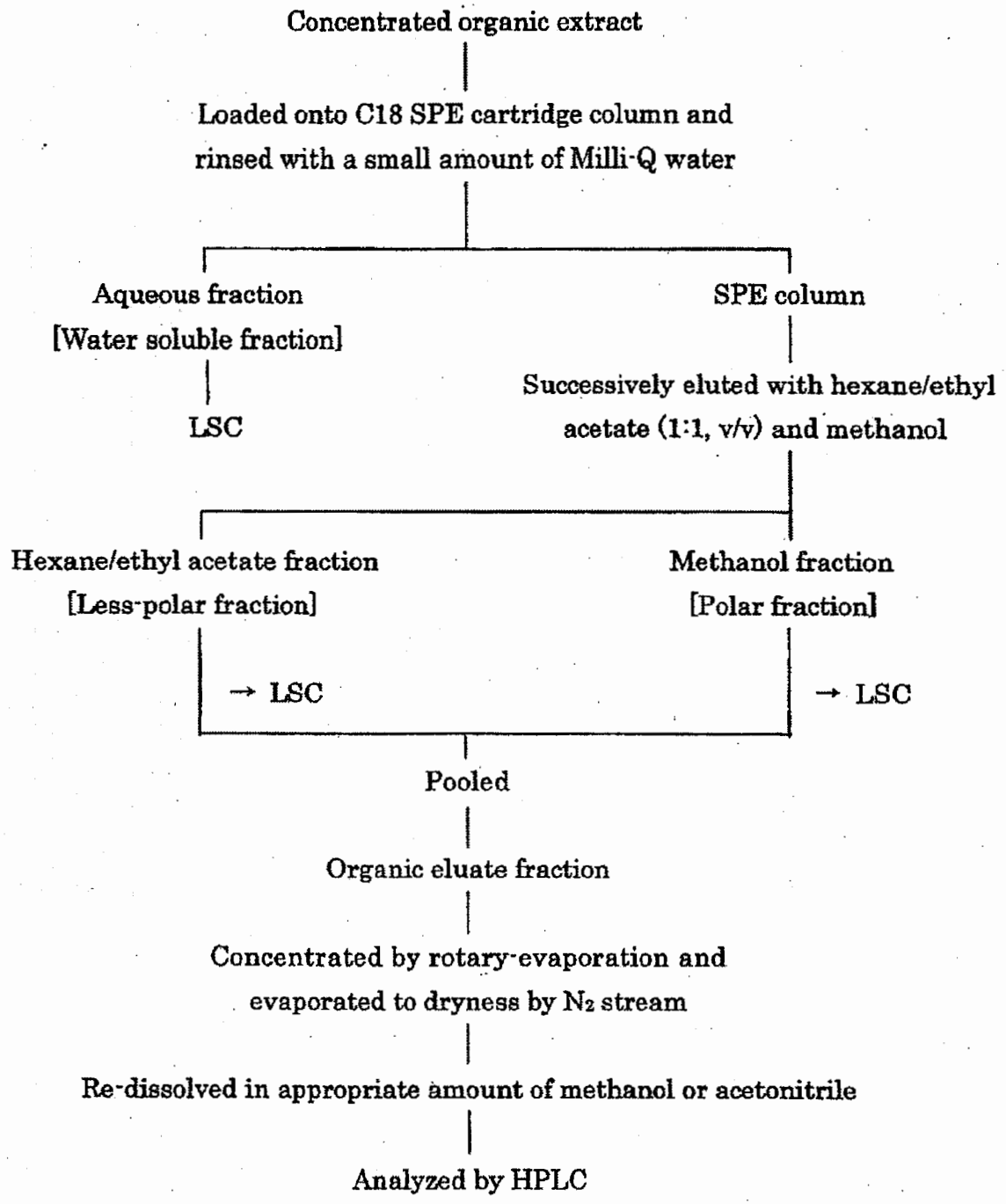
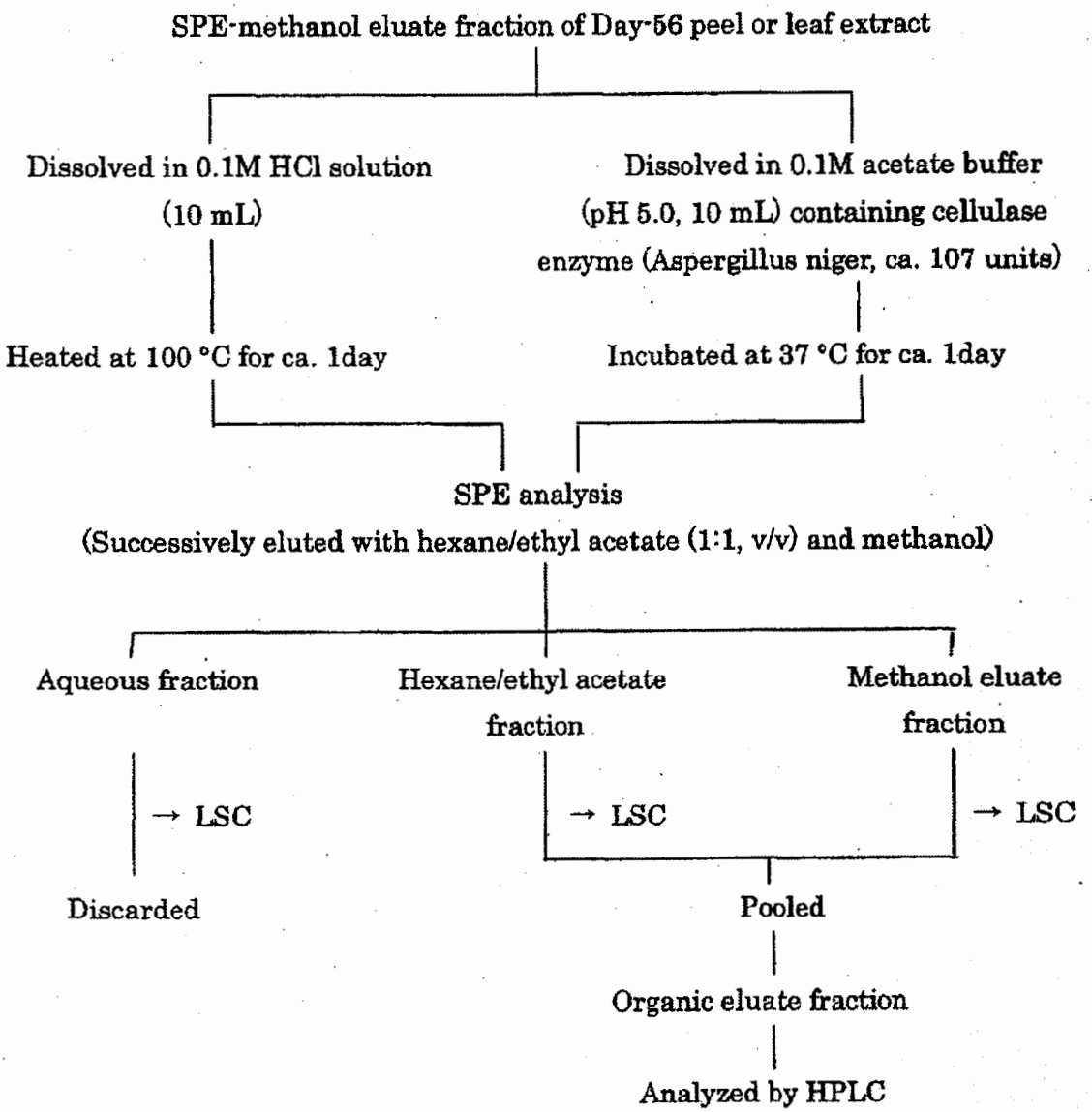


Figure B.4.1.3. Hydrolysis Flowchart for Mandarin Peel and Leaf



B.4.2. Analytical Methodology

TRR in samples of peel, flesh, and leaves were calculated by summing radioactivity in the surface wash, methanol/water extract, and nonextractable residues. Surface washes and extracts were radioassayed by LSC (in duplicate or more), and solid samples were radioassayed by combustion/LSC (in triplicate). The reported limit of detection for TRR determinations was 40 dpm (~2x natural radioactivity).

The surface rinses and SPE organic extracts of peel and leaves were analyzed by HPLC on a system equipped with a UV detector (268 nm), a flow-through radioactivity detector, and a fraction collector, and using a C18 column and a gradient mobile phase of 5 mM ammonium

acetate in water (pH 4.6)/ACN. Major radioactive components in the surface rinses and SPE organic extracts of peel and leaves were identified/characterized by HPLC retention time comparisons with reference standards as well as by one-dimensional TLC comparison of Rf values; the reference standards used in the study are listed in Appendix I.

TLC analyses were conducted on silica gel 60 F_{254} plates using solvent systems of: methylene chloride:ethyl acetate:methanol:formic acid (64:30:5:1, v:v:v:v); chloroform:ethyl acetate:methanol:formic acid (64:30:5:1, v:v:v:v); and ethyl acetate:ethanol:water (8:2:1, v:v:v). Radioactivity was visualized using a bioimaging analyzer, and nonlabeled standards were visualized by UV detection.

C. RESULTS AND DISCUSSION

The storage conditions and intervals for mandarin samples are presented in Table C.1. The petitioner provided the dates of sampling, homogenization, extraction, and analysis for all samples. All samples were extracted within 27 days of harvest, and analyzed by HPLC within 37 days of harvest. To demonstrate storage stability, subsamples of 56-DAT peel and leaf were extracted and subjected to SPE as described above 72-99 days after harvest. The resulting hexane/EtOAc and methanol fractions were analyzed by HPLC, and the results were compared with those of fractions originally analyzed 6-12 days (peel) or 5-9 days (leaves) after sampling. The study results indicate that residues were relatively stable in/on samples of peel and leaves stored frozen for up to 72-99 days. No additional storage stability data are required to support the study.

TRR in mandarin matrices, determined by summing radioactivity in the surface wash, methanol/water extract, and nonextractable residues, are reported in Table C.2.1. In mandarin fruit harvested 0, 28, and 56 days after a single broadcast foliar application of [cyclopentyl-^{14}C]metconazole or [triazole-3,5-^{14}C]metconazole at 0.178 lb ai/A, TRR were 0.1031, 0.0974, and 0.1127 ppm, respectively, following application of the cyclopentyl-labeled test substance and 0.1259, 0.0991, and 0.0716 ppm following application of the triazole-labeled test substance. In leaves harvested 0, 28, and 56 DAT, TRR were 4.2227, 3.4995, and 3.0903 ppm, respectively, following application of the cyclopentyl-labeled test substance, and 4.8372, 3.6605, and 3.3074 ppm following application of the triazole-labeled test substance.

The distribution of radioactivity in mandarin matrices is presented in Tables C.2.2.1 (cyclopentyl-label fruit), C.2.2.2 (triazole-label fruit), C.2.2.3 (cyclopentyl-label leaves), and C.2.2.4 (triazole-label leaves). The methanol surface wash released the majority of radioactivity, 80.33-83.95% TRR, from all 0-DAT samples. In 28-DAT samples, 18.15-19.85% TRR were released from fruit and 51.80-55.75% TRR were released from leaves. In 56-DAT samples, 11.53-15.24% TRR were released from fruit and 39.10-45.88% TRR were released from leaves. These data indicate that metconazole migrated rapidly into mandarin fruit tissues following application, and that translocation in leaves was slower than in fruit. Extraction with methanol/water released the majority of the remaining radioactivity from mandarin peel, flesh, and leaves, respectively: 15.74-18.16%, <0.17-0.26%, and 17.12-18.86% TRR, respectively, from 0-DAT samples; 73.83-74.66%, 1.32-1.88%, and 35.95-43.16% TRR, respectively, from

28-DAT samples; and 75.64-80.15%, 1.48-3.01%, and 47.34-51.34% TRR, respectively, from 56-DAT samples. Remaining nonextractable residues for all harvest intervals were ≤6.74% TRR (0.0076 ppm) in peel, ≤0.10% (0.001 ppm) in flesh, and ≤9.55% TRR (0.3163 ppm) in leaves. Residues in mandarin flesh were not further analyzed. These procedures adequately extracted the majority of the residues from mandarin matrices. Because TRR were determined by summing extractable and nonextractable radioactivity, accountabilities for all matrices were 100%.

The characterization and identification of residues in mandarin matrices are summarized in Tables C.2.3.1 (cyclopentyl-label fruit), C.2.3.2 (triazole-label fruit), C.2.3.3 (cyclopentyl-label leaves), and C.2.3.2 (triazole-label leaves). Metconazole (*cis* and *trans*) and M21 (in fraction 10) were identified and confirmed by HPLC and TLC co-chromatography with reference standards; based on TLC results, the petitioner concluded that M21 represented only a portion of HPLC fraction 10. No isomerization between *cis*- and *trans*-isomers of metconazole was observed. Remaining residues were characterized by SPE fractionation into aqueous, low polar (hexane/EtOAc), and polar (MeOH) residues, and were further characterized on the basis of HPLC retention time comparisons as polar unknowns (HPLC fractions 1-4), highly polar glucose conjugates (fractions 5-7), and free metabolites (fractions 8-9). Following mild acid hydrolysis of the SPE methanol fraction, the petitioner tentatively identified four aglycones in the regions corresponding to HPLC fractions 5-7; aglycones 1 and 3 were characterized as glucose conjugates of mono- or dihydroxylated metconazole metabolites, aglycone 2 was characterized as a glucose conjugate of M2, and glucose aglycone 4 was characterized as a conjugate of M1. Hydrolysis with cellulase did not release appreciable residues. The petitioner did not further address Fractions 12 and 13; however, these appear to be nonpolar unknowns based on comparison of their retention times with that of metconazole. HED notes that the petitioner did not include analysis for triazole metabolites (1,2,4-triazole, triazolylalanine, or triazolylacetic acid) in the study.

The metabolic profile was similar in samples from both labels. Metconazole was the primary residue identified in mandarin peel and leaves from both labels at all sampling intervals, accounting for 92.12-94.71% TRR (0.0972-0.1158 ppm for peel and 3.9240-4.5814 ppm for leaves) in 0-DAT samples; 54.06-56.90% TRR (0.0530-0.0537 ppm in peel and 1.9895-1.9949 ppm in leaves) in 28-DAT samples; and 45.22-48.93% TRR (0.0339-0.0553 ppm in peel and 1.4801-1.4958 ppm in leaves) in 56-DAT samples. Metabolite M21 was the only other identified residue, accounting for 0.22-0.57% TRR, 1.74-2.38% TRR, and 1.64-2.68% TRR, respectively, in 0-, 28-, and 56-DAT peel and leaves. Residues characterized as glucose conjugates (fractions 5-7) accounted for ≤2.55% TRR in 0-DAT peel and leaf samples; 23.72-26.38% TRR (0.0235-0.0255 ppm) and 28.62-29.79% TRR (0.0206-0.0335 ppm) in 28- and 56-DAT peel, respectively; and 17.70-18.48% TRR (0.6452-0.6475 ppm) and 20.97-22.25% TRR (0.6885 and 0.6930 ppm) in 28- and 56-DAT leaves. As noted above, portions of these residues were tentatively characterized/identified in 56-DAT samples as glucose conjugates of metconazole metabolites, including: (1) mono- or dihydroxylated metconazole, aglycones 1 and 3, respectively, at 7.95-8.58% and 2.96-3.37% TRR in peel, and 3.35-3.89% and 0.92-0.98% TRR in leaves; (2) metabolite M2, aglycone 2, at 1.82-1.94% TRR in peel and 0.69-0.82% TRR in leaves; and (3) metabolite M1, aglycone 4, at 2.96-2.98% TRR in peel and 1.36-1.39% TRR in leaves. Fraction 6, which represented up to 21% TRR in peel and 12% TRR in leaves was

shown to be comprised of multiple components, none exceeding 8.16% TRR in peel extracts or 3.61% TRR in leaves. Two fractions characterized as free metabolites (fractions 8 and 9) together accounted for up to 6.41% TRR in peel and up to 10.25% TRR in leaves. Remaining residues consisted of polar and nonpolar unknowns, which represented ≤2.14% TRR in peel and ≤2.68% TRR in leaves.

C.1. Storage Stability

The petitioner provided the dates of sampling, homogenization, extraction, and analysis for all samples. All samples were extracted within 27 days of harvest, and analyzed by HPLC within 37 days of harvest. To demonstrate storage stability, subsamples of 56-DAT peel and leaf were extracted and subjected to SPE as described above 72-99 days after harvest. The resulting hexane/EtOAc and methanol fractions were analyzed by HPLC, and the results were compared with those of fractions originally analyzed 6-12 days (peel) or 5-9 days (leaves) after sampling. Examination of the study results indicates that there was no significant difference in extractability of residues and distribution into SPE fractions for peel or leaves following storage. Comparison of the HPLC profiles of the SPE organic fractions for peel and leaf matrices confirms that the metabolic profile did not change during frozen storage. No additional data are required to support the study.

TABLE C.1. Summary of Storage Conditions.

Matrix	Storage Temperature (°C)	Actual Storage Duration[1]		Interval of Demonstrated Storage Stability
		Cyclopentyl label	Triazole label	
Mandarin peel and flesh	<-20	22-37 days (12-22 days)	23-36 days (6-27 days)	None submitted or required
Mandarin leaves		22-37 days (6-9 days)	23-36 days (5-26 days)	

[1] Interval from harvest to analysis; samples were extracted within 6-27 days of harvest for flesh and within 5-26 days of harvest for leaves.

C.2. Identification, Characterization, and Distribution of Residues

TABLE C.2.1. Total Radioactive Residues (TRR) in Mandarin Fruit and Leaves.

Matrix	No. of Applications	PHI (days)	Application rate (lb ai/A)	Cyclopentyl label (ppm)	Triazole label (ppm)
Immature fruit	1	0	0.178	0.1031	0.1259
		28		0.0974	0.0991
Mature fruit		56		0.1127	0.0716
Leaves	1	0	0.178	4.2227	4.8372
		28		3.4995	3.6605
		56		3.0903	3.3074

TABLE C.2.2.1. Distribution of the Parent and the Metabolites in Mandarin Fruit Following Application of [cyclopentyl-^{14}C]Metconazole at 0.178 lb ai/A.[1]

Metabolite Fraction[2]	0-DAT		28-DAT		56-DAT	
	TRR = 0.1031 ppm		TRR = 0.0974 ppm		TRR = 0.1127 ppm	
	%TRR	ppm	%TRR	ppm	%TRR	ppm
Methanol surface wash	81.83	0.0843	19.85	0.0195	11.53	0.0131
Metconazole	77.21	0.0796	13.75	0.0136	5.95	0.0068
cis-Metconazole	*10.46*	*0.0108*	*11.39*	*0.0113*	*5.05*	*0.0057*
trans-Metconazole	*66.75*	*0.0688*	*2.37*	*0.0023*	*0.90*	*0.0010*
M21/Fr. 10[2]	0.18	0.0002	0.61	0.0006	0.42	0.0005
Fr. 1-4 (polar unknowns)	--	--	0.70	0.0006	0.95	0.0011
Fr. 5 & 7 (glucose conjugates)	0.87	0.0008	1.75	0.0017	1.62	0.0018
Fr. 6 (glucose conjugates)[3]	0.45	0.0005	0.76	0.0007	1.05	0.0012
Fr. 8 & 9 (free metabolites)	2.18	0.0022	2.04	0.0019	1.39	0.0016
Fr. 12-13 (nonpolar unknowns)	0.95	0.0009	0.23	0.0002	0.15	0.0002
Peel	18.16	0.0188	78.68	0.0765	86.89	0.0978
Methanol/water	17.56	0.0182	73.83	0.0718	80.15	0.0902
Aqueous	<0.15	<0.0002	1.75	0.0017	2.36	0.0026
Hexane/EtOAc (comb. with methanol)	16.81	0.0174	50.82	0.0496	51.63	0.0582
Methanol (combine with hexane/EtOAc)[4]	1.37	0.0014	20.73	0.0200	26.25	0.0295
Aglycone 1					8.58	0.0091
Aglycone 2 (M2)					1.82	0.0019
Aglycone 3					2.96	0.0031
Aglycone 4 (M1)					2.98	0.0032
Combined SPE organic	18.18	0.0188	71.56	0.0696	77.88	0.0877
Metconazole	16.97	0.0176	40.31	0.0394	42.98	0.0485
cis-Metconazole	*14.78*	*0.0153*	*34.22*	*0.0335*	*36.49*	*0.0412*
trans-Metconazole	*2.19*	*0.0023*	*6.09*	*0.0059*	*6.49*	*0.0073*
M21/Fr 10[2]	0.04	<0.0001	1.13	0.0011	1.22	0.0014
Fr. 1-4 (polar unknowns)	0.04	<0.0001	0.81	0.0008	1.19	0.0014
Fr. 5 & 7 (glucose conjugates)	0.40	0.0004	6.90	0.0067	7.06	0.0080
Fr. 6 (glucose conjugates)[3]	0.17	0.0002	16.97	0.0164	20.06	0.0225
Fr. 8 & 9 (free metabolites)	0.53	0.0006	5.05	0.0049	5.02	0.0057
Fr. 12-13 (nonpolar unknowns)	0.03	<0.0001	0.38	0.0004	0.36	0.0004
Nonextractable	0.60	0.0006	4.86	0.0047	6.74	0.0076
Flesh	0.01	<0.0001	14.7	0.0014	1.58	0.0018
Methanol/water	<0.17	<0.0002	1.32	0.0013	1.48	0.0017
Aqueous			0.45	0.0004	0.55	0.0006
Hexane/EtOAc (comb. with methanol)			0.71	0.0007	0.51	0.0006
Methanol (combine with hexane/EtOAc)			0.18	0.0002	0.41	0.0005
Combined SPE organic			1.34	0.0013	1.47	0.0017
Nonextractable	0.01	<0.0001	0.15	0.0001	0.10	0.0001

[1] Shading indicates that the extraction step and/or characterization analysis was not conducted for the matrix in question.
[2] Metabolite M21 was identified as part of Fraction 10 in 28- and 56-DAT samples.

[3] Consisting of 5 Regions, each accounting for ≤0.21% and 0.37% in 28- and 56-DAT surface wash, respectively; and ≤7.15% and 8.16% TRR in 28- and 56-day peel extract, respectively.
[4] Aglycones were characterized by acid hydrolysis of a separate subsample of the methanol eluate.

TABLE C.2.2.2. Distribution of the Parent and the Metabolites in Mandarin Fruit Following Application of [triazole-3,5-^{14}C]Metconazole at 0.178 lb ai/A.[1]

Metabolite Fraction[2]	0-DAT		28-DAT		56-DAT	
	TRR = 0.1259 ppm		TRR = 0.0991 ppm		TRR = 0.0716 ppm	
	%TRR	ppm	%TRR	ppm	%TRR	ppm
Methanol surface wash	83.95	0.1053	18.15	0.0181	15.24	0.0108
Metconazole	78.04	0.0978	12.23	0.0123	8.33	0.0059
cis-Metconazole	*64.94*	*0.0814*	*9.72*	*0.0098*	*6.67*	*0.0047*
trans-Metconazole	*13.11*	*0.0164*	*2.51*	*0.0025*	*1.66*	*0.0012*
M21/Fr 10[2]	0.50	0.0006	0.56	0.0006	0.55	0.0004
Fr. 1-4 (polar unknowns)	--	--	0.78	0.0008	1.34	0.0009
Fr. 5 & 7 (glucose conjugates)	1.38	0.0018	1.71	0.0017	2.04	0.0015
Fr. 6 (glucose conjugates)[3]	0.64	0.0009	0.68	0.0007	1.04	0.0007
Fr. 8 & 9 (free metabolites)	2.43	0.0031	1.93	0.0019	1.81	0.0013
Fr. 12-13 (nonpolar unknowns)	0.96	0.0012	0.26	0.0002	0.13	0.0002
Peel	15.74	0.0202	79.87	0.0790	81.66	0.0586
Methanol/water	15.07	0.0193	74.66	0.0738	75.64	0.0543
Aqueous	0.06	0.0001	2.93	0.0029	4.47	0.0032
Hexane/EtOAc (comb. with methanol)	14.71	0.0188	49.74	0.0497	46.80	0.0336
Methanol (combine with hexane/EtOAc)[4]	0.51	0.0007	21.05	0.0203	24.42	0.0175
Aglycone 1					7.95	0.0054
Aglycone 2 (M2)					1.94	0.0013
Aglycone 3					3.37	0.0023
Aglycone 4 (M1)					2.96	0.0020
Combined SPE organic	15.22	0.0195	70.79	0.0699	71.22	0.0511
Metconazole	14.08	0.0180	41.84	0.0414	38.92	0.0280
cis-Metconazole	*11.98*	*0.0153*	*35.07*	*0.0348*	*31.97*	*0.0230*
trans-Metconazole	*2.10*	*0.0027*	*6.77*	*0.0067*	*6.96*	*0.0050*
M21/Fr 10[2]	0.07	0.0001	1.19	0.0012	1.14	0.0008
Fr. 1-4 (polar unknowns)	0.08	0.0001	1.14	0.0011	0.70	0.0005
Fr. 5 & 7 (glucose conjugates)	0.37	0.0004	6.39	0.0064	6.33	0.0046
Fr. 6 (glucose conjugates)[3]	0.16	0.0002	14.94	0.0147	19.21	0.0138
Fr. 8 & 9 (free metabolites)	0.44	0.0005	5.00	0.0049	4.57	0.0033
Fr. 12-13 (nonpolar unknowns)	0.02	<0.0001	0.30	0.0003	0.36	0.0002
Nonextractable	0.67	0.0009	5.21	0.0052	6.02	0.0043
Flesh	0.31	0.0004	1.98	0.0020	3.10	0.0022
Methanol/water	0.26	0.0003	1.88	0.0019	3.01	0.0022
Aqueous			1.15	0.0011	2.20	0.0016
Hexane/EtOAc			0.48	0.0005	0.45	0.0003
Methanol			0.23	0.0002	0.33	0.0002
Nonextractable	0.04	0.0001	0.10	0.0001	0.09	0.0001

[1] Shading indicates that the extraction step and/or characterization analysis was not conducted for the matrix in question.
[2] Metabolite M21 was identified as part of Fraction 10 in 28- and 56-DAT samples.

[3] Consisting of 5 Regions, each accounting for ≤0.22% and 0.32% in 28- and 56-DAT surface wash, respectively; and ≤5.81% and 7.55% TRR in 28- and 56-day peel extract, respectively.
[4] Aglycones were characterized by acid hydrolysis of a separate subsample of the methanol eluate.

TABLE C.2.2.3. Distribution of the Parent and the Metabolites in Mandarin Leaves Following Application of [cyclopentyl-^{14}C]Metconazole at 0.178 lb ai/A.[1]

Metabolite Fraction[2]	0-DAT		28-DAT		56-DAT	
	TRR = 4.2227 ppm		TRR =3.4995 ppm		TRR = 3.0903 ppm	
	%TRR	ppm	%TRR	ppm	%TRR	ppm
Methanol surface wash	80.33	3.3921	51.80	1.8139	45.88	1.4132
Metconazole	75.02	3.1682	33.74	1.1828	26.51	0.8154
cis-Metconazole	*63.95*	*2.7005*	*28.73*	*1.0073*	*22.87*	*0.7046*
trans-Metconazole	*11.07*	*0.4677*	*5.01*	*0.1755*	*3.64*	*0.1108*
M21/Fr 10[2]	0.37	0.0158	1.55	0.0542	1.65	0.0504
Fr. 1-4 (polar unknowns)	--	--	2.79	0.0974	3.03	0.0955
Fr. 5 & 7 (glucose conjugates)	1.15	0.0485	5.1	0.1782	5.58	0.1724
Fr. 6 (glucose conjugates)[3]	0.47	0.0200	2.13	0.0745	2.52	0.0779
Fr. 8 & 9 (free metabolites)	2.41	0.1016	5.77	0.2020	5.78	0.1773
Fr. 12-13 (nonpolar unknowns)	0.90	0.0379	0.71	0.0247	0.81	0.0244
Leaf	19.67	0.8306	48.20	1.6856	54.12	1.6771
Methanol/water	18.86	0.7964	43.16	1.5094	47.34	1.4655
Aqueous	0.12	0.0051	3.16	0.1103	4.43	0.1370
Hexane/EtOAc (comb. with methanol)	18.96	0.8005	31.38	1.1001	31.55	0.9708
Methanol (combine with hexane/EtOAc)[4]	0.49	0.0207	9.25	0.3224	11.81	0.3679
Aglycone 1					3.35	0.1393
Aglycone 2 (M2)					0.82	0.0343
Aglycone 3					0.98	0.0406
Aglycone 4 (M1)					1.36	0.0564
Combined SPE organic	19.45	0.8212	40.63	1.4225	43.36	1.3387
Metconazole	17.90	0.7558	23.16	0.8121	21.56	0.6647
cis-Metconazole	*15.58*	*0.6577*	*19.95*	*0.6992*	*18.38*	*0.5683*
trans-Metconazole	*2.32*	*0.0981*	*3.21*	*0.1129*	*3.18*	*0.0964*
M21/Fr 10[2]	0.10	0.0040	0.83	0.0291	1.03	0.0319
Fr. 1-4 (polar unknowns)	0.08	0.0033	1.21	0.0423	1.69	0.0520
Fr. 5 & 7 (glucose conjugates)	0.52	0.0218	4.57	0.1598	6.02	0.1858
Fr. 6 (glucose conjugates)[3]	0.22	0.0091	6.68	0.2327	8.13	0.2524
Fr. 8 & 9 (free metabolites)	0.60	0.0256	3.81	0.1336	4.47	0.1381
Fr. 12-13 (nonpolar unknowns)	0.11	0.0046	0.36	0.0128	0.45	0.0138
Nonextractable	0.81	0.0342	5.04	0.1762	6.78	0.2116

[1] Shading indicates that the extraction step and/or characterization analysis was not conducted for the matrix in question.
[2] Metabolite M21 was identified as part of Fraction 10 in 28- and 56-DAT samples.
[3] Consisting of 5 Regions, each accounting for ≤0.73% and 0.99% in 28- and 56-DAT surface wash, respectively; and ≤2.41% and 3.61% TRR in 28- and 56-day peel extract, respectively.
[4] Aglycones were characterized by acid hydrolysis of a separate subsample of the methanol eluate.

TABLE C.2.2.4. Distribution of the Parent and the Metabolites in Mandarin Leaves Following Application of [triazole-3,5-^{14}C]Metconazole at 0.178 lb ai/A.[1]

Metabolite Fraction[2]	0-DAT		28-DAT		56-DAT	
	TRR =4.8372 ppm		TRR = 3.6605 ppm		TRR = 3.3074 ppm	
	%TRR	ppm	%TRR	ppm	%TRR	ppm
Methanol surface wash	82.03	3.9666	55.75	2.0409	39.10	1.2937
Metconazole	77.24	3.7352	36.42	1.3334	22.74	0.7521
cis-Metconazole	*65.16*	*3.1512*	*30.33*	*1.1104*	*18.65*	*0.6168*
trans-Metconazole	*12.08*	*0.5841*	*6.09*	*0.2230*	*4.09*	*0.1353*
M21/Fr 10[2]	0.32	0.0155	1.60	0.0587	1.29	0.0426
Fr. 1-4 (polar unknowns)	--	--	3.78	0.1382	3.17	0.1048
Fr. 5 & 7 (glucose conjugates)	1.06	0.0512	5.21	0.1907	4.55	0.1506
Fr. 6 (glucose conjugates)[3]	0.44	0.0212	2.04	0.0746	1.88	0.0622
Fr. 8 & 9 (free metabolites)	2.15	0.1042	5.93	0.2171	4.81	0.1594
Fr. 12-13 (nonpolar unknowns)	0.81	0.0392	0.77	0.0281	0.67	0.0221
Leaf	17.97	0.8706	44.25	1.6196	60.90	2.0138
Methanol/water	17.12	0.8296	35.95	1.3159	51.34	1.6974
Aqueous	0.11	0.0056	3.81	0.1393	6.66	0.2202
Hexane/EtOAc (comb. with methanol)	18.30	0.8868	24.45	0.8956	32.60	1.0784
Methanol (combine with hexane/EtOAc)[4]	0.49	0.0237	9.23	0.3375	12.48	0.4120
Aglycone 1					3.89	0.1390
Aglycone 2 (M2)					0.69	0.0247
Aglycone 3					0.92	0.0330
Aglycone 4 (M1)					1.39	0.0496
Combined SPE organic	18.79	0.9105	33.69	1.2331	45.07	1.4904
Metconazole	17.47	0.8462	17.92	0.6561	22.48	0.7437
cis-Metconazole	*14.69*	*0.7116*	*14.92*	*0.5466*	*18.56*	*0.6138*
trans-Metconazole	*2.78*	*0.1347*	*2.99*	*0.1095*	*3.93*	*0.1300*
M21/Fr 10[2]	0.07	0.0035	0.67	0.0245	0.99	0.0326
Fr. 1-4 (polar unknowns)	0.07	0.0033	1.28	0.0467	2.01	0.0661
Fr. 5 & 7 (glucose conjugates)	0.42	0.0203	3.89	0.1425	6.11	0.2020
Fr. 6 (glucose conjugates)[3]	0.17	0.0080	6.56	0.2397	8.43	0.2782
Fr. 8 & 9 (free metabolites)	0.52	0.0249	3.06	0.1120	4.59	0.1517
Fr. 12-13 (nonpolar unknowns)	0.09	0.0042	0.32	0.0116	0.48	0.0158
Nonextractable	0.85	0.0410	8.30	0.3037	9.55	0.3163

[1] Shading indicates that the extraction step and/or characterization analysis was not conducted for the matrix in question.
[2] Metabolite M21 was identified as part of Fraction 10 .
[3] Consisting of 5 Regions, each accounting for ≤0.69% and 0.53% in 28- and 56-DAT surface wash, respectively; and ≤2.64% and 3.38% TRR in 28- and 56-day peel extract, respectively.
[4] Aglycones were characterized by acid hydrolysis of a separate subsample of the methanol eluate.

TABLE C.2.3.1. Summary of Characterization and Identification of Radioactive Residues in Mandarin Fruit Following Application of [cyclopentyl-^{14}C]Metconazole at 0.178 lb ai/A.

Compound	0-DAT		28-DAT		56-DAT	
	TRR = 0.1031 ppm		TRR = 0.0974 ppm		TRR = 0.1127 ppm	
	%TRR	ppm	%TRR	ppm	%TRR	ppm
Metconazole	94.18	0.0972	54.06	0.0530	48.93	0.0553
M21/Fr 10[2]	0.22	0.0003	1.74	0.0017	1.64	0.0019
Fr. 1-4 (polar unknowns)	0.04	0.0001	1.51	0.0014	2.14	0.0025
Fr. 5 & 7 (glucose conjugates)[1]	1.27	0.0012	8.65	0.0084	8.68	0.0098
Fr. 6 (glucose conjugates)[1]	0.62	0.0007	17.73	0.0171	21.11	0.0237
Fr. 8 & 9 (free metabolites)	2.71	0.0028	7.09	0.0068	6.41	0.0073
Fr. 12-13 (nonpolar unknowns)	0.98	0.0010	0.61	0.0006	0.51	0.0006
Methanol/water extractable (flesh)	<0.17	<0.0002	1.32	0.0013	1.48	0.0017
Total identified	94.40	0.0975	55.8	0.0547	50.57	0.0572
Total characterized	5.79	0.0060	36.91	0.0356	40.33	0.0456
Total extractable	99.56	0.1025	95.0	0.0926	93.16	0.1050
Unextractable (PES)[2]	0.61	0.0006	5.01	0.0048	6.84	0.0077
Accountability[3]	100		100		100	

[1] Based on retention times, including glucose conjugates of mono- or di-hydroxylated metconazole metabolites (aglycones 1 and 3) and metabolites M1 (aglycone 4) and M2 (aglycone 2); refer to Table C.2.2.1 for relative distribution of aglycones.
[2] Residues remaining after exhaustive extractions.
[3] Accountability = (Total extractable + Total unextractable)/(TRR from combustion analysis; see TABLE C.2.1) * 100.

TABLE C.2.3.2. Summary of Characterization and Identification of Radioactive Residues in Mandarin Fruit Following Application of [triazole-3,5-^{14}C]Metconazole at 0.178 lb ai/A.

Compound	0-DAT		28-DAT		56-DAT	
	TRR = 0.1259 ppm		TRR = 0.0991 ppm		TRR = 0.0716 ppm	
	%TRR	ppm	%TRR	ppm	%TRR	ppm
Metconazole	92.12	0.1158	54.07	0.0537	47.25	0.0339
M21/Fr 10[2]	0.57	0.0007	1.75	0.0018	1.69	0.0012
Fr. 1-4 (polar unknowns)	0.08	0.0001	1.92	0.0019	2.04	0.0014
Fr. 5 & 7 (glucose conjugates)[1]	1.75	0.0022	8.1	0.0081	8.37	0.0061
Fr. 6 (glucose conjugates)[1]	0.80	0.0011	15.62	0.0154	20.25	0.0145
Fr. 8 & 9 (free metabolites)	2.87	0.0036	6.93	0.0068	6.38	0.0046
Fr. 12-13 (nonpolar unknowns)	0.98	0.0013	0.56	0.0005	0.49	0.0004
Methanol/water extractable (flesh)	0.26	0.0003	1.88	0.0019	3.01	0.0022
Total identified	92.69	0.1165	55.82	0.0555	48.94	0.0351
Total characterized	6.74	0.0086	35.01	0.0346	40.54	0.0292
Total extractable	99.28	0.1249	94.69	0.0938	93.89	0.0673
Unextractable (PES)[2]	0.71	0.0010	5.31	0.0053	6.11	0.0044
Accountability[2]	100		100		100	

[1] Based on retention times, including glucose conjugates of mono- or di-hydroxylated metconazole metabolites (aglycones 1 and 3) and metabolites M1 (aglycone 4) and M2 (aglycone 2); refer to Table C.2.2.2 for relative distribution of aglycones.
[2] Residues remaining after exhaustive extractions.
[3] Accountability = (Total extractable + Total unextractable)/(TRR from combustion analysis; see TABLE C.2.1) * 100.

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TABLE C.2.3.3. Summary of Characterization and Identification of Radioactive Residues in Mandarin Leaves Following Application of [cyclopentyl-^{14}C]Metconazole at 0.178 lb ai/A.

Compound	0-DAT		28-DAT		56-DAT	
	TRR = 4.2227 ppm		TRR =3.4995 ppm		TRR = 3.0903 ppm	
	%TRR	ppm	%TRR	ppm	%TRR	ppm
Metconazole	92.92	3.9240	56.90	1.9949	48.07	1.4801
M21/Fr 10[2]	0.47	0.0198	2.38	0.0833	2.68	0.0823
Fr. 1-4 (polar unknowns)	0.08	0.0033	4.00	0.1397	4.72	0.1475
Fr. 5 & 7 (glucose conjugates)[3]	1.67	0.0703	9.67	0.3380	11.60	0.3582
Fr. 6 (glucose conjugates)[3]	0.69	0.0291	8.81	0.3072	10.65	0.3303
Fr. 8 & 9 (free metabolites)	3.01	0.1272	9.58	0.3356	10.25	0.3154
Fr. 12-13 (nonpolar unknowns)	1.01	0.0425	1.07	0.0375	1.26	0.0382
Total identified	93.39	3.9438	59.28	2.0782	50.75	1.5624
Total characterized	6.46	0.2724	33.13	1.158	38.48	1.1896
Total extractable	99.19	4.1885	94.96	3.3233	93.22	2.8787
Unextractable (PES)[1]	0.81	0.0342	5.04	0.1762	6.78	0.2116
Accountability[3]	100		100		100	

[1] Based on retention times, including glucose conjugates of mono- or di-hydroxylated metconazole metabolites (aglycones 1 and 3) and metabolites M1 (aglycone 4) and M2 (aglycone 2); refer to Table C.2.2.3 for relative distribution of aglycones.
[2] Residues remaining after exhaustive extractions.
[3] Accountability = (Total extractable + Total unextractable)/(TRR from combustion analysis; see TABLE C.2.1) * 100.

TABLE C.2.3.4. Summary of Characterization and Identification of Radioactive Residues in Mandarin Leaves Following Application of [triazole-3,5-^{14}C]Metconazole at 0.178 lb ai/A.

Compound	0-DAT		28-DAT		56-DAT	
	TRR =4.8372 ppm		TRR = 3.6605 ppm		TRR = 3.3074 ppm	
	%TRR	ppm	%TRR	ppm	%TRR	ppm
Metconazole	94.71	4.5814	54.34	1.9895	45.22	1.4958
M21/Fr 10[2]	0.39	0.0190	2.27	0.0832	2.28	0.0752
Fr. 1-4 (polar unknowns)	0.07	0.0033	5.06	0.1849	5.18	0.1709
Fr. 5 & 7 (glucose conjugates)	1.48	0.0715	9.10	0.3332	10.66	0.3526
Fr. 6 (glucose conjugates)[1]	0.61	0.0292	8.60	0.3143	10.31	0.3404
Fr. 8 & 9 (free metabolites)	2.67	0.1291	8.99	0.3291	9.40	0.3111
Fr. 12-13 (nonpolar unknowns)	0.90	0.0434	1.09	0.0397	1.15	0.0379
Total identified	95.1	4.6004	56.61	2.0727	47.50	1.5710
Total characterized	5.73	0.2765	32.84	1.2012	36.70	1.2129
Total extractable	99.15	4.7962	91.70	3.3568	90.44	2.9911
Unextractable (PES)[2]	0.85	0.0410	8.30	0.3037	9.55	0.3163
Accountability[3]	100		100		100	

[1] Based on retention times, including glucose conjugates of mono- or dihydroxylated metconazole metabolites (aglycones 1 and 3) and metabolites M1 (aglycone 4) and M2 (aglycone 2); refer to Table C.2.2.4 for relative distribution of aglycones.
[2] Residues remaining after exhaustive extractions.
[3] Accountability = (Total extractable + Total unextractable)/(TRR from combustion analysis; see TABLE C.2.1) * 100.

C.3. Proposed Metabolic Profile

Based on the submitted mandarin metabolism study, the petitioner proposed the following metabolic pathway for metconazole. The main metabolic route of metconazole in mandarin is

via hydroxylation to form several metabolites including M1 and M2. These metabolites are further metabolized to form glucose conjugates and/or bound residues. Hydroxylation in the 4-chlorobenzyl position to form M21 was also observed as a minor metabolic pathway.

FIGURE C.3.1. Proposed Metabolic Profile of Metconazole in Mandarin

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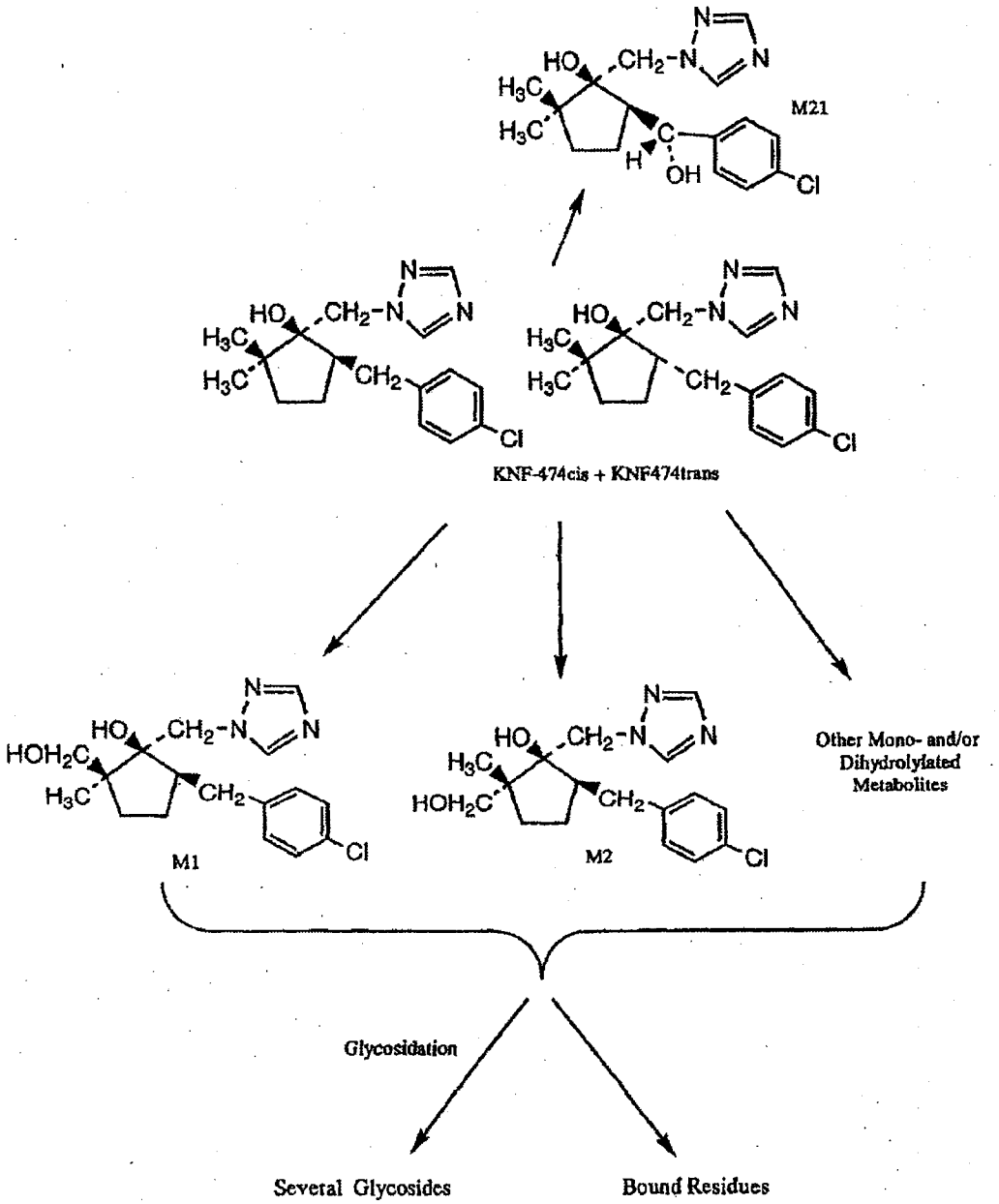
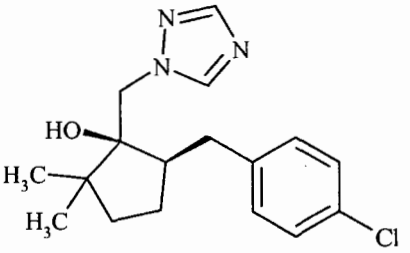
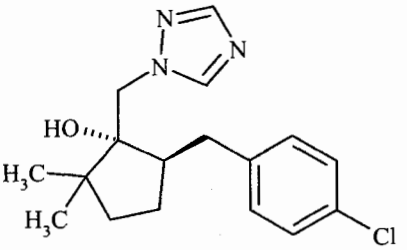
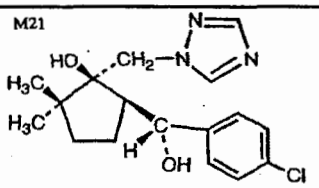
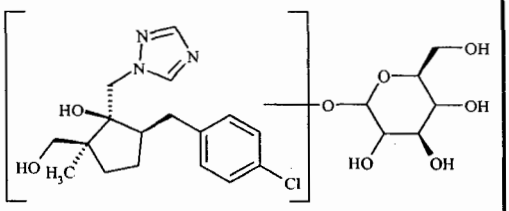
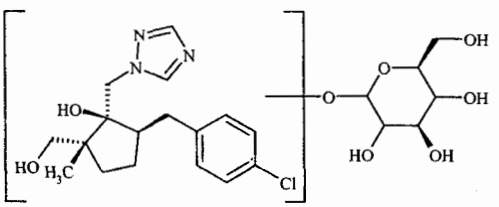
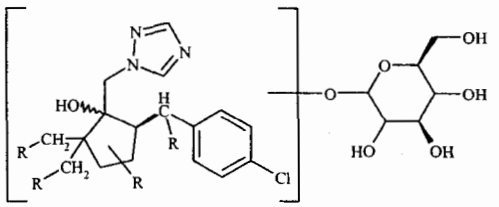


TABLE C.3.1. Identification of Compounds from Metabolism Study

Common name/code Figure C.3.1 ID No.	Chemical name	Chemical structure
Metconazole;	5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	 *cis*-isomer  *trans*-isomer
M21	5-[(4-chlorophenyl)methoxy]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)-1-cyclopentanol	
Glucose conjugate of M1 (tentative identification)	5-[(4-chlorophenyl)methyl]-2-methoxyl-2-methyl-1(1*H*-1,2,4-triazol-1-ylmethyl)-1-cyclopentanol	
Glucose conjugate of M2 (tentative identification)	5-[(4-chlorophenyl)methyl]-2-methoxyl-2-methyl-1(1*H*-1,2,4-triazol-1-ylmethyl)-1-cyclopentanol	
Glucose conjugate of mono- or dihydroxylated metconazole (tentative identification)		

D. CONCLUSION

In mandarin fruit harvested 0, 28, and 56 days after a single broadcast foliar application of [cyclopentyl-^{14}C]metconazole or [triazole-3,5-^{14}C]metconazole at 0.178 lb ai/A, TRR, determined by summing radioactivity in the surface wash, methanol/water extract, and nonextractable residues, were 0.1031, 0.0974, and 0.1127 ppm, respectively, following application of the cyclopentyl-labeled test substance and 0.1259, 0.0991, and 0.0716 ppm following application of the triazole-labeled test substance. In leaves harvested 0, 28, and 56 DAT, TRR were 4.2227, 3.4995, and 3.0903 ppm, respectively, following application of the cyclopentyl-labeled test substance, and 4.8372, 3.6605, and 3.3074 ppm following application of the triazole-labeled test substance.

Metconazole was the primary residue identified in mandarin peel and leaves at all sampling intervals, accounting for 92.12-94.71% TRR in 0-DAT samples; 54.06-56.90% TRR in 28-DAT samples; and 45.22-48.93% TRR in 56-DAT samples. Metabolite M21 was the only other identified residue, accounting for 0.22-0.57% TRR, 1.74-2.38% TRR, and 1.64-2.68% TRR, respectively, in 0-, 28-, and 56-DAT peel and leaves. Residues characterized as glucose conjugates (fractions 5-7) accounted for ≤2.55% TRR in 0-DAT peel and leaf samples; ≤26.38% TRR and ≤29.79% TRR in 28- and 56-DAT peel, respectively; and ≤18.48% TRR and ≤22.25% TRR in 28- and 56-DAT leaves. Portions of these residues were tentatively characterized/identified in 56-DAT samples as glucose conjugates of mono- or dihydroxylated metconazole, metabolite M2, and M1. Fraction 6 (21% TRR in peel and 12% TRR in leaves) was comprised of multiple components, none exceeding 8.16% TRR in peel extracts or 3.61% TRR in leaves. Two fractions characterized as free metabolites (fractions 8 and 9) together accounted for up to 6.41% TRR in peel and up to 10.25% TRR in leaves. Remaining residues consisted of polar and nonpolar unknowns, which represented ≤2.14% TRR in peel and ≤2.68% TRR in leaves.

The studies are supported by adequate storage stability data, and acceptable methods were used for extraction and characterization/identification of residues; however, the petitioner did not include analysis for triazole metabolites (1,2,4-triazole, triazolylalanine, or triazolylacetic acid) in the study.

Based on the submitted mandarin metabolism study, the petitioner proposed the following metabolic pathway for metconazole. The main metabolic route of metconazole in mandarin is via hydroxylation to form several metabolites including M1 and M2. These metabolites are further metabolized to form glucose conjugates and/or bound residues. Hydroxylation in the 4-chlorobenzyl position to form M21 was also observed as a minor metabolic pathway.

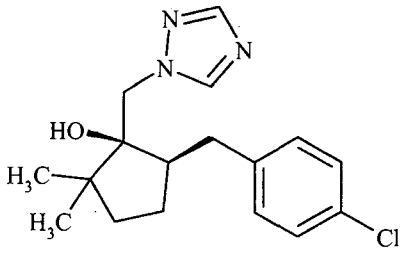
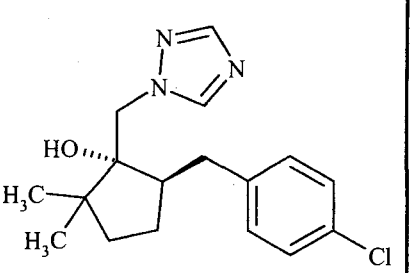
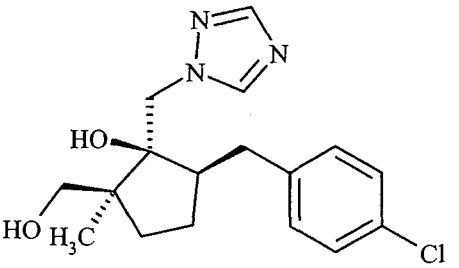
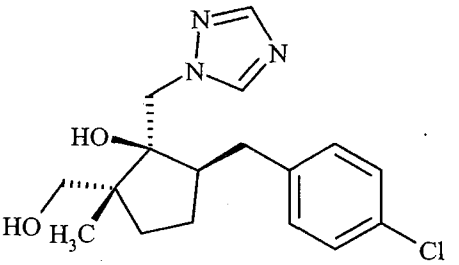
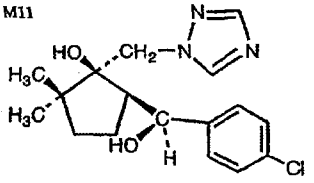
E. REFERENCES

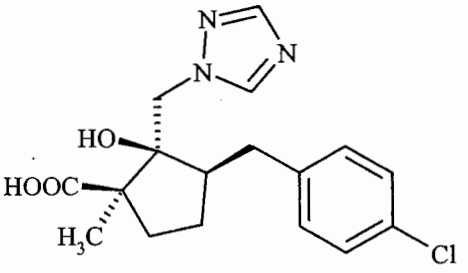
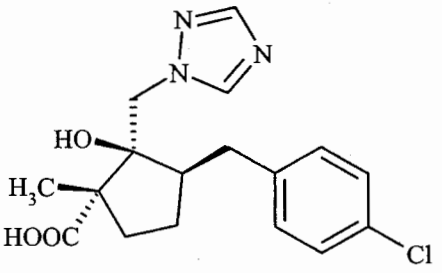
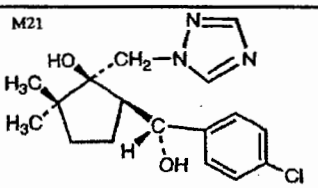
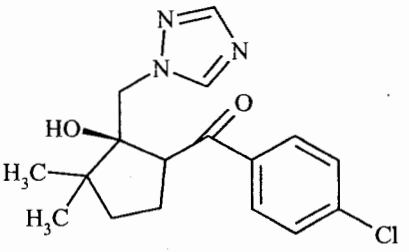
DP#:	324541
Subject:	Metconazole. Request for a Tolerance on Imported Bananas. Summary of Analytical Chemistry and Residue Data. Petition Number 9E05052.
From:	N. Dodd
To:	M. Waller
Date:	12/14/05
MRIDs:	44721506, 44721507, 44721508, 44721509, 44721510, and 44721511

F. DOCUMENT TRACKING

RDI: N. Dodd (2/20/08)
Petition Numbers: 6F7094 and 6F7095
DP#s: 348168 and 348206
PC Code: 125619

Template Version June 2005

APPENDIX I. Chemical Names and Structures of Reference Standards Used in the Mandarin Metabolism Study.		
Common name; Company code(s)	Chemical name	Chemical structure
Metconazole	5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	 *cis*-isomer  *trans*-isomer
M1; CL 359451	5-[(4-chlorophenyl)methyl]-2-methoxyl-2-methyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)-1-cyclopentanol or 3-(p-chlorobenzyl)-2-hydroxy-3-methyl-2-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanemethanol	
M2; CL 359452	5-[(4-chlorophenyl)methyl]-2-methoxyl-2-methyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)-1-cyclopentanol or 3-(p-chlorobenzyl)-2-hydroxy-3-methyl-2-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanemethanol	
M11; CL 382390; CL 197129; KNF-474-M-11	5-[(4-chlorophenyl)methoxyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)-1-cyclopentanol	

APPENDIX I. Chemical Names and Structures of Reference Standards Used in the Mandarin Metabolism Study.		
Common name; Company code(s)	Chemical name	Chemical structure
M12	5-[(4-chlorophenyl)methyl]-2-carboxyl-2-methyl-1-(1*H*-1,2,4-triazol-1-yl methyl)-1-cyclopentanol	
M13	5-[(4-chlorophenyl)methyl]-2-methyl-2-carboxyl-1-(1*H*-1,2,4-triazol-1-yl methyl)-1-cyclopentanol	
M21; CL 382391	5-[(4-chlorophenyl)methoxy]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)-1-cyclopentanol	
M30; CL 382389	5-[(4-chlorophenyl)keto]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)-1-cyclopentanol	

Primary Evaluator	This DER was originally prepared under contract by Dynamac Corporation.
Approved by	Nancy Dodd, Chemist Nancy Dodd Date: 2/20/08 Registration Action Branch 3 Health Effects Division (7509P)

This DER was originally prepared under contract by Dynamac Corporation (2275 Research Boulevard, Suite 300; Rockville, MD 20850; submitted 09/13/2007). The DER has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

46901908 Johnston, A.; Cameron, S.; Young, C. (1992) The Disposition of (Carbon 14)-WL148271 (KNF-S-474M) in the Lactating Goat. Project Number: IRI/143140, 200300446. Unpublished study prepared by Inveresk Research International. 170 p.

EXECUTIVE SUMMARY:

Valent U.S.A. Corporation has submitted a study investigating the metabolism of [cyclopentyl-^{14}C]metconazole (specific activity 10.33 µCi/mg) in goats. Two goats were orally dosed with the radiolabeled test substance at a target dose of 25 mg per day. Goat 1 was dosed for three consecutive days, and Goat 2 was dosed for four consecutive days; a third goat was dosed with a capsule containing ethanol only as a control. Based on the daily feed consumption, average dosing levels were equivalent to 14 and 25 ppm in the diet for Goat 1 and Goat 2, respectively. Milk was collected twice daily, and selected samples were separated into cream, curds, and whey. Goats were sacrificed 18 hours following the last dosing, and tissue samples of muscle (fore and hind leg), fat (renal and deep body), liver, and kidney were collected.

The in-life and initial analytical phases of the study were conducted by Inveresk Research International (IRI; Tranent, Scotland). Characterization and identification of metabolites in tissues were further investigated at Sittingbourne Research Center (SRC; Sittingbourne, England); these results were used to delineate the nature of the residue in goat matrices.

Total radioactive residues (TRR) in goat milk and tissues were determined at IRI. TRR were highest in liver (0.456 ppm, Goat 1; 0.559 ppm, Goat 2), then kidney (0.145 ppm, Goat 1; 0.276 ppm, Goat 2), and were very low in fat (ND-0.015 ppm), muscle (0.001-0.005 ppm) and milk (0.001-0.004 ppm). Fractionation of whole milk samples into cream, curds, and whey yielded average proportions of 4:23:73 (cream:curds:whey). The majority (55-69%) of the radioactivity was excreted, with relatively similar amounts in the urine and feces.

Only kidney and liver had TRR >0.015 ppm; therefore, extractions for metabolite identifications were focused mainly on the kidney and liver samples from Goat 2 (which bore higher residues than Goat 1). Initially at IRI, ~96-98% of the TRR in kidney and liver was extracted using acetonitrile (ACN) and ACN/water; nonextractable residues were 2.5-3.7% TRR. Kidney and liver samples were re-extracted for further residue characterization at SRC; ~88-89% of the TRR in kidney and liver was extracted using ACN/water; nonextractable residues were calculated by difference (11-12% TRR). The extracted radioactivity from SRC with the nonextractable radioactivity from IRI represented 92% of the TRR by combustion/LSC of kidney and liver. HED notes that samples of renal fat and muscle were also extracted at SRC, but because of very low radioactivity, these data are presented in the distribution table only for informational purposes and are not discussed below.

The extraction procedures and analytical methods used are adequate. The methods for identification and confirmation of residues included reverse and normal phase HPLC and TLC with fraction collection or co-chromatography with reference compounds. Adequate storage stability data demonstrate that the metabolic profile was relatively stable in kidney and liver for the study duration.

Approximately 40-42% TRR was identified in kidney and liver. The parent compound, metconazole, was the major compound identified in liver, accounting for 42.2% TRR (0.236 ppm); the parent only accounted for 2% TRR (0.006 ppm) in kidney. The metabolite M12 (with low levels of closely eluting M13) was identified as the major residue in kidney at 21% TRR (0.058 ppm). Following acid hydrolysis of the polar residues, at least 12 metabolites accounting for 50.5% TRR were characterized in liver (each present at ≤0.09 ppm). Insufficient kidney sample was available following acid hydrolysis for metabolite identification, but the metabolic profiles were essentially the same for kidney and urine; therefore, a urine extract was acid hydrolyzed and partitioned, and the data were converted to kidney equivalents. Based on the urine data, metabolite M1 accounted for 13.7% TRR (0.038 ppm), and co-eluting metabolites M2 and M15 accounted for 3.6% TRR (0.010 ppm) in kidney following acid hydrolysis. The petitioner reported that at least 14 metabolites were characterized in kidney (based on urine data) following acid hydrolysis (each present at ≤0.028 ppm). In general, the unknown metabolites in kidney and liver could only be characterized as monhydroxylated metabolites of metaconazole.

Based on the results of the cyclopentyl and triazole (refer to 46901909.der.doc) goat metabolism studies, the metabolic pathways of metconazole in goats include oxidative hydroxylation of the methyl group to yield monohydroxylated compounds M1 and M2, oxidative hydroxylation of the phenyl ring to yield monohydroxylated compounds M15 and/or M19, or oxidative hydroxylation of the cyclopentyl ring to yield monohydroxylated compounds M31 and M32. Further oxidation of the hydroxymethyl group to a carboxylic acid yields M12 and likely M13. Glucuronic acid conjugates of metconazole and the primary metabolites were also observed. In addition, the *cis:trans* isomer ratio determined in the liver extract (34:66) was very different from the *cis:trans* isomer ratio for the metconazole reference standard (80:20), indicating that the *trans* isomer of metconazole was metabolized more slowly than the *cis* isomer in liver.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the goat metabolism data are classified as scientifically acceptable.

The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP#s 348168 and 348206.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an impact on the validity of the study.

A. BACKGROUND INFORMATION

Metconazole [5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol] is a broad-spectrum triazole Group 3 fungicide (sterol biosynthesis inhibitors). There are currently no registered uses of metconazole in the U.S.; however, a tolerance has been established for banana, and a Section 18 emergency exemption and supporting time-limited tolerances have been granted for use on soybean. Valent U.S.A. Corporation has applied for registration of metconazole in the U.S. for use on peanut, stone fruits, and tree nuts.

The chemical structure and nomenclature of metconazole, and the physicochemical properties of the technical grade of metconazole are presented in Tables A.1 and A.2.

Table A.1. Metconazole Nomenclature.

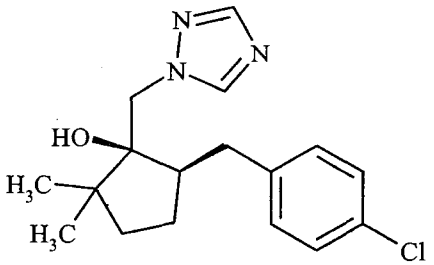
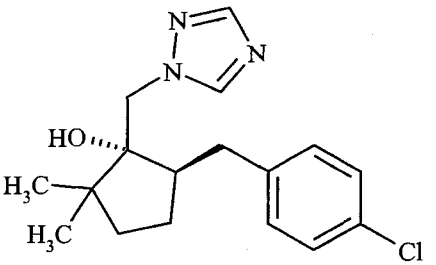
Chemical structure	 *cis*-isomer	 *trans*-isomer
Common name	Metconazole	
Company experimental name	KNF-S-474m (Kureha); BAS 555 F (BASF); V-10116 (Valent)	
IUPAC name	(1RS,5RS:1RS,5SR)-5-(4-chlorobenzyl)-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	
CAS name	5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	

Table A.1. Metconazole Nomenclature.	
CAS registry number	125116-23-6 (*cis*- and *trans*-isomers) 115850-27-6 (*cis*-isomer) 115850-28-7 (*trans*-isomer)
End-use products (EP)	50% WDG (Metconazole 50 WDG Fungicide, EPA File Symbol 59639-RUT) 0.75 lb/gal SC/L (Caramba™ Fungicide, EPA File Symbol No. 7969-EUA) 0.67 lb/gal SC/L formulation (BAS 556 01F Fungicide, EPA File Symbol No. 7969-EUT; also contains the active ingredient pyraclostrobin at 0.83 lb/gal)

Table A.2. Physicochemical Properties of Metconazole

Parameter	Value	References* (MRID)
Melting point/range	100.0-108.4°C (using Electrothermal Digital Melting Point Apparatus) (AC900,768 technical grade)	44721505
pH	5.81 at 25°C (1% aqueous suspension)	46808402
Relative density (20°C)	1.14 (relative density to water at 4°C, using capillary-stoppered, density-specific gravity bottle) (Lot No. AC 8879-140B)	44721505
Water solubility (20°C)	Using shake-flask method: 18.7 ± 1.0 mg/L (*cis*-isomer, WL148271, KNF-S-474m) 13.6 ± 1.7 mg/L (*trans*-isomer, WL148271, KNF-S-474m)	44721505

Solvent solubility (g/L) at 20°C — 44721505

Solvent	Metconazole	*cis*	*trans*
acetone	363	251	117
methanol	403	294	117
dichloromethane	481	343	141
ethyl acetate	260	173	90.0
propanol	132	86.6	46.7
toluene	103	66.2	38.0
Hexane	1.40	0.929	0.483

Vapor pressure (20°C)	Using gas-saturation method: $< 1.23 \times 10^{-5}$ Pa or 9.23×10^{-8} mm Hg (metconazole) $< 1.04 \times 10^{-5}$ Pa or 7.80×10^{-8} mm Hg (*cis*-isomer) $< 1.96 \times 10^{-6}$ Pa or 1.47×10^{-8} mm Hg (*trans*-isomer)	44721505
Dissociation constant (pK_a)	11.38±0.03 and 1.06±0.03 (in water at 29.1°C using spectrophotometric method; Lot No. AC 8879-140B)	44721505
Octanol/water partition coefficient, Log(K_{OW})	At 20 °C (using flask shaking method): K_{ow} (log K_{ow}) = 7090±989 (3.85) (Lot No. AC 8879-140B) (TGAI) K_{ow} (log K_{ow}) = 7150±803 (3.85) (*cis*-isomer, CL 354,801) K_{ow} (log K_{ow}) = 6800±1700 (3.8) (*trans*-isomer, CL 354,802)	44721505

UV/visible absorption spectrum — 46808403

pH	λ	A	log ε
cis-isomer			
2.0	221.4	0.828	4.03

Table A.2. Physicochemical Properties of Metconazole					
Parameter	Value				References* (MRID)
	6.8		0.8452	4.04	
	7.0		0.9126	4.08	
	10.3		0.7226	3.98	
	trans-isomer				
	2.0	221.4	0.9053	4.07	
	7.0		0.9547	4.10	
	10.1		0.9893	4.11	

* Product Chemistry Reviews: DP #256877, Shyam Mathur, Ph.D., 9/12/2000 and DP #329168, Shyam Mathur, Ph.D., 7/13/07.

B. EXPERIMENTAL DESIGN

B.1. Livestock

Two goats were orally dosed with [cyclopentyl-^{14}C]metconazole at a target dose of 25 mg per day. Goat 1 was dosed for three consecutive days, and Goat 2 was dosed for four consecutive days; a third goat was dosed with a capsule containing ethanol only as a control. Based on the daily feed consumption, average dosing levels were equivalent to 14 and 25 ppm in the diet for Goat 1 and Goat 2, respectively. The dose levels in dietary equivalents were higher than the target 10 ppm due to lower hay consumption than expected. One month prior to the start of the study and for the duration of the study, the animals were kept in individual stainless steel metabolism cages. The goats were fed ruminant feed supplemented with hay.

The test animals were sacrificed 18 hours after the last administration, and samples of edible organs and tissues were collected. Prior to sacrifice, milk samples were collected 17, 24, 41, 48, 65, 72 (Goat 2 only), and 89 (Goat 2 only) hours after the first dose administration.

Additional information relevant to the test goats is presented in Table B.1.1. Table B.1.2 presents the test animal dietary regime, and Table B.1.3 lists the test animal dosing regime.

TABLE B.1.1. General Test Animal Information.					
Species	Breed	Age	Weight at study initiation (kg)	Health Status	Description of housing/holding area
Goat	British Saanin	Not reported	50.5-51.0	Healthy; food intake declined in Goat 2 the last day of dosing, but the goat otherwise appeared healthy.	Individual stainless steel metabolism cages designed for separate collection of urine and feces. Controlled environment at 17-21 °C with 62-71% relative humidity; 12 hr. light/dark cycle and 15-20 air changes/hour.

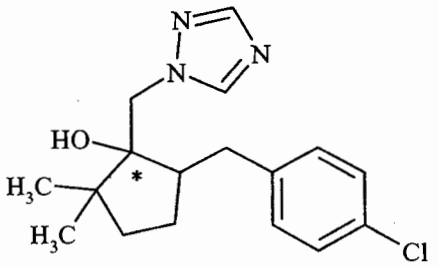
TABLE B.1.2. Test Animal Dietary Regime.				
Composition of Diet	Feed consumption (kg/day)	Water	Acclimation period	Predosing
250 g Course Goat Mixture twice daily at milking; hay *ad libitum*.	Goat 1: 1.4-2.1	*ad libitum*	1 month	None
	Goat 2: 1.1-1.7 and 0.5 on fourth dosing day			

TABLE B.1.3. Test Animal Dosing Regime.			
Treatment Type	Treatment Level [1] (ppm test material in vehicle)	Vehicle	Timing/Duration
Oral; esophageal tube into the rumen	Goat 1: 11.6-17.4 (average of 3 days = 13.7)	Dispensed in crushed diet in gelatin capsules	Goat 1: Once a day after evening milking for 3 consecutive days.
	Goat 2: 14.3-48.0 (average of 4 days = 25.1)		Goat 2: Once a day after evening milking for 4 consecutive days.

[1] Based on actual daily feed consumption and ~24 mg/day test substance.

B.2. Test Materials

The radiolabeled test substance was prepared in ethanol, and individual doses were dispensed onto crushed diet in a gelatin capsule each day. The characteristics of the test substance are presented in Table B.2.1.

TABLE B.2.1. Test Material Characteristics.	
Chemical structure	
Radiolabel position	[cyclopentyl-^{14}C]metconazole
Lot No.	S1157/1
cis:trans Ratio	79:21
Purity	99.0%
Specific activity	10.33 µCi/mg

B.3. Sampling Information

The in-life and initial analytical phases of the study were conducted by Inveresk Research International (IRI; Tranent, Scotland). Milk was collected twice daily (~9 am and 4 pm). The following organs and tissues were collected at goat sacrifice: liver, kidneys, two skeletal muscles (from fore leg and hind leg), two types of fat (renal and deep body along the spine), and the bile bladder. Sample collection information is summarized in Table B.3.1.

TABLE B.3.1. Sample Collection Information.			
Milk collected	Urine, feces and cage wash collected	Interval from last dose to sacrifice	Tissues harvested and analyzed
Milk collected twice daily (~9 am and 4 pm); 323-744 mL/milking from Goat 1 and 300-1,003 mL/milking from Goat 2 during dosing; milk production prior to dosing was not reported.	At each 24-hr period	18 hours	Fore and hind leg muscle, renal and body fat, liver, and kidney.

B.4. Identification/Characterization of Residues

B.4.1. Sample Handling and Preparation

Milk and tissue samples that were not analyzed immediately after collection were stored frozen (-20 °C).

Milk samples from Day 2 (17 and 24 hour), Day 4 am (65 hour), and Day 5 (89 hour, Goat 2 only) were fractionated into cream, curds, and whey. Cream was separated by centrifugation, and the remaining sample was acidified to precipitate the proteins (curds) from the whey fraction.

Only liver and kidney samples contained TRR >0.015 ppm; therefore, they were the only samples subjected to further extraction procedures at IRI. These results were used to demonstrate stability of the metabolic profile. Liver and kidney samples from Goat 2 were extracted with ACN (2x), centrifuged, and the supernatants were combined for TLC and HPLC analysis. Nonextractable residues were further extracted with ACN:water (1:1, v:v; 2x); these extracts were not subjected to chromatographic analysis.

Characterization and identification of metabolites in tissues was further investigated at Sittingbourne Research Center (SRC; Sittingbourne, England); these results were used to delineate the nature of the residue in goat matrices. Tissue samples were shipped frozen to SRC. Upon receipt, samples were immediately placed in deep frozen storage (at -25 to -10 °C) until analysis.

At SRC, liver and kidney samples were extracted 3x with ACN:water (9:1, v:v) and centrifuged. The combined supernatants were concentrated to dryness, and the residues were reconstituted in methanol. In kidney, when the methanol volume was reduced, precipitation occurred; radioassay of the liquid phase indicated 96% of the extracted radioactivity in solution.

Although residues were <0.015 ppm in fat and muscle, these samples were analyzed at SRC for metabolite identification. Muscle samples were extracted 2x with methanol, filtered, and the filtrate was concentrated to an oil. Residues were reconstituted in methanol and centrifuged to separate solid material. Finally, the methanol solution was concentrated (53% recovery).

Fat samples were extracted 2x with dichloromethane and filtered. The dichloromethane extract was concentrated to dryness and the white solid was redissolved in hexane and ACN. Following separation of the organic phases, the hexane layer was collected and washed twice again with

ACN. Radioactivity in the ACN and hexane phases was high, most likely due to low radioactivity and high volumes of extraction solvent.

The liver, kidney, and muscle residues in methanol, and fat residues in ACN were chromatographically analyzed. The liver and kidney extracts were also partitioned between diethyl ether and water several times, and like phases were combined. The aqueous phase containing the polar metabolites was concentrated, refluxed with 2 M HCl for 3 hours, and, after HPLC analysis, adjusted to pH 2 with sodium hydroxide and partitioned again under acidic conditions.

The residue fractionation/extraction procedures used for goat liver and kidney at SRC are depicted below (Figures B.4.1.1 and B.4.1.2; the flowcharts were copied without alteration from MRID 46901908). HED notes that the liver flowchart erroneously indicates the ether phase from the initial partitioning was acid treated; however, all of the data indicate that the aqueous phase (polar) was acid hydrolyzed.

Figure B.4.1.1. Flowchart of Residue Extraction/Fractionation Procedures in Goat Liver.

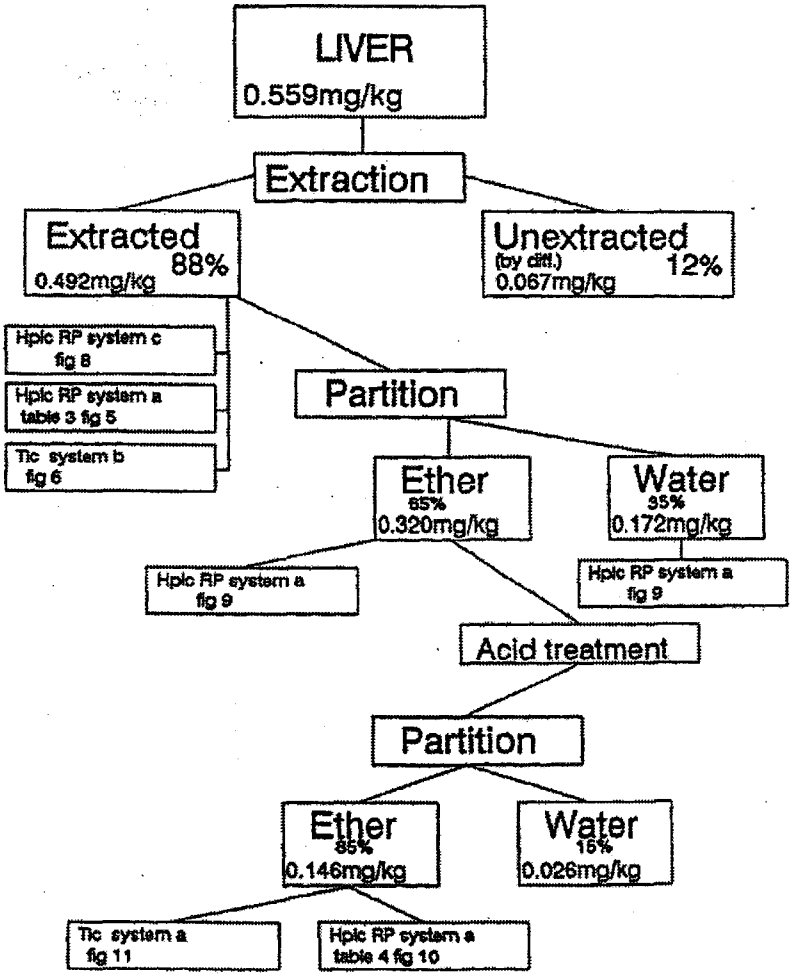
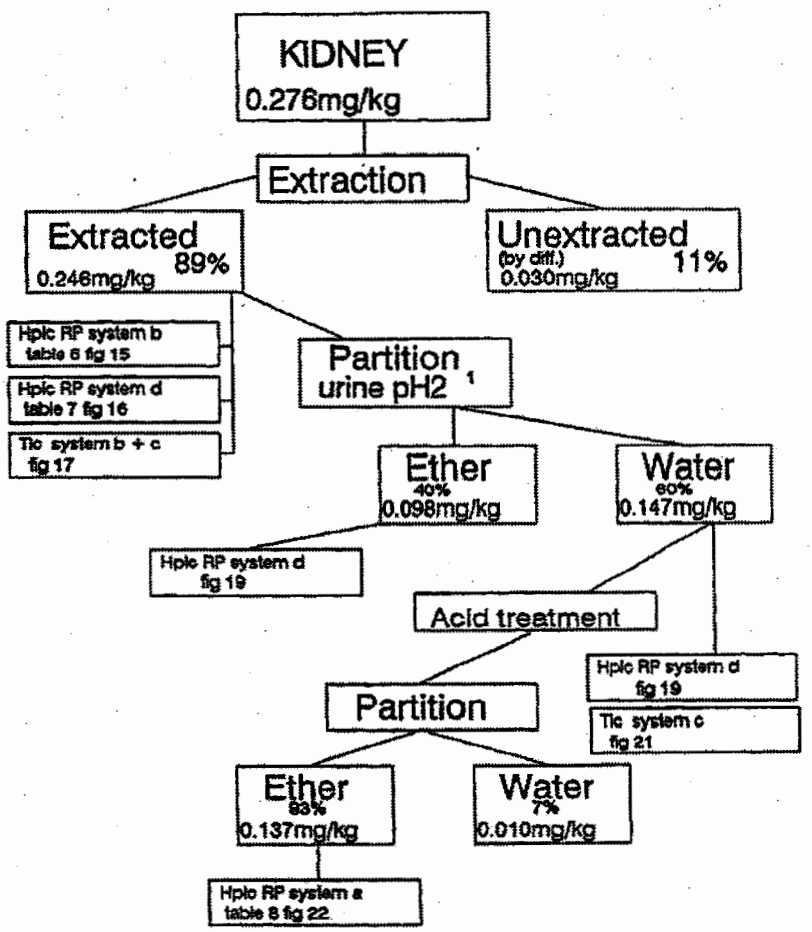


Figure B.4.1.2. Flowchart of Residue Extraction/Fractionation Procedures in Goat Kidney.



B.4.2. Analytical Methodology

Radioactivity in liquid samples was determined by direct liquid scintillation (LSC), and radioactivity in solid samples was determined using combustion/LSC. Limits of detection (LOD), based on the control goat samples, were 1-7 ppb for milk (whole, cream, curds, and whey), muscle, liver, kidney, and body fat, and 23 ppb for renal fat. The limit of reliable measurement (LRM) was set at 2x the net (average) LOD.

Liver and kidney extracts were initially analyzed at IRI using TLC (2 systems) and HPLC. The two TLC systems used silica gel plates and solvent systems of ethyl acetate:formic acid:water (70:1:1, v:v:v) or dichloromehane:acetone:formic acid:water (60:40:0.1:0.1, v:v:v:v). Radioactive areas were determined using a radioanalyzer; each extract was co-chromatographed with nonradiolabeled metconazole. The HPLC system utilized an ODS (C18) column, UV

detection (230 nm), online radiodetection, and a step gradient mobile phase of ACN and water, each acidified to pH 5-5.5 with formic acid and ammonia.

At SRC, kidney and liver extracts were analyzed using TLC and HPLC; these results were used to delineate the nature of the residue in goat matrices. TLC systems used silica gel plates and solvent systems of dichloromethane:acetone (3:1, v:v) and ethyl acetate:formic acid:water (70:2:2 or 70:8:8, v:v:v) for metabolite profiling. Radioactive areas were detected with autoradiography, and nonlabeled reference standards were observed using UV (254 nm) light; appropriate reference standards were co-chromatographed with each sample.

Normal phase HPLC analyses for isomer determination were conducted with a Nitro NC 100 column, UV (230 nm) detection, and an isocratic mobile phase of dichloromethane:hexane:tetrahydrofuran (80:18:2, v:v:v). Two reverse phase HPLC systems were used for metabolite profiling and identification. The first system utilized an ODS (C18) column, UV (230 or 254 nm) detection, and a gradient mobile phase of ACN and water containing ammonia solution and formic acid; or ACN and water each with formic acid. The second system utilized an S5-CN column, UV (254 nm) detection, and an isocratic mobile phase of ACN and water, each containing formic acid. Eluant fractions were collected with all HPLC systems, and the collected fractions were radioassayed by LSC. Metabolites were identified by comparison of retention times or co-chromatography with reference standards. The reference standards used in the study are presented in Appendix I.

Quantitation of residues by SRC was based on TRR measurements made by IRI. The proportions (%TRR in tissue) of radioactivity measured in the extracts, partition solutions, and chromatographic peaks were based on measurements made by SRC. When differences in the SRC and IRI values were observed, the IRI values were considered more accurate by the petitioner because control values were included in the calculations.

C. RESULTS AND DISCUSSION

Sample storage conditions and intervals are summarized in Table C.1. Initial residue characterization at IRI was performed within 1 month of sacrifice; tissue samples were further analyzed for metabolite characterization/identification at SRC within 10 months of collection. Re-extraction and analysis of kidney and liver samples at IRI demonstrated no significant changes in the metabolic profile ~7 months after collection; although the profiles showed differences in the ratio of the parent compound and polar components, no degradation products were detected. Therefore, it can be concluded that the residues in goat tissue samples were relatively stable during the experimental period.

Total radioactive residues in goat milk and tissues are presented in Table C.2.1; these values were determined at IRI. TRR were highest in liver (0.456 ppm, Goat 1; 0.559 ppm, Goat 2), then kidney (0.145 ppm, Goat 1; 0.276 ppm, Goat 2), and were very low in fat (ND-0.015 ppm), muscle (0.001-0.005 ppm) and milk (0.001-0.004 ppm). Fractionation of whole milk samples into cream, curds, and whey yielded average proportions of 4:23:73 (cream:curds:whey). The majority (55-69%) of the radioactivity was excreted, with relatively similar amounts in the urine

and feces. The pharmacokinetics of metconazole in goat excreta is presented in Figure C.2.1; a figure demonstrating the trend in milk was not generated because of the extremely low TRR levels in whole milk.

Only kidney and liver had TRR >0.015 ppm; therefore, extractions for metabolite identifications were focused mainly on the kidney and liver samples from Goat 2 (which bore higher residues than Goat 1). Initially at IRI, ~96-98% of the TRR in kidney and liver was extracted using ACN and ACN/water; nonextractable residues were 2.5-3.7% TRR. Kidney and liver samples were re-extracted for further residue characterization at SRC; ~88-89% of the TRR in kidney and liver was extracted using ACN/water; nonextractable residues were calculated by difference (11-12% TRR). The extracted radioactivity from SRC with the nonextractable radioactivity from IRI represented 92% of the TRR by combustion/LSC of kidney and liver. The distribution of residues based on the SRC results is presented in Table C.2.2. HED notes that samples of renal fat and muscle were also extracted at SRC, but because of very low radioactivity, these data are presented only in the distribution table for informational purposes.

The analytical methods used for identification and confirmation of residues are adequate. These included reverse and normal phase HPLC and TLC with fraction collection or co-chromatography with reference compounds. Approximately 40-42% TRR was identified in kidney and liver. A summary of the characterization and identification of residues in kidney and liver is presented in Table C.2.3.

The parent compound, metconazole, was the major compound identified in liver, accounting for 42.2% TRR (0.236 ppm); the parent only accounted for 2% TRR (0.006 ppm) in kidney. The metabolite M12 (with low levels of closely eluting M13) was identified as the major residue in kidney at 21% TRR (0.058 ppm). Following acid hydrolysis of the polar residues, at least 12 metabolites accounting for 50.5% TRR were characterized in liver (each present at ≤0.09 ppm). Insufficient kidney sample was available following acid hydrolysis for metabolite identification, but the metabolic profiles were essentially the same for kidney and urine; therefore, a urine extract was acid hydrolyzed and partitioned, and the data were converted to kidney equivalents. Based on the urine data, metabolite M1 accounted for 13.7% TRR (0.038 ppm), and co-eluting metabolites M2 and M15 accounted for 3.6% TRR (0.010 ppm) in kidney following acid hydrolysis. The petitioner reported that at least 14 metabolites were characterized in kidney (based on urine data) following acid hydrolysis (each present at ≤0.028 ppm). The chemical names and structures of compounds identified in the study are presented in Table C.3.1.

Identification of the parent, metconazole, in the liver extract was confirmed by reverse and normal phase HPLC analyses. The *cis:trans* isomer ratio was determined as 34:66 in the liver extract, which was very different from the *cis:trans* isomer ratio for the metconazole reference standard (80:20) indicating that the *trans* isomer of metconazole was metabolized more slowly than the *cis* isomer in liver.

Reverse phase HPLC (ODS column) analysis of liver at SRC, indicated two polar peaks at retention times similar to those of the carboxylic acid metabolites M12 and M13; however, when analyzed by reverse phase HPLC using a mobile phase with acidified solvents, the major polar

peak was not the same as M12, but was closer to the retention time of sulfate conjugates of monohydroxy or carboxylic metabolites of metconazole. These observations were confirmed with TLC analysis. The major polar peak in liver was similar to that in goat bile. The metabolite in bile was isolated by reverse phase HPLC, and attempts were made to identify it using MS detection; however, the spectra indicated that the residue was unstable.

When the liver extract was partitioned between diethyl ether and water, the majority (65%) of the radioactivity remained in the organic phase, but the major polar peak was found in the aqueous phase. The aqueous phase was acid hydrolyzed, and HPLC analysis of the hydrolysate indicated that the polar components were no longer present; however, the petitioner noted that the chromatography was poor. With partitioning of the acid hydrolysate (after adjustment to pH 2), the majority (85%) of the radioactivity remained in the organic phase, and HPLC analysis yielded seven distinct peaks. One peak co-chromatographed with metconazole. Identification of the other residues was inconclusive; however, two peaks appeared to be similar to metabolites M2/M15 (co-eluting) and M1. TLC analysis confirmed the parent and that the major polar component did not match the available monohydroxy metabolite reference standards. No further attempts were made to identify the polar components in liver, but, based on the chromatographic behavior, the majority of the nonpolar and deconjugated metabolites in liver were considered to be monohydroxy metabolites of metconazole. The acid hydrolyzed polar peaks in liver were the same as those in a goat fecal extract based on comparison of TLC and HPLC analyses. LC/MS of goat bile supported the tentative identification of the components in liver as monohydroxy metabolites of metconazole.

In kidney, identification of co-eluting M12/M13 was confirmed by HPLC under acidic conditions and by TLC analyses. The remaining three components were consistent with conjugated metabolites such as sulfates seen in rat fecal extracts. Further attempts to identify these metabolites in kidney were not possible because of the low radioactivity and limited tissue material; however, because of the similarities with the metabolic profile of urine, a urine sample was partitioned to further characterize the polar metabolites.

The radioactivity in urine upon partitioning with diethyl ether and water was split between the organic and aqueous phases almost equally. HPLC and TLC co-chromatography with reference standards confirmed the identification of M12 in the organic phase. Chromatography also indicated a small amount of M13 in the organic phase, but co-chromatography was not conducted to confirm M13. TLC showed that the polar components in kidney were the same as those in the aqueous phase of partitioned urine; therefore, the aqueous phase of urine was acid hydrolyzed and partitioned again: 93% of the radioactivity partitioned into the organic phase indicating the metabolites had changed. HPLC analysis indicated 16 peaks, with the major peak eluting at the same retention time as M1. A shoulder on the next largest component corresponded to M2 and/or M15. Identifications were not confirmed by co-chromatography because of the close proximity of the major components. For the remaining components, a major portion was considered to be a mixture of conjugates of monohydroxy metabolites of metconazole based on chromatographic behavior.

C.1. Storage Stability

Liver and kidney samples were extracted within 1 month of collection at IRI. Additional liver and kidney subsamples stored at -20 °C were extracted 3, 5, and 7 months after collection to demonstrate storage stability. These subsamples were extracted with ACN:water (9:1, v:v), and the extracts were analyzed by TLC and HPLC.

HPLC of the initial liver extract detected the parent as the major residue and three minor components. At the subsequent, 3- and 5-month intervals, the number of components detected by HPLC were the same but proportionally different; the parent accounted for only 10% in the 3-month sample. The petitioner proposes that the extract solvents used may have contributed to the differences in the residue levels detected; initial samples were extracted with ACN, in which the parent would likely be in solution, while more polar residues could be absent due to low solubility in ACN, and the later samples were extracted with ACN/water, which upon concentration would be mainly aqueous, allowing for greater solubility of the polar residues. Some precipitation of parent was thought to have also occurred with the more aqueous environment. To demonstrate this occurrence, the 7-month sample was extracted with ACN/water and reduced to a mixture of both ACN and water. HPLC analysis contained all residue peaks observed in earlier extractions, but at different proportions. The petitioner concluded that the 7-month extract was representative of the metabolic profile of liver, and that earlier proportions observed in liver were a result of the differing solubility of each radiolabeled compound in the final reduced extract rather than the breakdown of the radiolabeled component upon storage at -20 °C. Similar results were observed in the extracts of stored kidney; in addition, the metabolic profile for the 5-month sample was essentially the same as that found in urine, both in polarity and proportionally, thereby supporting the stability of the metabolic profile in kidney.

At SRC, samples, and when possible, extracts were stored at -25 to -10 °C until analysis. Working solutions were kept at room temperature during the day but were stored at -25 to -10 °C or 4 °C when not in use. Samples were stored for up to ~10 months from collection until analysis based on the experimental completion date; however, the petitioner stated that liver was stored frozen 5-11 months and kidney was stored up to 7 months prior to analysis at SRC. No significant differences were observed between the SRC and IRI analyses; therefore, the metabolic profile in kidney and liver appears to have been relatively stable for the study duration.

TABLE C.1. Summary of Storage Conditions.

Matrix	Storage Temperature (°C)	Actual Storage Duration [1]	Interval of Demonstrated Storage Stability
Goat liver and kidney at IRI	-20	25 days (<1 month)	7 months in frozen liver and kidney
Goat liver, kidney, fat and muscle at SRC	-10 to -25	≤294 days (9.7 months)	

[1] Storage interval from collection to initial extraction at IRI or storage interval from collection to experimental completion date at SRC. Actual analysis dates were not provided.

C.2. Identification, Characterization, and Distribution of Residues

TABLE C.2.1. Total Radioactive Residues (TRR) in Milk, Tissues, and Excreta.

Matrix	Collection Timing	Cyclopentyl Label			
		Goat 1		Goat 2	
		% AD	ppm [1]	% AD	ppm [1]
Urine	Dosing period	36.87	--	28.22	--
Feces		30.38	--	25.38	--
Cage wash		1.32	--	0.96	--
Total excreted		68.57	--	54.56	--
Milk	17 hour (Day 2 am)	NR [2]	0.003	NR	0.001
	24 hour (Day 2 pm)	NR	0.002	NR	0.001
	41 hour (Day 3 am)	NR	0.004	NR	0.002
	48 hour (Day 3 pm)	NR	0.003	NR	0.001
	65 hour (Day 4 am)	NR	0.004	NR	0.002
	72 hour (Day 4 pm)	--	--	NR	0.002
	89 hour (Day 5 am)	--	--	NR	0.004
Cream	17 hour (Day 2 am)	NR	0.007	NR	ND
	24 hour (Day 2 pm)	NR	ND	NR	ND
	65 hour (Day 4 am)	NR	0.012	NR	ND
	89 hour (Day 5 am)	--	--	NR	(0.008)
Curds	17 hour (Day 2 am)	NR	(0.005)	NR	ND
	24 hour (Day 2 pm)	NR	(0.004)	NR	(0.002)
	65 hour (Day 4 am)	NR	0.007	NR	(0.003)
	89 hour (Day 5 am)	--	--	NR	0.007
Whey	17 hour (Day 2 am)	NR	ND	NR	ND
	24 hour (Day 2 pm)	NR	(0.001)	NR	(0.001)
	65 hour (Day 4 am)	NR	(0.001)	NR	(0.001)
	89 hour (Day 5 am)	--	--	NR	(0.002)
Liver	At sacrifice	NR	0.456	NR	0.559
Kidney	At sacrifice	NR	0.145	NR	0.276
Muscle, fore leg	At sacrifice	NR	(0.001)	NR	(0.005)
Muscle, hind leg	At sacrifice	NR	0.004	NR	0.005
Fat, renal	At sacrifice	NR	ND	NR	ND
Fat, deep body	At sacrifice	NR	0.015	NR	0.003
Bile	At sacrifice	NR	3.781	NR	8.514
Bladder urine	At sacrifice	NR	11.206	NR	57.550

[1] ND = not detected. Ppm values reported in parentheses were calculated from residues below the limit of reliable measurement.
[2] NR = not reported.

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FIGURE C.2.1. Pharmacokinetics of Metconazole in Excreta of Lactating Goats

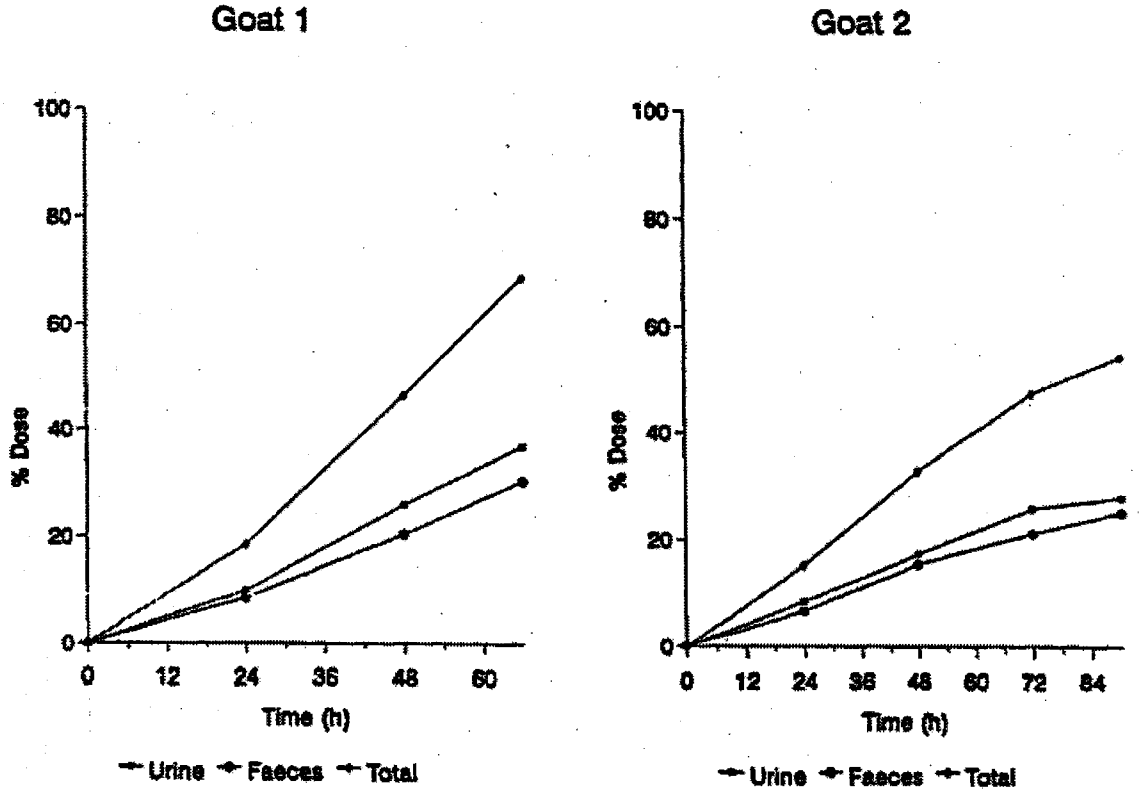

TABLE C.2.2. Distribution of the Parent and the Metabolites in Goat Matrices Following Dosing with [cyclopentyl-^{14}C]Metconazole at 25 ppm. [1]

Metabolite Fraction	Fat, renal		Muscle		Kidney[2]		Liver	
	TRR=0.023 ppm[3]		TRR=0.005 ppm		TRR=0.276 ppm		TRR=0.559 ppm	
	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm
Extractable	96	<0.012	82	0.004	89 [4]	0.246	88	0.492
Metconazole	14	<0.003	13.0	<0.001	1.0	0.003	37.5	0.210
M12	--	--	--	--	20.0	0.055	--	--
M13	--	--	--	--	1.0	0.003	--	--
Unknown conjugates	--	--	--	--	53.0 [5]	0.147	22.7 [6]	0.127
Unknowns (others)	--	--	69.0	0.003	12.0 [7]	0.003	27.8 [7]	0.155
Aqueous phase					53.4	0.147	30.8	0.172
Acidic aqueous phase					3.7	0.010	4.6	0.026
Acidic ether phase					49.7	0.137	26.2	0.146
Metconazole					--	--	4.7	0.026
Unknown (& metconazole)					2.7	0.007	--	--
M1					13.7	0.038	--	--
M2/M15					3.6	0.010	--	--
Unknowns (monohydroxy polarity)					23.5 [8]	0.065	1.9	0.011
Unknown (M1 polarity)					--	--	2.9	0.016
Unknown (M2/M15 polarity)					--	--	10.3	0.058

TABLE C.2.2. Distribution of the Parent and the Metabolites in Goat Matrices Following Dosing with [cyclopentyl-^{14}C]Metconazole at 25 ppm. [1]

Metabolite Fraction	Fat, renal		Muscle		Kidney[2]		Liver	
	TRR=0.023 ppm[3]		TRR=0.005 ppm		TRR=0.276 ppm		TRR=0.559 ppm	
	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm
Unknowns					5.6	0.015	6.3	0.035
Ether phase					35.6	0.098	57.2	0.320
Nonextractable [9]	4	<0.001	18	0.001	11 (2.5)	0.030 (0.007)	12 (3.7)	0.067 (0.021)

[1] Shading indicates that the extraction step and/or characterization analysis was not conducted for the matrix in question. TRR were determined by IRI in the initial analytical phase.
[2] Because of limited tissue availability the **values obtained from urine were converted to equivalent kidney residues** (partitioning and metabolites following acid hydrolysis).
[3] Based on the LRM (0.023 ppm) for fat; the actual value was below the LRM.
[4] Analyzed using two reverse phase HPLC systems; results from the one system under acidic conditions are presented because of better separation of M12/M13. For summarization of data, the petitioner used the results of the initial HPLC analysis for the parent compound (2% TRR, 0.006 ppm) because metconazole was confirmed with this system.
[5] Three separate components each present at ≤26.0% TRR (≤0.072 ppm).
[6] Two components each present at ≤16.1% TRR (≤0.090 ppm).
[7] Multiple components with a mixture of polarities; individual levels were not reported.
[8] A minimum of five components, each present at ≤11.1% TRR (≤0.031 ppm).
[9] Nonextractable residues were determined by SRC by difference (TRR - extractable); nonextractable residues, which were determined by combustion following extraction at IRI, are presented in parentheses (these values were used by the petitioner in summarizing the data).

TABLE C.2.3. Summary of Characterization and Identification of Radioactive Residues in Goat Matrices Following Dosing with [Cyclopentyl-^{14}C]Metconazole at 25 ppm. [1]

Compound	Kidney		Liver	
	TRR=0.276 ppm		TRR=0.559 ppm	
	% TRR	ppm	% TRR	ppm
Metconazole	2 [2]	0.006	42.2	0.236
M12/M13	21	0.058	--	--
M2/M15 (after acid hydrolysis)	3.6	0.010	--	--
M1 (after acid hydrolysis)	13.7	0.038	--	--
Others [3]	76	0.210	50.5	0.282
Total identified	40.3	0.112	42.2	0.236
Total characterized	76	0.210	50.5	0.282
Total extractable	89	0.246	88	0.492
Unextractable (PES) [4]	2.5	0.007	3.7	0.021
Accountability [5]	92	0.253	92	0.513

[1] Summarized results as presented by the petitioner in the tolerance petition volume.
[2] The petitioner used the metconazole values from IRI, since precipitation of the parent was suspected at SRC.
[3] In kidney, a minimum of 14 characterized metabolites after acid hydrolysis, each at ≤0.028 ppm; in liver, a minimum of 12 characterized metabolites after acid hydrolysis, each at ≤0.090 ppm.
[4] Residues remaining after extractions at IRI.
[5] Accountability = (Total extractable + Total unextractable)/(TRR from combustion analysis; see TABLE C.2.1) * 100.

C.3. Proposed Metabolic Profile

Based on the results of the cyclopentyl- and triazole-label (refer to 46901909.der.doc) goat metabolism studies, the metabolic pathways of metconazole in goats include oxidative

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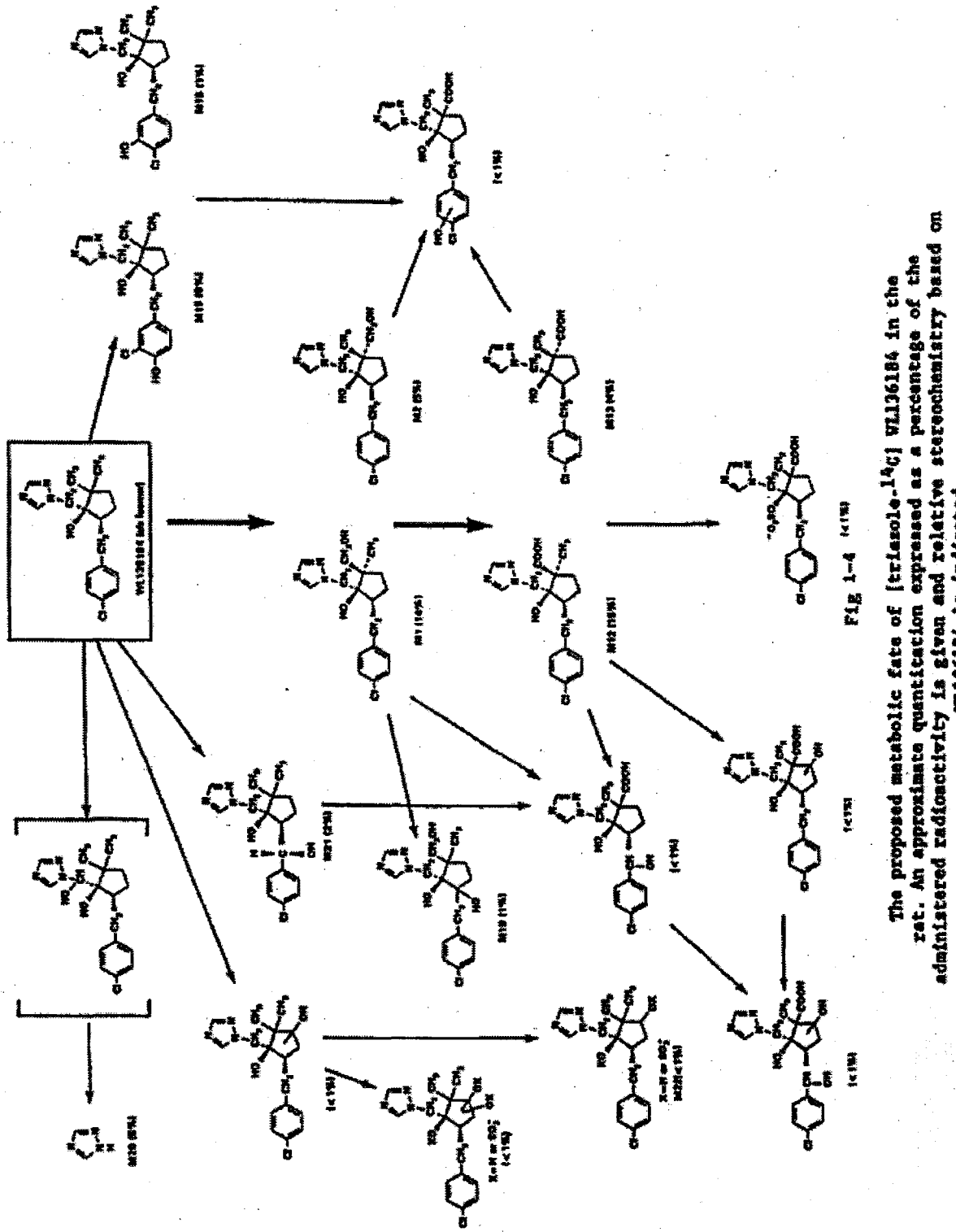
hydroxylation of the methyl group to yield monohydroxylated compounds M1 and M2, oxidative hydroxylation of the phenyl ring to yield monohydroxylated compounds M15 and/or M19, or oxidative hydroxylation of the cyclopentyl ring to yield monohydroxylated compounds M31 and M32. Further oxidation of the hydroxymethyl group to a carboxylic acid yields M12 and likely M13. Glucuronic acid conjugates of metconazole and the primary metabolites were also observed.

The petitioner did not include a metabolic pathway (flowchart) for metconazole in goat, but instead included the proposed metabolic fate of [triazole-^{14}C]metconazole in the rat. This is presented below in Figure C.3.1. for informational purposes.

FIGURE C.3.1. Proposed Metabolic Profile of Metconazole.



The proposed metabolic fate of [triazole-^{14}C] WL136184 in the rat. An approximate quantitation expressed as a percentage of the administered radioactivity is given and relative stereochemistry based on WL136184 is indicated

Fig 1-4

TABLE C.3.1. Identification of Compounds from Metabolism Study.

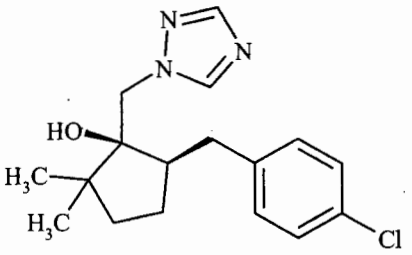
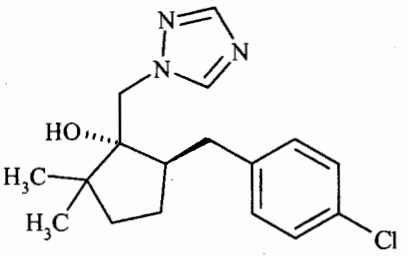
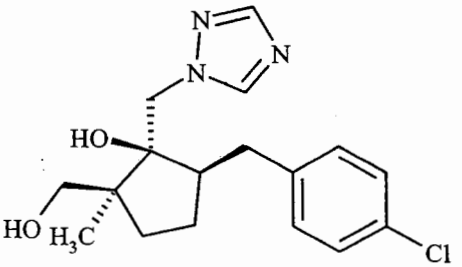
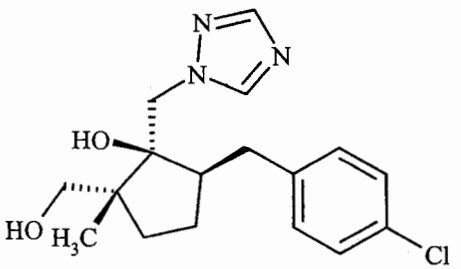
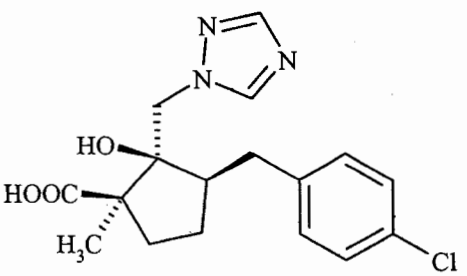
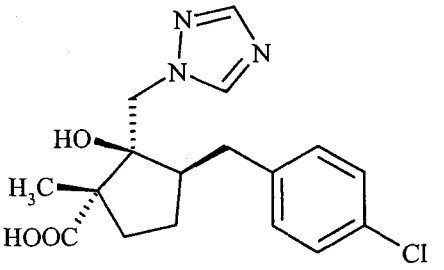
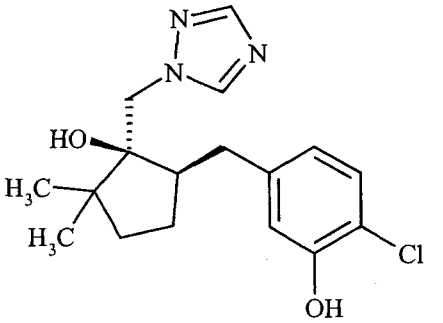
Common name/code Figure C.3.1 ID No.	Chemical name	Chemical structure
Metconazole	5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	 *cis*-isomer  *trans*-isomer
M1 (monohydroxylated metconazole metabolite)	5-[(4-chlorophenyl)methyl]-2-methoxyl-2-methyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)-1-cyclopentanol	
M2	5-[(4-chlorophenyl)methyl]-2-methoxyl-2-methyl-1(1*H*-1,2,4-triazol-1-yl methyl)-1-cyclopentanol	
M12 (carboxylic acid derivative of metconazole)	5-[(4-chlorophenyl)methyl]-2-carboxyl-2-methyl-1-(1*H*-1,2,4-triazol-1-yl methyl)-1-cyclopentanol	

TABLE C.3.1. Identification of Compounds from Metabolism Study.

Common name/code Figure C.3.1 ID No.	Chemical name	Chemical structure
M13 (isomer of M12)	5-[(4-chlorophenyl)methyl]-2-methyl-2-carboxyl-1-(1*H*-1,2,4-triazol-1-yl methyl)-1-cyclopentanol	
M15	5-[(3-hydroxy-4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-yl methyl)-1-cyclopentanol	

D. CONCLUSION

The metabolism study adequately delineates the nature of the residue in goats orally dosed with [cyclopentyl-^{14}C]metconazole for 3 or 4 consecutive days at 14 ppm (Goat 1) or 25 ppm (Goat 2), respectively, in the diet. TRR were highest in liver (0.456 ppm, Goat 1; 0.559 ppm, Goat 2), then kidney (0.145 ppm, Goat 1; 0.276 ppm, Goat 2), and were very low in fat (ND-0.015 ppm), muscle (0.001-0.005 ppm), and milk (0.001-0.004 ppm). Fractionation of whole milk samples into cream, curds, and whey yielded average proportions of 4:23:73 (cream:curds:whey). The majority (55-69%) of the radioactivity was excreted, with relatively similar amounts in the urine and feces. Only kidney and liver had TRR >0.015 ppm; therefore, extractions for metabolite identifications were focused mainly on the kidney and liver samples from Goat 2 (which bore higher residues than Goat 1).

The parent compound, metconazole, was the major compound identified in liver, accounting for 42.2% TRR; the parent only accounted for 2% TRR in kidney. The metabolite M12 (with low levels of closely eluting M13) was identified as the major residue in kidney at 21% TRR. Following acid hydrolysis of the polar residues, at least 12 metabolites accounting for 50.5% TRR were characterized in liver (each present at ≤0.09 ppm). Insufficient kidney sample was available following acid hydrolysis for metabolite identification, but the metabolic profiles were essentially the same for kidney and urine; therefore, a urine extract was acid hydrolyzed and partitioned, and the data were converted to kidney equivalents. Based on the urine data, metabolite M1 accounted for 13.7% TRR, and co-eluting metabolites M2 and M15 accounted for 3.6% TRR in kidney following acid hydrolysis. The petitioner reported that at least 14 metabolites were characterized in kidney (based on urine data) following acid hydrolysis (each

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present at ≤0.028 ppm). In general, the unknown metabolites in kidney and liver could only be characterized as monhydroxylated metabolites of metaconazole.

The study is supported by adequate storage stability data, and acceptable methods were used for extraction and characterization/identification of residues.

Based on the results of the cyclopentyl- and triazole-label (refer to 46901909.der.doc) goat metabolism studies, the metabolic pathways of metconazole in goats include oxidative hydroxylation of the methyl group to yield monohydroxylated compounds M1 and M2, oxidative hydroxylation of the phenyl ring to yield monohydroxylated compounds M15 and/or M19, or oxidative hydroxylation of the cyclopentyl ring to yield monohydroxylated compounds M31 and M32. Further oxidation of the hydroxymethyl group to a carboxylic acid yields M12 and likely M13. Glucuronic acid conjugates of metconazole and the primary metabolites were also observed.

E. REFERENCES

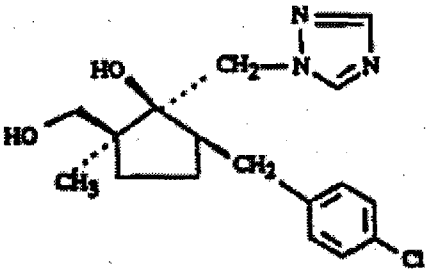
DP#:	324541
Subject:	Metconazole. Request for a Tolerance on Imported Bananas. Summary of Analytical Chemistry and Residue Data. Petition Number 9E05052.
From:	N. Dodd
To:	M. Waller
Date:	12/14/05
MRIDs:	44721506, 44721507, 44721508, 44721509, 44721510, and 44721511

F. DOCUMENT TRACKING

RDI: N. Dodd (2/20/08)
Petition Numbers: 6F7094 and 6F7095
DP#s: 348168 and 348206
PC Code: 125619

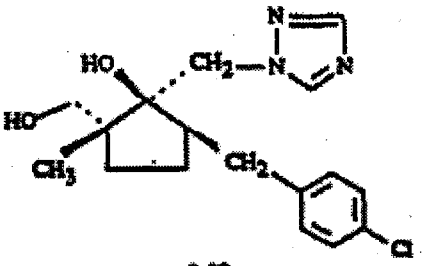
Template Version June 2005

APPENDIX I. Chemical Names and Structures of Reference Standards Used in Goat Metabolism Study. (Copied without alteration from MRID 46901908)



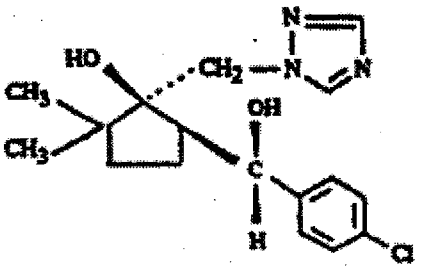
M1

(^{14}C-labelled, ref: 4191, B2-5)
(unlabelled, ref: MC1401)



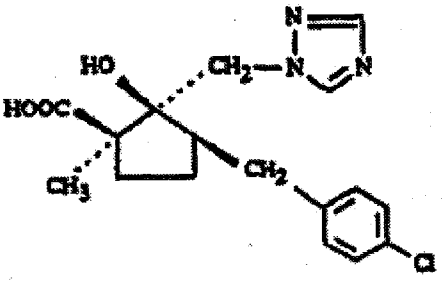
M2

(^{14}C-labelled, ref: 4191, B2-4)
(unlabelled, ref: MC1402)



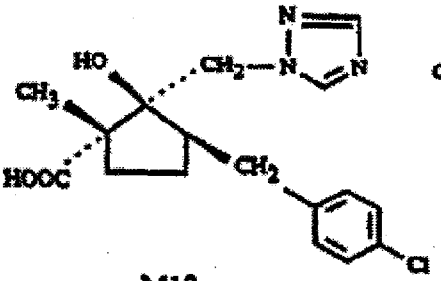
M11

(unlabelled, ref: MC1411)



M12

(^{14}C-labelled, ref: 4191, B1-5)
(unlabelled, ref: MC1417)



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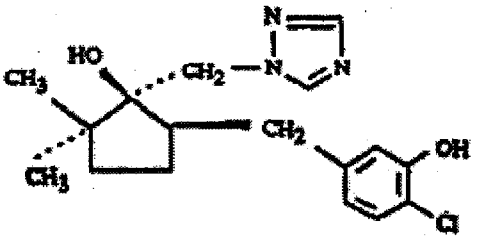
(^{14}C-labelled, ref: 4191, B1-4)
(unlabelled, ref: MC1418)



M15

(^{14}C-labelled, ref:4191, B3-3d)
(unlabelled, ref: MC1420)

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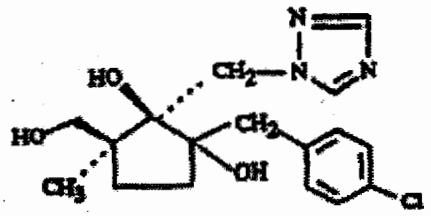
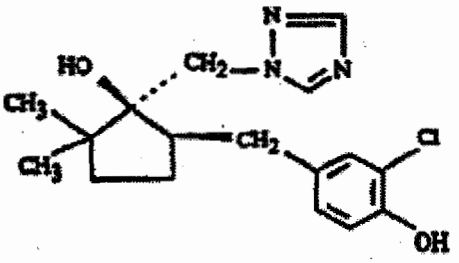
Appendix I (continued).



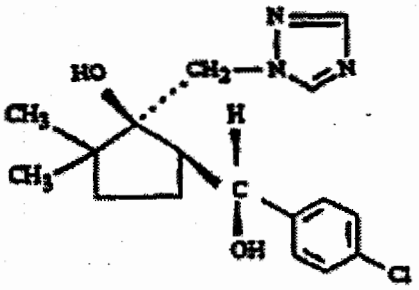
M18

(^{14}C-labelled, ref: 82-3d)



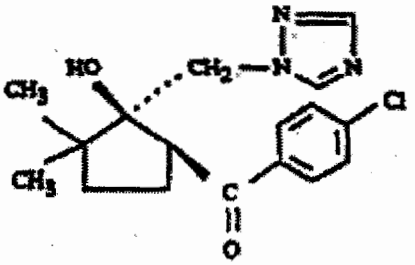
M19

(^{14}C-labelled, ref: 83-2c)



M21

(^{14}C-labelled, ref: 83-5c)



M30

(unlabelled, ref: MC1424)

Primary Evaluator	This DER was originally prepared under contract by Dynamac Corporation.
Approved by	Nancy Dodd, Chemist Nancy Dodd Date: 2/20/08 Registration Action Branch 3 Health Effects Division (7509P)

This DER was originally prepared under contract by Dynamac Corporation (2275 Research Boulevard, Suite 300; Rockville, MD 20850; submitted 09/13/2007). The DER has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

46901909 Jalal, M. (2006) Metconazole (KNF-S-474m): Metabolism by Lactating Goats. Project Number: 200600151, VP/28111, V/04/28111. Unpublished study prepared by Valent Dublin Laboratory and Genesis Midwest Laboratories. 294 p.

EXECUTIVE SUMMARY:

Valent U.S.A. Corporation has submitted a study investigating the metabolism of [triazole-^{14}C]metconazole (specific activity 2.07 GBq/mmole) in goats. A single goat was orally dosed with the radiolabeled test substance at a target dose of 10 mg/kg feed for four consecutive days; a second goat was dosed with a capsule containing corn meal and trace ethanol as a control. Based on the daily feed consumption, the average dosing level was equivalent to 10.36 ppm in the diet. Milk samples were collected twice daily, starting the morning prior to the first dosing and continuing until the morning of sacrifice. Goats were sacrificed 17 hours following the last dosing, and tissue samples of muscle (composite of loin, flank, and round), fat (composite of omental, renal, and subcutaneous), liver, and kidney were collected.

The in-life phase of the study was conducted by Genesis Midwest Laboratories (Neillsville, WI), and the analytical phase of the study was conducted by Valent Technical Center (Dublin, CA) and Acorn NMR Inc. (Livermore, CA; NMR analyses).

Total radioactive residues (TRR) were highest in liver (0.223 ppm), then kidney (0.110 ppm), and were very low in fat (0.003 ppm), muscle (0.004 ppm), and milk (0.003-0.005 ppm). The majority of the radioactivity was rapidly excreted from the treated goat via urine and feces, with higher levels in the feces. Although residues in milk were low, it appears that residues may have reached a plateau following 3 days of dosing.

Only kidney and liver had TRR >0.01 ppm; therefore, extractions for metabolite identifications were focused mainly on the kidney and liver. Milk Day 4 was also extracted for metabolite characterizations, but TRR levels were extremely low (0.005 ppm); therefore, chromatographic analyses were difficult and inconclusive; these data are presented in the distribution table for

informational purposes and are not discussed below. Approximately 94-96% of the TRR in kidney and liver was extracted using acetonitrile (ACN) and ethanol/water; nonextractable residues were 3.7-6.4% TRR (0.004-0.015 ppm).

The ACN and ethanol/water extracts were fractionated into organic and aqueous fractions for analysis; isolated peaks from the organic and aqueous fractions were also combined for chromatographic analysis. The analytical methods used for identification and confirmation of residues are adequate. These included HPLC and TLC with fraction collection and/or co-chromatography with reference compounds. Identification of selected metabolites was confirmed by LC/MS, LC/MS/MS, and/or NMR analysis of tissue metabolites isolated from goat urine. Adequate storage stability data demonstrate that the metabolic profile was relatively stable in kidney and liver for the study duration.

Approximately 65-70% TRR was identified in kidney and liver. The parent compound, metconazole, was the major compound identified in liver, accounting for 37.6% TRR (0.091 ppm); the parent only accounted for 2.3% TRR (0.003 ppm) in kidney. The metabolite M12 was identified as a major residue in kidney at 20.6% TRR (0.024 ppm) and was a minor residue in liver at 1.7% TRR (0.004 ppm). The glucuronic acid conjugate of M31 was also identified as a major residue in kidney at 24.2% TRR (0.028 ppm) and in liver at 13.5% TRR (0.033 ppm). The glucuronic acid conjugate of M1 accounted for 11.7% TRR (0.014 ppm) in kidney and 4.4% TRR (0.011 ppm) in liver. Other minor metabolites identified in kidney and liver, each accounting for ≤6% TRR (≤0.015 ppm) included M1, M31 (liver only; co-eluting with M1), *trans*-M31 (liver only), M32 (liver only), the glucuronic acid conjugate of *trans*-M31 (liver only), and the glucuronic acid conjugate of M32. Additional multicomponent unknowns accounting for 20.9-29.4% TRR were characterized in kidney and liver, each present at ≤0.01 ppm. The petitioner proposed that these unidentified components were likely structural isomers of M1, M31 and monohydroxylated analogues of metconazole based on their polarity and chromatographic similarities with the glucuronic acid conjugates of M1, M31 and M32.

The petitioner used reference standards for the triazole metabolites (M-20, M-34, and M-35 are 1,2,4-T, TAA, and TA, respectively) to analyze the residues in any extract containing >0.01 ppm or >10% TRR. No triazole metabolites were identified in such extracts. Unidentified residues in liver and kidney extracts which corresponded to the HPLC retention times of the triazole metabolites (2.3, 2.3, and 1.9 minutes for 1,2,4-T, TAA, and TA, respectively) totaled 1.2% TRR (0.003 ppm) in liver extracts and 2.4% TRR (0.003 ppm) in kidney extracts. The data are adequate to conclude that residues of 1,2,4-T, TAA, and TA, if present, are each <10% TRR (<0.01 ppm) in milk, meat, liver and kidney of the goat.

Based on the results of the triazole goat metabolism study, metconazole is extensively metabolized in goats through methyl group oxidation, cyclopentyl ring hydroxylation, and glucuronic acid conjugation. With the triazole label, the carboxylation/hydroxylation reactions were observed only in the cyclopentyl ring. Chemical modifications in other parts of the metconazole molecule (i.e., triazole and phenyl rings, and bridging methylene groups) were not observed. In addition, the *cis*:*trans* isomer ratio determined in the liver extract (59:41) was very

different from the *cis*:*trans* isomer ratio for the metconazole reference standard (80:20), indicating that the *cis* isomer of metconazole was preferentially metabolized in the goat.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the goat metabolism data are classified as scientifically acceptable.

The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP#s 348168 and 348206.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an impact on the validity of the study.

A. BACKGROUND INFORMATION

Metconazole [5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol] is a broad-spectrum triazole Group 3 fungicide (sterol biosynthesis inhibitors). There are currently no registered uses of metconazole in the U.S.; however, a tolerance has been established for banana, and a Section 18 emergency exemption and supporting time-limited tolerances have been granted for use on soybean. Valent U.S.A. Corporation has applied for registration of metconazole in the U.S. for use on peanut, stone fruits, and tree nuts.

The chemical structure and nomenclature of metconazole, and the physicochemical properties of the technical grade of metconazole are presented in Tables A.1 and A.2.

Table A.1. Metconazole Nomenclature.

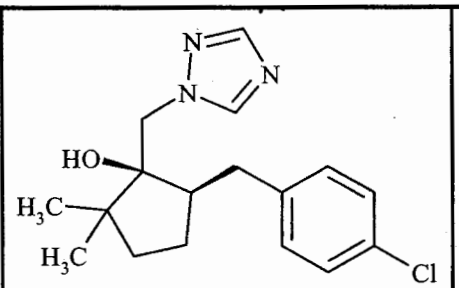
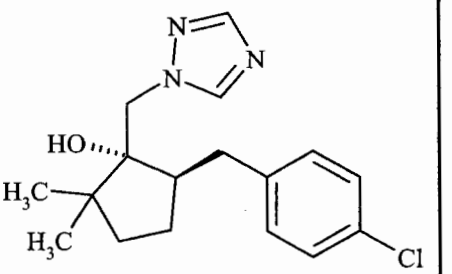
Chemical structure	 *cis*-isomer	 *trans*-isomer
Common name	Metconazole	
Company experimental name	KNF-S-474m (Kureha); BAS 555 F (BASF); V-10116 (Valent)	
IUPAC name	(1RS,5RS:1RS,5SR)-5-(4-chlorobenzyl)-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	

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Table A.1. Metconazole Nomenclature.	
CAS name	5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol
CAS registry number	125116-23-6 (*cis*- and *trans*-isomers) 115850-27-6 (*cis*-isomer) 115850-28-7 (*trans*-isomer)
End-use products (EP)	50% WDG (Metconazole 50 WDG Fungicide, EPA File Symbol 59639-RUT) 0.75 lb/gal SC/L (Caramba™ Fungicide, EPA File Symbol No. 7969-EUA) 0.67 lb/gal SC/L formulation (BAS 556 01F Fungicide, EPA File Symbol No. 7969-EUT; also contains the active ingredient pyraclostrobin at 0.83 lb/gal)

Table A.2. Physicochemical Properties of Metconazole

Parameter	Value				References* (MRID)
Melting point/range	100.0-108.4°C (using Electrothermal Digital Melting Point Apparatus) (AC900,768 technical grade)				44721505
pH	5.81 at 25°C (1% aqueous suspension)				46808402
Relative density (20°C)	1.14 (relative density to water at 4°C, using capillary-stoppered, density-specific gravity bottle) (Lot No. AC 8879-140B)				44721505
Water solubility (20°C)	Using shake-flask method: 18.7 ± 1.0 mg/L (*cis*-isomer, WL148271, KNF-S-474m) 13.6 ± 1.7 mg/L (*trans*-isomer, WL148271, KNF-S-474m)				44721505
Solvent solubility (g/L) at 20°C	Solvent	Metconazole	*cis*	*trans*	44721505
	acetone	363	251	117	
	methanol	403	294	117	
	dichloromethane	481	343	141	
	ethyl acetate	260	173	90.0	
	propanol	132	86.6	46.7	
	toluene	103	66.2	38.0	
	Hexane	1.40	0.929	0.483	
Vapor pressure (20°C)	Using gas-saturation method: $< 1.23 \times 10^{-5}$ Pa or 9.23×10^{-8} mm Hg (metconazole) $< 1.04 \times 10^{-5}$ Pa or 7.80×10^{-8} mm Hg (*cis*-isomer) $< 1.96 \times 10^{-6}$ Pa or 1.47×10^{-8} mm Hg (*trans*-isomer)				44721505
Dissociation constant (pK_a)	11.38±0.03 and 1.06±0.03 (in water at 29.1°C using spectrophotometric method; Lot No. AC 8879-140B)				44721505
Octanol/water partition coefficient, Log(K_{OW})	At 20 °C (using flask shaking method): K_{ow} (log K_{ow}) = 7090±989 (3.85) (Lot No. AC 8879-140B) (TGAI) K_{ow} (log K_{ow}) = 7150±803 (3.85) (*cis*-isomer, CL 354,801) K_{ow} (log K_{ow}) = 6800±1700 (3.8) (*trans*-isomer, CL 354,802)				44721505

Table A.2. Physicochemical Properties of Metconazole					
Parameter	Value				References* (MRID)
UV/visible absorption spectrum	pH	λ	A	log ε	46808403
	cis-isomer				
	2.0	221.4	0.828	4.03	
	6.8		0.8452	4.04	
	7.0		0.9126	4.08	
	10.3		0.7226	3.98	
	trans-isomer				
	2.0	221.4	0.9053	4.07	
	7.0		0.9547	4.10	
	10.1		0.9893	4.11	

* Product Chemistry Reviews: DP #256877, Shyam Mathur, Ph.D., 9/12/2000 and DP #329168, Shyam Mathur, Ph.D., 7/13/07.

B. EXPERIMENTAL DESIGN

B.1. Livestock

A single goat was orally dosed with the radiolabeled test substance at a target dose of 10 mg [triazole-^{14}C]metconazole per kg feed for four consecutive days; a second goat was dosed with a capsule containing corn meal and trace ethanol as a control. Based on the daily feed consumption, the average dosing level was equivalent to 10.36 ppm in the diet. The animals were kept in 8' x 4' x 4' pens inside the animal housing building at Genesis Midwest Laboratories (Neillsville, WI) for two weeks prior to the start of the study; 3 days prior to initial dosing, the goats were placed in individual metabolism cages for the study duration. The goats were fed ruminant feed supplemented with hay cubes.

The test animals were sacrificed 17 hours after the last administration, and samples of edible organs and tissues were collected. Prior to sacrifice, milk samples were collected twice daily, starting the morning prior to the first dosing and continuing until the morning of sacrifice.

Additional information relevant to the test goats is presented in Table B.1.1. Table B.1.2 presents the test animal dietary regime, and Table B.1.3 lists the test animal dosing regime.

TABLE B.1.1. General Test Animal Information.					
Species	Breed	Age	Weight at study initiation (kg)	Health Status	Description of housing/holding area
Goat	Capra hircus; crossbred	2-4 yrs.	48-55	Healthy	Individual metabolism cages designed for separate collection of urine and feces. Average minimum and maximum temperatures were 17-24 °C with an average 76% relative humidity and 14/10 hr. light/dark cycle.

TABLE B.1.2. Test Animal Dietary Regime.

Composition of Diet	Feed consumption (kg/day)	Water	Acclimation period	Predosing
Access to commercial goat pellets (grain) and alfalfa hay cubes via permanent bins; fresh feed added twice daily.	1.936-1.983 (average 1.967)	*ad libitum*	14 days	None

TABLE B.1.3. Test Animal Dosing Regime.

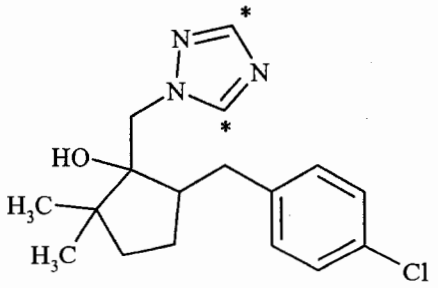
Treatment Type	Treatment Level [1] (ppm test material in vehicle)	Vehicle	Timing/Duration
Oral; balling gun	10.36 mg/kg feed	Dispensed in cornmeal in gelatin capsules	Twice a day after the morning and evening milking for 4 consecutive days.

[1] Based on actual daily feed consumption and ~10 mg test substance/kg feed per day.

B.2. Test Materials

The radiolabeled test substance in ethanol was isotopically diluted with non-labeled metconazole. The radio-diluted metconazole was diluted with ACN, and an aliquot was added to corn meal in a gelatin capsule and air dried prior to sealing. The characteristics of the test substance are presented in Table B.2.1.

TABLE B.2.1. Test Material Characteristics.

Chemical structure	
Radiolabel position	[triazole-^{14}C]metconazole (labeled in positions 3 and/or 5 in the triazole ring)
Lot No.	CFQ12045
cis:trans Ratio	87:13
Purity	99.9
Specific activity (test substance)	2.07 GBq/mmol (56 mCi/mmol)
Specific activity (radiodiluted test solution)	0.921 GBq/mmol (24.9 mCi/mmol)

B.3. Sampling Information

Afternoon milk samples were refrigerated and combined with the following morning sample to generate the daily milk sample. The following organs and tissues were collected at sacrifice: liver, kidneys, muscle (minimum 500 g composite of loin, flank and round), fat (minimum 500 g composite of omental, renal and subcutaneous), and bile. Sample collection information is summarized in Table B.3.1.

TABLE B.3.1. Sample Collection Information.			
Milk collected	Urine, feces and cage wash collected	Interval from last dose to sacrifice	Tissues harvested and analyzed
Milk collected twice daily (8-10 hours apart); 1,614-2,336 g/day during acclimation period and 1,858-2,097 g/day during dosing period from the treated goat.	Urine and feces collected at each milking (composited daily); cage wash collected at sacrifice	17 hours	Muscle (composite of loin, flank, and round); fat (composite of omental, renal, and subcutaneous); liver; and kidneys.

B.4. Identification/Characterization of Residues

B.4.1. Sample Handling and Preparation

Tissues were coarsely chopped, composited by tissue type, and homogenized with dry ice. All milk and tissue samples were frozen until shipment on dry ice to Valent (Dublin CA), where samples were stored frozen (ca. -20 °C) until analysis.

Only liver and kidney samples contained TRR >0.01 ppm; therefore, they were the only samples subjected to further extraction procedures. Briefly, homogenized liver and kidney samples were extracted with ACN (3x), centrifuged or filtered, and the ACN supernatants were combined, evaporated to dryness and redissolved in ACN for HPLC analysis. The ACN redissolved most of the residue, but the remaining residues of the ACN extract formed a milky solution which was dissolved in a small amount of water for radioassay. Nonextractable residues were further extracted once with water followed by rinsing with ethanol; the aqueous extract and ethanol rinse were combined, evaporated to dryness, redissolved in 50% ethanol/water and fractionated. The resulting ethanol fraction was analyzed by HPLC.

The extraction efficiency was determined using the control liver sample fortified with [triazole-^{14}C]metconazole at levels similar to those in the treated sample; 100% of the TRR was recovered in the ACN extract, with <0.1% TRR in the aqueous/ethanol extract and as nonextractable residues.

Although radioactivity in milk was low (≤0.005 ppm), the Day 4 sample was analyzed, and the residues were characterized. Briefly, milk was extracted 2x with ACN, resulting in an aqueous ACN extract. The extract was concentrated, yielding a concentrated aqueous extract and ACN extract. The ACN extract was evaporated to remove the solvent, then partitioned with ethyl acetate. The concentrated aqueous extract was adjusted to pH 4 to precipitate proteins, then centrifuged. No chromatographic analyses were conducted on milk extracts due to extremely low radioactivity.

The residue fractionation/extraction procedures used for goat liver, kidney, and milk are depicted below (Figures B.4.1.1-B.4.1.3; the flowcharts were copied without alteration from MRID 46901909).

Figure B.4.1.1. Flowchart of Residue Extraction/Fractionation Procedures in Goat Liver.

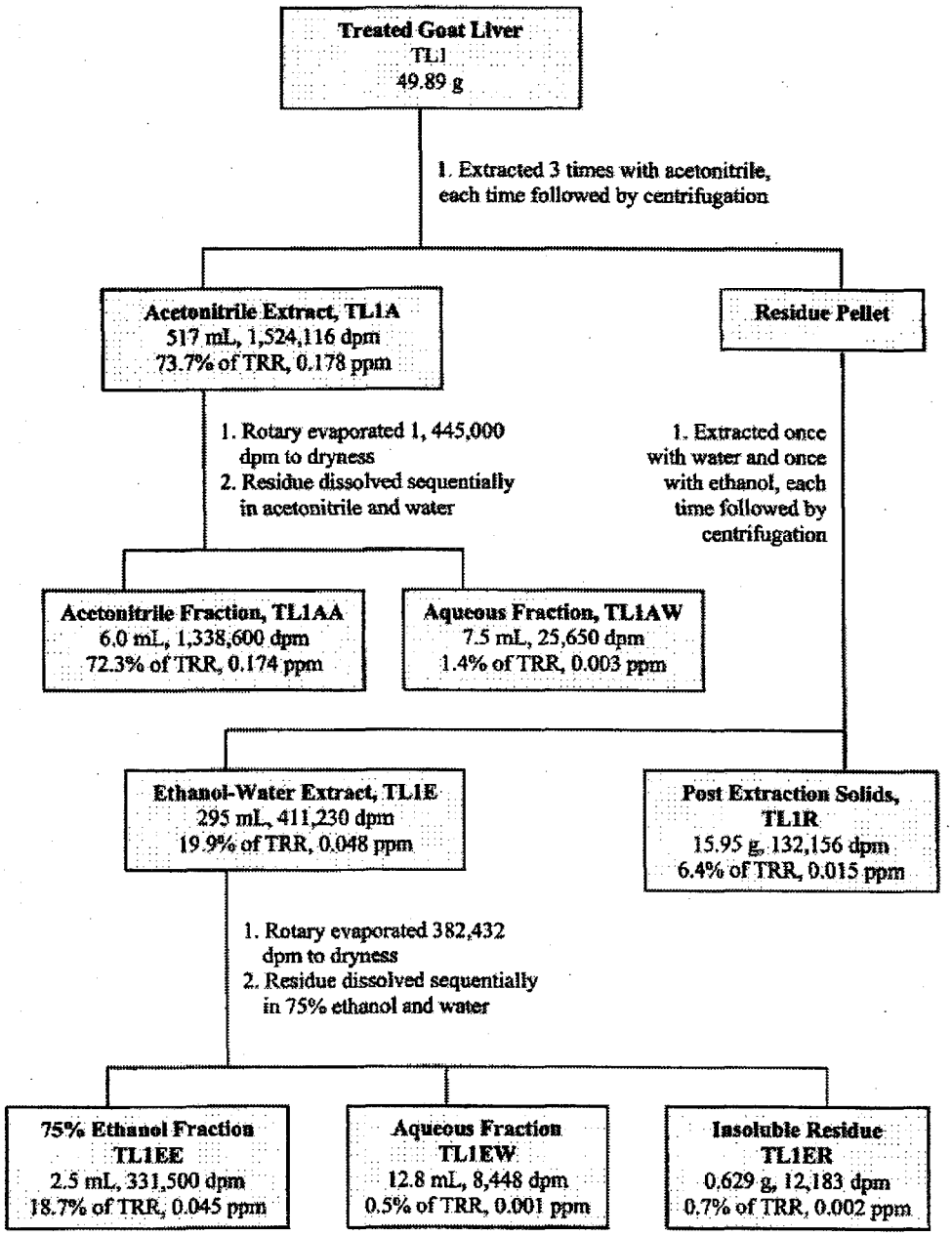


Figure B.4.1.2. Flowchart of Residue Extraction/Fractionation Procedures in Goat Kidney.

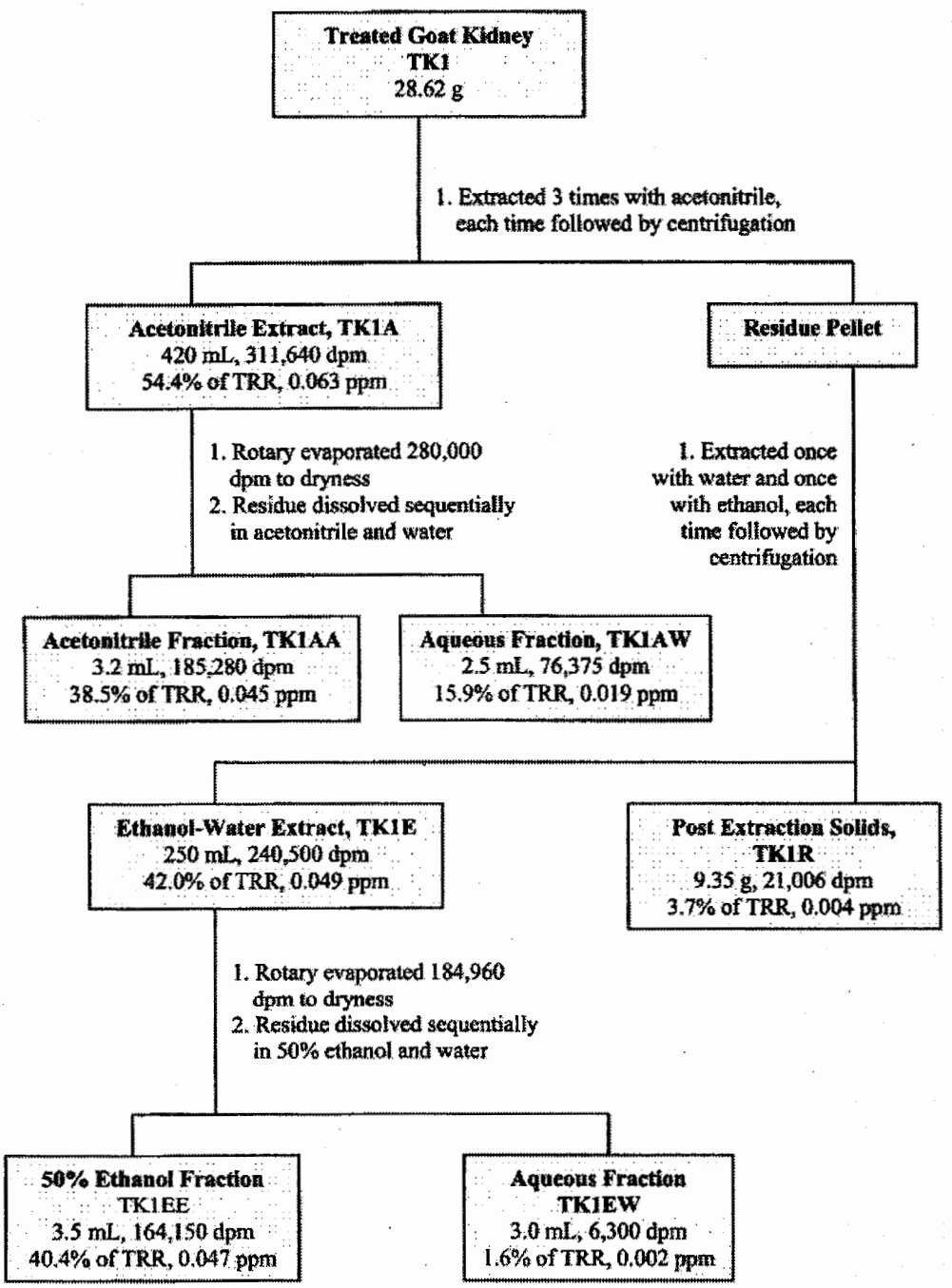


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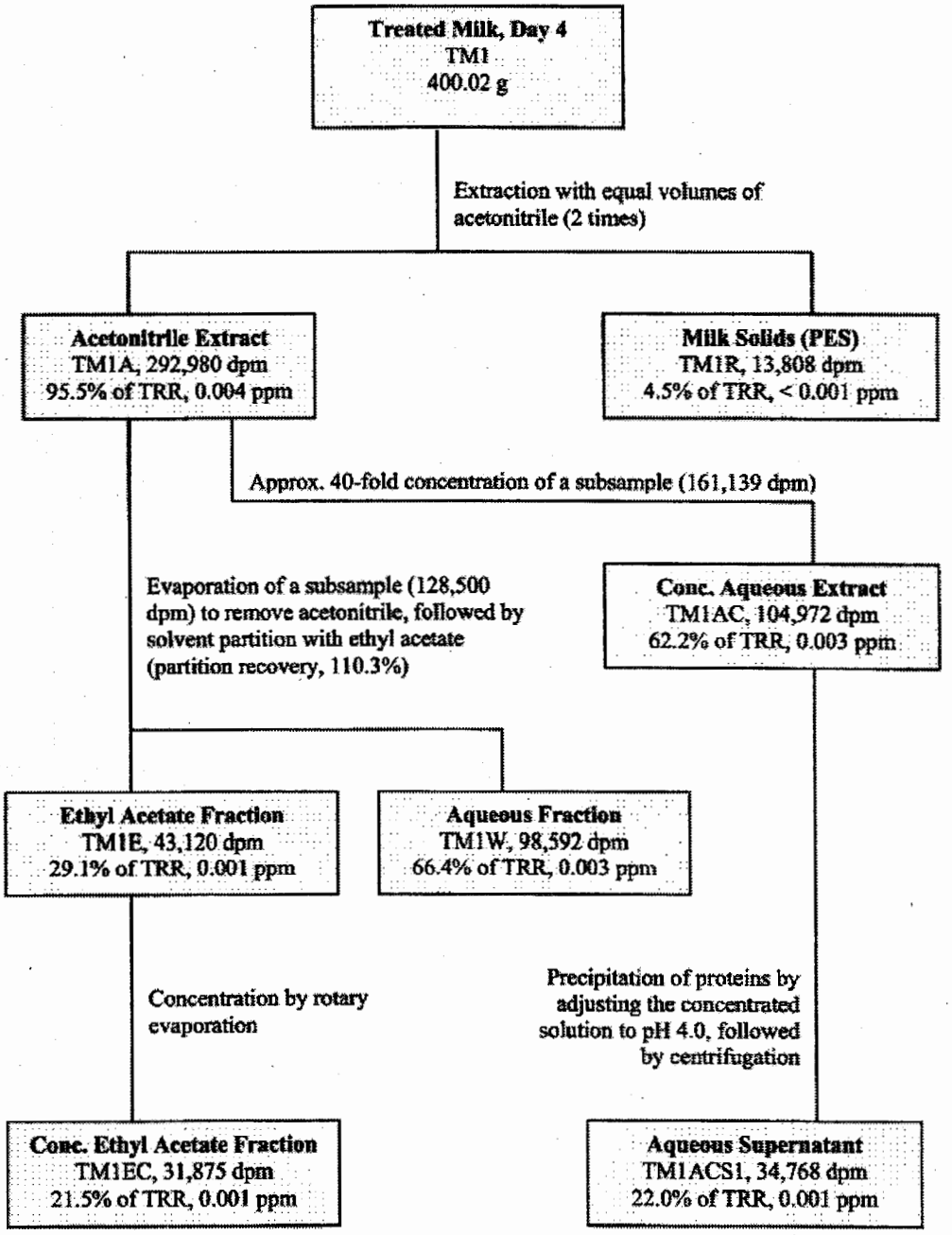
Figure B.4.1.3. Flowchart of Residue Extraction/Fractionation Procedures in Goat Milk.



B.4.2. Analytical Methodology

Radioactivity in liquid samples (milk and extracts) was determined by direct liquid scintillation (LSC), and radioactivity in solid samples (tissues and extracted solids) was determined using combustion/LSC. The TRR were also calculated by summing the extractable and nonextractable

radioactivity; summed TRR values were used for all further determinations. The combustion efficiency was determined by spiking a blank sample with [triazole-^{14}C]metconazole; recoveries were 95-102%. Example calculations of the limit of detection (LOD) and quantitation (LOQ) were provided; typical values were 0.0004 and 0.001 ppm, respectively.

Liver and kidney extracts were analyzed using HPLC and TLC to determine the metabolic profile and identify the metabolites. The HPLC system utilized a C8 column, UV detection (210 or 230 nm), flow-through radiodetection, and gradient mobile phases of ACN and water, each containing 0.05% trifluoroacetic acid. For peak isolation, eluted fractions were collected (preparative HPLC); metabolites were isolated by preparative HPLC before co-chromatography with reference standards. The two-dimensional TLC systems used silica gel plates and solvent systems of acetone:dichloromethane:acetic acid (40:10:1, v:v:v); toluene:ethyl acetate:formic acid (3:7:1, v:v:v); and/or 1-butanol:acetic acid:water (4:1:5, v:v:v). Radioactive areas were determined using phosphorimaging, and nonlabeled reference standards were detected with UV light; appropriate reference standards were co-chromatographed with each sample. The reference standards used in the study are presented in Appendix I.

LC/MS and LC/MS/MS analysis of isolated metabolites and metconazole standards was conducted using an LC system similar to above but with a C18 column, a mobile phase of ACN and water, each containing 0.05% formic acid, and MS APCI detection in the positive ion mode.

Metabolites were also confirmed with ^{1}H NMR by Acorn NMR Inc. (Livermore, CA). All NMR spectra were acquired at room temperature using an NMR spectrophotometer operating at 400 MHz.

C. RESULTS AND DISCUSSION

Sample storage conditions and intervals are summarized in Table C.1. TRR determinations and sample extractions were conducted within ~1 month of sample collection, and kidney and liver samples were analyzed (including metabolite identifications) within ~6 months of collection. Re-extraction and analysis of kidney and liver samples stored under frozen conditions for 7.5 months after collection demonstrated no significant changes in the metabolic profile over the duration of the study. These data adequately support the storage conditions and durations of samples from the goat metabolism study.

Total radioactive residues in goat milk and tissues are presented in Table C.2.1. TRR were highest in liver (0.223 ppm), then kidney (0.110 ppm), and were very low in fat (0.003 ppm), muscle (0.004 ppm), and milk (0.003-0.005 ppm). The majority of the radioactivity was rapidly excreted from the treated goat via urine and feces, with higher levels in the feces. Although residues in milk were low, it appears that residues may have reached a plateau following 3 days of dosing; a graph demonstrating the trend in milk was not generated because of the extremely low TRR levels in whole milk.

The distribution of radioactivity in goat milk, kidney, and liver is presented in Table C.2.2. Only kidney and liver had TRR >0.01 ppm; therefore, extractions for metabolite identifications were

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focused mainly on the kidney and liver. Milk Day 4 was also extracted for metabolite characterizations, but TRR levels were extremely low (0.005 ppm), therefore chromatographic analyses were difficult and inconclusive; these data are presented in the distribution table for informational purposes. Approximately 94-96% of the TRR in kidney and liver was extracted using ACN and ethanol/water; nonextractable residues were 3.7-6.4% TRR (0.004-0.015 ppm).

The ACN and ethanol/water extracts were fractionated into organic and aqueous fractions for analysis; isolated peaks from the organic and aqueous fractions were also combined for chromatographic analysis. The analytical methods used for identification and confirmation of residues are adequate. These included HPLC and TLC with fraction collection and/or co-chromatography with reference compounds. Identification of selected metabolites was confirmed by LC/MS, LC/MS/MS, and/or NMR analyses. A summary of the characterization and identification of residues in kidney and liver is presented in Table C.2.3.

The parent compound, metconazole, was the major compound identified in liver, accounting for 37.6% TRR (0.091 ppm); the parent only accounted for 2.3% TRR (0.003 ppm) in kidney. The metabolite M12 was identified as a major residue in kidney at 20.6% TRR (0.024 ppm) and was a minor residue in liver at 1.7% TRR (0.004 ppm). The glucuronic acid conjugate of M31 was also identified as a major residue in kidney at 24.2% TRR (0.028 ppm) and in liver at 13.5% TRR (0.033 ppm). The glucuronic acid conjugate of M1 accounted for 11.7% TRR (0.014 ppm) in kidney and 4.4% TRR (0.011 ppm) in liver. Other minor metabolites identified in kidney and liver, each accounting for ≤6% TRR (≤0.015 ppm) included M1, M31 (liver only; co-eluting with M1), *trans*-M31 (liver only), M32 (liver only), the glucuronic acid conjugate of *trans*-M31 (liver only) and the glucuronic acid conjugate of M32. Additional multicomponent unknowns accounting for 20.9-29.4% TRR were characterized in kidney and liver, each present at ≤0.01 ppm. The petitioner proposed that these unidentified components were likely structural isomers of M1, M31 and monohydroxylated analogues of metconazole based on their polarity and chromatographic similarities with the glucuronic acid conjugates of M1, M31, and M32. The chemical names and structures of compounds identified in the study are presented in Table C.3.1.

The petitioner used reference standards for the triazole metabolites (M-20, M-34, and M-35 are 1,2,4-T, TAA, and TA, respectively) to analyze the residues in any extract containing >0.01 ppm or >10% TRR. No triazole metabolites were identified in such extracts. Unidentified residues in liver and kidney extracts which corresponded to the HPLC retention times of the triazole metabolites (2.3, 2.3, and 1.9 minutes for 1,2,4-T, TAA, and TA, respectively) totaled 1.2% TRR (0.003 ppm) in liver extracts and 2.4% TRR (0.003 ppm) in kidney extracts. The data are adequate to conclude that residues of 1,2,4-T, TAA, and TA, if present, are each <10% TRR (<0.01 ppm) in milk, meat, liver and kidney of the goat.

Preliminary identification of the parent and metabolites was based on HPLC retention time comparisons. Bands with significant residues were isolated and the subjected to analysis with another HPLC system and/or TLC for quantification. The *cis* and *trans* isomers of metconazole were isolated separately from the liver ACN extract using preparative HPLC, and were identified by HPLC and TLC co-chromatography with the reference standard. The *cis*:*trans* isomer ratio was determined as 59:41 in the liver extract, which was very different from the *cis*:*trans* isomer

ratio for the metconazole reference standard (80:20), indicating that the *cis* isomer of metconazole was preferentially metabolized in the goat.

Three major and two minor metabolites (M12, M1 glucuronide, M31 glucuronide, *trans*-M31 glucuronide, and M32 glucuronide) present in liver and kidney were isolated/purified (Strata-X cartridge chromatography and preparative HPLC) from treated goat urine, and identified using LC/MS/MS, NMR, and/or TLC and HPLC co-chromatography. The glucuronic acid conjugates of M1, M31, *trans*-M31 and M32 were further confirmed with LC/MS of the aglycone released after acid hydrolysis of the metabolite. The identity of these metabolites in kidney and liver were then confirmed by co-chromatography with the isolated/identified urine metabolite.

C.1. Storage Stability

Samples were stored frozen after collection; TRR analyses were conducted within 2 weeks and extraction was conducted within ~1 month of collection. Analyses of liver and kidney were completed ~6 months after collection. To demonstrate stability of the metabolic profile, liver and kidney samples were re-extracted and re-analyzed after 7.5 months of frozen storage at the end of the analytical phase of the study. The distribution of the radioactivity in the initial and final extracts of liver and kidney were very similar. HPLC analyses demonstrated that the major metconazole metabolites were unchanged and that the metabolic profile in liver and kidney was stable for the duration of the study.

TABLE C.1. Summary of Storage Conditions.

Matrix	Storage Temperature (°C)	Actual Storage Duration[1]	Interval of Demonstrated Storage Stability
Goat kidney and liver	-20	193 days (6.3 months)	227 days (7.5 months) in frozen liver and kidney [collection to re-extraction]

[1] Storage interval from collection to final analysis including metabolite identification.

C.2. Identification, Characterization, and Distribution of Residues

TABLE C.2.1. Total Radioactive Residues (TRR) in Milk, Tissues, and Excreta.

Matrix	Collection Timing	Triazole Label	
		% AD	ppm[1]
Urine	Day 1	Not reported (NR)	2.132
	Day 2	NR	2.933
	Day 3	NR	2.594
	Day 4	NR	2.730
Feces	Day 1	NR	2.345
	Day 2	NR	5.261
	Day 3	NR	5.208
	Day 4	NR	5.025
Cage wash	Study duration	NR	0.131
Total excreted	Study duration	NR	28.36
Milk	Day 1	NR	0.003
	Day 2	NR	0.004

TABLE C.2.1. Total Radioactive Residues (TRR) in Milk, Tissues, and Excreta.

Matrix	Collection Timing	Triazole Label	
		% AD	ppm[1]
	Day 3	NR	0.005
	Day 4	NR	0.005
Liver	At sacrifice	NR	0.223 (0.241)
Kidney	At sacrifice	NR	0.110 (0.117)
Muscle	At sacrifice	NR	0.004
Fat	At sacrifice	NR	0.003
Bile	At sacrifice	NR	4.260

[1] TRR (ppm values) reported in parentheses were calculated by the summing extractable and nonextractable radioactivity; summed TRR values were used for all further determinations.

TABLE C.2.2. Distribution of the Parent and the Metabolites in Goat Matrices Following Dosing with [Triazole-^{14}C]Metconazole at 10.36 ppm. [1]

Metabolite Fraction	Milk, Day 4		Kidney		Liver	
	TRR=0.005 ppm		TRR=0.117 ppm		TRR=0.241 ppm	
	%TRR	ppm	%TRR	ppm	%TRR	ppm
ACN	95.5	0.004	54.4	0.063	73.7	0.178
ACN fraction (1AA)	29.1	0.001	38.5	0.045	72.3	0.174
Aqueous fraction (1AW)	66.4	0.003	15.9	0.019	1.4	0.003
Conc. Aqueous supernatant	22.0	0.001				
Ethanol/water			42.0	0.049	19.9	0.048
Ethanol fraction (1EE)			40.4	0.047	18.7	0.045
Aqueous fraction (1EW)			1.6	0.002	0.5	0.001
Insoluble fraction (1ER)			--	--	0.7	0.002
Combined fractions [2]			96.3	0.112	91.1	0.220
Metconazole			2.3	0.002	37.6	0.091
trans-Metconazole			1.1	0.001	15.5	0.037
cis-Metconazole			1.2	0.001	22.1	0.053
M12			20.6	0.024	1.7	0.004
M1			0.9	0.001	1.3	0.003
M31			--	--		
trans-M31			--	--	6.0	0.015
M32			--	--	0.8	0.002
M1 glucuronic acid conjugate			11.7	0.014	4.4	0.011
M31 glucuronic acid conjugate			24.2	0.028	13.5	0.033
M32 glucuronic acid conjugate			5.7	0.007	2.3	0.006
trans-M31 glucuronic acid conjugate			--	--	2.6	0.006
Others			29.4 [3]	0.034	20.9 [4]	0.050
Nonextractable	4.5	<0.001	3.7	0.004	6.4	0.015

[1] Shading indicates that the extraction step and/or characterization analysis was not conducted for the matrix in question.
[2] Consisting of fractions 1AA, 1EE, and 1AW for kidney, and 1AA and 1EE for liver. Peak regions were collected from the respective tissue fractions by preparative HPLC; isolated regions were combined in proportional ratios.
[3] Included 13 components each present at ≤8.9% TRR (≤0.01 ppm).
[4] Included 17 components each present at ≤2.6% TRR (<0.01 ppm).

TABLE C.2.3. Summary of Characterization and Identification of Radioactive Residues in Goat Matrices when Dosed with [Triazole-^{14}C]Metconazole at 10.36 ppm. [1]

Compound	Kidney		Liver	
	TRR = 0.117 ppm		TRR = 0.241 ppm	
	% TRR	ppm	% TRR	ppm
Total Metconazole (*cis:trans* ratio)	2.3 (52:48)	0.003	37.6 (59:41)	0.091
M12	20.6	0.024	1.7	0.004
M1	0.9	0.001	1.3	0.003
M31	--	--		
trans-M31	--	--	6.0	0.015
M32	--	--	0.8	0.002
M1 glucuronic acid conjugate	11.7	0.014	4.4	0.011
M31 glucuronic acid conjugate	24.2	0.028	13.5	0.033
M32 glucuronic acid conjugate	5.7	0.007	2.3	0.006
trans-M31 glucuronic acid conjugate	--	--	2.6	0.006
Unknown "others"	29.4	0.034	20.9	0.050
ACN, aqueous fraction (1AW)	--	--	1.4	0.003
Ethanol/water, aqueous fraction (1EW)	1.6	0.002	0.5	0.001
Ethanol/water, insoluble fraction (1ER)	--	--	0.7	0.002
Total identified	65.4	0.076	70.2	0.169
Total characterized	31.0	0.036	23.5	0.057
Total extractable	96.4	0.112	93.6	0.226
Unextractable (PES) [1]	3.7	0.004	6.4	0.015
Accountability [2]	106	0.117	108	0.241

[1] Residues remaining after exhaustive extractions.
[2] Accountability = (Total extractable + Total unextractable)/(TRR from combustion analysis; see TABLE C.2.1) * 100.

C.3. Proposed Metabolic Profile

Based on the results of the triazole goat metabolism study, metconazole is extensively metabolized in goats through methyl group oxidation, cyclopentyl ring hydroxylation, and glucuronic acid conjugation. With the triazole label, the carboxylation/hydroxylation reactions were observed only in the cyclopentyl ring. Chemical modifications in other parts of the metconazole molecule (i.e., triazole and phenyl rings, and bridging methylene groups) were not observed.

One of the major pathways of metabolism in goat is the oxidation of one of the methyl groups at position 2 of the cyclopentyl ring, yielding a carboxylic derivative (M12) and hydroxymethyl derivative (M1). As M12 is water soluble, it is not further metabolized but is eliminated from the body via urine. M1 is rapidly conjugated in the body to produce its glucuronic acid conjugate, which then being water soluble, is eliminated via urine.

Other major pathways involve the hydroxylation of the methylene group at position 3 of the cyclopentyl ring to form M31, followed by conjugation to its glucuronide acid conjugate, which is eliminated via urine. A minor pathway is hydroxylation of the methylene group at position 3

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of the cyclopentyl ring to form M32 (the configurational isomer of M31 at position 3). The glucuronic acid conjugate of M32 is formed, which is then eliminated via the urine.

A flowchart of the proposed metabolic pathway in goats is presented below in Figure C.3.1. This figure was copied without alteration from MRID 46901909.

FIGURE C.3.1. Proposed Metabolic Profile of Metconazole in Goat.

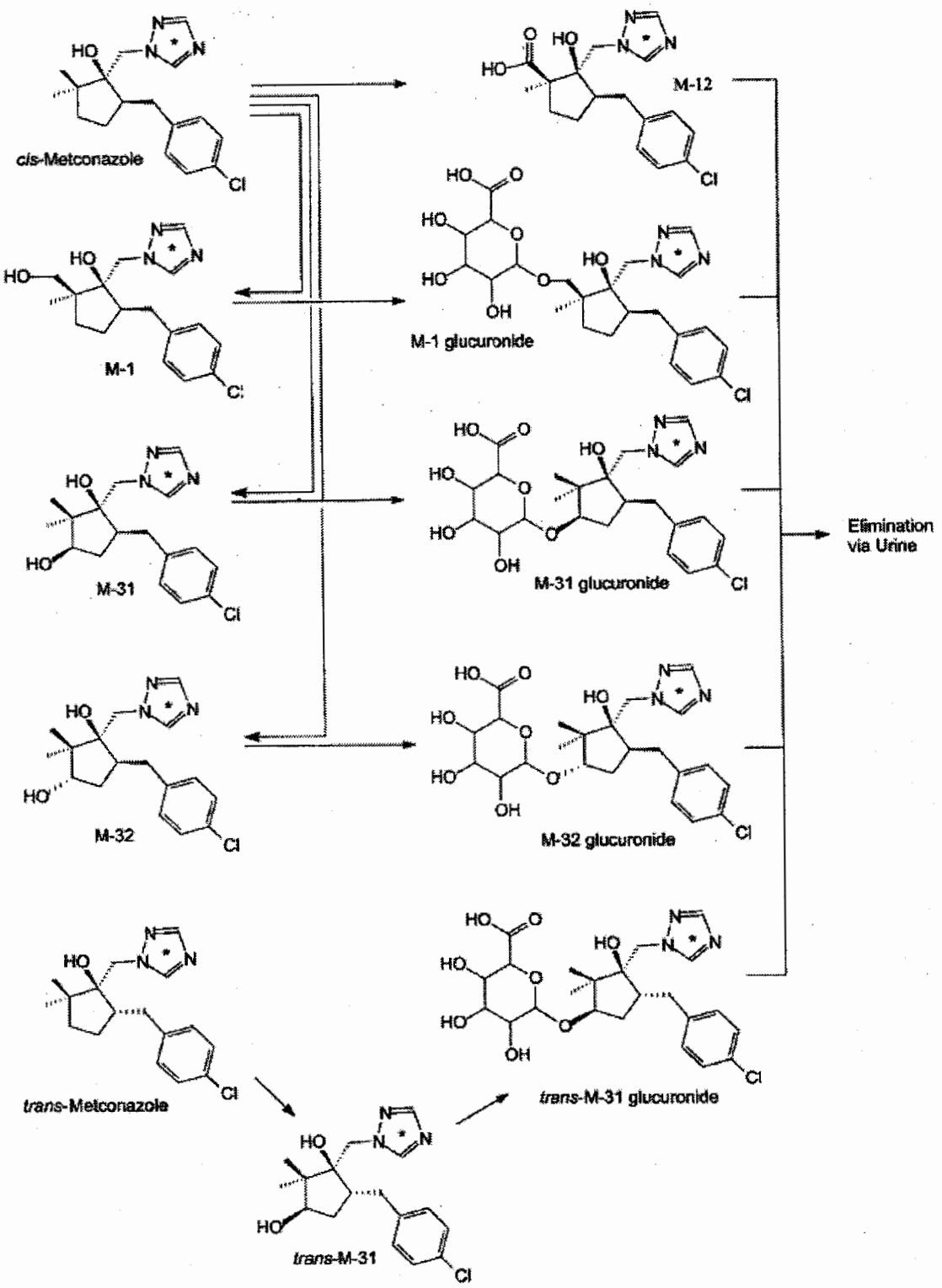


TABLE C.3.1. Identification of Compounds from Metabolism Study.

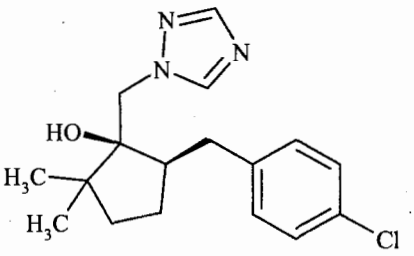
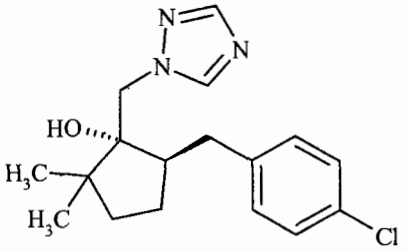
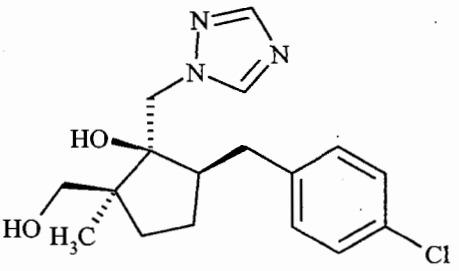
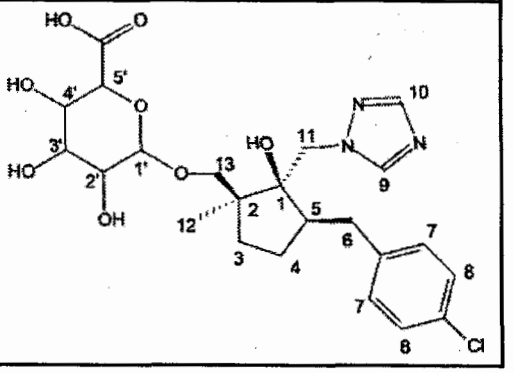
Common name/code Figure C.3.1 ID No.	Chemical name	Chemical structure
Metconazole (*cis* and *trans*)	5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	 *cis*-isomer  *trans*-isomer
M1 (2-hydroxymethyl-*cis*-metconazole)	5-[(4-chlorophenyl)methyl]-2-methoxyl-2-methyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)-1-cyclopentanol	
M1 glucuronide	Not provided.	

TABLE C.3.1. Identification of Compounds from Metabolism Study.

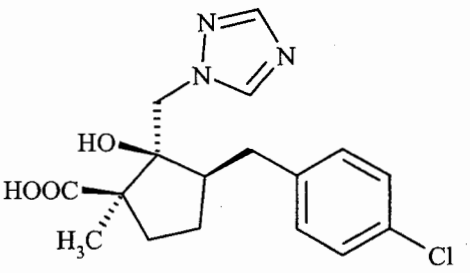
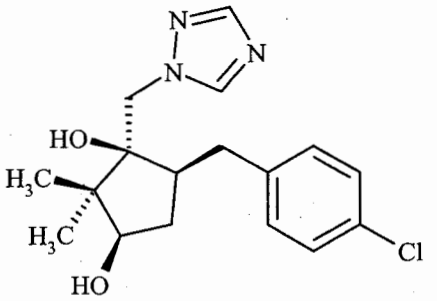
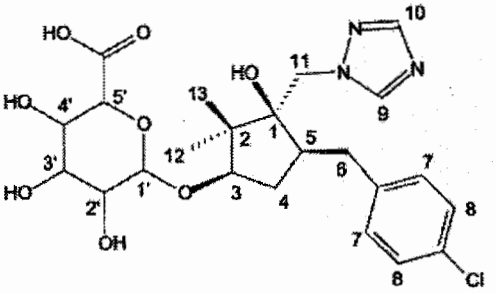
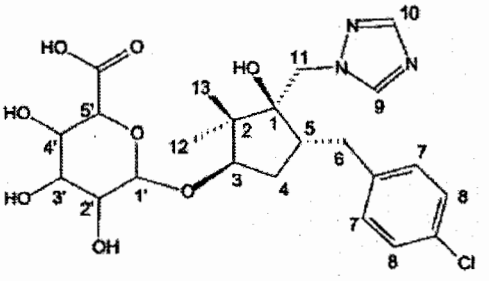
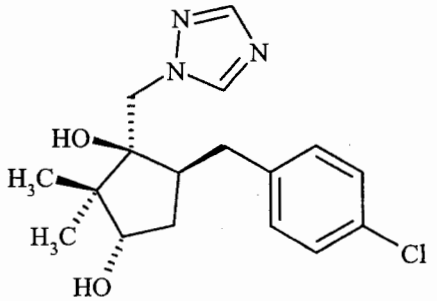
Common name/code Figure C.3.1 ID No.	Chemical name	Chemical structure
M12 (*cis*- metconazole-2-carboxylic acid)	5-[(4-chlorophenyl)methyl]-2-carboxyl-2-methyl-1-(1*H*-1,2,4-triazol-1-yl methyl)-1-cyclopentanol	
M31 [(1S*,3R*,5S*)-3-hydroxy-*cis*-metconazole]	Not provided.	
M31 glucuronide	Not provided.	
trans-M31 glucuronide	Not provided.	
M32 [(1S*,3S*,5S*)-3-hydroxy-*cis*-metconazole]	Not provided.	

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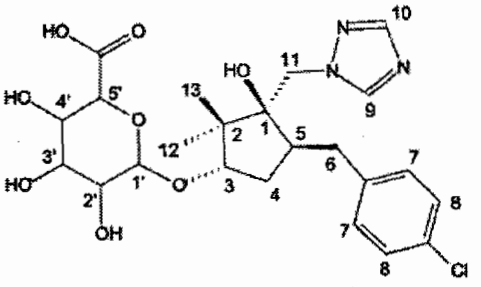
TABLE C.3.1. Identification of Compounds from Metabolism Study.		
Common name/code Figure C.3.1 ID No.	Chemical name	Chemical structure
M32 glucuronide	Not provided.	

D. CONCLUSION

In a single goat orally dosed with [triazole-^{14}C]metconazole for 4 consecutive days at 10.36 ppm in the diet, TRR were highest in liver (0.223 ppm), then kidney (0.110 ppm), and were very low in fat (0.003 ppm), muscle (0.004 ppm) and milk (0.003-0.005 ppm). The majority of the radioactivity was rapidly excreted from the treated goat via urine and feces, with higher levels in the feces. Only kidney and liver had TRR >0.01 ppm; therefore extractions for metabolite identifications were focused mainly on the kidney and liver samples.

The parent compound, metconazole, was the major compound identified in liver, accounting for 37.6% TRR; the parent only accounted for 2.3% TRR in kidney. The metabolite M12 was identified as a major residue in kidney at 20.6% TRR and was a minor residue in liver at 1.7% TRR. The glucuronic acid conjugate of M31 was also identified as a major residue in kidney at 24.2% TRR and in liver at 13.5% TRR. The glucuronic acid conjugate of M1 accounted for 11.7% TRR in kidney and 4.4% TRR in liver. Other minor metabolites identified in kidney and liver, each accounting for ≤6% TRR included M1, M31 (liver only; co-eluting with M1), *trans*-M31 (liver only), M32 (liver only), the glucuronic acid conjugate of *trans*-M31 (liver only), and the glucuronic acid conjugate of M32. Additional unknown components accounting for 20.9-29.4% TRR were characterized in kidney and liver, each present at ≤0.01 ppm. The petitioner proposes that these unidentified components were likely structural isomers of M1, M31 and monohydroxylated analogues of metconazole based on their polarity and chromatographic similarities with the glucuronic acid conjugates of M1, M31 and M32.

The study is supported by adequate storage stability data, and acceptable methods were used for extraction and characterization/identification of residues.

Based on the results of the triazole goat metabolism study, metconazole is extensively metabolized in goats through oxidative hydroxylation of the methyl group and further oxidation of the hydroxymethyl group to a carboxylic acid, oxidative hydroxylation of the cyclopentyl ring, and glucuronic acid conjugation. With the triazole label, the carboxylation/hydroxylation reactions were observed only in the cyclopentyl ring. Chemical modifications in other parts of the metconazole molecule (i.e., triazole and phenyl rings, and bridging methylene groups) were not observed.

E. REFERENCES

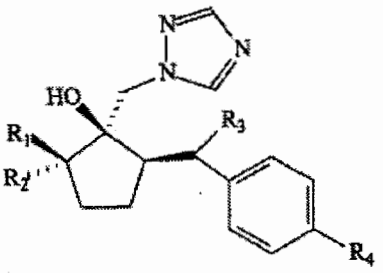
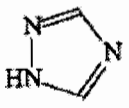
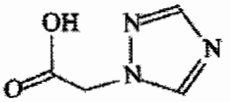
DP#: 324541
Subject: Metconazole. Request for a Tolerance on Imported Bananas. Summary of Analytical Chemistry and Residue Data. Petition Number 9E05052.
From: N. Dodd
To: M. Waller
Date: 12/14/05
MRIDs: 44721506, 44721507, 44721508, 44721509, 44721510, and 44721511

F. DOCUMENT TRACKING

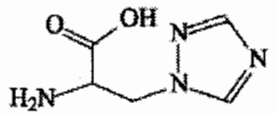
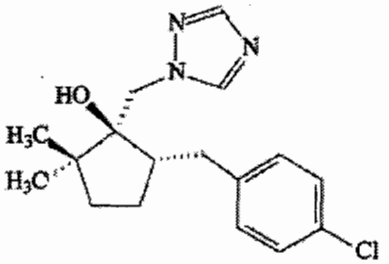
RDI: N. Dodd (2/20/08)
Petition Numbers: 6F7094 and 6F7095
DP#s: 348168 and 348206
PC Code: 125619

Template Version June 2005

APPENDIX I. Chemical Names and Structures of Reference Standards Used in Goat Metabolism Study. (Copied without alteration from MRID 46901909)

Standard Name (Abbreviated ID)	Chemical Structure				Purity %	Valent Inventory No.
						
	R_1	R_2	R_3	R_4		
Metconazole (Technical, *cis-trans* 85:15 mixture)	CH_3	CH_3	H	Cl	98.7	AS2122a
cis-Metconazole (*cis*-Met)	CH_3	CH_3	H	Cl	99.3	AS2025a
KNF-474-M-1 (M-1)	CH_2OH	CH_3	H	Cl	98.6	AS2104a
KNF-474-M-2 (M-2)	CH_3	CH_2OH	H	Cl	98.3	AS2105a
KNF-474-M-11 (M-11)	CH_3	CH_3	OH (α)	Cl	98.0	AS2106a
KNF-474-M-12 (M-12)	COOH	CH_3	H	Cl	98.7	AS2107a
KNF-474-M-13 (M-13)	CH_3	COOH	H	Cl	98.1	AS2108a
KNF-474-M-21 (M-21)	CH_3	CH_3	OH (β)	Cl	97.3	AS2110a
KNF-474-M-30 (M-30)	CH_3	CH_3	C=O in place of CHR_3	Cl	97.9	AS2111a
KNF-474-M-39 (M-39)	CH_3	CH_3	H	H	88.6	AS2114a
KNF-474-M-20 (M-20)					99.1	AS2109a
KNF-474-M-34 (M-34)					100.0	AS2112a

Appendix I (continued).

KNF-474-M-35 (M-35)		100.0	AS2113a
trans-Metconazole (*trans*-Met)		99.3	AS2026a

Primary Evaluator	This DER was originally prepared under contract by Dynamac Corporation.
Approved by	Nancy Dodd, Chemist Nancy Dodd Date: 2/20/08 Registration Action Branch 3 Health Effects Division (7509P)

This DER was originally prepared under contract by Dynamac Corporation (2275 Research Boulevard, Suite 300; Rockville, MD 20850; submitted 09/13/2007). The DER has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

46901912 Jalal, M. (2006) Metconazole (KNF-S-474m): Metabolism by Laying Hens. Project Number: 200600176, VP/28337, V/04/28337. Unpublished study prepared by Genesis Midwest Laboratories, Acorn NMR Inc and Valent Dublin Laboratory. 453 p.

EXECUTIVE SUMMARY:

Valent U.S.A. Corporation has submitted a study investigating the metabolism of [cyclopentyl-^{14}C]metconazole (specific activity 0.909 GBq/mmole) and [triazole-^{14}C]metconazole (specific activity 0.907 GBq/mmole) in laying hens. Two groups of five hens were orally dosed with the radiolabeled test substance at a target dose of 10 mg/kg feed for 4.5 consecutive days; a third group of hens (n=3) was dosed with a capsule containing corn meal and trace ethanol as a control. Based on the daily feed consumption, the average dosing level was equivalent to 14.0 ppm [cyclopentyl-^{14}C]metconazole or 12.6 ppm [triazole-^{14}C]metconazole in the diet. Eggs were collected twice daily and separated into yolks and whites. Hens were sacrificed 4.5 hours following the last dosing, and tissue samples of muscle (thigh and breast), liver, skin with fat, and abdominal fat were collected.

The in-life phase of the study was conducted by Genesis Midwest Laboratories (Neillsville, WI), and the analytical phase of the study was conducted by Valent Technical Center (Dublin, CA) and Acorn NMR Inc. (Livermore, CA; NMR analyses).

Total radioactive residues (TRR), determined by summing extractable and nonextractable radioactivity, were highest in liver (0.790-0.972 ppm), followed by fat (0.091-0.141 ppm), skin with fat (0.075-0.137 ppm), thigh muscle (0.049-0.152 ppm), and breast muscle (0.031-0.145 ppm). TRR in egg whites were <0.001-0.049 ppm and 0.017-0.174 ppm from hens treated with cyclopentyl- and triazole-labeled metconazole, respectively. TRR in egg yolks were <0.001-0.096 ppm and 0.005-0.163 ppm from hens treated with cyclopentyl- or triazole-labeled metconazole, respectively. Residues in egg whites appear to have reached a plateau following 3 or 4 days of dosing with cyclopentyl- and triazole-labeled metconazole, respectively. Maximum residues were observed in egg yolk (both labels) on Day 5. Egg whites from Day 4 and egg

yolks from Day 5 were used for extraction; TRR, determined by summing extractable and nonextractable radioactivity, were 0.047-0.186 ppm in Day 4 egg whites and 0.088-0.156 ppm in Day 5 egg yolks. Radioactivity was generally higher in the eggs and tissues from the triazole-treated hens. The majority of the radioactivity was rapidly excreted from the treated hens.

The majority of the radioactivity (78-98% TRR) was extracted from hen matrices with acetonitrile (ACN). Additional radioactivity (2-10% TRR) was released with water extraction, and small amounts of the TRR (<1-9% TRR) present as oil droplets in fat, skin with fat, egg yolks, and liver were hexane soluble. Nonextractable residues in egg yolk (cyclopentyl label) and liver (both labels) after solvent extraction were acid hydrolyzed which further released ~6-10% TRR. Nonextractable residues in egg whites and yolks and hen tissues were 1.6-7.1% TRR. Accountabilities based on combustion/LSC TRRs were 97-109%; the petitioner normalized the TRR (summation of extractable and nonextractable radioactivities) for the distribution of metabolites.

The ACN and aqueous extracts of eggs and tissues were analyzed by HPLC and/or TLC. The combined extracts of liver were also acid hydrolyzed to release any conjugated metabolites, and the hydrolysates were analyzed by HPLC; metabolites quantitated following acid hydrolysis in liver are discussed herein because the majority of the unhydrolyzed liver extract consisted of conjugated metabolites. The analytical methods used for identification and confirmation of residues are adequate. These included HPLC and TLC with fraction collection and/or co-chromatography with reference compounds. Identification of selected metabolites was confirmed by LC/MS and/or NMR analysis of tissue metabolites isolated from hen excreta. Approximately 68-93% TRR was identified in eggs and hen tissues (muscle, fat, skin with fat, and liver). Adequate storage stability data demonstrate that the metabolic profile was relatively stable in eggs and hen tissues for the study duration.

The parent, metconazole, was a major compound identified in fat and skin with fat from both labels, accounting for 35.3-36.7% TRR (0.033-0.050 ppm) in fat and 19.7-27.8% TRR (0.021-0.027 ppm) in skin. The parent was identified as a minor residue in all other hen matrices at 2.5-7.3% TRR (0.003-0.005 ppm) in egg whites, 6.6-11.4% TRR (0.010 ppm) in egg yolks, 3.3-9.8% TRR (0.005 ppm) in thigh muscle, 0.8-5.4% TRR (0.001-0.002 ppm) in breast muscle, and 1.7-4.1% TRR (0.017-0.033 ppm) in liver. Lower levels of the parent were observed in the triazole-label hen matrices, with 1,2,4-triazole as the major residue (except in fat); other metabolites were similar between the cyclopentyl and triazole labels in hen matrices.

In the cyclopentyl-label hen matrices, the metabolite M1 (co-eluting with small amounts of M31) was identified as a major residue in egg whites at 15.7% TRR (0.007 ppm), egg yolks at 18.2% TRR (0.016 ppm), muscle at 15.7-19.9% TRR (0.006-0.008 ppm), fat at 27.7% TRR (0.025 ppm), skin at 24.1% TRR (0.018 ppm), and liver at 16.2% TRR (0.128 ppm). The metabolite M31 was also identified as a single peak in liver, accounting for 8.1% TRR (0.064 ppm). The carboxylic acid metabolite, CM-2, was identified as a major residue in egg whites at 17.1% TRR (0.008 ppm) and at lower levels in muscle (8.5-10.2% TRR), fat and skin (9.6% TRR), and egg yolk (6.6% TRR); CM-2 was not detected in liver. Metabolite M12 (with co-eluting CM-2/3) was only detected in liver, at 11.5% TRR (0.091 ppm).

The sulfate conjugates of dihydroxy-metconazole (DHM), mono-hydroxy-metconazole (MHM) and M32 were identified in cyclopentyl-label hen matrices at varying levels. The MHM sulfate was a major residue in egg whites (16.3% TRR, 0.008 ppm), egg yolk (13.1% TRR, 0.012 ppm), and muscle (12.9-18.0% TRR, 0.006 ppm), but was a minor residue (≤6% TRR) in fat and skin. The DHM sulfate was a major residue in muscle (9.9-16.8% TRR, 0.003-0.008 ppm), but was a minor residue (<3% TRR) in skin and egg yolk. The sulfate of M32 was a major residue in egg whites (16.7% TRR, 0.008 ppm), but was present at lower levels in egg yolk (7.9% TRR), muscle (7.9-10.3% TRR), fat (1.6% TRR) and skin (3.7% TRR). The sulfates were not detected in acid-hydrolyzed liver, but various isomers of free DHM, MHM, and M32 (with co-eluting CM-1), and the carboxylic acid metabolite of monohydroxy-metconazole (CHM) and dicarboxylic acid metabolite of metconazole (DCM) were identified at 2.1%, 13.2%, 4.1%, 5.6%, and 9.3% TRR, respectively. The MHM-4 isomer was also detected at ≤8% TRR in egg whites, egg yolks, muscle, fat, and skin.

In the triazole-label hen matrices, 1,2,4-triazole was the major metabolite identified, at 64.8% TRR (0.120 ppm) in egg whites, 42.9% TRR (0.067 ppm) in egg yolk, 75.2-77.2% TRR (0.112-0.114 ppm) in muscle, 46.7% TRR (0.064 ppm) in skin, 13.3% TRR (0.019 ppm) in fat, and 27.3% TRR (0.265 ppm) in liver. The metabolite M1 (co-eluting with small amounts of M31) was also identified as a significant residue, in egg yolk at 12.8% TRR (0.020 ppm), fat at 13.4% TRR (0.019 ppm), and skin at 10.6% TRR (0.015 ppm), but was a minor residue (≤6% TRR) in egg whites and muscle. M1 and M31 (as individual peaks) were identified in liver at 9.7% TRR (0.094 ppm) and 5.1% TRR (0.049 ppm), respectively. M12, with co-eluting CM-2/3, was only identified in liver (8.3% TRR, 0.081 ppm).

The remaining minor metabolites (each ≤9.7% TRR) identified in triazole-label hen matrices included CM-2 (all matrices but liver), DHM sulfate (all matrices but skin, egg whites, and liver), M32 sulfate (all matrices but liver), and MHM sulfate (all matrices but liver). As for cyclopentyl-label liver, the sulfates were not detected in triazole-label acid hydrolyzed liver, but various isomers of free DHM, MHM, M32 (with co-eluting CM-1), CHM, DCM, and an oxo-metconazole metabolite (OCM) were identified, each at 0.5-9.7% TRR. The MHM-4 isomer was also detected at ≤5% TRR in egg whites, egg yolks, muscle, fat, and skin.

Additional unknown components accounting for 0.5-17.4% TRR were characterized in eggs and hen tissues (both labels), each present at ≤0.01 ppm.

Based on the metabolism study results, metconazole is extensively metabolized in hens through several major pathways involving: (i) oxidation of the methyl group at position 2 of the cyclopentyl ring to form either the carboxylic acid derivative, M12, and its isomers (M13, CM-1 to -3), or the hydroxymethyl derivative, M1, and its isomers (one or more MHM-1 to -6); (ii) oxidation of the methylene group at position 3 of the cyclopentyl ring to form M31 and M32 and their isomers (one or more MHM-1 to -6); (iii) oxidation of M1, M12, M31, M32 and their isomers to dihydroxy metconazole (DHM), monohydroxy metconazole carboxylic acid (CHM) and metconazole dicarboxylic acid (DCM); (iv) sulfate ester formation of the hydroxylated metconazole derivatives; and (v) C-N bond cleavage releasing 1,2,4-triazole from the parent and

likely from its metabolites. The metconazole metabolites are more water-soluble than the parent compound and are rapidly eliminated via excreta. In addition, the *cis* and *trans* isomers of metconazole were present approximately in equal portions in the fat and skin extracts, which differed significantly from the *cis*:*trans* isomer ratio for the parent test substance (~85:15), indicating that the *cis* isomer of metconazole was preferentially metabolized in the hen.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the hen metabolism data are classified as scientifically acceptable.

The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP#s 348168 and 348206.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an impact on the validity of the study.

A. BACKGROUND INFORMATION

Metconazole [5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol] is a broad-spectrum triazole Group 3 fungicide (sterol biosynthesis inhibitors). There are currently no registered uses of metconazole in the U.S.; however, a tolerance has been established for banana, and a Section 18 emergency exemption and supporting time-limited tolerances have been granted for use on soybean. Valent U.S.A. Corporation has applied for registration of metconazole in the U.S. for use on peanut, stone fruits, and tree nuts.

The chemical structure and nomenclature of metconazole, and the physicochemical properties of the technical grade of metconazole are presented in Tables A.1 and A.2.

Table A.1. Metconazole Nomenclature.

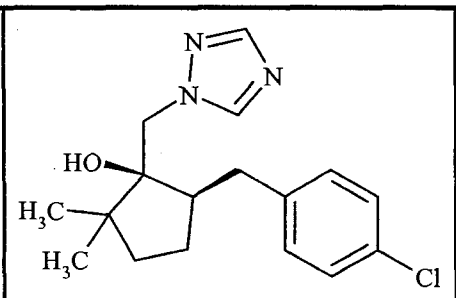
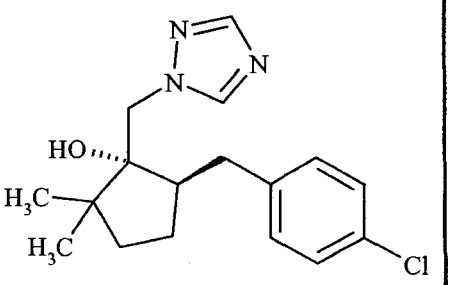
Chemical structure	 *cis*-isomer	 *trans*-isomer
Common name	Metconazole	

Table A.1. Metconazole Nomenclature.	
Company experimental name	KNF-S-474m (Kureha); BAS 555 F (BASF); V-10116 (Valent)
IUPAC name	(1RS,5RS:1RS,5SR)-5-(4-chlorobenzyl)-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol
CAS name	5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol
CAS registry number	125116-23-6 (*cis*- and *trans*-isomers) 115850-27-6 (*cis*-isomer) 115850-28-7 (*trans*-isomer)
End-use products (EP)	50% WDG (Metconazole 50 WDG Fungicide, EPA File Symbol 59639-RUT) 0.75 lb/gal SC/L (Caramba™ Fungicide, EPA File Symbol No. 7969-EUA) 0.67 lb/gal SC/L formulation (BAS 556 01F Fungicide, EPA File Symbol No. 7969-EUT; also contains the active ingredient pyraclostrobin at 0.83 lb/gal)

Table A.2. Physicochemical Properties of Metconazole

Parameter	Value				References* (MRID)
Melting point/range	100.0-108.4°C (using Electrothermal Digital Melting Point Apparatus) (AC900,768 technical grade)				44721505
pH	5.81 at 25°C (1% aqueous suspension)				46808402
Relative density (20°C)	1.14 (relative density to water at 4°C, using capillary-stoppered, density-specific gravity bottle) (Lot No. AC 8879-140B)				44721505
Water solubility (20°C)	Using shake-flask method: 18.7 ± 1.0 mg/L (*cis*-isomer, WL148271, KNF-S-474m) 13.6 ± 1.7 mg/L (*trans*-isomer, WL148271, KNF-S-474m)				44721505
Solvent solubility (g/L) at 20°C	Solvent	Metconazole	*cis*	*trans*	44721505
	acetone	363	251	117	
	methanol	403	294	117	
	dichloromethane	481	343	141	
	ethyl acetate	260	173	90.0	
	propanol	132	86.6	46.7	
	toluene	103	66.2	38.0	
	Hexane	1.40	0.929	0.483	
Vapor pressure (20°C)	Using gas-saturation method: $< 1.23 \times 10^{-5}$ Pa or 9.23×10^{-8} mm Hg (metconazole) $< 1.04 \times 10^{-5}$ Pa or 7.80×10^{-8} mm Hg (*cis*-isomer) $< 1.96 \times 10^{-6}$ Pa or 1.47×10^{-8} mm Hg (*trans*-isomer)				44721505
Dissociation constant (pK_a)	11.38±0.03 and 1.06±0.03 (in water at 29.1°C using spectrophotometric method; Lot No. AC 8879-140B)				44721505

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Table A.2. Physicochemical Properties of Metconazole					
Parameter	Value				References* (MRID)
Octanol/water partition coefficient, Log(K_{OW})	At 20 °C (using flask shaking method): K_{ow} (log K_{ow}) = 7090±989 (3.85) (Lot No. AC 8879-140B) (TGAI) K_{ow} (log K_{ow}) = 7150±803 (3.85) (*cis*-isomer, CL 354,801) K_{ow} (log K_{ow}) = 6800±1700 (3.8) (*trans*-isomer, CL 354,802)				44721505
UV/visible absorption spectrum	pH	λ	A	log ε	46808403
	cis-isomer				
	2.0	221.4	0.828	4.03	
	6.8		0.8452	4.04	
	7.0		0.9126	4.08	
	10.3		0.7226	3.98	
	trans-isomer				
	2.0	221.4	0.9053	4.07	
	7.0		0.9547	4.10	
	10.1		0.9893	4.11	

* Product Chemistry Reviews: DP #256877, Shyam Mathur, Ph.D., 9/12/2000 and DP #329168, Shyam Mathur, Ph.D., 7/13/07.

B. EXPERIMENTAL DESIGN

B.1. Livestock

Two groups of five hens were orally dosed with [cyclopentyl-^{14}C]metconazole or [triazole-^{14}C]metconazole at a target dose of 10 mg/kg feed for 4.5 consecutive days; a third group of hens (n=3) was dosed with a capsule containing corn meal and trace ethanol as a control. Based on the daily feed consumption, the average dosing level was equivalent to 14.0 ppm [cyclopentyl-^{14}C]metconazole or 12.6 ppm [triazole-^{14}C]metconazole in the diet. The test animals were chosen from a colony of hens and placed in individual cages housed in an animal building at Genesis Midwest Laboratories (Neillsville, WI) during the acclimation and study periods. The hens had free access to commercial poultry feed during the study.

The test animals were sacrificed 4.5 hours after the last administration, and samples of edible organs and tissues were collected. Prior to sacrifice, egg samples were collected by group twice daily.

Additional information relevant to the test hens is presented in Table B.1.1. Table B.1.2 presents the test animal dietary regime, and Table B.1.3 lists the test animal dosing regime.

TABLE B.1.1. General Test Animal Information.

Species	Breed	Age	Weight at study initiation (kg)	Health Status	Description of housing/holding area
Laying hens	White Leghorn	~24 weeks	1.6	Healthy	Individual 24" x 24" x 16" cages. Average minimum and maximum temperatures were 19-20 °C, with an average 51% relative humidity and 14/10 hr. light/dark cycle.

TABLE B.1.2. Test Animal Dietary Regime.

Composition of Diet	Feed consumption (g/day)	Water	Acclimation period	Predosing
Access to commercial poultry feed.	86-95 (range of group averages)	*ad libitum*	14 days	None

TABLE B.1.3. Test Animal Dosing Regime.

Treatment Type	Treatment Level [1] (ppm test material in vehicle)	Vehicle	Timing/Duration
Oral; inserted into the esophagus and gently massaged into the crop.	Cyclopentyl hens (Group T1) 14.0 mg/kg feed Triazole hens (Group T2) 12.6 mg/kg feed	Dispensed in cornmeal in gelatin capsules	Twice a day in the morning and evening for 4.5 consecutive days.

[1] Based on actual daily feed consumption and ~10 mg test substance/kg feed per day.

B.2. Test Materials

The radiolabeled test substances in ethanol were isotopically diluted with non-labeled metconazole. An aliquot of the radio-diluted metconazole stock solution was added to corn meal in a gelatin capsule, and air dried prior to sealing. The characteristics of the test substances are presented in Table B.2.1.

TABLE B.2.1. Test Material Characteristics.

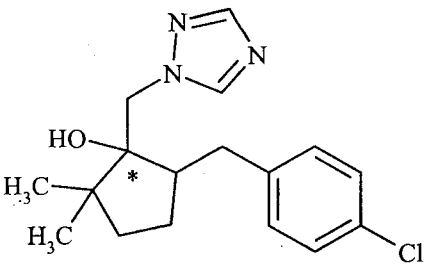
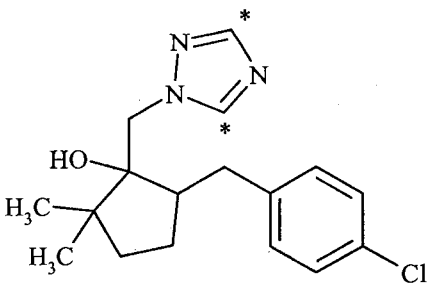
Chemical structure		
Radiolabel position	[cyclopentyl-1-^{14}C]metconazole (labeled at position 1 in the cyclopentyl ring)	[triazole-^{14}C]metconazole (labeled at positions 3 and/or 5 in the triazole ring)
Lot No.	CP-2397	CFQ12045
cis:trans Ratio	85:15	83:17
Purity	99.9%	99.8%
Specific activity – test substance	1.83 GBq/mmol (0.154 mCi/mg)	2.07 GBq/mmol (0.174 mCi/mg)

TABLE B.2.1. Test Material Characteristics.		
Specific activity – radiodiluted test solution	0.909 GBq/mmol (0.077 mCi/mg)	0.907 GBq/mmol (0.077 mCi/mg)

B.3. Sampling Information

Afternoon egg samples were refrigerated and combined with the following morning sample to generate the daily egg sample for each treatment group. Eggs from each 24-hour sampling were separated into yolks and whites, mixed thoroughly and frozen. The following organs and tissues were collected at hen sacrifice: liver, breast muscle, thigh muscle, abdominal fat and skin with fat.

TABLE B.3.1. Sample Collection Information.			
Eggs collected	Excreta collected	Interval from last dose to sacrifice	Tissues harvested and analyzed
Eggs collected twice daily (8-12 hours apart); average 1 egg/day/hen during acclimation and dosing periods.	Excreta collected at 24-hour intervals for each group of hens	4.5 hours	Breast muscle; thigh muscle; abdominal fat; skin with fat; and liver.

B.4. Identification/Characterization of Residues

B.4.1. Sample Handling and Preparation

Tissues collected from each group of hens were pooled, homogenized and frozen. All egg and tissue samples were frozen until shipment on dry ice to Valent (Dublin, CA), where samples were stored frozen (ca. -20 °C) until analysis.

Samples of tissue and egg white and yolk (Day 4 and 5 combined) were extracted with ACN(3x) and centrifuged or filtered. The ACN supernatants were combined, and any insoluble oily droplets were dissolved in hexane. The ACN extracts were concentrated by rotary evaporation for HPLC analysis. Nonextractable residues were then further extracted with water (2x); the aqueous extracts were combined. The aqueous extract was concentrated, and any precipitate was separated by centrifugation. The concentrated aqueous extract was analyzed by HPLC. The liver extracts (ACN + aqueous + hexane) were also combined and acid hydrolyzed to release conjugated residues, then reserved for HPLC.

The extraction efficiency was determined using the control tissue sample fortified with [triazole-^{14}C]metconazole at similar levels as in the treated sample; ~100% of the TRR was recovered in the ACN extract of egg white, thigh muscle, and liver, with <0.1% TRR in the aqueous extract and <0.1-0.2% TRR as nonextractable residues.

Nonextractable residues remaining in liver (both labels) and egg yolk (cyclopentyl only) after solvent extraction were acid hydrolyzed with 2 N HCl at reflux for one hour, cooled, and partitioned with ethyl acetate.

The extraction/fractionation procedures for fat and liver are outlined in Figures B.4.1.1 and B.4.1.2 presented below and are representative of the procedures used for all egg and tissue matrices. The flowcharts were copied without alteration from MRID 46901912.

Figure B.4.1.1. Flowchart of Residue Extraction/Fractionation Procedures in Hen Fat.

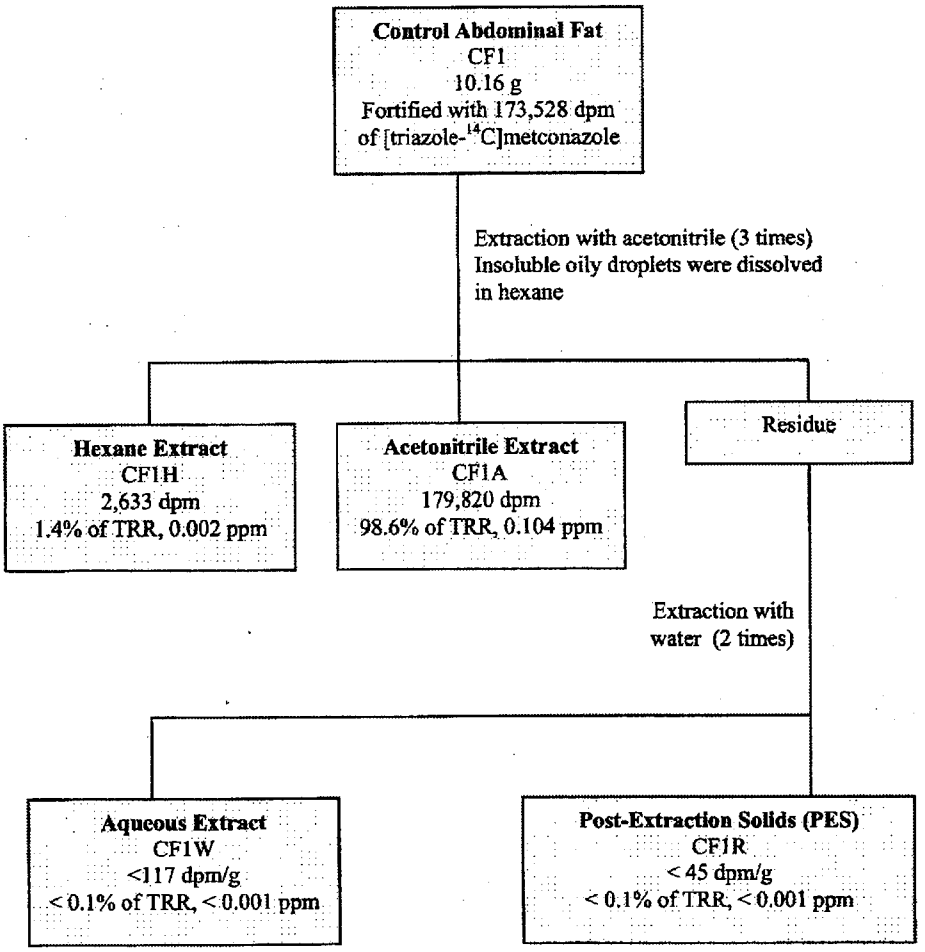
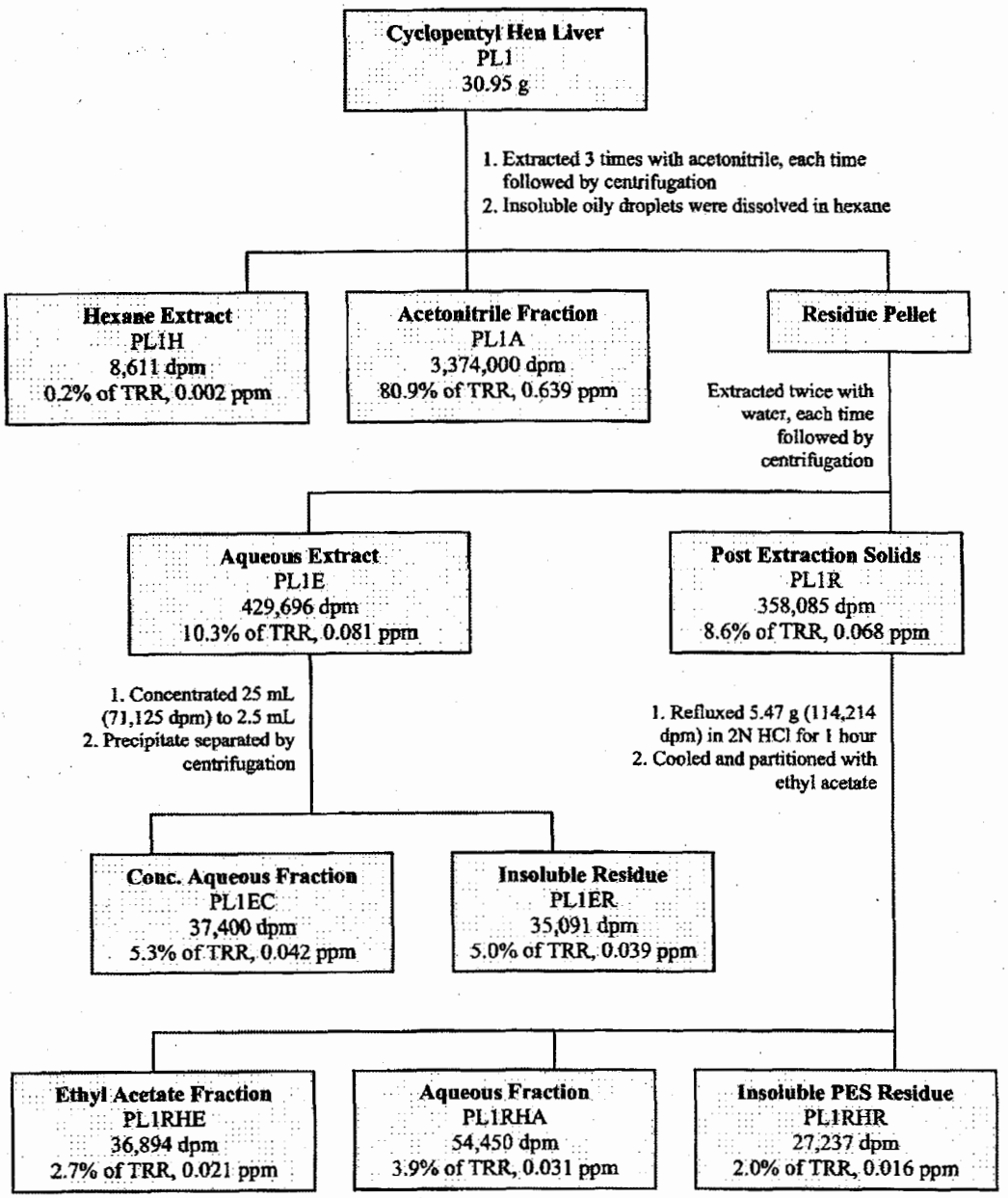


Figure B.4.1.2. Flowchart of Residue Extraction/Fractionation Procedures in Hen Liver.



B.4.2. Analytical Methodology

Radioactivity in egg yolks and whites and tissues was determined initially by combustion/liquid scintillation (LSC). TRR in fat were determined after solubilization in hexane with LSC. Radioactivity in liquid samples (extracts) was determined by direct LSC and by combustion/LSC in extracted solids. The TRR were also calculated by summing extractable and nonextractable radioactivity; summed TRR values were used for all further determinations. The combustion efficiency was determined by spiking a blank sample with [triazole-^{14}C]metconazole; recoveries were 96-99% for egg whites, thigh muscle, and liver. Example calculations of the limit of

detection (LOD) and quantitation (LOQ) were provided; typical values were 0.0004 and 0.001 ppm, respectively.

Egg and tissue extracts were analyzed by HPLC and TLC to determine the metabolic profile and identify the metabolites. The HPLC system utilized a C8 column, UV detection (210 or 230 nm), flow-through radiodetection, and gradient mobile phases of ACN and water, each containing 0.05% trifluoroacetic acid. For peak isolation, eluted fractions were collected by preparative HPLC. The two-dimensional TLC systems used silica gel plates and solvent systems of acetone:dichloromethane:acetic acid (40:10:1, v:v:v); toluene:ethyl formate:formic acid (5:7:1, v:v:v); and/or dichloromethane:acetone:formic acid:water (60:40:0.1:0.1, v:v:v:v). Radioactive areas were determined using phosphorimaging, and nonlabeled reference standards were detected with UV light; appropriate reference standards were co-chromatographed with each sample. The reference standards used in the study are presented in Appendix I.

LC/MS analysis of isolated metabolites and metconazole standards was conducted using an LC system similar to above but with a C18 column, a mobile phase of ACN and water, each containing 0.05% formic acid, and MS APCI or ESI detection in the positive or negative ion mode.

Metabolites were also confirmed with ^{1}H NMR by Acorn NMR Inc. (Livermore, CA). All NMR spectra were acquired at room temperature using an NMR spectrophotometer operating at 400 MHz for ^{1}H.

C. RESULTS AND DISCUSSION

Sample storage conditions and intervals are summarized in Table C.1. TRR determinations and sample extractions were conducted within ~1 month of sample collection, and egg and tissue samples were analyzed (including metabolite identifications) within 11 months of collection. Re-extraction and analysis of liver, thigh muscle, fat, and egg white samples stored under frozen conditions demonstrated no significant changes in the metabolic profile over the duration of the study (~11 months after collection). These data adequately support the storage conditions and intervals of samples from the hen metabolism study.

TRR in hen eggs and tissues are presented in Table C.2.1. TRR, determined by summing extractable and nonextractable radioactivity, were highest in liver (0.790-0.972 ppm), followed by fat (0.091-0.141 ppm), skin with fat (0.075-0.137 ppm), thigh muscle (0.049-0.152 ppm), and breast muscle (0.031-0.145 ppm). TRR in egg whites were <0.001-0.049 ppm and 0.017-0.174 ppm from hens treated with cyclopentyl- and triazole-labeled metconazole, respectively. TRR in egg yolks were <0.001-0.096 ppm and 0.005-0.163 ppm from hens treated with cyclopentyl- and triazole-labeled metconazole, respectively. Residues in egg whites appear to have reached a plateau following 3 or 4 days of dosing with cyclopentyl- or triazole-labeled metconazole, respectively. Maximum residues were observed in egg yolk (both labels) on Day 5. Egg whites from Day 4 and egg yolks from Day 5 were used for extraction; TRR, determined by summing extractable and nonextractable radioactivity were 0.047-0.186 ppm in Day 4 egg whites and 0.088-0.156 ppm in Day 5 egg yolks. Radioactivity was generally higher in the eggs and tissues

from the triazole-treated hens. The majority of the radioactivity was rapidly excreted from the treated hens. Graphs of the pharmacokinetics of metconazole in the eggs of laying hens are presented below in Figures C.2.1 (cyclopentyl label) and C.2.2 (triazole label).

The distribution of radioactivity in hen egg whites and yolks, and tissues is presented in Tables C.2.2.1. (cyclopentyl-label muscle, fat, skin, and egg), C.2.2.2 (triazole-label muscle, fat, skin, and egg) and C.2.2.3. (cyclopentyl- and triazole-label liver). Egg whites and yolks were respectively combined from Days 4 and 5 for extraction. The majority of the radioactivity (78-98% TRR) was extracted from hen matrices with ACN. Additional radioactivity (2-10% TRR) was released with water extraction, and small amounts of the TRR (<1-9% TRR) present as oil droplets in fat, skin with fat, egg yolk and liver were hexane soluble. Nonextractable residues in egg yolk (cyclopentyl label) and liver (both labels) after solvent extraction were acid hydrolyzed which further released ~6-10% TRR. Nonextractable residues in egg whites and yolks and hen tissues were 1.6-7.1% TRR.

The ACN and aqueous extracts of eggs and tissues were analyzed by HPLC and/or TLC. The combined extracts of liver were also acid hydrolyzed to release any conjugated metabolites, and the hydrolysates were analyzed by HPLC; metabolites quantitated following acid hydrolysis in liver are discussed herein because the majority of the unhydrolyzed liver extract consisted of conjugated metabolites. The analytical methods used for identification and confirmation of residues are adequate. These included HPLC and TLC with fraction collection and/or co-chromatography with reference compounds. Identification of selected metabolites was confirmed by LC/MS and/or NMR analysis of tissue metabolites isolated from hen excreta. Approximately 68-93% TRR was identified in eggs and hen tissues (muscle, fat, skin with fat, and liver). A summary of the characterization and identification of residues is presented in Tables C.2.3.1 (cyclopentyl-label tissues except liver), C.2.3.2 (cyclopentyl-label egg and liver), C.2.3.3 (triazole-label tissues except liver), and C.2.3.4 (triazole-label egg and liver).

The parent, metconazole, was a major compound identified in fat and skin with fat from both labels, accounting for 35.3-36.7% TRR (0.033-0.050 ppm) in fat and 19.7-27.8% TRR (0.021-0.027 ppm) in skin. The parent was identified as a minor residue in all other hen matrices at 2.5-7.3% TRR (0.003-0.005 ppm) in egg whites, 6.6-11.4% TRR (0.010 ppm) in egg yolks, 3.3-9.8% TRR (0.005 ppm) in thigh muscle, 0.8-5.4% TRR (0.001-0.002 ppm) in breast muscle, and 1.7-4.1% TRR (0.017-0.033 ppm) in liver. Lower levels of the parent were observed in the triazole-label hen matrices, with 1,2,4-triazole as the major residue (except in fat); other metabolites were similar between the cyclopentyl and triazole labels in hen matrices.

In the cyclopentyl-label hen matrices, the metabolite M1 (co-eluting with small amounts of M31) was identified as a major residue in egg whites at 15.7% TRR (0.007 ppm), egg yolks at 18.2% TRR (0.016 ppm), muscle at 15.7-19.9% TRR (0.006-0.008 ppm), fat at 27.7% TRR (0.025 ppm), skin at 24.1% TRR (0.018 ppm), and liver at 16.2% TRR (0.128 ppm). The metabolite M31 was also identified as a single peak in liver, accounting for 8.1% TRR (0.064 ppm). The carboxylic acid metabolite, CM-2, was identified as a major residue in egg whites at 17.1% TRR (0.008 ppm) and at lower levels in muscle (8.5-10.2% TRR), fat and skin (9.6% TRR), and egg

yolk (6.6% TRR); CM-2 was not detected in liver. Metabolite M12 (with co-eluting CM-2/3) was only detected in liver, at 11.5% TRR (0.091 ppm).

The sulfate conjugates of DHM, MHM and M32 were identified in cyclopentyl-label hen matrices at varying levels. The MHM sulfate was a major residue in egg whites (16.3% TRR, 0.008 ppm), egg yolk (13.1% TRR, 0.012 ppm), and muscle (12.9-18.0% TRR, 0.006 ppm), but was a minor residue (≤6% TRR) in fat and skin. The DHM sulfate was a major residue in muscle (9.9-16.8% TRR, 0.003-0.008 ppm), but was a minor residue (<3% TRR) in skin and egg yolk. The M32 sulfate was a major residue in egg whites (16.7% TRR, 0.008 ppm), but was present at lower levels in egg yolk (7.9% TRR), muscle (7.9-10.3% TRR), fat (1.6% TRR) and skin (3.7% TRR). The sulfates were not detected in acid-hydrolyzed liver, but various isomers of free DHM, MHM, M32 (with co-eluting CM-1), CHM, and DCM were identified at 2.1%, 13.2%, 4.1%, 5.6%, and 9.3% TRR, respectively. The MHM-4 isomer was also detected at ≤8% TRR in egg whites, egg yolks, muscle, fat, and skin.

In the triazole-label hen matrices, 1,2,4-triazole was the major metabolite identified, at 64.8% TRR (0.120 ppm) in egg whites, 42.9% TRR (0.067 ppm) in egg yolk, 75.2-77.2% TRR (0.112-0.114 ppm) in muscle, 46.7% TRR (0.064 ppm) in skin, 13.3% TRR (0.019 ppm) in fat and 27.3% TRR (0.265 ppm) in liver. The metabolite M1 (co-eluting with small amounts of M31) was also identified as a significant residue, in egg yolk at 12.8% TRR (0.020 ppm), fat at 13.4% TRR (0.019 ppm), and skin at 10.6% TRR (0.015 ppm), but was a minor residue (≤6% TRR) in egg whites and muscle. M1 and M31 (as individual peaks) were identified in liver at 9.7% TRR (0.094 ppm) and 5.1% TRR (0.049 ppm), respectively. M12, with co-eluting CM-2/3, was only identified in liver (8.3% TRR, 0.081 ppm).

The remaining minor metabolites (each ≤9.7% TRR) identified in triazole-label hen matrices included CM-2 (all matrices but liver), DHM sulfate (all matrices but skin, egg whites, and liver), M32 sulfate (all matrices but liver), and MHM sulfate (all matrices but liver). As for cyclopentyl-label liver, the sulfates were not detected in triazole-label acid hydrolyzed liver, but various isomers of free DHM, MHM, M32 (with co-eluting CM-1), CHM, DCM, and OCM were identified, each at 0.5-9.7% TRR. The MHM-4 isomer was also detected at ≤5% TRR in egg whites, egg yolks, muscle, fat, and skin.

Additional unknown components accounting for 0.5-17.4% TRR were characterized in eggs and hen tissues (both labels), each present at ≤0.01 ppm. The chemical names and structures of compounds identified in the study are presented in Table C.3.1.

Cis- and *trans*-isomers of metconazole were identified as major residues in fat and skin with fat. The isomers were isolated separately from the triazole-label fat ACN extract using preparative HPLC, and their identities were confirmed by HPLC and TLC co-chromatography with the reference standards. The *cis* and *trans* isomers were present approximately in equal portions in the fat and skin extracts, which differed significantly from the *cis*:*trans* isomer ratio for the parent test substance (~85:15) indicating that the *cis* isomer of metconazole was preferentially metabolized in the hen.

The major peak in all triazole-label hen matrices, 1,2,4-triazole, did not co-elute with the reference standard in the preliminary analysis of hen matrices likely due to other impurities. The metabolite was therefore isolated and purified using preparative HPLC from triazole-label hen excreta and identified with NMR and LC/MS co-chromatography with the reference standard.

Two broad bands of peaks were observed in all hen samples. The later-eluting region (11-15 minute Rt) corresponded to hydroxylated and carboxylated metabolites, such as M1, M31, and M12 and their isomers. The earlier-eluting region (7-11 minute Rt) did not correspond to any of the reference standards, but was thought to be comprised of conjugates of hydroxylated metconazole metabolites characterized as sulfate conjugated esters. To identify the unknown metabolites, large batches of excreta were extracted for metabolite isolation and identification. The metabolites were isolated/purified (Strata-X cartridge chromatography and preparative HPLC) from cyclopentyl- and/or triazole-label excreta and identified using spectroscopic techniques, NMR and/or LC/MS co-chromatography with reference standards or isolated/identified goat urine metabolites (M31). Metabolites M1, M12, M31, M32, CM, (3 isomers), CHM (5 isomers), DHM, MHM (6 isomers), DCM, OCM, M32 sulfate, and MHM sulfate were identified from the triazole-label excreta extracts; M32 sulfate and DHM sulfate (2 isomers) isolated from cyclopentyl-label excreta were also identified with NMR and/or LC/MS.

The exact position of the carboxyl and/or hydroxyl groups could not be determined for CM, MHM, and CHM, but, based on the pattern of carboxylation and hydroxylation in other common metabolites, it is likely that the carboxyl group was present in position 2 (as in M12) and the hydroxyl group was present in position 3 (as in M31 and M32). The possibility of the hydroxylation of other moieties (i.e., the benzylic methylene group of the aromatic ring) producing more isomers of MHM could not be dismissed; however, most of the metabolites identified to date in goat and hen indicate oxidation in the cyclopentyl moiety only. Likewise, the exact position of the hydroxyl groups and/or sulfate moiety could not be determined for DHM and the sulfates of MHM and DHM, but, based on the pattern of hydroxylation in other common metabolites, it is likely that the hydroxyl groups were present in position 2 (as in M1) and/or position 3 (as in M31 and M32). Additionally, OCM (and related DOM) was believed to be an oxidation product of metconazole, but exact structures could not be determined from the MS data. Generic structures were proposed for these metabolites.

To confirm metabolite identifications in hen matrices, HPLC regions with significant residues in liver (before and after acid hydrolysis) were isolated and analyzed by TLC co-chromatography with isolated/identified hen excreta metabolites. The distribution of the metabolites in muscle, fat, skin, egg white, and egg yolk extracts were based on the preliminary analyses with HPLC and metabolite retention times.

C.1. Storage Stability

Samples were stored frozen after collection; TRR analyses were initiated within 2 weeks of collection, and extraction was initiated within 1 month of collection. Analyses of eggs and tissues were completed within 11 months after collection. To demonstrate stability of the metabolic profile, samples of liver, thigh muscle, fat, and egg whites were re-extracted and re-

analyzed after ~11 months of frozen storage at the end of the analytical phase of the study. The distribution of the radioactivity in the initial and final extractions of liver, thigh muscle, fat, and egg whites were very similar. HPLC analyses demonstrated that the major metconazole metabolites were unchanged and that the metabolic profile in hen eggs and tissues was stable for the duration of the study.

TABLE C.1.Summary of Storage Conditions.

Matrix	Storage Temperature (°C)	Actual Storage Duration[1]	Interval of Demonstrated Storage Stability
Hen eggs and liver	-20	334 days (11.0 months)	339 days (11.2 months) in frozen liver, thigh muscle, fat, and egg whites [collection to re-extraction]
Hen fat, muscle, and skin		300 days (9.9 months)	

[1] Storage interval from collection to final analysis including metabolite identification.

C.2. Identification, Characterization, and Distribution of Residues

TABLE C.2.1. Total Radioactive Residues (TRR) in Eggs, Tissue and Excreta.

Matrix	Collection Timing	Cyclopentyl Label		Triazole Label	
		% AD	ppm [1]	% AD	ppm [1]
Excreta	Day 1	Not reported (NR)	10.748	NR	13.849
	Day 2	NR	11.325	NR	16.888
	Day 3	NR	12.610	NR	17.501
	Day 4	NR	14.655	NR	19.445
	Day 5	NR	14.685	NR	14.463
Egg whites	Day 1	NR	<0.001	NR	0.017
	Day 2	NR	0.037	NR	0.088
	Day 3	NR	0.049	NR	0.139
	Day 4	NR	0.041 (0.047)	NR	0.173 (0.186)
	Day 5	NR	0.046	NR	0.174
Egg yolk	Day 1	NR	<0.001	NR	0.005
	Day 2	NR	0.011	NR	0.036
	Day 3	NR	0.032	NR	0.092
	Day 4	NR	0.066 (0.088)	NR	0.126 (0.156)
	Day 5	NR	0.096	NR	0.163
Liver	At sacrifice	NR	0.745 (0.790)	NR	0.901 (0.972)
Muscle, breast	At sacrifice	NR	0.030 (0.031)	NR	0.138 (0.145)
Muscle, thigh	At sacrifice	NR	0.045 (0.049)	NR	0.140 (0.152)
Fat, abdominal	At sacrifice	NR	0.093 (0.091)	NR	0.131 (0.141)
Skin with fat	At sacrifice	NR	0.070 (0.075)	NR	0.127 (0.137)

[1] TRR (ppm values) reported in parentheses were calculated by the summing; summed TRR values were used for all further determinations.

FIGURE C.2.1. Pharmacokinetics of [Cyclopentyl -^{14}C]Metconazole in Eggs of Laying Hen.

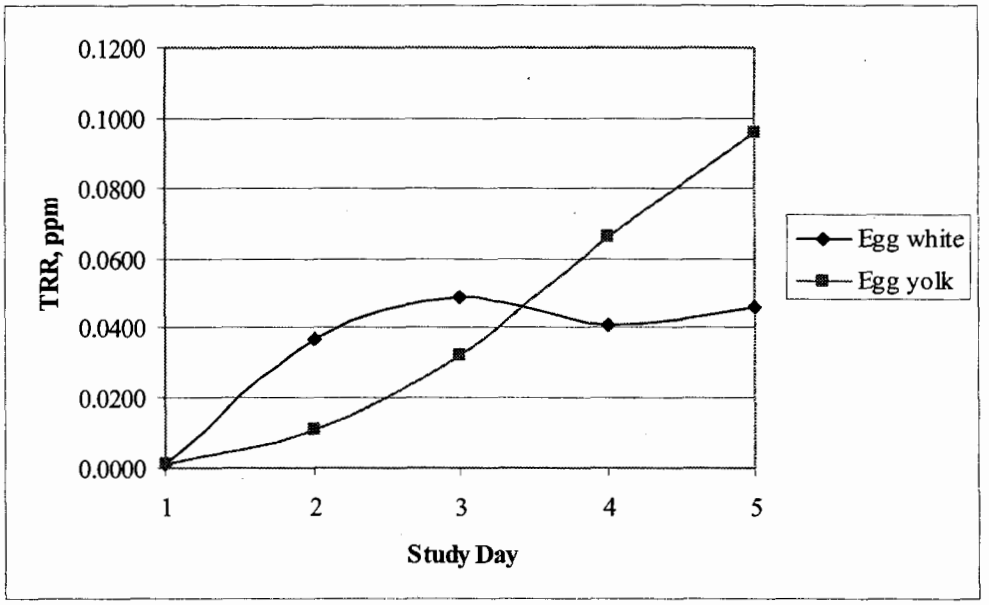


FIGURE C.2.2. Pharmacokinetics of [Triazole -^{14}C]Metconazole in Eggs of Laying Hen.

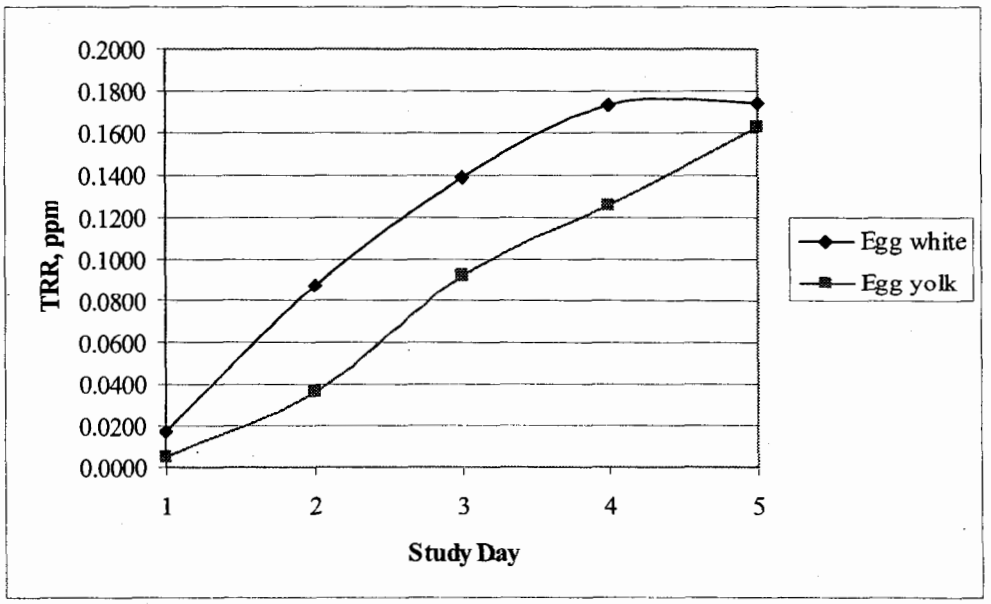


TABLE C.2.2.1. Distribution of the Parent and the Metabolites in Hen Matrices Following Dosing with [Cyclopentyl-^{14}C]Metconazole at 14.0 ppm. [1]

Metabolite Fraction	Muscle, thigh		Muscle, breast		Fat, abdominal		Skin with fat		Egg, white		Egg, yolk	
	TRR=0.049 ppm		TRR=0.031 ppm		TRR=0.091 ppm		TRR=0.075 ppm		TRR=0.047 ppm		TRR =0.088 ppm	
	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm
Hexane	--	--	--	--	9.1	0.008	2.5	0.002	--	--	0.6	0.001
ACN	87.2	0.042	89.4	0.028	85.4	0.078	85.0	0.064	95.8	0.045	78.2	0.069
Metconazole	9.7	0.005	5.4	0.002	36.7	0.033	27.8	0.021	7.3	0.003	11.5	0.010
trans-Metconazole	*6.0*	*0.003*	*3.6*	*0.001*	*17.7*	*0.016*	*13.4*	*0.010*	*5.2*	*0.002*	*7.1*	*0.006*
cis-Metconazole	*3.7*	*0.002*	*1.8*	*0.001*	*19.0*	*0.017*	*14.4*	*0.011*	*2.1*	*0.001*	*4.4*	*0.004*
M1 (+ M31)	15.7	0.008	19.9	0.006	27.7	0.025	24.1	0.018	15.7	0.007	18.2	0.016
CM-2	10.2	0.005	8.5	0.003	9.6	0.009	9.6	0.007	17.1	0.008	6.6	0.006
MHM-4 (& MHM-6 yolk)	6.1	0.003	7.7	0.002	3.5	0.003	5.3	0.004	7.1	0.003	8.4	0.007
DHM sulfate	16.8	0.008	9.9	0.003	--	--	2.3	0.002	--	--	2.8	0.003
M32 sulfate	7.9	0.004	10.3	0.003	1.6	0.001	3.7	0.003	16.7	0.008	7.9	0.007
MHM sulfate	12.9	0.006	18.0	0.006	4.5	0.004	6.0	0.005	16.3	0.008	13.1	0.012
Unknown "others"	7.8	0.004	9.8	0.003	1.7	0.002	6.2	0.005	15.8	0.007	9.7	0.009
Aqueous	5.9	0.003	4.0	0.001	3.9	0.004	6.8	0.005	2.2	0.001	7.1	0.006
Nonextractable	6.8	0.003	6.6	0.002	1.6	0.001	5.7	0.004	2.0	0.001	14.1	0.012
Acid - ethyl acetate											3.7	0.003
Acid - aqueous											5.8	0.005
Nonextractable											4.7	0.004

[1] Shading indicates that the extraction step and/or characterization analysis was not conducted for the matrix in question.

TABLE C.2.2.2. Distribution of the Parent and the Metabolites in Hen Matrices Following Dosing with [Triazole-^{14}C]Metconazole at 12.6 ppm. [1]

Metabolite Fraction	Muscle, thigh		Muscle, breast		Fat, abdominal		Skin with fat		Egg, white		Egg, yolk	
	TRR=0.152 ppm		TRR=0.1545 ppm		TRR=0.141 ppm		TRR=0.137 ppm		TRR=0.186 ppm		TRR =0.156 ppm	
	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm
Hexane	--	--	--	--	7.8	0.011	1.3	0.002	--	--	0.2	0.0003
ACN	90.5	0.138	87.8	0.128	81.5	0.115	89.6	0.122	97.8	0.182	88.5	0.138
Metconazole	3.2	0.005	0.8	0.001			19.7	0.027	2.5	0.004	6.6	0.010
trans-Metconazole	*1.5*	*0.002*	*0.8*	*0.001*			*9.5*	*0.013*	*1.7*	*0.003*	*4.6*	*0.007*
cis-Metconazole	*1.7*	*0.003*	--	--			*10.2*	*0.014*	*0.8*	*0.001*	*2.0*	*0.003*
1,2,4-triazole	70.8	0.108	71.0	0.103			46.7	0.064	64.8	0.120	42.9	0.067
M1 (+ M31)	3.8	0.006	3.8	0.006			10.6	0.015	6.2	0.011	12.8	0.020
CM-2	1.9	0.003	1.6	0.002			2.6	0.004	4.8	0.009	2.8	0.004
MHM-4 (& MHM-6 yolk)	1.5	0.002	1.4	0.002			1.9	0.003	2.5	0.005	4.5	0.007
DHM sulfate	1.3	0.002	1.9	0.003			--	--	--	--	1.3	0.002
M32 sulfate	3.8	0.006	2.1	0.003			2.8	0.004	3.9	0.007	3.1	0.005
MHM sulfate	2.4	0.004	3.7	0.005			2.5	0.003	5.3	0.010	8.3	0.013
Unknown "others"	1.7	0.003	1.6	0.002			2.8	0.004	7.8	0.014	6.2	0.010
Aqueous	6.6	0.010	8.6	0.013	8.7	0.012	5.1	0.007	1.6	0.003	4.2	0.007
1,2,4-triazole	4.3	0.007	6.2	0.009								

TABLE C.2.2.2. Distribution of the Parent and the Metabolites in Hen Matrices Following Dosing with [Triazole-^{14}C]Metconazole at 12.6 ppm. [1]

Metabolite Fraction	Muscle, thigh		Muscle, breast		Fat, abdominal		Skin with fat		Egg, white		Egg, yolk	
	TRR=0.152 ppm		TRR=0.1545 ppm		TRR=0.141 ppm		TRR=0.137 ppm		TRR=0.186 ppm		TRR =0.156 ppm	
	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm
M1 (+ M31)	0.2	<0.001	--	--								
Unknown "others"	2.1	0.003	2.4	0.003								
-Combined ACN/aqueous					90.2	0.127						
Metconazole					35.3	0.049						
trans-Metconazole					*17.3*	*0.024*						
cis-Metconazole					*18.0*	*0.025*						
1,2,4-triazole					13.3	0.019						
M1 (+ M31)					13.4	0.019						
CM-2					5.0	0.007						
MHM-4					2.6	0.004						
DHM sulfate					4.0	0.006						
M32 sulfate					9.7	0.014						
MHM sulfate					6.4	0.009						
Unknown "others"					0.5	0.001						
Nonextractable	2.9	0.004	3.6	0.005	2.0	0.003	4.0	0.005	0.6	0.001	7.1	0.011

[1] Shading indicates that the extraction step and/or characterization analysis was not conducted for the matrix in question.

TABLE C.2.2.3. Distribution of the Parent and the Metabolites in Hen Liver Following Dosing with [Cyclopentyl-^{14}C]Metconazole at 14.0 ppm or [Triazole-^{14}C]Metconazole at 12.6 ppm. [1]

Metabolite Fraction	Liver				Liver			
	TRR = 0.790 ppm				TRR=0.972 ppm			
	Pre-hydrolysis		Post-hydrolysis		Pre-hydrolysis		Post-hydrolysis	
	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm
Hexane	0.2	0.002			0.1	0.0005		
ACN (1AC)	80.9	0.639			82.0	0.797		
Aqueous	10.3	0.081			10.1	0.098		
Conc. aqueous (1EC)	5.3	0.042			6.9	0.067		
Insoluble precipitation	5.0	0.039			3.2	0.031		
-Combined fractions: [2]	86.2	0.681	91.4	0.722			92.1	0.895
Metconazole	4.3	0.034	4.1	0.033			1.7	0.017
trans-Metconazole	*0.4*	*0.003*						
cis-Metconazole	*3.9*	*0.031*						
1,2,4-triazole	--	--	--	--			27.3	0.265
M1	12.7	0.100	16.2	0.128			9.7	0.094
M12 (+CM-2/3)	4.1	0.033	11.5	0.091			8.3	0.081
M31	7.2	0.057	8.1	0.064			5.1	0.049
M32 (+ CM-1)	5.9	0.047	4.1	0.032			4.1	0.039
M32 sulfate	3.9	0.031	--	--			--	--
DHM sulfate	1.9	0.015	--	--			--	--
MHM sulfate	1.5	0.012	--	--			--	--
DCM	--	--	9.3	0.073			7.2	0.070

TABLE C.2.2.3. Distribution of the Parent and the Metabolites in Hen Liver Following Dosing with [Cyclopentyl-^{14}C]Metconazole at 14.0 ppm or [Triazole-^{14}C]Metconazole at 12.6 ppm. [1]

Metabolite Fraction	Liver				Liver			
	TRR = 0.790 ppm				TRR=0.972 ppm			
	Pre-hydrolysis		Post-hydrolysis		Pre-hydrolysis		Post-hydrolysis	
	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm
CHM (1-4 isomers)	0.9	0.007	5.6	0.044			4.9	0.048
DHM (2 isomers w/trace OCM)	--	--	2.1	0.017			1.9	0.018
MHM (4-6 isomers)	5.5	0.043	13.2	0.104			9.7	0.094
OCM	--	--	--	--			0.5	0.005
Unknown conjugates	33.2	0.262	--	--			--	--
Unknown "others"	5.1	0.040	17.4	0.137			11.8	0.115
Nonextractable	8.6	0.068			7.9	0.077		
Acid - ethyl acetate	2.7	0.021			2.6	0.025		
Acid - aqueous	3.9	0.031			3.7	0.036		
Nonextractable	2.0	0.016			1.6	0.015		

[1] Shading indicates that the extraction step and/or characterization analysis was not conducted for the matrix in question.
[2] Consisting of fractions 1AC + 1EC for prehydrolysis analysis, and consisting of hexane+ACN+Aq for post-hydrolysis analysis. The pre-hydrolysis concentrated ACN and aqueous fractions were analyzed separately; however, the petitioner reported totaled residue values. Levels in the separate extracts could not be determined by the study reviewer. In addition, the combined extracts (ACN, hexane and aqueous) were acid hydrolyzed to release the large number of conjugated metabolites, and analyzed.

TABLE C.2.3.1. Summary of Characterization and Identification of Radioactive Residues in Hen Muscle, Fat, and Skin Following Dosing with [Cyclopentyl-^{14}C]Metconazole at 14.0 ppm.

Metabolite Fraction	Muscle, thigh		Muscle, breast		Fat, abdominal		Skin with fat	
	TRR = 0.049 ppm		TRR = 0.031 ppm		TRR = 0.091 ppm		TRR = 0.075 ppm	
	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm
Total Metconazole (*cis:trans* ratio)	9.8 (38:61)	0.005	5.4 (33:67)	0.002	36.7 (52:48)	0.033	27.8 (52:48)	0.021
M1 (+ M31)	15.7	0.008	19.9	0.006	27.7	0.025	24.1	0.018
CM-2	10.2	0.005	8.5	0.003	9.6	0.009	9.6	0.007
MHM-4	6.1	0.003	7.7	0.002	3.5	0.003	5.3	0.004
DHM sulfate	16.8	0.008	9.9	0.003	--	--	2.3	0.002
M32 sulfate	7.9	0.004	10.3	0.003	1.6	0.001	3.7	0.003
MHM sulfate	12.9	0.006	18.0	0.006	4.5	0.004	6.0	0.005
Unknown "others"	7.8	0.004	9.8	0.003	1.7	0.002	6.2	0.005
Hexane soluble	--	--	--	--	9.1	0.008	2.5	0.002
Aqueous soluble	5.9	0.003	4.0	0.001	3.9	0.004	6.8	0.005
Total identified	79.5	0.039	79.6	0.025	83.7	0.076	78.8	0.059
Total characterized	13.7	0.007	13.8	0.004	14.7	0.014	15.5	0.012
Total extractable	93.2	0.045	93.4	0.029	98.4	0.089	94.3	0.071
Unextractable (PES) [1]	6.8	0.003	6.6	0.002	1.6	0.001	5.7	0.004
Accountability [2]	107	0.048	103	0.031	97	0.090	107	0.075

[1] Residues remaining after exhaustive extractions.
[2] Accountability = (Total extractable + Total unextractable)/(TRR from combustion analysis; see TABLE C.2.1) * 100.

TABLE C.2.3.2. Summary of Characterization and Identification of Radioactive Residues in Hen Egg White, Egg Yolk, and Liver Following Dosing with [Cyclopentyl-^{14}C]Metconazole at 14.0 ppm.

Metabolite Fraction	Egg, white		Egg, yolk		Liver (Post acid hydrolysis)	
	TRR = 0.047 ppm		TRR = 0.088 ppm		TRR= 0.790 ppm	
	%TRR	ppm	%TRR	ppm	%TRR	ppm
Total Metconazole (*cis:trans* ratio)	7.3 (29/71)	0.003	11.4 (39/62)	0.010	4.1	0.033
M1 (+ M31)	15.7	0.007	18.2	0.016	16.2	0.128
M31	--	--	--	--	8.1	0.064
M12 (+ CM-2/3)	--	--	--	--	11.5	0.091
CM-2	17.1	0.008	6.6	0.006	--	--
M32 (+ CM-1)	--	--	--	--	4.1	0.032
DCM	--	--	--	--	9.3	0.073
CHM (1-4 isomers)	--	--	--	--	5.6	0.044
DHM (2 isomers +OCM)	--	--	--	--	2.1	0.017
MHM (4-6 isomers)	7.1	0.003	8.4	0.007	13.2	0.104
DHM sulfate	--	--	2.8	0.003	--	--
M32 sulfate	16.7	0.008	7.9	0.007	--	--
MHM sulfate	16.3	0.008	13.1	0.012	--	--
Unknown "others"	15.8	0.007	9.7	0.009	17.3	0.137
Hexane soluble	--	--	0.6	0.001	--	--
Aqueous soluble	2.2	0.001	7.1	0.006	--	--
Acid - ethyl acetate phase	--	--	3.7	0.003	2.7	0.021
Acid - aqueous phase	--	--	5.8	0.005	3.9	0.031
Total identified	80.1	0.038	68.4	0.060	74.1	0.585
Total characterized	18.0	0.008	26.9	0.024	23.9	0.189
Total extractable	98.0	0.046	95.4	0.084	98.0	0.774
Unextractable (PES) [1]	2.0	0.001	4.7	0.004	2.0	0.016
Accountability [2]	107	0.047	109	0.088	106	0.790

[1] Residues remaining after exhaustive extractions.
[2] Accountability = (Total extractable + Total unextractable)/(TRR from combustion analysis; see TABLE C.2.1) * 100.

TABLE C.2.3.3. Summary of Characterization and Identification of Radioactive Residues in Hen Muscle, Fat, and Skin Following Dosing with [Triazole-^{14}C]Metconazole at 12.6 ppm.

Metabolite Fraction	Muscle, thigh		Muscle, breast		Fat, abdominal		Skin with fat	
	TRR = 0.152 ppm		TRR = 0.145 ppm		TRR = 0.141 ppm		TRR = 0.137 ppm	
	%TRR	ppm	%TRR	ppm	%TRR	ppm	%TRR	ppm
trans-Metconazole	1.5	0.002	0.8	0.001	17.3	0.024	9.5	0.013
cis-Metconazole	1.7	0.003	--	--	18.0	0.025	10.2	0.014
Total Metconazole (*cis:trans* ratio)	3.3 (52:45)	0.005	0.8 (0:100)	0.001	35.3 (51:49)	0.050	19.7 (52:48)	0.027
1,2,4-triazole	75.2	0.114	77.2	0.112	13.3	0.019	46.7	0.064
M1 (+ M31)	4.0	0.006	3.8	0.006	13.4	0.019	10.6	0.015
CM-2	1.9	0.003	1.6	0.002	5.0	0.007	2.6	0.004
MHM-4	1.5	0.002	1.4	0.002	2.6	0.004	1.9	0.003
DHM sulfate	1.3	0.002	1.9	0.003	4.0	0.006	--	--
M32 sulfate	3.8	0.006	2.1	0.003	9.7	0.014	2.8	0.004

TABLE C.2.3.3. Summary of Characterization and Identification of Radioactive Residues in Hen Muscle, Fat, and Skin Following Dosing with [Triazole-^{14}C]Metconazole at 12.6 ppm.

MHM sulfate	2.4	0.004	3.7	0.005	6.4	0.009	2.5	0.003
Unknown "others"	3.8	0.006	4.0	0.005	0.5	0.001	2.8	0.004
Hexane soluble	--	--	--	--	7.8	0.011	1.3	0.002
Aqueous soluble	--	--	--	--	--	--	5.1	0.007
Total identified	93.3	0.142	92.5	0.134	89.7	0.126	86.8	0.119
Total characterized	3.8	0.006	4.0	0.005	8.3	0.012	9.2	0.013
Total extractable	97.1	0.148	96.4	0.140	98.0	0.138	96.0	0.131
Unextractable (PES) [1]	2.9	0.004	3.6	0.005	2.0	0.003	4.0	0.005
Accountability [2]	109	0.152	105	0.145	108	0.141	107	0.136

[1] Residues remaining after exhaustive extractions.
[2] Accountability = (Total extractable + Total unextractable)/(TRR from combustion analysis; see TABLE C.2.1) * 100.

TABLE C.2.3.4. Summary of Characterization and Identification of Radioactive Residues in Hen Egg White, Egg Yolk, and Liver Following Dosing with [Triazole-^{14}C]Metconazole at 12.6 ppm.

Metabolite Fraction	Egg, white		Egg, yolk		Liver (Post acid hydrolysis)	
	TRR = 0.186 ppm		TRR = 0.156 ppm		TRR = 0.972 ppm	
	%TRR	ppm	%TRR	ppm	%TRR	ppm
Total Metconazole (*cis:trans* ratio)	2.5 (32:68)	0.005	6.6 (30:70)	0.010	1.7	0.017
1,2,4-triazole	64.8	0.120	42.9	0.067	27.3	0.265
M1	--	--	--	--	9.7	0.094
M1 (+ M31)	6.2	0.011	12.8	0.020	--	--
M31	--	--	--	--	5.1	0.049
M12 (+ CM-2/3)	--	--	--	--	8.3	0.081
CM-2	4.8	0.009	2.8	0.004	--	--
M32 (+ CM-1)	--	--	--	--	4.1	0.039
DCM	--	--	--	--	7.2	0.070
CHM (1-4 isomers)	--	--	--	--	4.9	0.048
DHM (2 isomers +OCM)	--	--	--	--	1.9	0.018
MHM (4-6 isomers)	2.5	0.005	4.5	0.007	9.7	0.094
OCM	--	--	--	--	0.5	0.005
DHM sulfate	--	--	1.3	0.002	--	--
M32 sulfate	3.9	0.007	3.1	0.005	--	--
MHM sulfate	5.3	0.010	8.3	0.013	--	--
Unknown "others"	7.8	0.014	6.2	0.010	11.8	0.115
Hexane soluble	--	--	0.2	<0.001	--	--
Aqueous soluble	1.6	0.003	4.2	0.007	--	--
Acid - ethyl acetate phase	--	--	--	--	2.6	0.025
Acid - aqueous phase	--	--	--	--	3.7	0.036
Total identified	90.0	0.167	82.3	0.128	80.3	0.781
Total characterized	9.4	0.017	10.6	0.017	18.1	0.176
Total extractable	99.4	0.185	92.9	0.145	98.4	0.956
Unextractable (PES) [1]	0.6	0.001	7.1	0.011	1.6	0.015
Accountability [2]	107	0.186	108	0.156	100	0.971

[1] Residues remaining after exhaustive extractions.

[2] Accountability = (Total extractable + Total unextractable)/(TRR from combustion analysis; see TABLE C.2.1) * 100.

C.3. Proposed Metabolic Profile

Based on the metabolism study results, metconazole is extensively metabolized in hens through several major pathways involving: (i) oxidation of the methyl group at position 2 of the cyclopentyl ring to form either the carboxylic acid derivative, M12, and its isomers (M13, CM-1 to -3), or the hydroxymethyl derivative, M1, and its isomers (one or more MHM-1 to -6); (ii) oxidation of the methylene group at position 3 of the cyclopentyl ring to form M31 and M32 and their isomers (one or more MHM-1 to -6); (iii) oxidation of M1, M12, M31, M32 and their isomers to dihydroxy metconazole (DHM), monohydroxy metconazole carboxylic acid (CHM) and metconazole dicarboxylic acid (DCM); (iv) sulfate ester formation of the hydroxylated metconazole derivatives; and (v) C-N bond cleavage releasing 1,2,4-triazole from the parent and likely from its metabolites. The metconazole metabolites are more water-soluble than the parent compound and are rapidly eliminated via excreta. A flowchart of the proposed metabolic pathway in hens is presented below in Figure C.3.1.

FIGURE C.3.1. Proposed Metabolic Profile of Metconazole in Hens.

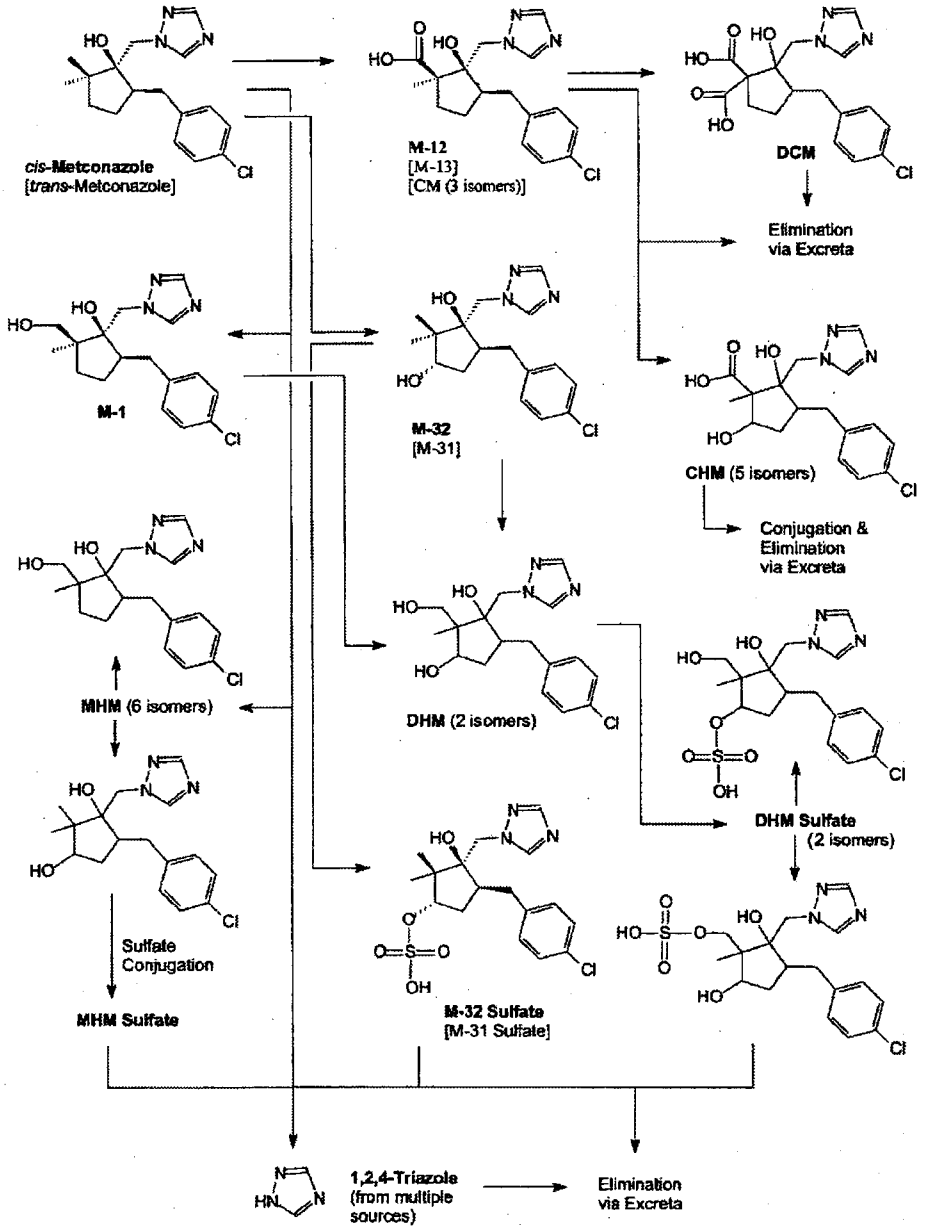


TABLE C.3.1. Identification of Compounds from Metabolism Study.

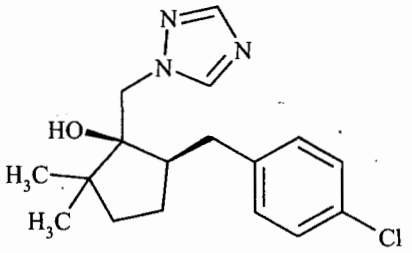
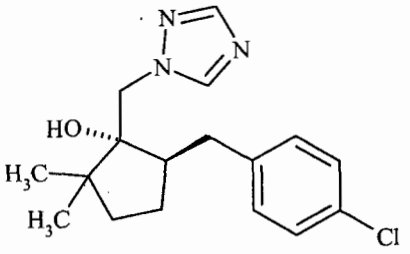
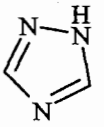
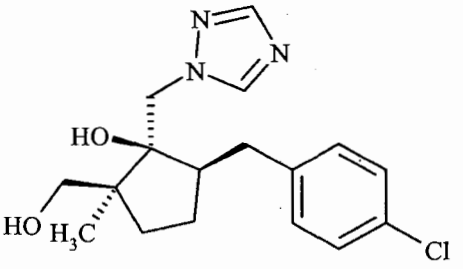
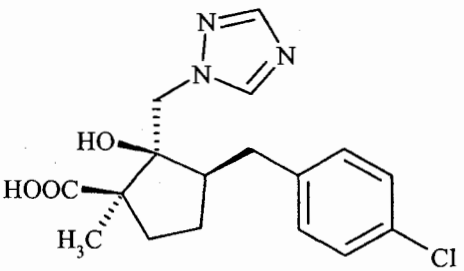
Common name/code Figure C.3.1 ID No.	Chemical name	Chemical structure
Metconazole	5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	 *cis*-isomer  *trans*-isomer
Triazole (1,2,4-T)	1*H*-1,2,4-triazole	
M1 (2-hydroxymethyl-*cis*-metconazole)	5-[(4-chlorophenyl)methyl]-2-methoxyl-2-methyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)-1-cyclopentanol	
M12 (*cis*- metconazole-2-carboxylic acid)	5-[(4-chlorophenyl)methyl]-2-carboxyl-2-methyl-1-(1*H*-1,2,4-triazol-1-yl methyl)-1-cyclopentanol	

TABLE C.3.1. Identification of Compounds from Metabolism Study.

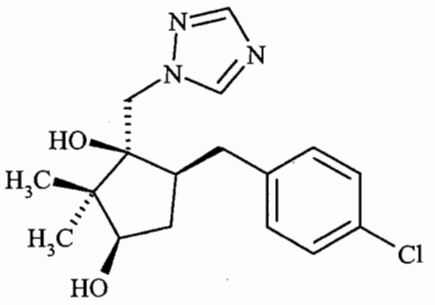
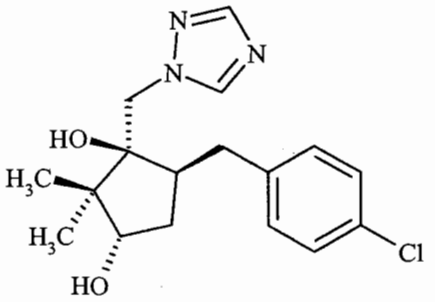
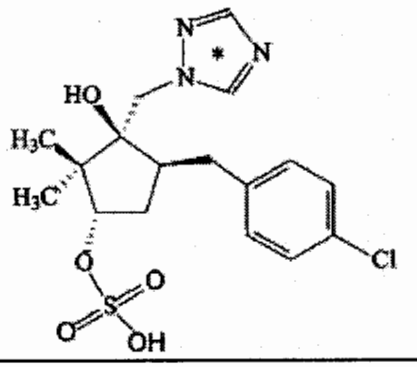
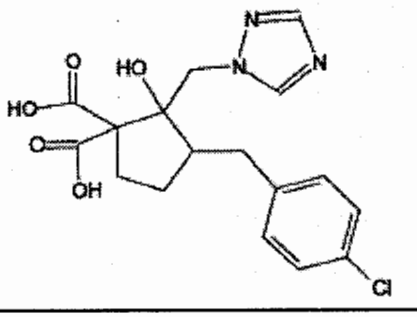
Common name/code Figure C.3.1 ID No.	Chemical name	Chemical structure
M31 [(1S*,3R*,5S*)-3-hydroxy-*cis*-metconazole]	Not provided	
M32 [(1S*,3S*,5S*)-3-hydroxy-*cis*-metconazole]	Not provided	
M32 sulfate (triazole-labeled figure shown; both triazole & cyclopentyl-labeled found in hen matrices)	Not provided	
DCM (metconazole dicarboxylic acid)	Not provided	

TABLE C.3.1. Identification of Compounds from Metabolism Study.

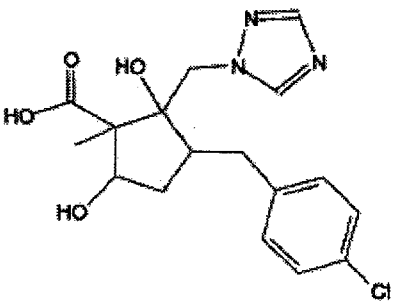
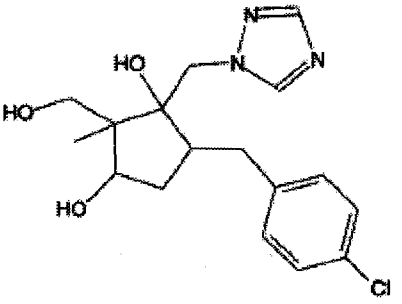
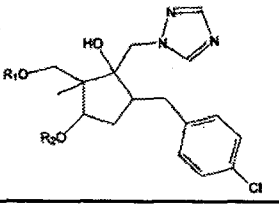
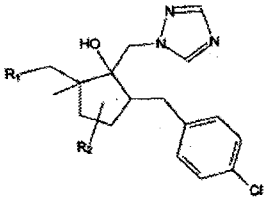
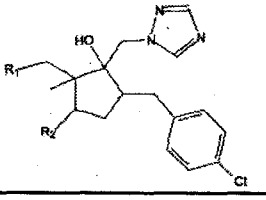
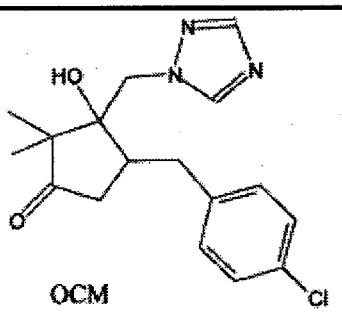
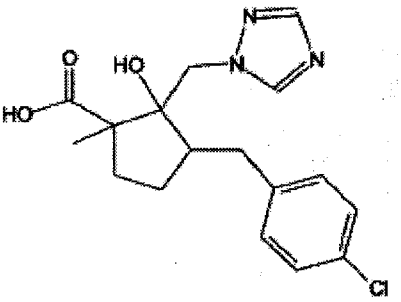
Common name/code Figure C.3.1 ID No.	Chemical name	Chemical structure
CHM (monohydroxy-metconazole carboxylic acid)	Not provided	
Dihydroxy-metconazole (DHM)	Not provided	
DHM sulfate	Not provided	 (1) $R_1 = H, R_2 = SO_3H$ (2) $R_1 = SO_3H, R_2 = H$
Monohydroxy-metconazole (MHM)	Not provided	 (1) $R_1 = OH, R_2 = H$ (2) $R_1 = H, R_2 = OH$
MHM sulfate	Not provided	 (1) $R_1 = H, R_2 = OSO_3H$ (2) $R_1 = OSO_3H, R_2 = H$

TABLE C.3.1. Identification of Compounds from Metabolism Study.		
Common name/code Figure C.3.1 ID No.	Chemical name	Chemical structure
Oxo-metconazole (OCM; one of many possible structures is presented)	Not provided	 OCM
CM-2 (metconazole carboxylic acid; proposed generic structure for CM isomers is presented)	Not provided	

D. CONCLUSION

The metabolism study adequately delineates the nature of the residue in hens orally dosed with [cyclopentyl-^{14}C]metconazole or [triazole-^{14}C]metconazole for 4.5 consecutive days at 14.0 ppm or 12.6 ppm, respectively, in the diet. TRR determined by summing extractable and nonextractable radioactivity, were highest in liver (0.790-0.972 ppm), followed by fat (0.091-0.141 ppm), skin with fat (0.075-0.137 ppm), thigh muscle (0.049-0.152 ppm) and breast muscle (0.031-0.145 ppm). TRR in egg whites were <0.001-0.049 ppm and 0.017-0.174 ppm from hens treated with cyclopentyl- and triazole-labeled metconazole, respectively. TRR in egg yolks were <0.001-0.096 ppm and 0.005-0.163 ppm from hens treated with cyclopentyl- or triazole-labeled metconazole, respectively. Residues in egg whites appear to have reached a plateau following 3 or 4 days of dosing with cyclopentyl- or triazole-labeled metconazole, respectively. Maximum residues were observed in egg yolk (both labels) on Day 5. Egg whites from Day 4 and egg yolks from Day 5 were used for extraction; TRR, determined by summing extractable and nonextractable radioactivity were 0.047-0.186 ppm in Day 4 egg whites and 0.088-0.156 ppm in Day 5 egg yolks. Radioactivity was generally higher in the eggs and tissues from the triazole-treated hens. The majority of the radioactivity was rapidly excreted from the treated hens.

The parent, metconazole, was a major compound identified in fat and skin with fat from both labels, accounting for 35.3-36.7% TRR in fat and 19.7-27.8% TRR in skin. The parent was identified as a minor residue in all other hen matrices at 0.8-11.4% TRR in egg whites, egg yolks, muscle and liver. Lower levels of the parent were observed in the triazole-label hen matrices, with 1,2,4-triazole as the major residue (except in fat); other metabolites were similar between the cyclopentyl and triazole labels in hen matrices. Metabolites quantitated following

acid hydrolysis in liver are discussed because the majority of the unhydrolyzed liver extract consisted of conjugated metabolites.

In the cyclopentyl-label hen matrices, the metabolite M1 (co-eluting with small amounts of M31) was identified as a major residue (15.7-27.7% TRR) in egg whites, egg yolks, muscle, fat, skin, and liver. The metabolite M31 was also identified as a single peak in liver, accounting for 8.1% TRR. The metabolite CM-2 was identified as a major residue in egg whites at 17.1% TRR and at lower levels (8.5-10.2% TRR) in muscle, fat, skin and egg yolk; CM-2 was not detected in liver. Metabolite M12 (with co-eluting CM-2/3) was only detected in liver at 11.5% TRR.

The sulfate conjugates of DHM, MHM and M32 were identified in cyclopentyl-label hen matrices at varying levels. The MHM sulfate was a major residue (12.9-18.0% TRR) in egg whites, egg yolk, and muscle, but was a minor residue (≤6% TRR) in fat and skin. The DHM sulfate was a major residue in muscle (9.9-16.8% TRR), but was a minor residue (<3% TRR) in skin and egg yolk. The M32 sulfate was a major residue in egg whites (16.7% TRR), but was present at lower levels (1.6-10.3% TRR) in egg yolk, muscle, fat and skin. The sulfates were not detected in acid hydrolyzed liver, but various isomers of free DHM, MHM, M32 (with co-eluting CM-1), CHM, and DCM were identified each at ≤9.3% TRR. The MHM4 isomer was also detected at ≤8% TRR in egg whites, egg yolks, muscle, fat, and skin.

In the triazole-label hen matrices, 1,2,4-triazole was the major metabolite identified, at 64.8% TRR in egg whites, 42.9% TRR in egg yolk, 75.2-77.2% TRR in muscle, 46.7% TRR in skin, 13.3% TRR in fat, and 27.3% TRR in liver. The metabolite M1 (co-eluting with small amounts of M31) was also identified as a significant residue (10.6-13.4% TRR) in egg yolk, fat, and skin, but as a minor residue (≤6% TRR) in egg whites and muscle. M1 and M31 (as individual peaks) were identified in liver at 9.7% TRR and 5.1% TRR, respectively. M12, with co-eluting CM-2/3, was only identified in liver (8.3% TRR).

The remaining minor metabolites (each ≤9.7% TRR) identified in triazole-label hen matrices included CM-2 (all matrices but liver), DHM sulfate (all matrices but skin, egg whites, and liver), M32 sulfate (all matrices but liver), and MHM sulfate (all matrices but liver). As for cyclopentyl-label liver, the sulfates were not detected in triazole-label acid hydrolyzed liver, but various isomers of free DHM, MHM, M32 (with co-eluting CM-1), CHM, DCM, and OCM were identified, each at 0.5-9.7% TRR. The MHM-4 isomer was also detected at ≤5% TRR in egg whites, egg yolks, muscle, fat, and skin.

Additional unknown components accounting for 0.5-17.4% TRR were characterized in eggs and hen tissues (both labels), each present at ≤0.01 ppm. The study is supported by adequate storage stability data, and acceptable methods were used for extraction and characterization/identification of residues.

Based on the metabolism study results, metconazole is extensively metabolized in hens through several major pathways involving: (i) oxidation of the methyl group at position 2 of the cyclopentyl ring to form either the carboxylic acid derivative, M12, and its isomers (M13, CM-1 to -3), or the hydroxymethyl derivative, M1, and its isomers (one or more MHM-1 to -6); (ii)

oxidation of the methylene group at position 3 of the cyclopentyl ring to form M31 and M32 and their isomers (one or more MHM-1 to -6); (iii) oxidation of M1, M12, M31, M32 and their isomers to dihydroxy metconazole (DHM), monohydroxy metconazole carboxylic acid (CHM) and metconazole dicarboxylic acid (DCM); (iv) sulfate ester formation of the hydroxylated metconazole derivatives; and (v) C-N bond cleavage releasing 1,2,4-triazole from the parent and likely from its metabolites. The metconazole metabolites are more water-soluble than the parent compound and are rapidly eliminated via excreta.

E. REFERENCES

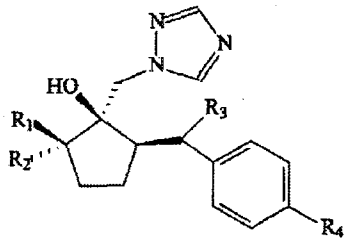
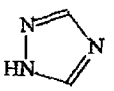
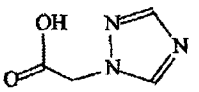
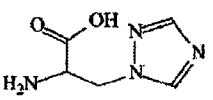
DP#:	324541
Subject:	Metconazole. Request for a Tolerance on Imported Bananas. Summary of Analytical Chemistry and Residue Data. Petition Number 9E05052.
From:	N. Dodd
To:	M. Waller
Date:	12/14/05
MRIDs:	44721506, 44721507, 44721508, 44721509, 44721510, and 44721511

F. DOCUMENT TRACKING

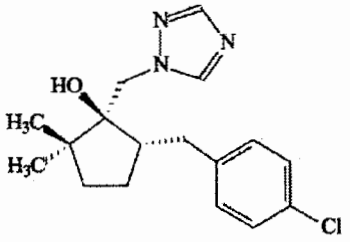
RDI: N. Dodd (2/20/08)
Petition Numbers: 6F7094 and 6F7095
DP#s: 348168 and 348206
PC Code: 125619

Template Version June 2005

APPENDIX I. Chemical Names and Structures of Reference Standards Used in Hen Metabolism Study. (Copied without alteration from MRID 46901912)

Standard Name (Abbreviated ID)	*Chemical Structure*				*Purity %*	*Valent Inventory No.*
						
	R_1	R_2	R_3	R_4		
Metconazole (Technical, *cis-trans* 85:15 mixture)	CH_3	CH_3	H	Cl	98.7	AS2122a
cis-Metconazole (*cis*-Met)	CH_3	CH_3	H	Cl	99.3	AS2025a
KNF-474-M-1 (M-1)	CH_2OH	CH_3	H	Cl	98.6	AS2104a
KNF-474-M-2 (M-2)	CH_3	CH_2OH	H	Cl	98.3	AS2105a
KNF-474-M-11 (M-11)	CH_3	CH_3	OH (α)	Cl	98.0	AS2106a
KNF-474-M-12 (M-12)	COOH	CH_3	H	Cl	98.7	AS2107a
KNF-474-M-13 (M-13)	CH_3	COOH	H	Cl	98.1	AS2108a
KNF-474-M-21 (M-21)	CH_3	CH_3	OH (β)	Cl	97.3	AS2110a
KNF-474-M-30 (M-30)	CH_3	CH_3	C=O in place of CHR_3	Cl	97.9	AS2111a
KNF-474-M-39 (M-39)	CH_3	CH_3	H	H	88.6	AS2114a
KNF-474-M-20 (M-20)					99.1	AS2109a
KNF-474-M-34 (M-34)					100.0	AS2112a
KNF-474-M-35 (M-35)					100.0	AS2113a

Appendix I (continued).

Standard Name (Abbreviated ID)	*Chemical Structure*	*Purity %*	*Valent Inventory No.*
trans-Metconazole (*trans*-Met)		99.3	AS2026a

Primary Evaluator	This DER was originally prepared under contract by Dynamac Corporation.
Approved by	Nancy Dodd, Chemist *Nancy Dodd* Date: 2/20/08 Registration Action Branch 3 Health Effects Division (7509P)

This DER was originally prepared under contract by Dynamac Corporation (2275 Research Boulevard, Suite 300; Rockville, MD 20850; submitted 09/13/2007). The DER has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

46901913 Hill, A.; Standen, M. (1993) Metconazole: Confined Rotational Crop Study Using [Cyclopentyl-(Carbon 14)]- and [Triazole-(Carbon 14)]-WL148271. Project Number: 200300437, SBGR/92/104. Unpublished study prepared by Sittingbourne Research Center. 201 p

EXECUTIVE SUMMARY:

Valent U.S.A. Corporation has submitted a confined rotational crop study with [cyclopentyl-^{14}C]metconazole (specific activity 17.0μCi/mg) and [triazole-3,5-^{14}C]metconazole (specific activity 20.4 μCi/mg). Each radiolabeled test substance was formulated as an emulsifiable concentrate and applied to bare sandy loam soil at a rate equivalent to 0.357 lb ai/A (400 g ai/ha). Rotational crops (radish, lettuce, and wheat) were planted 30 and 120 days after soil treatment, in a greenhouse/controlled chamber environment. Immature whole plants were sampled. Mature crops (radish roots and tops, lettuce, and wheat straw and grain) were harvested. The in-life and analytical phases of the study were conducted by Sittingbourne Research Centre (Sittingbourne, Kent, England).

Total radioactive residues (TRR) accumulated at ≥0.01 ppm in all rotational crop matrices planted at the 30- and 120-day plantback intervals (PBIs). In immature plants, TRR were comparable for both labels and were higher in 30-day radish, lettuce, and cyclopentyl-label wheat foliage and root than in 120-day samples; in triazole-label wheat foliage and root, TRR were the same or higher in 120-day samples than in 30-day samples. In mature radish roots and tops, lettuce, and wheat grain and straw, TRR were generally higher in triazole-label samples than in cyclopentyl-label samples, except for 120-day wheat straw, in which TRR were about the same; TRR were generally higher in 120-day samples for both labels than in 30-day samples, except for cyclopentyl-label wheat grain and straw, in which TRR were about the same. Immature crop samples including wheat foliage (forage) were not further analyzed. The following mature crop samples were subjected to extraction procedures and further analysis: 30-day cyclopentyl-label and 30- and 120-day triazole-label radish root and tops; 120-day cyclopentyl-label and 30- and 120-day triazole-label lettuce and wheat straw; and 30- and 120-day triazole-label wheat grain.

The majority of the radioactivity (81.4-88.6% TRR in radish root, 87.8-93.9% in radish tops; 72.7-91.6% in lettuce; 88.6-89.4% in wheat straw; and 83.2-84.7% in wheat grain) was extracted from rotational crop matrices using acetonitrile (ACN)/water. Further extraction with water released an additional <1.0-6.2% TRR from radish matrices, 10.9-16.7% TRR from lettuce, 1.1-2.1% TRR from wheat straw, and 12.3-14.1% TRR from wheat grain. Nonextractable residues following extraction procedures accounted for 4.6-16.1% TRR (≤0.07 ppm) in radish matrices, 6.0-16.4% (≤0.02 ppm) in lettuce, 9.3-9.6% TRR (≤0.07 ppm) in wheat straw, and 2.7-3.0% TRR (0.01 ppm) in wheat grain. These procedures adequately extracted the majority of the residues from rotational crop matrices. Extraction values were normalized; therefore, accountabilities were 100%.

In general, HPLC was used to generate initial profiles of the organic and aqueous phases following extraction of individual matrices. Identification of metconazole and M30 was confirmed in most matrices by HPLC and/or TLC co-chromatography. Triazolylalanine (TA) and triazolylacetic acid (TAA) were typically identified by TLC co-chromatography and were confirmed by GC/MS following derivatization of the isolated metabolites. In addition, metabolites M12/M13 and a related "ketone metabolite" were tentatively identified in a number of matrices by TLC co-chromatography and/or GC/MS. Glycoside conjugates were characterized on the basis of HPLC retention times and partitioning behavior following hydrolysis.

Metconazole was identified at both PBIs and for both labels in all rotational crop matrices except wheat grain. Metabolite M30 was identified at both PBIs and for both labels in radish root and tops and wheat straw. TA was also identified in triazole-label radish root, radish tops, lettuce, and wheat grain, and TAA was tentatively identified in lettuce and wheat grain. Metabolites M12/M13 and a related ketone metabolite were tentatively identified in radish root and tops and lettuce, and components characterized as glycoside conjugates were characterized in all matrices except wheat grain.

Metconazole was the major identified residue in 30-day radish root (both labels), accounting for 39.2% TRR (0.13 ppm) in cyclopentyl-label root and 28.8% TRR (0.11 ppm) in triazole-label root; metconazole was identified at 15.5% TRR (0.11 ppm) in 120-day radish root. TA was the major identified residue in 120-day triazole-label root, accounting for 45.2% TRR (0.33 ppm), and was identified in 30-day triazole-label root at 19.4% TRR (0.07 ppm). Metabolite M30 was identified as a minor residue in all samples, accounting for 1.4-4.8% TRR. A ketone metabolite was also characterized at 3.1-6.3% TRR in all samples, and M13 and glycoside conjugates were characterized but not quantitated in the aqueous-soluble residues. No remaining individual component accounted for >8% TRR in any radish root sample.

In radish tops, metconazole was identified at 18.4% TRR (0.07 ppm) and 15.5% TRR (0.10 ppm) in 30-day cyclopentyl- and triazole-label tops, respectively, and at 10.8% TRR (0.09 ppm) in 120-day triazole-label tops. TA was identified in 30- and 120-day day triazole-label tops at 30.1% TRR (0.20 ppm) and 33.6% TRR (0.28 ppm; tentative identification), respectively, and metabolite M12 was identified in all samples at 33.6% TRR (0.13 ppm) and 26.8% TRR (0.17

ppm) in 30-day cyclopentyl- and triazole-label tops, respectively, and at 13.3% TRR (0.11 ppm; tentative identification) in 120-day tops. Metabolite M30 was a minor residue in all samples, accounting for 2.3-5.4% TRR. The petitioner additionally characterized glycoside conjugates in the organic and aqueous phases (1.1-11.3% and 2.3-5.3% TRR, respectively) of 30-day radish tops, and the ketone metabolite at 4.7-9.6% TRR in all samples. No remaining individual component accounted for >7% TRR in any radish top sample.

Metconazole was identified at 16.5% TRR (0.02 ppm) in 120-day cyclopentyl-label lettuce, and in triazole-label lettuce (both PBIs) at 1.2-5.0% TRR (0.01 ppm). The petitioner also tentatively identified TA in 30-day triazole-label lettuce (at >18.8%, >0.15 ppm), and TAA in 120-day triazole-label lettuce (at 32.5% TRR, 0.05 ppm). Glycoside conjugates or M12/M13 were characterized but not quantitated in the aqueous-soluble residues.

In wheat straw, metconazole accounted for 3.5-4.0% TRR (0.03 ppm) in 120-day samples (both labels), and for 12.0% TRR (0.07 ppm) in 30-day triazole-label straw. Metabolite M30 was identified at 4.5-5.5% TRR (0.03-0.04 ppm) in all samples. Glycoside conjugates were also characterized at 17.7-18.3% TRR (0.12-0.13 ppm) in 120-day samples (both labels) based on acid hydrolysis and partitioning behavior of aqueous-soluble residues.

Only triazole-label wheat grain samples were subjected to characterization/identification analysis. TA was identified as the major metabolite in 30- and 120-day samples, at 37.0% TRR (0.13 ppm) and 59.4% TRR (0.29 ppm), respectively. TAA was also identified in 120-day samples at 20.6% TRR (0.10 ppm). Remaining residues were characterized as organosoluble (based on partitioning into ethyl acetate [EtOAc], ≤1.3% TRR) or aqueous-soluble. Aqueous-soluble residues were characterized on the basis of TLC distribution in 120-day samples (where no individual component accounted for >11.2% TRR) but were not further investigated in 30-day samples (remaining residues = 58.9% TRR, 0.13 ppm).

The dates of sample combustion, extraction and analysis were not reported; however, a limited number of dated HPLC and TLC chromatograms and GC/MS spectra were included in the study, which indicated that the majority of analyses for characterization/identification of residues were completed within 5-16 months of sample harvest. The petitioner conducted a concurrent storage stability study indicating that the metabolic profile was stable for 7 months in wheat straw. Additional storage stability data are available demonstrating the stability of: (1) metconazole *per se* in carrots, lettuce, and wheat grain and straw for up to 12 months (refer to 46902218.der.doc); (2) metconazole, M30, TA, and TAA in radish roots and tops and wheat grain and straw for up to 6 months (refer to 46902223.der.doc); and (3) TA in wheat grain for up to 12 months (refer to 46902221.der.doc). The available storage stability data are adequate to support the confined rotational crop study.

Based on the submitted confined rotational crop study, the petitioner concluded that the main metabolic transformations were oxidation at the benzylic methylene to form M30, and oxidation of the methyl groups on the cyclopentane ring to form M12/M13. The presence of TA and TAA in radish tops and roots and wheat grain indicate that oxidative transformation occurs in the plant at the methylene group bearing the triazole ring. The metabolism of metconazole in rotational

crops appeared to be extensive; however, detailed characterization and identification of metabolites was limited due to generally low residue levels.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the confined rotational crop data are classified as scientifically acceptable.

The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP#s 348168 and 348206.

COMPLIANCE:

Signed and dated Good Laboratory Practices (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an impact on the validity of the study.

A. BACKGROUND INFORMATION

Metconazole [5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol] is a broad-spectrum triazole Group 3 fungicide (sterol biosynthesis inhibitors). There are currently no registered uses of metconazole in the U.S.; however, a tolerance has been established for banana, and a Section 18 emergency exemption and supporting time-limited tolerances have been granted for use on soybean. Valent U.S.A. Corporation has applied for registration of metconazole in the U.S. for use on peanut, stone fruits, and tree nuts.

The chemical structure and nomenclature of metconazole, and the physicochemical properties of the technical grade of metconazole are presented in Tables A.1 and A.2.

Table A.1. Metconazole Nomenclature.

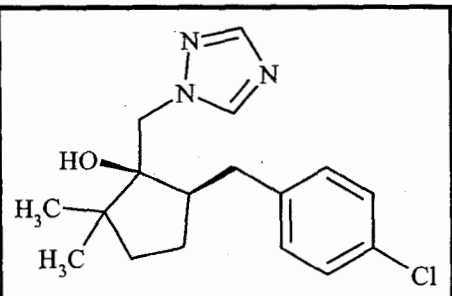
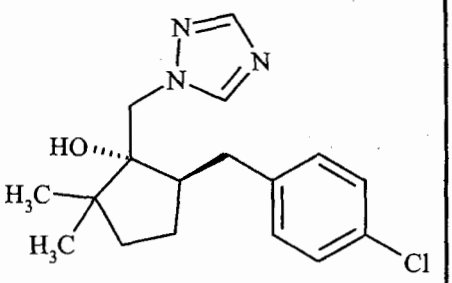
Chemical structure	 *cis*-isomer	 *trans*-isomer
Common name	Metconazole	
Company experimental name	KNF-S-474m (Kureha); BAS 555 F (BASF); V-10116 (Valent)	
IUPAC name	(1RS,5RS:1RS,5SR)-5-(4-chlorobenzyl)-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	

Table A.1. Metconazole Nomenclature.	
CAS name	5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol
CAS registry number	125116-23-6 (*cis*- and *trans*-isomers) 115850-27-6 (*cis*-isomer) 115850-28-7 (*trans*-isomer)
End-use products (EP)	50% WDG (Metconazole 50 WDG Fungicide, EPA File Symbol 59639-RUT) 0.75 lb/gal SC/L (Caramba™ Fungicide, EPA File Symbol No. 7969-EUA) 0.67 lb/gal SC/L formulation (BAS 556 01F Fungicide, EPA File Symbol No. 7969-EUT; also contains the active ingredient pyraclostrobin at 0.83 lb/gal)

Table A.2. Physicochemical Properties of Metconazole

Parameter	Value				References* (MRID)
Melting point/range	100.0-108.4°C (using Electrothermal Digital Melting Point Apparatus) (AC900,768 technical grade)				44721505
pH	5.81 at 25°C (1% aqueous suspension)				46808402
Relative density (20°C)	1.14 (relative density to water at 4°C, using capillary-stoppered, density-specific gravity bottle) (Lot No. AC 8879-140B)				44721505
Water solubility (20°C)	Using shake-flask method: 18.7 ± 1.0 mg/L (*cis*-isomer, WL148271, KNF-S-474m) 13.6 ± 1.7 mg/L (*trans*-isomer, WL148271, KNF-S-474m)				44721505
Solvent solubility (g/L) at 20°C	Solvent	Metconazole	*cis*	*trans*	44721505
	acetone	363	251	117	
	methanol	403	294	117	
	dichloromethane	481	343	141	
	ethyl acetate	260	173	90.0	
	propanol	132	86.6	46.7	
	toluene	103	66.2	38.0	
	Hexane	1.40	0.929	0.483	
Vapor pressure (20°C)	Using gas-saturation method: $< 1.23 \times 10^{-5}$ Pa or 9.23×10^{-8} mm Hg (metconazole) $< 1.04 \times 10^{-5}$ Pa or 7.80×10^{-8} mm Hg (*cis*-isomer) $< 1.96 \times 10^{-6}$ Pa or 1.47×10^{-8} mm Hg (*trans*-isomer)				44721505
Dissociation constant (pK_a)	11.38±0.03 and 1.06±0.03 (in water at 29.1°C using spectrophotometric method; Lot No. AC 8879-140B)				44721505
Octanol/water partition coefficient, Log(K_{OW})	At 20 °C (using flask shaking method): K_{ow} (log K_{ow}) = 7090±989 (3.85) (Lot No. AC 8879-140B) (TGAI) K_{ow} (log K_{ow}) = 7150±803 (3.85) (*cis*-isomer, CL 354,801) K_{ow} (log K_{ow}) = 6800±1700 (3.8) (*trans*-isomer, CL 354,802)				44721505

4 90

Table A.2. Physicochemical Properties of Metconazole					
Parameter	Value				References* (MRID)
UV/visible absorption spectrum	pH	λ	A	log ε	46808403
	cis-isomer				
	2.0	221.4	0.828	4.03	
	6.8		0.8452	4.04	
	7.0		0.9126	4.08	
	10.3		0.7226	3.98	
	trans-isomer				
	2.0	221.4	0.9053	4.07	
	7.0		0.9547	4.10	
	10.1		0.9893	4.11	

* Product Chemistry Reviews: DP #256877, Shyam Mathur, Ph.D., 9/12/2000 and DP #329168, Shyam Mathur, Ph.D., 7/13/07.

B. EXPERIMENTAL DESIGN

B.1. Test Site and Crop Information

Radish and lettuce were grown in pots in a greenhouse; wheat was grown in pots in controlled environmental growth chambers simulating typical conditions in March, April, May, and June/July. Lettuce, radish, and wheat were planted 30 and 120 days after a single application to bare sandy loam soil of [cyclopentyl-^{14}C]metconazole or [triazole-3,5-^{14}C]metconazole at 0.357 lb ai/A (400 g ai/ha). The in-life and analytical phases of the study were conducted by Sittingbourne Research Centre (Sittingbourne, Kent, England). Soil characteristics are presented in Table B.1.1, and crop information is presented in Table B.1.2.

Plants were maintained according to standard agricultural practices; temperature and humidity were strictly controlled, and extremes of light were avoided in the greenhouse. The pots were weeded and thinned periodically by hand. The mean day temperature in the greenhouse was 22 ± 2 °C and the mean night temperature was 18 ± 2 °C over the course of the study. Programs for the simulated conditions in the growth chambers were based on 9-year averages; a table of the programmed temperatures for the growth chambers was included. Watering was based on the approximate soil moisture content. Fertilizer was applied weekly, starting 4 weeks after germination for radish and lettuce, and 3 weeks after germination for wheat.

TABLE B.1.1. Test Site Information.

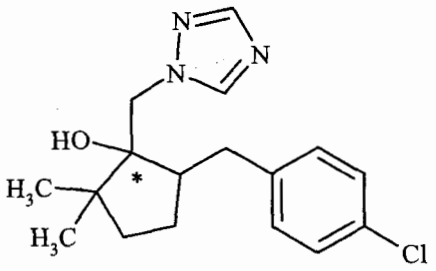
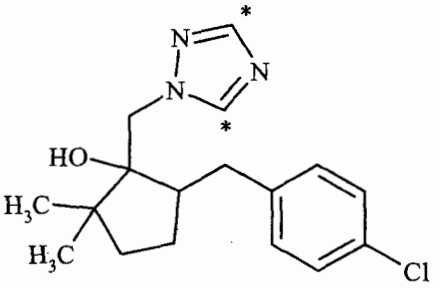
Testing Environment and location	Soil characteristics						
	Type	% Sand	% Silt	% Clay	%OM	pH	CEC (meq/g)
Radish and lettuce were grown in greenhouses. Wheat was grown in controlled environmental growth chambers simulating typical weather for March, April, May, June/July.	Sandy loam	58	28	14	1.3	6.7	0.171

TABLE B.1.2. Crop Information.

Crop; crop group	Variety	Plantback intervals (days)	Growth stage at harvest	Harvested Matrix	Harvesting procedure
Radish; Vegetable, root and tuber, group 1, and Vegetable, leaves of root and tuber, group 2	Cherry Belle	30, 120	Immature	Whole plant	Removed from pots; separated from soil
			Mature	Roots and tops	Tops separated from roots; roots separated from soil; remaining soil rinsed from roots with water
Lettuce; Vegetable, leafy, except *Brassica*, group 4	Bellona	30,120	Immature	Whole plant	Plants removed from pots; separated from soil; remaining soil rinsed from roots with water
			Mature	Roots and tops	
Spring wheat; Grain, cereal, group 15, and Grain, cereal, forage, fodder and straw, group 16	Axona	30,120	Immature	Whole plant	Stem and leaves removed; root separated from soil
			Mature	Straw, grain, and root	Ears (grain and chaff) removed with scissors. Stem cut just above soil surface; roots separated from soil by rinsing

B.2. Test Materials

The radiolabeled test substances were isotopically diluted with nonlabeled metconazole and formulated as EC formulations by dissolving in formulation blank containing nonlabeled metconazole, n-butanol, and the surfactants Surfadone LP100 and Shellsol A. The formulated test substances were diluted with tap water prior to application. The characteristics of the test substances are presented in Table B.2.1.

TABLE B.2.1. Test Material Characteristics.		
Chemical structure		
Radiolabel position	[cyclopentyl-^{14}C]metconazole	[triazole-3,5-^{14}C]metconazole
Lot No.	1160	1163
cis/trans Ratio	79:21	80:20
Purity	99.0%	99.0%
Specific activity	17.0µCi/mg (37794 dpm/µg)	20.4 µCi/mg (45334 dpm/µg)

B.3. Study Use Pattern

The application solution was applied directly to bare soil using a calibrated microsyringe at a rate equivalent to 0.357 lb ai/A (400 g ai/ha). Rotational crops radish, lettuce, and wheat were planted 30 and 120 days after soil treatment. The study use pattern is summarized in Table B.3.1.

TABLE B.3.1. Use Pattern Information.		
Chemical name	[cyclopenty-l^{14}C]metconazole	[triazole-3,5-^{14}C]metconazole
Application method	Bare soil treated with microsyringe.	
Application rate	0.357 lb ai/A (400 g ai/ha)*	
Number of application (s)	One	
Timing of application (s)	30 and 120 days prior to planting of rotational crops	
Days after treatment	30, 120	

* Nominal rate; verified rates were 0.346-0.348 lb ai/A (388-390 g ai/ha).

B.4. Identification/Characterization of Residues

B.4.1. Sample Handling and Preparation

Immature plant samples and the roots of mature lettuce and wheat were subjected to radioassay, but were not further investigated. Immature radish plants were not processed prior to radioassay; samples of immature lettuce were processed with a crop processor, and samples of immature wheat were chopped. Mature radish tops and roots and lettuce samples were prepared by chopping with a knife. Representative subsamples of radish, lettuce, and immature wheat were freeze-dried prior to combustion. Wheat grain was separated from chaff using a thresher, and ground to a fine powder prior to extraction; straw was milled in a knife cutter, and wheat roots were freeze-dried prior to radioassay. Processed samples were stored at ≤-18 °C prior to further analysis. The petitioner included a complete discussion of soil sampling and limited analysis results which are not addressed herein.

All crop samples except wheat straw were subjected to initial extraction followed by filtration with ACN:water (7:3, v:v; 2x) and water (2x for grain; 1x for remaining matrices). The ACN/water extracts of 30-day radish root and tops and 120-day wheat straw were combined prior to further procedures. For all remaining samples, the ACN/water and water extracts were combined.

The combined extracts of 30-day radish roots were diluted with water, then sequentially partitioned with hexane, ethyl acetate (EtOAc), and dichloromethane (DCM) at neutral pH. The aqueous phase following partitioning was combined with the original water extract and reserved for HPLC and TLC analysis. The hexane and EtOAc phases were combined and reserved for HPLC analysis, and the DCM phase was not further investigated.

The combined extracts of remaining matrices were diluted with water if necessary and partitioned with EtOAc (3x) at neutral pH; selected aqueous extracts or aqueous phases were acidified to pH 2 with concentrated HCl prior to further partitioning with EtOAc.

Samples of 30-day triazole-label straw and 120-day straw from both labels were soaked for 1.5 hours in ACN:water (9:1, v:v), and then homogenized and filtered. Remaining residues were extracted with ACN:water (1:1, v:v) followed by water, and filtered. As for radish and lettuce, selected aqueous extracts or aqueous phases were subjected to hydrolysis followed by re-partitioning with EtOAc. These procedures are discussed in further detail where applicable under "Results and Discussion".

To generate additional material for metabolite identification, a separate subsample of 120-day cyclopentyl-label straw was soaked in ACN:water (7:3, v:v), homogenized and filtered, and then extracted 3x with ACN:water (7:3, v:v).

Flow charts depicting the extraction procedures for radish roots are presented below. The flow charts were copied without alteration from MRID 46901913.

Figure B.4.1.1. Extraction Procedure for Radish Root Samples With 30-Day PBI.

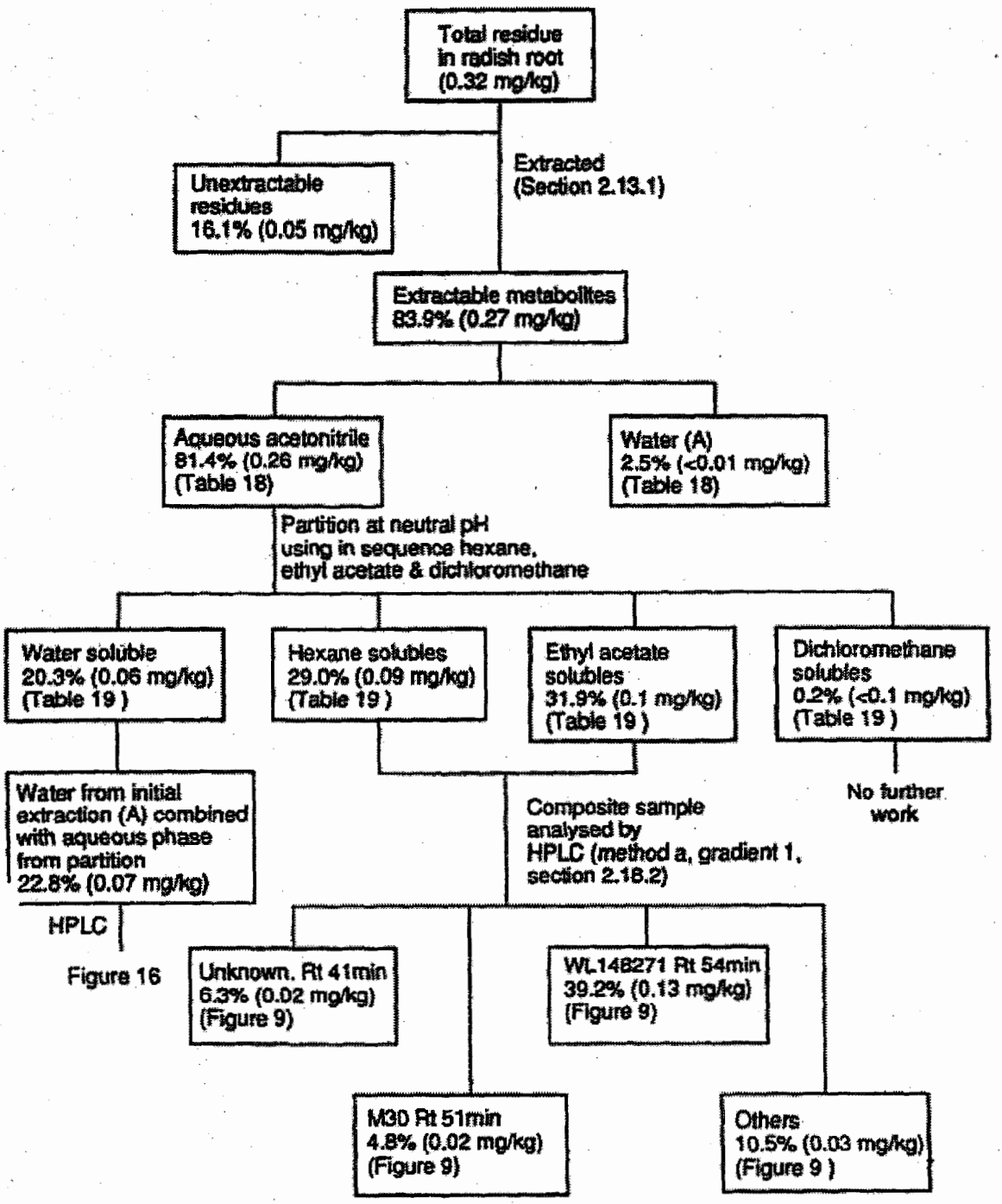


Figure B.4.1.2. Extraction Procedure for Radish Root Samples, Continued.

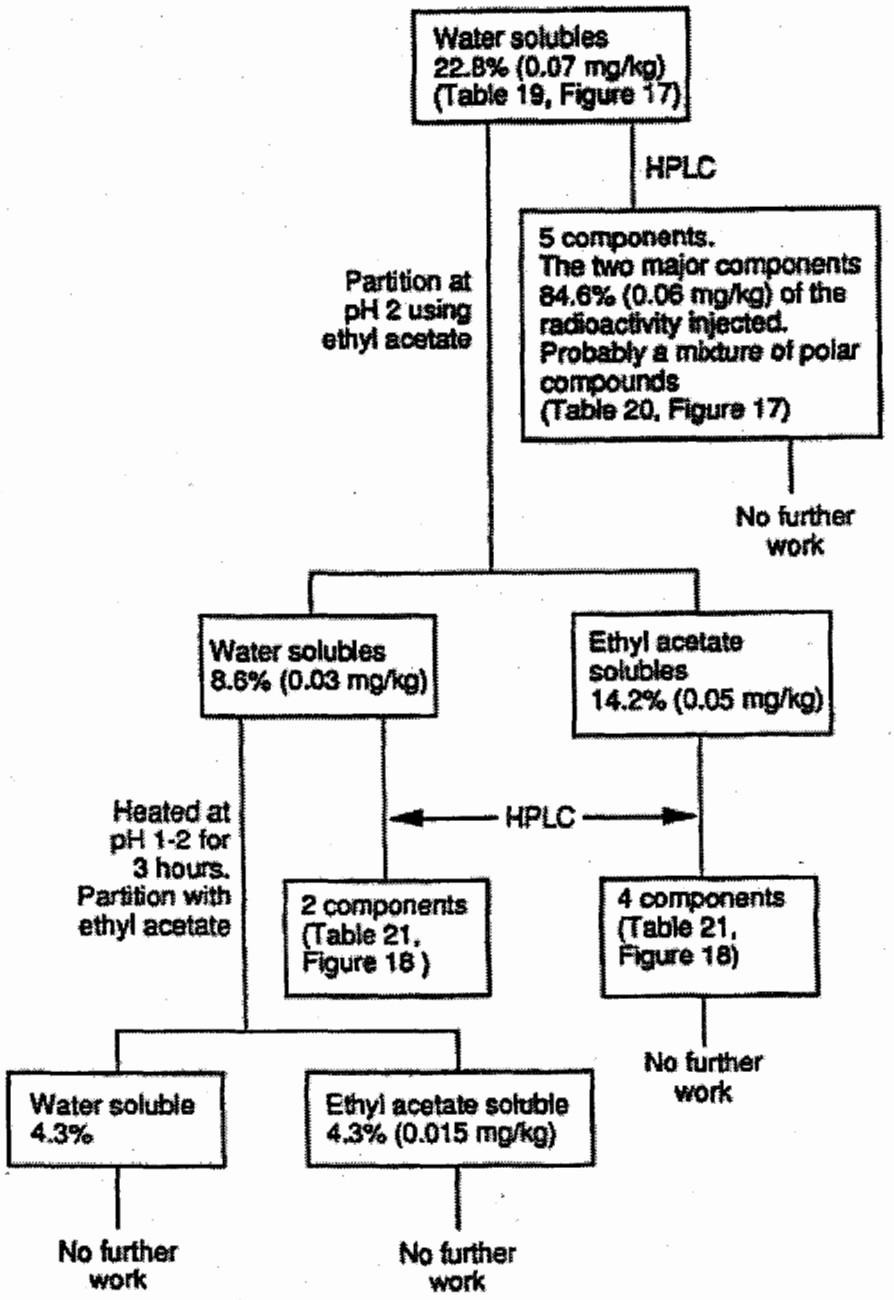
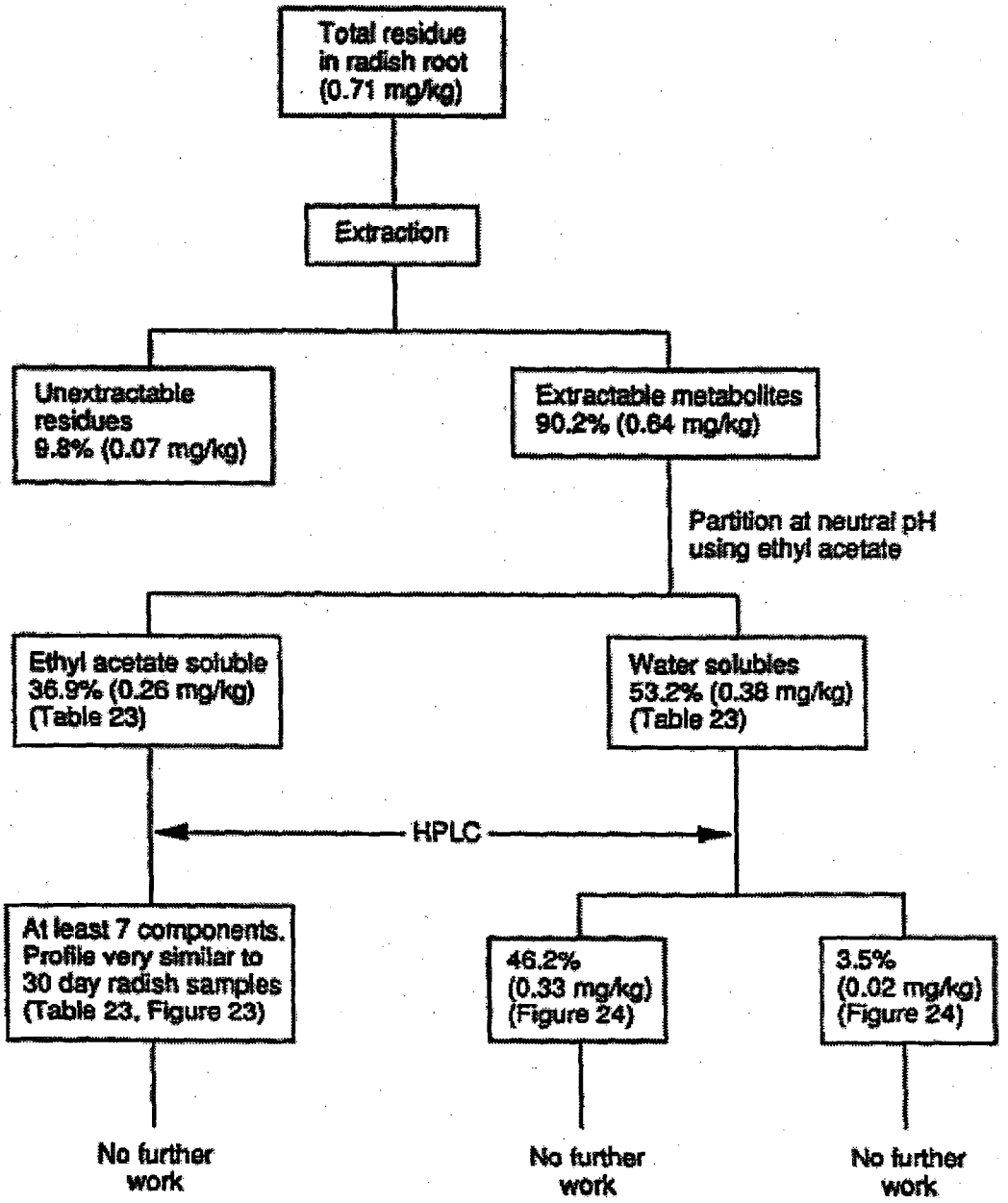


Figure B.4.1.3. Extraction Procedure for Samples of Radish Roots with 120-Day PBI.



B.4.2. Analytical Methodology

Total radioactive residues (TRR) were determined by combustion/LSC in all rotational crop matrices. Extracts were radioassayed by LSC in duplicate, and nonextractable residues were radioassayed by combustion/LSC. The limit of quantitation for TRR determinations was not reported.

Sample extracts were analyzed by HPLC and TLC. HPLC analyses were conducted on systems equipped with a UV detector, a radiodetector, and, for some systems, a fraction collector. Systems **a** and **b** used a reverse-phase silica ODS 30 column and a gradient mobile phase of water and ACN; system **a** was used for metabolite profiling of all extracts as well as for fractionation, and system **b** was used for semipreparative clean-up procedures. Remaining systems were used for analysis of isolated fractions/zones, except system **i**, which was used for determination of the isomer ratio of metconazole determined in organosoluble residues. Systems **d** and **e** used an SCX column and a mobile phase of 0.001 M citric acid and 0.001 M sodium dihydrogen citrate. Systems **f** and **g** used an amino column and a mobile phase of hexane and tetrahydrofuran. System **h** used an amino column and a mobile phase of hexane and tetrahydrofuran, and system **i** used an NO_2 column and a mobile phase of DCM:hexane:tetrahydrofuran (80:18:2, v:v:v). TLC analyses were conducted using silica gel plates (Merck F254, 0.25 mm, or Schleicher and Schuell, 0.5 and 1.0 mm) and one of three solvent systems: (a) acetone:DCM (1:4, v:v or 1:3, v:v), (b) EtOAc:hexane (5:1, v:v) or (c) isopropan-2-ol:water:triethylamine (6:1.5:0.1, v:v:v). A radioanalyzer was used to locate and quantify radioactive components. Metabolites were identified by co-chromatography with reference standards; chemical names and structures of the reference standards used in this study are presented in Appendix I.

Selected aqueous-soluble residues were subjected to further cleanup using strong anion exchange (SAX)/strong cation exchange (SCX) on a BondElut cartridge; residues were eluted with 1% formic acid in water for SAX and 10% NH_4OH in methanol for SCX.

For determination of TA and TAA by GC/MS, residues were derivatized by butylation, with 15% HCl in 1-butanol, and, if necessary, acylation (TA only) with heptafluorobutyric acid anhydride (HFBA).

GC/MS was used for confirmation of the identification of metconazole, M30, TA, and TAA in selected extracts. GC/MS was conducted using phenyl columns; the GC was linked to a radiodetector and a mass selective detector. LC/MS was used to investigate a polar unknown in 120-day grain. LC/MS was conducted using a carbon ODS 30 column, a gradient mobile phase of water and ACN (HPLC system **c**), and thermospray ionization and a radiodetector linked in series.

C. RESULTS AND DISCUSSION

The storage conditions and intervals for rotational crop commodities are presented in Table C.1. The dates of sample combustion, extraction, and analysis were not reported; however, a limited number of dated HPLC and TLC chromatograms and GC/MS spectra were included in the study, which indicated that the majority of analyses for characterization/identification of residues were completed within 5-16 months of sample harvest. The petitioner conducted a concurrent storage stability study indicating that the metabolic profile was stable for 7 months in wheat straw. Additional storage stability data are available demonstrating the stability of: (1) metconazole *per se* in carrots, lettuce, and wheat grain and straw for up to 12 months (refer to 46902218.der.doc); (2) metconazole, M30, TA, and TAA in radish root and tops and wheat grain and straw for up to

six months (refer to 46902223.der.doc); and (3) TA in wheat grain for up to 12 months (refer to 46902221.der.doc). The available storage stability data are adequate to support the confined rotational crop study.

The TRR in rotational crop matrices are presented in Table C.2.1. TRR accumulated at ≥0.01 ppm in all rotated crop matrices planted 30 or 120 days following application of [cyclopentyl-^{14}C]metconazole or [triazole-3,5-^{14}C]metconazole directly to bare soil at 0.357 lb ai/A. In immature plants, TRR were comparable for both labels and were higher in 30-day radish, lettuce, and cyclopentyl-label wheat foliage and root than in 120-day samples; in triazole-label wheat foliage and root, TRR were the same or higher in 120-day samples than in 30-day samples. In mature radish roots and tops, lettuce, and wheat grain and straw, TRR were generally higher in triazole-label samples than in cyclopentyl-label samples, except for 120-day wheat straw, in which TRR were about the same; TRR were generally higher in 120-day samples for both labels than in 30-day samples, except for cyclopentyl-label wheat grain and straw, in which TRR were about the same. Immature crop samples including wheat foliage (forage) were not further analyzed. The following mature crop samples were subjected to extraction procedures and further analysis: 30-day cyclopentyl-label and 30- and 120-day triazole-label radish root and tops; 120-day cyclopentyl-label and 30- and 120-day triazole-label lettuce and wheat straw; and 30- and 120-day triazole-label wheat grain.

The extraction profiles and distribution of the radioactivity in rotational crop commodities are presented in Tables C.2.2.1 through C.2.2.5. The majority of the radioactivity (81.4-88.6% TRR in radish root, 87.8-93.9% in radish tops; 72.7-91.6% in lettuce; 88.6-89.4% in wheat straw; and 83.2-84.7% in wheat grain) was extracted from rotational crop matrices using ACN/water. Further extraction with water released an additional <1.0-6.2% TRR from radish matrices, 10.9-16.7% TRR from lettuce, 1.1-2.1% TRR from wheat straw, and 12.3-14.1% TRR from wheat grain. Nonextractable residues following extraction procedures accounted for 4.6-16.1% TRR (≤0.07 ppm) in radish matrices, 6.0-16.4% (≤0.02 ppm) in lettuce, 9.3-9.6% TRR (≤0.07 ppm) in wheat straw, and 2.7-3.0% TRR (0.01 ppm) in wheat grain. These procedures adequately extracted the majority of the residues from rotational crop matrices. Extraction values were normalized; therefore, accountabilities were 100%.

In general, HPLC was used to generate initial profiles of the organic and aqueous phases following extraction of individual matrices. Identification of metconazole and M30 was confirmed in most matrices by HPLC and/or TLC co-chromatography. TA and TAA were typically identified by TLC co-chromatography and were confirmed by GC/MS following derivatization of the isolated metabolites. In addition, metabolites M12/M13 and a related "ketone metabolite" were tentatively identified in a number of matrices by TLC co-chromatography and/or GC/MS. Glycoside conjugates were characterized on the basis of HPLC retention times and partitioning behavior following hydrolysis. A more detailed discussion of the characterization/identification procedures by matrix is presented below.

HED notes that information and data pertaining to the distribution of metabolites in the rotational crop matrices appeared variously in the submission in text, tables, and/or flow charts. This

information was consolidated as accurately as possible into the distribution and summary tables presented in this DER.

The characterization and identification of residues in rotational crop matrices are summarized in Tables C.2.3.1 through C.2.3.5. Metconazole was identified at both PBIs and for both labels in all rotational crop matrices except wheat grain. Metabolite M30 was identified at both PBIs and for both labels in radish root and tops and wheat straw. TA was also identified in triazole-label radish root, radish tops, lettuce, and wheat grain, and TAA was tentatively identified in lettuce and wheat grain. Metabolites M12/M13 and a related ketone metabolite were tentatively identified in radish root and tops and lettuce. Glycoside conjugates were characterized on the basis of HPLC retention times and partitioning behavior following hydrolysis.

Metconazole was the major identified residue in 30-day radish root (both labels), accounting for 39.2% TRR (0.13 ppm) in cyclopentyl-label root and 28.8% TRR (0.11 ppm) in triazole-label root; metconazole was identified at 15.5% TRR (0.11 ppm) in 120-day radish root. TA was the major identified residue in 120-day triazole-label root, accounting for 45.2% TRR (0.33 ppm), and was identified in 30-day triazole-label root at 19.4% TRR (0.07 ppm). Metabolite M30 was identified as a minor residue in all samples, accounting for 1.4-4.8% TRR. A ketone metabolite was also characterized at 3.1-6.3% TRR in all samples, and glycoside conjugates were characterized but not quantitated in the aqueous-soluble residues. No remaining individual component accounted for >8% TRR in any radish root sample.

In radish tops, metconazole was identified at 18.4% TRR (0.07 ppm) and 15.5% TRR (0.10 ppm) in 30-day cyclopentyl- and triazole-label tops, respectively, and at 10.8% TRR (0.09 ppm) in 120-day triazole-label tops. TA was identified in 30- and 120-day day triazole-label tops at 30.1% TRR (0.20 ppm) and 33.6% TRR (0.28 ppm; tentative identification), respectively, and metabolite M12 was identified in all samples at 33.6% TRR (0.13 ppm) and 26.8% TRR (0.17 ppm) in 30-day cyclopentyl- and triazole-label tops, respectively, and at 13.3% TRR (0.11 ppm; tentative identification) in 120-day tops. Metabolite M30 was a minor residue in all samples, accounting for 2.3-5.4% TRR. The petitioner additionally characterized glycoside conjugates in the organic and aqueous phases (1.1-11.3% and 2.3-5.3% TRR, respectively) of 30-day radish tops, and the ketone metabolite at 4.7-9.6% TRR in all samples. No remaining individual component accounted for >7% TRR in any radish top sample.

Metconazole was identified at 16.5% TRR (0.02 ppm) in 120-day cyclopentyl-label lettuce, and in triazole-label lettuce (both PBIs) at 1.2-5.0% TRR (0.01 ppm). The petitioner also tentatively identified TA in 30-day triazole-label lettuce (at >18.8% TRR, >0.15 ppm), and TAA in 120-day triazole-label lettuce (at 32.5% TRR, 0.05 ppm). Glycoside conjugates or M12/M13 were characterized but not quantitated in the aqueous-soluble residues.

In wheat straw, metconazole accounted for 3.5-4.0% TRR (0.03 ppm) in 120-day samples (both labels), and for 12.0% TRR (0.07 ppm) in 30-day triazole-label straw. Metabolite M30 was identified at 4.5-5.5% TRR (0.03-0.04 ppm) in all samples. Glycoside conjugates were also characterized at 17.7-18.3% TRR (0.12-0.13 ppm) in 120-day samples (both labels) based on acid hydrolysis and partitioning behavior of aqueous-soluble residues.

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Only triazole-label wheat grain samples were subjected to characterization/identification analysis. TA was identified as the major metabolite in 30- and 120-day samples, at 37.0% TRR (0.13 ppm) and 59.4% TRR (0.29 ppm), respectively. TAA was also identified in 120-day samples at 20.6% TRR (0.10 ppm). Remaining residues were characterized as organosoluble (based on partitioning into EtOAc, ≤1.3% TRR) or aqueous-soluble. Aqueous-soluble residues were characterized on the basis of TLC distribution in 120-day samples (where no individual component accounted for >11.2% TRR) but were not further investigated in 30-day samples (remaining residues = 58.9% TRR, 0.13 ppm).

The combined hexane/EtOAc phases of 30-day radish root (both labels) were subjected to fractionation on HPLC System **a**, which yielded similar profiles. Identification of metconazole and M30 in the hexane/EtOAc phase of 30-day cyclopentyl radish root was confirmed by HPLC co-chromatography on systems **a** and **h**; the isomer ratio for metconazole was determined using HPLC system **i**. Identification of these residues in the triazole-label samples was based on the results for the cyclopentyl label. The water-soluble residues of 30-day radish root were initially analyzed by HPLC on system **a**, which indicated five components (two major polar components, three minor polar/nonpolar components) in cyclopentyl-label root, and three components (one major polar component, two minor nonpolar components) in triazole-label root. The major polar component in triazole-label root was identified as TA by TLC co-chromatography in 30-day samples, and was confirmed by derivatization followed by GC/MS analysis. The water-soluble residues were also subjected to additional procedures to attempt to characterize carboxylic acid metabolites, such as M12 and M13 (acidified to pH 2 with 2 M HCl and re-partitioned with EtOAc), and to establish whether remaining residues consisted of conjugated material (hydrolysis with 2 M HCl at reflux, followed by re-partitioning with EtOAc). Based on these procedures, metabolite M13 was tentatively identified as a possible metabolite in cyclopentyl-label root, and the presence of small amounts of glycoside conjugates was suggested in triazole-label root from both labels.

Metconazole and M30 were identified in 30-day radish tops by reverse-phase HPLC fractionation of the triazole-label extract followed by HPLC and TLC co-chromatography. The three additional components of the organosoluble residues were characterized as glycoside conjugates (following acid hydrolysis), a ketone metabolite (following semi-preparative TLC and GC/MS), and a minor unknown. The water-soluble residues were found to be similar to those of 30-day radish root. Small amounts of conjugated material and some metabolites containing the carboxylic acid function were indicated in the cyclopentyl-label residues; TA was identified in triazole-label residues, and M12 was identified in both labels by TLC co-chromatography. Identification of TA was confirmed by HPLC co-chromatography following SCX cleanup and derivatization; HPLC analysis suggested that the peak identified as M12 by TLC was either M12 or a similar metabolite containing a carboxylic functional group. Because the only significant difference between the 30-day tops samples from the two labels was the presence of TA, only the triazole-label 120-day tops sample was analyzed. Based on comparison of the HPLC profiles, the petitioner concluded that the metabolic profile was similar to that of 30-day tops.

Metconazole was identified in the EtOAc phases of 30-day (triazole label) and 120-day lettuce (both labels) by retention time on HPLC system **a**, and confirmed by TLC co-chromatography in the 120-day extracts. In the water-soluble residues for the cyclopentyl label, TRR were higher for the triazole-label, and different metabolic profiles were observed on HPLC. HPLC analysis suggested the presence of glycoside conjugates or unconjugated components containing the carboxylic acid function. Following adjustment to pH 2 and re-partitioning with EtOAc, the major component was tentatively identified as M13 based on retention time comparisons. The triazole-label water-soluble residues, which represented significantly higher TRR, were subjected to hydrolysis followed by EtOAc partitioning at pH 9 with 0.1 M NaOH at room temperature, at pH 11 at room temperature, and at pH 2 with heating. Based on these procedures, the petitioner concluded that the major metabolites in the aqueous phase were not glycoside conjugates. TLC co-chromatography suggested the presence of TAA and minor amounts, if any, of TA and 1,2,4-T; however, the presence of TAA could not be confirmed either by a residue method developed for that purpose or by GC/MS analysis following butylation and extensive cleanup (SCX and HPLC fractionation). GC/MS analysis suggested that the major metabolite in this phase was an unknown. TLC analysis of the water-soluble residues of 30-day triazole-label lettuce following butylation and acylation suggested the presence of TA; however, this was not confirmed.

Metconazole and M30 were identified in the EtOAc phases of 30-day (triazole-label) and 120-day wheat straw (both labels) by retention time on HPLC system **a**; identification was confirmed by GC/MS in the 120-day triazole-label extract. HPLC analysis of the water-soluble residues in cyclopentyl- and triazole-label straw indicated similar profiles and suggested the presence of glycoside conjugates. HPLC analysis following hydrolysis at pH 2 and re-partitioning with EtOAc indicated the presence of free metabolite unknowns. Comparison of the metabolite profiles for 30- and 120-day triazole-label straw indicated that they were similar except that metconazole was present at higher levels (~2x) in the 30-day samples.

Only triazole-label grain samples were subjected to characterization/identification procedures. Only minor amounts of radioactivity partitioned into the EtOAc phases; therefore, these were not further investigated. The water-soluble residues of 120-day grain were concentrated to precipitate co-extractives and were subjected to HPLC which suggested the presence of glycoside conjugates; however, this was not supported by further analyses. Following hydrolysis at pH 2 and re-partitioning into EtOAc the water-soluble residues were analyzed by TLC, HPLC, and a residue method developed specifically for determination of triazole metabolites, which suggested the presence of TA and TAA. GC/MS following butylation and acylation confirmed the presence of TA; however, there was not sufficient material to confirm the presence of TAA. Residues in the 30-day samples were characterized/identified based on TLC co-chromatography and comparison with the results for 120-day grain.

C.1. Storage Stability

Samples of the rotational crop commodities were stored frozen (≤-18 °C) prior to analysis. The dates of sample combustion, extraction and analysis were not reported; however, a limited number of dated HPLC and TLC chromatograms and GC/MS spectra were included in the study, which indicated that the majority of analyses for characterization/identification of residues was completed within 5-16 months of sample harvest. Sample storage intervals based on the dated chromatograms are presented in Table C.1.

To demonstrate storage stability of metconazole residues, a subsample of wheat straw that was originally extracted 63 days after harvest was re-extracted and analyzed after frozen storage for 5 months (6.7 months after harvest). Residues were extracted with ACN/water, and the ACN/water extract was partitioned with EtOAc. The distribution of residues following extraction and partitioning was similar in both samples. Further comparison of the HPLC profiles for the aqueous and organic phases indicated no significant changes in the water soluble profile; a slight increase in the component with a retention time of 5 min was observed in the EtOAc phase. Additional storage stability data are available demonstrating the stability of: (1) metconazole *per se* in carrots, lettuce, and wheat grain and straw for up to 12 months (refer to 46902218.der.doc); (2) metconazole, M30, TA, and TAA in radish roots and tops and wheat grain and straw for up to 6 months (refer to 46902223.der.doc); and (3) TA in wheat grain for up to 12 months (refer to 46902221.der.doc). The available storage stability data are adequate to support the confined rotational crop study.

TABLE C.1. Summary of Storage Conditions.

Matrix	Plantback interval (days)	Storage Temp. (°C)	Maximum Storage Duration[1]	Interval of Demonstrated Storage Stability
Radish	30	-18	274 days (9.0 months)	The metabolic profile was stable for 7 months in wheat straw based on a concurrent storage stability study. Storage stability has been demonstrated for up to 12 months for metconazole *per se* in carrots, lettuce, and wheat grain and straw; for up to 6 months for metconazole, M30, TA, and TAA in radish roots and tops and wheat grain and straw; and for up to 12 months for TA in wheat grain.[2]
	120		Not available	
Lettuce	30		470 days (15.5 months)	
	120		180 days (5.9 months)	
Wheat, straw	30		Not available	
	120		217 days (7.1 months)	
Wheat, grain	30		Not available	
	120		152-262 days (5.0-8.6 months)	

[1] Interval from harvest to analysis for characterization/identification based on dated chromatograms.
[2] Refer to 46902218.der.doc, 46902223.der.doc, and 46902221.der.doc.

C.2. Identification, Characterization, and Distribution of Residues

TABLE C.2.1. Total Radioactive Residues (TRR) in Rotational Radish, Lettuce, and Wheat.

Crop	Matrix	Cyclopentyl label, ppm		Triazole label, ppm	
		30-day PBI	120-day PBI	30-day PBI	120-day PBI
Immature radish	Whole plant	0.24	0.19	0.31	0.14
Immature lettuce	Whole plant	0.13	0.04	0.13	0.06
Immature wheat	Foliage	0.15	0.13	0.12	0.20
	Root	0.35	0.25	0.29	0.30
Mature radish	Tops	0.40	0.68	0.65	0.84
	Root	0.32	0.37	0.38	0.71
Mature lettuce	Foliage	0.03	0.10	0.08	0.20
	Root	0.36	0.63	0.50	0.62
Mature wheat	Straw	0.73	0.70	0.61	0.73
	Grain	0.01	0.01	0.35	0.49
	Chaff	0.17	0.15	0.28	0.32
	Root	0.90	0.65	0.85	0.78

TABLE C.2.2.1. Distribution of the Parent and the Metabolites in Rotational Radish Root Following Application of [^{14}C]Metconazole at 0.357 lb ai/A.[1]

Metabolite Fraction	Cyclopentyl label		Triazole label			
	30-day PBI		30-day PBI		120-day PBI	
	TRR = 0.32 ppm		TRR = 0.38 ppm		TRR = 0.71 ppm	
	%TRR	ppm	%TRR	ppm	%TRR	ppm
Water/CAN	81.4	0.26	88.6	0.34	83.9	0.60
Hexane (combined with EtOAc)	29.0	0.09	14.4	0.05		
EtOAc (combined with hexane)	31.9	0.10	25.6	0.10	36.9	0.26
Combined organic	60.9	0.19	40.0	0.15		
Metconazole[2]	39.2	0.13	28.8	0.11	15.5	0.11
M30[3]	4.8	0.02	2.5	0.01	1.4	0.01
Rt ~ 7 min.	--	--	--	--	<1.4	<0.01
Rt ~ 14 min.	--	--	--	--	2.8	0.02
Rt ~ 22 min.	--	--	--	--	1.4	0.01
Rt ~ 32 min.	--	--	--	--	1.4	0.01
Rt ~ 39-41 min. (ketone metabolite)[3]	6.3	0.02	3.1	0.01	5.6	0.04
Rt ~ 45 min.	--	--	2.6	0.01	--	--
Others	10.5	0.03	5.6	0.02	7.0	0.05
DCM	<0.2	<0.01	<0.3	<0.01		
Water (combined with water ext)	20.3	0.06	48.4	0.18	47.0	0.34
Water (combined with water phase)	2.5	<0.01	1.4	<0.01	6.2	0.04
Combined water	22.8	0.07	49.8	0.19	53.2	0.38
Rt ~ 4-5 min. (poss. TA)	--	--	--	--	45.2	0.33
Rt ~7-8 min.	11.3	0.04	24.9	0.09	--	--
TA (by TLC)	--	--	19.4	0.07		
Rt ~ 15-17 min.	--	--	--	--	3.5	0.02
Rt ~19 min	8.0	0.03	2.9	0.01	--	--

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TABLE C.2.2.1. Distribution of the Parent and the Metabolites in Rotational Radish Root Following Application of [^{14}C]Metconazole at 0.357 lb ai/A.[1]

Metabolite Fraction	Cyclopentyl label		Triazole label			
	30-day PBI		30-day PBI		120-day PBI	
	TRR = 0.32 ppm		TRR = 0.38 ppm		TRR = 0.71 ppm	
	%TRR	ppm	%TRR	ppm	%TRR	ppm
Rt ~ 67 min.	--	--	9.6	0.04	--	--
Others	3.5	<0.03	12.4	0.05	3.6	0.03
pH 2 EtOAc	14.2	0.05	8.5	0.03		
pH 2 aqueous	8.6	0.03	41.3	0.16		
Heated pH 2 aqueous (M13?)	4.3	0.015	34.8	0.13		
Heated pH 2 EtOAc (glycoside conjugates)	4.3	0.015	6.5	0.02		
Unextractable	16.1	0.05	10.0	0.04	9.8	0.07

[1] Shading indicates that the extraction step and/or characterization analysis was not conducted for the matrix in question. Where TRR were reported by the petitioner as "% of radioactivity injected," % TRR were calculated by the study reviewer as [% of radioactivity injected] x [% TRR in fraction].
[2] Based on identification in 30-day cyclopentyl-label roots.
[3] Based on characterization in 30-day triazole-label radish tops.

TABLE C.2.2.2. Distribution of the Parent and the Metabolites in Rotational Radish Tops Following Application of [^{14}C]Metconazole at 0.357 lb ai/A.[1]

Metabolite Fraction	Cyclopentyl label		Triazole label			
	30-day PBI		30-day PBI		120-day PBI	
	TRR = 0.40 ppm		TRR = 0.65 ppm		TRR = 0.84 ppm	
	%TRR	ppm	%TRR	ppm	%TRR	ppm
Water/CAN	93.9	0.38	93.5	0.61	87.8	0.74
EtOAc[2]	55.0	0.22	35.4	0.23	36.3	0.30
Metconazole	18.4	0.07	15.5	0.10	10.8	0.09
M30	5.4	0.02	2.9	0.02	2.3	0.02
Rt ~ 4 min.	--	--	--	--	1.4	0.01
Rt ~ 19 min. (glycoside conjugates)	11.3	0.05	8.1	0.05	1.1	0.01
Rt ~ 22 min.	--	--	--	--	2.0	0.02
Rt ~ 32 min.	--	--	--	--	1.4	0.01
Rt ~ 39-41 min. (ketone metabolite)	9.6	0.04	4.7	0.03	7.0	0.06
Rt ~ 45 min.	4.1	0.02	1.9	0.01	2.0	0.02
Others	6.3	0.03	2.3	0.01	8.2	0.07
Water (combined with water extract)	NR[3]	NR	NR	NR	NR	NR
Water (combined with water phase)	<1.0	<0.01	2.0	0.01	4.0	0.03
Combined water	39.9	0.16	60.1	0.39	55.5	0.47
Rt ~ 4-5 min.[4]	4.7	0.02	32.6	0.21	33.6	0.28
TA (by TLC)	--	--	30.1	0.20	--	--
Rt ~ 7-8 min.	3.1	0.01	--	--	2.8	0.02
Rt ~ 15-17 min.[5]	26.8	0.11	23.6	0.15	13.3	0.11
M12 (by TLC)	33.6	0.13	26.8	0.17	--	--
Rt ~ 19 min. (glycoside conjugates)[2]	5.3	0.02	2.3	0.01	--	--
Others	--	--	1.7	0.01	5.8	0.05

TABLE C.2.2.2. Distribution of the Parent and the Metabolites in Rotational Radish Tops Following Application of [^{14}C]Metconazole at 0.357 lb ai/A.[1]

Metabolite Fraction	Cyclopentyl label		Triazole label			
	30-day PBI		30-day PBI		120-day PBI	
	TRR = 0.40 ppm		TRR = 0.65 ppm		TRR = 0.84 ppm	
	%TRR	ppm	%TRR	ppm	%TRR	ppm
Unextractable	5.1	0.02	4.6	0.03	8.2	0.07

[1] Shading indicates that the extraction step and/or characterization analysis was not conducted for the matrix in question. Where TRR were reported by the petitioner as "% of radioactivity injected," % TRR were calculated by the study reviewer as [% of radioactivity injected] x [% TRR in fraction].
[2] Characterization of glycoside conjugates and the ketone metabolite based on 30-day triazole-label tops.
[3] NR = Not reported.
[4] TA was identified and quantitated in 30-day triazole-label tops; this fraction believed to be mostly TA in 120-day triazole-label tops.
[5] M12 was identified and quantitated in 30-day tops (both labels); this fraction believed to be M12 or a related metabolite in 120-day tops.

TABLE C.2.2.3. Distribution of the Parent and the Metabolites in Rotational Lettuce Following Application of [^{14}C]Metconazole at 0.357 lb ai/A.[1]

Metabolite Fraction	Cyclopentyl label		Triazole label			
	120-day PBI		30-day PBI		120-day PBI	
	TRR = 0.10 ppm		TRR = 0.08 ppm		TRR = 0.20 ppm	
	%TRR	ppm	%TRR	ppm	%TRR	ppm
Water/CAN (combined with water)	72.7	0.07	91.6	0.07	74.9	0.15
Water (combined with ACN)	10.9	0.01	12.4	<0.01	16.7	0.03
Combined water/ACN	83.6	0.08	94.0	0.08	91.5	0.18
EtOAc soluble	44.9	0.04	25.0	0.02	18.4	0.04
Metconazole	16.5	0.02	1.2	0.01	5.0	0.01
Rt ~ 5 min.	1.2	<0.01	3.2	<0.01	0.3	<0.01
Rt ~ 20 min.	5.8	<0.01	1.5	<0.01	1.7	<0.01
Rt ~ 23 min.	2.4	<0.01	--	--	1.7	<0.01
Rt ~ 34 min.	6.2	<0.01	--	--	1.3	<0.01
Rt ~ 41 min.	2.3	<0.01	--	--	1.2	<0.01
Rt ~ 46 min.	2.6	<0.01	1.3	<0.01	1.1	<0.01
Rt ~ 51 min.	4.3	<0.01	14.4	<0.01	1.2	<0.01
Water soluble[2]	38.7	0.04	69.0	0.06	73.1	0.15
Rt ~ 5 min.	10.1	0.01	61.2	0.05	59.9	0.12
TA (30-day)/poss. TAA (120-day)	--	--	>18.8	>0.015	32.5	0.05
Rt ~ 15 min.	14.4	0.02	4.1	<0.01	5.1	0.01
Rt ~ 19 min.	5.7	<0.01	0.9	<0.01	2.1	<0.01
Rt ~ 31 min.	0.8	<0.01	--	--	--	--
pH 2 EtOAc (poss. M13)[3]	23.5	0.02			58.4	0.12
pH 2 aqueous	15.2	0.02			14.7	0.03
Unextractable	16.4	0.02	6.0	<0.01	8.5	0.02

[1] Shading indicates that the extraction step and/or characterization analysis was not conducted for the matrix in question. Where TRR were reported by the petitioner as "% of radioactivity injected," % TRR were calculated by the study reviewer as [% of radioactivity injected] x [% TRR in fraction].
[2] Components characterized as glycoside conjugates or unconjugated compounds containing the carboxylic acid function (e.g., M12/M13) based on polarity on HPLC.
[3] Based on HPLC of 120-day cyclopentyl-label lettuce.

TABLE C.2.2.4. Distribution of the Parent and the Metabolites in Rotational Wheat Straw Following Application of [^{14}C]Metconazole at 0.357 lb ai/A.[1]

Metabolite Fraction	Cyclopentyl label		Triazole label			
	120-day PBI		30-day PBI		120-day PBI	
	TRR = 0.70 ppm		TRR = 0.61 ppm		TRR = 0.73 ppm	
	%TRR	ppm	%TRR	ppm	%TRR	ppm
Water/ACN[2]	89.0	0.62	89.4	0.55	88.6	0.64
Combined water/ACN			90.4	0.55		
EtOAc soluble	36.8	0.26	44.3	0.27	30.9	0.22
Metconazole	4.0	0.03	12.0	0.07	3.5	0.03
M30	5.4	0.04	5.5	0.03	4.5	0.03
Rt ~ 5 min.	0.6	<0.01	1.3	<0.01	0.7	<0.01
Rt ~ 20 min.	7.9	0.06	3.1	0.02	5.8	0.04
Rt ~ 28 min.	5.0	0.04	1.8	0.01	4.2	0.03
Rt ~ 33 min.	4.4	0.03	1.9	0.01	3.2	0.02
Rt ~ 37 min.	1.7	0.01	1.1	<0.01	2.0	0.01
Rt ~ 41 min.	5.0	0.04	4.8	0.03	4.0	0.03
Rt ~ 45 min.	2.5	0.02	2.4	0.01	2.6	0.02
Others	0.4	<0.01	10.5	0.06	0.4	<0.01
Water soluble[3]	52.2	0.36	46.1	0.28	57.7	0.42
Rt ~ 4 min.	26.5	0.18	21.5	0.13	35.1	0.26
Rt ~ 10 min.	--	--	4.7	0.03	6.5	0.05
Rt ~ 15 min.	20.3	0.14	16.6	0.10	11.7	0.09
Rt ~ 19 min.	4.5	0.03	2.8	0.02	4.0	0.03
Rt ~ 53 min.	0.6	<0.01	--	--	0.5	<0.01
Others	0.3	<0.01	0.8	<0.01	--	--
pH 2 EtOAc	11.2	0.08			5.5	0.04
pH 2 water	41.0	0.28			52.3	0.38
2 M HCl EtOAc (glycoside conj's.)	18.3	0.12			17.7	0.13
2M HCl water	22.7	0.16			34.6	0.25
Water[2]	1.7	0.01	1.1	<0.01	2.1	0.015
Unextractable	9.3	0.07	9.6	0.06	9.3	0.07

[1] Shading indicates that the extraction step and/or characterization analysis was not conducted for the matrix in question.
[2] Water/ACN and water extracts were combined for 30-day straw only.
[3] Believed to contain conjugated metabolites based on HPLC profile.

TABLE C.2.2.5. Distribution of the Parent and the Metabolites in Rotational Wheat Grain Following Application of [Triazole-3,5-^{14}C]Metconazole at 0.357 lb ai/A.[1]

Metabolite Fraction	30-day PBI		120-day PBI	
	TRR = 0.35 ppm		TRR = 0.49 ppm	
	%TRR	ppm	%TRR	ppm
Water/CAN (combined with water)	84.7	0.30	83.2	0.41
Water (combined with water/ACN)	12.3	0.05	14.1	0.07
Combined water/ACN	97.0	0.34	97.3	0.48
EtOAc soluble	1.1	<0.01	1.3	<0.01
Water soluble[2]	95.9	0.34	95.9	0.47

TABLE C.2.2.5. Distribution of the Parent and the Metabolites in Rotational Wheat Grain Following Application of [Triazole-3,5-^{14}C]Metconazole at 0.357 lb ai/A.[1]

Metabolite Fraction	30-day PBI		120-day PBI	
	TRR = 0.35 ppm		TRR = 0.49 ppm	
	%TRR	ppm	%TRR	ppm
TA[3]	37.0	0.13	59.4	0.29
TAA[3]	--	--	20.6	0.1
Rf 0.34	NR[4]	NR	11.2	0.05
Rf 0.79	NR	NR	1.6	<0.01
Other	NR	NR	3.1	0.02
pH 2 EtOAc			0.8	<0.01
pH 2 water			95.1	0.47
Unextractable	3.0	0.01	2.7	0.01

[1] Shading indicates that the extraction step and/or characterization analysis was not conducted for the matrix in question.
[2] Metabolite distribution reflects TLC analysis. The presence of glycoside conjugates was indicated by HPLC profile; however, distribution on pH 2 partitioning suggested absence of conjugates.
[3] Presence confirmed by HPLC and GC/MS (TA only) of 120-day sample.
[4] NR = Not reported.

TABLE C.2.3.1. Summary of Characterization and Identification of Radioactive Residues in Rotational Radish Root Following Application of [^{14}C]Metconazole at 0.357 lb ai/A.

Compound	Cyclopentyl label		Triazole label			
	30-day PBI		30-day PBI		120-day PBI	
	TRR = 0.32 ppm		TRR = 0.38 ppm		TRR = 0.71 ppm	
	% TRR	ppm	% TRR	ppm	% TRR	ppm
Metconazole	39.2	0.13	28.8	0.11	15.5	0.11
M30	4.8	0.02	2.5	0.01	1.4	0.01
TA[1]	--	--	19.4	0.07	45.2	0.33
Characterized organic:						
Rt ~ 7 min.	--	--	--	--	<1.4	<0.01
Rt ~ 14 min.	--	--	--	--	2.8	0.02
Rt ~ 22 min.	--	--	--	--	1.4	0.01
Rt ~ 32 min.	--	--	--	--	1.4	0.01
Rt ~ 39-41 min. (ketone metabolite)	6.3	0.02	3.1	0.01	5.6	0.04
Rt ~ 45 min.	--	--	2.6	0.01	--	--
Others	10.5	0.03	5.6	0.02	7.0	0.05
DCM	<0.2	<0.01	<0.3	<0.01	--	--
Characterized aqueous (containing M13 and glycoside conjugates):						
Rt ~7-8 min.	11.3	0.04	--	--	--	--
Rt ~ 15-17 min.	--	--	--	--	3.5	0.02
Rt ~19 min	8.0	0.03	2.9	0.01	--	--
Rt ~ 67 min.	--	--	9.6	0.04	--	--
Others	3.5	<0.03	12.4	0.05	3.6	0.03
Total identified	44.0	0.15	50.7	0.19	62.1	0.45
Total characterized	39.8	0.12	36.5	0.15	26.7	0.19
Total extractable	83.9	0.27	90.0	0.34	90.2	0.64
Unextractable (PES)[2]	16.1	0.05	10.0	0.04	9.8	0.07
Accountability[3]	100%		100%		100%	

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[1] Identified by TLC in 30-day root at Rt ~7-8 min.; tentatively identified in 120-day root at Rt ~4-5 min.
[2] Residues remaining after exhaustive extractions.
[3] Accountability = (Total extractable + Total unextractable)/(TRR from combustion analysis; see TABLE C.2.1) * 100.

TABLE C.2.3.2. Summary of Characterization and Identification of Radioactive Residues in Rotational Radish Tops Following Application of [^{14}C]Metconazole at 0.357 lb ai/A.

Compound	Cyclopentyl label		Triazole label			
	30-day PBI		30-day PBI		120-day PBI	
	TRR = 0.40 ppm		TRR = 0.65 ppm		TRR = 0.84 ppm	
	% TRR	ppm	% TRR	ppm	% TRR	ppm
Metconazole	18.4	0.07	15.5	0.10	10.8	0.09
M30	5.4	0.02	2.9	0.02	2.3	0.02
TA (by TLC)[1]	--	--	30.1	0.20	33.6	0.28
M12 (by TLC)[1]	33.6	0.13	26.8	0.17	13.3	0.11
Characterized organic:						
Rt ~ 4 min.	--	--	--	--	1.4	0.01
Rt ~ 19 min. (glycoside conjugates)	11.3	0.05	8.1	0.05	1.1	0.01
Rt ~ 22 min.	--	--	--	--	2.0	0.02
Rt ~ 32 min.	--	--	--	--	1.4	0.01
Rt ~ 39-41 min. (ketone metabolite)	9.6	0.04	4.7	0.03	7.0	0.06
Rt ~ 45 min.	4.1	0.02	1.9	0.01	2.0	0.02
Others	6.3	0.03	2.3	0.01	8.2	0.07
Characterized aqueous:						
Rt ~ 4-5 min.	4.7	0.02	--	--	--	--
Rt ~ 7-8 min.	3.1	0.01	--	--	2.8	0.02
Rt ~ 19 min. (glycoside conjugates)	5.3	0.02	2.3	0.01	--	--
Others	--	--	1.7	0.01	5.8	0.05
Total identified	57.4	0.22	75.3	0.49	60.0	0.50
Total characterized	44.4	0.19	21.0	0.12	31.7	0.38
Total extractable	94.9	0.38	95.4	0.62	91.8	0.77
Unextractable (PES)[2]	5.1	0.02	4.6	0.03	8.2	0.07
Accountability[3]	100%		100%		100%	

[1] Identified and quantitated in 30-day tops; believed to be mostly TA and M12 or a related metabolite, respectively, in 120-day tops.
[2] Residues remaining after exhaustive extractions.
[3] Accountability = (Total extractable + Total unextractable)/(TRR from combustion analysis; see TABLE C.2.1) * 100.

TABLE C.2.3.3. Summary of Characterization and Identification of Radioactive Residues in Rotational Lettuce Following Application of [^{14}C]Metconazole at 0.357 lb ai/A.

Compound	Cyclopentyl label		Triazole label			
	120-day PBI		30-day PBI		120-day PBI	
	TRR = 0.10 ppm		TRR = 0.08 ppm		TRR = 0.20 ppm	
	% TRR	ppm	% TRR	ppm	% TRR	ppm
Metconazole	16.5	0.02	1.2	0.01	5.0	0.01
TA (tentative)	--	--	>18.8	>0.015	--	--
TAA (tentative)	--	--	--	--	32.5	0.05
Characterized organic:						
Rt ~ 5 min.	1.2	<0.01	3.2	<0.01	0.3	<0.01

TABLE C.2.3.3. Summary of Characterization and Identification of Radioactive Residues in Rotational Lettuce Following Application of [^{14}C]Metconazole at 0.357 lb ai/A.

Compound	Cyclopentyl label		Triazole label			
	120-day PBI		30-day PBI		120-day PBI	
	TRR = 0.10 ppm		TRR = 0.08 ppm		TRR = 0.20 ppm	
	% TRR	ppm	% TRR	ppm	% TRR	ppm
Rt ~ 20 min.	5.8	<0.01	1.5	<0.01	1.7	<0.01
Rt ~ 23 min.	2.4	<0.01	--	--	1.7	<0.01
Rt ~ 34 min.	6.2	<0.01	--	--	1.3	<0.01
Rt ~ 41 min.	2.3	<0.01	--	--	1.2	<0.01
Rt ~ 46 min.	2.6	<0.01	1.3	<0.01	1.1	<0.01
Rt ~ 51 min.	4.3	<0.01	14.4	<0.01	1.2	<0.01
Characterized aqueous (including possibly glycoside conjugates or M12/M13):						
Rt ~ 5 min.[1]	10.1	0.01	61.2	0.05	59.9	0.12
Rt ~ 15 min.	14.4	0.02	4.1	<0.01	5.1	0.01
Rt ~ 19 min.	5.7	<0.01	0.9	<0.01	2.1	<0.01
Rt ~ 31 min.	0.8	<0.01	--	--	--	--
Total identified	16.5	0.02	1.2	0.01	5.0	0.01
Total characterized	55.8	0.06	86.6	0.07	75.6	0.15
Total extractable	83.6	0.08	94	0.08	91.5	0.18
Unextractable (PES)[2]	16.4	0.02	6.0	<0.01	8.5	0.02
Accountability[3]	100%		100%		100%	

[1] % TRR and ppm values for triazole samples were calculated by the study reviewer by subtracting TA/TAA quantitated for each sample.
[2] Residues remaining after exhaustive extractions.
[3] Accountability = (Total extractable + Total unextractable)/(TRR from combustion analysis; see TABLE C.2.1) * 100.

TABLE C.2.3.4. Summary of Characterization and Identification of Radioactive Residues in Rotational Wheat Straw Following Application of [^{14}C]Metconazole at 0.357 lb ai/A.

Compound	Cyclopentyl label		Triazole label			
	120-day PBI		30-day PBI		120-day PBI	
	TRR = 0.70 ppm		TRR = 0.61 ppm		TRR = 0.73 ppm	
	%TRR	ppm	% TRR	ppm	% TRR	ppm
Metconazole	4.0	0.03	12.0	0.07	3.5	0.03
M30	5.4	0.04	5.5	0.03	4.5	0.03
Characterized organic:						
Rt ~ 5 min.	0.6	<0.01	1.3	<0.01	0.7	<0.01
Rt ~ 20 min.	7.9	0.06	3.1	0.02	5.8	0.04
Rt ~ 28 min.	5.0	0.04	1.8	0.01	4.2	0.03
Rt ~ 33 min.	4.4	0.03	1.9	0.01	3.2	0.02
Rt ~ 37 min.	1.7	0.01	1.1	<0.01	2.0	0.01
Rt ~ 41 min.	5.0	0.04	4.8	0.03	4.0	0.03
Rt ~ 45 min.	2.5	0.02	2.4	0.01	2.6	0.02
Others	0.4	<0.01	10.5	0.06	0.4	<0.01
Characterized aqueous (containing glycoside conjugates)[1]:						
Rt ~ 4 min.	26.5	0.18	21.5	0.13	35.1	0.26

TABLE C.2.3.4. Summary of Characterization and Identification of Radioactive Residues in Rotational Wheat Straw Following Application of [^{14}C]Metconazole at 0.357 lb ai/A.

Compound	Cyclopentyl label		Triazole label			
	120-day PBI		30-day PBI		120-day PBI	
	TRR = 0.70 ppm		TRR = 0.61 ppm		TRR = 0.73 ppm	
	%TRR	ppm	% TRR	ppm	% TRR	ppm
Rt ~ 10 min.	--	--	4.7	0.03	6.5	0.05
Rt ~ 15 min.	20.3	0.14	16.6	0.10	11.7	0.09
Rt ~ 19 min.	4.5	0.03	2.8	0.02	4.0	0.03
Rt ~ 53 min.	0.6	<0.01	--	--	0.5	<0.01
Others	0.3	<0.01	0.8	<0.01	--	--
Water	1.7	0.01	--	--	2.1	0.015
Total identified	9.4	0.07	17.5	0.10	8.0	0.06
Total characterized	81.4	0.57	73.3	0.45	82.8	0.60
Total extractable	90.7	0.63	90.4	0.55	90.7	0.66
Unextractable (PES)[2]	9.3	0.07	9.6	0.06	9.3	0.07
Accountability[3]	100%		100%		100%	

[1] Characterized at 18.3% TRR (0.12 ppm) and 17.7% TRR (0.13 ppm) in 120-day cyclopentyl- and triazole-label samples.
[2] Residues remaining after exhaustive extractions.
[3] Accountability = (Total extractable + Total unextractable)/(TRR from combustion analysis; see TABLE C.2.1) * 100.

TABLE C.2.3.5. Summary of Characterization and Identification of Radioactive Residues in Rotational Wheat Grain Following Application of [Triazole-3,5-^{14}C]Metconazole at 0.357 lb ai/A.

Compound	30-day PBI		120-day PBI	
	TRR = 0.35 ppm		TRR = 0.49 ppm	
	% TRR	ppm	% TRR	ppm
TA[1]	37.0	0.13	59.4	0.29
TAA[1]	--	--	20.6	0.10
Characterized organic (EtOAc):	1.1	<0.01	1.3	<0.01
Characterized aqueous:				
Rf 0.34	58.9[2]	0.21	11.2	0.05
Rf 0.79			1.6	<0.01
Other			3.1	0.02
Total identified	37.0	0.13	80.0	0.39
Total characterized	58.9	0.21	14.3	0.07
Total extractable	97.0	0.34	97.3	0.48
Unextractable (PES)[3]	3.0	0.01	2.7	0.01
Accountability[4]	100%		100%	

[1] Presence was confirmed by HPLC and GC/MS (TA only) of 120-day sample.
[2] Calculated by study reviewer by subtraction.
[3] Residues remaining after exhaustive extractions.
[4] Accountability = (Total extractable + Total unextractable)/(TRR from combustion analysis; see TABLE C.2.1) * 100.

C.3. Proposed Metabolic Profile

Based on the submitted confined rotational crop study, the petitioner concluded that the main metabolic transformations were oxidation at the benzylic methylene to form M30 and oxidation of the methyl groups on the cyclopentane ring to form M12/M13. The presence of TA and TAA

in radish tops and roots and wheat grain indicated that oxidative transformation occurs in the plant at the methylene group bearing the triazole ring. The metabolism of metconazole in rotational crops appeared to be extensive; however, detailed characterization and identification of metabolites was limited due to generally low residue levels. The MRID did not include a figure illustrating the metabolic pathway.

TABLE C.3.1. Identification of Compounds from the Confined Rotational Crop Study.

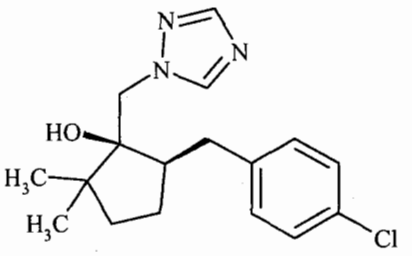
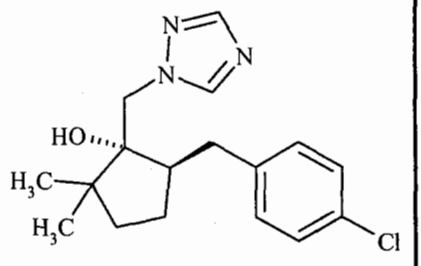
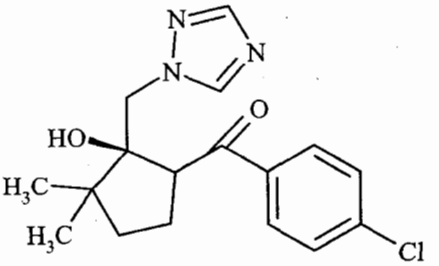
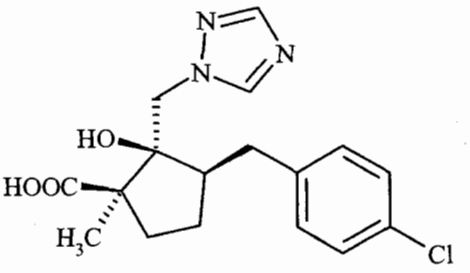
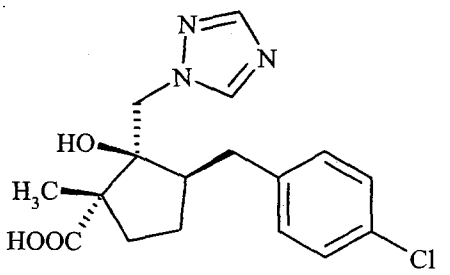
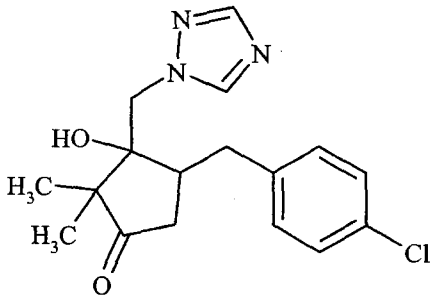
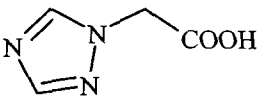
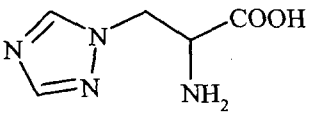
Common name/code Figure C.3.1 ID No.	Chemical name	Chemical structure
Metconazole (WL148271)	5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	 *cis*-isomer  *trans*-isomer
M30	5-[(4-chlorophenyl)keto]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)-1-cyclopentanol	
M12; MC 1417	5-[(4-chlorophenyl)methyl]-2-carboxyl-2-methyl-1-(1*H*-1,2,4-triazol-1-yl methyl)-1-cyclopentanol	

TABLE C.3.1. Identification of Compounds from the Confined Rotational Crop Study.

Common name/code Figure C.3.1 ID No.	Chemical name	Chemical structure
M13; MC 1417	5-[(4-chlorophenyl)methyl]-2-methyl-2-carboxyl-1-(1*H*-1,2,4-triazol-1-yl methyl)-1-cyclopentanol	
Ketone metabolite (putative structure)	Not provided	
Triazolylacetic acid (WL161417)	1*H*-1,2,4-triazol-1-yl acetic acid	
Triazolylalanine (WL161416)	2-amino-3-(1*H*-1,2,4-triazol-1-yl)propanoic acid	

D. CONCLUSION

The extent and nature of the residue uptake by crops planted 30 and 120 days following treatment of bare soil with [cyclopentyl-^{14}C]metconazole or [triazole-3,5-^{14}C]metconazole at 0.357 lb ai/A (400 g ai/ha) was determined. TRR accumulated at ≥0.01 ppm in all rotated crop matrices planted 30 or 120 days following application of [cyclopentyl-^{14}C]metconazole or [triazole-3,5-^{14}C]metconazole directly to bare soil at 0.357 lb ai/A. In immature plants, TRR were comparable for both labels and were higher in 30-day radish, lettuce, and cyclopentyl-label wheat foliage and root than in 120-day samples; in triazole-label wheat foliage and root, TRR were the same or higher in 120-day samples than in 30-day samples. In mature radish roots and tops, lettuce, and wheat grain and straw, TRR were generally higher in triazole-label samples than in cyclopentyl-label samples, except 120-day wheat straw, where TRR were about the same; TRR were generally higher in 120-day samples for both labels than in 30-day samples, except cyclopentyl-label wheat grain and straw, where TRR were about the same.

Metconazole was identified at both PBIs and for both labels in all rotational crop matrices except wheat grain. Metabolite M30 was identified at both PBIs and for both labels in radish root and tops and wheat straw. TA was also identified in triazole-label radish root, radish tops, lettuce,

and wheat grain, and TAA was tentatively identified in lettuce and wheat grain. Metabolites M12/M13 and a related ketone metabolite were tentatively identified in radish root and tops and lettuce, and components characterized as glycoside conjugates were characterized in all matrices except wheat grain.

Based on the submitted confined rotational crop study, the petitioner concluded that the main metabolic transformations were oxidation at the benzylic methylene to form M30, and oxidation of the methyl groups on the cyclopentane ring to form M12/M13. The presence of TA and TAA in radish tops and roots and wheat grain indicated that oxidative transformation occurs in the plant at the methylene group bearing the triazole ring. The metabolism of metconazole in rotational crops appeared to be extensive; however, detailed characterization and identification of metabolites was limited due to generally low residue levels.

The study is supported by adequate storage stability data, and acceptable methods were used for the characterization/identification and quantitation of residues.

E. REFERENCES

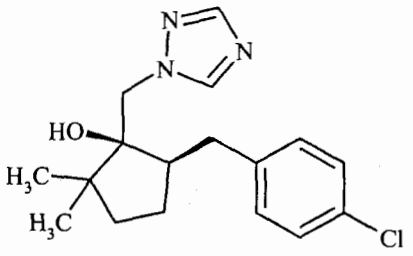
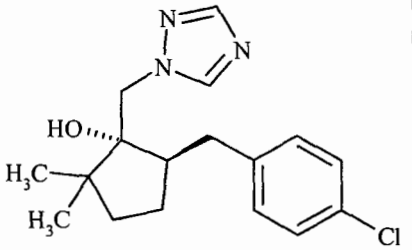
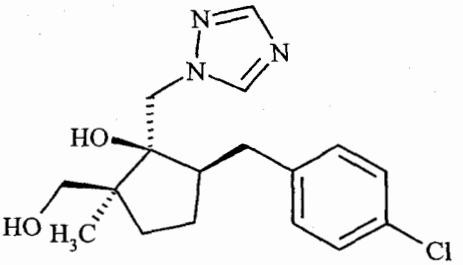
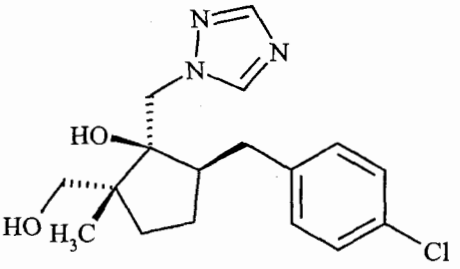
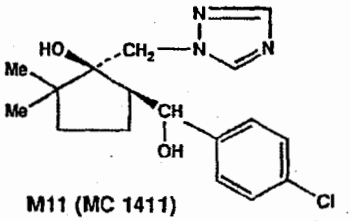
DP#:	324541
Subject:	Metconazole. Request for a Tolerance on Imported Bananas. Summary of Analytical Chemistry and Residue Data. Petition Number 9E05052.
From:	N. Dodd
To:	M. Waller
Date:	12/14/05
MRIDs:	44721506, 44721507, 44721508, 44721509, 44721510, and 44721511

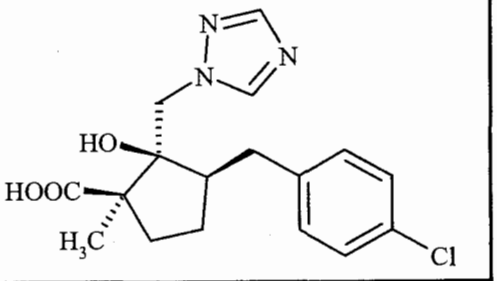
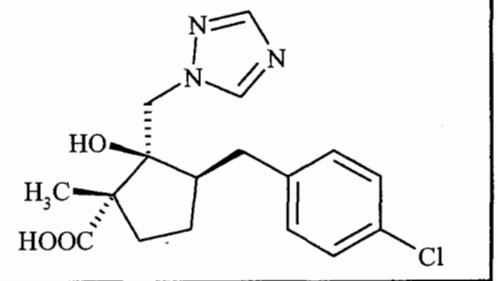
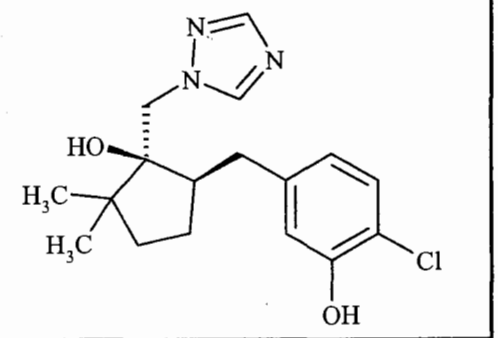
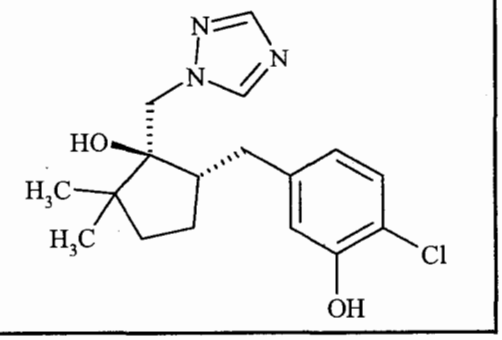
F. DOCUMENT TRACKING

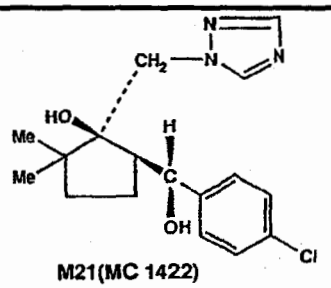
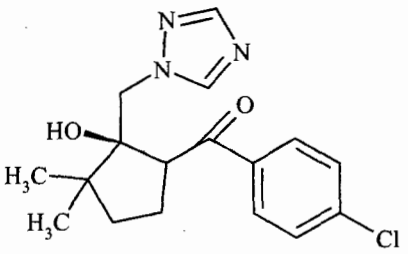
RDI: N. Dodd (2/20/08)
Petition Numbers: 6F7094 and 6F7095
DP#s: 348168 and 348206
PC Code: 125619

Template Version June 2005

APPENDIX I. Chemical Names and Structures of Reference Standards Used in Confined Rotational Crop Study.

Common name; Company code	Chemical name	Chemical structure
Metconazole	5-[(4-chlorophenyl)methyl]-2,2-. dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	 *cis*-isomer  *trans*-isomer
M1 (MC 1401)	5-[(4-chlorophenyl)methyl]-2-methoxyl-2-methyl-1(1*H*-1,2,4-triazol-1-ylmethyl)-1-cyclopentanol	
M2 (MC 1402)	5-[(4-chlorophenyl)methyl]-2-methoxyl-2-methyl-1(1*H*-1,2,4-triazol-1-yl methyl)-1-cyclopentanol	
M11 (MC 1411)	5-[(4-chlorophenyl)methoxyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)-1-cyclopentanol	 **M11 (MC 1411)**

APPENDIX I. Chemical Names and Structures of Reference Standards Used in Confined Rotational Crop Study.		
Common name; Company code	Chemical name	Chemical structure
M12 (MC 1417)	5-[(4-chlorophenyl)methyl]-2-carboxyl-2-methyl-1-(1*H*-1,2,4-triazol-1-yl methyl)-1-cyclopentanol	
M13 (MC 1418)	5-[(4-chlorophenyl)methyl]-2-methyl-2-carboxyl-1-(1*H*-1,2,4-triazol-1-yl methyl)-1-cyclopentanol	
M15 (MC 1420)	5-[(3-hydroxy-4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-yl methyl)-1-cyclopentanol	
M16 (MC 1421)	5-[(3-hydroxy-4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-yl methyl)-1-cyclopentanol	

APPENDIX I. Chemical Names and Structures of Reference Standards Used in Confined Rotational Crop Study.		
Common name; Company code	Chemical name	Chemical structure
M21 (MC 1422)	5-[(4-chlorophenyl)methoxy]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)-1-cyclopentanol	 M21(MC 1422)
M30 (MC 1424)	5-[(4-chlorophenyl)keto]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)-1-cyclopentanol	

Primary Evaluator	This DER was originally prepared under contract by Dynamac Corporation.
Approved by	Nancy Dodd, Chemist Nancy Dodd Date: 2/20/08 Registration Action Branch 3 Health Effects Division (7509P)

This DER was originally prepared under contract by Dynamac Corporation (2275 Research Boulevard, Suite 300; Rockville, MD 20850; submitted 09/17/2007). The DER has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

46901914 Green, C. (2006) Magnitude of the Residues of Metconazole in Dairy Cattle Milk and Meat. Project Number: 200600291, 29111, V/05/29111. Unpublished study prepared by Genesis Midwest Laboratories and Valent Dublin Laboratory. 401 p.

EXECUTIVE SUMMARY:

Valent USA Corporation has submitted a cattle feeding study with metconazole. Three treatment groups of three dairy cows each were dosed orally with gelatin capsules containing metconazole at dose rates of 4.73, 14.6, and 45.7 ppm (low, mid, and high dose) in the diet (dry-weight basis) for 28 consecutive days. Cows were milked twice daily, and samples were composited daily for each cow. On Day 29 of the study, two of the control cows and all surviving dosed cows were sacrificed within 24 hours of the last dose; one cow from the low dose group was severely injured and euthanized on dosing day 11. Samples of liver, kidney, muscle (hindquarter, pectoral, and abductor), and fat (perirenal, abdominal, and subcutaneous) were collected from each cow. Samples of milk collected on study days 1, 2, 4, 7, 10, 14, 17, 21, 24, and 28 from the high dose cattle were analyzed. In addition, milk from Day 24 was centrifuged to form cream and skim milk samples; samples from the high dose group were analyzed.

Whole milk, skim milk, and cream samples were analyzed for residues of *cis*- and *trans*-metconazole using GC/NPD method RM-41M-1. Tissue samples were analyzed for residues of *cis*- and *trans*-metconazole using LC/MS/MS method RM-41M-2. These methods were adequate for data collection based on acceptable method recoveries. The validated limits of quantitation (LOQs) for RM-41M-1 were 0.02 ppm for each analyte in milk and 0.04 ppm for each analyte in cream. The validated LOQ for RM-41M-2 was 0.02 ppm for each analyte in tissues.

Liver and kidney samples were also analyzed for residues of metabolites M1 (free and conjugated) and M12 using LC/MS/MS method RM-41M-3. The method was adequate for data collection; however, recoveries were generally low, ranging from 57.4 to 61.6% for M1 in liver,

66.2-67.4% for M12 in liver, 69.7-78.5% for M1 in kidney, and 67.6-73.9% for M12 in kidney. The LOQs for method RM-41M-3 were 0.02 ppm for each analyte in liver and kidney.

The LOD for all methods, analytes, and matrices except cream was 0.01 ppm. The LOD for *cis*- and *trans*-metconazole in cream was 0.02 ppm.

Milk and tissue samples were stored frozen at -20 °C prior to analysis. Maximum storage durations were 32 days (1.1 months) for milk and cream samples, 54 days (1.8 months) for tissues analyzed for *cis*- and *trans*-metconazole, and 182 days (6.0 months) for liver and kidney analyzed for M1 and M12. No storage stability data are required to support the storage conditions and durations of whole milk, skim milk or cream because samples were stored for ~30 days. To support the sample storage durations for *cis*- and *trans*-metconazole residues in tissues, a concurrent storage stability study was conducted which indicated that residues were relatively stable in liver, fat, and muscle stored frozen for 108-112 days (~3.6 months). These data for *cis*- and *trans*-metconazole are adequate to support the cattle feeding study.

Except as noted below, samples of cattle matrices from the mid- and low-dose groups were not analyzed because residues were low (nondetectable or nonquantifiable) on analysis of samples from the high-dose group. Residues of *cis*- and *trans*-metconazole were below the LOQ (<0.04 ppm for each isomer in cream; <0.02 ppm for remaining matrices) in all samples of whole milk, skim milk, cream, fat, muscle, and kidney from the high-dose group. In liver, residues of *cis*- and *trans*- metconazole were <0.02-0.021 ppm and <0.02 ppm, respectively, in samples from the high-dose group and below the LOQ (both isomers) in samples from the low- and mid-dose groups. Maximum total metconazole residues (sum of *cis*- and *trans*-isomers) were 0.041 ppm in liver from the high-dose group; total metconazole residues were <0.04 ppm in all samples of whole and skim milk and tissues from all dosing levels and <0.08 ppm in all samples of cream from all dosing levels.

Residues of metabolites M1 and M12 were below the LOQ (<0.02 ppm) in samples of liver and kidney from the low- and mid-dose groups. Residues of M1 were <0.02-0.049 ppm and <0.02-0.027 ppm in samples of liver and kidney, respectively, from the high-dose group, and residues of M12 were <0.02 ppm and <0.02-0.057 ppm in samples of liver and kidney, respectively, from the high-dose group.

Residues of metconazole, M1, and M12 were less than the LOQ except for meat byproducts at the highest dosing level (12x the dietary burden for beef cattle and 5.2x the dietary burden for dairy cattle).

HED notes that samples from the cattle feeding study were not analyzed for the triazole metabolites [1,2,4-triazole (1,2,4-T), triazolylalanine (TA), and triazolylacetic acid (TAA)].

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the data depicting residues in livestock are classified as scientifically acceptable.

The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP#s 348168 and 348206.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an impact on the validity of the study.

A. BACKGROUND INFORMATION

Metconazole [5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol] is a broad-spectrum triazole Group 3 fungicide (sterol biosynthesis inhibitors). There are currently no registered uses of metconazole in the U.S.; however, a tolerance has been established for banana, and a Section 18 emergency exemption and supporting time-limited tolerances have been granted for use on soybean. Valent U.S.A. Corporation has applied for registration of metconazole in the U.S. for use on peanut, stone fruits, and tree nuts.

The chemical structure and nomenclature of metconazole, and the physicochemical properties of the technical grade of metconazole are presented in Tables A.1 and A.2.

TABLE A.1. Metconazole Nomenclature.

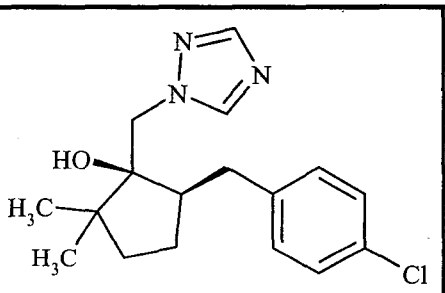
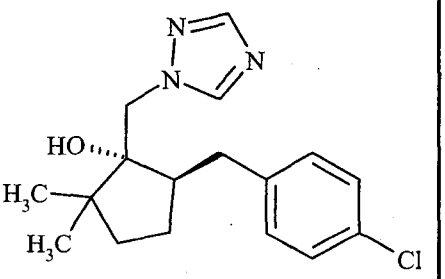
Chemical structure	 *cis*-isomer	 *trans*-isomer
Common name	Metconazole	
Company experimental name	KNF-S-474m (Kureha); BAS 555 F (BASF); V-10116 (Valent)	
IUPAC name	(1RS,5RS:1RS,5SR)-5-(4-chlorobenzyl)-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	
CAS name	5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	
CAS registry number	125116-23-6 (*cis*- and *trans*-isomers) 115850-27-6 (*cis*-isomer) 115850-28-7 (*trans*-isomer)	
End-use products (EP)	50% WDG (Metconazole 50 WDG Fungicide, EPA File Symbol 59639-RUT) 0.75 lb/gal SC/L (Caramba™ Fungicide, EPA File Symbol No. 7969-EUA) 0.67 lb/gal SC/L formulation (BAS 556 01F Fungicide, EPA File Symbol No. 7969-EUT; also contains the active ingredient pyraclostrobin at 0.83 lb/gal)	

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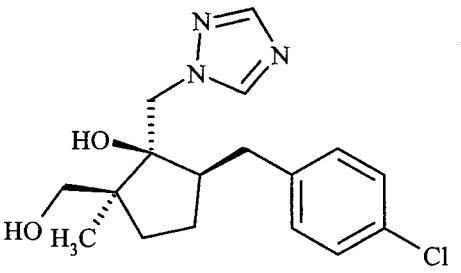
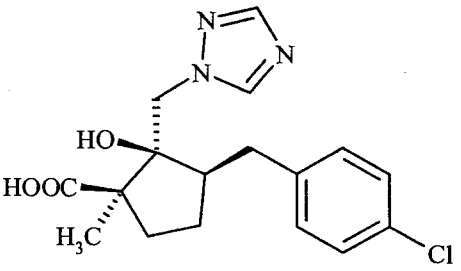
TABLE A.1. Metconazole Nomenclature.	
Metconazole metabolite M1	
Metconazole metabolite M12	

Table A.2. Physicochemical Properties of Metconazole

Parameter	Value				References* (MRID)
Melting point/range	100.0-108.4°C (using Electrothermal Digital Melting Point Apparatus) (AC900,768 technical grade)				44721505
pH	5.81 at 25°C (1% aqueous suspension)				46808402
Relative density (20°C)	1.14 (relative density to water at 4°C, using capillary-stoppered, density-specific gravity bottle) (Lot No. AC 8879-140B)				44721505
Water solubility (20°C)	Using shake-flask method: 18.7 ± 1.0 mg/L (*cis*-isomer, WL148271, KNF-S-474m) 13.6 ± 1.7 mg/L (*trans*-isomer, WL148271, KNF-S-474m)				44721505
Solvent solubility (g/L) at 20°C	Solvent	Metconazole	*cis*	*trans*	44721505
	acetone	363	251	117	
	methanol	403	294	117	
	dichloromethane	481	343	141	
	ethyl acetate	260	173	90.0	
	propanol	132	86.6	46.7	
	toluene	103	66.2	38.0	
	Hexane	1.40	0.929	0.483	
Vapor pressure (20°C)	Using gas-saturation method: $< 1.23 \times 10^{-5}$ Pa or 9.23×10^{-8} mm Hg (metconazole) $< 1.04 \times 10^{-5}$ Pa or 7.80×10^{-8} mm Hg (*cis*-isomer) $< 1.96 \times 10^{-6}$ Pa or 1.47×10^{-8} mm Hg (*trans*-isomer)				44721505

Table A.2. Physicochemical Properties of Metconazole

Parameter	Value	References* (MRID)
Dissociation constant (pK_a)	11.38±0.03 and 1.06±0.03 (in water at 29.1°C using spectrophotometric method; Lot No. AC 8879-140B)	44721505
Octanol/water partition coefficient, Log(K_{OW})	At 20 °C (using flask shaking method): K_{ow} (log K_{ow}) = 7090±989 (3.85) (Lot No. AC 8879-140B) (TGAI). K_{ow} (log K_{ow}) = 7150±803 (3.85) (*cis*-isomer, CL 354,801) K_{ow} (log K_{ow}) = 6800±1700 (3.8) (*trans*-isomer, CL 354,802)	44721505
UV/visible absorption spectrum	See below	46808403

pH	λ	A	log ε
cis-isomer			
2.0	221.4	0.828	4.03
6.8		0.8452	4.04
7.0		0.9126	4.08
10.3		0.7226	3.98
trans-isomer			
2.0	221.4	0.9053	4.07
7.0		0.9547	4.10
10.1		0.9893	4.11

* Product Chemistry Reviews: DP #256877, Shyam Mathur, Ph.D., 9/12/2000 and DP #329168, Shyam Mathur, Ph.D., 7/13/07.

B. EXPERIMENTAL DESIGN

B.1. Livestock

The in-life phase of the feeding study was conducted at Genesis Midwest Laboratories (Neillsville, WI). Twelve lactating dairy cattle were divided into four treatment groups, one control and three dosed groups. Each group consisted of three cows. The three dosed groups were dosed orally with gelatin capsules containing metconazole at 4.73, 14.6, and 45.7 ppm (low, mid, and high dose) in the feed (dry-weight basis) at a nominal *cis:trans* ratio of 85:15. The nine treated cows were dosed once a day following the am milking for 28 consecutive days. The three control cows received placebos (empty capsules) once a day.

Cows were milked twice daily; the evening milk for each cow was combined with the following morning milk. At each milking, cows were offered 4 kg dairy ration, 5 kg alfalfa hay cubes, and 3 kg baled hay; the quantity of alfalfa cubes offered was adjusted based on consumption. Feed consumption was monitored daily. Two of the control cows and the eight surviving treated cows were sacrificed on day 29, within 24 hours of the last dose; one cow from the low dose group was severely injured and euthanized on dosing day 11. Following termination, samples of liver, kidney, fat (perinephric, abdominal, and subcutaneous), and muscle (hind-quarter, pectoral, and abductor) were collected from each cow. Descriptions of the test animals used and the dietary

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regime are presented in Tables B.1.1 and B.1.2; the dosing regime and sample collection procedures are summarized in Tables B.1.3 and B.1.4.

TABLE B.1.1. Description of Livestock Used in the Feeding Study.

Species	Breed	Age	Weight at study initiation (kg)	Health status	Description of housing/holding area
Bos Taurus	Holstein	3-7 years	470-720	Healthy[1]	4'x7' individual stalls with stanchions, located in a dairy barn. Untreated wood shavings for bedding and a photoperiod of 12 hours light/12 hours dark.

[1] On dose Day 11, the low-dose cow #3 was severely injured. It was removed from the study and euthanized. On dose Day 14, control cow #3 developed a hoof ulcer and wart; an oxytet bandage was applied. All other cows appeared normal for the study duration.

TABLE B.1.2. Test Animal Dietary Regime.

Composition of Diet	Feed consumption (kg/cow/day)	Water	Acclimation period	Predosing
4 kg dairy ration, 5 kg alfalfa hay cubes, and 3 kg baled hay twice daily at milkings. Quantity of alfalfa cubes offered was adjusted based on consumption.	Control: 19.2 1X: 20.3 3X: 20.6 10X: 20.3	*Ad libitum*	15 days	None

TABLE B.1.3. Dosing Regime.

Treatment group	Treatment Type	Level of administered dose (mg/day)	Residue intake in diet (ppm)	Vehicle	Timing/ Duration
Control	Oral	0	0	Gelatin capsule	Cows were dosed daily following the am milking for 29 consecutive days.
1X		1910	4.73		
3X		7320	14.6		
10X		22840	45.7		

TABLE B.1.4. Sample Collection.

Milk collected	Amount of milk produced during normal production	Urine, feces and cage wash collected	Interval from last dose to sacrifice (days)	Tissues harvested and analyzed
Milk collected twice daily; milk collected in the pm was combined with milk collected in the following am.	Average daily milk production during dosing: Control: 20.2-23.3 kg Group 1X: 28.1-31.1kg Group 3X: 18.7-21.4 kg Group 10X: 24.6-25.5 kg Average daily milk production during acclimation: Control: 25.0-25.8 kg Group 1X: 28.3-30.3 kg Group 3X: 20.5-20.6 kg Group 10X: 21.0-22.8 kg	Not collected	≤24 hours	Liver, kidneys, fat (perinephric, abdominal, and subcutaneous), and muscle (hind-quarter, pectoral, and abductor)

B.2. Sampling Handling and Preparation

Milk was collected twice daily, and milk was retained on Days 1, 2, 4, 7, 10, 14, 17, 21, 24 and 28. Day 24 whole milk was centrifuged to obtain cream and skim milk fractions. Composite samples of whole milk, skim milk, cream, and tissues collected at sacrifice were stored frozen (temperature unspecified) prior to shipment to the analytical facility.

Tissue samples were macerated in the presence of dry ice, and the dry ice was allowed to sublime prior to shipment. Samples of milk and tissues were shipped frozen via FedEx to the Valent Technical Center (Dublin, CA), where they were stored frozen (-20 °C) prior to extraction and analysis.

B.3. Analytical Methodology

Whole milk, skim milk, and cream samples were analyzed for residues of *cis*- and *trans*-metconazole using GC/NPD method RM-41M-1. Tissue samples were analyzed for residues of *cis*- and *trans*-metconazole using LC/MS/MS method RM-41M-2. Residues of metabolites M1 and M12 in liver and kidney were determined using LC/MS/MS method RM-41M-3. Descriptions of these methods were included in the submission.

For method RM-41M-1, samples of whole milk, skim milk, and cream were extracted with ethyl acetate:methanol (2:1, v:v; 2x) and filtered. The extracts were combined and concentrated by rotary evaporation. The residue was mixed with 10% NaCl and partitioned with methylene chloride (3x). The methylene chloride layer was drained through sodium sulfate and concentrated to an oily residue. The resulting residue was dissolved in hexane and partitioned with acetonitrile (ACN). The ACN phase was concentrated by evaporation, rinsed with ethyl acetate, and evaporated to dryness. Residues were redissolved in toluene for determination by GC/NPD. The LOQs were 0.02 ppm for each isomer in whole and skim milk and 0.04 ppm for each isomer in cream.

For method RM-41M-2, tissue samples were extracted with ACN (3x) and filtered, and the extracts were combined. The ACN extract was partitioned with hexane, and the ACN layer was concentrated to an oily residue, then partitioned with hexane:ethyl acetate (9:1, v:v) using a 10% NaCl rinse. The hexane/ethyl acetate layer was drained through sodium sulfate and partitioned with ACN, and the ACN layer was evaporated to dryness. The residue was dissolved in methanol and applied to a C18 SPE cartridge; residues were eluted with methanol:water (5:1, v:v). The eluate was combined with ethyl acetate, evaporated to dryness, and redissolved in methanol:water (2:1, v:v) for LC/MS/MS analysis. The LOQ was 0.02 ppm for each isomer

For method RM-41M-3, samples of liver and kidney were extracted with methanol followed by methanol:water (9:1, v:v) and filtered. The extracts were combined and concentrated by rotary evaporation to remove methanol. The residue was redissolved in methanol and mixed with ACN and hexane. The ACN/methanol layer was adjusted to volume with ACN and divided into two fractions for separate determination of M12 and M1. For M12, the fraction was concentrated, combined with ethyl acetate, and evaporated to dryness, then redissolved in methanol and water

and applied to a C18 SPE cartridge. For M1, the fraction was concentrated, combined with ethyl acetate, and evaporated to dryness, then redissolved in methylene chloride and evaporated to dryness. The residue was redissolved in 3 N HCl and hydrolyzed at 80-85 °C for 1.5 hr to release conjugated residues. The hydrolysate was diluted with water and applied to a C18 cartridge. For both analytes, residues were eluted from the SPE cartridge with methanol:water (5:1, v:v). The resulting eluates were combined with ethyl acetate, evaporated to dryness, and redissolved in methanol:water (2:1, v:v) for LC/MS/MS analysis. The LOQ was 0.02 ppm for each isomer.

The LOD for all methods, analytes, and matrices except cream was 0.01 ppm. The LOD for *cis*- and *trans*-metconazole in cream was 0.02 ppm.

Method RM-41M-1 was validated concurrently with the analysis of whole milk, skim milk, and cream using samples from undosed cattle fortified with *cis*- and *trans*-metconazole, each at 0.02 and 0.10 ppm for milk and 0.04 and 0.20 ppm for cream. Method RM-41M-2 was validated concurrently with the analysis of liver, kidney, muscle, and fat using samples from undosed cattle fortified with each isomer at 0.02 and 0.10 ppm. Method RM-41M-3 was validated concurrently with the analysis of liver and kidney samples using samples from undosed cattle fortified with M1 and M12, each at 0.02 and 0.10 ppm.

C. RESULTS AND DISCUSSION

Sample storage conditions are summarized in Table C.2.1. Whole milk samples were stored frozen for up to 20 days (0.7 months), skim milk samples for up to 25 days (0.8 months), and cream samples for up to 32 days (1.1 months). Tissue samples analyzed for *cis*- and *trans*-metconazole were stored frozen for up to 54 days (1.8 months) for liver, 42 days (1.4 months) for kidney, 43 days(1.4 months) for muscle, and 49 days (1.6 months) for fat. For M1 and M12 analysis, liver samples were stored for up to 182 days (6.0 months) and kidney samples were stored for up to 173 days (5.7 months). No storage stability data are required to support the storage conditions and durations of whole milk, skim milk or cream because samples were stored for ~30 days. To support the sample storage durations for *cis*- and *trans*-metconazole residues in tissues, a concurrent storage stability study was conducted which indicated that residues were relatively stable in liver, fat, and muscle stored frozen for 108-112 days (~3.6 months). These data for *cis*- and *trans*-metconazole are adequate to support the cattle feeding study.

Concurrent recovery data are presented in Table C.1. Methods RM-41M-1 and RM-41M-2 were adequate for data collection based on acceptable concurrent recoveries. The fortification levels encompassed the residues found in cattle milk and tissues, and the recoveries were within the acceptable range of 70-120%. Apparent residues of *cis*- and *trans*-metconazole were each below the LOQ (<0.02 ppm) in five samples of whole milk, one sample of skim milk, three samples of liver, one sample of kidney, two samples of muscle, and three samples of fat from undosed cattle. Residues of *cis*-metconazole at 0.018-0.021 ppm were initially detected in cream from undosed cattle; however, upon reanalysis residues were not detected. The petitioner stated that the initial results were due to background interference in those chromatograms. Adequate representative chromatograms were provided.

Method RM-41M-3 was acceptable for data collection; however, recoveries were generally low, ranging from 57.4 to 61.6% for M1 in liver, 66.2-67.4% for M12 in liver, 69.7-78.5% for M1 in kidney and 67.6-73.9% for M12 in kidney. Apparent residues of M1 and M12 were each below the LOQ (<0.02 ppm) in two samples each of liver and kidney from undosed cattle. Adequate representative chromatograms were provided.

The results of the feeding study are reported in Table C.3, and a summary of the residues in milk and cattle tissues is presented in Table C.4. Except as noted below, samples of cattle matrices from the mid- and low-dose groups were not analyzed because residues were low (nondetectable or nonquantifiable) on analysis of samples from the high-dose group. Residues of *cis*- and *trans*-metconazole were below the LOQ (<0.04 for each isomer in cream; <0.02 ppm for remaining matrices) in all samples of whole milk, skim milk, cream, fat, muscle, and kidney from the high-dose group. In liver, residues of *cis*- and *trans*- metconazole were <0.02-0.021 ppm and <0.02 ppm, respectively, in samples from the high-dose group and below the LOQ (both isomers) in samples from the low- and mid-dose groups. Maximum total metconazole residues (sum of *cis*- and *trans*-isomers) were 0.041 ppm in liver from the high-dose group; total metconazole residues were <0.04 ppm in all samples of whole and skim milk and tissues from all dosing levels and <0.08 ppm in all samples of cream from all dosing levels.

Residues of metabolites M1 and M12 were each below the LOQ (<0.02 ppm) in samples of liver and kidney from the low- and mid-dose groups. Residues of M1 were <0.02-0.049 ppm and <0.02-0.027 ppm, respectively, in samples of liver and kidney from the high-dose group, and residues of M12 were <0.02 ppm and <0.02-0.057 ppm, respectively, in samples of liver and kidney from the high-dose group.

Because residues were largely nonquantifiable in cattle matrices, it was not possible to determine a relationship between the feeding level and the residue level for any matrix. Due to the lack of quantifiable residues in milk samples, it was not possible to determine if a plateau in residue levels was reached.

TABLE C.1. Summary of Concurrent Recoveries of Metconazole and Metabolites M1 and M12 from Dairy Cattle Matrices.

Matrix	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev.[1] (%)
***cis*-Metconazole**				
Whole milk	0.02	5	92.0, 96.9, 96.9, 103, 103	98.4 ± 4.7
	0.10	5	92.2, 92.3, 93.1, 93.3, 103	94.8 ± 4.6
Skim milk	0.02	1	92.7	--
	0.10	1	92.8	--
Cream	0.04	1	96.7	--
	0.20	1	92.0	--
Liver	0.02	2	70.3, 72.3	71.3
	0.10	2	75.1, 81.9	78.5
Kidney	0.02	1	74.5	--
	0.10	1	81.4	--
Muscle	0.02	1	80.4	--

TABLE C.1. Summary of Concurrent Recoveries of Metconazole and Metabolites M1 and M12 from Dairy Cattle Matrices.

Matrix	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev.[1] (%)
	0.10	1	74.8	--
Fat	0.02	1	79.0	--
	0.10	1	85.2	--
***trans*-Metconazole**				
Whole milk	0.02	5	90.7, 92.7, 94.9, 96.7, 104	95.8 ± 5.1
	0.10	5	90.6, 93.2, 95.4, 96.8, 97.2	94.6 ± 2.7
Skim milk	0.02	1	94.2	--
	0.10	1	96.0	--
Cream	0.04	1	105	--
	0.20	1	97.6	--
Liver	0.02	2	71.5, 75.3	73.4
	0.10	2	75.9, 81.1	78.5
Kidney	0.02	1	77.8	--
	0.10	1	82.6	--
Muscle	0.02	1	77.9	--
	0.10	1	75.7	--
Fat	0.02	1	82.2	--
	0.10	1	84.5	--
M1				
Liver	0.02	2	57.4, 58.8	58.1
	0.10	2	60.4, 61.6	61.0
Kidney	0.02	2	73.9, 78.5	76.2
	0.10	2	69.7, 72.4	71.0
M12				
Liver	0.02	1	67.4	--
	0.10	1	66.2	--
Kidney	0.02	2	67.6, 68.3	68.0
	0.10	2	70.0, 73.9	72.0

[1] Standard deviation not applicable for sample sizes of fewer than 3 samples.

TABLE C.2.1. Summary of Storage Conditions.

Matrix	Storage Temperature (°C)	Actual Storage Duration[1]	Interval of Demonstrated Storage Stability
Whole milk	-20	2-20 days (0.1-0.7 months)	No storage stability submitted or required.
Skim milk		25 days (0.8 months)	
Cream		11-32 days (0.4-1.1 months)	
Liver		42-54 days (1.4-1.8 months)	Residues of *cis*- and *trans*-metconazole are relatively stable in cow liver, muscle, and fat for 108-112 days (See Table C.2.2).
Kidney		42 days (1.4 months)	
Muscle		43 days (1.4 months)	
Fat		49 days (1.6 months)	
Liver (M1 and M12 analysis)		176-182 days (5.8-6.0 months)	No storage stability data were submitted.[2]
Kidney (M1 and M12 analysis)		162-173 days (5.3-5.7 months)	

[1] From collection or sacrifice to last analysis. Samples were analyzed within 1-22 days of extraction.
[2] Acceptable storage stability data are available from the goat metabolism studies to support the storage durations for liver and kidney for purposes of the metabolism studies. Refer 46901908.der.doc and 46901909.der.doc.

TABLE C.2.2. Stability of Metconazole Residues in Cattle Tissues Following Storage at -20°C.

Commodity	Spike Level (ppm)	Storage Interval (days)	Recovered Residues (ppm)	Mean Recovered Residues (ppm)	Mean Recovery[1] (%)	Corrected % recovery[2]
***cis*-Metconazole**						
Liver	0.1	108	0.0707, 0.0684	0.0696	65.2	79.5
Muscle	0.1	112	0.0657, 0.0649	0.0653	60.3	76.1
Fat	0.1	111	0.0790, 0.0873	0.0832	79.8	96.2
***trans*-Metconazole**						
Liver	0.1	108	0.0698, 0.0664	0.0681	67.0	79.1
Muscle	0.1	112	0.0672, 0.0639	0.0656	64.0	77.0
Fat	0.1	111	0.0812, 0.0838	0.0825	81.6	99.5

[1] Corrected for recovery in control.
[2] Corrected for mean concurrent recovery.

TABLE C.3. Residue Data from the Dairy Cattle Feeding Study with Metconazole.

Animal identification #	Matrix; Collection Time	Feeding Level (ppm)	Residues (ppm)[1]				
			cis-Metconazole	*trans*-Metconazole	Total Metconazole[2]	M1	M12
T-III-1	Milk; Day 1	45.7	ND[3]	ND	0.04		
	Milk; Day 2	45.7	ND	ND	0.04		
	Milk; Day 4	45.7	ND	ND	0.04		
	Milk; Day 7	45.7	ND	ND	0.04		
	Milk; Day 10	45.7	ND	ND	0.04		
	Milk; Day 14	45.7	ND[4]	ND[4]	0.04		
	Milk, Day 17	45.7	ND	ND	0.04		
	Milk; Day 21	45.7	ND	ND	0.04		
	Milk; Day 24	45.7	ND	ND	0.04		
	Milk; Day 28	45.7	ND	ND	0.04		

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TABLE C.3. Residue Data from the Dairy Cattle Feeding Study with Metconazole.

Animal identification #	Matrix; Collection Time	Feeding Level (ppm)	Residues (ppm)[1]				
			cis-Metconazole	*trans*-Metconazole	Total Metconazole[2]	M1	M12
T-III-2	Milk; Day 1	45.7	ND	ND	0.04		
	Milk; Day 2	45.7	ND	ND	0.04		
	Milk; Day 4	45.7	ND	ND	0.04		
	Milk; Day 7	45.7	ND	ND	0.04		
	Milk; Day 10	45.7	ND	ND	0.04		
	Milk; Day 14	45.7	ND[4]	ND[4]	0.04		
	Milk, Day 17	45.7	ND	ND	0.04		
	Milk; Day 21	45.7	ND	ND	0.04		
	Milk; Day 24	45.7	ND	ND	0.04		
	Milk; Day 28	45.7	ND	ND	0.04		
T-III-3	Milk; Day 1	45.7	ND	ND	0.04		
	Milk; Day 2	45.7	ND	ND	0.04		
	Milk; Day 4	45.7	ND	ND	0.04		
	Milk; Day 7	45.7	ND	ND	0.04		
	Milk; Day 10	45.7	ND	ND	0.04		
	Milk; Day 14	45.7	ND[4]	ND[4]	0.04		
	Milk, Day 17	45.7	ND	ND	0.04		
	Milk; Day 21	45.7	ND	ND	0.04		
	Milk; Day 24	45.7	ND	ND	0.04		
	Milk; Day 28	45.7	ND	ND	0.04		
T-III-1	Cream; Day 24	45.7	ND[4]	ND[4]	0.08		
T-III-2	Cream; Day 24	45.7	ND[4]	ND[4]	0.08		
T-III-3	Cream; Day 24	45.7	ND[4]	ND[4]	0.08		
T-III-1	Skim milk; Day 24	45.7	ND[4]	ND[4]	0.04		
T-III-2	Skim milk; Day 24	45.7	ND[4]	ND[4]	0.04		
T-III-3	Skim milk; Day 24	45.7	ND[4]	ND[4]	0.04		
T-I-1	Liver, Day 29	4.73				ND	
T-I-2	Liver, Day 29	4.73				ND	
T-II-1	Liver; Day 29	14.6	ND	ND	0.04	ND	ND
T-II-2	Liver; Day 29	14.6	ND	ND	0.04	ND	ND
T-II-3	Liver; Day 29	14.6	ND	ND	0.04	(0.011)	ND
T-III-1	Liver; Day 29	45.7	0.021	ND	0.041	ND	ND
T-III-2	Liver; Day 29	45.7	(0.011)	ND	0.04	0.049	(0.014)
T-III-3	Liver; Day 29	45.7	(0.010)	ND	0.04	(0.015)	(0.015)
T-I-1	Kidney; Day 29	4.73				ND	ND
T-I-2	Kidney; Day 29	4.73				ND	ND
T-II-1	Kidney; Day 29	14.6				ND	(0.016)
T-II-2	Kidney; Day 29	14.6				ND	(0.011)
T-II-3	Kidney; Day 29	14.6				(0.012)	(0.013)

TABLE C.3. Residue Data from the Dairy Cattle Feeding Study with Metconazole.

Animal identification #	Matrix; Collection Time	Feeding Level (ppm)	Residues (ppm)[1]				
			cis-Metconazole	*trans*-Metconazole	Total Metconazole[2]	M1	M12
T-III-1	Kidney; Day 29	45.7	ND	ND	0.04	(0.014)	(0.015)
T-III-2	Kidney; Day 29	45.7	ND	ND	0.04	0.027	0.057
T-III-3	Kidney; Day 29	45.7	ND	ND	0.04	(0.019)	0.035
T-III-1	Muscle; Day 29	45.7	ND	ND	0.04		
T-III-2	Muscle; Day 29	45.7	ND	ND	0.04		
T-III-3	Muscle; Day 29	45.7	ND	ND	0.04		
T-III-1	Fat; Day 29	45.7	ND	ND	0.04		
T-III-2	Fat; Day 29	45.7	ND	ND	0.04		
T-III-3	Fat; Day 29	45.7	ND	ND	0.04		

[1] For milk and skim milk, the LOD was 0.01 ppm and the LOQ was 0.02 ppm for each analyte. For cream, the LOD was 0.02 ppm and the LOQ was 0.04 ppm for each analyte. For tissues, the LOD was 0.01 ppm and the LOQ was 0.02 ppm for *cis*- and *trans*-metconazole, M1 and M12. Values between the LOD and LOQ are reported in parentheses.
[2] For calculation of total residues, the LOQ (0.04 ppm for cream; 0.02 ppm for all other matrices) was used for any results reported as ND or <LOQ.
[3] ND = Not detected.
[4] Results of duplicate analyses.

TABLE C.4. Summary of Residue Data from the Dairy Cattle Feeding Study with Metconazole.

Matrix	Feeding Level (ppm)	Residue Levels (ppm)[1]					
		n	Min.	Max.	Median (STMdR)	Mean (STMR)	Std. Dev.
***cis*-Metconazole**							
Liver	14.6	3	<0.02	<0.02	0.02	0.02	--
Whole milk	45.7	30	<0.02	<0.02	0.02	0.02	--
Cream	45.7	3	<0.04	<0.04	0.04	0.04	--
Skim milk	45.7	3	<0.02	<0.02	0.02	0.02	--
Liver	45.7	3	<0.02	0.021	0.02	0.02	--
Kidney	45.7	3	<0.02	<0.02	0.02	0.02	--
Muscle	45.7	3	<0.02	<0.02	0.02	0.02	--
Fat	45.7	3	<0.02	<0.02	0.02	0.02	--
***trans*-Metconazole**							
Liver	14.6	3	<0.02	<0.02	0.02	0.02	--
Whole milk	45.7	30	<0.02	<0.02	0.02	0.02	--
Cream	45.7	3	<0.04	<0.04	0.04	0.04	--
Skim milk	45.7	3	<0.02	<0.02	0.02	0.02	--
Liver	45.7	3	<0.02	<0.02	0.02	0.02	--
Kidney	45.7	3	<0.02	<0.02	0.02	0.02	--
Muscle	45.7	3	<0.02	<0.02	0.02	0.02	--
Fat	45.7	3	<0.02	<0.02	0.02	0.02	--
Total Metconazole							
Liver	14.6	3	<0.04	<0.04	0.04	0.04	--
Whole milk	45.7	30	<0.04	<0.04	0.04	0.04	--
Cream	45.7	3	<0.08	<0.08	0.08	0.08	--
Skim milk	45.7	3	<0.04	<0.04	0.04	0.04	--

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TABLE C.4. Summary of Residue Data from the Dairy Cattle Feeding Study with Metconazole.

Matrix	Feeding Level (ppm)	Residue Levels (ppm)[1]					
		n	Min.	Max.	Median (STMdR)	Mean (STMR)	Std. Dev.
Liver	45.7	3	<0.04	0.041	0.04	0.04	--
Kidney	45.7	3	<0.04	<0.04	0.04	0.04	--
Muscle	45.7	3	<0.04	<0.04	0.04	0.04	--
Fat	45.7	3	<0.04	<0.04	0.04	0.04	--
M1							
Liver	4.73	2	<0.02	<0.02	0.02	0.02	--
Kidney	4.73	2	<0.02	<0.02	0.02	0.02	--
Liver	14.6	3	<0.02	<0.02	0.02	0.02	--
Kidney	14.6	3	<0.02	<0.02	0.02	0.02	--
Liver	45.7	3	<0.02	0.049	0.02	0.030	0.017
Kidney	45.7	3	<0.02	0.027	0.02	0.022	0.004
M12							
Kidney	4.73	2	<0.02	<0.02	0.02	0.02	--
Liver	14.6	3	<0.02	<0.02	0.02	0.02	--
Kidney	14.6	3	<0.02	<0.02	0.02	0.02	--
Liver	45.7	3	<0.02	<0.02	0.02	0.02	--
Kidney	45.7	3	<0.02	0.057	0.035	0.037	0.019

[1] For calculation of the median, mean, and standard deviation, the LOQ was used for all values less than 0.01 ppm.

D. CONCLUSION

The submitted dairy cattle feeding study is adequate and reflects oral dosing with metconazole at levels of 4.73 ppm, 14.6 ppm, and 45.7 ppm. Maximum total metconazole residues (sum of *cis*- and *trans*-isomers) were 0.041 ppm in liver from the high-dose group; total metconazole residues were <0.04 ppm in all samples of whole and skim milk and tissues from all dosing levels and <0.08 ppm in all samples of cream from all dosing levels.

Residues of metabolites M1 and M12 were below the LOQ (<0.02 ppm) in samples of liver and kidney from the low- and mid-dose groups. Residues of M1 were <0.02-0.049 ppm and <0.02-0.027 ppm in samples of liver and kidney, respectively, from the high-dose group, and residues of M12 were <0.02 ppm and <0.02-0.057 ppm in samples of liver and kidney, respectively, from the high-dose group.

Acceptable methods were used for the quantitation of residues of cis- and trans-metconazole, M1, and M12. The study is supported by adequate storage stability data for *cis*- and *trans*-metconazole.

E. REFERENCES

DP#: 324541
Subject: Metconazole. Request for a Tolerance on Imported Bananas. Summary of Analytical Chemistry and Residue Data. Petition Number 9E05052.
From: N. Dodd
To: M. Waller
Date: 12/14/05
MRIDs: 44721506, 44721507, 44721508, 44721509, 44721510, and 44721511

F. DOCUMENT TRACKING

RDI: N. Dodd (2/20/08)
Petition Numbers: 6F7094 and 6F7095
DP#s: 348168 and 348206
PC Code: 125619

Template Version June 2005

Primary Evaluator	This DER was originally prepared under contract by Dynamac Corporation.
Approved by	Nancy Dodd, Chemist Nancy Dodd Date: 2/20/08 Registration Action Branch 3 Health Effects Division (7509P)

This DER was originally prepared under contract by Dynamac Corporation (2275 Research Boulevard, Suite 300; Rockville, MD 20850; submitted 09/13/2007). The DER has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORTS:

46902216 Saha, M.; Gooding, R. (2006) The Determination of Residues of Metconazole (BAS 555 F) and its Metabolites in Plant Matrices Using LC/MS/MS: Final Report. Project Number: 2005/5000141, 238522. Unpublished study prepared by BASF Agro Research. 221 p.

46902217 Perez, R.; Ibrahim, A.; Hauser, R.; et. al. (2006) Independent Method Validation of BASF Analytical Method D0508: The Determination of Residues of Metconazole (BAS 555 F) and Its Metabolites in Plant Matrices Using LC/MS/MS. Project Number: 238582, 2006/7007032, 2K6/238582. Unpublished study prepared by Adpen Labs. 296 p.

EXECUTIVE SUMMARY:

BASF has submitted LC/MS/MS method D0508 for the determination of residues of metconazole (*cis* and *trans* isomers), and metabolites M21, M11, M30, 1,2,4-triazole (1,2,4-T), triazolylacetic acid (TAA) and triazolylalanine (TA) in/on wheat grain, wheat straw, soybean seed, soybean hay, sugar beet root, sugar beet tops, wheat flour, soybean oil, sugar beet juice, and sugar beet molasses. Method D0508 was used for data collection in samples from the storage stability study, the small grain, soybean, and sugar beet crop field trials and processing studies, and the field rotational crop studies submitted by BASF and reviewed under DP#s 348168 and 348206. BASF is proposing method D0508 as an enforcement method and has submitted supporting method validation data and an independent laboratory validation (ILV) for method D0508.

Briefly, samples of wheat grain, straw, and flour, sugar beet roots and tops, and soybean seed and hay are extracted with ACN:water (70:30, v:v), and the extract is diluted with methanol/water, and filtered for analysis of metconazole and metabolites M21, M11, and M30, or evaporated to dryness and redissolved in 0.1% formic acid for analysis of triazole metabolites. Samples of soybean seed are extracted as above for analysis of all analytes except TA; for TA, the ACN/water extract is combined with water, concentrated, and hydrolyzed with 6 N HCl, and the hydrolysate is evaporated to dryness and redissolved in 0.1% formic acid. Samples of soybean oil are combined with ACN/0.1% formic acid, and partitioned with hexane. The

aqueous layer is evaporated to dryness and redissolved in methanol/water for analysis of metconazole, M21, M11, and M30, or redissolved in 0.1% formic acid for analysis of triazole metabolites. Samples of sugar beet molasses, sugar, and juice are extracted with ACN:water (50:50, v:v) and centrifuged. The extract is evaporated to dryness, and redissolved in methanol/water for analysis for metconazole, M21, M11, and M30, or mixed with water, concentrated, and diluted with 0.1% formic acid for analysis of TAA and TA. The following optional clean-up steps are included: partitioning with hexane/ethyl acetate for soybean forage and hay; and SPE column cleanup (residues eluted with NH_4OH in methanol) for sugar beet roots and tops (for analysis of TA) and sugar beet processed fractions (for analysis of 1,2,4-T and TA). The method uses three different LC/MS/MS systems (Methods I-III) and monitors a single ion transition for each analyte.

The method limits of quantitation (LOQs), determined as the lower limit of method validation (LLMV), are 0.01 ppm for metconazole (0.005 ppm for *cis* and *trans* isomers), 0.01 ppm for M21, M11, and M30, and 0.05 ppm for 1,2,4-T, TAA and TA.

Acceptable method validation recoveries were obtained for *cis*- and *trans*-metconazole, M21, M11, M30, 1,2,4-T, TAA, and TA from samples of wheat grain, wheat straw, soybean seed, soybean hay, sugar beet root, sugar beet tops, wheat flour, soybean oil, sugar beet juice, and molasses fortified at the LOQ and 10x LOQ with *cis*- and *trans*-metconazole (0.005 and 0.05 ppm); M21, M11, and M30 (0.01 and 0.1 ppm); and 1,2,4-T, TAA, and TA (0.05 and 0.5 ppm). Recoveries were generally in the acceptable range of 70-120% for all analytes in all matrices with the exception of M30 in molasses, for which recoveries ranged from 60 to 69%.

Concurrent recovery data were generated in conjunction with the storage stability, crop field trial, processing, and field rotational crop studies submitted by BASF and reviewed under DP#s 348168 and 348206. Maximum fortification levels for the concurrent recovery investigations were generally 0.5 ppm for *cis*- and *trans*-metconazole, 1 ppm for metabolites M21, M11, and M30, and 5 ppm for the triazole metabolites. Together, the fortification levels used in method validation and concurrent method validation bracket expected residue levels (i.e., fortification levels were at least within an order of magnitude of residues found) in crop commodities except for *cis*-metconazole in/on oat and wheat hay (maximum residues of 10.01 and 10.98 ppm, respectively) and rye and wheat straw (maximum residues of 7.36 and 8.39 ppm, respectively) from the crop field trials. For wheat aspirated grain fractions, the petitioner provided concurrent recovery data for *cis*- and *trans*-metconazole only at 0.5 ppm each; concurrent method fortification levels did not bracket expected residue levels for *cis*-metconazole (maximum residues of 21.19 ppm), and no recovery data were provided for M21, M11, and M30 (maximum residues of 0.71 ppm, 7.15 ppm, and 1.44 ppm, respectively). HED notes that low concurrent recoveries were obtained for metabolite M30 in molasses fortified at 0.01 and 1.0 ppm (68% and 63%, respectively).

No confirmatory analysis procedures were included in the method.

No radiovalidation data were submitted for method D0508; however, HED has concluded that because the extraction solvents used for the data collection method are similar to the aqueous

organic solvent mixtures used in the plant metabolism studies, radiovalidation of the method is not required.

Method D0508 has undergone a successful ILV with wheat grain, wheat straw, soybean seed, soybean hay, and sugar beet root, fortified at 0.005 and 0.5 ppm for *cis*- and *trans*-metconazole, 0.01 and 1.0 ppm for metabolites M21, M11 and M30, and 0.05 and 0.5 ppm for metabolites 1,2,4-T, TAA and TA. Generally, adequate recoveries within the acceptable 70-120% range were obtained for all analytes in all commodities. The ILV laboratory noted that the retention times listed for LC/MS/MS Method III (for determination of TA if matrix suppression is observed) appeared to be incorrect and should be corrected. The laboratory also recommended that a comment be added to Section 3.2.6.ii of the method (optional MCS SPE cleanup for sugar beet matrices) indicating that, for sugar beet roots, the extract should be transferred from Section 3.2.4. The laboratory further recommended that the method be revised to include a statement that duplicate injection of each standard level should be performed when generating the calibration curves to confirm instrument stability during the run.

Method D0508 was forwarded to ACB/BEAD (DP#339992, N. Dodd, 5/29/07), along with the ILV recommendations, for petition method review. ACB/BEAD reviewed the method (Paul Golden, ACB Project #B07-18, 2/8/08).

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the analytical method test data are classified as scientifically acceptable pending receipt of additional information:

- The petitioner should modify the plant method D0508 to incorporate the recommendations of the ILV laboratory in an official enforcement method document reviewed by the petitioner's quality assurance unit.

- The petitioner must modify the plant method D0508 to provide information for a second MS/MS ion transition to provide a confirmation of analyte identity. If two ion transitions are not available, the Agency recommends that the petitioner provide an alternate chromatographic column and/or mobile-phase combination. Until this revision can be made, multiresidue methods will serve as the confirmatory method.

The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP#s 348168 and 348206.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an impact on the validity of the study.

A. BACKGROUND INFORMATION

Metconazole [5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol] is a broad-spectrum triazole Group 3 fungicide (sterol biosynthesis inhibitors). There are currently no registered uses of metconazole in the U.S.; however, a tolerance has been established for banana, and a Section 18 emergency exemption and supporting time-limited tolerances have been granted for use on soybean. BASF Corporation has applied for registration of metconazole in the U.S. for use on barley, oats, rye, soybeans, sugar beets, triticale, and wheat.

The chemical structure and nomenclature of metconazole, and the physicochemical properties of the technical grade of metconazole are presented in Tables A.1 and A.2.

TABLE A.1. Metconazole Nomenclature.

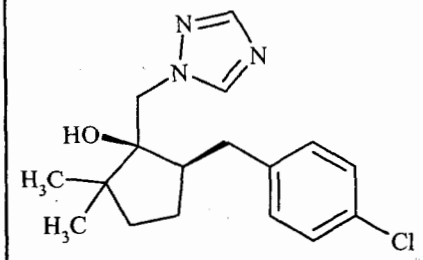
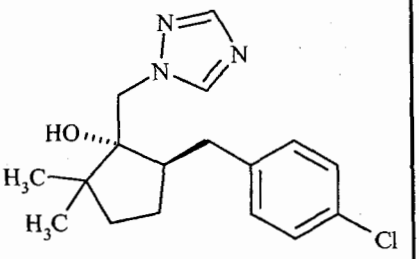
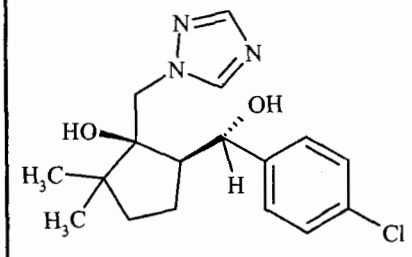
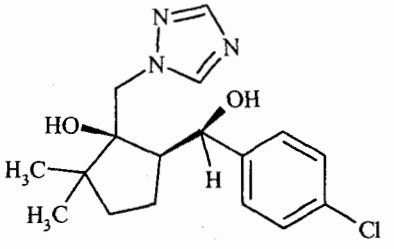
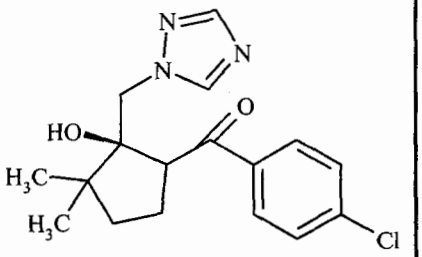
Chemical structure	 *cis*-isomer	 *trans*-isomer
Common name	Metconazole	
Company experimental name	KNF-S-474m (Kureha); BAS 555 F (BASF); V-10116 (Valent)	
IUPAC name	(1RS,5RS:1RS,5SR)-5-(4-chlorobenzyl)-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	
CAS name	5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	
CAS registry number	125116-23-6 (*cis*- and *trans*-isomers) 115850-27-6 (*cis*-isomer) 115850-28-7 (*trans*-isomer)	
End-use products (EP)	50% WDG (Metconazole 50 WDG Fungicide, EPA File Symbol 59639-RUT) 0.75 lb/gal SC/L (Caramba™ Fungicide, EPA File Symbol No. 7969-EUA) 0.67 lb/gal SC/L formulation (BAS 556 01F Fungicide, EPA File Symbol No. 7969-EUT; also contains the active ingredient pyraclostrobin at 0.83 lb/gal)	
 Metconazole metabolite M11	 Metconazole metabolite M21	 Metconazole metabolite M30

TABLE A.1. Metconazole Nomenclature.

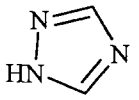
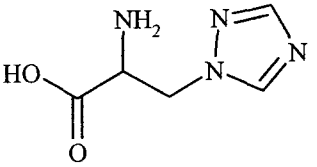
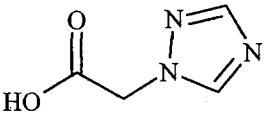
 Triazole metabolite 1,2,4-triazole (1,2,4-T)	 Triazole metabolite triazolylalanine (TA)	 Triazole metabolite triazolylacetic acid (TAA)

Table A.2. Physicochemical Properties of Metconazole

Parameter	Value				References* (MRID)
Melting point/range	100.0-108.4°C (using Electrothermal Digital Melting Point Apparatus) (AC900,768 technical grade)				44721505
pH	5.81 at 25°C (1% aqueous suspension)				46808402
Relative density (20°C)	1.14 (relative density to water at 4°C, using capillary-stoppered, density-specific gravity bottle) (Lot No. AC 8879-140B)				44721505
Water solubility (20°C)	Using shake-flask method: 18.7 ± 1.0 mg/L (*cis*-isomer, WL148271, KNF-S-474m) 13.6 ± 1.7 mg/L (*trans*-isomer, WL148271, KNF-S-474m)				44721505
Solvent solubility (g/L) at 20°C	Solvent	Metconazole	*cis*	*trans*	44721505
	acetone	363	251	117	
	methanol	403	294	117	
	dichloromethane	481	343	141	
	ethyl acetate	260	173	90.0	
	propanol	132	86.6	46.7	
	toluene	103	66.2	38.0	
	Hexane	1.40	0.929	0.483	
Vapor pressure (20°C)	Using gas-saturation method: $< 1.23 \times 10^{-5}$ Pa or 9.23×10^{-8} mm Hg (metconazole) $< 1.04 \times 10^{-5}$ Pa or 7.80×10^{-8} mm Hg (*cis*-isomer) $< 1.96 \times 10^{-6}$ Pa or 1.47×10^{-8} mm Hg (*trans*-isomer)				44721505
Dissociation constant (pK_a)	11.38±0.03 and 1.06±0.03 (in water at 29.1°C using spectrophotometric method; Lot No. AC 8879-140B)				44721505
Octanol/water partition coefficient, Log(K_{OW})	At 20 °C (using flask shaking method): K_{ow} (log K_{ow}) = 7090±989 (3.85) (Lot No. AC 8879-140B) (TGAI) K_{ow} (log K_{ow}) = 7150±803 (3.85) (*cis*-isomer, CL 354,801) K_{ow} (log K_{ow}) = 6800±1700 (3.8) (*trans*-isomer, CL 354,802)				44721505
UV/visible absorption spectrum	pH	λ	A	log ε	46808403
	cis-isomer				

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Table A.2. Physicochemical Properties of Metconazole					
Parameter	Value				References* (MRID)
	2.0	221.4	0.828	4.03	
	6.8		0.8452	4.04	
	7.0		0.9126	4.08	
	10.3		0.7226	3.98	
	trans-isomer				
	2.0	221.4	0.9053	4.07	
	7.0		0.9547	4.10	
	10.1		0.9893	4.11	

* Product Chemistry Reviews: DP #256877, Shyam Mathur, Ph.D., 9/12/2000 and DP #329168, Shyam Mathur, Ph.D., 7/13/07.

B. MATERIALS AND METHODS

B.1. Data-Gathering Method

Samples of aspirated grain fractions (soybean and wheat); barley, oat, and wheat forage and/or hay, grain, and straw; lettuce; radish roots and tops; spinach; soybean forage, hay, and seed; sugar beet roots and tops, soybean hulls, meal, and oil; sugar beet dried pulp, molasses, and sugar; wheat bran, flour, middlings, shorts, and germ from the storage stability, crop field trial, processing, and/or limited rotational crop studies submitted by BASF and reviewed under DP#s 348168 and 348206 were analyzed for residues of *cis*- and *trans*-metconazole, metabolites M21, M11, and M30, and the triazole metabolites 1,2,4-T, TAA and TA using LC/MS/MS method D0508. The method is entitled "The Determination of Residues of Metconazole (BAS 555 F) and its Metabolites in Plant Matrices Using LC/MS/MS." The petitioner noted that the method was originally developed for analysis of *cis*- and *trans*-metconazole and was modified to include additional metabolites.

B.1.1. Principle of the Method:

Method D0508 is an LC/MS/MS method developed to determine the residues of metconazole and its metabolites in/on a variety of plant matrices. The parameters of the method are described in Table B.1.1.

Briefly, samples of wheat grain, straw, and flour, sugar beet roots and tops, and soybean seed and hay are extracted with ACN:water (70:30, v:v), and the extract is diluted with methanol/water, and filtered for analysis of metconazole, M21, M11, and M30, or evaporated to dryness and redissolved in 0.1% formic acid for analysis of triazole metabolites. Samples of soybean seed are extracted as above for analysis of all analytes except TA; for TA, the ACN/water extract is combined with water, concentrated, and hydrolyzed with 6 N HCl, and the hydrolysate is evaporated to dryness and redissolved in 0.1% formic acid. Samples of soybean oil are combined with ACN/0.1% formic acid, and partitioned with hexane. The aqueous layer is evaporated to dryness and redissolved in methanol/water for analysis of metconazole, M21,

M11, and M30, or redissolved in 0.1% formic acid for analysis of triazole metabolites. Samples of sugar beet molasses, sugar, and juice are extracted with ACN:water (50:50, v:v) and centrifuged. The extract is evaporated to dryness and redissolved in methanol/water for analysis of metconazole, M21, M11, and M30, or mixed with water, concentrated, and diluted with 0.1% formic acid for analysis for TAA and TA. The following optional clean-up steps are included: partitioning with hexane/ethyl acetate for soybean forage and hay; and SPE column cleanup (residues eluted with NH_4OH in methanol) for sugar beet roots and tops (for analysis of TA) and sugar beet processed fractions (for analysis of 1,2,4-T and TA). The method uses three different LC/MS/MS systems (Methods I-III) and monitors a single ion transition for each analyte.

TABLE B.1.1. Summary Parameters for the Analytical Method Used for the Quantitation of Metconazole Residues in Wheat Grain, Wheat Straw, Soybean Seed, Soybean Hay, Sugar Beet Root, Sugar Beet Tops, Wheat Flour, Soybean Oil, Sugar Beet Juice, and Molasses.

Method ID	BASF Analytical Method D0508
Analytes	*cis*-metconazole, *trans*-metconazole, M21, M11, M30, 1,2,4-T, TA, TAA
Extraction solvent/technique	Wheat grain, straw, flour, sugar beet roots and tops, soybean seed and hay: Samples are extracted with ACN:water (70:30, v:v) and centrifuged, and the extract is diluted with methanol:water (80:20, v:v), and filtered for analysis of metconazole, M21, M11, and M30, or evaporated to dryness and redissolved in 0.1% formic acid for analysis for triazole metabolites. Soybean seed: Samples are extracted for analysis as above for all analytes except TA. For TA, the extract is combined with water, concentrated, and hydrolyzed with 6 N HCl at 110 °C for 0.5 hr. The hydrolysate is evaporated to dryness and redissolved in 0.1% formic acid. Soybean oil: The sample is combined with ACN:0.1% formic acid (80:20, v:v), and partitioned with hexane. The aqueous layer is adjusted to volume with ACN, and an aliquot is evaporated to dryness and redissolved in methanol:water (80:20, v:v) for analysis for metconazole, M21, M11, and M30 or evaporated to dryness and redissolved in 0.1% formic acid for analysis for triazole metabolites. Sugar beet molasses, sugar, and juice: Samples are extracted with ACN:water (50:50, v:v) and centrifuged. The extract is adjusted to volume with ACN/water, evaporated to dryness, and redissolved in methanol:water (80:20, v:v) for analysis for metconazole and metabolites, or the extract is mixed with water, concentrated, and diluted with 0.1% formic acid for analysis for TAA and TA.
Cleanup strategies	Soybean hay and forage (optional): An aliquot of the extract is concentrated to aqueous and partitioned with hexane:ethyl acetate (9:1, v:v). The organic layer is evaporated to dryness and redissolved in methanol:water (80:20, v:v) for analysis. Sugar beet roots and tops (optional for TA), molasses, sugar, and juice (optional for 1,2,4-T and TA): The initial aqueous extract is combined with water and methanol:water (50:50, v:v) and applied to an MCX SPE column. Residues are eluted with 1% NH_4OH in methanol. The eluate is evaporated to dryness and redissolved in 0.1% formic acid.
Instrument/Detector	For metconazole, M21, M11, and M30 (Method I): LC/MS/MS is conducted using a reverse phase C18 column and a gradient mobile phase of water and ACN, each containing 0.1% formic acid. MS/MS is conducted using turbospray ionization in the positive ion mode. The following ion transitions are monitored: 320.1→ 40.1 for metconazole (*cis* and *trans*), 336.1 → 125.1 for M21 and M11, and 334.1 → 111.1 for M30. For 1,2,4-T, TAA and TA (Method II): LC/MS/MS is conducted using a graphite column and a gradient mobile phase of water and methanol, each containing 0.1% formic acid. MS/MS is conducted using turbospray ionization in the positive ion mode. The following ion transitions are monitored: 70.1 → 43.2 for 1,2,4-T, 128.1 → 70.2 for TAA, and 157.1 → 88.1 for TA. For TA if matrix suppression is observed (Method III): LC/MS/MS is conducted using the same system as Method II but with a different gradient program. The following ion transitions are monitored: 70.1 → 43.2 for 1,2,4-T, 128.1 → 70.2 for TAA, and 157.1 → 88.1 for TA.
Standardization method	External standardization using a calibration curve prepared by plotting peak area vs. weight and using a linear least squares equation.

TABLE B.1.1. Summary Parameters for the Analytical Method Used for the Quantitation of Metconazole Residues in Wheat Grain, Wheat Straw, Soybean Seed, Soybean Hay, Sugar Beet Root, Sugar Beet Tops, Wheat Flour, Soybean Oil, Sugar Beet Juice, and Molasses.	
Stability of std solutions	Stock standards of metconazole, M21, M11, and M30 in methanol and triazole metabolites in water: 90 days. Fortification standards of metconazole, M21, M11, and M30 in methanol: 41 days. Fortification standards of triazole metabolites in water: 60 days. Calibration standards of metconazole, M21, M11, and M30 in methanol:water (80:20, v:v) and triazole metabolites in 0.1% formic acid: 30 days.
Retention times	Method I: *cis*-metconazole: 9.80 min; *trans*-metconazole: 9.43 min; M21: 9.15 min; M11: 8.27 min; and M30: 9.04 min Methods II and III: 1,2,4-T: 1.64 min; TAA: 3.99 min; TA: 3.12 min

B.2. Enforcement Method

The proposed enforcement method is the same as the data gathering method.

C. RESULTS AND DISCUSSION

C.1. Data-Gathering Method

The method validation data are presented in Table C.1.1. The method validation recoveries of *cis*- and *trans*-metconazole and metabolites M21, M11, M30, 1,2,4-T, TAA, and TA were adequate from samples of wheat grain, wheat straw, soybean seed, soybean hay, sugar beet root, sugar beet tops, wheat flour, soybean oil, sugar beet juice and molasses fortified at the LOQ and 10x LOQ with *cis*- and *trans*-metconazole (0.005 and 0.05 ppm); M21, M11, and M30 (0.01 and 0.1 ppm); and 1,2,4-T, TAA, and TA (0.05 and 0.5 ppm). Recoveries were generally in the acceptable range of 70-120% for all analytes in all matrices with the exception of M30 in molasses, for which recoveries ranged from 60 to 69%.

Concurrent recovery data were generated in conjunction with the storage stability, crop field trial, processing, and field rotational crop studies submitted by BASF and reviewed under DP#s 348168 and 348206. Fortification levels for the concurrent recovery investigations were generally 0.5 ppm for *cis*- and *trans*-metconazole, 1 ppm for metabolites M21, M11, and M30, and 5 ppm for the triazole metabolites. Together, the fortification levels used in method validation and concurrent method validation bracket expected residue levels (i.e., fortification levels were at least within an order of magnitude of residues found) in crop commodities, except for *cis*-metconazole in/on oat and wheat hay (maximum residues of 10.01 and 10.98 ppm, respectively) and rye and wheat straw (maximum residues of 7.36 and 8.39 ppm, respectively) from the crop field trials. For wheat aspirated grain fractions, the petitioner provided concurrent method fortifications for *cis*- and *trans*-metconazole only at 0.5 ppm each; concurrent method fortification levels did not bracket expected residue levels for *cis*-metconazole (maximum residues of 21.19 ppm), and no recovery data were provided for M21, M11, and M30 (maximum residues of 0.71 ppm, 7.15 ppm, and 1.44 ppm, respectively). HED notes that low concurrent recoveries were obtained for metabolite M30 in molasses fortified at 0.01 and 1.0 ppm (68% and 63%, respectively).

The method characteristics for method D0508 are presented in Table C.1.2. No confirmatory analysis procedures were included in the method, and no interference study was submitted. The petitioner considers LC/MS/MS to be highly selective and self-confirmatory; however, ACB/BEAD currently recommends that enforcement methods include information for two MS/MS ion transitions per analyte in order to be considered sufficiently specific. When two transitions are not available, ACB/BEAD recommends providing an alternate chromatographic column and/or mobile-phase combination to reduce the possibility of false positive residues.

No radiovalidation data were submitted for method D0508; however, HED has concluded that because the extraction solvents used for the data collection method are similar to the aqueous organic solvent mixtures used in the plant metabolism studies, radiovalidation of the method is not required.

TABLE C.1.1. Recovery Results from Method Validation of Wheat Grain, Wheat Straw, Soybean Seed, Soybean Hay, Sugar Beet Root, Sugar Beet Tops, Wheat Flour, Soybean Oil, Sugar Beet Juice, and Molasses using the Data-Gathering Analytical Method. [1]

Matrix	Spiking Level (ppm)	Recoveries Obtained (%)	Mean Recovery ± Std. Dev. [CV], (%)
***cis*-Metconazole**			
Wheat grain	0.005	92, 92, 98, 102, 102	97 ± 5.0 [5.2]
	0.05	94, 94, 98, 99, 102	97 ± 3.4 [3.5]
Wheat straw	0.005	69, 72, 75, 80, 86	76 ± 6.7 [8.8]
	0.05	91, 92, 94, 98, 98	95 ± 3.3 [3.5]
Soybean seed	0.005	81, 84, 86, 90, 92	87 ± 4.4 [5.1]
	0.05	95, 97, 102, 104, 107	101± 4.9 [4.9]
Soybean hay	0.005	93, 98, 102, 105, 111	102 ± 6.8 [6.7]
	0.05	95, 102, 104, 112, 112	105 ± 7.2 [6.9]
Sugar beet root	0.005	82, 88, 89, 99, 110	94 ± 11 [12]
	0.05	95, 101, 103, 104, 104	101 ± 3.8 [3.7]
Sugar beet tops	0.005	85, 86, 89, 93, 94	89 ± 4.0 [4.5]
	0.05	90, 92, 92, 100, 102	95 ± 5.4 [5.7]
Wheat flour	0.005	80, 80, 90, 90, 94	87 ± 6.4 [7.4]
	0.05	90, 92, 94, 99, 105	96 ± 6.0 [6.3]
Soybean oil	0.005	82, 88, 91, 104, 106	94 ± 10 [11]
	0.05	80, 86, 86, 91, 92	87 ± 4.8 [5.5]
Sugar beet juice	0.005	88, 88, 97, 98, 106	95 ± 7.6 [8.0]
	0.05	99, 99, 102, 104, 113	103 ± 5.8 [5.6]
Molasses	0.005	86, 94, 97, 98, 124	100 ± 14 [14]
	0.05	93, 97, 98, 100, 103	98 ± 3.7 [3.8]
***trans*-Metconazole**			
Wheat grain	0.005	84, 87, 90, 90, 94	89 ± 3.7 [4.2]
	0.05	84, 94, 98, 102, 107	97 ± 8.7 [9.0]
Wheat straw	0.005	75, 75, 86, 86, 86	82 ± 6.0 [7.4]
	0.05	90, 93, 96, 100, 106	97 ± 6.2 [6.4]
Soybean seed	0.005	77, 82, 83, 97, 96	85 ± 7.1 [8.4]
	0.05	86, 90, 97, 98, 106	95 ± 7.7 [8.1]

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TABLE C.1.1. Recovery Results from Method Validation of Wheat Grain, Wheat Straw, Soybean Seed, Soybean Hay, Sugar Beet Root, Sugar Beet Tops, Wheat Flour, Soybean Oil, Sugar Beet Juice, and Molasses using the Data-Gathering Analytical Method. [1]

Matrix	Spiking Level (ppm)	Recoveries Obtained (%)	Mean Recovery ± Std. Dev. [CV], (%)
Soybean hay	0.005	102, 104, 108, 111, 115	108 ± 5.2 [4.9]
	0.05	104, 105, 108, 114, 117	110 ± 5.7 [5.2]
Sugar beet root	0.005	93, 98, 102, 105, 111	102 ± 6.8 [6.7]
	0.05	95, 102, 104, 112, 112	105 ± 7.2 [6.9]
Sugar beet tops	0.005	81, 81, 84, 89, 89	85 ± 4.0 [4.7]
	0.05	74, 89, 89, 90, 92	87 ± 7.3 [8.4]
Wheat flour	0.005	68, 69, 75, 77, 78	73 ± 4.6 [6.3]
	0.05	94, 95, 96, 104, 104	99 ± 5.0 [5.1]
Soybean oil	0.005	81, 82, 84, 84, 91	84 ± 3.9 [4.6]
	0.05	77, 78, 78, 80, 83	79 ± 2.4 [3.0]
Sugar beet juice	0.005	78, 85, 86, 91, 93	87 ± 5.9 [6.8]
	0.05	93, 101, 101, 104, 107	101 ± 5.2 [5.2]
Molasses	0.005	79, 80, 82, 85, 95	84 ± 6.5 [7.7]
	0.05	89, 90, 98, 99, 100	95 ± 5.3 [5.5]
M21			
Wheat grain	0.01	87, 90, 91, 96, 97	92 ± 4.2 [4.6]
	0.1	94, 97, 102, 104, 107	101 ± 5.3 [5.2]
Wheat straw	0.01	74, 75, 78, 82, 88	79 ± 5.7 [7.2]
	0.1	82, 83, 85, 86, 92	86 ± 3.9 [4.6]
Soybean seed	0.01	75, 80, 83, 90, 100	86 ± 9.7 [11]
	0.1	88, 91, 97, 104, 108	98 ± 8.4 [8.7]
Soybean hay	0.01	84, 90, 93, 106, 109	96 ± 11 [11]
	0.1	88, 89, 109, 109, 113	102 ± 12 [12]
Sugar beet root	0.01	80, 83, 84, 94, 105	89 ± 10 [12]
	0.1	73, 77, 88, 94, 101	87 ± 12 [13]
Sugar beet tops	0.01	82, 83, 84, 91, 91	86 ± 4.4 [5.1]
	0.1	82, 90, 96, 102, 106	95 ± 9.5 [10]
Wheat flour	0.01	71, 89, 90, 91, 91	86 ± 8.6 [10]
	0.1	87, 91, 97, 98, 102	95 ± 6.0 [6.3]
Soybean oil	0.01	71, 78, 84, 92, 99	85 ± 11 [13]
	0.1	72, 72, 91, 94, 94	85 ± 11 [13]
Sugar beet juice	0.01	87, 94, 97, 101, 104	97 ± 6.6 [6.8]
	0.1	89, 92, 96, 100, 101	96 ± 5.1 [5.4]
Molasses	0.01	76, 80, 80, 83, 94	83 ± 6.8 [8.3]
	0.1	98, 106, 106, 112, 116	108 ± 6.8 [6.4]
M11			
Wheat grain	0.01	90, 91, 91, 92, 94	92 ± 1.5 [1.7]
	0.1	99, 101, 101, 102, 103	101 ± 1.5 [1.5]
Wheat straw	0.01	72, 73, 74, 84, 87	78 ± 7.0 [8.9]
	0.1	76, 78, 87, 92, 97	86 ± 9.0 [10]
Soybean seed	0.01	67, 72, 73, 78, 79	74 ± 4.9 [6.6]
	0.1	89, 90, 90, 96, 113	96 ± 10 [11]

TABLE C.1.1. Recovery Results from Method Validation of Wheat Grain, Wheat Straw, Soybean Seed, Soybean Hay, Sugar Beet Root, Sugar Beet Tops, Wheat Flour, Soybean Oil, Sugar Beet Juice, and Molasses using the Data-Gathering Analytical Method. [1]

Matrix	Spiking Level (ppm)	Recoveries Obtained (%)	Mean Recovery ± Std. Dev. [CV], (%)
Soybean hay	0.01	88, 89, 90, 99, 104	94 ± 7.1 [7.6]
	0.1	84, 92, 94, 96, 97	93 ± 5.2 [5.6]
Sugar beet root	0.01	92, 93, 93, 96, 107	96 ± 6.2 [6.5]
	0.1	96, 103, 104, 106, 107	103 ± 4.3 [4.2]
Sugar beet tops	0.01	77, 78, 80, 82, 91	82 ± 5.6 [6.9]
	0.1	78, 87, 88, 92, 96	88 ± 6.7 [7.6]
Wheat flour	0.01	88, 89, 100, 101, 101	96 ± 6.7 [7.0]
	0.1	87, 89, 98, 100, 104	96 ± 7.3 [7.6]
Soybean oil	0.01	89, 90, 94, 95, 116	97 ± 11 [11]
	0.1	92, 94, 95, 96, 100	95 ± 3.0 [3.1]
Sugar beet juice	0.01	86, 90, 90, 97, 99	92 ± 5.4 [5.9]
	0.1	90, 98, 101, 102, 102	99 ± 5.1 [5.2]
Molasses	0.01	66, 70, 78, 80, 86	76 ± 8.0 [11]
	0.1	87, 90, 91, 93, 95	91 ± 3.0 [3.3]
M30			
Wheat grain	0.01	87, 89, 90, 90, 95	90 ± 2.9 [3.3]
	0.1	97, 98, 101, 102, 111	102 ± 5.5 [5.4]
Wheat straw	0.01	67, 68, 74, 74, 76	72 ± 4.0 [5.6]
	0.1	83, 88, 88, 98, 103	92 ± 8.2 [8.9]
Soybean seed	0.01	77, 82, 87, 89, 100	87 ± 8.6 [9.9]
	0.1	84, 91, 92, 94, 95	91 ± 4.3 [4.7]
Soybean hay	0.01	95, 97, 99, 101, 107	100 ± 4.6 [4.6]
	0.1	98, 104, 106, 107, 107	104 ± 3.8 [3.6]
Sugar beet root	0.01.	82, 94, 94, 96, 96	92 ± 5.9 [6.4]
	0.1	93, 95, 95, 104, 111	100 ± 7.7 [7.7]
Sugar beet tops	0.01	73, 83, 84, 92, 95	85 ± 8.6 [10]
	0.1	90, 91, 95, 95, 116	97 ± 11 [11]
Wheat flour	0.01	91, 92, 92, 93, 93	92 ± 0.8 [0.9]
	0.1	90, 95, 95, 96, 99	95 ± 3.2 [3.4]
Soybean oil	0.01	79, 87, 92, 94, 99	90 ± 7.6 [8.4]
	0.1	82, 90, 91, 98, 102	93 ± 7.7 [8.4]
Sugar beet juice	0.01	87, 96, 96, 97, 102	96 ± 5.4 [5.7]
	0.1	93, 93, 96, 99, 100	96 ± 3.3 [3.4]
Molasses	0.01	60, 61, 64, 64, 65	63 ± 2.2 [3.5]
	0.1	60, 66, 68, 68, 69	66 ± 3.6 [5.5]
1,2,4-T			
Wheat grain	0.05	81, 93, 94, 108, 113	98 ± 13 [13]
	0.5	75, 89, 101, 104, 117	97 ±16 [16]
Soybean seed	0.05	93, 94, 95, 102, 103	97 ± 4.7 [4.8]
	0.5	88, 94, 100, 106, 109	99 ± 8.6 [8.6]
Soybean hay	0.05	47[2]; 69, 74, 81, 84	77 ± 6.8 [8.8]
	0.5	79, 90, 91, 97, 103	92 ± 8.9 [9.7]

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TABLE C.1.1. Recovery Results from Method Validation of Wheat Grain, Wheat Straw, Soybean Seed, Soybean Hay, Sugar Beet Root, Sugar Beet Tops, Wheat Flour, Soybean Oil, Sugar Beet Juice, and Molasses using the Data-Gathering Analytical Method. [1]

Matrix	Spiking Level (ppm)	Recoveries Obtained (%)	Mean Recovery ± Std. Dev. [CV], (%)
Sugar beet root	0.05	80, 86, 106, 106, 110	98 ± 14 [14]
	0.5	68, 79, 82, 83, 102	83 ± 12 [15]
Sugar beet tops	0.05	84, 87, 91, 93, 94	90 ± 4.2 [4.7]
	0.5	91, 92, 108, 115, 118	105 ± 13 [12]
Wheat flour	0.05	67, 76, 86, 105, 112	89 ± 19 [21]
	0.5	90, 97, 97, 97, 100	96 ± 3.7 [3.8]
Soybean oil	0.05	83, 86, 89, 92, 94	89 ± 4.4 [5.0]
	0.5	79, 88, 91, 95, 97	90 ± 7.1 [7.9]
Sugar beet juice	0.05	76, 77, 85, 97, 107	88 ± 13 [15]
	0.5	82, 93, 96, 100, 111	96 ± 11 [11]
Molasses (without SPE cleanup)	0.05	80, 94, 96, 96, 107	95 ± 9.6 [10]
	0.5	73, 78, 79, 80, 80	78 ± 2.9 [3.7]
Molasses (with SPE cleanup)	0.05	69, 78, 90, 94, 99	86 ± 12 [14]
	0.5	75, 76, 77, 82, 85	79 ± 4.3 [5.4]
TAA			
Wheat grain	0.05	58[2]; 90, 93, 96, 104	96 ± 6.0 [6.3]
	0.5	84, 86, 93, 94, 99	91 ± 6.1 [6.7]
Soybean seed	0.05	73, 79, 80, 98, 104	87 ± 13 [15]
	0.5	89, 92, 93, 105, 108	97 ± 8.5 [8.7]
Soybean hay	0.05	91, 99, 102, 105, 110	101 ± 7.1 [7.0]
	0.5	100, 101, 103, 111, 115	106 ± 6.6 [6.3]
Sugar beet root	0.05	93, 100, 101, 102, 105	100 ± 4.4 [4.4]
	0.5	89, 89, 90, 93, 112	95 ± 9.9 [10]
Sugar beet tops	0.05	88, 93, 93, 94, 104	94 ± 5.9 [6.2]
	0.5	89, 92, 100, 102, 102	97 ± 6.1 [6.3]
Wheat flour	0.05	71, 72, 75, 80, 84	76 ± 5.5 [7.2]
	0.5	86, 88, 91, 92, 92	90 ± 2.7 [3.0]
Soybean oil	0.05	82, 90, 92, 93, 98	91 ± 5.8 [6.4]
	0.5	83, 85, 94, 96, 100	92 ± 7.3 [8.0]
Sugar beet juice	0.05	96, 103, 104, 105, 107	103 ± 4.2 [4.1]
	0.5	103, 105, 108, 109, 122	109 ± 7.4 [6.8]
Molasses	0.05	74, 79, 89, 101, 103	89 ± 13 [15]
	0.5	83, 84, 94, 99, 102	92 ± 8.6 [9.3]
TA			
Wheat grain	0.05	66, 72, 74, 83, 92	77 ± 10 [13]
	0.5	70, 75, 77, 77, 82	76 ± 4.3 [5.7]
Soybean seed	0.05	82, 82, 82, 93, 98	87 ± 7.6 [8.7]
	0.5	68, 70, 72, 75, 77	72 ± 3.6 [5.0]
Soybean hay	0.05	68, 71, 75, 77, 79	74 ± 4.5 [6.0]
	0.5	86, 86, 86, 88, 89	87 ± 1.4 [1.6]
Sugar beet root (without SPE cleanup)	0.05	90, 102, 108, 111, 114	105 ± 9.5 [9.0]
	0.5	89, 91, 91, 92, 100	93 ± 9.8 [11]

TABLE C.1.1. Recovery Results from Method Validation of Wheat Grain, Wheat Straw, Soybean Seed, Soybean Hay, Sugar Beet Root, Sugar Beet Tops, Wheat Flour, Soybean Oil, Sugar Beet Juice, and Molasses using the Data-Gathering Analytical Method. [1]

Matrix	Spiking Level (ppm)	Recoveries Obtained (%)	Mean Recovery ± Std. Dev. [CV], (%)
Sugar beet root (with SPE cleanup	0.05	88, 91, 92, 98, 99	94 ± 4.7 [5.0]
	0.5	91, 95, 95, 98, 100	96 ± 3.4 [3.6]
Sugar beet tops (without SPE cleanup)	0.05	68, 70, 74, 77, 77	73 ± 4.1 [5.6]
	0.5	80, 82, 82, 89, 89	84 ± 4.3 [5.1]
Sugar beet tops (with SPE cleanup	0.05	79, 89, 92, 92, 98	90 ± 7.0 [7.7]
	0.5	94, 95, 98, 100, 101	98 ± 3.0 [3.1]
Wheat flour	0.05	64, 71, 77, 79, 83	75 ± 7.4 [9.9]
	0.5	75, 77, 79, 87, 92	82 ± 7.2 [8.8]
Soybean oil	0.05	76, 78, 80, 83, 91	82 ± 5.9 [7.2]
	0.5	77, 79, 82, 82, 90	82 ± 4.9 [6.0]
Sugar beet juice	0.05	96, 97, 103, 103, 104	101 ± 3.8 [3.8]
	0.5	106, 106, 110, 116, 118	111 ± 5.6 [5.0]
Molasses (without SPE cleanup)	0.05	75, 76, 81, 86, 87	81 ± 5.5 [6.8]
	0.5	72, 78, 88, 93, 93	85 ± 9.4 [11]
Molasses (with SPE cleanup)	0.05	83, 87, 87, 89, 96	88 ± 4.8 [5.4]
	0.5	82, 83, 99, 101, 101	93 ± 9.8 [11]

[1] Fortification standards prepared in methanol for *cis*- and *trans*-metconazole, M21, M11, and M30, and in water for 1,2,4-T, TAA and TA; calibration standards prepared in methanol/water for *cis*- and *trans*-metconazole, M21, M11, and M30, and in 0.1% formic acid for 1,2,4-T, TAA and TA.
[2] Considered an outlier by the petitioner; not included in calculation of mean and standard deviation.

TABLE C.1.2. Characteristics for the Data-Gathering Analytical Method Used for the Quantitation of Metconazole Residues in Wheat Grain, Wheat Straw, Soybean Seed, Soybean Hay, Sugar Beet Root, Sugar Beet Tops, Wheat Flour, Soybean Oil, Sugar Beet Juice, and Molasses.

Analytes	Metconazole (*cis* and *trans* isomers), M21, M11, M30, 1,2,4-T, TA, TAA
Equipment ID	PE Sciex API 4000 Q Trap Biomolecular Mass Analyzer system equipped with a Luna C18 (2) column for metconazole, M21, M11, and M30 and a Thermo Hypercarb column for triazole metabolites.
Limit of quantitation (LOQ)	0.01 ppm for metconazole (0.005 ppm for *cis* and *trans* isomers) 0.01 ppm for M21, M11 and M30 0.05 ppm for 1,2,4-T, TAA and TA Based on LLMV
Limit of detection (LOD)	20% of the LOQ
Accuracy/Precision	Recoveries for most analytes in most commodities were in the acceptable range of 70-120%, except for M30 in molasses, where recoveries were 60-69% (average 65%).
Reliability of the Method [ILV]	An independent laboratory method validation [ILV], Study No. 238582, was conducted to verify the reliability of method No. D0508 for the determination of *cis*- and *trans*-metconazole, M21, M11, M30, 1,2,4-T, TAA, and TA residues in wheat grain, wheat straw, soybean seed, soybean hay, and sugar beet root. The values obtained are indicative that method No. D0508 is reliable.
Linearity	The method/detector response was linear (coefficient of determination, $r^2 \geq 0.9900$) within the range of 1.25-200 pg.
Specificity	The control chromatograms generally have no peaks above the chromatographic background and the spiked sample chromatograms contain only the analyte peak of interest. Peaks were well defined and symmetrical. There appeared to be no carryover to the following chromatograms.

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C.2. Enforcement Method

The proposed enforcement method is the same as the data-gathering method.

C.3. Independent Laboratory Validation

An ILV study for method D0508 was conducted by Adpen Laboratories (Jacksonville, FL). Samples of untreated wheat grain, wheat straw, soybean seed, soybean hay, and sugar beet root (supplied by the petitioner) were fortified with *cis*- and *trans*-metconazole at 0.005 and 0.05 ppm and metabolites M21, M11, and M30 at 0.01 and 1.0 ppm each. Separate samples of untreated wheat grain, soybean seed, soybean hay and sugar beet root were fortified with 1,2,4-T, TAA, and TA at 0.05 and 0.5 ppm each.

Samples were analyzed according to the method procedures described in Table B.1.1. The ILV laboratory reported that they used the optional clean-up steps for determination of metconazole, M21, M11, and M30 in soybean hay (partitioning with hexane:ethyl acetate) and for determination of TA in sugar beet root (MCX SPE).

The ILV was successful on the first trial for all analytes and matrices except TA and TAA in soybean hay, for which the second trial was successful. Recoveries are reported in Table C.3.1.

The ILV laboratory reported that the method, though complex, was well written and contained no deficiencies, but noted that adherence and close attention to the method instructions and notes are critical to achieving acceptable recoveries. The laboratory noted that the retention times listed for LC/MS/MS Method III (for determination of TA if matrix suppression is observed) appeared to be incorrect and should be corrected. The laboratory also recommended that a comment be added to Section 3.2.6.ii of the method (optional MCS SPE cleanup for sugar beet matrices) indicating that, for sugar beet roots, the extract should be transferred from Section 3.2.4. The laboratory further recommended that the method be revised to include a statement that duplicate injection of each standard level should be performed when generating the calibration curves, to confirm instrument stability during the run. Finally, the laboratory noted that although matrix effects were observed in the initial analysis of 1,2,4-T and TA when instrument check was performed, these were reduced significantly by exhaustive cleaning of the LC/MS/MS instrument hardware.

The ILV laboratory did not report the number of worker hours or calendar days required to complete analysis of a sample set. According to the method description, eight person-hours are required to prepare a set of 13 samples, exclusive of LC/MS/MS analysis time, and provided that no problems, such as matrix interference, arise. Contact with the petitioner was required after the first trial to obtain guidance on how to proceed with the analysis for triazole metabolites in/on soybean hay. A second contact was made after successful completion of the second trial.

TABLE C.3.1. Recovery Results Obtained by an Independent Laboratory Validation of the Enforcement Method for the Determination of *cis*-metconazole, *trans*-metconazole, M21, M11, M30, 1,2,4-T, TAA, and TA in Wheat Grain, Wheat Straw, Soybean Seed, Soybean Hay, and Sugar Beet Root.

Matrix	Spiking Level (ppm)	Recoveries Obtained (%)	Mean Recovery ± Std. Dev. [CV][1] (%)
		***cis*-Metconazole**	
Wheat grain	0.005	91.6, 93.6	92.6
	0.5	98.2, 102.6	100.4
Wheat straw	0.005	83.2, 88.4	85.8
	0.5	98.4, 98.4	98.4
Soybean seed	0.005	96.0, 100.0	98.0
	0.5	101.0, 101.6	101.3
Soybean hay	0.005	80.0, 84.0	82.0
	0.5	81.6, 85.2	83.4
Sugar beet root	0.005	80.0, 80.0	80.0
	0.5	81.2, 83.8	82.5
		***trans*-Metconazole**	
Wheat grain	0.005	89.8, 100.5	95.2
	0.5	106.6, 114.5	110.6
Wheat straw	0.005	83.0, 82.6	82.8
	0.5	99.2, 96.4	97.8
Soybean seed	0.005	96.0, 100.0	98.0
	0.5	94.8, 96.0	95.4
Soybean hay	0.005	84.0, 87.2	85.6
	0.5	80.4, 85.4	82.9
Sugar beet root	0.005	86.0, 90.0	88.0
	0.5	79.6, 82.2	80.9
		M21	
Wheat grain	0.01	99.9, 106.9	103.4
	1.0	99.0, 104.3	101.7
Wheat straw	0.01	85.7, 83.2	84.5
	1.0	94.7, 93.5	94.1
Soybean seed	0.01	98.9, 109.7	104.3
	1.0	98.1, 100.9	99.5
Soybean hay	0.01	91.6, 89.0	90.3
	1.0	84.1, 80.2	82.2
Sugar beet root	0.01	82.0, 75.0	78.5
	1.0	73.4, 79.3	76.4
		M11	
Wheat grain	0.01	110.4, 107.6	109
	1.0	102.2, 107.3	104.8
Wheat straw	0.01	85.3, 90.6	88.0
	1.0	95.4, 92.1	93.8
Soybean seed	0.01	105.0, 110.0	107.5
	1.0	99.4, 105.9	102.7

TABLE C.3.1. Recovery Results Obtained by an Independent Laboratory Validation of the Enforcement Method for the Determination of *cis*-metconazole, *trans*-metconazole, M21, M11, M30, 1,2,4-T, TAA, and TA in Wheat Grain, Wheat Straw, Soybean Seed, Soybean Hay, and Sugar Beet Root.

Matrix	Spiking Level (ppm)	Recoveries Obtained (%)	Mean Recovery ± Std. Dev. [CV][1] (%)
Soybean hay	0.01	86.0, 94.0	90.0
	1.0	75.2, 67.8	71.5
Sugar beet root	0.01	86.0, 93.0	89.5
	1.0	78.6, 84.6	81.6
M30			
Wheat grain	0.01	112.4, 112.6	112.5
	1.0	100.3, 100.0	100.2
Wheat straw	0.01	96.1, 92.1	94.1
	1.0	105.3, 111.0	108.2
Soybean seed	0.01	97.0, 108.0	102.5
	1.0	101.9, 106.0	104.0
Soybean hay	0.01	101.6, 86.8	94.2
	1.0	89.2, 89.4	89.3
Sugar beet root	0.01	102.0, 94.0	98.0
	1.0	75.2, 82.5	78.9
1, 2, 4-T			
Wheat grain	0.05	102.2, 80.1	91.2
	0.5	98.7, 100.9	99.8
Soybean seed	0.05	100.5, 110.1	105.3
	0.5	78.1, 78.1	78.1
Soybean hay	0.05	110.1, 101.8	106.0
	0.5	128.0, 85.8	106.9
Sugar beet root	0.05	86.0, 90.8	88.4
	0.5	113.1, 92.4	102.8
TAA			
Wheat grain	0.05	72.7, 73.2	73.0
	0.5	76.6, 76.8	76.7
Soybean seed	0.05	109.4, 96.6	103.0
	0.5	105.6, 103.6	104.6
Soybean hay	0.05	100.5, 110.7	105.6
	0.5	79.9, 87.0	83.5
Sugar beet root	0.05	96.8, 97.2	97.0
	0.5	99.8, 93.5	96.7
TA			
Wheat grain	0.05	70.2, 82.7	76.5
	0.5	76.4, 75.6	76.0
Soybean seed	0.05	84.9, 91.3	88.1
	0.5	70.2, 71.5	70.9
Soybean hay	0.05	101.1, 113.9	107.5
	0.5	70.5, 75.0	72.8

TABLE C.3.1. Recovery Results Obtained by an Independent Laboratory Validation of the Enforcement Method for the Determination of *cis*-metconazole, *trans*-metconazole, M21, M11, M30, 1,2,4-T, TAA, and TA in Wheat Grain, Wheat Straw, Soybean Seed, Soybean Hay, and Sugar Beet Root.			
Matrix	Spiking Level (ppm)	Recoveries Obtained (%)	Mean Recovery ± Std. Dev. [CV][1] (%)
Sugar beet root	0.05	82.2, 84.5	83.4
	0.5	88.0, 86.9	87.5

[1] Standard deviation and CV only applicable for sample sizes ≥ 3 samples.

D. CONCLUSION

The submitted LC/MS/MS method, D0508, appears to be adequate for determining residues of *cis*- and *trans*-metconazole, M21, M11, M30, 1,2,4-T, TAA and TA, although recoveries of M30 in sugar beet molasses were low and fortification levels did not bracket expected residue levels for some commodities.

The petitioner is proposing Method D0508 for the enforcement of tolerances for crop commodities. Adequate independent laboratory validation data have been submitted. Method D0508 was forwarded to ACB/BEAD (DP#339992, N. Dodd, 5/29/07), along with the ILV recommendations, for petition method review.

ACB/BEAD reviewed the method (Paul Golden, ACB Project #B07-18, 2/8/08) and indicated that 1) the petitioner should modify the plant method D0508 to incorporate the recommendations of the ILV laboratory in an official enforcement method document reviewed by the petitioner's quality assurance unit; and 2) the petitioner must modify the plant method D0508 to provide information for a second MS/MS ion transition to provide a confirmation of analyte identity. If two ion transitions are not available, the Agency recommends that the petitioner provide an alternate chromatographic column and/or mobile-phase combination. Until this revision can be made, multiresidue methods will serve as the confirmatory method.

E. REFERENCES

DP#: 324541
Subject: Metconazole. Request for a Tolerance on Imported Bananas. Summary of Analytical Chemistry and Residue Data. Petition Number 9E05052.
From: N. Dodd
To: M. Waller
Date: 12/14/05
MRIDs: 44721506, 44721507, 44721508, 44721509, 44721510, and 44721511

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F. DOCUMENT TRACKING

RDI: N. Dodd (2/20/08)
Petition Numbers: 6F7094 and 6F7095
DP#s: 348168 and 348206
PC Code: 125619

Template Version June 2005

Primary Evaluator	This DER was originally prepared under contract by Dynamac Corporation.
Approved by	Nancy Dodd, Chemist Nancy Dodd Date: 2/20/08 Registration Action Branch 3 Health Effects Division (7509P)

This DER was originally prepared under contract by Dynamac Corporation (2275 Research Boulevard, Suite 300; Rockville, MD 20850; submitted 09/13/2007). The DER has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORTS:

46902218 Memmesheimer, H. (1997) Metconazole (CL 900768): Storage Stability of CL 900768 Residues as cis-(CL 354801) and trans-(CL 354802) Isomer at < -18Degrees Celsius in Cereal Grain (Germany, 1995). Project Number: DER31, CFS/1997/001, MK/326/004. Unpublished study prepared by Cyanamid Forshung Gmbh (CFS). 38 p.

46902219 Memmesheimer, H. (1997) Metconazole (CL 900768): Storage Stability of CL 900768 Residues as cis-(CL 354801) and trans-(CL 354802) Isomer at < -18 Degrees Celsius in Cereal Green Plant and Straw (Germany, 1996). Project Number: DER43, CFS/1997/022, MK/326/005. Unpublished study prepared by Cyanamid Forshung Gmbh (CFS). 49 p.

46902220 Memmesheimer, H. (1997) Metconazole (CL 900768): Storage Stability of CL 900768 Residues as cis-(CL 354801) and trans-(CL 354802) Isomer at < -18 Degrees Celsius in Carrots and Lettuce (Germany, 1996). Project Number: DER48, CFS/1997/060, MK/326/006. Unpublished study prepared by Cyanamid Forshung Gmbh (CFS). 55 p.

46902222 Memmesheimer, H. (1997) Metconazole (CL 900768): Storage Stability of CL 900768 Residues as cis-(CL 354801) and trans-(CL 354802) Isomer at < -18 Degrees Celsius in Rape Seed and Rape Oil (Germany, 1996). Project Number: DER49, CFS/1977/061, MK/326/007. Unpublished study prepared by Cyanamid Forshung Gmbh (CFS). 55 p.

EXECUTIVE SUMMARY:

BASF Corporation has submitted the results of storage stability studies with *cis*- and *trans*-metconazole in carrots, lettuce, rapeseed and rapeseed oil, rye green plant (forage), and wheat grain and straw. Samples of untreated carrots, lettuce, rapeseed, rapeseed oil, and wheat grain were fortified with *cis*- and *trans*-metconazole at 0.10 ppm; samples of rye forage and wheat straw bearing incurred residues of metconazole were obtained from crop field trials. All samples were stored frozen (≤-18 °C) and analyzed at intervals of 0, 1 and/or 3, 6, 9, and 12 months.

Samples were analyzed for residues of *cis*- and *trans*-metconazole by GC/NPD methods FAMS 050-01 for rye forage, wheat straw, and wheat grain, FAMS 057-01 for carrots and lettuce, and FAMS 059-01 and FAMS 059-02 for rapeseed and rapeseed oil. Methods FAMS 050-01 and FAMS 057-01 are essentially identical; FAMS 059-02 reflects a slight a modification of the extraction procedures of FAMS 059-01 for rapeseed. The methods were adequate for data collection based on acceptable concurrent method recoveries. The validated LOQs were 0.01 ppm for each analyte in carrot, lettuce, rapeseed, rapeseed oil, and wheat grain, and 0.03 ppm for each analyte in rye forage and wheat straw.

The results indicate that residues of *cis*- and *trans*-metconazole are relatively stable in/on fortified samples of carrot, lettuce, rapeseed and rapeseed oil, and wheat grain, and weathered residues of *cis*- and *trans*-metconazole are relatively stable in/on rye forage and wheat straw stored frozen for up to 12 months.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the storage stability data are classified as scientifically acceptable.

The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP#s 348168 and 348206.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an impact on the validity of the study.

A. BACKGROUND INFORMATION

Metconazole [5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cycopentanol] is a broad-spectrum triazole Group 3 fungicide (sterol biosynthesis inhibitors). There are currently no registered uses of metconazole in the U.S.; however, a tolerance has been established for banana, and a Section 18 emergency exemption and supporting time-limited tolerances have been granted for use on soybean. BASF Corporation has applied for registration of metconazole in the U.S. for use on barley, oats, rye, soybeans, sugar beets, triticale, and wheat.

The chemical structure and nomenclature of metconazole, and the physicochemical properties of the technical grade of metconazole are presented in Tables A.1 and A.2.

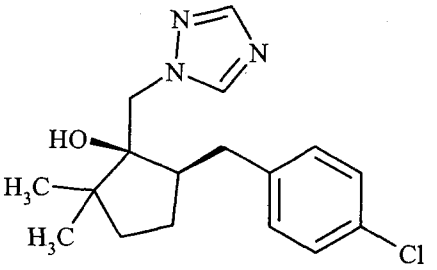
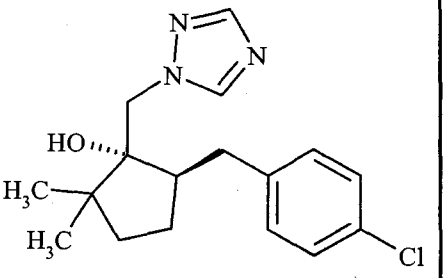
Table A.1. Metconazole Nomenclature.		
Chemical structure	 *cis*-isomer	 *trans*-isomer
Common name	Metconazole	
Company experimental name	KNF-S-474m (Kureha); BAS 555 F (BASF); V-10116 (Valent)	
IUPAC name	(1RS,5RS:1RS,5SR)-5-(4-chlorobenzyl)-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	
CAS name	5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	
CAS registry number	125116-23-6 (*cis*- and *trans*-isomers) 115850-27-6 (*cis*-isomer) 115850-28-7 (*trans*-isomer)	
End-use products (EP)	50% WDG (Metconazole 50 WDG Fungicide, EPA File Symbol 59639-RUT) 0.75 lb/gal SC/L (Caramba™ Fungicide, EPA File Symbol No. 7969-EUA) 0.67 lb/gal SC/L formulation (BAS 556 01F Fungicide, EPA File Symbol No. 7969-EUT; also contains the active ingredient pyraclostrobin at 0.83 lb/gal)	

Table A.2. Physicochemical Properties of Metconazole					
Parameter	Value				References* (MRID)
Melting point/range	100.0-108.4°C (using Electrothermal Digital Melting Point Apparatus) (AC900,768 technical grade)				44721505
pH	5.81 at 25°C (1% aqueous suspension)				46808402
Relative density (20°C)	1.14 (relative density to water at 4°C, using capillary-stoppered, density-specific gravity bottle) (Lot No. AC 8879-140B)				44721505
Water solubility (20°C)	Using shake-flask method: 18.7 ± 1.0 mg/L (*cis*-isomer, WL148271, KNF-S-474m) 13.6 ± 1.7 mg/L (*trans*-isomer, WL148271, KNF-S-474m)				44721505
Solvent solubility (g/L) at 20°C	Solvent	Metconazole	*cis*	*trans*	44721505
	acetone	363	251	117	
	methanol	403	294	117	
	dichloromethane	481	343	141	
	ethyl acetate	260	173	90.0	
	propanol	132	86.6	46.7	
	toluene	103	66.2	38.0	

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Table A.2. Physicochemical Properties of Metconazole

Parameter	Value				References* (MRID)
	Hexane	1.40	0.929	0.483	
Vapor pressure (20°C)	Using gas-saturation method: $< 1.23x10^{-5}$ Pa or 9.23×10^{-8} mm Hg (metconazole) $< 1.04x10^{-5}$ Pa or 7.80×10^{-8} mm Hg (*cis*-isomer) $< 1.96x10^{-6}$ Pa or 1.47×10^{-8} mm Hg (*trans*-isomer)				44721505
Dissociation constant (pK_a)	11.38±0.03 and 1.06±0.03 (in water at 29.1°C using spectrophotometric method; Lot No. AC 8879-140B)				44721505
Octanol/water partition coefficient, Log(K_{OW})	At 20 °C (using flask shaking method): K_{ow} (log K_{ow}) = 7090±989 (3.85) (Lot No. AC 8879-140B) (TGAI) K_{ow} (log K_{ow}) = 7150±803 (3.85) (*cis*-isomer, CL 354,801) K_{ow} (log K_{ow}) = 6800±1700 (3.8) (*trans*-isomer, CL 354,802)				44721505
UV/visible absorption spectrum	pH	λ	A	log ε	46808403
	cis-isomer				
	2.0	221.4	0.828	4.03	
	6.8		0.8452	4.04	
	7.0		0.9126	4.08	
	10.3		0.7226	3.98	
	trans-isomer				
	2.0	221.4	0.9053	4.07	
	7.0		0.9547	4.10	
	10.1		0.9893	4.11	

* Product Chemistry Reviews: DP #256877, Shyam Mathur, Ph.D., 9/12/2000 and DP #329168, Shyam Mathur, Ph.D., 7/13/07.

B. EXPERIMENTAL DESIGN

Storage stability studies with *cis*- and *trans*-metconazole in carrots, lettuce, rapeseed and rapeseed oil, rye forage, and wheat grain and straw were conducted by Cyanamid Forschung GmbH (Schwabenheim Germany).

B.1. Sample Handling and Preparation

Samples of untreated carrot, lettuce, and rapeseed oil were obtained from commercial sources, and samples of untreated rapeseed and wheat grain and treated rye forage and wheat straw were obtained from experimental trials. Untreated samples were fortified separately with either *cis*- or *trans*-metconazole at 0.10 ppm for each analyte. Fortified and unfortified samples of carrots, lettuce, rapeseed, rapeseed oil, and wheat grain were stored frozen (≤-18°C) and analyzed at 0-, 1-, 3-, 6-, 9-, and 12-month storage intervals; samples of rye forage and wheat straw bearing weathered resides were stored frozen (≤-18°C) and were analyzed at 0-, 3-, 6-, 9-, and 12-month storage intervals

B.2. Analytical Methodology

Samples were analyzed for residues of *cis*- and *trans*-metconazole by GC/NPD methods FAMS 050-01 for rye forage, wheat straw, and wheat grain, FAMS 057-01 for carrots and lettuce, and FAMS 059-01 and FAMS 059-02 for rapeseed and rapeseed oil. Brief descriptions of the methods were included in the MRIDs. Methods FAMS 050-01 and FAMS 057-01 are essentially identical; FAMS 059-02 reflects a slight a modification of the extraction procedures of FAMS 059-01 for rapeseed. The validated LOQs were 0.01 ppm for each analyte in carrot, lettuce, rapeseed, rapeseed oil, and wheat grain, and 0.03 ppm for each analyte in rye forage and wheat straw.

For methods FAMS 050-01 and 057-01, samples were extracted with acetone:hexane (1:1, v:v) and centrifuged. Water and NaCl were added, and the extracts were partitioned 2x with ethyl acetate. The ethyl acetate phases were combined, evaporated to near dryness, redissolved in methanol, and cleaned up by gel permeation chromatography (GPC) for GC/NPD analysis.

For methods FAMS 059-01 and FAMS 059-02, samples of rapeseed were extracted 2x with acetonitrile (ACN) and centrifuged; samples of rapeseed oil were diluted with hexane and extracted 3x with ACN. The respective extracts were combined, water was added, and the extracts were partitioned 2x with ethyl acetate. The ethyl acetate phases were combined, evaporated to near dryness, redissolved in methanol, and cleaned up by GPC for GC/NPD analysis.

C. RESULTS AND DISCUSSION

Concurrent recovery data are presented in Table C.1. The date indicate that GC/NPD methods FAMS 050-01, FAMS 057-01, and FAMS 059-01/059-02 are adequate for the determination of residues of *cis*- and *trans*-metconazole in/on carrots, lettuce, rapeseed and rapeseed oil, rye forage, and wheat grain and straw. Concurrent method recoveries were within the acceptable range of 70-120% for both analytes in all matrices. Apparent residues of *cis*- and *trans*-metconazole were not detected in any of the control samples.

The results of the storage stability studies are presented in Tables C.2.1 (fortified samples) and C.2.2 (treated samples bearing weathered residues). Based on the reported data, residues of *cis*-

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and *trans*-metconazole are relatively stable in/on plant samples stored frozen for up to 12 months. Graphs indicating the residue stability of metconazole in/on fortified samples of carrots/lettuce, rapeseed/oil, and wheat grain, are presented in Figures C.1, C.2, and C.3, respectively; a graph indicating the stability of weathered residues of metconazole in/on rye forage and wheat straw is presented in Figure C.4.

TABLE C.1. Summary of Concurrent Recoveries of Metconazole from Plant Samples.

Matrix	Analyte	Spike Level (ppm)	Storage Interval Months	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. (%)
Carrot (MRID 46902220)	*cis*-Metconazole	0.10	0	2	88, 90	89
			1	2	87, 88	88
			3	2	89, 92	91
			6	2	93, 93	93
			9	2	87, 89	88
			12	2	90, 91	91
	trans-Metconazole	0.10	0	2	91, 92	92
			1	2	89, 90	90
			3	2	90, 94	92
			6	2	94, 94	94
			9	2	88, 89	89
			12	2	90, 91	91
Lettuce (MRID 46902220)	*cis*-Metconazole	0.10	0	2	74, 81	78
			1	2	95, 97	96
			3	2	83, 92	88
			6	2	92, 94	93
			9	2	85, 87	86
			12	2	97, 99	98
	trans-Metconazole	0.10	0	2	70, 79	75
			1	2	93, 96	95
			3	2	81, 84	83
			6	2	92, 93	93
			9	2	84, 86	85
			12	2	98, 99	99
Rapeseed (MRID 46902222)	*cis*-Metconazole	0.10	0	2	79, 80	80
			1	2	79, 80	80
			3	2	90, 92	91
			6	2	77, 91	84
			9	2	90, 91	91
			12	2	87, 91	89
	trans-Metconazole	0.10	0	2	80, 80	80
			1	2	81, 81	81
			3	2	91, 94	93
			6	2	78, 95	87
			9	2	94, 95	95
			12	2	90, 96	93

TABLE C.1. Summary of Concurrent Recoveries of Metconazole from Plant Samples.

Matrix	Analyte	Spike Level (ppm)	Storage Interval Months	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. (%)
Rapeseed oil (MRID 46902222)	*cis*-Metconazole	0.1	0	2	98, 99	99
			1	2	96	96
			3	2	97, 100	99
			6	2	97, 100	99
			9	2	94, 94	94
			12	2	94, 95	95
	trans-Metconazole	0.10	0	2	99, 101	100
			1	2	96	96
			3	2	97, 99	98
			6	2	97, 99	98
			9	2	95, 95	95
			12	2	94, 95	95
Wheat grain	*cis*-Metconazole	0.1	0	2	77, 78	78
			1	2	81, 82	82
			3	2	88, 89	89
			6	2	83, 86	85
			9	2	84, 85	85
			12	2	76, 81	79
	trans-Metconazole	0.1	0	2	78, 79	79
			1	2	81, 82	82
			3	2	89, 91	90
			6	2	86, 89	88
			9	2	85, 86	86
			12	2	80, 83	82
Rye forage (MRID 46902219)	*cis*-Metconazole	0.90	0	2	86, 90	88
			3	2	86, 87	87
			6	2	85, 89	87
			9	2	82, 85	84
			12	2	79, 81	80
	trans-Metconazole	0.90	0	2	87, 91	89
			3	2	85, 85	85
			6	2	84, 88	86
			9	2	82, 82	82
			12	2	78, 79	79
Wheat straw (MRID 46902219)	*cis*-Metconazole	0.30	0	2	76, 78	77
			3	2	79, 81	80
			6	2	72, 78	75
			9	2	72, 78	75
			12	2	73, 73	73
	trans-Metconazole	0.30	0	2	79, 80	80
			3	2	79, 80	80
			6	2	71, 79	75
			9	2	73, 76	75

TABLE C.1. Summary of Concurrent Recoveries of Metconazole from Plant Samples.						
Matrix	Analyte	Spike Level (ppm)	Storage Interval Months	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. (%)
			12	2	72, 74	73

FIGURE C.1. ***Graph of residue stability in carrots and lettuce***

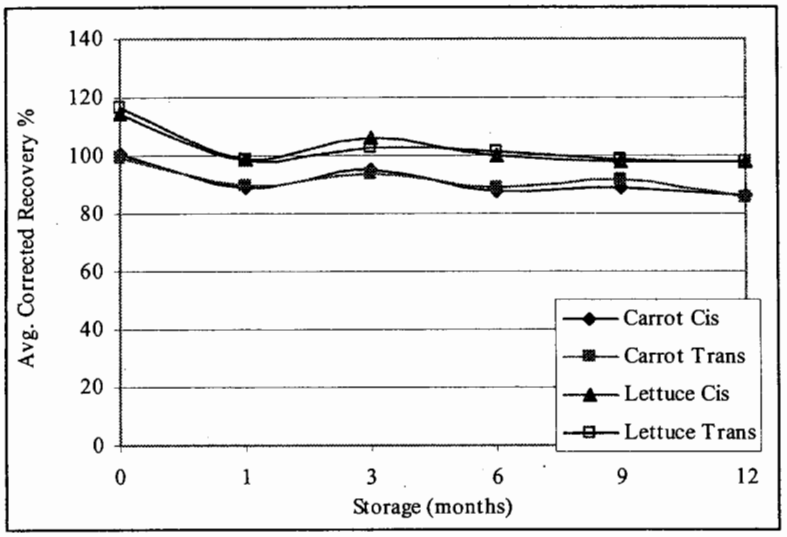

FIGURE C.2. ***Graph of residue stability in rapeseed and rapeseed oil***

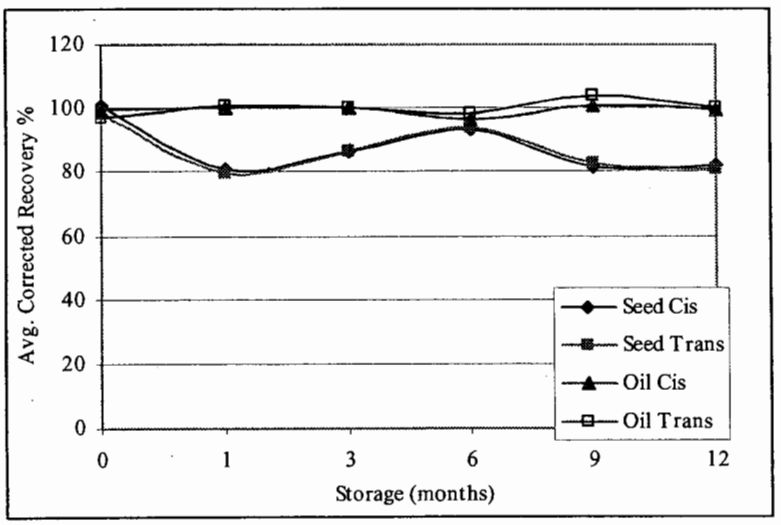

FIGURE C.3. ***Graph of residue stability in wheat grain***

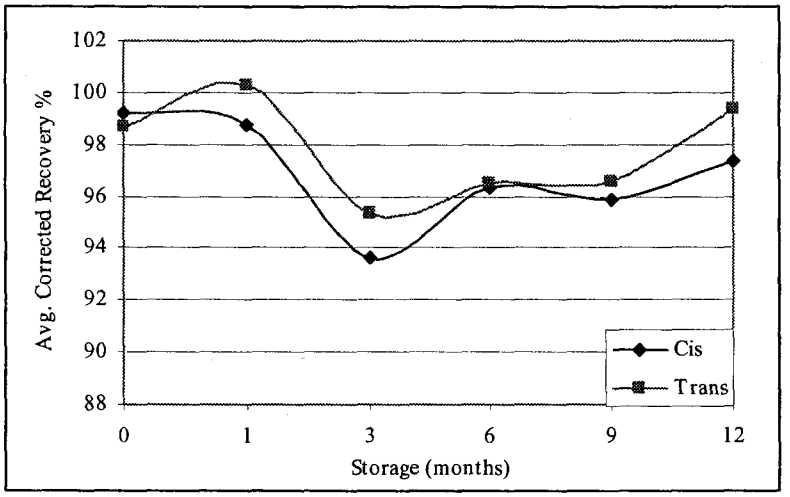

Figure C.4. ***Graph of residue stability in rye forage and wheat straw***

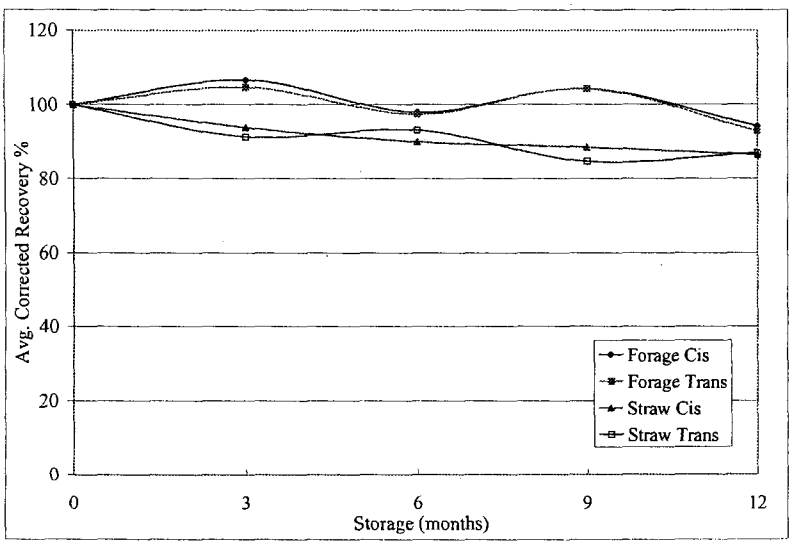

TABLE C.2.1. Stability of Metconazole Residues in Plant Samples Following Storage at ≤-18 °C.

Commodity	Analyte	Spike Level (ppm)	Storage Interval (months)	Recovered Residues (ppm)	Mean Recovered Residues (ppm)	Mean Recovery (%)	Corrected % recovery[1]
Wheat Grain (MRID 46902218)	*cis*-Metconazole	0.10	0	0.0768, 0.0772, 0.0782	0.0774	77	99
			1	0.0793, 0.0812, 0.0825	0.0810	81	99
			3	0.0832, 0.0834, 0.0834	0.0833	83	93
			6	0.0811, 0.0812, 0.0834	0.0819	82	96
			9	0.0813, 0.0815, 0.0818	0.0815	82	96
			12	0.0765, 0.0771, 0.0772	0.0769	77	97

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TABLE C.2.1. Stability of Metconazole Residues in Plant Samples Following Storage at ≤-18 °C.

Commodity	Analyte	Spike Level (ppm)	Storage Interval (months)	Recovered Residues (ppm)	Mean Recovered Residues (ppm)	Mean Recovery (%)	Corrected % recovery[1]
	trans-Metconazole	0.10	0	0.0775, 0.0778, 0.0785	0.0779	78	99
			1	0.0804, 0.0824, 0.0839	0.0822	82	100
			3	0.0855, 0.0859, 0.0860	0.0858	86	96
			6	0.0840, 0.0845, 0.0862	0.0849	85	97
			9	0.0824, 0.0831, 0.0837	0.0831	83	97
			12	0.0809, 0.0816, 0.0819	0.0810	81	100
Carrot (MRID 46902220)	*cis*-Metconazole	0.10	0	0.0878, 0.0891, 0.0913	0.0894	89	101
			1	0.0773, 0.0777, 0.0793	0.0781	78	89
			3	0.0839, 0.0854, 0.0886	0.0860	86	95
			6	0.0802, 0.0821, 0.0825	0.0816	82	88
			9	0.0779, 0.0782, 0.0794	0.0785	79	90
			12	0.0763, 0.0785, 0.0785	0.0778	78	86
	trans-Metconazole	0.10	0	0.0893, 0.0906, 0.0922	0.0907	91	99
			1	0.0789, 0.0798, 0.0814	0.0800	80	89
			3	0.0835, 0.0861, 0.0891	0.0862	86	93
			6	0.0819, 0.0841, 0.0842	0.0834	83	88
			9	0.0809, 0.0811, 0.0814	0.0811	81	91
			12	0.0752, 0.0779, 0.0787	0.0773	77	85
Lettuce (MRID 46902220)	*cis*-Metconazole	0.10	0	0.0859, 0.0888, 0.0917	0.0888	89	114
			1	0.0914, 0.0952, 0.0976	0.0947	95	99
			3	0.0910, 0.0931, 0.0945	0.0929	93	106
			6	0.0923, 0.0931, 0.0935	0.0930	93	100
			9	0.0832, 0.0837, 0.0866	0.0845	85	99
			12	0.0949, 0.0949, 0.0982	0.0960	96	98
	trans-Metconazole	0.10	0	0.0831, 0.0871, 0.0896	0.0866	87	116
			1	0.0905, 0.0934, 0.0966	0.0935	94	99
			3	0.0824, 0.0836, 0.089	0.0850	85	102
			6	0.0931, 0.0944, 0.0947	0.0941	94	101
			9	0.0814, 0.0832, 0.0875	0.0840	84	99
			12	0.0949, 0.0956, 0.0983	0.0963	96	97
Rapeseed (MRID 46902222)	*cis*-Metconazole	0.10	0	0.0789, 0.0793, 0.0815	0.0799	80	100
			1	0.0633, 0.0644, 0.0645	0.0641	64	80
			3	0.0776, 0.0792, 0.0795	0.0788	79	87
			6	0.0761, 0.0793, 0.0797	0.0784	78	93
			9	0.0704, 0.075, 0.0765	0.0740	74	81
			12	0.0713, 0.0737, 0.0743	0.0731	73	82
	trans-Metconazole	0.10	0	0.0775, 0.0777, 0.0813	0.0788	79	99
			1	0.0639, 0.0639, 0.0652	0.0643	64	79
			3	0.0783, 0.0802, 0.0811	0.0799	80	86
			6	0.0782, 0.0819, 0.0833	0.0811	81	93
			9	0.0751, 0.0786, 0.0813	0.0783	78	82
			12	0.0728, 0.0763, 0.0770	0.0754	75	81

TABLE C.2.1. Stability of Metconazole Residues in Plant Samples Following Storage at ≤-18 °C.

Commodity	Analyte	Spike Level (ppm)	Storage Interval (months)	Recovered Residues (ppm)	Mean Recovered Residues (ppm)	Mean Recovery (%)	Corrected % recovery[1]
Rapeseed oil (MRID 46902222)	*cis*-Metconazole	0.10	0	0.0980, 0.0982, 0.0985	0.0982	98	99
			1	0.0950, 0.0959, 0.0982	0.0964	96	100
			3	0.0984, 0.0985, 0.0991	0.0987	99	100
			6	0.0938, 0.0945, 0.0963	0.0949	95	96
			9	0.0931, 0.0947, 0.0965	0.0948	95	101
			12	0.0927, 0.095, 0.0951	0.0943	94	99
	trans-Metconazole	0.10	0	0.0958, 0.0965, 0.0981	0.0968	97	97
			1	0.0948, 0.0959, 0.0985	0.0964	96	100
			3	0.098, 0.0981, 0.0983	0.0981	98	100
			6	0.0953, 0.0962, 0.0976	0.0964	96	98
			9	0.0966, 0.0978, 0.1009	0.0984	98	103
			12	0.0924, 0.0952, 0.0955	0.0944	94	99
Wheat Grain (MRID 46902218)	*cis*-Metconazole	0.10	0	0.0768, 0.0772, 0.0782	0.0774	77	99
			1	0.0793, 0.0812, 0.0825	0.0810	81	99
			3	0.0832, 0.0834, 0.0834	0.0833	83	93
			6	0.0811, 0.0812, 0.0834	0.0819	82	96
			9	0.0813, 0.0815, 0.0818	0.0815	82	96
			12	0.0765, 0.0771, 0.0772	0.0769	77	97
	trans-Metconazole	0.10	0	0.0775, 0.0778, 0.0785	0.0779	78	99
			1	0.0804, 0.0824, 0.0839	0.0822	82	100
			3	0.0855, 0.0859, 0.0860	0.0858	86	96
			6	0.0840, 0.0845, 0.0862	0.0849	85	97
			9	0.0824, 0.0831, 0.0837	0.0831	83	97
			12	0.0809, 0.0816, 0.0819	0.0810	81	100

[1] Corrected for mean concurrent recovery (see Table C.1.).

TABLE C.2.2. Stability of Weathered Residues of Metconazole in Rye Forage and Wheat Straw Following Storage at ≤-18 °C.

Commodity	Analyte	Storage Interval (months)	Recovered Weathered Residues (ppm)	Mean Recovered Residues (ppm)	Corrected Recovered Residues (ppm)[1]	Corrected % recovery[2]
Rye Forage (MRID 46902219)	*cis*-Metconazole	0	0.74, 0.78, 0.73, 0.70, 0.75	0.74	0.84	100
		3	0.74, 0.79, 0.81	0.78	0.90	107
		6	0.71, 0.73, 0.71	0.72	0.82	98
		9	0.78, 0.68, 0.75	0.74	0.88	104
		12	0.61, 0.65, 0.64	0.63	0.79	94
	trans-Metconazole	0	0.17, 0.18, 0.17, 0.17, 0.17	0.17	0.19	100
		3	0.16, 0.17, 0.18	0.17	0.20	105
		6	0.16, 0.16, 0.16	0.16	0.19	97
		9	0.17, 0.15, 0.17	0.16	0.20	104
		12	0.14, 0.14, 0.14	0.14	0.18	93

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TABLE C.2.2. Stability of Weathered Residues of Metconazole in Rye Forage and Wheat Straw Following Storage at ≤-18 °C.

Commodity	Analyte	Storage Interval (months)	Recovered Weathered Residues (ppm)	Mean Recovered Residues (ppm)	Corrected Recovered Residues (ppm)[1]	Corrected % recovery[2]
Wheat straw (MRID 46902219)	*cis*-Metconazole	0	0.22, 0.22, 0.23, 0.25, 0.26	0.24	0.31	100
		3	0.23, 0.22, 0.24	0.23	0.29	94
		6	0.20, 0.20, 0.22	0.21	0.28	90
		9	0.20, 0.20, 0.21	0.20	0.27	88
		12	0.20, 0.18, 0.20	0.19	0.26	86
	trans-Metconazole	0	0.08, 0.08, 0.08, 0.09, 0.09	0.08	0.11	100
		3	0.08, 0.07, 0.08	0.08	0.10	91
		6	0.07, 0.07, 0.08	0.07	0.10	93
		9	0.06, 0.07, 0.07	0.07	0.09	85
		12	0.07, 0.06, 0.07	0.07	0.09	87

[1] Corrected for mean concurrent recovery (Table C.1).
[2] Calculated as (ppm corrected recovered residues in sample ÷ ppm corrected recovered residues in 0-day sample) * 100.

D. CONCLUSION

The submitted storage stability results adequately demonstrate the stability of *cis*- and *trans*-metconazole residues in/on samples of untreated carrots, lettuce, rapeseed and rapeseed oil, and wheat grain fortified with *cis*- and *trans*-metconazole, and samples of rye forage and wheat straw bearing weathered residues of metconazole samples stored frozen for up to 12 months. Acceptable methods were used for the quantitation of residues.

E. REFERENCES

DP#: 324541
Subject: Metconazole. Request for a Tolerance on Imported Bananas. Summary of Analytical Chemistry and Residue Data. Petition Number 9E05052.
From: N. Dodd
To: M. Waller
Date: 12/14/05
MRIDs: 44721506, 44721507, 44721508, 44721509, 44721510, and 44721511

F. DOCUMENT TRACKING

RDI: N. Dodd (2/20/08)
Petition Numbers: 6F7094 and 6F7095
DP#s: 348168 and 348206
PC Code: 125619

Template Version June 2005

Primary Evaluator	This DER was originally prepared under contract by Dynamac Corporation.
Approved by	Nancy Dodd, Chemist *Nancy Dodd* Date: 2/20/08 Registration Action Branch 3 Health Effects Division (7509P)

This DER was originally prepared under contract by Dynamac Corporation (2275 Research Boulevard, Suite 300; Rockville, MD 20850; submitted 09/13/2007). The DER has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

46902221 Kretschmer, S. (2000) Metconazole (CL 900768): Storage Stability of Residues of the Metabolite Triazolylalanine (CL 147267) in Wheat Grain. Project Number: P/342/G, B/342, MK/326/016. Unpublished study prepared by PTRL Europe Gmbh. 37 p.

EXECUTIVE SUMMARY:

BASF Corporation has submitted the results of a storage stability study with the triazole metabolite, triazolylalanine (TA) in wheat grain. Samples of untreated wheat grain were fortified with TA at 5.0 ppm, stored frozen (≤-20°C), and analyzed at intervals of 0, 6, and 12 months.

Samples were analyzed for residues of TA using a GC/MS method. The method was adequate for data collection based on acceptable concurrent method recoveries. The validated LOQ was 0.10 ppm for TA.

The results indicate that residues of TA are stable in/on wheat grain for up to 12 months.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the storage stability data are classified as scientifically acceptable.

The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP#s 348168 and 348206.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an impact on the validity of the study.

A. BACKGROUND INFORMATION

Metconazole [5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol] is a broad-spectrum triazole Group 3 fungicide (sterol biosynthesis inhibitors). There are currently no registered uses of metconazole in the U.S.; however, a tolerance has been established for banana, and a Section 18 emergency exemption and supporting time-limited tolerances have been granted for use on soybean. BASF Corporation has applied for registration of metconazole in the U.S. for use on barley, oats, rye, soybeans, sugar beets, triticale, and wheat.

The chemical structure and nomenclature of metconazole, and the physicochemical properties of the technical grade of metconazole are presented in Tables A.1 and A.2.

TABLE A.1. Metconazole Nomenclature.

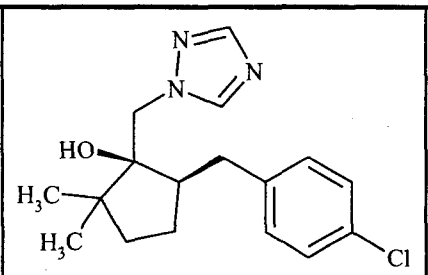
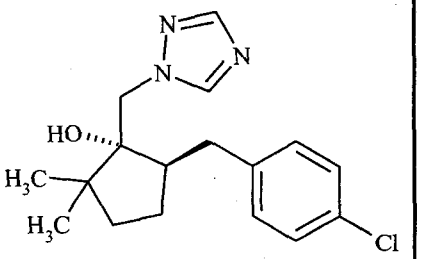
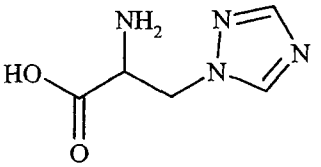
Chemical structure	 *cis*-isomer  *trans*-isomer
Common name	Metconazole
Company experimental name	KNF-S-474m (Kureha); BAS 555 F (BASF); V-10116 (Valent)
IUPAC name	(1RS,5RS:1RS,5SR)-5-(4-chlorobenzyl)-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol
CAS name	5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol
CAS registry number	125116-23-6 (*cis*- and *trans*-isomers) 115850-27-6 (*cis*-isomer) 115850-28-7 (*trans*-isomer)
End-use products (EP)	50% WDG (Metconazole 50 WDG Fungicide, EPA File Symbol 59639-RUT) 0.75 lb/gal SC/L (Caramba™ Fungicide, EPA File Symbol No. 7969-EUA) 0.67 lb/gal SC/L formulation (BAS 556 01F Fungicide, EPA File Symbol No. 7969-EUT; also contains the active ingredient pyraclostrobin at 0.83 lb/gal)
Triazole metabolite triazolylalanine (TA)	

Table A.2. Physicochemical Properties of Metconazole

Parameter	Value	References* (MRID)
Melting point/range	100.0-108.4°C (using Electrothermal Digital Melting Point Apparatus) (AC900,768 technical grade)	44721505
pH	5.81 at 25°C (1% aqueous suspension)	46808402
Relative density (20°C)	1.14 (relative density to water at 4°C, using capillary-stoppered, density-specific gravity bottle) (Lot No. AC 8879-140B)	44721505
Water solubility (20°C)	Using shake-flask method: 18.7 ± 1.0 mg/L (*cis*-isomer, WL148271, KNF-S-474m) 13.6 ± 1.7 mg/L (*trans*-isomer, WL148271, KNF-S-474m)	44721505
Solvent solubility (g/L) at 20°C	See nested table below	44721505
Vapor pressure (20°C)	Using gas-saturation method: $< 1.23 \times 10^{-5}$ Pa or 9.23×10^{-8} mm Hg (metconazole) $< 1.04 \times 10^{-5}$ Pa or 7.80×10^{-8} mm Hg (*cis*-isomer) $< 1.96 \times 10^{-6}$ Pa or 1.47×10^{-8} mm Hg (*trans*-isomer)	44721505
Dissociation constant (pK_a)	11.38±0.03 and 1.06±0.03 (in water at 29.1°C using spectrophotometric method; Lot No. AC 8879-140B)	44721505
Octanol/water partition coefficient, Log(K_{OW})	At 20 °C (using flask shaking method): K_{ow} (log K_{ow}) = 7090±989 (3.85) (Lot No. AC 8879-140B) (TGAI) K_{ow} (log K_{ow}) = 7150±803 (3.85) (*cis*-isomer, CL 354,801) K_{ow} (log K_{ow}) = 6800±1700 (3.8) (*trans*-isomer, CL 354,802)	44721505
UV/visible absorption spectrum	See nested table below	46808403

Solvent	Metconazole	*cis*	*trans*
acetone	363	251	117
methanol	403	294	117
dichloromethane	481	343	141
ethyl acetate	260	173	90.0
propanol	132	86.6	46.7
toluene	103	66.2	38.0
Hexane	1.40	0.929	0.483

pH	λ	A	log ε
cis-isomer			
2.0	221.4	0.828	4.03
6.8		0.8452	4.04
7.0		0.9126	4.08
10.3		0.7226	3.98
trans-isomer			
2.0	221.4	0.9053	4.07
7.0		0.9547	4.10
10.1		0.9893	4.11

* Product Chemistry Reviews: DP #256877, Shyam Mathur, Ph.D., 9/12/2000 and DP #329168, Shyam Mathur, Ph.D., 7/13/07.

B. EXPERIMENTAL DESIGN

A storage stability study with TA in wheat grain was conducted by PTRL Europe (Ulm, Germany).

B.1. Sample Handling and Preparation

Samples of untreated wheat grain were obtained from crop field trial studies. Samples were homogenized and fortified with TA at 5.0 ppm. The fortification standards were prepared in methanol:water (1:1, v:v); the stability of the fortification standards was not reported. Fortified and unfortified samples were stored frozen (≤-20°C) and analyzed at 0-, 6-, and 12-month storage intervals.

B.2. Analytical Methodology

Samples of wheat grain were analyzed for residues of TA using a GC/MS method. A full description of the method was included in the submission.

Briefly, residues of TA were extracted with water:methanol (2:1, v:v, followed by 1:1, v:v), vacuum filtered, and then diluted with water and centrifuged. The resulting supernatant was acidified with concentrated HCl and purified on a cation exchange column; residues were eluted with 2 M ammonia solution, and the eluate was concentrated to dryness. The purified extract was esterified with isobutanol/acetyl chloride at reflux, then derivatized with heptafluorobutyric acid anhydride (HFBA) at reflux. The resulting oily residue was sequentially purified on a silica gel column followed by an aluminum oxide column. Residues were eluted from the silica gel column with hexane:acetone (1:1, v:v) and from the aluminum oxide column with cyclohexane:ethyl acetate (1:1, v:v). The resulting eluate was evaporated to dryness and redissolved in ethyl acetate for GC/MS analysis. The validated LOQ was 0.10 ppm.

C. RESULTS AND DISCUSSION

Concurrent method recovery data are presented in Table C.1. The data indicate that the GC/MS method was adequate for determination of residues of TA in wheat grain. Concurrent method recoveries were acceptable, ranging from 72 to 93%. Apparent residues of TA were less than the LOQ in/on all control samples.

The results of the storage stability studies are presented in Table C.2. Based on the reported data, residues of TA are stable in/on wheat grain for up to 12 months when stored frozen at ≤-20 °C. A graph of residue stability in wheat grain was not generated because only three storage intervals were analyzed.

TABLE C.1. Summary of Concurrent Recoveries of TA from Wheat Grain.					
Matrix	Spike Level (ppm)	Storage Interval (months)	Sample Size (n)	Recoveries (%)	Mean (%)
Wheat grain	5.0	0	2[1]	72, 72	72
		6	2	84, 92, 97, 99	93
		12	2	78, 78, 79	78

[1] Unacceptable recoveries of 37% and 52% in two samples were attributed by the petitioner to incomplete derivatization.

TABLE C.2. Stability of TA Residues in Wheat Grain Following Storage at - 20°C.						
Commodity	Spike Level (ppm)	Storage Interval (months)	Recovered Residues (ppm)	Mean Recovered Residues (ppm)	Mean Recovery (%)	Corrected % recovery[1]
Wheat grain	5.0	0	3.58, 3.60	3.59	72	100
		6	4.6, 3.9, 4.0	4.2	84	90
		12	4.2, 4.3, 4.1	4.2	84	108

[1] Corrected for mean concurrent recovery (see Table C.1.).

D. CONCLUSION

The submitted storage stability results adequately demonstrate the stability of the triazole metabolite TA in/on wheat grain stored frozen at ≤-20 °C for up to 12 months. An acceptable method was used for the quantitation of residues.

E. REFERENCES

DP#: 324541
Subject: Metconazole. Request for a Tolerance on Imported Bananas. Summary of Analytical Chemistry and Residue Data. Petition Number 9E05052.
From: N. Dodd
To: M. Waller
Date: 12/14/05
MRIDs: 44721506, 44721507, 44721508, 44721509, 44721510, and 44721511

F. DOCUMENT TRACKING

RDI: N. Dodd (2/20/08)
Petition Numbers: 6F7094 and 6F7095
DP#s: 348168 and 348206
PC Code: 125619

Template Version June 2005

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Primary Evaluator	This DER was originally prepared under contract by Dynamac Corporation.
Approved by	Nancy Dodd, Chemist *Nancy Dodd* Date: 2/20/08 Registration Action Branch 3 Health Effects Division (7509P)

This DER was originally prepared under contract by Dynamac Corporation (2275 Research Boulevard, Suite 300; Rockville, MD 20850; submitted 09/13/2007). The DER has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

46902223 Gooding, R.; Saha, M. (2006) Freezer Storage Stability of BAS 555 F (Metconazole) and its Metabolites in Plant Samples: Amended Final Report. Project Number: 2006/7007240, 138032. Unpublished study prepared by BASF Agro Research. 177 p.

EXECUTIVE SUMMARY:

BASF Corporation has submitted the results of storage stability studies with *cis*- and *trans*-metconazole, the metabolites M11, M21, and M30, and the triazole metabolites [triazole (1,2,4-T), triazolylalanine (TA), and triazolyl-acetic acid (TAA)] in radish root and tops, soybean seed, sugar beet root, and wheat hay, straw, and grain. Samples of untreated crop commodities were fortified with selected analytes at 0.10 ppm for each analyte as follows: (1) radish root with *cis*- and *trans*-metconazole and the triazole metabolites; (2) radish tops and wheat grain with M11, M21, M30, and the triazole metabolites; (3) soybean seed with all analytes; (4) sugar beet root and wheat straw with M11, M21, and M30; and (4) wheat hay with *cis*- and *trans*-metconazole, M11, M21, and M30. All fortified samples were stored frozen (≤-5 °C) and analyzed at intervals of 0, 1, 3, and 6 months. The petitioner noted that further samples are to be analyzed at the 9- and 12-month storage intervals.

Samples were analyzed for residues of *cis*- and *trans*-metconazole, M11, M21, and M30, and the triazole metabolites using an LC/MS/MS method (BASF Method D0508). The method was adequate for data collection based on acceptable concurrent method recoveries. The validated limits of quantitation (LOQs) were 0.01 ppm for the parent metconazole (sum of *cis* and *trans* isomers at 0.005 ppm each) and the metabolites M11, M21, and M30 in/on all plant samples. The validated LOQ was 0.05 ppm for 1,2,4-T, TA, and TAA.

The results of the study are summarized in the table below.

Stability of Residues of Metconazole, M11, M21, M30, and Triazole Metabolites (1,2,4-T, TA, and TAA) in/on Radish, Soybean, Sugar Beet, and Wheat Commodities Following Storage for up to 6 months at ≤- 5 °C.								
Commodity	% Corrected Recovery Following Storage for 6 Months							
	Metconazole		M11	M21	M30	1,2,4-T	TAA	TA
	cis	*trans*						
Radish root	83	98	--	--	--	105	102	104
Radish top	--	--	111	88	114	106	81	101
Soybean seed	85	91	117	110	89	78	108	99
Sugar beet root	--	--	110	97	94	--	--	--
Wheat hay	95	95	108	107	98	--	--	--
Wheat straw	--	--	113	96	108	--	--	--
Wheat grain	--	--	86	96	111	85	70	70

The results indicate residues of *cis*- and *trans*-metconazole in/on radish root, soybean seed, and wheat hay; residues of M11, M21, and M30 in/on radish top, soybean seed, sugar beet root, and wheat hay, straw, and grain; and residues of the triazole metabolites are stable in/on radish root, radish top, soybean seed, and wheat grain during frozen storage for up to 6 months.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the storage stability data are classified as scientifically acceptable.

The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP#s 348168 and 348206.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported.

A. BACKGROUND INFORMATION

Metconazole [5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol] is a broad-spectrum triazole Group 3 fungicide (sterol biosynthesis inhibitors). There are currently no registered uses of metconazole in the U.S.; however, a tolerance has been established for banana, and a Section 18 emergency exemption and supporting time-limited tolerances have been granted for use on soybean. BASF Corporation has applied for registration of metconazole in the U.S. for use on barley, oats, rye, soybeans, sugar beets, triticale, and wheat.

The chemical structure and nomenclature of metconazole, and the physicochemical properties of the technical grade of metconazole are presented in Tables A.1 and A.2.

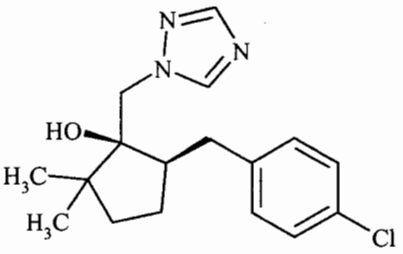
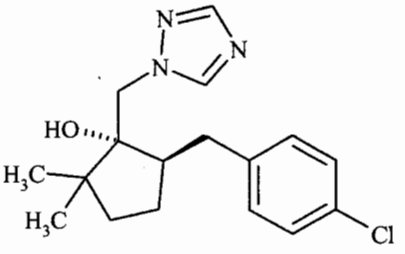
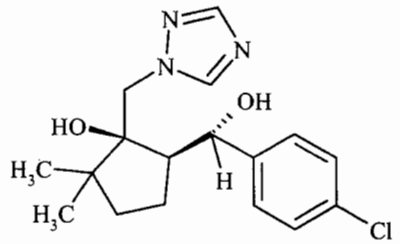
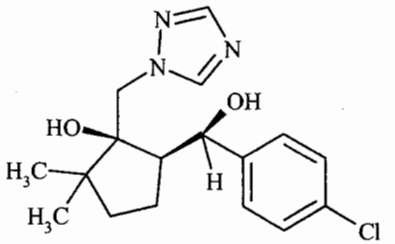
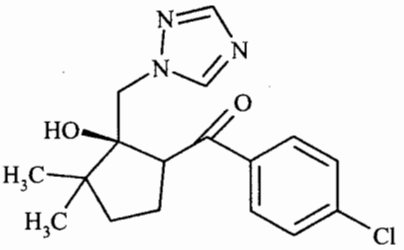
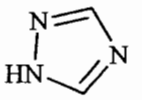
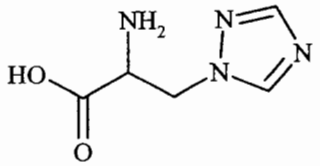
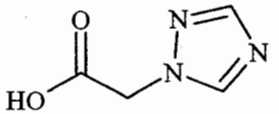
TABLE A.1. Metconazole Nomenclature.		
Chemical structure	 *cis*-isomer	 *trans*-isomer
Common name	Metconazole	
Company experimental name	KNF-S-474m (Kureha); BAS 555 F (BASF); V-10116 (Valent)	
IUPAC name	(1RS,5RS:1RS,5SR)-5-(4-chlorobenzyl)-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	
CAS name	5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	
CAS registry number	125116-23-6 (*cis*- and *trans*-isomers) 115850-27-6 (*cis*-isomer) 115850-28-7 (*trans*-isomer)	
End-use products (EP)	50% WDG (Metconazole 50 WDG Fungicide, EPA File Symbol 59639-RUT) 0.75 lb/gal SC/L (Caramba™ Fungicide, EPA File Symbol No. 7969-EUA) 0.67 lb/gal SC/L formulation (BAS 556 01F Fungicide, EPA File Symbol No. 7969-EUT; also contains the active ingredient pyraclostrobin at 0.83 lb/gal)	
 Metconazole metabolite M11	 Metconazole metabolite M21	 Metconazole metabolite M30
 Triazole metabolite 1,2,4-triazole (1,2,4-T)	 Triazole metabolite triazolylalanine (TA)	 Triazole metabolite triazolylacetic acid (TAA)

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Table A.2. Physicochemical Properties of Metconazole

Parameter	Value	References* (MRID)
Melting point/range	100.0-108.4°C (using Electrothermal Digital Melting Point Apparatus) (AC900,768 technical grade)	44721505
pH	5.81 at 25°C (1% aqueous suspension)	46808402
Relative density (20°C)	1.14 (relative density to water at 4°C, using capillary-stoppered, density-specific gravity bottle) (Lot No. AC 8879-140B)	44721505
Water solubility (20°C)	Using shake-flask method: 18.7 ± 1.0 mg/L (*cis*-isomer, WL148271, KNF-S-474m) 13.6 ± 1.7 mg/L (*trans*-isomer, WL148271, KNF-S-474m)	44721505

Solvent solubility (g/L) at 20°C — 44721505

Solvent	Metconazole	*cis*	*trans*
acetone	363	251	117
methanol	403	294	117
dichloromethane	481	343	141
ethyl acetate	260	173	90.0
propanol	132	86.6	46.7
toluene	103	66.2	38.0
Hexane	1.40	0.929	0.483

Vapor pressure (20°C)	Using gas-saturation method: $< 1.23 \times 10^{-5}$ Pa or 9.23×10^{-8} mm Hg (metconazole) $< 1.04 \times 10^{-5}$ Pa or 7.80×10^{-8} mm Hg (*cis*-isomer) $< 1.96 \times 10^{-6}$ Pa or 1.47×10^{-8} mm Hg (*trans*-isomer)	44721505
Dissociation constant (pK_a)	11.38±0.03 and 1.06±0.03 (in water at 29.1°C using spectrophotometric method; Lot No. AC 8879-140B)	44721505
Octanol/water partition coefficient, Log(K_{OW})	At 20 °C (using flask shaking method): K_{ow} (log K_{ow}) = 7090±989 (3.85) (Lot No. AC 8879-140B) (TGAI) K_{ow} (log K_{ow}) = 7150±803 (3.85) (*cis*-isomer, CL 354,801) K_{ow} (log K_{ow}) = 6800±1700 (3.8) (*trans*-isomer, CL 354,802)	44721505

UV/visible absorption spectrum — 46808403

pH	λ	A	log ε
cis-isomer			
2.0	221.4	0.828	4.03
6.8		0.8452	4.04
7.0		0.9126	4.08
10.3		0.7226	3.98
trans-isomer			
2.0	221.4	0.9053	4.07
7.0		0.9547	4.10
10.1		0.9893	4.11

* Product Chemistry Reviews: DP #256877, Shyam Mathur, Ph.D., 9/12/2000 and DP #329168, Shyam Mathur, Ph.D., 7/13/07.

B. EXPERIMENTAL DESIGN

A storage stability study with *cis*- and *trans*-metconazole, the metabolites M11, M21, and M30, and the triazole metabolites (1,2,4-T, TA, and TAA) in radish, soybean, sugar beet, and wheat commodities was conducted by BASF Agro Research (Research Triangle Park, NC).

B.1. Sample Handling and Preparation

Samples of untreated radish root and top, soybean seed, sugar beet root, and wheat grain were obtained from crop field trial studies. Samples were fortified separately with standards/mixed standards of: (1) *cis*- and *trans*-metconazole; (2) M11 and M21; (3) M30; and/or (4) 1,2,4-T, TA, and TAA. Fortification standards for metconazole, M11, M21, and M30 were prepared in methanol, and standards for the triazole metabolites were prepared in water. The stabilities of the fortification standards were reported to be 41 days for metconazole, M11, M21, and M30, and 60 days for the triazole metabolites when stored refrigerated at 4 °C.

Samples of untreated crop commodities were fortified with selected analytes at 0.10 ppm for each analyte as follows: (1) radish root with *cis*- and *trans*-metconazole and the triazole metabolites; (2) radish tops and wheat grain with M11, M21, M30, and the triazole metabolites; (3) soybean seed with all analytes; (4) sugar beet root and wheat straw with M11, M21, and M30; and (4) wheat hay with *cis*- and *trans*-metconazole, M11, M21, and M30.

A single freshly fortified homogenized sample was analyzed at 0-time for all plant commodities. Fortified and unfortified samples were stored frozen and analyzed at 0-, 1-, 3- and 6-month storage intervals. HED notes that the storage temperature was reported in the MRID as "about -20 °C" in the study abstract, and as "≤-5 °C" in the Sample History and Preparation section.

B.2. Analytical Methodology

Plant samples were analyzed for residues of metconazole, its metabolites M11, M21, and M30, and the triazole metabolites (1,2,4-T, TA, and TAA) using an LC/MS/MS method (BASF Method D0508). A brief description of the method was included in the MRID.

Briefly, samples were extracted with acetonitrile (ACN):water (70:30, v:v). The extract was diluted with methanol:water (80:20, v:v), and filtered for analysis for *cis*- and *trans*-metconazole, M11, M21, and M30, or evaporated to dryness and redissolved in 0.1% formic acid for analysis for triazole metabolites. Alternatively, for determination of TA in soybean seed, the ACN/water extract was combined with water, concentrated, hydrolyzed with 3 N HCl, and the hydrolysate was evaporated to dryness and re-dissolved in 0.1% formic acid.

The validated LOQ was 0.01 ppm for the parent metconazole (sum of *cis* and *trans* isomers at 0.005 ppm each) and the metabolites M11, M21, and M30 in/on plant samples. The validated LOQ was 0.05 ppm for 1,2,4-T, TA, and TAA. The reported limit of detection was 20% LOQ.

C. RESULTS AND DISCUSSION

Concurrent recovery data are presented in Table C.1. The data indicate that LC/MS/MS method D0508 is adequate for the determination of residues of metconazole (*cis* and *trans* isomers), metabolites M11, M21, and M30, and the triazole metabolites 1,2,4-T, TA, and TAA in/on selected radish, soybean, sugar beet, and wheat commodities. Concurrent method recoveries were generally within the acceptable range of 70-120% for all analytes and all matrices. Apparent residues of all analytes were less than the LOQ in/on all control samples.

The results of the storage stability studies are presented in Table C.2. Based on the reported data, following frozen storage for 6 months, residues of *cis*- and *trans*-metconazole are stable in/on radish root, soybean seed, and wheat hay; residues of M11, M21, and M30 are stable in/on radish top, soybean seed, sugar beet root, and wheat hay, straw, and grain; residues of the triazole metabolites are stable/relatively stable in/on radish root, radish top, soybean seed, and wheat grain. Graphs of residue stability in plant samples were not generated because only three to four storage intervals were analyzed.

TABLE C.1. Summary of Concurrent Recoveries of Metconazole, M11, M21, M30, and the Triazole Metabolites (1,2,4-T, TAA, and TA) from Plant Samples.

Matrix	Analyte	Spike Level (ppm)	Storage Interval (months)	Sample Size (n)	Recoveries (%)	Mean (%)
Radish root	*cis*-Metconazole	0.10	0	2	85, 96	90
			1	2	85, 96	90
			3	2	73, 80	76
			6	2	97, 101	99
	trans-Metconazole	0.10	0	2	85, 89	87
			1	2	85, 89	87
			3	2	81, 87	84
			6	2	95, 97	96
	1,2,4-T	0.10	0	2	110, 119	114
			1	2	110, 119	114
			3	2	76, 81	78
			6	2	75, 79	77
	TA	0.10	0	2	95, 96	96
			1	2	95, 96	96
			3	2	81, 90	86
			6	2	102, 106	104
	TAA	0.10	0	2	112, 126	119
			1	2	112, 126	119
			3	2	94, 97	96
			6	2	105, 106	106
Radish tops	M11	0.10	0	2	91, 108	100
			1	2	91, 108	100
			3	2	109, 113	111
			6	2	86, 93	90
	M21	0.10	0	2	82, 87	84

TABLE C.1. Summary of Concurrent Recoveries of Metconazole, M11, M21, M30, and the Triazole Metabolites (1,2,4-T, TAA, and TA) from Plant Samples.

Matrix	Analyte	Spike Level (ppm)	Storage Interval (months)	Sample Size (n)	Recoveries (%)	Mean (%)
			1	2	82, 87	84
			3	2	91, 112	102
			6	2	104, 104	104
	M30	0.10	0	2	97, 101	99
			1	2	97, 101	99
			3	2	82, 93	88
			6	2	95, 101	98
	1,2,4-T	0.10	0	2	111, 132	122
			1	2	111, 132	122
			3	2	79, 82	80
			6	2	79, 90	84
	TA	0.10	0	2	120, 123	122
			1	2	120, 123	122
			3	2	63, 74	68
			6	2	102, 120	111
	TAA	0.10	0	2	91, 106	98
			1	2	91, 106	98
			3	2	99, 103	101
			6	2	98, 107	102
Soybean seed	*cis*-Metconazole	0.10	0	2	105, 106	106
			3	2	105, 106	106
			6	2	96, 99	98
	trans-Metconazole	0.10	0	2	100, 109	104
			3	2	100, 109	104
			6	2	99, 101	100
	M11	0.10	0	2	94, 106	100
			3	2	94, 106	100
			6	2	76, 108	92
	M21	0.10	0	2	100, 109	104
			3	2	100, 109	104
			6	2	84, 111	98
	M30	0.10	0	2	103, 117	110
			3	2	103, 117	110
			6	2	100, 110	105
	1,2,4-T	0.10	0	2	56, 81	68
			3	2	56, 81	68
			6	2	114, 116	115
	TA	0.10	0	2	68, 74	71
			3	2	68, 74	71
			6	2	84, 86	85
	TAA	0.10	0	2	100, 101	100
			3	2	100, 101	100

TABLE C.1. Summary of Concurrent Recoveries of Metconazole, M11, M21, M30, and the Triazole Metabolites (1,2,4-T, TAA, and TA) from Plant Samples.

Matrix	Analyte	Spike Level (ppm)	Storage Interval (months)	Sample Size (n)	Recoveries (%)	Mean (%)
			6	2	96, 108	102
	TA Hydrolysis	0.10	0	2	63, 70	66
			3	2	63, 70	66
Sugar beet root	M11	0.10	0	2	86, 97	92
			1	2	86, 97	92
			3	2	93, 102	98
			6	2	120, 121	120
	M21	0.10	0	2	82, 95	88
			1	2	82, 95	88
			3	2	107, 110	108
			6	2	102, 121	112
	M30	0.10	0	2	88, 95	92
			1	2	88, 95	92
			3	2	87, 113	100
			6	2	115, 115	115
Wheat hay	*cis*-Metconazole	0.10	0	2	91, 94	92
			1	2	91, 94	92
			3	2	81, 91	86
			6	2	90, 98	94
	trans-Metconazole	0.10	0	2	90, 97	94
			1	2	90, 97	94
			3	2	77, 89	83
			6	2	99, 101	100
	M11	0.10	0	2	93, 98	96
			1	2	93, 98	96
			3	2	90, 92	91
			6	2	89, 101	95
	M21	0.10	0	2	84, 95	90
			1	2	84, 95	90
			3	2	77, 84	80
			6	2	86, 97	92
	M30	0.10	0	2	92, 95	94
			1	2	92, 95	94
			3	2	88, 104	96
			6	2	92, 102	97
Wheat straw	M11	0.10	0	2	93, 103	98
			1	2	93, 103	98
			3	2	100, 104	102
			6	2	93, 94	94
	M21	0.10	0	2	85, 93	89
			1	2	85, 93	89
			3	2	89, 106	98

TABLE C.1. Summary of Concurrent Recoveries of Metconazole, M11, M21, M30, and the Triazole Metabolites (1,2,4-T, TAA, and TA) from Plant Samples.

Matrix	Analyte	Spike Level (ppm)	Storage Interval (months)	Sample Size (n)	Recoveries (%)	Mean (%)
			6	2	102, 104	103
	M30	0.10	0	2	96, 102	99
			1	2	96, 102	99
			3	2	91, 100	96
			6	2	88, 97	92
Wheat grain	M11	0.10	0	2	92, 94	93
			1	2	92, 94	93
			3	2	100, 107	104
			6	2	130, 131	130
	M21	0.10	0	2	85, 99	92
			1	2	85, 99	92
			3	2	90, 93	92
			6	2	110, 114	112
	M30	0.10	0	2	99, 103	101
			1	2	99, 103	101
			3	2	112, 113	112
			6	2	111, 119	115
	1,2,4-T	0.10	0	2	113, 116	114
			1	2	113, 116	114
			3	2	70, 72	71
			6	2	72, 73	73
	TA	0.10	0	2	88, 96	92
			1	2	88, 96	92
			3	2	74, 76	75
			6	2	79, 80	80
	TAA	0.10	0	2	118, 123	120
			1	2	118, 123	120
			3	2	77, 85	81
			6	2	89, 93	91

TABLE C.2. Stability of Residues of Metconazole, Metabolites M11, M21, M30, and the Triazole Metabolites 1,2,4-T, TAA, and TA in Plant Samples Following Storage at ≤-5 °C.

Matrix	Analyte	Spike Level (ppm)	Storage Interval (months)	Recovered Residues (ppm)	Mean Recovered Residues (ppm)	Mean Recovery (%)	Corrected % recovery[1]
Radish root	*cis*-Metconazole	0.10	0	0.0888, 0.0884	0.0886	89	98
			1	0.0920, 0.0898	0.0909	91	100
			3	0.0792, 0.0820	0.0806	81	105
			6	0.0796, 0.0838	0.0817	82	83
	trans-Metconazole	0.10	0	0.0878, 0.0908	0.0893	89	102
			1	0.0952, 0.0974	0.0963	96	110
			3	0.0956, 0.1012	0.0984	98	117

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TABLE C.2. Stability of Residues of Metconazole, Metabolites M11, M21, M30, and the Triazole Metabolites 1,2,4-T, TAA, and TA in Plant Samples Following Storage at ≤-5 °C.

Matrix	Analyte	Spike Level (ppm)	Storage Interval (months)	Recovered Residues (ppm)	Mean Recovered Residues (ppm)	Mean Recovery (%)	Corrected % recovery[1]
			6	0.0918, 0.0956	0.0937	94	98
	1,2,4-T	0.10	0	0.1123, 0.0837	0.098	98	85
			1	0.1037, 0.0979	0.1008	101	88
			3	0.0797, 0.0746	0.0772	77	97
			6	0.0754, 0.0864	0.0809	81	105
	TAA	0.10	0	0.1008, 0.119	0.1099	110	115
			1	0.1046, 0.1114	0.108	108	113
			3	0.0906, 0.0952	0.0929	93	108
			6	0.1104, 0.1018	0.1061	106	102
	TA	0.10	0	0.1123, 0.0946	0.1035	103	87
			1	0.0845, 0.0749	0.0797	80	67
			3	0.0971, 0.1046	0.1009	101	105
			6	0.0979, 0.1229	0.1104	110	104
Radish tops	M11	0.10	0	0.0866, 0.0974	0.092	92	92
			1	0.0976, 0.0798	0.0887	89	89
			3	0.0804, 0.1120	0.0962	96	86
			6	0.0928, 0.1064	0.0996	100	111
	M21	0.10	0	0.0876, 0.0924	0.09	90	106
			1	0.1004, 0.0872	0.0938	94	111
			3	0.0892, 0.1066	0.0979	98	96
			6	0.0880, 0.0944	0.0912	91	88
	M30	0.10	0	0.0948, 0.0868	0.0908	91	92
			1	0.0934, 0.0892	0.0913	91	92
			3	0.0692, 0.086	0.0776	78	89
			6	0.107, 0.1166	0.1118	112	114
	1,2,4-T	0.10	0	0.1373, 0.1056	0.1215	121	99
			1	0.119, 0.1133	0.1162	116	95
			3	0.0785, 0.065	0.0718	72	89
			6	0.097, 0.0834	0.0902	90	106
	TAA	0.10	0	0.1056, 0.1104	0.108	108	89
			1	0.1037, 0.1037	0.1037	104	85
			3	0.0948, 0.0936	0.0942	94	136
			6	0.0853, 0.0949	0.0901	90	81
	TA	0.10	0	0.1286, 0.0898	0.1092	109	110
			1	0.1056, 0.1056	0.0915	91	92
			3	0.0773, 0.0851	0.0925	92	91
			6	0.0998, 0.1037	0.1037	104	101
Soybean seed	*cis*-Metconazole	0.10	0	0.0922, 0.1030	0.0976	98	92
			3	0.0862, 0.0860	0.0861	86	81
			6	0.0748, 0.0914	0.0831	83	85

TABLE C.2. Stability of Residues of Metconazole, Metabolites M11, M21, M30, and the Triazole Metabolites 1,2,4-T, TAA, and TA in Plant Samples Following Storage at ≤-5 °C.

Matrix	Analyte	Spike Level (ppm)	Storage Interval (months)	Recovered Residues (ppm)	Mean Recovered Residues (ppm)	Mean Recovery (%)	Corrected % recovery[1]
	trans-Metconazole	0.10	0	0.1112, 0.0936	0.1024	102	97
			3	0.0870, 0.0830	0.085	85	81
			6	0.0872, 0.0952	0.0912	91	91
	M11	0.10	0	0.0942, 0.1080	0.1011	101	101
			3	0.0840, 0.0822	0.0831	83	83
			6	0.1142, 0.1018	0.108	108	117
	M21	0.10	0	0.1074, 0.1136	0.1105	111	106
			3	0.0946, 0.1118	0.1032	103	98
			6	0.1166, 0.0996	0.1081	108	110
	M30	0.10	0	0.096, 0.1046	0.1003	100	91
			3	0.092, 0.0926	0.0923	92	84
			6	0.08, 0.1066	0.0933	93	89
	1,2,4-T	0.10	0	0.1114, 0.0959	0.1037	104	151
			3	0.1046, 0.0876	0.0961	96	139
			6	0.0932, 0.0875	0.0904	90	78
	TAA	0.10	0	0.0949, 0.0947	0.0948	95	134
			3	0.0894, 0.084	0.0867	87	123
			6	0.096, 0.0875	0.0918	92	108
	TA	0.10	0	0.0769, 0.0712	0.0741	74	73
			3	0.079, 0.0734	0.0762	76	75
			6	0.1085, 0.0931	0.1008	101	99
	TA Hydrolysis	0.10	0	0.0738, 0.0619	0.0679	68	101
			3	0.0878, 0.0719	0.0799	80	119
Sugar beet root	M11	0.10	0	0.0976, 0.0910	0.0943	94	102
			1	0.0952, 0.0874	0.0913	91	99
			3	0.1058, 0.1052	0.1055	106	108
			6	0.1254, 0.1404	0.1329	133	110
	M21	0.10	0	0.0832, 0.0812	0.0822	82	92
			1	0.0890, 0.0896	0.0893	89	100
			3	0.0998, 0.1058	0.1028	103	94
			6	0.1074, 0.1102	0.1088	109	97
	M30	0.10	0	0.0878, 0.0926	0.0902	90	98
			1	0.09, 0.0748	0.0824	82	89
			3	0.1158, 0.091	0.1034	103	103
			6	0.1092, 0.1064	0.1078	108	94
Wheat hay	*cis*-Metconazole	0.10	0	0.09640, 0.09420	0.0953	95	102
			1	0.08960, 0.08300	0.0863	86	92
			3	0.0734, 0.0834	0.0784	78	91
			6	0.0912, 0.0870	0.0891	89	95

TABLE C.2. Stability of Residues of Metconazole, Metabolites M11, M21, M30, and the Triazole Metabolites 1,2,4-T, TAA, and TA in Plant Samples Following Storage at ≤-5 °C.

Matrix	Analyte	Spike Level (ppm)	Storage Interval (months)	Recovered Residues (ppm)	Mean Recovered Residues (ppm)	Mean Recovery (%)	Corrected % recovery[1]
	trans-Metconazole	0.10	0	0.0866, 0.0868	0.0867	87	93
			1	0.0842, 0.0850	0.0846	85	90
			3	0.0812, 0.0972	0.0892	89	107
			6	0.0930, 0.0974	0.0952	95	95
	M11	0.10	0	0.1020, 0.1024	0.1022	102	106
			1	0.0822, 0.0886	0.0854	85	89
			3	0.0986, 0.0926	0.0956	96	105
			6	0.1000, 0.1054	0.1027	103	108
	M21	0.10	0	0.0822, 0.0942	0.0882	88	98
			1	0.0878, 0.0828	0.0853	85	94
			3	0.1076, 0.0930	0.1003	100	123
			6	0.0930, 0.1030	0.098	98	107
	M30	0.10	0	0.0970, 0.0864	0.0917	92	98
			1	0.0846, 0.0924	0.0885	89	95
			3	0.1114, 0.0960	0.1037	104	108
			6	0.0944, 0.0962	0.0953	95	98
Wheat straw	M11	0.10	0	0.1084, 0.0832	0.0958	96	98
			1	0.0780, 0.0924	0.0852	85	87
			3	0.1072, 0.1078	0.1075	108	106
			6	0.1084, 0.1038	0.1061	106	113
	M21	0.10	0	0.0968, 0.0944	0.0956	96	108
			1	0.0858, 0.0884	0.0871	87	98
			3	0.1186, 0.1088	0.1137	114	116
			6	0.1000, 0.0986	0.0993	99	96
	M30	0.10	0	0.0960, 0.0922	0.0941	94	95
			1	0.0978, 0.0862	0.092	92	93
			3	0.0800, 0.0806	0.0803	80	83
			6	0.103, 0.097	0.1	100	108
Wheat grain	M11	0.10	0	0.0894, 0.0914	0.0904	90	97
			1	0.0930, 0.0978	0.0954	95	102
			3	0.0954, 0.0966	0.0960	96	92
			6	0.0932, 0.1322	0.1127	113	86
	M21	0.10	0	0.0912, 0.1014	0.0963	96	104
			1	0.0924, 0.0986	0.0955	96	104
			3	0.0926, 0.1148	0.1037	104	113
			6	0.1186, 0.0970	0.1078	108	96
	M30	0.10	0	0.0960, 0.0980	0.097	97	96
			1	0.0940, 0.0778	0.0859	86	85
			3	0.1216, 0.1120	0.1168	117	104
			6	0.1226, 0.1326	0.1276	128	111

TABLE C.2. Stability of Residues of Metconazole, Metabolites M11, M21, M30, and the Triazole Metabolites 1,2,4-T, TAA, and TA in Plant Samples Following Storage at ≤-5 °C.

Matrix	Analyte	Spike Level (ppm)	Storage Interval (months)	Recovered Residues (ppm)	Mean Recovered Residues (ppm)	Mean Recovery (%)	Corrected % recovery[1]
	1,2,4-T	0.10	0	0.1142, 0.1248	0.1195	120	104
			1	0.1219, 0.0858	0.1039	104	90
			3	0.0884, 0.0835	0.086	86	121
			6	0.0561, 0.0679	0.062	62	85
	TAA	0.10	0	0.0989, 0.0801	0.0895	90	98
			1	0.0828, 0.0938	0.0883	88	96
			3	0.0801, 0.0847	0.0824	82	109
			6	0.0596, 0.0519	0.0558	56	70
	TA	0.10	0	0.1286, 0.1037	0.1162	116	96
			1	0.1238, 0.1248	0.1243	124	102
			3	0.0858, 0.0888	0.0873	87	107
			6	0.0673, 0.061	0.0642	64	70

[1] Corrected for mean concurrent recovery (see Table C.1.).

D. CONCLUSION

Residues of *cis*- and *trans*-metconazole in/on radish root, soybean seed, and wheat hay; residues of M11, M21, and M30 in/on radish top, soybean seed, sugar beet root, and wheat hay, straw, and grain; and residues of the triazole metabolites in/on radish root, radish top, soybean seed, and wheat grain are stable in frozen storage for up to 6 months. An acceptable method was used for the quantitation of residues.

E. REFERENCES

DP#: 324541
Subject: Metconazole. Request for a Tolerance on Imported Bananas. Summary of Analytical Chemistry and Residue Data. Petition Number 9E05052.
From: N. Dodd
To: M. Waller
Date: 12/14/05
MRIDs: 44721506, 44721507, 44721508, 44721509, 44721510, and 44721511

F. DOCUMENT TRACKING

RDI: N. Dodd (2/20/08)
Petition Numbers: 6F7094 and 6F7095
DP#s: 348168 and 348206
PC Code: 125619

Template Version June 2005

Primary Evaluator	This DER was originally prepared under contract by Dynamac Corporation.
Approved by	Nancy Dodd, Chemist *Nancy Dodd* Date: 2/20/08 Registration Action Branch 3 Health Effects Division (7509P)

This DER was originally prepared under contract by Dynamac Corporation (2275 Research Boulevard, Suite 300; Rockville, MD 20850; submitted 09/18/2007). The DER has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

46902224 White, M.; Saha, M. (2006) The Magnitude of Residues of Metconazole (BAS 555 F) and its Metabolites in Wheat: Final Report. Project Number: 137711, 2006/7006723. Unpublished study prepared by BASF Agro Research, Southeast Ag Research, Inc. and Shoffner Farm Research. 203 p.

EXECUTIVE SUMMARY:

BASF Corporation has submitted field trial data for metconazole on wheat. Fifteen field trials (eight winter wheat and seven spring wheat) were conducted in the United States and Canada in Zones 2 (GA, 1 trial), 4 (AR; 1 trial), 5 (IL, NE; 2 trials), 6 (OK; 1 trial), 7 (ND, NE; 3 trials), 8 (OK, TX; 2 trials), 11 (ID; 1 trial), and 14 (AB, MB, SK; 4 trials) during the 2004-2005 growing season. Because Canadian Zone 14 is contiguous with two major U.S. wheat-growing regions, Zones 5 and 7, HED has concluded that results from the Canadian trials may be used to address U.S. data requirements for wheat.

Each test site included one control plot and two treated plots. The treated plots received two broadcast foliar applications of a 0.75 lb ai/gal soluble concentrate/liquid (SC/L) formulation of metconazole at 0.08-0.10 lb ai/A/application, with a 6- to 8-day retreatment interval, for a total seasonal rate of 0.18-0.21 lb ai/A. Applications were initiated four weeks prior to the harvest of mature grain (plot 2) or two weeks prior to the cutting of hay (plot 3). Applications were made in 11-30 gal/A spray volumes using ground equipment. A nonionic surfactant was added as a spray adjuvant for all applications.

Wheat hay was harvested 6-8 days after the last application and allowed to dry in the field or under cover for 0-14 days prior to collection. Wheat grain and straw were harvested 20-22 days after the last application. Additional hay samples were collected from two trials 0, 7-8, and 14 days after the last application, and grain and straw samples were harvested 14, 21-22, 28, and 35-36 days after the last application to generate residue decline data.

Samples were analyzed for residues of *cis*- and *trans*-metconazole, the metabolites M11, M21, and M30, and the triazole metabolites [wheat grain only; 1,2,4-triazole (1,2,4-T), triazolylalanine (TA), and triazolylacetic acid (TAA)], using an LC/MS/MS method (BASF Method D0508). Residues of metabolites M11, M21, and M30 were converted to parent equivalents using molecular weight conversion factors of 0.95 for M11 and M21 and 0.96 for M30. The validated limits of quantitation (LOQs) were 0.01 ppm for the parent metconazole (sum of *cis* and *trans* isomers at 0.005 ppm each), M11, M21, and M30 in/on wheat samples. The validated LOQ was 0.05 ppm for 1,2,4-T, TA, and TAA. The method was adequate for data collection based on acceptable concurrent method recoveries.

Samples were stored frozen (<-10 °C) from harvest to extraction for 122-249 days (4.0-8.2 months) for wheat hay, 122-237 days (4.0-7.8 months) for wheat grain, and 82-192 days (2.7-6.3 months) for wheat straw, and were analyzed within 0-4 days of extraction. Adequate storage stability data are available to support the storage conditions and durations of samples for the wheat field trials.

Maximum residues of *cis*-and *trans*-metconazole in/on wheat hay were 10.98 and 1.72 ppm, respectively; maximum total metconazole residues (sum of *cis* and *trans* isomers) were 12.66 ppm. In wheat grain, maximum residues of *cis*- and *trans*-metconazole were 0.097 and 0.019 ppm, respectively, and maximum total metconazole residues were 0.116 ppm. In wheat straw, maximum residues of *cis*- and *trans*-metconazole were 8.39 and 4.720 ppm, respectively, and maximum total metconazole residues were 9.842 ppm. Maximum residues of metabolite M11 were 0.48, 0.03, and 1.29 ppm for hay, grain, and straw, respectively; maximum residues of M21 were 0.19, 0.010, and 0.45 ppm for hay, grain, and straw, respectively; and maximum residues of metabolite M30 were 0.06, <0.01, and 0.14 ppm in hay, grain, and straw.

Maximum residues of 1,2,4-T, TA, and TAA in/on samples of wheat grain were below the LOQ (<0.05 ppm), 0.691 ppm, and 0.360 ppm, respectively.

The submitted residue decline data indicated that total metconazole residues (sum of *cis* and *trans* isomers) generally declined or did not increase in wheat hay, grain, and straw with increasing preharvest intervals.

HED notes that wheat forage was not collected from any trial site because applications were initiated at a later growth stage.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the field trial residue data are classified as scientifically acceptable. Wheat forage was not collected; however, data on wheat forage are not required for late-season applications (after flag leaf emergence).

The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP#s 348168 and 348206.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an impact on the validity of the study.

A. BACKGROUND INFORMATION

Metconazole [5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol] is a broad-spectrum triazole Group 3 fungicide (sterol biosynthesis inhibitors). There are currently no registered uses of metconazole in the U.S.; however, a tolerance has been established for banana, and a Section 18 emergency exemption and supporting time-limited tolerances have been granted for use on soybean. BASF Corporation has applied for registration of metconazole in the U.S. for use on barley, oats, rye, soybeans, sugar beets, triticale, and wheat.

The chemical structure and nomenclature of metconazole, and the physicochemical properties of the technical grade of metconazole are presented in Tables A.1 and A.2.

TABLE A.1. Metconazole Nomenclature.

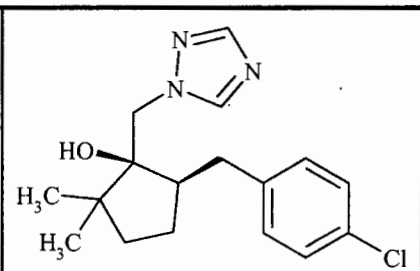
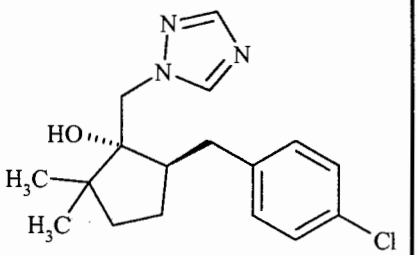
Chemical structure	 *cis*-isomer	 *trans*-isomer
Common name	Metconazole	
Company experimental name	KNF-S-474m (Kureha); BAS 555 F (BASF); V-10116 (Valent)	
IUPAC name	(1RS,5RS:1RS,5SR)-5-(4-chlorobenzyl)-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	
CAS name	5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	
CAS registry number	125116-23-6 (*cis*- and *trans*-isomers) 115850-27-6 (*cis*-isomer) 115850-28-7 (*trans*-isomer)	
End-use products (EP)	50% WDG (Metconazole 50 WDG Fungicide, EPA File Symbol 59639-RUT) 0.75 lb/gal SC/L (Caramba™ Fungicide, EPA File Symbol No. 7969-EUA) 0.67 lb/gal SC/L formulation (BAS 556 01F Fungicide, EPA File Symbol No. 7969-EUT; also contains the active ingredient pyraclostrobin at 0.83 lb/gal)	

TABLE A.1. Metconazole Nomenclature.

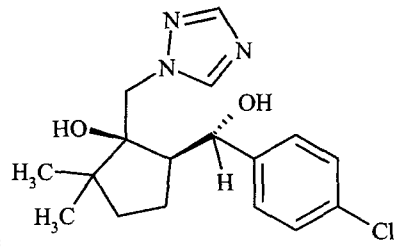
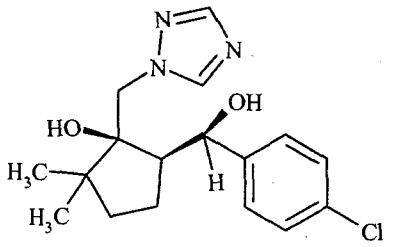
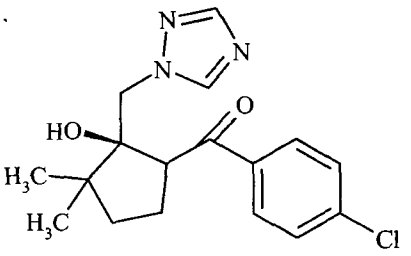
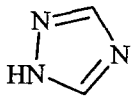
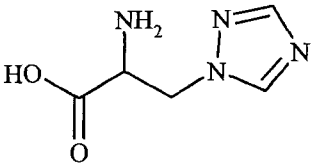
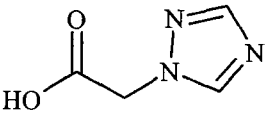
 Metconazole metabolite M11	 Metconazole metabolite M21	 Metconazole metabolite M30
 Triazole metabolite 1,2,4-triazole (1,2,4-T)	 Triazole metabolite triazolylalanine (TA)	 Triazole metabolite triazolylacetic acid (TAA)

Table A.2. Physicochemical Properties of Metconazole

Parameter	Value				References* (MRID)
Melting point/range	100.0-108.4°C (using Electrothermal Digital Melting Point Apparatus) (AC900,768 technical grade)				44721505
pH	5.81 at 25°C (1% aqueous suspension)				46808402
Relative density (20°C)	1.14 (relative density to water at 4°C, using capillary-stoppered, density-specific gravity bottle) (Lot No. AC 8879-140B)				44721505
Water solubility (20°C)	Using shake-flask method: 18.7 ± 1.0 mg/L (*cis*-isomer, WL148271, KNF-S-474m) 13.6 ± 1.7 mg/L (*trans*-isomer, WL148271, KNF-S-474m)				44721505
Solvent solubility (g/L) at 20°C	Solvent	Metconazole	*cis*	*trans*	44721505
	Acetone	363	251	117	
	Methanol	403	294	117	
	dichloromethane	481	343	141	
	ethyl acetate	260	173	90.0	
	Propanol	132	86.6	46.7	
	Toluene	103	66.2	38.0	
	Hexane	1.40	0.929	0.483	
Vapor pressure (20°C)	Using gas-saturation method: $< 1.23 \times 10^{-5}$ Pa or 9.23×10^{-8} mm Hg (metconazole) $< 1.04 \times 10^{-5}$ Pa or 7.80×10^{-8} mm Hg (*cis*-isomer) $< 1.96 \times 10^{-6}$ Pa or 1.47×10^{-8} mm Hg (*trans*-isomer)				44721505
Dissociation constant (pK_a)	11.38±0.03 and 1.06±0.03 (in water at 29.1°C using spectrophotometric method; Lot No. AC 8879-140B)				44721505

Table A.2. Physicochemical Properties of Metconazole					
Parameter	Value				References* (MRID)
Octanol/water partition coefficient, Log(K_{OW})	At 20 °C (using flask shaking method): K_{ow} (log K_{ow}) = 7090±989 (3.85) (Lot No. AC 8879-140B) (TGAI) K_{ow} (log K_{ow}) = 7150±803 (3.85) (*cis*-isomer, CL 354,801) K_{ow} (log K_{ow}) = 6800±1700 (3.8) (*trans*-isomer, CL 354,802)				44721505
UV/visible absorption spectrum	pH	λ	A	log ε	46808403
	cis-isomer				
	2.0	221.4	0.828	4.03	
	6.8		0.8452	4.04	
	7.0		0.9126	4.08	
	10.3		0.7226	3.98	
	trans-isomer				
	2.0	221.4	0.9053	4.07	
	7.0		0.9547	4.10	
	10.1		0.9893	4.11	

* Product Chemistry Reviews: DP #256877, Shyam Mathur, Ph.D., 9/12/2000 and DP #329168, Shyam Mathur, Ph.D., 7/13/07.

B. EXPERIMENTAL DESIGN

B.1. Study Site Information

Fifteen field trials (eight winter wheat and seven spring wheat) were conducted in the United States and Canada in Zones 2 (GA, 1 trial), 4 (AR; 1 trial), 5 (IL, NE; 2 trials), 6 (OK; 1 trial), 7 (ND, NE; 3 trials), 8 (OK, TX; 2 trials), 11 (ID; 1 trial), and 14 (AB, MB, SK; 4 trials) during the 2004-2005 growing season.

Each test site included one control plot and two treated plots. The treated plots received two broadcast foliar applications of a 0.75 lb ai/gal soluble concentrate/liquid (SC/L) formulation of metconazole at 0.08-0.10 lb ai/A/application, with a 6- to 8-day retreatment interval, for a total seasonal rate of 0.18-0.21 lb ai/A. Applications were initiated four weeks prior to the harvest of mature grain (plot 2) or two weeks prior to the cutting of hay (plot 3). Applications were made in 11-30 gal/A spray volumes using ground equipment. A nonionic surfactant was added as a spray adjuvant for all applications.

Wheat hay was harvested 6-8 days after the last application and allowed to dry in the field or under cover for up to 14 days prior to collection. Wheat grain and straw were harvested 20-22 days after the last application. Additional hay samples were collected from two trials 0, 7-8, and 14 days after the last application and grain and straw samples were harvested 14, 21-22, 28, and 35-36 days after the last application to generate residue decline data. Wheat forage was not collected from any trial site because applications were initiated at a later growth stage.

The test crops were grown and maintained according to typical agricultural practices for each region; maintenance pesticides and fertilizers were used to produce a commercial quality crop. Irrigation was used to supplement rainfall as needed. Trial site conditions are presented in Table B.1.1, and the study use pattern is presented in Table B.1.2. The crop varieties grown are identified in Table C.3.

For each field trial, the petitioner presented the weather conditions at application and summarized the weather conditions for the duration of the trials. The petitioner reported abnormal meteorological conditions in several trial sites, which are summarized in Table B.1.1. These unusual weather conditions did not have an adverse effect on the wheat crops.

TABLE B.1.1. Trial Site Conditions.

Trial Identification (City, State; Year)	Soil characteristics				Meteorological Data	
	Type	%OM	pH	CEC (meq/g)	Overall rainfall range	Overall Temperature Range (°C)
Winter Wheat						
Tift, GA; 2004 (RCN R05044)	Loamy Sand	1.0	5.5	Not provided	Higher than normal	Normal
Jackson, AR; 2004 (RCN R05045)	Loamy Sand	0.8	5.8	Not provided	Below normal in May	Normal
York, NE; 2004 (RCN R05046)	Silty Clay Loam	2.8	6.4	Not provided	Below normal in May. Above normal in July	Normal
Clinton, IL; 2004 (RCN R05047)	Silt Loam	1.8	6.8	Not provided	Normal	Normal
Hall, NE; 2004 (RCN R05048)	Clay Loam	2.7	6.6	Not provided	Above normal for May-June. Below normal for July	Above normal for May-July
Caddo, OK; 2005 (RCN R05051)	Sandy Loam	0.9	5.5	Not provided	Below normal in March-April. Above normal in June	Normal
Caddo, OK; 2004 (RCN R05052)	Silt Loam	1.0	6.5	Not provided	Well below normal in March-April	Normal
Lubbock, TX; 2005 (RCN R05053)	Sandy Loam	0.4	8.4	Not provided	Normal	Normal
Spring Wheat						
Mc Henry, ND; 2005 (RCN R05049)	Loam	3.2	5.6	Not provided	Much above normal in June	Normal
Cass, ND; 2005 (RCN R05050)	Loam	4.1	8.2	Not provided	Above normal in June and August	Normal
Payette, ID; 2005 (RCN R05054)	Silty Clay Loam	0.7	6.2	Not provided	Normal	Normal
SK, Canada; 2005 (RCN R05055)	Fine Silty Loam	5.6	5.8	Not provided	Generally wetter than normal	Generally cooler than normal.
MB, Canada; 2005 (RCN R05056)	Loam	4.9	7.5	Not provided	May-July above normal. Below normal in August.	Cooler than normal in May-August.
AB, Canada; 2005 (RCN R05057)	Clay Loam	7.6	6.2	Not provided	Generally wetter than normal.	Normal
AB, Canada; 2005 (RCN R05058)	Loam	5.6	6.5	Not provided	Generally wetter than normal.	Normal

TABLE B.1.2. Study Use Pattern.

Trial identification: County, State; Year (Trial ID)	EP[1]	Application					Tank Mix/ Adjuvants[4]
		Method; Timing	Volume[2] GPA [L/ha]	Rate (lb ai/A) [kg ai/ha]	RTI[3] (days)	Total Rate (lb ai/A) [kg ai/ha]	
Tift, GA; 2004 (RCN R05044)	0.75 SC/L lb/gal	1. Broadcast foliar; first grains half final size	14.3 [134]	0.102 [0.11]	8	0.20 [0.23]	Penatron (NIS)
		2. Broadcast foliar; soft dough	15.0 [140]	0.102 [0.11]			
		1. Broadcast foliar; beginning of stem elongation	18.3 [171]	0.100 [0.11]	8	0.20 [0.23]	
		2. Broadcast foliar; flag leaf stage	17.4 [162]	0.102 [0.11]			
Jackson, AR; 2004 (RCN R05045)	0.75 lb/gal SC/L	1. Broadcast foliar; early milk	20.0 [187]	0.100 [0.11]	6	0.20 [0.23]	LI-700 (NIS)
		2. Broadcast foliar; medium milk	20.2 [189]	0.101 [0.11]			
		1. Broadcast foliar; beginning of flowering	20.2 [189]	0.101 [0.11]	7	0.20 [0.23]	
		2. Broadcast foliar; full flowering	20.0 [187]	0.100 [0.11]			
York, NE; 2004 (RCN R05046)	0.75 lb/gal SC/L	1. Broadcast foliar; medium milk	19.9 [186]	0.099 [0.11]	7	0.20 [0.22]	Activator plus (NIS)
		2. Broadcast foliar; early dough	20.1 [188]	0.101 [0.11]			
		1. Broadcast foliar; beginning of flowering	19.8 [185]	0.101 [0.11]	7	0.20 [0.22]	
		2. Broadcast foliar; end of flowering	19.9 [186]	0.100 [0.11]			
Clinton, IL; 2004 (RCN R05047)	0.75 lb/gal SC/L	1. Broadcast foliar; late milk	12.3 [115]	0.099 [0.11]	7	0.20 [0.22]	Preference (NIS)
		2. Broadcast foliar; early dough	16.9 [158]	0.101 [0.11]			
		1. Broadcast foliar; beginning of heading	14.3 [133]	0.099 [0.11]	7	0.20 [0.22]	
		2. Broadcast foliar; early dough	16.3 [152]	0.100 [0.11]			
Hall, NE; 2004 (RCN R05048)	0.75 lb/gal SC/L	1. Broadcast foliar; medium milk	20.2 [188]	0.101 [0.11]	7	0.20 [0.23]	Activator plus (NIS)
		2. Broadcast foliar; late milk	20.2 [189]	0.101 [0.11]			
		1. Broadcast foliar; beginning of flowering	19.8 [185]	0.099 [0.11]	8	0.20 [0.22]	
		2. Broadcast foliar; end of flowering	19.4 [181]	0.100 [0.11]			

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TABLE B.1.2. Study Use Pattern.

Trial identification: County, State; Year (Trial ID)	EP[1]	Application					Tank Mix/ Adjuvants[4]
		Method; Timing	Volume[2] GPA [L/ha]	Rate (lb ai/A) [kg ai/ha]	RTI[3] (days)	Total Rate (lb ai/A) [kg ai/ha]	
Mc Henry, ND; 2005 (RCN R05049)	0.75 lb/gal SC/L	1. Broadcast foliar; early milk	12.0 [113]	0.099 [0.11]	7	0.20 [0.22]	R-11 (NIS)
		2. Broadcast foliar; medium milk	12.1 [113]	0.102 [0.11]			
		1. Broadcast foliar; late boot stage	12.1 [113]	0.100 [0.11]	7	0.20 [0.22]	
		2. Broadcast foliar; full flowering	12.1 [114]	0.101 [0.11]			
Cass, ND; 2005 (RCN R05050)	0.75 lb/gal SC/L	1. Broadcast foliar; early milk	16.3 [152]	0.103 [0.12]	6	0.21 [0.23]	Activator 90 (NIS)
		2. Broadcast foliar; late milk	15.7 [147]	0.103 [0.12]			
		1. Broadcast foliar; end of flowering	16.3 [153]	0.103 [0.12]	6	0.21 [0.23]	
		2. Broadcast foliar; early milk	16.0 [150]	0.102 [0.11]			
Caddo, OK; 2005 (RCN R05051)	0.75 lb/gal SC/L	1. Broadcast foliar; medium milk	13.1 [122]	0.100 [0.11]	7	0.20 [0.22]	Baron (NIS)
		2. Broadcast foliar; soft dough	13.5 [126]	0.100 [0.11]			
		1. Broadcast foliar; end of heading	13.5 [126]	0.101 [0.11]	8	0.20 [0.22]	
		2. Broadcast foliar; first grains half final size	13.8 [129]	0.100 [0.11]			
Caddo, OK; 2004 (RCN R05052)	0.75 lb/gal SC/L	1. Broadcast foliar; early dough	13.7 [128]	0.100 [0.11]	7	0.18 [0.20]	Baron (NIS)
		2. Broadcast foliar; soft dough	11.3 [105]	0.083 [0.09]			
		1. Broadcast foliar; first grains half final size	13.4 [125]	0.100 [0.11]	6	0.20 [0.22]	
		2. Broadcast foliar; late milk	13.7 [129]	0.100 [0.11]			
Lubbock, TX; 2005 (RCN R05053)	0.75 lb/gal SC/L	1. Broadcast foliar; end of flowering	15.1 [141]	0.101 [0.11]	8	0.20 [0.22]	R-11 (NIS)
		2. Broadcast foliar; hard dough	14.8 [138]	0.099 [0.11]			
		1. Broadcast foliar; beginning of flowering	15.0 [141]	0.099 [0.11]	6	0.20 [0.22]	
		2. Broadcast foliar; end of heading	15.0 [140]	0.099 [0.11]			

TABLE B.1.2. Study Use Pattern.

Trial identification: County, State; Year (Trial ID)	EP[1]	Application					Tank Mix/ Adjuvants[4]
		Method; Timing	Volume[2] GPA [L/ha]	Rate (lb ai/A) [kg ai/ha]	RTI[3] (days)	Total Rate (lb ai/A) [kg ai/ha]	
Payette, ID; 2005 (RCN R05054)	0.75 lb/gal SC/L	1. Broadcast foliar; soft dough	29.7 [278]	0.099 [0.11]	6	0.20 [0.22]	R-11 (NIS)
		2. Broadcast foliar; hard dough	30.3 [283]	0.101 [0.11]			
		1. Broadcast foliar; middle of heading	30.3 [284]	0.103 [0.12]	7	0.20 [0.23]	
		2. Broadcast foliar; full flowering	30.2 [283]	0.101 [0.11]			
SK, Canada; 2005 (RCN R05055)	0.75 lb/gal SC/L	1. Broadcast foliar; late milk	14.4 [135]	0.099 [0.11]	6	0.20 [0.22]	AgSurf (NIS)
		2. Broadcast foliar; soft dough	15.9 [149]	0.100 [0.11]			
		1. Broadcast foliar; first awns visible	14.9 [139]	0.100 [0.11]	7	0.20 [0.22]	
		2. Broadcast foliar; full flowering	14.3 [134]	0.100 [0.11]			
MB, Canada; 2005 (RCN R05056)	0.75 lb/gal SC/L	1. Broadcast foliar; early dough	23.3 [218]	0.102 [0.11]	6	0.20 [0.23]	AgSurf (NIS)
		2. Broadcast foliar; soft dough	21.0 [197]	0.101 [0.11]			
		1. Broadcast foliar; middle of heading	21.3 [199]	0.101 [0.11]	7	0.20 [0.22]	
		2. Broadcast foliar; first grains half final size	21.4 [200]	0.099 [0.11]			
AB, Canada; 2005 (RCN R05057)	0.75 lb/gal SC/L	1. Broadcast foliar; early dough	24.2 [226]	0.100 [0.11]	7	0.20 [0.22]	Merge (NIS)
		2. Broadcast foliar; soft dough	24.9 [233]	0.100 [0.11]			
		1. Broadcast foliar; middle of heading	26.0 [243]	0.101 [0.11]	7	0.20 [0.23]	
		2. Broadcast foliar; beginning of flowering	26.2 [245]	0.100 [0.11]			
AB, Canada; 2005 (RCN R05058)	0.75 lb/gal SC/L	1. Broadcast foliar; soft dough	21.6 [202]	0.100 [0.11]	7	0.20 [0.22]	Merge (NIS)
		2. Broadcast foliar; soft dough	24.1 [225]	0.100 [0.11]			
		1. Broadcast foliar; end of heading	25.8 [241]	0.098 [0.11]	7	0.19 [0.22]	
		2. Broadcast foliar; full flowering	24.2 [226]	0.097 [0.11]			

[1] EP = End-use Product
[2] Gallons per acre or L/ha
[3] RTI = Retreatment Interval
[4] NIS=Nonionic surfactant

TABLE B.1.3. Trial Numbers and Geographical Locations.

NAFTA Growing Zones	Wheat		
	Submitted	Requested [1]	
		Canada	U.S.
1			
1A			
2	1		1
3			
4	1		1
5	2	2	5 [3]
5A			
5B			
6	1		1
7	3	7	5 [4]
7A		1	
8	2		6 [4]
9			
10			
11	1		1
12			
13			
14	4	10	
15			
16			
17			
18			
19			
20			
21			
Total	15	20	20 [15]

[1] The requested number and geographic distribution of field trials for wheat, according to OPPTS Guideline 860.1500 and PMRA Directive 98-2, are shown. Where two entries are provided for a region, the second number [given in brackets] is for situations where a 25% reduction in the number of trials is possible due to the crop being a representative commodity used to obtain a crop group tolerance.

B.2. Sample Handling and Preparation

Wheat samples were placed in coolers and stored frozen at the field sites 5 hours after harvest or collection for hay. Samples remained in frozen storage at the field facilities for up to 51 days until shipment via ACDS freezer truck to the analytical laboratory, BASF Agro Research (Research Triangle Park, NC), for analysis. In preparation for analysis, wheat samples were homogenized in the presence of dry ice. All samples remained frozen at all times except during homogenization and subsampling for analysis.

B.3. Analytical Methodology

Wheat samples were analyzed for residues of metconazole, the metabolites M11, M21, and M30, and the triazole metabolites (wheat grain only), 1,2,4-T, TA, and TAA, using an LC/MS/MS method (BASF Method D0508). A brief description of the method was included in the MRID. Briefly, residues of metconazole, M11, M21, and M30 were extracted with acetonitrile (ACN):water (70:30, v:v). The extracts were diluted with methanol:water (80:20, v:v), filtered, and reserved for LC/MS/MS analysis. For determination of residues of 1,2,4-T, TA, and TAA, a separate aliquot of the initial extract was evaporated to dryness, redissolved in 0.1% formic acid in water, filtered, and reserved for LC/MS/MS analysis. An optional clean-up step was used for determination of TA in wheat grain if needed. A separate aliquot of the initial extract was diluted with methanol/water and applied to an SPE cartridge; residues were eluted with 1% NH_4OH in methanol. The resulting eluate was evaporated to dryness and redissolved in 0.1% formic acid in water as for other extracts. Residues of metabolites M11, M21, and M30 were converted to parent equivalents using molecular weight conversion factors of 0.95 for M11 and M21 and 0.96 for M30.

The validated LOQ was 0.01 ppm for the parent metconazole (sum of *cis* and *trans* isomers at 0.005 ppm each), M11, M21, and M30 in/on wheat samples. The validated LOQ was 0.05 ppm for 1,2,4-T, TA, and TAA. The reported limit of detection was 20% LOQ.

The method was validated concurrently with the analysis of field samples using samples of untreated wheat hay, grain, and straw fortified at 0.005 and 0.5 ppm with *cis*- and *trans*-metconazole; at 0.01 and 1.00 ppm with M11, M21, and M30; and at 0.05 and 5.00 ppm with 1,2,4-T, TA, and TAA.

C. RESULTS AND DISCUSSION

Samples were stored frozen (<-10 °C) from harvest to extraction for 122-249 days (4.0-8.2 months) for wheat hay, 122-237 days (4.0-7.8 months) for wheat grain, and 82-192 days (2.7-6.3 months) for wheat straw, and were analyzed within 0-4 days of extraction. Adequate storage stability data are available indicating that: (1) residues of *cis*- and *trans*-metconazole are relatively stable under frozen storage conditions in wheat grain, rye forage, and wheat straw for up to 12 months (refer to 46902218.der.doc); (2) residues of M11, M21, and M30 are stable in/on wheat hay, straw, and grain for up to 6 months (refer to 46902223.der.doc); and (3) residues of 1,2,4-T, TA, and TAA are stable/relatively stable in/on wheat grain for up to 6 months (refer to 46902223.der.doc). These data are sufficient to support the storage conditions and durations for the wheat field trials.

Concurrent method recovery data are presented in Table C.1. Samples were analyzed for residues of metconazole, metabolites M11, M21, and M30, and the triazole metabolites 1,2,4-T, TA, and TAA using LC/MS/MS Method D0508. Residues of metabolites M11, M21, and M30 were converted to parent equivalents using molecular weight conversion factors of 0.95 for M11 and M21 and 0.96 for M30. The method was adequate for data collection based on acceptable concurrent method recovery data. Concurrent method recoveries were generally within the

acceptable range of 70-120% for wheat hay, grain, and straw fortified at 0.005 and 0.5 ppm with *cis*- and *trans*-metconazole; at 0.01 and 1.00 ppm with M11, M21, and M30; and at 0.05 and 5.00 ppm with 1,2,4-T, TA, and TAA. Apparent residues of *cis*- and *trans*-metconazole, metabolites M11, M21, and M30, and 1,2,4-T were each below the respective LOQs in/on 15 samples each of untreated wheat hay, grain, and straw. Residues of TA above the LOQ (0.057-0.296 ppm) were recovered in seven of the fifteen untreated samples, and residues of TAA above the LOQ (0.061-0.121 ppm) were recovered in four of the fifteen untreated samples. These residues were generally lower than residues in the associated treated samples.

Residue data from the wheat field trials are reported in Tables C.3.1 and C.3.2, and the residue data for wheat are summarized in Tables C.4.1 and C.4.2. Residues of *cis*-and *trans*-metconazole in/on wheat hay were 1.16-10.98 and 0.17-1.72 ppm, respectively; total metconazole residues (sum of *cis* and *trans* isomers) were 1.33-12.66 ppm. In wheat grain, residues of *cis*- and *trans*-metconazole were 0.006-0.097 and <0.005-0.019 ppm, respectively, and total metconazole residues were 0.011-0.116 ppm. In wheat straw, residues of *cis*- and *trans*-metconazole were 1.53-8.39 and 0.048-4.720 ppm, respectively, and total metconazole residues were 0.266-9.842 ppm. Residues of metabolite M11 were <0.01-0.48, <0.01-0.03, and 0.03-1.29 ppm for hay, grain, and straw, respectively; residues of M21 were 0.03-0.19, <0.01-0.01, and 0.04-0.45 ppm for wheat hay, grain, and straw, respectively; and residues of M30 were <0.01-0.06 ppm, <0.01, and 0.01-0.14 ppm for hay, grain, and straw.

Residues of 1,2,4-T, TA, and TAA in/on samples of wheat grain were <0.05 ppm, <0.05-0.691 ppm, and <0.05-0.360 ppm, respectively.

The submitted residue decline data indicated that total metconazole residues (sum of *cis* and *trans* isomers) generally declined or did not increase in wheat hay, grain, and straw with increasing harvest intervals.

TABLE C.1. Summary of Concurrent Recoveries of Metconazole and Metabolites from Wheat.

Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. (%)
Grain	*cis*-Metconazole	0.005	3	76, 85, 98	86 ± 11
		0.500	3	92, 100, 105	99 ± 6
	trans-Metconazole	0.005	3	78, 88, 115	94 ± 19
		0.500	3	90, 99, 119	103 ± 15
	M11	0.010	3	90, 91, 105	95 ± 8
		1.000	3	89, 99, 106	98 ± 9
	M21	0.010	3	97, 98, 99	98 ± 1
		1.000	3	84, 106, 113	101 ± 15
	M30	0.010	3	98, 101, 106	102 ± 4
		1.000	3	87, 108, 115	103 ± 15
	1,2,4-T	0.050	3	86, 97, 116	100 ± 15
		5.000	3	82, 86, 98	89 ± 8
	TA	0.050	3	65, 95, 125	95 ± 30
		5.000	3	91, 92, 99	94 ± 4
	TAA	0.050	3	74, 80, 82	79 ± 4

TABLE C.1. Summary of Concurrent Recoveries of Metconazole and Metabolites from Wheat.

Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. (%)
		5.000	3	75, 82, 99	86 ± 13
Hay	*cis*-Metconazole	0.005	3	70, 74, 88	77 ± 10
		0.500	3	85, 88, 100	91 ± 8
	trans-Metconazole	0.005	3	84, 89, 98	90 ± 7
		0.500	3	94, 104, 120	106 ± 14
	M11	0.010	3	73, 75, 81	77 ± 4
		1.000	3	87, 88, 108	95 ± 12
	M21	0.010	3	87, 93, 108	96 ± 11
		1.000	3	93, 99, 107	99 ± 7
	M30	0.010	3	79, 88, 95	87 ± 8
		1.000	3	91, 96, 106	98 ± 7
Straw	*cis*-Metconazole	0.005	3	70, 72, 81	74 ± 6
		0.500	3	86, 100, 112	99 ± 13
	trans-Metconazole	0.005	3	74, 82, 88	81 ± 7
		0.500	3	102, 112, 117	110 ± 8
	M11	0.010	3	57, 70, 94	74 ± 19
		1.000	3	102, 104, 129	112 ± 15
	M21	0.010	3	60, 71, 90	74 ± 15
		1.000	3	105, 106, 113	108 ± 5
	M30	0.010	3	71, 72, 74	72 ± 2
		1.000	3	104, 106, 112	107 ± 4

TABLE C.2. Summary of Storage Conditions.

Matrix	Storage Temperature (°C)	Actual Storage Duration [1] Days (Months)	Interval of Demonstrated Storage Stability
Hay	< -10	122-249 (4.0-8.2)	The available storage stability data indicate that residues of *cis*- and *trans*-metconazole are relatively stable in wheat grain, rye forage, and wheat straw for up to 12 months; and that residues of M11, M21, and M30 are stable in/on wheat hay, straw, and grain, and residues of 1,2,4-T, TA, and TAA are stable/relatively stable in/on wheat grain for up to 6 months.[2]
Grain		122-237 (4.0-7.8)	
Straw		82-192 (2.7-6.3)	

[1] Storage duration from harvest to extraction is reported by the petitioner. Samples were analyzed within 0-2 days of extraction.
[2] Refer to 46902218.der.doc and 46902223.der.doc.

TABLE C.3.1 Residue Data for Metconazole, M11, M21, and M30 from Wheat Field Trials with Metconazole.

Trial ID (County, State; Year)	Zone	Crop; Variety	Matrix	Total Rate (lb ai/A)	PHI (days)[1]	Metconazole Residues (ppm parent equivalents)						
						Metconazole			Metabolites			Total[2]
						cis	*trans*	Total	M11	M21	M30	
Tift, GA; 2004 (RCN R05044)	2	Winter; Pioneer 26R24	Hay	0.20	7 [8]	3.160	0.628	3.788	0.02	0.04	<0.01	<3.9
						3.800	0.736	4.536	0.02	0.05	<0.01	<4.6
			Grain	0.02	21	0.030	0.007	0.037	0.02	<0.01	<0.01	<0.08
						0.027	0.007	0.035	0.02	<0.01	<0.01	<0.08
			Straw	0.20	21	1.200	0.269	1.469	0.86	0.09	0.08	2.5
						1.630	0.349	1.979	1.29	0.12	0.11	3.5
Jackson, AR; 2004 (RCN R05045)	4	Winter; Genesis R033	Hay	0.20	7 [5]	5.140	0.868	6.008	0.05	0.06	0.01	6.1
						5.420	0.940	6.360	0.05	0.06	0.01	6.5
			Grain	0.20	21	0.076	0.011	0.087	<0.01	<0.01	<0.01	<0.12
						0.083	0.017	0.100	<0.01	<0.01	<0.01	<0.13
			Straw	0.20	21	6.500	1.130	7.630	0.39	0.19	0.05	8.3
						6.800	1.280	8.080	0.38	0.21	0.05	8.7
York, NE; 2004 (RCN R05046)	5	Winter; Millenium	Hay	0.20	8 [0]	1.164	0.168	1.332	0.13	0.08	0.04	1.6
						1.204	0.178	1.382	0.13	0.09	0.03	1.6
			Grain	0.20	20	0.012	0.005	0.017	<0.01	<0.01	<0.01	<0.05
						0.016	<0.005	<0.021	<0.01	<0.01	<0.01	<0.05
			Straw	0.20	20	3.300	0.553	3.853	0.56	0.21	0.10	4.7
						5.750	0.999	6.749	0.76	0.32	0.12	7.9
Clinton, IL; 2004 (RCN R05047)	5	Winter; Excel 201	Hay	0.20	0	9.000	1.544	10.544	0.03	0.06	<0.01	<10.6
						9.860	1.464	11.324	0.03	0.05	<0.01	<11.4
					7 [5]	6.740	1.176	7.916	0.05	0.07	0.01	8.0
						5.640	1.012	6.652	0.03	0.06	0.01	6.7
					14	4.940	0.820	5.760	0.06	0.07	0.02	5.9
						3.820	0.824	4.644	0.05	0.07	0.01	4.8
			Grain	0.20	14	0.028	0.007	0.034	0.01	<0.01	<0.01	<0.06
						0.040	<0.005	<0.045	0.02	<0.01	<0.01	<0.09
					21	0.065	0.011	0.077	0.03	<0.01	<0.01	<0.13
						0.051	0.010	0.062	0.03	<0.01	<0.01	<0.11
					28	0.042	0.008	0.051	0.02	<0.01	<0.01	<0.09
						0.046	<0.005	<0.051	0.02	<0.01	<0.01	<0.09
					35	0.031	<0.005	<0.036	0.04	<0.01	<0.01	<0.10
						0.039	0.009	0.048	0.04	<0.01	<0.01	<0.11
			Straw	0.20	14	2.510	0.515	3.025	0.48	0.14	0.05	3.7
						3.075	0.578	3.653	0.50	0.16	0.07	4.4
					21	3.860	0.816	4.676	0.93	0.30	0.14	6.0
						3.805	0.741	4.546	0.78	0.23	0.11	5.7
					28	3.660	0.743	4.403	1.24	0.38	0.17	6.2
						4.250	0.849	5.099	1.22	0.44	0.18	6.9
					35	3.435	0.661	4.096	1.51	0.47	0.22	6.3
						3.195	0.628	3.823	1.64	0.37	0.23	6.1

TABLE C.3.1 Residue Data for Metconazole, M11, M21, and M30 from Wheat Field Trials with Metconazole.

Trial ID (County, State; Year)	Zone	Crop; Variety	Matrix	Total Rate (lb ai/A)	PHI (days)[1]	Metconazole Residues (ppm parent equivalents)						
						Metconazole			Metabolites			Total[2]
						cis	*trans*	Total	M11	M21	M30	
Hall, NE; 2004 (RCN R05048)	7	Winter; Jagalene HRW	Hay	0.20	7 [0]	1.824	0.362	2.186	0.02	0.03	<0.01	<2.2
						1.520	0.306	1.826	0.02	0.03	<0.01	<1.9
			Grain	0.20	22	0.012	<0.005	<0.017	<0.01	<0.01	<0.01	<0.05
						0.008	<0.005	<0.013	<0.01	<0.01	<0.01	<0.04
			Straw	0.20	22	1.410	0.305	1.715	0.45	0.14	0.08	2.4
						2.340	0.538	2.878	0.59	0.20	0.12	3.8
Mc Henry, ND; 2005 (RCN R05049)	7	Spring; Dapps	Hay	0.20	8 [1]	4.080	0.740	4.820	<0.01	0.04	<0.01	<4.9
						5.920	1.092	7.012	0.01	0.05	<0.01	<7.1
			Grain	0.20	20	0.031	0.009	0.039	<0.01	<0.01	<0.01	<0.07
						0.032	0.009	0.040	<0.01	<0.01	<0.01	<0.07
			Straw	0.20	20	2.004	0.347	2.351	0.07	0.08	0.02	2.5
						2.212	0.412	2.624	0.07	0.09	0.02	2.8
Cass, ND; 2005 (RCN R05050)	5	Spring; Knudson	Hay	0.21	0	10.000	1.764	11.764	0.04	0.07	0.01	11.9
						10.320	1.600	11.920	0.04	0.06	0.01	12.0
					8 [6]	5.080	0.868	5.948	0.36	0.13	0.05	6.5
						5.180	0.940	6.120	0.37	0.13	0.04	6.7
					14	3.180	0.592	3.772	0.09	0.08	0.02	4.0
						3.468	0.640	4.108	0.10	0.08	0.02	4.3
			Grain	0.20	14	0.013	<0.005	<0.018	<0.01	<0.01	<0.01	<0.05
						0.017	<0.005	<0.022	<0.01	<0.01	<0.01	<0.05
					22	0.009	<0.005	<0.014	<0.01	<0.01	<0.01	<0.04
						0.011	<0.005	<0.016	<0.01	<0.01	<0.01	<0.05
					28	0.008	<0.005	<0.013	<0.01	<0.01	<0.01	<0.04
						0.008	<0.005	<0.013	0.01	<0.01	<0.01	<0.04
					36	0.007	<0.005	<0.012	0.01	<0.01	<0.01	<0.04
						0.008	<0.005	<0.013	0.01	<0.01	<0.01	<0.04
			Straw	0.21	14	1.108	0.177	1.285	0.12	0.06	0.02	1.5
						1.108	0.170	1.278	0.12	0.06	0.02	1.5
					22	1.260	0.161	1.421	0.17	0.07	0.03	1.7
						0.936	0.126	1.062	0.14	0.07	0.03	1.3
					28	1.044	0.154	1.198	0.17	0.07	0.04	1.5
						1.032	0.147	1.179	0.18	0.07	0.04	1.5
					36	0.660	0.097	0.757	0.14	0.05	0.03	1.0
						0.860	0.118	0.978	<0.01	0.06	0.04	<1.1
Caddo, OK; 2005 (RCN R05051)	6	Winter; Jagalene	Hay	0.20	7 [6]	6.720	1.136	7.856	0.13	0.17	0.04	8.2
						5.720	0.964	6.684	0.14	0.17	0.04	7.0
			Grain	0.20	22	0.006	<0.005	<0.011	<0.01	<0.01	<0.01	<0.04
						0.006	<0.005	<0.011	<0.01	<0.01	<0.01	<0.04
			Straw	0.20	22	0.218	0.048	0.266	0.08	0.04	0.02	0.4
						0.504	0.070	0.574	0.11	0.06	0.03	0.8

TABLE C.3.1 Residue Data for Metconazole, M11, M21, and M30 from Wheat Field Trials with Metconazole.

Trial ID (County, State; Year)	Zone	Crop; Variety	Matrix	Total Rate (lb ai/A)	PHI (days)[1]	Metconazole Residues (ppm parent equivalents)						
						Metconazole			Metabolites			Total[2]
						cis	*trans*	Total	M11	M21	M30	
Caddo, OK; 2004 (RCN R05052)	8	Winter; Jagger	Hay	0.20	6 [7]	8.540	1.400	9.940	0.09	0.12	0.02	10.2
						8.120	1.392	9.512	0.08	0.11	0.02	9.7
			Grain	0.20	21	0.097	0.019	0.116	0.02	<0.01	<0.01	<0.16
						0.063	0.013	0.075	0.01	<0.01	<0.01	<0.11
			Straw	0.18	21	8.180	1.436	9.616	0.91	0.45	0.12	11.1
						8.390	1.452	9.842	0.86	0.45	0.12	11.3
Lubbock, TX; 2005 (RCN R05053)	8	Winter; TAM 200	Hay	0.20	7 [9]	8.440	1.644	10.084	0.07	0.08	0.02	10.2
						9.500	1.720	11.220	0.07	0.07	0.02	11.4
			Grain	0.20	21	0.026	0.005	0.032	<0.01	<0.01	<0.01	<0.06
						0.031	0.006	0.037	<0.01	<0.01	<0.01	<0.07
			Straw	0.20	21	3.080	0.564	3.644	0.18	0.05	0.04	3.9
						3.852	0.760	4.612	0.40	0.08	0.05	5.1
Payette, ID; 2005 (RCN R05054)	11	Spring; Penawawa	Hay	0.20	7 [5]	4.860	0.916	5.776	0.03	0.08	0.01	5.9
						5.300	0.740	6.040	0.03	0.08	0.01	6.2
			Grain	0.20	21	0.043	0.008	0.051	<0.01	<0.01	<0.01	<0.08
						0.038	0.007	0.045	<0.01	<0.01	<0.01	<0.08
			Straw	0.20	21	0.632	3.544	4.176	0.03	0.05	0.01	4.3
						0.912	4.720	5.632	0.04	0.06	0.01	5.7
SK, Canada; 2005 (RCN R05055)	14	Spring; Bounty	Hay	0.20	7 [8]	10.980	1.684	12.664	0.03	0.08	0.02	12.8
						10.900	1.596	12.496	0.03	0.08	0.02	12.6
			Grain	0.20	21	0.019	<0.005	<0.024	<0.01	<0.01	<0.01	<0.05
						0.017	<0.005	<0.022	<0.01	<0.01	<0.01	<0.05
			Straw	0.20	21	0.153	1.044	1.197	0.06	0.07	0.01	1.3
						0.160	1.020	1.180	0.07	0.07	0.01	1.3
MB, Canada; 2005 (RCN R05056)	14	Spring; AC Barrie	Hay	0.20	7 [4]	5.520	0.956	6.476	0.06	0.08	0.02	6.6
						5.240	0.816	6.056	0.05	0.08	0.02	6.2
			Grain	0.20	21	0.020	<0.005	<0.025	0.02	<0.01	<0.01	<0.07
						0.023	<0.005	<0.028	0.02	<0.01	<0.01	<0.07
			Straw	0.20	21	0.416	2.040	2.456	0.14	0.12	0.03	2.8
						0.358	2.196	2.554	0.14	0.13	0.03	2.8
AB, Canada; 2005 (RCN R05057)	14	Spring; AC Intrepid	Hay	0.20	7 [13]	4.780	0.744	5.524	0.11	0.13	0.03	5.8
						4.660	0.836	5.496	0.13	0.13	0.03	5.8
			Grain	0.20	21	0.022	0.005	0.028	<0.01	<0.01	<0.01	<0.06
						0.022	0.005	0.027	<0.01	<0.01	<0.01	<0.06
			Straw	0.20	21	0.353	2.068	2.421	0.08	0.08	0.01	2.6
						0.404	2.112	2.516	0.07	0.09	0.01	2.7

TABLE C.3.1 Residue Data for Metconazole, M11, M21, and M30 from Wheat Field Trials with Metconazole.

Trial ID (County, State; Year)	Zone	Crop; Variety	Matrix	Total Rate (lb ai/A)	PHI (days)[1]	Metconazole Residues (ppm parent equivalents)						
						Metconazole			Metabolites			Total[2]
						cis	*trans*	Total	M11	M21	M30	
AB, Canada; 2005 (RCN R05058)	14	Spring; 5700PR	Hay	0.19	7 [14]	5.500	1.012	6.512	0.19	0.16	0.04	6.9
						5.980	0.824	6.804	0.48	0.19	0.06	7.5
			Grain	0.20	21	0.044	0.010	0.054	0.02	0.01	<0.01	<0.09
						0.044	0.010	0.054	0.02	<0.01	<0.01	<0.09
			Straw	0.20	21	0.544	2.820	3.364	0.45	0.20	0.04	4.1
						0.544	3.068	3.612	0.43	0.21	0.04	4.3

[1] Hay samples were cut, then allowed to dry in the field or under cover prior to collection; the drying interval is presented in brackets.
[2] Total = total residue; the sum of *cis*- and *trans*-metconazole, M11, M21, and M30; values presented as calculated and reported by the petitioner.

TABLE C.3.2 Residue Data for the Triazole Metabolites from Wheat Field Trials with Metconazole.

Trial ID (County, State; Year)	Zone	Crop; Variety	Matrix	Total Rate (lb ai/A)	PHI (days)	Triazole Residues (ppm)		
						1,2,4-T	TA	TAA
Tift, GA; 2004 (RCN R05044)	2	Winter; Pioneer 26R24	Grain	0.02	21	<0.05	0.691	0.360
						<0.05	0.614	0.322
Jackson, AR; 2004 (RCN R05045)	4	Winter; Genesis R033	Grain	0.20	21	<0.05	0.091	<0.05
						<0.05	0.086	<0.05
York, NE; 2004 (RCN R05046)	5	Winter; Millenium	Grain	0.20	20	<0.05	0.128	0.081
						<0.05	0.144	0.105
Clinton, IL; 2004 (RCN R05047)	5	Winter; Excel 201	Grain	0.20	14	<0.05	<0.05	<0.05
						<0.05	0.059	<0.05
					21	<0.05	0.060	<0.05
						<0.05	<0.05	0.054
					28	<0.05	0.060	0.051
						<0.05	<0.05	<0.05
					35	<0.05	<0.05	<0.05
						<0.05	0.053	<0.05
Hall, NE; 2004 (RCN R05048)	7	Winter; Jagalene HRW	Grain	0.20	22	<0.05	0.113	0.088
						<0.05	0.068	0.056
Mc Henry, ND; 2005 (RCN R05049)	7	Spring; Dapps	Grain	0.20	20	<0.05	0.114	<0.05
						<0.05	0.136	<0.05
Cass, ND; 2005 (RCN R05050)	5	Spring; Knudson	Grain	0.20	14	<0.05	0.150	0.093
						<0.05	0.152	0.080
					22	<0.05	0.146	0.076
						<0.05	0.144	0.076
					28	<0.05	0.126	0.068
						<0.05	0.140	0.070
					36	<0.05	0.149	0.063
						<0.05	0.132	0.071

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TABLE C.3.2 Residue Data for the Triazole Metabolites from Wheat Field Trials with Metconazole.

Trial ID (County, State; Year)	Zone	Crop; Variety	Matrix	Total Rate (lb ai/A)	PHI (days)	Triazole Residues (ppm)		
						1,2,4-T	TA	TAA
Caddo, OK; 2005 (RCN R05051)	6	Winter; Jagalene	Grain	0.20	22	<0.05	0.053	<0.05
						<0.05	<0.05	<0.05
Caddo, OK; 2004 (RCN R05052)	8	Winter; Jagger	Grain	0.20	21	<0.05	<0.05	<0.05
						<0.05	<0.05	<0.05
Lubbock, TX; 2005 (RCN R05053)	8	Winter; TAM 200	Grain	0.20	21	<0.05	<0.05	<0.05
						<0.05	<0.05	<0.05
Payette, ID; 2005 (RCN R05054)	11	Spring; Penawawa	Grain	0.20	21	<0.05	<0.05	<0.05
						<0.05	<0.05	<0.05
SK, Canada; 2005 (RCN R05055)	14	Spring; Bounty	Grain	0.20	21	<0.05	0.097	<0.05
						<0.05	0.095	<0.05
MB, Canada; 2005 (RCN R05056)	14	Spring; AC Barrie	Grain	0.20	21	<0.05	0.610	0.271
						<0.05	0.662	0.289
AB, Canada; 2005 (RCN R05057)	14	Spring; AC Intrepid	Grain	0.20	21	<0.05	0.068	<0.05
						<0.05	0.078	<0.05
AB, Canada; 2005 (RCN R05058)	14	Spring; 5700PR	Grain	0.20	21	<0.05	0.245	0.183
						<0.05	0.228	0.183

TABLE C.4.1 Summary of Residue Data for Metconazole, M11, M21, and M30 from Wheat Field Trials with Metconazole.

Commodity	Total Applic. Rate (lb ai/A)	PHI	Analyte	Residue Levels[1] (ppm)						
				n	Min.	Max.	HAFT[2]	Median (STMdR)	Mean (STMR)	Std. Dev.
Hay	0.18-0.21	6-8 [0-14]	*cis*-Metconazole	30	1.16	10.98	10.94	5.36	5.55	2.51
			trans-Metconazole	30	0.17	1.72	1.682	0.93	0.95	0.41
			Metconazole	30	1.33	12.66	12.58	6.24	6.50	2.91
			M11	30	<0.01	0.48	0.365	0.06	0.10	0.11
			M21	30	0.03	0.19	0.175	0.08	0.09	0.04
			M30	30	<0.01	0.06	0.05	0.02	0.02	0.01
			Total Residues	30	1.60	12.80	12.7	6.55	6.71	2.915
Grain	0.18-0.21	20-22	*cis*-Metconazole	30	0.006	0.097	0.08	0.027	0.033	0.024
			trans-Metconazole	30	<0.005	0.019	0.016	0.006	0.008	0.004
			Metconazole	30	0.011	0.116	0.0955	0.034	0.041	0.027
			M11	30	<0.010	0.030	0.03	0.010	0.014	0.006
			M21	30	<0.010	0.010	0.01	0.010	0.010	---
			M30	30	<0.010	<0.010	0.01	0.010	0.010	---
			Total Residues	30	0.040	0.160	0.04	0.070	0.075	0.031

TABLE C.4.1 Summary of Residue Data for Metconazole, M11, M21, and M30 from Wheat Field Trials with Metconazole.

Commodity	Total Applic. Rate (lb ai/A)	PHI	Analyte	Residue Levels[1] (ppm)						
				n	Min.	Max.	HAFT[2]	Median (STMdR)	Mean (STMR)	Std. Dev.
Straw	0.18-0.21	20-22	*cis*-Metconazole	30	0.153	8.390	8.285	1.335	2.390	2.476
			trans-Metconazole	30	0.048	4.720	4.132	0.908	1.233	1.143
			Metconazole	30	0.266	9.842	9.729	2.751	3.623	2.565
			M11	30	0.030	1.290	1.075	0.280	0.383	0.347
			M21	30	0.040	0.450	0.45	0.105	0.151	0.111
			M30	30	0.010	0.140	0.125	0.040	0.055	0.043
			Total Residues	30	0.400	11.300	11.2	3.650	4.210	2.850

[1] For calculations of median, mean, and standard deviation, the LOQ was used for any results reported as <LOQ in Table C.3.1.
[2] HAFT = Highest Average Field Trial.

TABLE C.4.2. Summary of Residue Data for the Triazole Metabolites from Wheat Field Trials with Metconazole.

Commodity	Total Applic. Rate (lb ai/A)	PHI	Analyte	Residue Levels[1] (ppm)						
				n	Min.	Max.	HAFT[2]	Median (STMdR)	Mean (STMR)	Std. Dev.
Grain	0.18-0.21	20-22	1,2,4-T	30	<0.05	<0.05	0.05	0.05	0.05	--
			TA	30	<0.05	0.691	0.65	0.09	0.17	0.20
			TAA	30	<0.05	0.360	0.34	0.05	0.10	0.09

[1] For calculations of median, mean, and standard deviation, the LOQ was used for any results reported as <LOQ in Table C.3.2.
[2] HAFT = Highest Average Field Trial.

D. CONCLUSION

The submitted field trial data are adequate and reflect the use of two broadcast foliar applications of a 0.75 lb ai/gal SC/L formulation of metconazole at a total rate of 0.18-0.21 lb ai/A, with a 6- to 8-day retreatment interval. Samples were harvested at PHIs of 6-8 days for wheat hay and 20-22 days for grain and straw. An acceptable method was used for quantitation of residues of *cis*- and *trans*-metconazole, M11, M21, and M30, and 1,2,4-T, TA, and TAA in/on wheat samples. The study is supported by adequate storage stability data for *cis*- and trans-metconazole.

E. REFERENCES

DP#: 324541
Subject: Metconazole. Request for a Tolerance on Imported Bananas. Summary of Analytical Chemistry and Residue Data. Petition Number 9E05052.
From: N. Dodd
To: M. Waller
Date: 12/14/05
MRIDs: 44721506, 44721507, 44721508, 44721509, 44721510, and 44721511

F. DOCUMENT TRACKING

RDI: N. Dodd (2/20/08)
Petition Numbers: 6F7094 and 6F7095
DP#s: 348168 and 348206
PC Code: 125619

Template Version June 2005

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Primary Evaluator	This DER was originally prepared under contract by Dynamac Corporation.
Approved by	Nancy Dodd, Chemist *Nancy Dodd* Date: 2/20/08 Registration Action Branch 3 Health Effects Division (7509P)

This DER was originally prepared under contract by Dynamac Corporation (2275 Research Boulevard, Suite 300; Rockville, MD 20850; submitted 09/18/2007). The DER has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

46902225 White, M.; Saha, M. (2006) The Magnitude of Residues of Metconazole (BAS 555 F) and its Metabolites in Barley: Final Report. Project Number: 137714, 2006/7006917. Unpublished study prepared by BASF Agro Research, ACDS Research, Inc. and Alvey Lab & Agr Research Services. 175 p.

EXECUTIVE SUMMARY:

BASF Corporation has submitted field trial data for metconazole on barley. Twelve field trials were conducted in the United States and Canada in Zones 1 (NY, 1 trial), 5 (IL, NE; 2 trials), 7 (ND, NE; 2 trials), 9 (UT; 1 trial), 10 (CA; 1 trial), 11 (ID; 1 trial), and 14 (AB, MB, SK; 4 trials) during the 2004-2005 growing season. Because Canadian Zone 14 is contiguous with the two major U.S. barley-growing regions, Zones 5 and 7, HED has concluded that results from the Canadian trials may be used to address U.S. data requirements for barley.

Each test site included one control plot and two treated plots. The treated plots received two broadcast foliar applications of a 0.75 lb ai/gal soluble concentrate/liquid (SC/L) formulation of metconazole at ~0.10 lb ai/A/application, with a 6- to 8-day retreatment interval, for a total seasonal rate of ~0.20 lb ai/A. Applications were initiated four weeks prior to the harvest of mature grain (plot 2) or two weeks prior to the cutting of hay (plot 3). Applications were made in 12-30 gal/A spray volumes using ground equipment. A nonionic surfactant was added as a spray adjuvant for all applications.

Barley hay was harvested 7-8 days after the last application and allowed to dry in the field for 0-14 days prior to collection. Barley grain and straw were harvested 20-21 days after the last application. Additional hay samples were collected from one trial 0, 7, and 14 days after the last application, and grain and straw samples were harvested 14, 21, 28, and 35 days after the last application to generate residue decline data.

Samples were analyzed for residues of *cis*- and *trans*-metconazole, metabolites M11, M21, and M30, and the triazole metabolites (barley grain only), triazole (1,2,4-T), triazolylalanine (TA),

and triazolylacetic acid (TAA), using an LC/MS/MS method (BASF Method D0508). Residues of metabolites M11, M21, and M30 were converted to parent equivalents using molecular weight conversion factors of 0.95 for M11 and M21 and 0.96 for M30. The validated limits of quantitation (LOQs) were 0.01 ppm for the parent metconazole (sum of *cis* and *trans* isomers at 0.005 ppm each), M11, M21, and M30 in/on barley samples. The validated LOQ was 0.05 ppm for 1,2,4-T, TA, and TAA. The method was adequate for data collection based on acceptable concurrent method recoveries.

Samples were stored frozen (<-10 °C) from harvest to extraction for 160-241 days (5.3-7.9 months) for barley hay, 131-228 days (4.3-7.5 months) for barley grain, and 137-225 days (4.5-7.4 months) for barley straw, and were analyzed within 0-2 days of extraction. Adequate storage stability data are available to support the storage conditions and durations of samples for the barley field trials.

Maximum residues of *cis*-and *trans*-metconazole in barley hay were 3.69 and 0.74 ppm, respectively; maximum total metconazole residues (sum of *cis* and *trans* isomers) were 4.43 ppm. In barley grain, maximum residues of *cis*- and *trans*-metconazole were 1.33 and 0.27 ppm, respectively, and maximum total metconazole residues were 1.60 ppm. In barley straw, maximum residues of *cis*- and *trans*-metconazole were 3.94 and 0.82 ppm, respectively, and maximum total metconazole residues were 4.65 ppm. Maximum residues of metabolite M11 were 0.38, 0.33, and 1.08 ppm for hay, grain, and straw, respectively; maximum residues of M21 were 0.20, 0.08, and 0.46 ppm for hay, grain, and straw, respectively; and maximum residues of metabolite M30 were 0.07, 0.05, 0.15 ppm for hay, grain, and straw, respectively.

Maximum residues of 1,2,4-T, TA, and TAA in/on samples of barley grain were below the LOQ (<0.05 ppm), 0.45 ppm, and 0.18 ppm, respectively.

The submitted residue decline data indicated that total metconazole residues (sum of *cis* and *trans* isomers) generally declined in barley hay, grain, and straw with increasing preharvest intervals.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the field trial residue data are classified as scientifically acceptable.

The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP#s 348168 and 348206.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an impact on the validity of the study.

A. BACKGROUND INFORMATION

Metconazole [5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cycopentanol] is a broad-spectrum triazole Group 3 fungicide (sterol biosynthesis inhibitors). There are currently no registered uses of metconazole in the U.S.; however, a tolerance has been established for banana, and a Section 18 emergency exemption and supporting time-limited tolerances have been granted for use on soybean. BASF Corporation has applied for registration of metconazole in the U.S. for use on barley, oats, rye, soybeans, sugar beets, triticale, and wheat.

The chemical structure and nomenclature of metconazole, and the physicochemical properties of the technical grade of metconazole are presented in Tables A.1 and A.2.

TABLE A.1. Metconazole Nomenclature.

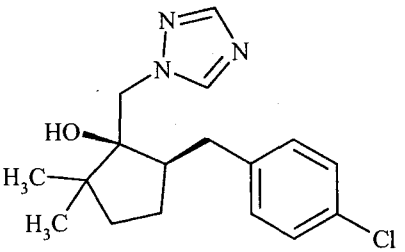
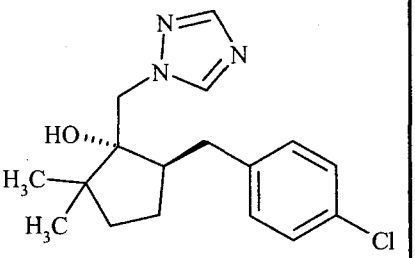
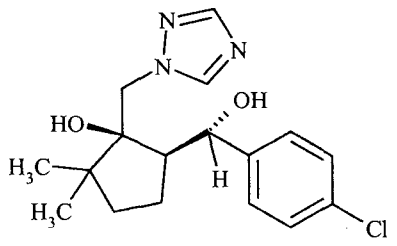
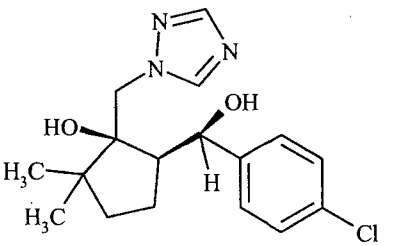
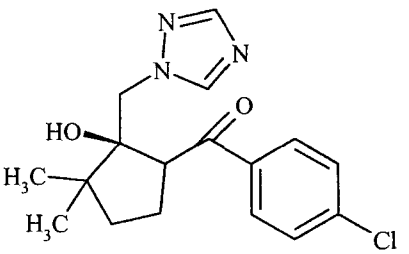
Chemical structure	 *cis*-isomer	 *trans*-isomer
Common name	Metconazole	
Company experimental name	KNF-S-474m (Kureha); BAS 555 F (BASF); V-10116 (Valent)	
IUPAC name	(1RS,5RS:1RS,5SR)-5-(4-chlorobenzyl)-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	
CAS name	5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	
CAS registry number	125116-23-6 (*cis*- and *trans*-isomers) 115850-27-6 (*cis*-isomer) 115850-28-7 (*trans*-isomer)	
End-use products (EP)	50% WDG (Metconazole 50 WDG Fungicide, EPA File Symbol 59639-RUT) 0.75 lb/gal SC/L (Caramba™ Fungicide, EPA File Symbol No. 7969-EUA) 0.67 lb/gal SC/L formulation (BAS 556 01F Fungicide, EPA File Symbol No. 7969-EUT; also contains the active ingredient pyraclostrobin at 0.83 lb/gal)	
 Metconazole metabolite M11	 Metconazole metabolite M21	 Metconazole metabolite M30

TABLE A.1. Metconazole Nomenclature.

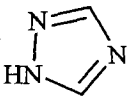
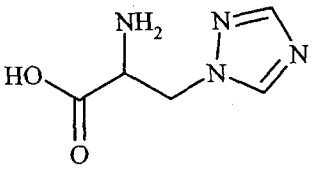
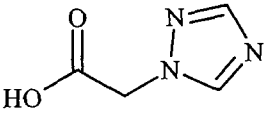
		
Triazole metabolite 1,2,4-triazole (1,2,4-T)	Triazole metabolite triazolylalanine (TA)	Triazole metabolite triazolylacetic acid (TAA)

Table A.2. Physicochemical Properties of Metconazole

Parameter	Value	References* (MRID)
Melting point/range	100.0-108.4°C (using Electrothermal Digital Melting Point Apparatus) (AC900,768 technical grade)	44721505
pH	5.81 at 25°C (1% aqueous suspension)	46808402
Relative density (20°C)	1.14 (relative density to water at 4°C, using capillary-stoppered, density-specific gravity bottle) (Lot No. AC 8879-140B)	44721505
Water solubility (20°C)	Using shake-flask method: 18.7 ± 1.0 mg/L (*cis*-isomer, WL148271, KNF-S-474m) 13.6 ± 1.7 mg/L (*trans*-isomer, WL148271, KNF-S-474m)	44721505
Solvent solubility (g/L) at 20°C	Solvent / Metconazole / *cis* / *trans* acetone: 363 / 251 / 117 methanol: 403 / 294 / 117 dichloromethane: 481 / 343 / 141 ethyl acetate: 260 / 173 / 90.0 propanol: 132 / 86.6 / 46.7 toluene: 103 / 66.2 / 38.0 Hexane: 1.40 / 0.929 / 0.483	44721505
Vapor pressure (20°C)	Using gas-saturation method: $< 1.23 \times 10^{-5}$ Pa or 9.23×10^{-8} mm Hg (metconazole) $< 1.04 \times 10^{-5}$ Pa or 7.80×10^{-8} mm Hg (*cis*-isomer) $< 1.96 \times 10^{-6}$ Pa or 1.47×10^{-8} mm Hg (*trans*-isomer)	44721505
Dissociation constant (pK_a)	11.38±0.03 and 1.06±0.03 (in water at 29.1°C using spectrophotometric method; Lot No. AC 8879-140B)	44721505
Octanol/water partition coefficient, Log(K_{OW})	At 20 °C (using flask shaking method): K_{ow} (log K_{ow}) = 7090±989 (3.85) (Lot No. AC 8879-140B) (TGAI) K_{ow} (log K_{ow}) = 7150±803 (3.85) (*cis*-isomer, CL 354,801) K_{ow} (log K_{ow}) = 6800±1700 (3.8) (*trans*-isomer, CL 354,802)	44721505
UV/visible absorption spectrum	pH / λ / A / log ε *cis*-isomer	46808403

Table A.2. Physicochemical Properties of Metconazole					
Parameter	Value				References* (MRID)
	2.0	221.4	0.828	4.03	
	6.8		0.8452	4.04	
	7.0		0.9126	4.08	
	10.3		0.7226	3.98	
	trans-isomer				
	2.0	221.4	0.9053	4.07	
	7.0		0.9547	4.10	
	10.1		0.9893	4.11	

* Product Chemistry Reviews: DP #256877, Shyam Mathur, Ph.D., 9/12/2000 and DP #329168, Shyam Mathur, Ph.D., 7/13/07.

B. EXPERIMENTAL DESIGN

B.1. Study Site Information

Twelve field trials were conducted in the United States and Canada in zones 1 (NY, 1 trial), 5 (IL, NE; 2 trials), 7 (ND, NE; 2 trials), 9 (UT; 1 trial), 10 (CA; 1 trial), 11 (ID; 1 trial), and 14 (AB, MB, SK; 4 trials) during the 2004-2005 growing season.

Each test site included one control plot and two treated plots. The treated plots received two broadcast foliar applications of a 0.75 lb ai/gal soluble concentrate/liquid (SC/L) formulation of metconazole at 0.10-0.11 lb ai/A/application, with a 6- to 8-day retreatment interval, for a total seasonal rate of 0.20-0.21 lb ai/A. Applications were initiated four weeks prior to the harvest of mature grain (plot 2) or two weeks prior to the cutting of hay (plot 3). Applications were made in spray volumes of 12-30 gal/A using ground equipment. A nonionic surfactant was added as a spray adjuvant for all applications.

Samples of barley hay were harvested 7-8 days after the last application and allowed to dry in the field for 0-14 days prior to collection. Barley grain and straw were harvested 20-21 days after the last application. Additional hay samples were collected from one trial 0, 7, and 14 days after the last application, and grain and straw samples were harvested 14, 21, 28, and 35 days after the last application to generate residue decline data.

The test crops were grown and maintained according to typical agricultural practices for each region; maintenance pesticides and fertilizers were used to produce a commercial quality crop. Irrigation was used to supplement rainfall as needed. Trial site conditions are presented in Table B.1.1, and the study use pattern is presented in Table B.1.2. The crop varieties grown are identified in Table C.3; HED notes that the crop variety was listed as "not specified" for the St. Clair, IL site.

For each field trial, the petitioner presented the weather conditions at application and summarized the weather conditions for the duration of the trials. The trials at Innisfail, AB,

Minto, MB, and Rosthern, SK in Canada experienced wetter than normal weather, which resulted in a delay in harvesting the crops at these sites. This unusual weather did not damage the crops. No unusual weather events occurred in the United States trials which had an adverse impact on the barley crops.

TABLE B.1.1. Trial Site Conditions.

Trial Identification: County, State; Year (Trial ID)	Soil characteristics				Meteorological Data	
	Type	%OM	pH	CEC (meq/g)	Overall Rainfall range	Overall Temperature range (°C)
Wayne, NY; 2005 (RCN R05155)	Silt Loam	4.1	5.0	Not provided	Above normal in April and July; below normal in May and June.	Normal
St. Clair, IL; 2004 (RCN R05156)	Silt Loam	2.2	6.6	Not provided	Normal	Normal
York, NE; 2005 (RCN R05157)	Silty Clay Loam	2.8	6.4	Not provided	Below normal in May; above normal in July	Normal
McHenry, ND; 2005 (RCN R05158)	Loam	3.2	5.6	Not provided	Much above normal in June	Normal
Hall, NE; 2005 (RCN R05159)	Clay Loam	2.7	6.6	Not provided	Above normal in May and June; below normal in July	Above normal for the trial period
Cache, UT; 2005 (RCN R05160)	Loam	1.3	7.8	Not provided	Normal	Normal
Madera, CA; 2005 (RCN R05161)	Loamy Sand	0.5	8.4	Not provided	Normal	Normal
Payette, ID; 2005 (RCN R05162)	Silty Clay Loam	0.65	6.2	Not provided	Normal	Normal
Rosthern, SK; 2005 (RCN R05163)	Loam	7.2	7.0	Not provided	Generally wetter than normal. Much above normal in August and September	Generally cooler than normal
Minto, MB; 2005 (RCN R05164)	Loam	4.9	7.5	Not provided	Above normal in May, June and July. Below normal in August and September	Generally cooler than normal
Innisfail, AB; 2005 (RCN R05165)	Clay Loam	7.6	6.2	Not provided	Generally wetter than normal	Normal
Innisfail, AB; 2005 (RCN R05166)	Loam	5.6	6.5	Not provided	Generally wetter than normal	Normal

TABLE B.1.2. Study Use Pattern.

Trial Identification: County, State; Year (Trial ID)	EP[1]	Application					Tank Mix/ Adjuvants[4]
		Method; timing	Volume[2] (GPA)	Rate (lb ai/A)	RTI[3] (days)	Total Rate (lb ai/A)	
Wayne, NY; 2005 (RCN R05155)	0.75 lb/gal SC/L	1. Broadcast foliar; early dough	24.7	0.101	8	0.20	Induce (NIS)
		2. Broadcast foliar; soft dough	24.6	0.100			
		1. Broadcast foliar; beginning of flowering	25.3	0.103	7	0.21	Induce (NIS)
		2. Broadcast foliar; first grains half final size	25.3	0.104			

TABLE B.1.2. Study Use Pattern.

Trial Identification: County, State; Year (Trial ID)	EP[1]	Application					Tank Mix/ Adjuvants[4]
		Method; timing	Volume[2] (GPA)	Rate (lb ai/A)	RTI[3] (days)	Total Rate (lb ai/A)	
St. Clair, IL; 2005 (RCN R05156)	0.75 lb/gal SC/L	1. Broadcast foliar; soft dough	12.6	0.101	7	0.20	Preference (NIS)
		2. Broadcast foliar; soft dough	16.7	0.100			
		1. Broadcast foliar; beginning of flowering	14.8	0.103	7	0.20	Preference (NIS)
		2. Broadcast foliar; end of flowering	16.4	0.101			
York, NE; 2005 (RCN R05157)	0.75 lb/gal SC/L	1. Broadcast foliar; early dough	19.8	0.099	7	0.20	Activate Plus (NIS)
		2. Broadcast foliar; soft dough	19.9	0.100			
		1. Broadcast foliar; beginning of heading	20.1	0.100	7	0.20	Activate Plus (NIS)
		2. Broadcast foliar; 80% of inflorescence emerged	19.8	0.099			
McHenry, ND; 2005 (RCN R05158)	0.75 lb/gal SC/L	1. Broadcast foliar; early mild	12.1	0.100	7	0.20	R-11 (NIS)
		2. Broadcast foliar; soft dough	11.9	0.099			
		1. Broadcast foliar; flag leaf sheath opening	12.1	0.099	7	0.20	R-11 (NIS)
		2. Broadcast foliar; full flowering	12.0	0.100			
Hall, NE; 2005 (RCN R05159)	0.75 lb/gal SC/L	1. Broadcast foliar; early dough	19.9	0.100	7	0.20	Activate Plus (NIS)
		2. Broadcast foliar; soft dough	20.1	0.101			
		1. Broadcast foliar; beginning of heading	19.3	0.100	7	0.20	Activate Plus (NIS)
		2. Broadcast foliar; 80% of inflorescence emerged	20.0	0.101			
Cache, UT; 2005 (RCN R05160)	0.75 lb/gal SC/L	1. Broadcast foliar; soft dough	17.2	0.100	8	0.20	Agri-Dex (NIS)
		2. Broadcast foliar; hard dough	17.1	0.096			
		1. Broadcast foliar; full flowering	18.8	0.105	7	0.21	Agri-Dex (NIS)
		2. Broadcast foliar; late milk	19.1	0.106			
Madera, CA; 2005 (RCN R05161)	0.75 lb/gal SC/L	1. Broadcast foliar; hard dough	29.9	0.099	7	0.20	Penetrator plus (NIS)
		2. Broadcast foliar; hard dough	29.8	0.099			
		1. Broadcast foliar; early dough	30.0	0.100	7	0.20	Penetrator plus (NIS)
		2. Broadcast foliar; hard dough	30.1	0.099			
Payette, ID; 2005 (RCN R05162)	0.75 lb/gal SC/L	1. Broadcast foliar; soft dough	30.2	0.100	7	0.20	R-11 (NIS)
		2. Broadcast foliar; hard dough	30.0	0.100			
		1. Broadcast foliar; beginning of heading	30.4	0.104	7	0.20	R-11 (NIS)
		2. Broadcast foliar; 80% of inflorescence emerged	29.8	0.099			

TABLE B.1.2. Study Use Pattern.

Trial Identification: County, State; Year (Trial ID)	EP[1]	Application					Tank Mix/ Adjuvants[4]
		Method; timing	Volume[2] (GPA)	Rate (lb ai/A)	RTI[3] (days)	Total Rate (lb ai/A)	
Rosthern, SK; 2005 (RCN R05163)	0.75 lb/gal SC/L	1. Broadcast foliar; soft dough	21.9	0.099	6	0.20	Ag-Surf (NIS)
		2. Broadcast foliar; soft dough	21.8	0.101			
		1. Broadcast foliar; beginning of flowering	21.5	0.099	7	0.20	Ag-Surf (NIS)
		2. Broadcast foliar; early milk	20.9	0.100			
Minto, MB; 2005 (RCN R05164)	0.75 lb/gal SC/L	1. Broadcast foliar; soft dough	22.2	0.101	8	0.20	Ag-Surf (NIS)
		2. Broadcast foliar; hard dough	20.8	0.099			
		1. Broadcast foliar; beginning of heading	22.0	0.101	7	0.20	Ag-Surf (NIS)
		2. Broadcast foliar; medium milk	22.2	0.102			
Innisfail, AB; 2005 (RCN R05165)	0.75 lb/gal SC/L	1. Broadcast foliar; soft dough	24.2	0.100	7	0.20	Merge (NIS)
		2. Broadcast foliar; soft dough	24.9	0.100			
		1. Broadcast foliar; beginning of heading	26.1	0.101	7	0.20	Merge (NIS)
		2. Broadcast foliar; beginning of flowering	26.0	0.100			
Innisfail, AB; 2005 (RCN R05166)	0.75 lb/gal SC/L	1. Broadcast foliar; soft dough	21.6	0.100	7	0.20	Merge (NIS)
		2. Broadcast foliar; hard dough	24.2	0.100			
		1. Broadcast foliar; middle of heading	26.6	0.101	7	0.20	Merge (NIS)
		2. Broadcast foliar; 70% of inflorescence emerged	24.6	0.098			

[1] EP = End-use Product
[2] Gallons per acre
[3] RTI = Retreatment Interval
[4] NIS=Nonionic surfactant

TABLE B.1.3. Trial Numbers and Geographical Locations.

NAFTA Growing Zones	Barley		
	Submitted	Requested[1]	
		Canada	U.S.
1	1		1[2]
1A			
2			1[2]
3			
4			
5	2	1	3 [2]
5A			
5B		1	
6			
7	2	2	4 [3]
7A			
8			
9	1		1
10	1		1
11	1		2 [1]
12			
13			
14	4	12	
15			
16			
17			
18			
19			
20			
21			
Total	12	16	12 [9]

[1] The requested number and geographic distribution of field trials for barley, according to OPPTS Guideline 860.1500 and PMRA Directive 98-2, are shown. Where two entries are provided for a region, the second number [given in brackets] is for situations where a 25% reduction in the number of trials is possible due to the crop being a representative commodity used to obtain a crop group tolerance.

[2] Either Zone 1 or 2 is acceptable.

B.2. Sample Handling and Preparation

Barley samples were placed in coolers and stored frozen at the field sites five hours after harvest. Samples remained in frozen storage at the field facilities for up to 52 days until shipment via ACDS freezer truck to the analytical laboratory, BASF Agro Research (Research Triangle Park, NC), for analysis. In preparation for analysis, barley samples were homogenized in the presence of dry ice. All samples remained frozen at all times except during homogenization and subsampling for analysis.

B.3. Analytical Methodology

Barley samples were analyzed for residues of metconazole, metabolites M11, M21, and M30, and the triazole metabolites (barley grain only), 1,2,4-T, TA, and TAA, using an LC/MS/MS method (BASF Method D0508). A brief description of the method was included in the MRID.

Briefly, residues of metconazole and its metabolites (M11, M21, and M30) were extracted with acetonitrile (ACN):water (70:30, v:v). The extracts were diluted with methanol:water (80:20, v:v), filtered, and reserved for LC/MS/MS analysis. For determination of residues of 1,2,4-T, TA, and TAA, a separate aliquot of the initial extract was evaporated to dryness, redissolved in 0.1% formic acid in water, filtered, and reserved for LC/MS/MS analysis. An optional clean-up step was used for determination of TA in barley grain if needed. A separate aliquot of the initial extract was diluted with methanol/water and applied to an SPE cartridge; residues were eluted with 1% NH_4OH in methanol. The resulting eluate was evaporated to dryness and redissolved in 0.1% formic acid in water as for other extracts. Residues of metabolites M11, M21, and M30 were converted to parent equivalents using molecular weight conversion factors of 0.95 for M11 and M21 and 0.96 for M30.

The validated LOQ was 0.01 ppm for the parent metconazole (sum of *cis* and *trans* isomers at 0.005 ppm each), M11, M21, and M30 in/on barley samples. The validated LOQ was 0.05 ppm for 1,2,4-T, TA, and TAA. The reported limit of detection was 20% LOQ.

The method was validated concurrently with the analysis of field samples using samples of untreated barley hay, grain, and straw fortified at 0.005 and 0.5 ppm with *cis*- and *trans*-metconazole; at 0.01 and 1.00 ppm with M11, M21, and M30; and at 0.05 and 5.00 ppm with 1,2,4-T, TA, and TAA.

C. RESULTS AND DISCUSSION

Samples were stored frozen (<-10 °C) from harvest to extraction for 160-241 days (5.3-7.9 months) for barley hay, 131-228 days (4.3-7.5 months) for barley grain, and 137-225 days (4.5-7.4 months) for barley straw, and were analyzed within 0-2 days of extraction. Adequate storage stability data are available indicating that: (1) residues of *cis*- and *trans*-metconazole are relatively stable under frozen storage conditions in wheat grain, rye forage, and wheat straw for up to 12 months (refer to 46902218.der.doc); (2) residues of M11, M21, and M30 are stable in/on wheat hay, straw, and grain for up to 6 months (refer to 46902223.der.doc); and (3) residues of 1,2,4-T, TA, and TAA are stable/relatively stable in/on wheat grain for up to 6 months (refer to 46902223.der.doc). These data are sufficient to support the storage conditions and durations for the barley field trials.

Concurrent method recovery data are presented in Table C.1. Samples were analyzed for residues of metconazole, metabolites M11, M21, and M30, and the triazole metabolites (barley grain only), 1,2,4-T, TA, and TAA, using LC/MS/MS Method D0508. Residues of metabolites M11, M21, and M30 were converted to parent equivalents using molecular weight conversion factors of 0.95 for M11 and M21 and 0.96 for M30. The method was adequate for data

collection based on acceptable concurrent method recovery data. Concurrent method recoveries were generally within the acceptable range of 70-120% for barley hay, grain, and straw fortified at 0.005 and 0.5 ppm with *cis*- and *trans*-metconazole; at 0.01 and 1.00 ppm with M11, M21, and M30; and at 0.05 and 5.00 ppm with 1,2,4-T, TA, and TAA.

Apparent residues of *cis*- and *trans*-metconazole, metabolites M11, M21, and M30, and 1,2,4-T were each below the respective LOQs in/on 12 samples each of untreated barley hay, grain, and straw with the exception of one hay sample which contained residues of *cis*- and *trans*-metconazole at 0.06 ppm and 0.40 ppm, respectively, and one straw sample which contained *cis*-metconazole at 0.01 ppm. Apparent residues of TA were detectable in eight of the twelve samples of untreated barley grain samples (0.06-0.43 ppm). Apparent residues of TAA were detectable in four of the twelve untreated barley samples (0.07-0.14 ppm).

Residue data from the barley field trials are reported in Table C.3.1 (metconazole, M11, M21, and M30) and Table C.3.2 (triazole metabolites), and summaries of the residue data for barley are presented in Tables C.4.1 and C.4.2. Residues of *cis*-and *trans*-metconazole in barley hay were 0.64-3.69 ppm and 0.09-0.74 ppm, respectively; total metconazole residues (sum of *cis* and *trans* isomers) were 0.73-4.43 ppm. In barley grain, residues of *cis*- and *trans*-metconazole were 0.09-1.33 ppm and 0.02-0.27 ppm, respectively, and total metconazole residues were 0.11-1.60 ppm. In barley straw, residues of *cis*- and *trans*-metconazole were 0.54-3.94 and 0.09-0.82 ppm, respectively, and total metconazole residues were 0.64-4.65 ppm. Residues of metabolite M11 were <0.01-0.38, <0.01-0.33, and 0.03-1.08 ppm for hay, grain, and straw, respectively; residues of M21 were <0.01-0.20, <0.01-0.08, and 0.04-0.46 ppm for hay, grain, and straw, respectively; and residues of metabolite M30 were <0.01-0.07 ppm, <0.01-0.05 ppm, and 0.01-0.15 for hay, grain, and straw, respectively.

Residues of 1,2,4-T, TA, and TAA in/on samples of barley grain were <0.05 ppm, <0.05-0.45 ppm, and <0.05-0.18 ppm, respectively.

The submitted residue decline data indicated that total metconazole residues (sum of *cis* and *trans* isomers) generally declined in barley hay, grain, and straw with increasing preharvest intervals.

TABLE C.1. Summary of Concurrent Recoveries of Metconazole and Metabolites from Barley.

Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev.[1] (%)
Grain	*cis*-Metconazole	0.005	2	74, 94	84
		0.500	2	75, 108	92
	trans-Metconazole	0.005	2	78, 83	80
		0.500	2	101, 107	104
	M11	0.010	2	85, 87	86
		1.000	2	86, 101	94
	M21	0.010	2	87, 100	94
		1.000	2	98, 107	102

TABLE C.1. Summary of Concurrent Recoveries of Metconazole and Metabolites from Barley.

Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev.[1] (%)
	M30	0.010	2	84, 102	93
		1.000	2	93, 104	98
	1,2,4-T	0.050	2	121, 129	125
		5.000	2	94, 101	98
	TAA	0.050	2	73, 77	75
		5.000	2	92, 101	96
	TA	0.050	2	69, 77	73
		5.000	2	82, 83	82
Hay	*cis*-Metconazole	0.005	3	65, 78, 85	76 ± 10
		0.500	3	71, 78, 110	86 ± 21
	trans-Metconazole	0.005	3	73, 78, 83	78 ± 5
		0.500	3	98, 100, 121	107 ± 13
	M11	0.010	3	69, 84, 86	80 ± 9
		1.000	3	91, 100, 112	101 ± 11
	M21	0.010	3	71, 76, 99	82 ± 15
		1.000	3	91, 95, 98	95 ± 4
	M30	0.010	3	82, 82, 92	85 ± 6
		1.000	3	91, 95, 103	96 ± 6
Straw	cis-Metconazole	0.005	2	72, 77	74
		0.500	2	92, 100	96
	trans-Metconazole	0.005	2	73, 85	79
		0.500	2	88, 94	91
	M11	0.010	2	75, 86	81
		1.000	2	84, 90	87
	M21	0.010	2	69, 83	76
		1.000	2	82, 99	91
	M30	0.010	2	77, 83	80
		1.000	2	94, 102	98

[1] Standard deviation is applicable only for groups ≥3 samples.

TABLE C.2. Summary of Storage Conditions.

Matrix	Storage Temperature (°C)	Actual Storage Duration [1] Days (Months)	Interval of Demonstrated Storage Stability
Hay	< -10	160-241 (5.3-7.9)	The available storage stability data indicate that residues of *cis*- and *trans*-metconazole are relatively stable in wheat grain, rye forage, and wheat straw for up to 12 months; and that residues of M11, M21, and M30 are stable in/on wheat hay, straw, and grain, and residues of 1,2,4-T, TA, and TAA are stable/relatively stable in/on wheat grain for up to 6 months.[2]
Grain		131-228 (4.3-7.5)	
Straw		137-225 (4.5-7.4)	

[1] Storage duration from harvest to extraction is reported by the petitioner. Samples were analyzed within 0-2 days of extraction.

[2] Refer to 46902218.der.doc and 46902223.der.doc.

TABLE C.3.1. Residue Data for Metconazole, M11, M21, and M30 from Crop Field Trials with Metconazole.

Trial Identification: County, State; Year (Trial ID)	Zone	Crop; Variety	Commodity or Matrix	Total Rate (lb ai/A)	PHI (days)[1]	Metconazole Residues (ppm parent equivalents)						
						Parent metconazole			Metabolites			Total[2]
						Cis	*Trans*	Total	M11	M21	M30	
Wayne, NY; 2005 (RCN R05155)	1	Spring barley, Chapais	Hay	0.21	7 [3]	2.472	0.393	2.865	0.05	0.04	0.01	3.0
						2.688	0.492	3.180	0.04	0.04	<0.01	3.3
			Grain	0.20	20	0.196	0.029	0.225	0.12	0.01	0.04	0.39
						0.173	0.029	0.203	0.12	0.01	0.03	0.37
			Straw	0.20	20	0.852	0.119	0.971	0.54	0.07	0.07	1.7
						0.736	0.111	0.847	0.48	0.06	0.07	1.5
St. Clair, IL; 2005 (RCN R05156)	5	Winter barley; Not specified	Hay	0.20	0	9.400	1.568	10.968	0.05	0.04	0.01	11.1
						9.380	1.540	10.920	0.05	0.04	0.01	11.0
					7 [5]	2.296	0.408	2.704	0.06	0.03	0.01	2.8
						2.460	0.504	2.964	0.07	0.04	0.01	3.1
					14	1.340	0.220	1.560	0.19	0.05	0.03	1.8
						1.248	0.224	1.472	0.15	0.05	0.03	1.7
			Grain	0.20	14	1.504	0.362	1.866	0.40	0.10	0.06	2.42
						1.502	0.164	1.216	0.29	0.07	0.05	1.62
					21	1.224	0.177	1.401	0.30	0.08	0.05	1.83
						0.828	0.127	0.955	0.33	0.06	0.04	1.38
					28	0.808	0.136	0.944	0.25	0.06	0.04	1.30
						0.624	0.091	0.715	0.19	0.05	0.04	0.98
					35	0.564	0.086	0.650	0.18	0.04	0.03	0.91
						0.608	0.095	0.703	0.28	0.05	0.04	1.08
			Straw	0.20	14	2.984	0.716	3.700	0.90	0.42	0.14	5.2
						3.328	0.704	4.032	0.81	0.40	0.13	5.4
					21	2.720	0.592	3.312	1.08	0.46	0.15	5.0
						2.496	0.524	3.020	0.95	0.40	0.14	4.5
					28	2.504	0.568	3.072	1.14	0.48	0.17	4.9
						1.716	0.378	2.094	0.95	0.36	0.14	3.5
					35	1.460	0.290	1.750	0.87	0.36	0.14	3.1
						1.420	0.288	1.708	0.97	0.32	0.15	3.1
York, NE; 2005 (RCN R05157)	5	Spring barley; Robust	Hay	0.20	7 [0]	0.732	0.125	0.857	<0.01	<0.01	<0.01	0.9
						0.636	0.090	0.726	<0.01	<0.01	<0.01	0.8
			Grain	0.20	21	0.172	0.035	0.207	0.03	<0.01	<0.01	0.26
						0.140	0.028	0.168	0.03	<0.01	<0.01	0.22
			Straw	0.20	21	1.628	0.208	1.836	0.50	0.12	0.06	2.5
						1.788	0.343	2.131	0.51	0.12	0.06	2.8
McHenry, ND; 2005 (RCN R05158)	7	Spring barley; Excel	Hay	0.20	8 [1]	0.764	0.120	0.884	<0.01	0.01	<0.01	0.9
						1.320	0.177	1.497	0.01	0.02	<0.01	1.5
			Grain	0.20	20	0.137	0.026	0.162	0.02	<0.01	<0.01	0.20
						0.145	0.028	0.173	0.02	<0.01	<0.01	0.21
			Straw	0.20	20	1.756	0.330	2.086	0.10	0.07	0.02	2.3
						1.332	0.181	1.513	0.08	0.06	0.02	1.7

TABLE C.3.1. Residue Data for Metconazole, M11, M21, and M30 from Crop Field Trials with Metconazole.

Trial Identification: County, State; Year (Trial ID)	Zone	Crop; Variety	Commodity or Matrix	Total Rate (lb ai/A)	PHI (days)[1]	Metconazole Residues (ppm parent equivalents)						
						Parent metconazole			Metabolites			Total [2]
						Cis	*Trans*	Total	M11	M21	M30	
Hall, NE; 2005 (RCN R05159)	7	Spring barley; Robust	Hay	0.20	7 [0]	0.684	0.105	0.789	<0.01	<0.01	<0.01	0.8
						0.760	0.090	0.850	<0.01	<0.01	<0.01	0.9
			Grain	0.20	21	0.432	0.066	0.498	0.05	0.01	0.01	0.58
						0.404	0.056	0.460	0.05	0.01	0.01	0.54
			Straw	0.20	21	2.652	0.532	3.184	0.49	0.13	0.06	3.9
						3.060	0.564	3.624	0.54	0.14	0.07	4.4
Cache, UT; 2005 (RCN R05160)	9	Spring barley; Baronesse	Hay	0.21	7	1.912	0.331	2.243	0.06	0.07	0.01	2.4
						1.732	0.368	2.100	0.06	0.07	0.01	2.2
			Grain	0.20	20	0.490	0.092	0.582	<0.01	<0.01	<0.01	0.61
						0.466	0.101	0.567	<0.01	<0.01	<0.01	0.60
			Straw	0.20	20	3.512	0.680	4.192	0.11	0.11	0.03	4.4
						3.536	0.672	4.208	0.11	0.11	0.03	4.5
Madera, CA; 2005 (RCN R05161)	10	Spring barley; Farmers Best	Hay	0.20	7 [3]	2.616	0.580	3.196	0.02	0.03	<0.01	3.3
						2.776	0.496	3.272	0.02	0.03	<0.01	3.3
			Grain	0.20	21	0.884	0.198	1.082	0.01	0.01	<0.01	1.11
						1.330	0.268	1.598	0.01	0.02	<0.01	1.64
			Straw	0.20	21	3.936	0.712	4.648	0.03	0.05	0.01	4.7
						3.700	0.780	4.480	0.03	0.05	0.01	4.6
Payette, ID; 2005 (RCN R05162)	11	Spring barley; Baronesse	Hay	0.20	7 [5]	2.556	0.476	3.032	0.04	0.05	0.01	3.1
						2.716	0.568	3.284	0.04	0.05	0.01	3.4
			Grain	0.20	21	0.576	0.111	0.687	<0.01	0.01	<0.01	0.72
						0.520	0.114	0.634	<0.01	0.01	<0.01	0.66
			Straw	0.20	21	2.760	0.568	3.328	0.04	0.06	0.01	3.4
						2.444	0.476	2.920	0.03	0.04	0.01	3.0
Rosthern, SK; 2005 (RCN R05163)	14	Spring barley; AC Metcalfe	Hay	0.20	7 [13]	3.320	0.516	3.836	0.06	0.08	0.01	4.0
						3.628	0.720	4.348	0.04	0.06	0.01	4.5
			Grain	0.20	21	0.093	0.019	0.112	0.01	0.01	<0.01	0.15
						0.104	0.020	0.124	0.02	0.01	<0.01	0.17
			Straw	0.20	21	0.544	0.094	0.638	0.09	0.09	0.03	0.8
						0.592	0.105	0.697	0.10	0.09	0.03	0.9
Minto, MB; 2005 (RCN R05164)	14	Spring barley; AC Metcalfe	Hay	0.20	7 [6]	2.584	0.440	3.024	0.12	0.07	0.03	3.2
						2.752	0.496	3.248	0.11	0.06	0.03	3.5
			Grain	0.20	20	0.268	0.043	0.311	0.04	0.01	<0.01	0.38
						0.191	0.034	0.225	0.03	<0.01	<0.01	0.28
			Straw	0.20	20	2.648	0.468	3.116	0.68	0.36	0.08	4.2
						2.964	0.540	3.504	0.55	0.33	0.08	4.5

TABLE C.3.1. Residue Data for Metconazole, M11, M21, and M30 from Crop Field Trials with Metconazole.

Trial Identification: County, State; Year (Trial ID)	Zone	Crop; Variety	Commodity or Matrix	Total Rate (lb ai/A)	PHI (days)[1]	Metconazole Residues (ppm parent equivalents)						
						Parent metconazole			Metabolites			Total [2]
						Cis	*Trans*	Total	M11	M21	M30	
Innisfail, AB; 2005 (RCN R05165)	14	Spring barley; CDC Bold	Hay	0.20	7 [14]	2.804	0.528	3.332	0.15	0.13	0.03	3.6
						3.144	0.660	3.804	0.13	0.12	0.03	4.1
			Grain	0.20	21	0.480	0.102	0.582	0.07	0.05	0.01	0.71
						0.462	0.101	0.563	0.07	0.04	0.01	0.68
			Straw	0.20	21	1.612	0.333	1.945	0.33	0.13	0.05	2.5
						1.864	0.373	2.237	0.36	0.13	0.05	2.8
Innisfail, AB; 2005 (RCN R05166)	14	Spring barley; CDC Bold	Hay	0.20	7 [14]	3.688	0.740	4.428	0.38	0.20	0.07	5.1
						3.688	0.628	4.316	0.33	0.19	0.06	4.9
			Grain	0.20	21	0.404	0.076	0.480	0.07	0.04	<0.01	0.59
						0.400	0.072	0.472	0.06	0.04	<0.01	0.60
			Straw	0.20	21	3.476	0.812	4.288	0.75	0.42	0.05	5.5
						3.712	0.824	4.536	0.85	0.41	0.05	5.8

[1] Hay samples were cut, then allowed to dry in the field prior to collection; the drying interval is presented in brackets.
[2] Total= total residues; sum of *cis*- and *trans*-metconazole, M11, M21, and M30; values presented as calculated and reported by the petitioner.

TABLE C.3.2. Residue Data for the Triazole Metabolites from Crop Field Trials with Metconazole.

Trial ID: City, State; Year (Trial ID)	Zone	Crop; Variety	Commodity or Matrix	Total Rate (lb ai/A)	PHI (days)	Triazole Residues (ppm)		
						1,2,4-T	TA	TAA
Wayne, NY; 2005 (RCN R05155)	1	Spring barley, Chapais	Grain	0.20	20	<0.05	0.18	0.09
						<0.05	0.18	0.08
St. Clair, IL; 2005 (RCN R05156)	5	Winter barley; Not specified	Grain	0.20	14	<0.05	0.07	0.06
						<0.05	0.07	0.05
					21	<0.05	0.06	<0.05
						<0.05	0.06	0.06
					28	<0.05	0.07	0.07
						<0.05	0.06	<0.05
					35	<0.05	0.06	<0.05
						<0.05	0.07	0.06
York, NE; 2005 (RCN R05157)	5	Spring barley; Robust	Grain	0.20	21	<0.05	0.14	0.06
						<0.05	0.12	<0.05
McHenry, ND; 2005 (RCN R05158)	7	Spring barley; Excel	Grain	0.20	20	<0.05	0.10	<0.05
						<0.05	0.10	<0.05
Hall, NE; 2005 (RCN R05159)	7	Spring barley; Robust	Grain	0.20	21	<0.05	0.09	<0.05
						<0.05	0.08	<0.05
Cache, UT; 2005 (RCN R05160)	9	Spring barley; Baronesse	Grain	0.20	20	<0.05	<0.05	<0.05
						<0.05	<0.05	<0.05
Madera, CA; 2005 (RCN R05161)	10	Spring barley; Farmers Best	Grain	0.20	21	<0.05	<0.05	<0.05
						<0.05	<0.05	<0.05

TABLE C.3.2. Residue Data for the Triazole Metabolites from Crop Field Trials with Metconazole.

Trial ID: City, State; Year (Trial ID)	Zone	Crop; Variety	Commodity or Matrix	Total Rate (lb ai/A)	PHI (days)	Triazole Residues (ppm)		
						1,2,4-T	TA	TAA
Payette, ID; 2005 (RCN R05162)	11	Spring barley; Baronesse	Grain	0.20	21	<0.05	<0.05	<0.05
						<0.05	<0.05	<0.05
Rosthern, SK; 2005 (RCN R05163)	14	Spring barley; AC Metcalfe	Grain	0.20	21	<0.05	<0.05	<0.05
						<0.05	0.05	<0.05
Minto, MB; 2005 (RCN R05164)	14	Spring barley; AC Metcalfe	Grain	0.20	20	<0.05	0.45	0.18
						<0.05	0.42	0.18
Innisfail, AB; 2005 (RCN R05165)	14	Spring barley; CDC Bold	Grain	0.20	21	<0.05	0.05	<0.05
						<0.05	<0.05	<0.05
Innisfail, AB; 2005 (RCN R05166)	14	Spring barley; CDC Bold	Grain	0.20	21	<0.05	0.31	0.07
						<0.05	0.32	0.06

TABLE C.4.1 Summary of Residue Data for Metconazole, M11, M21, and M30 from Barley Field Trials with Metconazole.

Commodity	Total Applic. Rate (lb ai/A)	PHI (days)	Analyte	Residue Levels[1] (ppm)						
				n	Min.	Max.	HAFT[2]	Median (STMdR)	Mean (STMR)	Std. Dev.
Hay	0.20-0.21	6-8 [0-14]	*cis*-Metconazole	24	0.64	3.69	3.69	2.57	2.28	0.99
			trans-Metconazole	24	0.09	0.74	0.68	0.48	0.42	0.20
			Metconazole	**24**	**0.73**	**4.43**	**4.37**	**3.03**	**2.70**	**1.19**
			M11	24	<0.01	0.38	0.36	0.05	0.08	0.10
			M21	24	<0.01	0.2	0.2	0.05	0.06	0.05
			M30	24	<0.01	0.07	0.07	0.01	0.02	0.02
			Total Residues	24	0.80	5.10	5.00	3.15	2.86	1.31
Grain	0.20	20-21	*cis*-Metconazole	24	0.09	1.33	1.11	0.40	0.44	0.34
			trans-Metconazole	24	0.02	0.27	0.23	0.07	0.08	0.06
			Metconazole	**24**	**0.11**	**1.60**	**1.34**	**0.48**	**0.52**	**0.40**
			M11	24	<0.01	0.33	0.32	0.03	0.06	0.08
			M21	24	<0.01	0.08	0.07	0.01	0.02	0.02
			M30	24	<0.01	0.05	0.05	0.01	0.02	0.01
			Total Residues	24	0.15	1.83	1.61	0.59	0.62	0.45
Straw	0.20	20-21	*cis*-Metconazole	24	0.54	3.94	3.82	2.57	2.35	1.06
			trans-Metconazole	24	0.09	0.82	0.82	0.50	0.46	0.23
			Metconazole	**24**	**0.64**	**4.65**	**4.56**	**3.07**	**2.80**	**1.29**
			M11	24	0.03	1.08	1.02	0.42	0.39	0.32
			M21	24	0.04	0.46	0.43	0.12	0.17	0.14
			M30	24	0.01	0.15	0.15	0.05	0.05	0.04
			Total Residues	24	0.80	5.80	5.65	3.65	3.41	1.45

[1] For calculation of mean, median, and standard deviation, the LOQ was used for any results reported as <LOQ in Table C.3.1.
[2] HAFT = Highest Average Field Trial.

TABLE C.4.2 Summary of Residue Data for the Triazole Metabolites from Barley Field Trials with Metconazole.

Commodity	Total Applic. Rate (lb ai/A)	PHI (days)	Analyte	Residue Levels[1] (ppm)						
				n	Min.	Max.	HAFT[2]	Median (STMdR)	Mean (STMR)	Std. Dev.
Grain	0.20	20-21	1,2,4-T	24	<0.05	<0.05	0.05	0.05	0.05	--
			TA	24	<0.05	0.45	0.44	0.07	0.13	0.12
			TAA	24	<0.05	0.18	0.18	0.05	0.07	0.04

[1] For calculation of mean, median, and standard deviation, the LOQ was used for any results reported as <LOQ in Table C.3.2.
[2] HAFT = Highest Average Field Trial.

D. CONCLUSION

The submitted field trial data are adequate and reflect the use of two broadcast foliar applications of a 0.75 lb ai/gal SC/L formulation of metconazole at a total rate of ~0.20 lb ai/A, with a 6- to 8-day retreatment interval. Samples were harvested at PHIs of 6-8 days for barley hay and 20-21 days for grain and straw. An acceptable method was used for quantitation of residues of *cis*- and *trans*-metconazole, M11, M21, and M30, 1,2,4-T, TA, and TAA in/on barley samples. The study is supported by adequate storage stability data for *cis*- and *trans*-metconazole.

E. REFERENCES

DP#: 324541
Subject: Metconazole. Request for a Tolerance on Imported Bananas. Summary of Analytical Chemistry and Residue Data. Petition Number 9E05052.
From: N. Dodd
To: M. Waller
Date: 12/14/05
MRIDs: 44721506, 44721507, 44721508, 44721509, 44721510, and 44721511

F. DOCUMENT TRACKING

RDI: N. Dodd (2/20/08)
Petition Numbers: 6F7094 and 6F7095
DP#s: 348168 and 348206
PC Code: 125619

Template Version June 2005

615

Primary Evaluator	This DER was originally prepared under contract by Dynamac Corporation.
Approved by	Nancy Dodd, Chemist Nancy Dodd Date: 2/20/08 Registration Action Branch 3 Health Effects Division (7509P)

This DER was originally prepared under contract by Dynamac Corporation (2275 Research Boulevard, Suite 300; Rockville, MD 20850; submitted 09/18/2007). The DER has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

46902226 Jordan, J.; Saha, M. (2006) The Magnitude of Metconazole (BAS 555 F) and its Metabolites and Pyraclostrobin (BAS 500 F) Residues in Oats: Final Report. Project Number: 137717, 2006/7006724. Unpublished study prepared by BASF Agro Research, ACDS Research, Inc. and Southeast Ag Research, Inc. 255 p.

EXECUTIVE SUMMARY:

BASF Corporation has submitted field trial data for metconazole on oats. Twelve field trials were conducted in the United States and Canada in Zones 1 (NY; 1 trial), 2 (GA, 1 trial), 5 (IL, ND, WI; 3 trials), 5B (QB; 1 trial), 6 (OK; 1 trial), 7 (ND, NE; 2 trials), and 14 (AB, MB, SK; 3 trials) during the 2004-2005 growing season. Because Canadian Zones 5B and 14 are contiguous with the two major U.S. oat-growing regions, Zones 5 and 7, HED has concluded that results from the Canadian trials may be used to address U.S. data requirements for oats.

Each test site included one control plot and two treated plots. The treated plots received two broadcast foliar applications of a 0.75 lb ai/gal soluble concentrate/liquid (SC/L) formulation of metconazole at 0.10-0.11 lb ai/A/application, with a 6- to 8-day retreatment interval, for a total seasonal rate of 0.20-0.21 lb ai/A. Applications were initiated four weeks prior to the harvest of mature grain (plot 2) or two weeks prior to the cutting of hay (plot 3). Applications were made in 10-27 gal/A spray volumes. A nonionic surfactant was added as a spray adjuvant for all applications.

Oat hay was harvested 6-8 days after the last application and was allowed to dry in the field for 0-29 days before collection. Oat grain and straw were harvested 20-21 days after the last application, except for one trial in which grain and straw were harvested 26 days after the last application due to adverse weather conditions. Additional hay samples were collected from one trial 0, 7, and 14 days after the last application, and grain and straw samples were harvested 14, 21, 28, and 36 days after the last application to generate residue decline data.

Samples were analyzed for residues of *cis*- and *trans*-metconazole, metabolites M11, M21, and M30, and the triazole metabolites (oat grain only), triazole (1,2,4-T), triazolylalanine (TA), and triazolylacetic acid (TAA), using an LC/MS/MS method (BASF Method D0508). Residues of metabolites M11, M21, and M30 were converted to parent equivalents using molecular weight conversion factors of 0.95 for M11 and M21 and 0.96 for M30. The validated limits of quantitation (LOQs) were 0.01 ppm for the parent metconazole (sum of *cis* and *trans* isomers at 0.005 ppm each), M11, M21, and M30 in/on oat samples. The validated LOQ was 0.05 ppm for 1,2,4-T, TA, and TAA. The method was adequate for data collection based on acceptable concurrent method recoveries.

Samples were stored frozen (<-10 °C) from harvest to extraction for 230-372 days (7.6-12.2 months) for oat hay, 221-364 days (7.3-12.0 months) for oat grain, and 213-355 days (7.0-11.7 months) for oat straw, and were analyzed within 0-3 days of extraction. Adequate storage stability data are available to support the storage conditions and durations of samples for the oat field trials.

Maximum residues of *cis*-and *trans*-metconazole in/on oat hay were 10.013 and 1.659 ppm, respectively; maximum total metconazole residues (sum of *cis* and *trans* isomers) were 11.672 ppm. In oat grain, maximum residues of *cis*- and *trans*-metconazole were 0.566 and 0.218 ppm, respectively, and maximum total metconazole residues were 0.680 ppm. In oat straw, maximum residues of *cis*- and *trans*-metconazole were 5.067 and 0.869 ppm, respectively, and maximum total metconazole residues were 5.937 ppm. Maximum residues of metabolite M11 were 0.43, 0.34, and 2.48 ppm for oat hay, grain, and straw, respectively; maximum residues of M21 were 0.12, 0.06, and 0.49 ppm for oat hay, grain, and straw, respectively; and maximum residues of metabolite M30 were 0.05, 0.06, and 0.18 ppm for oat hay, grain, and straw, respectively.

Maximum residues of 1,2,4-T, TA, and TAA in/on samples of oat grain were 0.08, 1.22, and 0.40 ppm, respectively.

The submitted residue decline data indicated that total metconazole residues (sum of *cis* and *trans* isomers) generally declined in oat hay, grain, and straw with increasing preharvest intervals.

HED notes that oat forage was not collected from any trial site because applications were initiated at a later growth stage.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the field trial residue data are classified as scientifically acceptable. Oat forage was not collected; however, data on oat forage are not required for late-season applications (after flag leaf emergence).

The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP#s 348168 and 348206.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an impact on the validity of the study.

A. BACKGROUND INFORMATION

Metconazole [5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol] is a broad-spectrum triazole Group 3 fungicide (sterol biosynthesis inhibitors). There are currently no registered uses of metconazole in the U.S.; however, a tolerance has been established for banana, and a Section 18 emergency exemption and supporting time-limited tolerances have been granted for use on soybean. BASF Corporation has applied for registration of metconazole in the U.S. for use on barley, oats, rye, soybeans, sugar beets, triticale, and wheat.

The chemical structure and nomenclature of metconazole, and the physicochemical properties of the technical grade of metconazole are presented in Tables A.1 and A.2.

TABLE A.1. Metconazole Nomenclature.

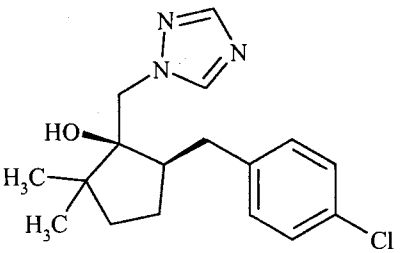
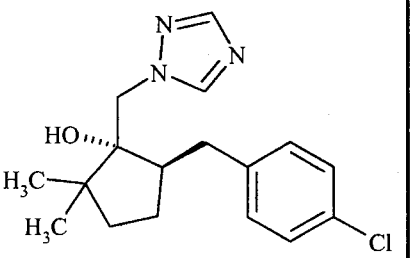
Chemical structure	 *cis*-isomer	 *trans*-isomer
Common name	Metconazole	
Company experimental name	KNF-S-474m (Kureha); BAS 555 F (BASF); V-10116 (Valent)	
IUPAC name	(1RS,5RS:1RS,5SR)-5-(4-chlorobenzyl)-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	
CAS name	5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	
CAS registry number	125116-23-6 (*cis*- and *trans*-isomers) 115850-27-6 (*cis*-isomer) 115850-28-7 (*trans*-isomer)	
End-use products (EP)	50% WDG (Metconazole 50 WDG Fungicide, EPA File Symbol 59639-RUT) 0.75 lb/gal SC/L (Caramba™ Fungicide, EPA File Symbol No. 7969-EUA) 0.67 lb/gal SC/L formulation (BAS 556 01F Fungicide, EPA File Symbol No. 7969-EUT; also contains the active ingredient pyraclostrobin at 0.83 lb/gal)	

TABLE A.1. Metconazole Nomenclature.

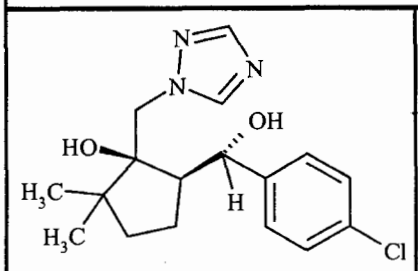
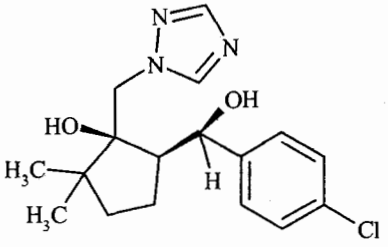
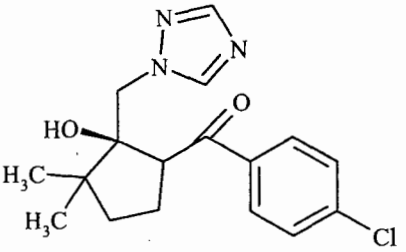
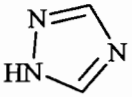
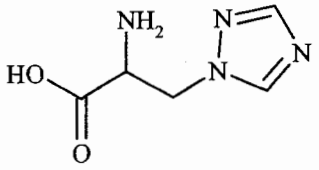
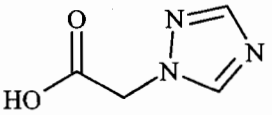
 Metconazole metabolite M11	 Metconazole metabolite M21	 Metconazole metabolite M30
 Triazole metabolite 1,2,4-triazole (1,2,4-T)	 Triazole metabolite triazolylalanine (TA)	 Triazole metabolite triazolylacetic acid (TAA)

Table A.2. Physicochemical Properties of Metconazole

Parameter	Value				References* (MRID)
Melting point/range	100.0-108.4°C (using Electrothermal Digital Melting Point Apparatus) (AC900,768 technical grade)				44721505
pH	5.81 at 25°C (1% aqueous suspension)				46808402
Relative density (20°C)	1.14 (relative density to water at 4°C, using capillary-stoppered, density-specific gravity bottle) (Lot No. AC 8879-140B)				44721505
Water solubility (20°C)	Using shake-flask method: 18.7 ± 1.0 mg/L (*cis*-isomer, WL148271, KNF-S-474m) 13.6 ± 1.7 mg/L (*trans*-isomer, WL148271, KNF-S-474m)				44721505
Solvent solubility (g/L) at 20°C	Solvent	Metconazole	*cis*	*trans*	44721505
	acetone	363	251	117	
	methanol	403	294	117	
	dichloromethane	481	343	141	
	ethyl acetate	260	173	90.0	
	propanol	132	86.6	46.7	
	toluene	103	66.2	38.0	
	Hexane	1.40	0.929	0.483	
Vapor pressure (20°C)	Using gas-saturation method: $< 1.23 \times 10^{-5}$ Pa or 9.23×10^{-8} mm Hg (metconazole) $< 1.04 \times 10^{-5}$ Pa or 7.80×10^{-8} mm Hg (*cis*-isomer) $< 1.96 \times 10^{-6}$ Pa or 1.47×10^{-8} mm Hg (*trans*-isomer)				44721505
Dissociation constant (pK_a)	11.38±0.03 and 1.06±0.03 (in water at 29.1°C using spectrophotometric method; Lot No. AC 8879-140B)				44721505

Table A.2. Physicochemical Properties of Metconazole

Parameter	Value				References* (MRID)
Octanol/water partition coefficient, Log(K_{OW})	At 20 °C (using flask shaking method): K_{ow} (log K_{ow}) = 7090±989 (3.85) (Lot No. AC 8879-140B) (TGAI) K_{ow} (log K_{ow}) = 7150±803 (3.85) (*cis*-isomer, CL 354,801) K_{ow} (log K_{ow}) = 6800±1700 (3.8) (*trans*-isomer, CL 354,802)				44721505
UV/visible absorption spectrum	pH	λ	A	log ε	46808403
	cis-isomer				
	2.0	221.4	0.828	4.03	
	6.8		0.8452	4.04	
	7.0		0.9126	4.08	
	10.3		0.7226	3.98	
	trans-isomer				
	2.0	221.4	0.9053	4.07	
	7.0		0.9547	4.10	
	10.1		0.9893	4.11	

* Product Chemistry Reviews: DP #256877, Shyam Mathur, Ph.D., 9/12/2000 and DP #329168, Shyam Mathur, Ph.D., 7/13/07.

B. EXPERIMENTAL DESIGN

B.1. Study Site Information

Twelve field trials were conducted in the United States and Canada in Zones 1 (NY; 1 trial), 2 (GA, 1 trial), 5 (IL, ND, WI; 3 trials), 5B (QB; 1 trial), 6 (OK; 1 trial), 7 (ND, NE; 2 trial), and 14 (AB, MB, SK; 3 trials) during the 2004-2005 growing season.

Each test site included one control plot and two treated plots. The treated plots received two broadcast foliar applications of a 0.75 lb ai/gal soluble concentrate/liquid (SC/L) formulation of metconazole at 0.10-0.11 lb ai/A/application, with a 6- to 8-day retreatment interval, for a total seasonal rate of 0.20-0.21 lb ai/A. Applications were initiated four weeks prior to the harvest of mature grain (plot 2) or two weeks prior to the cutting of hay (plot 3). Applications were made in 10-27 gal/A spray volumes. A nonionic surfactant was added as a spray adjuvant for all applications.

Oat hay was harvested 6-8 days after the last application and was allowed to dry in the field for 0-29 days before collection. Oat grain and straw were harvested 20-21 days after the last application, except for one trial where grain and straw were harvested 26 days after the last application due to adverse weather conditions. Additional hay samples were collected from one trial 0, 7, and 14 days after the last application, and grain and straw samples were harvested 14, 21, 28, and 36 days after the last application to generate residue decline data. Oat forage was not collected from any trial site because applications were initiated at a later growth stage.

The test crops were grown and maintained according to typical agricultural practices for each region; maintenance pesticides and fertilizers were used to produce a commercial quality crop. Irrigation was used to supplement rainfall as needed. Trial site conditions are presented in Table B.1.1, and the study use pattern is presented in Table B.1.2. The crop varieties grown are identified in Table C.3.

For each field trial, the petitioner presented the weather conditions at application and summarized the weather conditions for the duration of the trials. The petitioner reported abnormal meteorological conditions in several trial sites, which are summarized in Table B.1.1. These unusual weather conditions did not have an adverse effect on the oat crops.

TABLE B.1.1. Trial Site Conditions.

Trial Identification: County, State; Year (Trial ID)	Soil Characteristics				Meteorological Data	
	Type	%OM	pH	CEC (meq/g)	Overall Rainfall range	Overall Temperature range (°C)
Wayne, NY; 2005 (RCN R05126)	Silt Loam	4.1	5.0	Not provided	Above normal in April and July. Below normal in May and June	Normal
Tift, GA; 2004 (RCN R05127)	Loamy Sand	1.0	5.5	Not provided	Normal	Normal
Clinton, IL; 2005 (RCN R05128)	Silt Loam	2.3	7.0	Not provided	Normal	Normal
Pepin, WI; 2005 (RCN R05129)	Sandy Loam	2.9	5.7	Not provided	Normal	Cooler during May and warmer during June
Stutsman, ND; 2005 (RCN R05130)	Sandy Loam	4.7	5.7	Not provided	Above normal in May, June, August, and September	Normal
Hall, NE; 2005 (RCN R05131)	Clay Loam	2.7	6.6	Not provided	Above normal for May and June, and below normal in July	Above normal
Cass, ND; 2005 (RCN R05132)	Loam	4.1	8.2	Not provided	Above normal in June and August	Normal
Caddo, OK; 2005 (RCN R05133)	Sandy Loam	Not provided			Much below normal in March and April. Much above normal in June	Cooler than normal
St-Cesaire, QB; 2005 (RCN R05134)	Loamy Sand	4.1	4.7	Not provided	Generally above normal	Normal
Rosthern, SK; 2005 (RCN R05135)	Loam	7.2	7.0	Not provided	Above normal in August and September	Generally cooler than normal
Minto, MB; 2005 (RCN R05136)	Loam	4.9	7.5	Not provided	Above normal for May-July. Below normal in August	Cooler than normal for May-August
Innisfail, AB; 2005 (RCN R05137)	Clay Loam	7.6	6.2	Not provided	Generally above normal, especially in June, August, and September	Normal

TABLE B.1.2. Study Use Pattern.

Trial Identification: County, State; Year (Trial ID)	EP[1]	Application					Tank Mix/ Adjuvants[4]
		Method; Timing	Volume GPA[2]	Rate (lb ai/A)	RTI[3] (days)	Total Rate (lb ai/A)	
Wayne, NY; 2005 (RCN R05126)	0.75 lb/gal SC/L	1. Broadcast foliar; early milk	24.25	0.0991	8	0.20	Induce (NIS)
		2. Broadcast foliar; early dough	24.96	0.1020			
		1. Broadcast foliar; beginning of flowering	25.03	0.1023	7	0.20	
		2. Broadcast foliar; first grains half final size	24.88	0.1018			
Tift, GA; 2004 (RCN R05127)	0.75 lb/gal SC/L	1. Broadcast foliar; medium milk	14.03	0.0977	7	0.20	Penetron (NIS)
		2. Broadcast foliar; soft dough	14.55	0.1042			
		1. Broadcast foliar; 1st node >1 cm above tillering node	18.42	0.1011	8	0.20	
		2. Broadcast foliar; late boot stage	16.98	0.0999			
Clinton, IL; 2005 (RCN R05128)	0.75 lb/gal SC/L	1. Broadcast foliar; medium milk	17.75	0.1011	7	0.20	NIS
		2. Broadcast foliar; soft dough	17.81	0.0979			
		1. Broadcast foliar; beginning of flowering	12.60	0.1034	8	0.21	
		2. Broadcast foliar; early milk	16.68	0.1016			
Pepin, WI; 2005 (RCN R05129)	0.75 lb/gal SC/L	1. Broadcast foliar; first grains half final size	20.15	0.1003	7	0.20	Induce (NIS)
		2. Broadcast foliar; medium milk	20.18	0.1010			
		1. Broadcast foliar; beginning of heading	20.15	0.1033	7	0.20	
		2. Broadcast foliar; beginning of flowering	20.14	0.1007			
Stutsman, ND; 2005 (RCN R05130)	0.75 lb/gal SC/L	1. Broadcast foliar; end of flowering	19.91	0.0997	7	0.20	Activator 90 (NIS)
		2. Broadcast foliar; medium milk	15.16	0.1007			
		1. Broadcast foliar; node 3 >2 cm above node 2	10.12	0.1007	8	0.20	
		2. Broadcast foliar; flag leaf stage	12.47	0.1024			
Hall, NE; 2005 (RCN R05131)	0.75 lb/gal SC/L	1.. Broadcast foliar; medium milk	20.21	0.1010	7	0.20	Activate Plus (NIS)
		2. Broadcast foliar; soft dough	20.21	0.1010			

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TABLE B.1.2. Study Use Pattern.

Trial Identification: County, State; Year (Trial ID)	EP[1]	Application					Tank Mix/ Adjuvants[4]
		Method; Timing	Volume GPA[2]	Rate (lb ai/A)	RTI[3] (days)	Total Rate (lb ai/A)	
		1. Broadcast foliar; 60% of inflorescence emerged	20.07	0.1035	7	0.20	
		2. Broadcast foliar; beginning of flowering	20.00	0.1004			
Cass, ND; 2005 (RCN R05132)	0.75 lb/gal SC/L	1. Broadcast foliar; end of flowering	15.89	0.1003	6	0.20	Activator 90 (NIS)
		2. Broadcast foliar; medium milk	15.91	0.1013			
		1. Broadcast foliar; node 2 >2 cm above node 1	17.06	0.1028	7	0.20	
		2. Broadcast foliar; flag leaf stage	15.94	0.1018			
Caddo, OK; 2005 (RCN R05133)	0.75 lb/gal SC/L	1. Broadcast foliar; first grains half final size	13.45	0.1010	7	0.20	Baron (NIS)
		2. Broadcast foliar; late milk	14.10	0.1023			
		1. Broadcast foliar; beginning of heading	13.70	0.1000	7	0.20	
		2. Broadcast foliar; first grains half final size	13.46	0.1010			
St-Cesaire, QB; 2005 (RCN R05134)	0.75 lb/gal SC/L	1. Broadcast foliar; late milk	21.62	0.0965	7	0.20	Surf 92 (NIS)
		2. Broadcast foliar; hard dough	24.35	0.0987			
		1. Broadcast foliar; late milk	25.07	0.1060	7	0.20	
		2. Broadcast foliar; hard dough	24.29	0.0985			
Rosthern, SK; 2005 (RCN R05135)	0.75 lb/gal SC/L	1. Broadcast foliar; late milk	21.85	0.1004	8	0.20	AgSurf (NIS)
		2. Broadcast foliar; early dough	21.36	0.0999			
		1. Broadcast foliar; late boot stage	21.53	0.0993	7	0.20	
		2. Broadcast foliar; beginning of flowering	20.97	0.1001			
Minto, MB; 2005 (RCN R05136)	0.75 lb/gal SC/L	1. Broadcast foliar; medium milk	22.28	0.1013	7	0.20	AgSurf (NIS)
		2. Broadcast foliar; hard dough	21.30	0.0990			
		1. Broadcast foliar; 80% of inflorescence emerged	22.33	0.0991	6	0.20	
		2. Broadcast foliar; end of flowering	21.94	0.1019			

TABLE B.1.2. Study Use Pattern.

Trial Identification: County, State; Year (Trial ID)	EP[1]	Application					Tank Mix/ Adjuvants[4]
		Method; Timing	Volume GPA[2]	Rate (lb ai/A)	RTI[3] (days)	Total Rate (lb ai/A)	
Innisfail, AB; 2005 (RCN R05137)	0.75 lb/gal SC/L	1. Broadcast foliar; early dough	24.16	0.1001	7	0.20	Merge (NIS)
		2. Broadcast foliar; soft dough	25.07	0.1009			
		1. Broadcast foliar; beginning of flowering	26.95	0.0992	7	0.20	
		2. Broadcast foliar; end of flowering	23.79	0.0968			

[1] EP = End-use Product
[2] Gallons per acre
[3] RTI = Retreatment Interval
[4] NIS = Nonionic surfactant

TABLE B.1.3. Trial Numbers and Geographical Locations.

NAFTA Growing Zones	Oat		
	Submitted	Requested[1]	
		Canada	U.S.
1	1	1	1
1A			
2	1		1
3			
4			
5	3	1	9 [6]
5A		1	
5B	1	1	
6	1		1
7	2	2	3 [2]
7A			
8			1
9			
10			
11			
12			
13			
14	3	10	
15			
16			
17			
18			
19			
20			
21			
Total	12	16	16 [12]

624

[1] The requested number and geographic distribution of field trials for oats, according to OPPTS Guideline 860.1500 and PMRA Directive 98-2, are shown. Where two entries are provided for a region, the second number [given in brackets] is for situations where a 25% reduction in the number of trials is possible due to the crop being a representative commodity used to obtain a crop group tolerance.

B.2. Sample Handling and Preparation

Oat samples were stored frozen at the field sites promptly after harvest. Samples remained in frozen storage at the field facilities for up to 52 days until shipment via ACDS freezer truck to the analytical laboratory, BASF Agro Research (Research Triangle Park, NC), for analysis. In preparation for analysis, oat samples were homogenized in the presence of dry ice. All samples remained frozen at all times except during homogenization and subsampling for analysis.

B.3. Analytical Methodology

Oat samples were analyzed for residues of metconazole, M11, M21, and M30, and the triazole metabolites (oat grain only), 1,2,4-T, TA, and TAA, using an LC/MS/MS method (BASF Method D0508). A brief description of the method was included in the MRID.

Briefly, residues of metconazole, M11, M21, and M30 were extracted with acetonitrile (ACN):water (70:30, v:v). The extracts were diluted with methanol:water (80:20, v:v), filtered, and reserved for LC/MS/MS analysis. For determination of residues of 1,2,4-T, TA, and TAA, a separate aliquot of the initial extract was evaporated to dryness, redissolved in 0.1% formic acid in water, filtered, and reserved for LC/MS/MS analysis. Residues of metabolites M11, M21, and M30 were converted to parent equivalents using molecular weight conversion factors of 0.95 for M11 and M21 and 0.96 for M30.

The validated LOQ was 0.01 ppm for the parent metconazole (sum of *cis* and *trans* isomers at 0.005 ppm each), M11, M21, and M30 in/on oat samples. The validated LOQ was 0.05 ppm for 1,2,4-T, TA, and TAA. The reported limit of detection was 20% LOQ.

The method was validated concurrently with the analysis of field samples using samples of untreated oat hay, grain, and straw fortified at 0.005 and 0.5 ppm with *cis*- and *trans*-metconazole; at 0.01 and 1.00 ppm with M11, M21, and M30; and at 0.05 and 5.00 ppm with 1,2,4-T, TA, and TAA.

C. RESULTS AND DISCUSSION

Samples were stored frozen (<-10 °C) prior to extraction for 230-372 days (7.6-12.2 months) for oat hay, 221-364 days (7.3-12.0 months) for oat grain, and 213-355 days (7.0-11.7 months) for oat straw, and were analyzed within 0-3 days of extraction. Adequate storage stability data are available indicating that: (1) residues of *cis*- and *trans*-metconazole are relatively stable under frozen storage conditions in wheat grain, rye forage, and wheat straw for up to 12 months (refer to 46902218.der.doc); (2) residues of M11, M21, and M30 are stable in/on wheat hay, straw, and grain for up to 6 months (refer to 46902223.der.doc); and (3) residues of 1,2,4-T, TA, and TAA

are stable/relatively stable in/on wheat grain for up to 6 months (refer to 46902223.der.doc). These data are sufficient to support the storage conditions and durations for the oat field trials.

Concurrent method recovery data are presented in Table C.1. Samples were analyzed for residues of metconazole, metabolites M11, M21, and M30, and the triazole metabolites (oat grain only), 1,2,4-T, TA, and triazolylacetic acid TAA, using LC/MS/MS Method D0508. Residues of metabolites M11, M21, and M30 were converted to parent equivalents using molecular weight conversion factors of 0.95 for M11 and M21 and 0.96 for M30. The method was adequate for data collection based on acceptable concurrent method recovery data. Concurrent method recoveries were generally within the acceptable range of 70-120% for oat hay, grain, and straw fortified at 0.005 and 0.5 ppm with *cis*- and *trans*-metconazole; at 0.01 and 1.00 ppm with M11, M21, and M30; and at 0.05 and 5.00 ppm with 1,2,4-T, TA, and TAA. Apparent residues of *cis*- and *trans*-metconazole, M11, M21, and M30, and 1,2,4-T, TA, and TAA were each below the respective LOQs in/on 12 samples each of untreated oat hay, grain, and straw, with the exception pf two hay samples which contained residues of parent metconazole at 0.10 ppm and 0.06 ppm. These residue levels were relatively low compared to the residues in the associated treated hay samples.

Residue data from the oat field trials are reported in Tables C.3.1 (metconazole, M11, M21, and M30) and C.3.2 (triazole metabolites), and the residue data for oat are summarized in Tables C.4.1 and C.4.2. Residues of *cis*-and *trans*-metconazole in/on oat hay were 1.860-10.013 and 0.389-1.659 ppm, respectively; total metconazole residues (sum of *cis* and *trans* isomers) were 2.294-11.672 ppm. In oat grain, residues of *cis*- and *trans*-metconazole were 0.041-0.566 and 0.024-0.218 ppm, respectively, and total metconazole residues were 0.127-0.680 ppm. In oat straw, residues of *cis*- and *trans*-metconazole were 0.834-5.067 and 0.154-0.869 ppm, respectively, and total metconazole residues were 0.992-5.937 ppm. Residues of metabolite M11 were <0.01-0.43, 0.01-0.34, and 0.02-2.48 ppm for oat hay, grain, and straw, respectively; residues of M21 were 0.03-0.12, 0.02-0.06, and 0.02-0.49 ppm for oat hay, grain, and straw, respectively; and residues of metabolite M30 were 0.01-0.05, 0.01-0.06 ppm, and 0.01-0.18 for oat hay, grain, and straw, respectively.

Residues of 1,2,4-T, TA, and TAA in/on samples of oat grain were <0.05-0.08, 0.06-1.22, and <0.05-0.40 ppm, respectively.

The submitted residue decline data indicated that total metconazole residues (sum of *cis* and *trans* isomers) generally declined in oat hay, grain, and straw with increasing harvest intervals.

TABLE C.1. Summary of Concurrent Recoveries of Metconazole and Metabolites from Oat.

Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean
Grain	*trans*-Metconazole	0.005	2	74, 85	80
		0.500	2	104, 111	108
	cis-Metconazole	0.005	2	74, 93	84
		0.500	2	106, 116	111

TABLE C.1. Summary of Concurrent Recoveries of Metconazole and Metabolites from Oat.

Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean
	M11	0.010	2	94, 109	102
		1.000	2	107, 167	137
	M21	0.010	2	94, 109	102
		1.000	2	118, 135	127
	M30	0.010	2	100, 102	101
		1.000	2	115, 153	134
	1,2,4-T	0.050	2	88, 92	90
		5.000	2	84, 95	90
	TA	0.050	2	79, 86	83
		5.000	2	77, 98	88
	TAA	0.050	2	72, 83	78
		5.000	2	81, 109	95
Hay	*trans*-Metconazole	0.005	2	67, 84	76
		0.500	2	79, 95	87
	cis-Metconazole	0.005	2	76, 80	78
		0.500	2	91, 93	92
	M11	0.010	2	84, 94	89
		1.000	2	93, 102	98
	M21	0.010	2	76, 84	80
		1.000	2	79, 90	85
	M30	0.010	2	84, 84	84
		1.000	2	91, 96	94
Straw	*trans*-Metconazole	0.005	2	82, 95	89
		0.500	2	98, 125	112
	cis-Metconazole	0.005	2	75, 91	83
		0.500	2	95, 122	109
	M11	0.010	2	74, 87	81
		1.000	2	97, 125	111
	M21	0.010	2	77, 95	86
		1.000	2	102, 122	112
	M30	0.010	2	73, 98	86
		1.000	2	101, 120	111

TABLE C.2. Summary of Storage Conditions.

Matrix	Storage Temperature (°C)	Actual Storage Duration [1] Days (Months)	Interval of Demonstrated Storage Stability
Hay	< -10	230-372 (7.6-12.2)	The available storage stability data indicate that residues of *cis*- and *trans*-metconazole are relatively stable in wheat grain, rye forage, and wheat straw for up to 12 months; and that residues of M11, M21, and M30 are stable in/on wheat hay, straw, and grain, and residues of 1,2,4-T, TA, and TAA are stable/relatively stable in/on wheat grain for up to 6 months.[2]
Grain		221-364 (7.3-12.0)	
Straw		213-355 (7.0-11.7)	

[1] Storage duration from harvest to extraction is reported by the petitioner. Samples were analyzed within 0-3 days of extraction.
[2] Refer to 46902218.der.doc and 46902223.der.doc.

TABLE C.3.1 Residue Data for Metconazole, M11, M21, and M30 from Oat Field Trials with Metconazole.

Trial ID (County, State; Year)	Zone	Crop; Variety	Matrix	Total Rate (lb ai/A)	PHI (days)[1]	Metconazole Residues (ppm parent equivalents)						
						Metconazole			Metabolites			Total[2]
						cis	*trans*	Total	M11	M21	M30	
Wayne, NY; 2005 (RCN R05126)	1	Winter; AC Alymer	Hay	0.20	7 [3]	7.880	1.395	9.276	0.03	0.11	0.01	9.43
						8.101	1.510	9.611	0.04	0.12	0.02	9.78
			Grain	0.20	20	0.310	0.049	0.359	0.15	0.04	0.02	0.57
						0.297	0.048	0.345	0.17	0.04	0.03	0.59
			Straw	0.20	20	1.258	0.268	1.526	0.30	0.05	0.04	1.92
						1.218	0.194	1.412	0.37	0.04	0.04	1.86
Tift, GA; 2004 (RCN R05127)	2	Spring; Horizon 314	Hay	0.20	7 [8]	3.161	0.634	3.794	0.01	0.03	<0.01	3.85
						2.956	0.561	3.518	0.01	0.03	<0.01	3.57
			Grain	0.20	21	0.488	0.069	0.558	0.08	0.03	0.01	0.68
						0.433	0.060	0.493	0.07	0.02	0.01	0.59
			Straw	0.20	21	1.799	0.417	2.216	0.42	0.06	0.03	2.73
						1.795	0.428	2.223	0.43	0.06	0.03	2.75
Clinton, IL; 2005 (RCN R05128)	5	Spring; Seed Oat	Hay	0.21	7 [4]	3.514	0.722	4.235	0.02	0.06	<0.01	4.33
						2.976	0.389	3.365	0.01	0.05	<0.01	3.44
			Grain	0.20	21	0.483	0.091	0.574	0.16	0.04	0.02	0.80
						0.471	0.068	0.538	0.16	0.03	0.02	0.76
			Straw	0.20	21	1.374	0.299	1.673	0.52	0.07	0.05	2.31
						1.486	0.313	1.799	0.55	0.07	0.05	2.46
Pepin, WI; 2005 (RCN R05129)	5	Spring; Vista	Hay	0.20	7 [5]	10.013	1.659	11.672	0.08	0.12	0.02	11.90
						9.155	1.659	10.814	0.08	0.12	0.02	11.03
			Grain	0.20	20	0.322	0.044	0.367	0.20	0.03	0.04	0.64
						0.362	0.068	0.430	0.24	0.04	0.05	0.77
			Straw	0.20	20	4.575	0.786	5.361	2.16	0.44	0.15	8.12
						5.067	0.869	5.937	2.48	0.49	0.18	9.09
Stutsman, ND; 2005 (RCN R05130)	7	Spring; Morton	Hay	0.20	8 [4]	6.801	1.269	8.071	0.03	0.08	0.01	8.19
						4.127	0.933	5.059	0.02	0.05	<0.01	5.14
			Grain	0.20	21	0.103	0.024	0.127	0.01	0.02	<0.01	0.17
						0.123	0.027	0.150	0.02	0.02	<0.01	0.20
			Straw	0.20	21	1.544	0.216	1.760	0.08	0.04	0.01	1.90
						0.949	0.154	1.102	0.04	0.03	<0.01	1.18
Hall, NE; 2005 (RCN R05131)	7	Spring; Jerry	Hay	0.20	6 [0]	2.232	0.425	2.657	<0.01	0.04	<0.01	2.72
						5.968	1.001	6.969	0.02	0.10	<0.01	7.10
			Grain	0.20	21	0.154	0.029	0.183	0.03	0.02	<0.01	0.25
						0.155	0.033	0.187	0.03	0.02	<0.01	0.25
			Straw	0.20	21	2.727	0.614	3.341	0.28	0.12	0.04	3.78
						1.955	0.476	2.430	0.19	0.09	0.03	2.73

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TABLE C.3.1 Residue Data for Metconazole, M11, M21, and M30 from Oat Field Trials with Metconazole.

Trial ID (County, State; Year)	Zone	Crop; Variety	Matrix	Total Rate (lb ai/A)	PHI (days)[1]	Metconazole Residues (ppm parent equivalents)						
						Metconazole			Metabolites			Total[2]
						cis	*trans*	Total	M11	M21	M30	
Cass, ND; 2005 (RCN R05132)	5	Spring; Morton	Hay	0.20	0	7.880	1.522	9.402	0.05	0.08	0.02	9.55
						7.806	1.418	9.225	0.04	0.08	0.02	9.37
					7 [5]	3.012	0.603	3.615	0.02	0.03	<0.01	3.68
						3.606	0.643	4.249	0.02	0.04	<0.01	4.32
					14	1.656	0.371	2.028	0.02	0.03	<0.01	2.09
						2.251	0.528	2.779	0.02	0.03	<0.01	2.84
			Grain	0.20	14	0.147	0.032	0.179	0.01	0.02	<0.01	0.22
						0.172	0.034	0.207	0.02	0.02	<0.01	0.26
					21	0.117	0.027	0.144	0.02	0.02	<0.01	0.19
						0.112	0.029	0.141	0.02	0.02	<0.01	0.19
					28	0.184	0.039	0.223	0.07	0.03	0.01	0.33
						0.153	0.034	0.187	0.04	0.02	<0.01	0.26
					36	0.157	0.031	0.189	0.08	0.03	0.02	0.31
						0.110	0.025	0.135	0.07	0.03	0.02	0.25
			Straw	0.20	14	2.587	0.619	3.207	0.04	0.05	<0.01	3.30
						2.355	0.492	2.847	0.04	0.04	<0.01	2.94
					21	1.065	0.157	1.222	0.02	0.02	<0.01	1.27
						1.070	0.199	1.269	0.03	0.02	<0.01	1.32
					28	1.329	0.210	1.539	0.09	0.04	0.01	1.67
						1.683	0.416	2.099	0.11	0.04	0.02	2.27
					36	1.280	0.175	1.456	0.18	0.04	0.03	1.70
						0.752	0.117	0.869	0.15	0.03	0.02	1.07
Caddo, OK; 2005 (RCN R05133)	6	Spring; Jerry	Hay	0.20	6 [8]	5.003	0.961	5.964	0.33	0.10	0.05	6.45
						5.150	1.057	6.208	0.29	0.12	0.05	6.67
			Grain	0.20	26	0.283	0.070	0.352	0.20	0.06	0.04	0.66
						0.222	0.050	0.272	0.16	0.05	0.03	0.52
			Straw	0.20	26	0.834	0.158	0.992	0.42	0.07	0.05	1.53
						0.845	0.161	1.006	0.43	0.08	0.05	1.57
St-Cesaire, QB; 2005 (RCN R05134)	5B	Spring; Rigodon	Hay	0.20	7 [1]	4.286	0.871	5.157	0.43	0.11	0.04	5.73
						3.839	0.784	4.622	0.39	0.10	0.04	5.15
			Grain	0.20	21	0.339	0.092	0.430	0.19	0.05	0.04	0.71
						0.566	0.114	0.680	0.34	0.06	0.06	1.14
			Straw	0.20	21	1.218	0.214	1.432	0.37	0.06	0.04	1.91
						1.532	0.185	1.717	0.47	0.07	0.05	2.30
Rosthern, SK; 2005 (RCN R05135)	14	Spring; Furlong	Hay	0.20	7 [27]	7.949	1.492	9.441	0.05	0.11	0.02	9.62
						7.826	1.441	9.267	0.07	0.11	0.02	9.47
			Grain	0.20	20	0.179	0.036	0.215	0.02	0.02	<0.01	0.27
						0.139	0.028	0.167	0.02	0.02	<0.01	0.22
			Straw	0.20	20	1.224	0.206	1.430	0.05	0.03	<0.01	1.52
						1.339	0.302	1.642	0.05	0.04	<0.01	1.74

TABLE C.3.1 Residue Data for Metconazole, M11, M21, and M30 from Oat Field Trials with Metconazole.

Trial ID (County, State; Year)	Zone	Crop; Variety	Matrix	Total Rate (lb ai/A)	PHI (days)[1]	Metconazole Residues (ppm parent equivalents)						
						Metconazole			Metabolites			Total[2]
						cis	*trans*	Total	M11	M21	M30	
Minto, MB; 2005 (RCN R05136)	14	Spring; Triple crown	Hay	0.20	7 [16]	4.360	0.981	5.341	0.11	0.10	0.03	5.57
						5.469	1.118	6.587	0.07	0.09	0.02	6.76
			Grain	0.20	20	0.041	0.218	0.260	0.09	0.02	0.01	0.39
						0.194	0.050	0.244	0.10	0.03	0.02	0.39
			Straw	0.20	20	2.144	0.505	2.649	0.33	0.15	0.05	3.18
						2.716	0.574	3.290	0.49	0.34	0.06	4.18
Innisfail, AB; 2005 (RCN R05137)	14	Spring; AC Lu	Hay	0.20	7 [29]	1.860	0.434	2.294	0.16	0.09	0.02	2.57
						2.390	0.521	2.911	0.18	0.10	0.03	3.21
			Grain	0.20	21	0.234	0.042	0.276	0.02	0.02	<0.01	0.33
						0.197	0.042	0.239	0.02	0.02	<0.01	0.29
			Straw	0.20	21	1.977	0.446	2.423	0.06	0.05	<0.01	2.55
						2.153	0.541	2.694	0.07	0.06	0.01	2.83

[1] Hay samples were cut, then allowed to dry in the field or under cover prior to collection; the drying interval is presented in brackets.
[2] Total = total residues; sum of *cis*- and *trans*-metconazole, M11, M21, and M30; values presented as calculated and reported by the petitioner.

TABLE C.3.2 Residue Data for the Triazole Metabolites from Oat Field Trials with Metconazole.

Trial ID (County, State; Year)	Zone	Crop; Variety	Matrix	Total Rate (lb ai/A)	PHI (days)	Triazole Residues (ppm)		
						1,2,4-T	TAA	TA
Wayne, NY; 2005 (RCN R05126)	1	Winter; AC Alymer	Grain	0.20	20	<0.05	0.16	0.48
						<0.05	0.18	0.51
Tift, GA; 2004 (RCN R05127)	2	Spring; Horizon 314	Grain	0.20	21	<0.05	0.38	1.09
						<0.05	0.40	1.10
Clinton, IL; 2005 (RCN R05128)	5	Spring; Seed Oat	Grain	0.20	21	<0.05	0.07	0.25
						<0.05	0.08	0.26
Pepin, WI; 2005 (RCN R05129)	5	Spring; Vista	Grain	0.20	20	<0.05	<0.05	0.09
						<0.05	<0.05	0.08
Stutsman, ND; 2005 (RCN R05130)	7	Spring; Morton	Grain	0.20	21	<0.05	<0.05	0.14
						<0.05	<0.05	0.16
Hall, NE; 2005 (RCN R05131)	7	Spring; Jerry	Grain	0.20	21	<0.05	0.05	0.16
						<0.05	<0.05	0.15
Cass, ND; 2005 (RCN R05132)	5	Spring; Morton	Grain	0.20	14	<0.05	<0.05	0.15
						<0.05	<0.05	0.17
					21	0.08	<0.05	0.16
						0.06	<0.05	0.17
					28	0.05	<0.05	0.15
						0.06	<0.05	0.16
					26	0.05	<0.05	0.14
						0.07	<0.05	0.13

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TABLE C.3.2 Residue Data for the Triazole Metabolites from Oat Field Trials with Metconazole.

Trial ID (County, State; Year)	Zone	Crop; Variety	Matrix	Total Rate (lb ai/A)	PHI (days)	Triazole Residues (ppm)		
						1,2,4-T	TAA	TA
Caddo, OK; 2005 (RCN R05133)	6	Spring; Jerry	Grain	0.20	26	<0.05	0.34	1.07
						<0.05	0.36	1.22
St-Cesaire, QB; 2005 (RCN R05134)	5B	Spring; Rigodon	Grain	0.20	21	<0.05	<0.05	0.12
						<0.05	<0.05	0.10
Rosthern, SK; 2005 (RCN R05135)	14	Spring; Furlong	Grain	0.20	20	<0.05	<0.05	0.09
						<0.05	<0.05	0.10
Minto, MB; 2005 (RCN R05136)	14	Spring; Triple crown	Grain	0.20	20	<0.05	0.40	1.12
						<0.05	0.37	0.98
Innisfail, AB; 2005 (RCN R05137)	14	Spring; AC Lu	Grain	0.20	21	<0.05	<0.05	0.06
						<0.05	<0.05	0.06

TABLE C.4.1 Summary of Residue Data for Metconazole, M11, M21, and M30 from Oat Field Trials with Metconazole.

Commodity	Total Applic. Rate (lb ai/A)	PHI	Analyte	Residue Levels[1] (ppm)						
				n	Min.	Max.	HAFT[2]	Median (STMdR)	Mean (STMR)	Std. Dev.
Hay	0.20-0.21	6-8 [0-29]	*cis*-Metconazole	24	1.860	10.013	9.584	4.323	5.068	2.363
			trans-Metconazole	24	0.389	1.659	1.659	0.947	0.961	0.406
			Metconazole	**24**	**2.294**	**11.672**	**11.243**	**5.249**	**6.029**	**2.762**
			M11	24	0.01	0.43	0.41	0..05	0.10	0.13
			M21	24	0.03	0.12	0.12	0.10	0.08	0.03
			M30	24	0.01	0.05	0.05	0.02	0.02	0.01
			Total Residues	24	2.57	11.90	11.47	5.68	6.24	2.78
Grain	0.20-0.21	20-26	*cis*-Metconazole	24	0.041	0.566	0.477	0.228	0.264	0.145
			trans-Metconazole	24	0.024	0.218	0.134	0.049	0.059	0.041
			Metconazole	**24**	**0.127**	**0.680**	**0.556**	**0.274**	**0.322**	**0.159**
			M11	24	0.01	0.34	0.27	0.09	0.11	0.09
			M21	24	0.02	0.06	0.06	0.03	0.03	0.02
			M30	24	0.01	0.06	0.05	0.01	0.02	0.02
			Total Residues	24	0.17	1.14	0.93	0.46	0.48	0.26
Straw	0.20-0.21	20-26	*cis*-Metconazole	24	0.834	5.067	4.821	1.509	1.828	1.062
			trans-Metconazole	24	0.154	0.869	0.828	0.301	0.362	0.205
			Metconazole	**24**	**0.992**	**5.937**	**5.649**	**1.739**	**2.189**	**1.257**
			M11	24	0.02	2.48	2.32	0.35	0.44	0.61
			M21	24	0.02	0.49	0.47	0.06	0.11	0.14
			M30	24	0.01	0.18	0.17	0.04	0.04	0.04
			Total Residues	24	1.18	9.09	8.61	2.31	2.78	1.95

[1] For calculations of median, mean, and standard deviation, the LOQ was used for any results reported as <LOQ in Table C.3.1.
[2] HAFT = Highest Average Field Trial.

TABLE C.4.2 Summary of Residue Data for the Triazole Metabolites from Oat Field Trials with Metconazole.

Commodity	Total Applic. Rate (lb ai/A)	PHI	Analyte	Residue Levels[1] (ppm)						
				n	Min.	Max.	HAFT[2]	Median (STMdR)	Mean (STMR)	Std. Dev.
Grain	0.20-0.21	20-26	1,2,4-T	24	<0.05	0.08	0.07	0.05	0.05	0.01
			TA	24	0.06	1.22	1.14	0.16	0.41	0.42
			TAA	24	<0.05	0.40	0.38	0.05	0.14	0.14

[1] For calculations of median, mean, and standard deviation, the LOQ was used for any results reported as <LOQ in Table C.3..2
[2] HAFT = Highest Average Field Trial

D. CONCLUSION

The submitted field trial data are adequate and reflect the use of two broadcast foliar applications of a 0.75 lb ai/gal SC/L formulation of metconazole at a total rate of 0.20-0.21 lb ai/A, with a 6- to 8- day retreatment interval. Samples were harvested at PHIs of 6-8 days for barley hay and 20-26 days for grain and straw. An acceptable method was used for quantitation of residues of *cis*- and *trans*-metconazole, M11, M21, M30, 1,2,4-T, TA, and TAA in/on oat samples. The study is supported by adequate storage stability data for *cis*- and *trans*-metconazole.

E. REFERENCES

DP#: 324541
Subject: Metconazole. Request for a Tolerance on Imported Bananas. Summary of Analytical Chemistry and Residue Data. Petition Number 9E05052.
From: N. Dodd
To: M. Waller
Date: 12/14/05
MRIDs: 44721506, 44721507, 44721508, 44721509, 44721510, and 44721511

F. DOCUMENT TRACKING

RDI: N. Dodd (2/20/08)
Petition Numbers: 6F7094 and 6F7095
DP#s: 348168 and 348206
PC Code: 125619

Template Version June 2005

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Primary Evaluator	This DER was originally prepared under contract by Dynamac Corporation.
Approved by	Nancy Dodd, Chemist Nancy Dodd Date: 2/20/08 Registration Action Branch 3 Health Effects Division (7509P)

This DER was originally prepared under contract by Dynamac Corporation (2275 Research Boulevard, Suite 300; Rockville, MD 20850; submitted 09/18/2007). The DER has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

46902227 Jordan, J.; Saha, M. (2006) The Magnitude of Residues of Metconazole (BAS 555 F) and its Metabolites in Rye: Final Report. Project Number: 137720, 2006/7006725. Unpublished study prepared by BASF Agro Research, Southeast Ag Research, Inc. and Midwest Research, Inc. 146 p.

EXECUTIVE SUMMARY:

BASF Corporation has submitted field trial data for metconazole on rye. Five field trials were conducted in the United States and Canada in Zones 2 (GA; 1 trial), 5 (NE; 1 trial), 7 (ND; 1 trial), and 14 (MB, SK; 2 trials) during the 2004-2005 growing season. Because Canadian Zone 14 is contiguous with the two major U.S. rye-growing regions, Zones 5 and 7, HED has concluded that results from the Canadian trials may be used to address U.S. data requirements for rye.

Each test site included one control plot and one treated plot. The treated plot received two broadcast foliar applications of a 0.75 lb ai/gal soluble concentrate/liquid (SC/L) formulation of metconazole at 0.10 lb ai/A/application, with a 6- to 8-day retreatment interval, for a total seasonal rate of 0.20-0.21 lb ai/A. Applications were initiated four weeks prior to the harvest of mature grain. Applications were made in spray volumes of 14-22 gal/A. A nonionic surfactant was added as a spray adjuvant for all applications.

Rye grain and straw were harvested 20-22 days after the last application. Additional grain and straw samples were harvested from one trial 14, 21, 28, and 34 days after the last application to generate residue decline data.

Samples were analyzed for residues of *cis*- and *trans*-metconazole, metabolites M11, M21, and M30, and the triazole metabolites (rye grain only), 1,2,4-triazole (1,2,4-T), triazolylalanine (TA), and triazolylacetic acid (TAA), using an LC/MS/MS method (BASF Method D0508). Residues of metabolites M11, M21, and M30 were converted to parent equivalents using molecular weight conversion factors of 0.95 for M11 and M21 and 0.96 for M30. The validated limits of quantitation (LOQs) were 0.01 ppm for the parent metconazole (sum of *cis* and *trans* isomers at 0.005 ppm each), M11, M21, and M30 in/on rye samples. The validated LOQ was 0.05 ppm for 1,2,4-T, TA, and TAA. The method was adequate for data collection based on acceptable concurrent method recoveries.

Samples were stored frozen (<-10 °C) from harvest to extraction for 231-350 days (7.6-11.5 months) for rye grain, and 237-353 days (7.8-11.6 months) for rye straw, and were analyzed within 0-6 days of extraction. Adequate storage stability data are available to support the storage conditions and durations of samples for the rye field trials.

Maximum residues of *cis*-and *trans*-metconazole in/on rye grain were 0.131 and 0.026 ppm, respectively; maximum total metconazole residues (sum of *cis* and *trans* isomers) were 0.157 ppm. In rye straw, maximum residues of *cis*- and *trans*-metconazole were 7.358 and 1.426 ppm, respectively, and maximum total metconazole residues were 8.784 ppm. Maximum residues of metabolite M11 were 0.040, and 0.910 ppm for grain and straw, respectively; maximum residues of M21 were 0.010, and 0.140 ppm for grain and straw, respectively; and maximum residues of metabolite M30 were 0.010 and 0.060 ppm in grain and straw, respectively.

Maximum residues of 1,2,4-T, TA, and TAA in/on samples of rye grain were below the LOQ (<0.05 ppm), 1.27 ppm, and 1.73 ppm, respectively.

The submitted residue decline data indicated that total metconazole residues (sum of *cis* and *trans* isomers) generally remained the same or increased slightly in rye grain and straw with increasing preharvest intervals.

HED notes that rye forage was not collected from any trial site because applications were initiated at a later growth stage.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the field trial residue data are classified as scientifically acceptable. Rye forage was not collected; however, data on rye forage are not required for late-season applications (after flag leaf emergence).

The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP#s 348168 and 348206.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an impact on the validity of the study.

A. BACKGROUND INFORMATION

Metconazole [5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol] is a broad-spectrum triazole Group 3 fungicide (sterol biosynthesis inhibitors). There are currently no registered uses of metconazole in the U.S.; however, a tolerance has been established for banana, and a Section 18 emergency exemption and supporting time-limited tolerances have been granted for use on soybean. BASF Corporation has applied for registration of metconazole in the U.S. for use on barley, oats, rye, soybeans, sugar beets, triticale, and wheat.

The chemical structure and nomenclature of metconazole, and the physicochemical properties of the technical grade of metconazole are presented in Tables A.1 and A.2.

TABLE A.1. Metconazole Nomenclature.

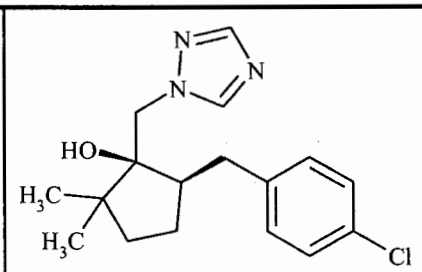
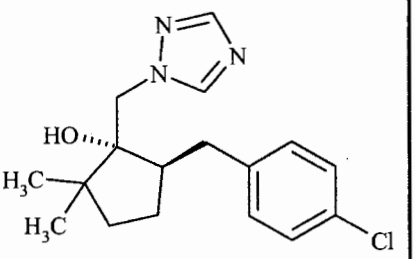
Chemical structure	 *cis*-isomer  *trans*-isomer
Common name	Metconazole
Company experimental name	KNF-S-474m (Kureha); BAS 555 F (BASF); V-10116 (Valent)
IUPAC name	(1RS,5RS:1RS,5SR)-5-(4-chlorobenzyl)-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol
CAS name	5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol
CAS registry number	125116-23-6 (*cis*- and *trans*-isomers) 115850-27-6 (*cis*-isomer) 115850-28-7 (*trans*-isomer)
End-use products (EP)	50% WDG (Metconazole 50 WDG Fungicide, EPA File Symbol 59639-RUT) 0.75 lb/gal SC/L (Caramba™ Fungicide, EPA File Symbol No. 7969-EUA) 0.67 lb/gal SC/L formulation (BAS 556 01F Fungicide, EPA File Symbol No. 7969-EUT; also contains the active ingredient pyraclostrobin at 0.83 lb/gal)

TABLE A.1. Metconazole Nomenclature.

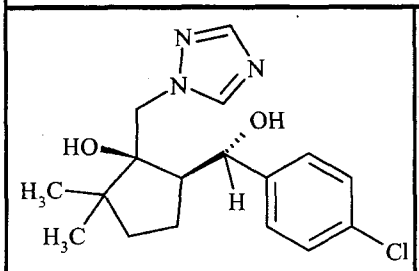
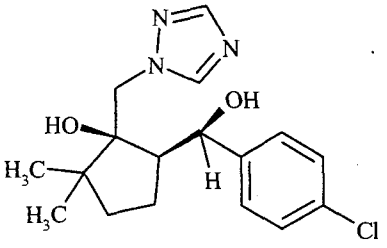
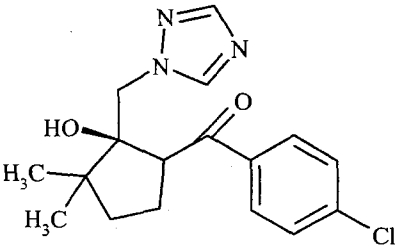
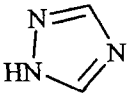
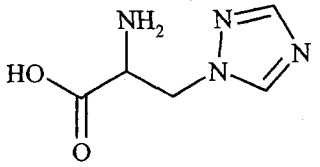
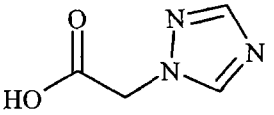
 Metconazole metabolite M11	 Metconazole metabolite M21	 Metconazole metabolite M30
 Triazole metabolite 1,2,4-triazole (1,2,4-T)	 Triazole metabolite triazolylalanine (TA)	 Triazole metabolite triazolylacetic acid (TAA)

Table A.2. Physicochemical Properties of Metconazole					
Parameter	Value				References* (MRID)
Melting point/range	100.0-108.4°C (using Electrothermal Digital Melting Point Apparatus) (AC900,768 technical grade)				44721505
pH	5.81 at 25°C (1% aqueous suspension)				46808402
Relative density (20°C)	1.14 (relative density to water at 4°C, using capillary-stoppered, density-specific gravity bottle) (Lot No. AC 8879-140B)				44721505
Water solubility (20°C)	Using shake-flask method: 18.7 ± 1.0 mg/L (*cis*-isomer, WL148271, KNF-S-474m) 13.6 ± 1.7 mg/L (*trans*-isomer, WL148271, KNF-S-474m)				44721505
Solvent solubility (g/L) at 20°C	Solvent	Metconazole	*cis*	*trans*	44721505
	acetone	363	251	117	
	methanol	403	294	117	
	dichloromethane	481	343	141	
	ethyl acetate	260	173	90.0	
	propanol	132	86.6	46.7	
	toluene	103	66.2	38.0	
	Hexane	1.40	0.929	0.483	
Vapor pressure (20°C)	Using gas-saturation method: $< 1.23 \times 10^{-5}$ Pa or 9.23×10^{-8} mm Hg (metconazole) $< 1.04 \times 10^{-5}$ Pa or 7.80×10^{-8} mm Hg (*cis*-isomer) $< 1.96 \times 10^{-6}$ Pa or 1.47×10^{-8} mm Hg (*trans*-isomer)				44721505
Dissociation constant (pK_a)	11.38±0.03 and 1.06±0.03 (in water at 29.1°C using spectrophotometric method; Lot No. AC 8879-140B)				44721505

Table A.2. Physicochemical Properties of Metconazole

Parameter	Value				References* (MRID)
Octanol/water partition coefficient, Log(K_{OW})	At 20 °C (using flask shaking method): K_{ow} (log K_{ow}) = 7090±989 (3.85) (Lot No. AC 8879-140B) (TGAI) K_{ow} (log K_{ow}) = 7150±803 (3.85) (*cis*-isomer, CL 354,801) K_{ow} (log K_{ow}) = 6800±1700 (3.8) (*trans*-isomer, CL 354,802)				44721505
UV/visible absorption spectrum	pH	λ	A	log ε	46808403
	cis-isomer				
	2.0	221.4	0.828	4.03	
	6.8		0.8452	4.04	
	7.0		0.9126	4.08	
	10.3		0.7226	3.98	
	trans-isomer				
	2.0	221.4	0.9053	4.07	
	7.0		0.9547	4.10	
	10.1		0.9893	4.11	

* Product Chemistry Reviews: DP #256877, Shyam Mathur, Ph.D., 9/12/2000 and DP #329168, Shyam Mathur, Ph.D., 7/13/07.

B. EXPERIMENTAL DESIGN

B.1. Study Site Information

Five field trials were conducted in the United States and Canada in Zones 2 (GA; 1 trial), 5 (NE; 1 trial), 7 (ND; 1 trial), and 14 (MB, SK; 2 trials) during the 2004-2005 growing season.

Each test site included one control plot and one treated plot. The treated plot received two broadcast foliar applications of a 0.75 lb ai/gal soluble concentrate/liquid (SC/L) formulation of metconazole at 0.10 lb ai/A/application, with a 6- to 8-day retreatment interval, for a total seasonal rate of 0.20-0.21 lb ai/A. Applications were initiated four weeks prior to the harvest of mature grain. Applications were made in 14-22 gal/A spray volumes. A nonionic surfactant was added as a spray adjuvant for all applications.

Rye grain and straw were harvested 20-22 days after the last application. Additional grain and straw samples were harvested from one trial 14, 21, 28, and 34 days after the last application to generate residue decline data. Rye forage was not collected from any trial site because applications were initiated at a later growth stage.

The test crops were grown and maintained according to typical agricultural practices for each region; maintenance pesticides and fertilizers were used to produce a commercial quality crop. Irrigation was used to supplement rainfall as needed. Trial site conditions are presented in Table

B.1.1, and the study use pattern is presented in Table B.1.2. The crop varieties grown are identified in Table C.3.

For each field trial, the petitioner presented the weather conditions at application and summarized the weather conditions for the duration of the trials. The petitioner reported abnormal meteorological conditions in several trial sites, which are summarized in Table B.1.1. These unusual weather conditions did not have an adverse effect on the rye crops.

TABLE B.1.1. Trial Site Conditions.

Trial Identification: County, State; Year (Trial ID)	Soil characteristics				Meteorological Data	
	Type	%OM	pH	CEC (meq/g)	Overall Rainfall Range	Overall Temperature Range (°C)
Tift, GA; 2004 (RCN R05145)	Loamy Sand	<1.0	5.5	Not provided	Above normal, especially in April	Slightly lower than normal
York, NE; 2004 (RCN R05146)	Silty Clay Loam	2.8	6.4	Not provided	Below normal in May; above normal in July	Normal
Stutsman, ND; 2005 (RCN R05147)	Sandy Loam	4.7	5.7	Not provided	Above normal	Normal
Rosthern, SK; 2004 (RCN R05148)	Loam	7.2	7.0	Not provided	Above normal in August and September	Generally cooler than normal
Minto, MB; 2004 (RCN R05149)	Loam	5.7	7.8	Not provided	May-July above normal; below normal in August	Cooler than normal May-August

TABLE B.1.2. Study Use Pattern.

Trial Identification: County, State; Year (Trial ID)	EP[1]	Application					Tank Mix/ Adjuvants[4]
		Method; Timing	Volume[2] (GPA)	Rate (lb ai/A)	RTI[3] (days)	Total Rate (lb ai/A)	
Tift, GA; 2004 (RCN R05145)	0.75 lb/gal SC/L	1. Broadcast foliar; early milk	14.57	0.1012	7	0.20	Penetron (NIS)
		2. Broadcast foliar; soft dough	13.56	0.0971			
York, NE; 2004 (RCN R05146)	0.75 lb/gal SC/L	1. Broadcast foliar; medium milk	20.15	0.1000	7	0.20	Active Plus (NIS)
		2. Broadcast foliar; late milk	20.14	0.1000			
Stutsman, ND; 2005 (RCN R05147)	0.75 lb/gal SC/L	1. Broadcast foliar; first grains half final size	15.31	0.1017	6	0.21	Activator 90 (NIS)
		2. Broadcast foliar; late milk	15.92	0.1033			
Rosthern, SK; 2004 (RCN R05148)	0.75 lb/gal SC/L	1. Broadcast foliar; early dough	21.86	0.1005	8	0.20	Ag Surf (NIS)
		2. Broadcast foliar; soft dough	21.37	0.1000			
Minto, MB; 2004 (RCN R05149)	0.75 lb/gal SC/L	1. Broadcast foliar; hard dough	22.09	0.0982	6	0.20	AgSurf (NIS)
		2. Broadcast foliar; hard dough	22.03	0.1021			

[1] EP = End-use Product
[2] Gallons per acre
[3] RTI = Retreatment Interval
[4] NIS = Nonionic surfactant

TABLE B.1.3. Trial Numbers and Geographical Locations.

NAFTA Growing Zones	Rye		
	Submitted	Requested [1]	
		Canada	U.S.
1			
1A			
2	1		1
3			
4			
5	1	1	2
5A			
5B			
6			
7	1	3	2
7A			
8			
9			
10			
11			
12			
13			
14	2	4	
15			
16			
17			
18			
19			
20			
21			
Total	5	8	5

[1] The requested number and geographic distribution of field trials for rye, according to OPPTS Guideline 860.1500 and PMRA Directive 98-2, are shown.

B.2. Sample Handling and Preparation

Rye samples were placed in placed in frozen storage at the field sites promptly after harvest. Samples remained in frozen storage at the field facilities for up to 41 days until shipment via ACDS freezer truck to the analytical laboratory, BASF Agro Research (Research Triangle Park, NC), for analysis. In preparation for analysis, rye samples were homogenized in the presence of dry ice. All samples remained frozen at all times except during homogenization and subsampling for analysis.

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B.3. Analytical Methodology

Rye samples were analyzed for residues of metconazole, metabolites M11, M21, and M30, and the triazole metabolites (rye grain only), 1,2,4-T, TA, and TAA, using an LC/MS/MS method (BASF Method D0508). A brief description of the method was included in the MRID. Briefly, residues of metconazole, M11, M21, and M30 were extracted with acetonitrile (ACN):water (70:30, v:v). The extracts were diluted with methanol:water (80:20, v:v), filtered, and reserved for LC/MS/MS analysis. For determination of residues of 1,2,4-T, TA, and TAA, a separate aliquot of the initial extract was evaporated to dryness, redissolved in 0.1% formic acid in water, filtered, and reserved for LC/MS/MS analysis. Residues of metabolites M11, M21, and M30 were converted to parent equivalents using molecular weight conversion factors of 0.95 for M11 and M21 and 0.96 for M30.

The validated LOQ was 0.01 ppm for the parent metconazole (sum of *cis* and *trans* isomers at 0.005 ppm each), M11, M21, and M30 in/on rye samples. The validated LOQ was 0.05 ppm for 1,2,4-T, TA, and TAA. The reported limit of detection was 20% LOQ.

The method was validated concurrently with the analysis of field samples using samples of untreated rye grain and straw fortified at 0.005 and 0.5 ppm with *cis*- and *trans*-metconazole; at 0.01 and 1.00 ppm with M11, M21, and M30; and at 0.05 and 5.00 ppm with 1,2,4-T, TA, and TAA.

C. RESULTS AND DISCUSSION

Samples were stored frozen (<-10 °C) from harvest to extraction for 231-350 days (7.6-11.5 months) for rye grain, and 237-353 days (7.8-11.6 months) for rye straw, and were analyzed within 0-6 days of extraction. Adequate storage stability data are available indicating that: (1) residues of *cis*- and *trans*-metconazole are relatively stable under frozen storage conditions in wheat grain, rye forage, and wheat straw for up to 12 months (refer to 46902218.der.doc); (2) residues of M11, M21, and M30 are stable in/on wheat hay, straw, and grain for up to 6 months (refer to 46902223.der.doc); and (3) residues of 1,2,4-T, TA, and TAA are stable/relatively stable in/on wheat grain for up to 6 months (refer to 46902223.der.doc). These data are sufficient to support the storage conditions and durations for the rye field trials.

Concurrent method recovery data are presented in Table C.1. Samples were analyzed for residues of metconazole, metabolites M11, M21, and M30, and the triazole metabolites (1,2,4-T, TA, and TAA) using LC/MS/MS Method D0508. Residues of metabolites M11, M21, and M30 were converted to parent equivalents using molecular weight conversion factors of 0.95 for M11 and M21 and 0.96 for M30. The method was adequate for data collection based on acceptable concurrent method recovery data. Concurrent method recoveries were generally within the acceptable range of 70-120% for rye grain and straw fortified at 0.005 and 0.5 ppm with *cis*- and *trans*-metconazole, at 0.01 and 1.00 ppm with M11, M21, and M30, and at 0.05 and 5.00 ppm with 1,2,4-T, TA, and TAA, except that low recoveries were obtained from rye grain fortified with *cis*-metconazole and *trans*-metconazole at 0.5 ppm (68-69%) and with M11 and M30 at 1.0 ppm (63% for each). Apparent residues of *cis*- and *trans*-metconazole, metabolites M11, M21,

and M30, and 1,2,4-T, TA, and TAA were each below the respective LOQs in/on five samples each of untreated rye grain, and straw.

Residue data from the rye field trials are reported in Table C.3.1 (metconazole, M11, M21, and M30) and C.3.2 (triazole metabolites), and the residue data for rye are summarized in Tables C.4.1 and C.4.2. Residues of *cis*-and *trans*-metconazole in/on rye grain were 0.032-0.131 ppm and 0.008-0.026 ppm, respectively; total metconazole residues (sum of *cis* and *trans* isomers) were 0.040-0.157 ppm. In rye straw, residues of *cis*- and *trans*-metconazole were 1.803-7.358 ppm and 0.128-1.426 ppm, respectively; total metconazole residues were 1.931-8.784 ppm. Residues of metabolite M11 were <0.010-0.040 ppm and 0.050-0.910 ppm in grain and straw, respectively; residues of M21 were <0.010-0.010 ppm and 0.040-0.140 ppm in grain and straw, respectively; and residues of M30 were <0.010-0.010 ppm and 0.010-0.060 ppm in grain and straw, respectively.

Residues of 1,2,4-T, TA, and TAA in/on samples of rye grain were <0.05, <0.05-1.27, and 0.06-1.73 ppm, respectively.

The submitted residue decline data indicated that total metconazole residues (sum of *cis* and *trans* isomers) generally remained the same or increased slightly in rye grain and straw with increasing preharvest intervals. Residues in grain increased from 0.064-0.070 ppm at the 21-day PHI to 0.070-0.078 ppm at the 34-day PHI, and residues in straw increased from 3.449-4.716 ppm at the 21-day PHI to 4.460-5.626 ppm at the 34-day PHI.

TABLE C.1. Summary of Concurrent Recoveries of Metconazole, its Metabolites M11, M21, and M30, and Triazole Metabolites from Rye.

Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean (%)
Grain	*trans*-metconazole	0.005	1	92	92
		0.5	1	68	68
	cis-Metconazole	0.005	1	118	118
		0.5	1	69	69
	M11	0.01	1	92	92
		1.0	1	63	63
	M21	0.01	1	95	95
		1.0	1	72	72
	M30	0.01	1	95	95
		1.0	1	63	63
	1,2,4-T	0.05	1	100	100
		5.0	1	108	108
	TAA	0.05	1	128	128
		5.0	1	102	102
	TA	0.05	1	102	102
		5.0	1	92	92
Straw	*trans*-metconazole	0.005	1	103	103
		0.5	1	114	114
	cis-Metconazole	0.005	1	97	97

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TABLE C.1. Summary of Concurrent Recoveries of Metconazole, its Metabolites M11, M21, and M30, and Triazole Metabolites from Rye.

Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean (%)
		0.5	1	99	99
	M11	0.01	1	75	75
		1.0	1	83	83
	M21	0.01	1	83	83
		1.0	1	82	82
	M30	0.01	1	80	80
		1.0	1	86	86

TABLE C.2. Summary of Storage Conditions.

Matrix	Storage Temperature (°C)	Actual Storage Duration Days (Months)	Interval of Demonstrated Storage Stability[1]
Grain	< -10	231-350 (7.6-11.5)	The available storage stability data indicate that residues of *cis*- and *trans*-metconazole are relatively stable in wheat grain, rye forage, and wheat straw for up to 12 months; and that residues of M11, M21, and M30 are stable in/on wheat hay, straw, and grain, and residues of 1,2,4-T, TA, and TAA are stable/relatively stable in/on wheat grain for up to 6 months.[2]
Straw		237-353 (7.8-11.6)	

[1] Storage duration from harvest to extraction is reported by the petitioner. Samples were analyzed within 0-6 days of extraction.
[2] Refer to 46902218.der.doc and 46902223.der.doc.

TABLE C.3.1. Residue Data for Metconazole, M11, M21, and M30 from Rye Field Trials with Metconazole.

Trial Identification: County, State; Year (Trial ID)	Zone	Crop; Variety	Matrix	Total Rate (lb ai/A)	PHI (days)	Metconazole Residues (ppm parent equivalents)						
						Metconazole			Metabolites			Total[1]
						cis	*trans*	Total	M11	M21	M30	
Tift, GA; 2004 (RCN R05145)	2	Winter; Wrens Abruzzi	Grain	0.20	21	0.044	0.011	0.05	<0.01	<0.01	<0.01	0.09
						0.032	0.008	0.040	<0.01	<0.01	<0.01	0.07
			Straw		21	3.580	0.866	4.446	0.57	0.04	0.03	5.08
						3.531	0.817	4.348	0.19	0.04	0.02	4.59
York, NE; 2004 (RCN R05146)	5	Winter; VNS	Grain	0.20	22	0.048	0.009	0.057	0.02	<0.01	<0.01	0.10
						0.066	0.013	0.079	0.03	<0.01	<0.01	0.12
			Straw		22	2.045	0.137	2.181	0.69	0.06	0.04	2.96
						2.282	0.155	2.437	0.18	0.06	0.04	2.71

TABLE C.3.1. Residue Data for Metconazole, M11, M21, and M30 from Rye Field Trials with Metconazole.

Trial Identification: County, State; Year (Trial ID)	Zone	Crop; Variety	Matrix	Total Rate (lb ai/A)	PHI (days)	Metconazole Residues (ppm parent equivalents)						
						Metconazole			Metabolites			Total[1]
						cis	*trans*	Total	M11	M21	M30	
Stutsman, ND; 2005 (RCN R05147)	7	Winter; Dahcold	Grain	0.21	14	0.051	0.011	0.062	0.01	<0.01	<0.01	0.09
						0.067	0.015	0.082	0.02	<0.01	<0.01	0.12
					21	0.053	0.012	0.064	0.04	<0.01	<0.01	0.13
						0.057	0.013	0.070	0.04	<0.01	0.01	0.13
					28	0.052	0.012	0.064	0.04	<0.01	0.01	0.13
						0.045	0.010	0.055	0.04	<0.01	0.01	0.12
					34	0.057	0.013	0.070	0.06	0.01	0.01	0.15
						0.064	0.014	0.078	0.06	0.01	0.01	0.17
			Straw		14	4.019	0.899	4.918	0.18	0.08	0.03	5.21
						3.844	0.828	4.672	0.17	0.07	0.03	4.94
					21	3.795	0.921	4.716	0.91	0.11	0.04	5.78
						2.846	0.603	3.449	0.60	0.14	0.06	4.24
					28	2.636	0.576	3.211	0.72	0.08	0.04	4.04
						3.114	0.724	3.838	1.10	0.10	0.06	5.10
					34	3.643	0.817	4.460	1.46	0.14	0.07	6.13
						4.627	0.998	5.626	1.71	0.17	0.08	7.58
Rosthern, SK; 2004 (RCN R05148)	14	Spring; Gazelle	Grain	0.20	20	0.074	0.019	0.093	0.01	<0.01	<0.01	0.13
						0.074	0.018	0.092	0.01	<0.01	<0.01	0.13
			Straw		20	1.803	0.128	1.931	0.05	0.04	0.01	2.02
						2.031	0.156	2.188	0.06	0.05	0.01	2.31
Minto, MB; 2004 (RCN R05149)	14	Winter; Common	Grain	0.20	22	0.131	0.026	0.157	0.04	0.01	<0.01	0.22
						0.120	0.023	0.144	0.04	0.01	<0.01	0.20
			Straw		22	7.358	1.426	8.784	0.68	0.13	0.04	9.63
						6.955	1.207	8.162	0.19	0.12	0.04	8.51

[1] Total = total residues; sum of *cis*- and *trans*-metconazole, M11, M21, and M30; values presented as calculated and reported by the petitioner.

TABLE C.3.2. Residue Data for the Triazole Metabolites from Rye Field Trials with Metconazole.

Trial Identification: County, State; Year (Trial ID)	Zone	Crop; Variety	Matrix	Total Rate (lb ai/A)	PHI (days)	Triazole Residues (ppm)		
						1,2,4-T	TAA	TA
Tift, GA; 2004 (RCN R05145)	2	Winter; Wrens Abruzzi	Grain	0.20	21	<0.05	1.73	1.27
						<0.05	1.57	1.06
York, NE; 2004 (RCN R05146)	5	Winter; VNS	Grain	0.20	22	<0.05	0.15	0.08
						<0.05	0.12	0.06

TABLE C.3.2. Residue Data for the Triazole Metabolites from Rye Field Trials with Metconazole.

Trial Identification: County, State; Year (Trial ID)	Zone	Crop; Variety	Matrix	Total Rate (lb ai/A)	PHI (days)	Triazole Residues (ppm)		
						1,2,4-T	TAA	TA
Stutsman, ND; 2005 (RCN R05147)	7	Winter; Dahcold	Grain	0.21	14	<0.05	0.06	<0.05
						<0.05	0.06	<0.05
					21	<0.05	0.07	<0.05
						<0.05	0.07	<0.05
					28	<0.05	0.07	<0.05
						<0.05	0.07	<0.05
					34	<0.05	0.07	<0.05
						<0.05	0.07	<0.05
Rosthern, SK; 2004 (RCN R05148)	14	Spring; Gazelle	Grain	0.20	20	<0.05	0.08	<0.05
						<0.05	0.08	<0.05
Minto, MB; 2004 (RCN R05149)	14	Winter; Common	Grain	0.20	22	<0.05	0.06	<0.05
						<0.05	0.06	<0.05

TABLE C.4. Summary of Residue Data for Metconazole, M11, M21, and M30 from Rye Crop Field Trials with Metconazole.

Commodity	Total Applic. Rate (lb ai/A)	PHI (days)	Analyte	Residues (ppm)[1]						
				n	Min.	Max.	HAFT[2]	Median (STMdR)	Mean (STMR)	Std. Dev.
Grain	0.20-0.21	20-22	*cis*-Metconazole	10	0.032	0.131	0.126	0.062	0.070	0.032
			trans-Metconazole	10	0.008	0.026	0.025	0.013	0.015	0.006
			Metconazole	**10**	**0.040**	**0.157**	**0.150**	**0.075**	**0.085**	**0.039**
			M11	10	<0.010	0.040	0.040	0.025	0.025	0.014
			M21	10	<0.010	0.010	0.010	0.010	0.010	---
			M30	10	<0.010	0.010	0.010	0.010	0.010	---
			Total Residues	10	0.070	0.220	0.210	0.130	0.132	0.046
Straw	0.20-0.21	20-22	*cis*-Metconazole	10	1.803	7.358	7.157	3.189	3.623	1.995
			trans-Metconazole	10	0.128	1.426	1.317	0.710	0.642	0.482
			Metconazole	**10**	**1.931**	**8.784**	**8.473**	**3.899**	**4.264**	**2.449**
			M11	10	0.050	0.910	0.755	0.380	0.412	0.310
			M21	10	0.040	0.140	0.125	0.060	0.079	0.041
			M30	10	0.010	0.060	0.050	0.040	0.033	0.016
			Total Residues	10	2.020	9.630	9.070	4.415	4.783	2.586

[1] For calculation of mean, median, and standard deviation, the LOQ was used for any results reported as <LOQ in Table C.3.1.
[2] HAFT = Highest Average Field Trial.

TABLE C.4.2. Summary of Residue Data for the Triazole Metabolites from Rye Crop Field Trials with Metconazole.

Commodity	Total Applic. Rate (lb ai/A)	PHI (days)	Analyte	Residues (ppm)[1]						
				n	Min.	Max.	HAFT[2]	Median (STMdR)	Mean (STMR)	Std. Dev.
Grain	0.20-0.21	20-22	1,2,4-T	10	<0.05	<0.05	0.05	0.05	0.05	--
			TA	10	<0.05	1.27	1.17	0.05	0.28	0.47
			TAA	10	0.06	1.73	1.65	0.08	0.40	0.66

[1] For calculation of mean, median, and standard deviation, the LOQ was used for any results reported as <LOQ in Table C.3.2.
[2] HAFT = Highest Average Field Trial.

D. CONCLUSION

The submitted field trial data are adequate and reflect the use of two broadcast foliar applications of a 0.75 lb ai/gal SC/L formulation of metconazole at a total rate of ~0.20 lb ai/A with a 6- to 8-day retreatment interval. Samples were harvested at a PHI of 20-22 days. An acceptable method was used for quantitation of residues of *cis*- and *trans*-metconazole, M11, M21, and M30, and 1,2,4-T, TA, and TAA in/on rye samples. The study is supported by adequate storage stability data for *cis*- and *trans*-metconazole.

E. REFERENCES

DP#: 324541
Subject: Metconazole. Request for a Tolerance on Imported Bananas. Summary of Analytical Chemistry and Residue Data. Petition Number 9E05052.
From: N. Dodd
To: M. Waller
Date: 12/14/05
MRIDs: 44721506, 44721507, 44721508, 44721509, 44721510, and 44721511

F. DOCUMENT TRACKING

RDI: N. Dodd (2/20/08)
Petition Numbers: 6F7094 and 6F7095
DP#s: 348168 and 348206
PC Code: 125619

Template Version June 2005

Primary Evaluator	This DER was originally prepared under contract by Dynamac Corporation.
Approved by	Nancy Dodd, Chemist *Nancy Dodd* Date: 2/20/08 Registration Action Branch 3 Health Effects Division (7509P)

This DER was originally prepared under contract by Dynamac Corporation (2275 Research Boulevard, Suite 300; Rockville, MD 20850; submitted 09/18/2007). The DER has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

46902228 White, M.; Saha, M. (2006) The Magnitude of Residues of Metconazole (BAS 555 F) and Its Metabolites in Soybean: Final Report. Project Number: 137726, 2006/7006995. Unpublished study prepared by BASF Agro Research, Southeast Ag Research, Inc. and Agresources, Inc. 213 p.

46902229 Leonard, R. (2005) The Magnitude of Metconazole Residues in Soybeans: Final Report. Project Number: 204640, 2004/5000755. Unpublished study prepared by BASF Agro Research, Southeast Ag Research, Inc. and Shoffner Farm Research. 113 p.

EXECUTIVE SUMMARY:

BASF Corporation has submitted field trial data for metconazole on soybean. Twenty-one field trials were conducted in the United States and Canada in Zones 2 (GA, 2 trials), 4 (AR, MS; 3 trials), 5 (IA, IL, MI, MN, NE, WI, and ON; 15 trials), and 5B (QB, 1 trial) during the 2004 and 2005 growing seasons. Because the Canadian trials were conducted in Zones which extend into the U.S. (Zone 5) or are contiguous with the major U.S. soybean-growing zone (Zone 5b), HED has concluded that results from the Canadian trials may be used to address U.S. data requirements for soybean.

Each test site included one control plot and one treated plot. The treated plot received two broadcast foliar applications of a 0.75 lb ai/gal soluble concentrate/liquid (SC/L) formulation of metconazole at 0.07-0.08 lb ai/A/application, with a 9- to 11-day retreatment interval, for a total seasonal rate of ~0.14 lb ai/A. Applications were made approximately 40 days prior to harvest of mature seed. Applications were made in 10-32 gal/A spray volumes. A nonionic surfactant was added as a spray adjuvant for all applications.

Soybean forage and hay were harvested 6-8 days after the last application and soybean seed were harvested 28-32 days after the last application. Soybean hay was allowed to dry in the field for 0-11 days prior to collection. Additional hay samples were collected from two trials 0, 7, 14, and

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20-21 days after the last application, and seed samples were harvested 23, 30, 36-37, and 43-44 days after the last application to generate residue decline data.

Samples from the 15 trials conducted in 2005 were analyzed for residues of *cis*- and *trans*-metconazole, the metabolites M11, M21, and M30, and the triazole metabolites [1,2,4-triazole (1,2,4-T), triazolylalanine (TA), and triazolylacetic acid (TAA)] using an LC/MS/MS method (BASF Method D0508). Residues of metabolites M11, M21, and M30 were converted to parent equivalents using molecular weight conversion factors of 0.95 for M11 and M21 and 0.96 for M30. Samples from the six trials conducted in 2004 were analyzed for residues of *cis*- and *trans*-metconazole using an LC/MS/MS method, BASF Method 550/0. The validated limits of quantitation (LOQs) were 0.01 ppm for the parent metconazole (sum of *cis* and *trans* isomers at 0.005 ppm each for both methods), M11, M21, and M30 in/on soybean samples. The validated LOQ was 0.05 ppm for 1,2,4-T, TA, and TAA. The methods were adequate for data collection based on acceptable concurrent method recoveries.

Samples were stored frozen (<-10 °C) from harvest to extraction for 61-195 days (2.0-6.4 months) for soybean forage, 68-179 days (2.2-5.9 months) for soybean hay, and 40-161 days (1.3-5.3 months) for soybean seed, and were analyzed within 0-5 days of extraction. Adequate storage stability data are available to support the storage conditions and durations of samples for the soybean field trials.

Maximum residues of *cis*-and *trans*-metconazole in/on soybean forage were 2.040 and 0.405 ppm, respectively; maximum total metconazole residues (sum of *cis* and *trans* isomers) were 2.430 ppm. In soybean hay, maximum residues of *cis*- and *trans*-metconazole were 3.930 and 0.808 ppm, respectively, and maximum total metconazole residues were 4.738 ppm. In soybean seed, maximum residues of *cis*- and *trans*-metconazole were 0.036 and 0.090 ppm, respectively, and maximum total metconazole residues were 0.050 ppm. Maximum residues of metabolite M11 was 0.09, 0.20, and <0.01 ppm for forage, hay and seed, respectively; maximum residues of M21 were 0.03, 0.08, and <0.01 ppm for forage, hay and seed, respectively; and maximum residues of metabolite M30 were 0.01, 0.04, and <0.01 ppm, respectively, for forage, hay, and seed.

Maximum residues of 1,2,4-T were <0.05, 0.08, and 0.10 ppm in/on soybean forage, hay, and seed, respectively; maximum residues of TA were 0.23, <0.05, and 0.69 ppm for forage, hay, and seed, respectively; and maximum residues of TAA were <0.05, 0.08, and <0.05 ppm for forage, hay, and seed, respectively.

The submitted residue decline data indicated that total metconazole residues (sum of *cis* and *trans* isomers) generally declined in soybean forage, hay, and seed with increasing preharvest intervals.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the field trial residue data are classified as scientifically acceptable.

The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP#s 348168 and 348206.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an impact on the validity of the study.

A. BACKGROUND INFORMATION

Metconazole [5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol] is a broad-spectrum triazole Group 3 fungicide (sterol biosynthesis inhibitors). There are currently no registered uses of metconazole in the U.S.; however, a tolerance has been established for banana, and a Section 18 emergency exemption and supporting time-limited tolerances have been granted for use on soybean. BASF Corporation has applied for registration of metconazole in the U.S. for use on barley, oats, rye, soybeans, sugar beets, triticale, and wheat.

The chemical structure and nomenclature of metconazole, and the physicochemical properties of the technical grade of metconazole are presented in Tables A.1 and A.2.

TABLE A.1. Metconazole Nomenclature.

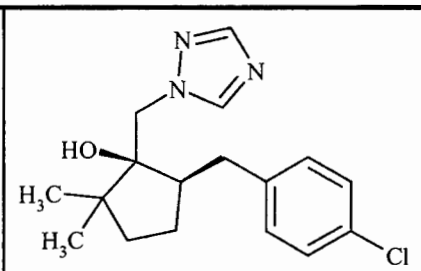
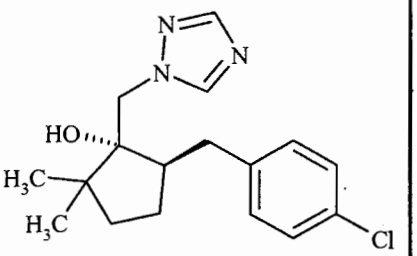
Chemical structure	 *cis*-isomer	 *trans*-isomer
Common name	Metconazole	
Company experimental name	KNF-S-474m (Kureha); BAS 555 F (BASF); V-10116 (Valent)	
IUPAC name	(1RS,5RS:1RS,5SR)-5-(4-chlorobenzyl)-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	
CAS name	5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	
CAS registry number	125116-23-6 (*cis*- and *trans*-isomers) 115850-27-6 (*cis*-isomer) 115850-28-7 (*trans*-isomer)	

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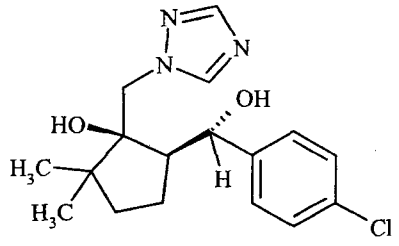
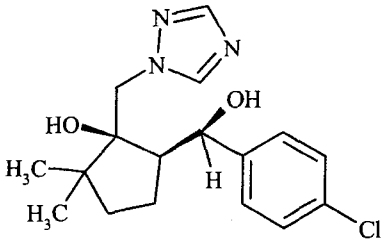
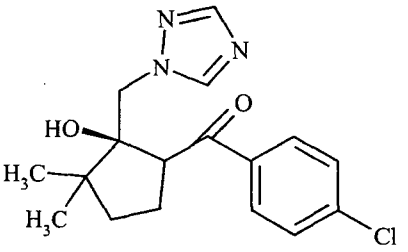
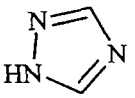
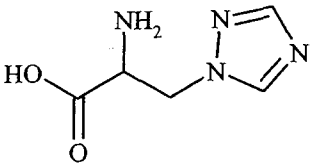
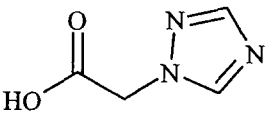
TABLE A.1. Metconazole Nomenclature.		
End-use products (EP)	50% WDG (Metconazole 50 WDG Fungicide, EPA File Symbol 59639-RUT) 0.75 lb/gal SC/L (Caramba™ Fungicide, EPA File Symbol No. 7969-EUA) 0.67 lb/gal SC/L formulation (BAS 556 01F Fungicide, EPA File Symbol No. 7969-EUT; also contains the active ingredient pyraclostrobin at 0.83 lb/gal)	
 Metconazole metabolite M11	 Metconazole metabolite M21	 Metconazole metabolite M30
 Triazole metabolite 1,2,4-triazole (1,2,4-T)	 Triazole metabolite triazolylalanine (TA)	 Triazole metabolite triazolylacetic acid (TAA)

Table A.2. Physicochemical Properties of Metconazole					
Parameter	Value				References* (MRID)
Melting point/range	100.0-108.4°C (using Electrothermal Digital Melting Point Apparatus) (AC900,768 technical grade)				44721505
pH	5.81 at 25°C (1% aqueous suspension)				46808402
Relative density (20°C)	1.14 (relative density to water at 4°C, using capillary-stoppered, density-specific gravity bottle) (Lot No. AC 8879-140B)				44721505
Water solubility (20°C)	Using shake-flask method: 18.7 ± 1.0 mg/L (*cis*-isomer, WL148271, KNF-S-474m) 13.6 ± 1.7 mg/L (*trans*-isomer, WL148271, KNF-S-474m)				44721505
Solvent solubility (g/L) at 20°C	Solvent	Metconazole	*cis*	*trans*	44721505
	acetone	363	251	117	
	methanol	403	294	117	
	dichloromethane	481	343	141	
	ethyl acetate	260	173	90.0	
	propanol	132	86.6	46.7	
	toluene	103	66.2	38.0	
	Hexane	1.40	0.929	0.483	

Table A.2. Physicochemical Properties of Metconazole

Parameter	Value				References* (MRID)
Vapor pressure (20°C)	Using gas-saturation method: $< 1.23x10^{-5}$ Pa or 9.23 x 10^{-8} mm Hg (metconazole) $< 1.04x10^{-5}$ Pa or 7.80 x 10^{-8} mm Hg (*cis*-isomer) $< 1.96x10^{-6}$ Pa or 1.47 x 10^{-8} mm Hg (*trans*-isomer)				44721505
Dissociation constant (pK_a)	11.38±0.03 and 1.06±0.03 (in water at 29.1°C using spectrophotometric method; Lot No. AC 8879-140B)				44721505
Octanol/water partition coefficient, Log(K_{OW})	At 20 °C (using flask shaking method): K_{ow} (log K_{ow}) = 7090±989 (3.85) (Lot No. AC 8879-140B) (TGAI) K_{ow} (log K_{ow}) = 7150±803 (3.85) (*cis*-isomer, CL 354,801) K_{ow} (log K_{ow}) = 6800±1700 (3.8) (*trans*-isomer, CL 354,802)				44721505
UV/visible absorption spectrum	pH	λ	A	log ε	46808403
	cis-isomer				
	2.0	221.4	0.828	4.03	
	6.8		0.8452	4.04	
	7.0		0.9126	4.08	
	10.3		0.7226	3.98	
	trans-isomer				
	2.0	221.4	0.9053	4.07	
	7.0		0.9547	4.10	
	10.1		0.9893	4.11	

* Product Chemistry Reviews: DP #256877, Shyam Mathur, Ph.D., 9/12/2000 and DP #329168, Shyam Mathur, Ph.D., 7/13/07.

B. EXPERIMENTAL DESIGN

Twenty-one field trials were conducted in the United States and Canada in Zones 2 (GA, 2 trials), 4 (AR, MS; 3 trials), 5 (IA, IL, MI, MN, NE, WI, and ON; 15 trials), and 5B (QB, 1 trial) during the 2004 and 2005 growing seasons.

Each test site included one control plot and treated plot. The treated plot received two broadcast foliar applications of a 0.75 lb ai/gal SC/L formulation of metconazole at 0.07-0.08 lb ai/A/application, with a 9- to 11-day retreatment interval, for a total seasonal rate of ~0.14 lb ai/A. Applications were made approximately 40 days prior to harvest of mature seed. Applications were made in spray volumes of 14-32 gal/A. A nonionic surfactant was added as a spray adjuvant for all applications.

Soybean forage and hay were harvested 6-8 days after the last application, and soybean seed was harvested 28-32 days after the last application. Soybean hay was allowed to dry in the field for 0-11 days prior to collection. Additional hay samples were collected from two trials 0, 7, 14, and

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20-21 days after the last application, and seed samples were harvested 23, 30, 36-37, and 43-44 days after the last application to generate residue decline data.

The test crops were grown and maintained according to typical agricultural practices for each region; maintenance pesticides and fertilizers were used to produce a commercial quality crop. Irrigation was used to supplement rainfall as needed. Trial site conditions are presented in Table B.1.1, and the study use pattern is presented in Table B.1.2. The crop varieties grown are identified in Table C.3.

For each field trial, the petitioner presented the weather conditions at application and summarized the weather conditions for the duration of the trials. The petitioner reported abnormal meteorological conditions in several trial sites, which are summarized in Table B.1.1. These unusual weather conditions did not have an adverse effect on the soybean crops.

B.1. Study Site Information

TABLE B.1.1. Trial Site Conditions.

Trial Identification: County, State; Year (Trial ID)	Soil characteristics				Meteorological Data	
	Type	%OM	pH	CEC (meq/g)	Overall Rainfall Range	Overall Temperature Range (°C)
Tift, GA; 2005 (RCN R05111)	Loamy Sand	0.7	5.7	NA[1]	Above normal prior to September and below normal in September and October	Normal
Wabasha, MN; 2005 (RCN R05112)	Silt Loam	3.1	6.7	NA	Above normal in August	Normal
Wabasha, MN; 2005 (RCN R05113)	Loam	2.3	6.3	NA	Above normal in August	Normal
Madison, IL; 2005 (RCN R05114)	Silt Loam	2.0	6.8	NA	Normal	Normal
Clinton, IL; 2005 (RCN R05115)	Silt Loam	1.8	6.6	NA	Normal	Normal
Stark, IL; 2005 (RCN R05116)	Silt Loam	3.0	6.6	NA	Below normal in July and August	Normal
Polk, NE; 2005 (RCN R05117)	Sandy Loam	1.5	8.3	NA	Below normal in May-September	Slightly higher than normal.
York, NE; 2005 (RCN R05118)	Silty Clay Loam	2.8	6.4	NA	Below normal in May, August and September. Above normal in July	Normal
Hall, NE; 2005 (RCN R05119)	Clay Loam	2.7	6.6	NA	Above normal in July	Above normal in May-July
Branchton, ON; 2005 (RCN R05120)	Silt Loam	1.3	6.8	NA	Above normal in July and August	Generally above normal
Wapello, IA; 2005 (RCN R05121)	Loam	3.5	6.9	NA	Generally below normal	Above normal late July-early August
Jefferson, IA; 2005 (RCN R05122)	Silty Clay Loam	3.9	6.8	NA	Generally below normal	Above normal late July-early August
Keokuk, IA; 2005 (RCN R05123)	Silty Clay Loam	3.0	6.6	NA	Generally below normal	Above normal late July-early August

TABLE B.1.1. Trial Site Conditions.

Trial Identification: County, State; Year (Trial ID)	Soil characteristics				Meteorological Data	
	Type	%OM	pH	CEC (meq/g)	Overall Rainfall Range	Overall Temperature Range (°C)
Ottawa, MI; 2005 (RCN R05124)	Loam	2.2	6.9	NA	Below normal in May, June and August. Above normal in July and September	Below normal in May. Above normal in June-September
St-Pie-de-Bagot, QB; 2005 (RCN R05125)	Loamy Fine Sand	3.3	5.9	NA	Generally above normal/	Normal
Chula, GA; 2004 (RCN 20041912)	Loamy Sand	1.0	5.0	NA	Normal	Normal
Newport, AR; 2004 (RCN 2004193)	Loamy Sand	1.4	5.6	NA	Normal	Normal
Proctor, AR; 2004 (RCN 2004194)	Clay Loam	0.8	5.8	NA	Normal	Normal
Stoneville, MS; 2004 (RCN 2004195)	Silty Clay	2.4	7.3	NA	Normal	Normal
Arkansaw, WI; 2004 (RCN 2004196)	Sandy Loam	1.5	6.6	NA	Normal	Normal
Carlyle, IL; 2004 (RCN 2004197)	Silt Loam	1.5	6.5	NA	Normal	Normal

NA = not applicable. Data not provided.

TABLE B.1.2. Study Use Pattern.

Location (City, State; Year) Trial ID	EP[1]	Application					Tank Mix/ Adjuvants[4]
		Method; Timing	Volume GPA[2] [L/ha]	Rate lb ai/A [kg ai/ha]	RTI[3] (days)	Total Rate lb ai/A [kg ai/ha]	
Tift, GA; 2005 (RCN R05111)	0.75 lb/gal SC/L	1. Broadcast foliar; all pods final length	18.82 [176]	0.0696 [0.08]	10	0.14 [0.16]	Penetrator Plus (NIS)
		2. Broadcast foliar; all pods final length	19.22 [180]	0.0688 [0.08]			
Wabasha, MN; 2005 (RCN R05112)	0.75 lb/gal SC/L	1. Broadcast foliar; 30% pods final length	20.24 [189]	0.0709 [0.08]	10	0.14 [0.16]	Agridex (NIS)
		2. Broadcast foliar; 70% pods final length	19.96 [187]	0.0702 [0.08]			
Wabasha, MN; 2005 (RCN R05113)	0.75 lb/gal SC/L	1. Broadcast foliar; 30% pods final length	20.10 [188]	0.0704 [0.08]	10	0.14 [0.16]	Agridex (NIS)
		2. Broadcast foliar; 70% pods final length	19.82 [185]	0.0697 [0.08]			
Madison, IL; 2005 (RCN R05114)	0.75 lb/gal SC/L	1. Broadcast foliar; 70% pods final length	15.95 [149]	0.0712 [0.08]	10	0.14 [0.16]	Preference (NIS)
		2. Broadcast foliar; all pods final length	16.12 [151]	0.0693 [0.08]			
Clinton, IL; 2005 (RCN R05115)	0.75 lb/gal SC/L	1. Broadcast foliar; 70% pods final length	18.67 [175]	0.0709 [0.08]	11	0.14 [0.16]	Preference (NIS)
		2. Broadcast foliar; all pods final length	19.68 [184]	0.0700 [0.08]			
Stark, IL; 2005 (RCN R05116)	0.75 lb/gal	1. Broadcast foliar; all pods final length	18.83 [176]	0.0695 [0.08]	11	0.14 [0.16]	Preference (NIS)

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TABLE B.1.2. Study Use Pattern.

Location (City, State; Year) Trial ID	EP[1]	Application					Tank Mix/ Adjuvants[4]
		Method; Timing	Volume GPA[2] [L/ha]	Rate lb ai/A [kg ai/ha]	RTI[3] (days)	Total Rate lb ai/A [kg ai/ha]	
	SC/L	2. Broadcast foliar; 60% of pods ripe	18.67 [175]	0.0717 [0.08]			
Polk, NE; 2005 (RCN R05117)	0.75 lb/gal SC/L	1. Broadcast foliar; 50% pods final length	19.64 [184]	0.0701 [0.08]	10	0.14 [0.16]	Activate Plus (NIS)
		2. Broadcast foliar; 70% pods final length	20.18 [189]	0.0721 [0.08]			
York, NE; 2005 (RCN R05118)	0.75 lb/gal SC/L	1. Broadcast foliar; 50% pods final length	19.97 [187]	0.0707 [0.08]	9	0.14 [0.16]	Activate Plus (NIS)
		2. Broadcast foliar; 70% pods final length	20.04 [187]	0.0703 [0.08]			
Hall, NE; 2005 (RCN R05119)	0.75 lb/gal SC/L	1. Broadcast foliar; 50% pods final length	19.68 [184]	0.0703 [0.08]	10	0.14 [0.16]	Activate Plus (NIS)
		2. Broadcast foliar; 70% pods final length	19.95 [187]	0.0713 [0.08]			
Branchton, ON; 2005 (RCN R05120)	0.75 lb/gal SC/L	1. Broadcast foliar; 50% pods final length	28.03 [262]	0.0659 [0.07]	9	0.14 [0.16]	Agral 90 (NIS)
		2. Broadcast foliar; 70% pods final length	31.99 [299]	0.0768 [0.09]			
Wapello, IA; 2005 (RCN R05121)	0.75 lb/gal SC/L	1. Broadcast foliar; 40% pods final length	14.40 [135]	0.0691 [0.08]	10	0.14 [0.16]	Agri-Dex (NIS)
		2. Broadcast foliar; 50% pods final length	14.65 [137]	0.0701 [0.08]			
Jefferson, IA; 2005 (RCN R05122)	0.75 lb/gal SC/L	1. Broadcast foliar; 40% pods final length	14.76 [138]	0.0702 [0.08]	9	0.14 [0.16]	Agri-Dex (NIS)
		2. Broadcast foliar; 50% pods final length	14.03 [131]	0.0696 [0.08]			
Keokuk, IA; 2005 (RCN R05123)	0.75 lb/gal SC/L	1. Broadcast foliar; 40% pods final length	14.77 [138]	0.0705 [0.08]	10	0.14 [0.16]	Agri-Dex (NIS)
		2. Broadcast foliar; 50% pods final length	15.20 [142]	0.0694 [0.08]			
Ottawa, MI; 2005 (RCN R05124)	0.75 lb/gal SC/L	1. Broadcast foliar; 30% of leaves discolored	20.52 [192]	0.0702 [0.08]	10	0.14 [0.16]	Penetrator Plus (NIS)
		2. Broadcast foliar; 10% of pods ripe	20.45 [191]	0.0707 [0.08]			
St-Pie-de-Bagot, QB; 2005 (RCN R05125)	0.75 lb/gal SC/L	1. Broadcast foliar; 70% pods final length	24.38 [228]	0.0727 [0.08]	11	0.14 [0.16]	Surf 92 (NIS)
		2. Broadcast foliar; all pods final length	23.01 [215]	0.0701 [0.08]			
Chula, GA; 2004 (RCN 20041912)	0.75 lb/gal SC/L	1. Broadcast foliar; all pods final length	21.99 [206]	0.07 [0.08]	10	0.14 [0.16]	Induce (NIS)
		2. Broadcast foliar; all pods final length	22.13 [207]	0.07 [0.08]			
Newport, AR; 2004 (RCN 2004193)	0.75 lb/gal SC/L	1. Broadcast foliar; 50% pods final length	20.06 [188]	0.07 [0.08]	10	0.14 [0.16]	X-77 (NIS)
		2. Broadcast foliar; 50% pods final length	22.26 [189]	0.07 [0.08]			

TABLE B.1.2. Study Use Pattern.

Location (City, State; Year) Trial ID	EP[1]	Application					Tank Mix/ Adjuvants[4]
		Method; Timing	Volume GPA[2] [L/ha]	Rate lb ai/A [kg ai/ha]	RTI[3] (days)	Total Rate lb ai/A [kg ai/ha]	
Proctor, AR; 2004 (RCN 2004194)	0.75 lb/gal SC/L	1. Broadcast foliar; 70% pods final length	20.16 [189]	0.07 [0.08]	10	0.14 [0.16]	X-77 (NIS)
		2. Broadcast foliar; all pods final length	20.29 [190]	0.07 [0.08]			
Stoneville, MS; 2004 (RCN 2004195)	0.75 lb/gal SC/L	1. Broadcast foliar; 70% pods final length	20.32 [188]	0.07 [0.08]	10	0.14 [0.16]	Surf AC 820 (NIS)
		2. Broadcast foliar; all pods final length	21.65 [189]	0.07 [0.08]			
Arkansaw, WI; 2004 (RCN 2004196)	0.75 lb/gal SC/L	1. Broadcast foliar; 30% pods final length	20.13 [188]	0.07 [0.08]	10	0.14 [0.16]	Latron CS-7 (NIS)
		2. Broadcast foliar; 50% pods final length	20.19 [189]	0.07 [0.08]			
Carlyle, IL; 2004 (RCN 2004197)	0.75 lb/gal SC/L	1. Broadcast foliar; 70% pods final length	10.17 [95]	0.07 [0.08]	10	0.14 [0.16]	Lantron CS-7 (NIS)
		2. Broadcast foliar; all pods final length	10.72 [100]	0.07 [0.08]			

[1] EP = End-use Product
[2] Gallons per acre or L/ha
[3] RTI = Retreatment Interval
[4] NIS = nonionic surfactant

TABLE B.1.3. Trial Numbers and Geographical Locations.

NAFTA Growing Zones	Soybean		
	Submitted	Requested [1]	
		Canada	U.S.
1			
1A			
2	2		2
3			
4	3		3
5	15	11	15
5A			
5B	1	1	
6			
7			
7A			
8			
9			
10			
11			
12			
13			
14			
15			

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TABLE B.1.3. Trial Numbers and Geographical Locations.

NAFTA Growing Zones	Soybean		
	Submitted	Requested [1]	
		Canada	U.S.
16			
17			
18			
19			
20			
21			
Total	21	12	20

[1] The requested number and geographic distribution of field trials for rye, according to OPPTS Guideline 860.1500 and PMRA Directive 98-2, are shown.

B.2. Sample Handling and Preparation

Soybean samples were placed in coolers and stored frozen at the field sites within 5 hours of harvest or collection. Samples remained in frozen storage at the field facilities for up to 53 days until shipment via ACDS freezer truck to the analytical laboratory, BASF Agro Research (Research Triangle Park, NC), for analysis. In preparation for analysis, soybean samples were homogenized in the presence of dry ice. All samples remained frozen at all times except during homogenization and subsampling for analysis.

B.3. Analytical Methodology

Soybean samples from the 2005 trials were analyzed for residues of metconazole, metabolites M11, M21, and M30, and the triazole metabolites 1,2,4-T, TA, and TAA using an LC/MS/MS method (BASF Method D0508). A brief description of the method was included in MRID 46902228.

Briefly, residues of metconazole, M11, M21, and M30 were extracted with acetonitrile (ACN):water (70:30, v:v). The extracts were diluted with methanol:water (80:20, v:v), filtered, and reserved for LC/MS/MS analysis. For forage and hay, the extract was concentrated, diluted with water, and partitioned with hexane:ethyl acetate (9:1, v:v). For determination of residues of 1,2,4-T, TA, and TAA, a separate aliquot of the initial extract was evaporated to dryness, redissolved in 0.1% formic acid in water, filtered, and reserved for LC/MS/MS analysis. Residues of metabolites M11, M21, and M30 were converted to parent equivalents using molecular weight conversion factors of 0.95 for M11 and M21 and 0.96 for M30. The reported limit of detection was 20% LOQ.

Soybean samples from the six 2004 trials were analyzed for residues of *cis*- and *trans*-metconazole using a LC/MS/MS method, BASF Method 550/0. A brief description of the method was included in MRID 46902229.

Briefly, residues of metconazole were extracted with methanol:water:2N HCl (70:25:5 v:v:v), isolated via centrifugation, diluted with water, and partitioned with dichloromethane (DCM). The DCM phase was collected, evaporated to dryness, and redissolved in methanol:water (80:20, v:v) for LC/MS/MS analysis. The limit of detection (LOD) was 0.001 ppm.

The validated LOQ was 0.01 ppm for the parent metconazole (sum of *cis* and *trans* isomers at 0.005 ppm each, for both methods) and the metabolites M11, M21, and M30 in/on soybean samples. The validated LOQ was 0.05 ppm for 1,2,4-T, TA, and TAA.

Both methods were validated concurrently with the analysis of field samples using samples of untreated soybean forage, hay, and seed fortified at 0.005 and 0.5 ppm with *cis*- and *trans*-metconazole; at 0.01 and 1.00 ppm with M11, M21, and M30; and at 0.05 and 5.00 ppm with 1,2,4-T, TA, and TAA. Method validation data were also submitted for method 550/0, reflecting fortification levels of 0.005 and 0.5 ppm for both isomers.

C. RESULTS AND DISCUSSION

Samples were stored frozen (<-10 °C) from harvest to extraction for 61-195 days (2.0-6.4 months) for soybean forage, 68-179 days (2.2-5.9 months) for soybean hay, and 40-161 days (1.3-5.3 months) for soybean seed, and were analyzed within 0-5 days of extraction. Adequate storage stability data are available indicating that: (1) residues of all analytes are stable/relatively stable under frozen storage conditions in/on soybean seed for up to 6 months (refer to 46902223.der.doc); (2) residues of M11, M21, M30, and the triazole metabolites are stable/relatively stable in/on radish tops for up to 6 months (refer to 46902223.der.doc); and (3)

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residues of *cis*- and *trans*-metconazole< M11, M21, and M30 are stable in/on wheat hay for up to 6 months (refer to 46902223.der.doc);and (4) residues of *cis*- and *trans*-metconazole are relatively stable in/on lettuce and rye forage for up to 12 months (refer to 46902218.der.doc). These data are sufficient to support the storage conditions and durations for the soybean field trials.

The petitioner conducted a concurrent storage stability study with soybean hay to investigate the stability of residues in extracts stored under refrigeration. The initial (ACN/water) and final (methanol/water) extracts of selected samples of fortified soybean hay that had been analyzed on the day of extraction were stored refrigerated (temperature unspecified) and re-analyzed 6-7 days later. The results indicated that residues of *cis*- and *trans*-metconazole, M11, M21, M30, 1,2,4-T, TA, and TAA were stable in refrigerated extracts for up to 7 days.

Method validation and concurrent method recovery data are presented in Table C.1. Samples from the 15 trials conducted in 2005 were analyzed for residues of *cis*- and *trans*-metconazole, metabolites M11, M21, and M30, and the triazole metabolites 1,2,4-T, TA, and TAA using an LC/MS/MS method (BASF Method D0508). Residues of metabolites M11, M21, and M30 were converted to parent equivalents using molecular weight conversion factors of 0.95 for M11 and M21 and 0.96 for M30. Samples from the six trials conducted in 2004 were analyzed for residues of *cis*- and *trans*-metconazole using a LC/MS/MS method, BASF Method 550/0. The validated limits of quantitation (LOQs) were 0.01 ppm for the parent metconazole (sum of *cis* and *trans* isomers at 0.005 ppm each for both methods), M11, M21, and M30 in/on soybean samples. The validated LOQ was 0.05 ppm for 1,2,4-T, TA, and TAA. The methods were adequate for data collection based on acceptable concurrent recovery and method validation recovery data. Concurrent and method validation recoveries were generally within the acceptable range of 70-120% for soybean forage, hay, and seed fortified at 0.005 and 0.5 ppm with *cis*- and *trans*-metconazole (both methods); at 0.01 and 1.00 ppm with M11, M21, and M30; and at 0.05 and 5.00 ppm with 1,2,4-T, TA, and TAA. Apparent residues of *cis*- and *trans*-metconazole, metabolites M11, M21, and M30, and 1,2,4-T, TA, and TAA were each below the respective LOQs in/on 21 samples each of untreated soybean forage, hay, and seed.

Residue data from the soybean field trials are reported in Tables C.3.1 (metconazole, M11, M21, and M30) and C.3.2 (triazole metabolites), and the residue data for wheat are summarized in Tables C.4.1 and C.4.2. Residues of *cis*-and *trans*-metconazole in/on soybean forage were 0.404-2.040 and 0.0.070-0.405 ppm, respectively; total metconazole residues (sum of *cis* and *trans* isomers) were 0.474-2.430 ppm. In soybean hay, residues of *cis*- and *trans*-metconazole were 0.995-3.930 and 0.173-0.808 ppm, respectively, and total metconazole residues were 1.168-4.738 ppm. In soybean seed, residues of *cis*- and *trans*-metconazole were <0.005-0.036 and <0.005-0.090 ppm, respectively, and total metconazole residues were <0.01-0.050 ppm. Residues of metabolite M11 were <0.01-0.09, 0.02-0.20, and <0.01 ppm for forage, hay and seed, respectively; residues of M21 were <0.01-0.03, 0.01-0.08, and <0.01 ppm for forage, hay and seed, respectively; and residues of M30 were <0.01-0.01, <0.01-0.04, and <0.01 ppm for forage, hay, and seed, respectively.

Residues of 1,2,4-T were <0.05, <0.05-0.08, and <0.05-0.10 ppm in/on forage, hay, and seed, respectively; maximum residues of TA were <0.05-0.23, <0.05, and <0.05-0.69 ppm for forage, hay, and seed, respectively; and maximum residues of TAA were <0.05, <0.05-0.08, and <0.05 ppm for forage, hay, and seed, respectively.

The submitted residue decline data indicated that total metconazole residues (sum of *cis* and *trans* isomers) generally declined in soybean forage, hay, and seed with increasing preharvest intervals.

TABLE C.1. Summary of Concurrent Recoveries of Metconazole, its Metabolites M11, M21, and M30, and Triazole Metabolites from Soybeans.

Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. (%)
Concurrent Recovery (Method D0508)					
Forage	*Cis*-Metconazole	0.005	3	79, 110, 110	100 ± 18
		0.5	3	96, 103, 111	103 ± 8
	Trans-metconazole	0.005	3	82, 87, 90	86 ± 4
		0.5	3	90, 92, 98	93 ± 4
	M11	0.01	3	79, 89, 104	91 ± 13
		1.0	3	86, 88, 113	96 ± 15
	M21	0.01	3	70, 73, 88	77 ± 9
		1.0	3	86, 90, 105	94 ± 10
	M30	0.01	3	75, 103, 94	90 ± 14
		1.0	3	87, 102, 106	98 ± 10
	1,2,4-T	0.05	3	75, 105, 107	95 ± 18
		5.0	3	64, 99, 108	90 ± 23
	TAA	0.05	3	92, 93, 97	94 ± 3
		5.0	3	87, 89, 90	89 ± 2
	TA	0.05	3	99, 99, 119	106 ± 12
		5.0	3	88, 92, 100	93 ± 6
Hay	*Cis*-Metconazole	0.005	3	96, 101, 104	100 ± 4
		0.5	3	87, 98, 114	100 ± 14
	Trans-metconazole	0.005	3	90, 100, 103	97 ± 7
		0.5	3	97, 99, 116	104 ± 11
	M11	0.01	3	74, 82, 84	80 ± 5
		1.0	3	79, 93, 95	89 ± 8
	M21	0.01	3	81, 86, 115	94 ± 18
		1.0	3	93, 94, 106	97 ± 7
	M30	0.01	3	91, 96, 100	96 ± 5
		1.0	3	96, 101, 113	103 ± 9
	1,2,4-T	0.05	3	75, 78, 105	86 ± 16
		5.0	3	81, 99, 108	96 ± 13
	TAA	0.05	3	81, 95, 95	90 ± 8
		5.0	3	84, 106, 113	101 ± 15
	TA	0.05	3	69, 75, 79	74 ± 5
		5.0	3	77, 80, 85	81 ± 4

TABLE C.1. Summary of Concurrent Recoveries of Metconazole, its Metabolites M11, M21, and M30, and Triazole Metabolites from Soybeans.

Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. (%)
Seed	*Cis*-Metconazole	0.005	4	84, 91, 113, 123	103 ± 18
		0.5	4	84, 96, 102, 108	97 ± 11
	Trans-metconazole	0.005	4	72, 96, 105, 112	96 ± 17
		0.5	4	85, 105, 108, 118	104 ± 14
	M11	0.01	4	67, 74, 75, 80	74 ± 5
		1.0	4	94, 99, 104, 104	100 ± 5
	M21	0.01	4	80, 89, 91, 98	90 ± 7
		1.0	4	88, 89, 104, 111	98 ± 11
	M30	0.01	4	76, 86, 94, 97	88 ± 9
		1.0	4	93, 97, 103, 109	101 ± 7
	1,2,4-T	0.05	4	78, 88, 89, 95	87 ± 7
		5.0	3	89, 90, 91	90 ± 1
	TAA	0.05	4	83, 98, 101, 102	96 ± 9
		5.0	4	90, 93, 101, 101	96 ± 6
	TA	0.05	4	68, 69, 79, 91	77 ± 11
		5.0	4	66, 76, 77, 80	74 ± 6
Concurrent Recovery (Method 550/0)					
Forage	*Cis*-Metconazole	0.005	1	86	86
		0.5	1	93	93
	Trans-metconazole	0.005	1	86	86
		0.5	1	93	93
Hay	*Cis*-Metconazole	0.005	1	94	94
		0.5	1	107	107
	Trans-metconazole	0.005	1	92	92
		0.5	1	76	76
Seed	*Cis*-Metconazole	0.005	2	87, 96	92
		0.5	1	114	114
	Trans-metconazole	0.005	2	91, 92	92
		0.5	1	104	104
Method Validation (Method 550/0)					
Forage	*Cis*-Metconazole	0.005	5	88, 92, 98, 101, 101	96 ± 6
		0.5	5	80, 84, 85, 85, 87	84 ± 2
	Trans-metconazole	0.005	5	93, 94, 98, 98, 108	98 ± 5
		0.5	5	84, 88, 89, 90, 93	89 ± 3
Hay	*Cis*-Metconazole	0.005	5	97, 102, 104, 106, 108	103 ± 4
		0.5	5	98, 101, 103, 112, 124	108 ± 11
	Trans-metconazole	0.005	5	98, 99, 101, 104, 108	102 ± 4
		0.5	5	97, 104, 106, 109, 110	105 ± 5
Seed	*Cis*-Metconazole	0.005	5	97, 97, 100, 102, 103	100 ± 3
		0.5	5	94, 100, 100, 106, 113	103 ± 7
	Trans-metconazole	0.005	5	92, 96, 97, 102, 103	98 ± 5
		0.5	5	94, 98, 99, 102, 109	100 ± 6

TABLE C.2. Summary of Storage Conditions.]

Matrix	Storage Temperature (°C)	Actual Storage Duration Days (Months)	Interval of Demonstrated Storage Stability
Forage	< -10	61-195 (2.0-6.4)	The available storage stability data indicate that residues of all analytes are stable/relatively stable in/on soybean seed for up to 6 months; residues of M11, M21, M30, and the triazole metabolites are stable/relatively stable in/on radish tops for up to 6 months; (3) residues of *cis*- and *trans*-metconazole, M11, M21, and M30 are stable in/on wheat hay for up to 6 months; and residues of *cis*- and *trans*-metconazole are relatively stable in/on lettuce and rye forage for up to 12 months.[2]
Hay		68-179 (2.2-5.9)	
Seed		40-161 (1.3-5.3)	

[1] Storage duration from harvest to extraction is reported by the petitioner. Samples were analyzed within 0-5 days of extraction.
[2] Refer to 46902218.der.doc and 46902223.der.doc.

TABLE C.3.1 Residue Data for Metconazole, M11, M21, and M30 from Soybean Field Trials with Metconazole.

Trial ID (County, State; Year)	Zone	Crop; Variety	Matrix	Total Rate lb ai/A [kg ai/ha]	PHI (days)[1]	Metconazole Residues (ppm parent equivalents)						
						Metconazole			Metabolites			Total[2]
						cis	*trans*	Total	M11	M21	M30	
Tift, GA; 2005 (RCN R05111)	2	Soybean; Dekalb H7242	Forage	0.14	7	0.894	0.198	1.092	0.02	0.01	<0.01	1.14
						0.785	0.183	0.968	0.03	0.01	<0.01	1.02
			Hay	0.14	7 [11]	1.690	0.340	2.030	0.06	0.04	0.02	2.15
						1.640	0.329	1.969	0.06	0.03	0.02	2.08
			Seed	0.14	30	<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04
Wabasha, MN; 2005 (RCN R05112)	5	Soybean; Asgrow AG1603	Forage	0.14	7	0.556	0.112	0.668	0.01	0.01	<0.01	0.70
						0.649	0.141	0.790	0.02	0.01	<0.01	0.83
			Hay	0.14	7 [4]	3.360	0.633	3.993	0.07	0.06	0.02	4.15
						2.330	0.494	2.824	0.06	0.04	0.02	2.95
			Seed	0.14	30	<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04
Wabasha, MN; 2005 (RCN R05113)	5	Soybean; Asgrow AG1603	Forage	0.14	7	0.876	0.160	1.036	0.02	0.01	<0.01	1.08
						0.824	0.165	0.989	0.02	0.01	<0.01	1.04
			Hay	0.14	7 [4]	3.240	0.668	3.908	0.10	0.06	0.03	4.09
						3.370	0.605	3.975	0.13	0.07	0.04	4.22
			Seed	0.14	30	<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04
Madison, IL; 2005 (RCN R05114)	5	Soybean; DKB38-52	Forage	0.14	7	0.783	0.147	0.930	0.05	0.01	0.01	1.01
						0.819	0.166	0.985	0.06	0.02	0.01	1.08
			Hay	0.14	7 [3]	1.080	0.199	1.279	0.06	0.03	0.02	1.38
						1.210	0.233	1.443	0.09	0.03	0.02	1.57
			Seed	0.14	30	0.007	<0.005	<0.012	<0.01	<0.01	<0.01	0.04
						0.005	<0.005	<0.010	<0.01	<0.01	<0.01	0.04

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TABLE C.3.1 Residue Data for Metconazole, M11, M21, and M30 from Soybean Field Trials with Metconazole.

Trial ID (County, State; Year)	Zone	Crop; Variety	Matrix	Total Rate lb ai/A [kg ai/ha]	PHI (days)[1]	Metconazole Residues (ppm parent equivalents)						
						Metconazole			Metabolites			Total[2]
						cis	*trans*	Total	M11	M21	M30	
Clinton, IL; 2005 (RCN R05115)	5	Soybean; NK 43-B1	Forage	0.14	7	0.888	0.167	1.055	0.03	0.01	<0.01	1.11
						0.910	0.176	1.086	0.03	0.01	0.01	1.14
			Hay	0.14	7 [6]	1.390	0.297	1.687	0.04	0.03	0.02	1.77
						2.140	0.407	2.547	0.07	0.04	0.03	2.68
			Seed	0.14	29	<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04
Stark, IL; 2005 (RCN R05116)	5	Soybean; Asgrow 3202	Forage	0.14	7	1.670	0.336	2.006	0.08	0.02	0.01	2.12
						1.930	0.405	2.335	0.09	0.03	0.01	2.46
			Hay	0.14	7 [6]6	1.770	0.336	2.106	0.09	0.03	0.01	2.24
						1.750	0.291	2.041	0.10	0.03	0.01	2.19
			Seed	0.14	29	<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04
Polk, NE; 2005 (RCN R05117)	5	Soybean; Pioneer 92M80	Forage	0.14	7	0.918	0.179	1.097	<0.01	<0.01	<0.01	1.13
						1.140	0.229	1.369	0.01	<0.01	<0.01	1.40
			Hay	0.14	7 [0]	1.550	0.333	1.883	0.02	0.02	0.01	1.94
						2.160	0.496	2.656	0.02	0.02	0.02	2.72
			Seed	0.14	29	<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04
York, NE; 2005 (RCN R05118)	5	Soybean; Pioneer 92M80	Forage	0.14	7	1.300	0.286	1.586	0.02	0.02	<0.01	1.64
						1.350	0.315	1.665	0.03	0.02	0.01	1.73
			Hay	0.14	0	8.010	1.490	9.500	0.07	0.05	0.02	9.64
						8.820	1.640	10.46	0.08	0.05	0.03	10.6
					7 [0]	3.930	0.808	4.738	0.08	0.05	0.03	4.89
						3.610	0.723	4.333	0.08	0.05	0.03	4.49
					14	2.180	0.460	2.640	0.05	0.04	0.02	2.74
						2.310	0.452	2.762	0.05	0.04	0.02	2.88
					20	0.902	0.183	1.085	0.03	0.02	<0.01	1.14
						0.968	0.196	1.164	0.03	0.02	0.01	1.22
			Seed	0.14	23	<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
						0.006	<0.005	<0.011	<0.01	<0.01	<0.01	0.04
					30	<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04
					36	<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04
					43	0.005	<0.005	<0.010	<0.01	<0.01	<0.01	0.04
						<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04

TABLE C.3.1 Residue Data for Metconazole, M11, M21, and M30 from Soybean Field Trials with Metconazole.

Trial ID (County, State; Year)	Zone	Crop; Variety	Matrix	Total Rate lb ai/A [kg ai/ha]	PHI (days)[1]	Metconazole Residues (ppm parent equivalents)						
						Metconazole			Metabolites			Total[2]
						cis	*trans*	Total	M11	M21	M30	
Hall, NE; 2005 (RCN R05119)	5	Soybean; Dyna-Gro-37B28RR	Forage	0.14	8	0.596	0.121	0.717	0.01	0.01	<0.01	0.75
						0.591	0.121	0.712	0.01	0.01	<0.01	0.75
			Hay	0.14	8 [0]	1.300	0.303	1.603	0.03	0.02	0.01	1.67
						1.480	0.305	1.785	0.04	0.03	0.02	1.87
			Seed	0.14	30	<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04
Branchton, ON; 2005 (RCN R05120)	5	Soybean; Mycogen 5140 RR	Forage	0.14	7	1.150	0.250	1.400	0.05	0.02	0.01	1.49
						1.030	0.212	1.242	0.05	0.02	<0.01	1.32
			Hay	0.14	7 [11]	2.620	0.494	3.114	0.20	0.07	0.03	3.42
						2.670	0.574	3.244	0.19	0.08	0.04	3.55
			Seed	0.14	32	0.023	0.006	0.029	<0.01	<0.01	<0.01	0.06
						0.025	0.006	0.031	<0.01	<0.01	<0.01	0.06
Wapello, IA; 2005 (RCN R05121)	5	Soybean; Pioneer 93M11	Forage	0.14	6	1.224	0.254	1.478	0.02	0.02	0.01	1.53
						1.860	0.357	2.217	0.04	0.03	0.01	2.30
			Hay	0.14	6 [0]	2.370	0.552	2.922	0.06	0.04	0.02	3.04
						2.440	0.552	2.992	0.06	0.04	0.02	3.11
			Seed	0.14	31	0.006	<0.005	<0.011	<0.01	<0.01	<0.01	0.04
						0.007	<0.005	<0.012	<0.01	<0.01	<0.01	0.04
Jefferson, IA; 2005 (RCN R05122)	5	Soybean; Pioneer 93B87	Forage	0.14	7	1.484	0.296	1.780	0.03	0.02	0.01	1.85
						1.476	0.314	1.790	0.03	0.03	0.01	1.86
			Hay	0.14	0	5.490	1.130	6.620	0.11	0.05	0.03	6.80
						5.340	1.130	6.470	0.09	0.04	0.02	6.63
					7 [0]	2.630	0.546	3.176	0.07	0.05	0.02	3.32
						3.160	0.614	3.774	0.08	0.05	0.03	3.93
					14	1.880	0.349	2.229	0.10	0.05	0.03	2.41
						1.860	0.380	2.240	0.10	0.05	0.03	2.42
					21	0.474	0.095	0.569	0.02	0.01	<0.01	0.61
						0.522	0.113	0.635	0.02	0.01	<0.01	0.68
			Seed	0.14	23	<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04
					30	<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04
					37	<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04
					44	<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04

TABLE C.3.1 Residue Data for Metconazole, M11, M21, and M30 from Soybean Field Trials with Metconazole.

Trial ID (County, State; Year)	Zone	Crop; Variety	Matrix	Total Rate lb ai/A [kg ai/ha]	PHI (days)[1]	Metconazole Residues (ppm parent equivalents)						
						Metconazole			Metabolites			Total[2]
						cis	*trans*	Total	M11	M21	M30	
Keokuk, IA; 2005 (RCN R05123)	5	Soybean; DeKalb 3451	Forage	0.14	8	1.116	0.232	1.348	0.02	0.02	<0.01	1.40
						1.732	0.336	2.068	0.03	0.02	<0.01	2.13
			Hay	0.14	8 [0]	2.370	0.480	2.850	0.04	0.03	0.02	2.94
						2.810	0.731	3.541	0.04	0.04	0.02	3.64
			Seed	0.14	30	<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04
Ottawa, MI; 2005 (RCN R05124)	5	Soybean; Asgrow AG1903	Forage	0.14	7	1.208	0.202	1.410	0.04	0.02	0.01	1.48
						1.180	0.206	1.386	0.04	0.01	0.01	1.45
			Hay	0.14	7 [2]	1.150	0.187	1.337	0.05	0.02	0.01	1.42
						1.230	0.204	1.434	0.06	0.02	0.01	1.53
			Seed	0.14	28	<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04
St-Pie-de-Bagot, QB; 2005 (RCN R05125)	5	Soybean; 26-02RR	Forage	0.14	7	0.548	0.091	0.639	0.01	<0.01	<0.01	0.67
						0.404	0.070	0.474	<0.01	<0.01	<0.01	0.50
			Hay	0.14	7 [2]	0.995	0.173	1.168	0.02	0.01	<0.01	1.21
						1.290	0.206	1.496	0.02	0.01	<0.01	1.54
			Seed	0.14	30	<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04
Chula, GA; 2004 (RCN 20041912)	2	Soybean; Dekalb H7242RR	Forage	0.14	7	1.62	0.33	1.95	---	---	---	---
						1.54	0.32	1.86	---	---	---	---
			Hay	0.14	7 [3]	2.80	0.56	3.36	---	---	---	---
						2.62	0.59	3.21	---	---	---	---
			Seed	0.14	30	<0.005	<0.005	<0.010	---	---	---	---
						<0.005	<0.005	<0.010	---	---	---	---
Newport, AR; 2004 (RCN 2004193)	4	Soybean; Genesis C444NRR	Forage	0.14	7	0.82	0.18	1.00	---	---	---	---
						1.13	0.23	1.36	---	---	---	---
			Hay	0.14	7 [2-7]	1.23	0.24	1.47	---	---	---	---
						1.08	0.21	1.29	---	---	---	---
			Seed	0.14	30	<0.005	<0.005	<0.010	---	---	---	---
						<0.005	<0.005	<0.010	---	---	---	---
Proctor, AR; 2004 (RCN 2004194)	4	Soybean; BP563RR	Forage	0.14	7	1.47	0.29	1.76	---	---	---	---
						1.66	0.33	1.99	---	---	---	---
			Hay	0.14	7 [2-7]	1.88	0.37	2.25	---	---	---	---
						1.52	0.31	1.83	---	---	---	---
			Seed	0.14	30	<0.005	<0.005	<0.010	---	---	---	---
						<0.005	<0.005	<0.010	---	---	---	---

TABLE C.3.1 Residue Data for Metconazole, M11, M21, and M30 from Soybean Field Trials with Metconazole.

Trial ID (County, State; Year)	Zone	Crop; Variety	Matrix	Total Rate lb ai/A [kg ai/ha]	PHI (days)[1]	Metconazole Residues (ppm parent equivalents)						
						Metconazole			Metabolites			Total[2]
						cis	*trans*	Total	M11	M21	M30	
Stoneville, MS; 2004 (RCN 2004195)	4	Soybean; Pioneer 95B96	Forage	0.14	7	1.22	0.25	1.47	---	---	---	---
						1.88	0.38	2.26	---	---	---	---
			Hay	0.14	7 [2-7]	1.96	0.40	2.36	---	---	---	---
						2.36	0.41	2.77	---	---	---	---
			Seed	0.14	30	<0.005	<0.005	<0.010	---	---	---	---
						<0.005	<0.005	<0.010	---	---	---	---
Arkansaw, WI; 2004 (RCN 2004196)	5	Soybean; NK S-20-G4	Forage	0.14	7	1.00	0.20	1.20	---	---	---	---
						1.02	0.21	1.23	---	---	---	---
			Hay	0.14	7 [2-7]	1.85	0.32	2.16	---	---	---	---
						2.52	0.54	3.06	---	---	---	---
			Seed	0.14	30	0.035[3]	0.09[3]	0.04[2]	---	---	---	---
						0.036[3]	0.011[3]	0.05[2]	---	---	---	---
Carlyle, IL; 2004 (RCN 2004197)	5	Soybean; BT-383 CR	Forage	0.14	7	1.56	0.34	1.90	---	---	---	---
						2.04	0.39	2.43	---	---	---	---
			Hay	0.14	7 [2-7]	2.02	0.40	2.42	---	---	---	---
						2.28	0.48	2.76	---	---	---	---
			Seed	0.14	30	<0.005	<0.005	<0.010	---	---	---	---
						<0.005	<0.005	<0.010	---	---	---	---

[1] Hay samples were cut, then allowed to dry in the field prior to collection; the drying interval is presented in brackets; only the range of intervals was provided for the 2004 trials.
[2] Total = total residues; sum of *cis*- and *trans*-metconazole, M11, M21, and M30; values presented as calculated and reported by the petitioner.
[3] The average value of duplicate analyses is reported (residues ranged 0.034-0.038 ppm for *cis*-metconazole and 0.009-0.011 ppm for *trans*-metconazole)..

TABLE C.3.1.2. Residue Data for the Triazole Metabolites from Soybean Field Trials with Metconazole.

Trial ID (County, State; Year)	Zone	Crop; Variety	Matrix	Total Rate lb ai/A	PHI[1] (days)	Triazole Residues (ppm)		
						1,2,4-T	TAA	TA
Tift, GA; 2005 (RCN R05111)	2	Soybean; Dekalb H7242	Forage	0.14	7	<0.05	<0.05	0.23
						<0.05	<0.05	0.22
			Hay	0.14	7 [11]	<0.05	0.08	<0.05
						0.053	0.07	<0.05
			Seed	0.14	30	<0.05	<0.05	0.69
						<0.05	<0.05	0.64
Wabasha, MN; 2005 (RCN R05112)	5	Soybean; Asgrow AG1603	Forage	0.14	7	<0.05	<0.05	<0.05
						<0.05	<0.05	<0.05
			Hay	0.14	7 [4]	0.052	<0.05	<0.05
						0.061	<0.05	<0.05
			Seed	0.14 [0.16]	30	<0.05	<0.05	<0.05
						<0.05	<0.05	<0.05

TABLE C.3.1.2. Residue Data for the Triazole Metabolites from Soybean Field Trials with Metconazole.

Trial ID (County, State; Year)	Zone	Crop; Variety	Matrix	Total Rate lb ai/A	PHI[1] (days)	Triazole Residues (ppm)		
						1,2,4-T	TAA	TA
Wabasha, MN; 2005 (RCN R05113)	5	Soybean; Asgrow AG1603	Forage	0.14 [0.16]	7	<0.05	<0.05	<0.05
						<0.05	<0.05	<0.05
			Hay	0.14 [0.16]	7 [4]	<0.05	<0.05	<0.05
						0.081	<0.05	<0.05
			Seed	0.14 [0.16]	30	<0.05	<0.05	0.08
						<0.05	<0.05	0.06
Madison, IL; 2005 (RCN R05114)	5	Soybean; DKB38-52	Forage	0.14 [0.16]	7	<0.05	<0.05	<0.05
						<0.05	<0.05	<0.05
			Hay	0.14 [0.16]	7 [3]	<0.05	<0.05	<0.05
						<0.05	<0.05	<0.05
			Seed	0.14 [0.16]	30	<0.05	<0.05	0.08
						<0.05	<0.05	0.07
Clinton, IL; 2005 (RCN R05115)	5	Soybean; NK 43-B1	Forage	0.14 [0.16]	7	<0.05	<0.05	<0.05
						<0.05	<0.05	<0.05
			Hay	0.14 [0.16]	7 [6]	0.078	<0.05	<0.05
						0.076	<0.05	<0.05
			Seed	0.14 [0.16]	29	<0.05	<0.05	0.08
						<0.05	<0.05	0.08
Stark, IL; 2005 (RCN R05116)	5	Soybean; Asgrow 3202	Forage	0.14 [0.16]	7	<0.05	<0.05	<0.05
						<0.05	<0.05	<0.05
			Hay	0.14 [0.16]	7 [6]	<0.05	<0.05	<0.05
						<0.05	<0.05	<0.05
			Seed	0.14 [0.16]	29	<0.05	<0.05	0.06
						<0.05	<0.05	0.07
Polk, NE; 2005 (RCN R05117)	5	Soybean; Pioneer 92M80	Forage	0.14 [0.16]	7	<0.05	<0.05	<0.05
						<0.05	<0.05	<0.05
			Hay	0.14 [0.16]	7 [0]	0.066	<0.05	<0.05
						0.080	<0.05	<0.05
			Seed	0.14 [0.16]	29	<0.05	<0.05	0.06
						<0.05	<0.05	0.05
York, NE; 2005 (RCN R05118)	5	Soybean; Pioneer 92M80	Forage	0.14 [0.16]	7	<0.05	<0.05	0.05
						<0.05	<0.05	<0.05
			Hay	0.14 [0.16]	0	<0.05	<0.05	<0.05
						<0.05	<0.05	<0.05
					7 [0]	<0.05	<0.05	<0.05
						<0.05	<0.05	<0.05
					14	<0.05	<0.05	<0.05
						<0.05	<0.05	<0.05
					20	<0.05	<0.05	<0.05
						<0.05	<0.05	<0.05
			Seed	0.14 [0.16]	23	<0.05	<0.05	0.15
						<0.05	<0.05	0.11
					30	<0.05	<0.05	0.07

TABLE C.3.1.2. Residue Data for the Triazole Metabolites from Soybean Field Trials with Metconazole.

Trial ID (County, State; Year)	Zone	Crop; Variety	Matrix	Total Rate lb ai/A	PHI[1] (days)	Triazole Residues (ppm)		
						1,2,4-T	TAA	TA
						<0.05	<0.05	0.09
					36	<0.05	<0.05	0.09
						<0.05	<0.05	<0.05
					43	<0.05	<0.05	0.06
						<0.05	<0.05	0.06
Hall, NE; 2005 (RCN R05119)	5	Soybean; Dyna-Gro-37B28RR	Forage	0.14 [0.16]	8	<0.05	<0.05	<0.05
						<0.05	<0.05	<0.05
			Hay	0.14 [0.16]	8 [0]	0.072	<0.05	<0.05
						0.060	<0.05	<0.05
			Seed	0.14 [0.16]	30	0.07	<0.05	0.06
						0.05	<0.05	0.10
Branchton, ON; 2005 (RCN R05120)	5	Soybean; Mycogen 5140 RR	Forage	0.14 [0.16]	7	<0.05	<0.05	<0.05
						<0.05	<0.05	<0.05
			Hay	0.14 [0.16]	7 [11]	0.075	<0.05	<0.05
						0.084	<0.05	<0.05
			Seed	0.14 [0.16]	32	0.07	<0.05	0.08
						0.10	<0.05	0.07
Wapello, IA; 2005 (RCN R05121)	5	Soybean; Pioneer 93M11	Forage	0.14 [0.16]	6	<0.05	<0.05	<0.05
						<0.05	<0.05	<0.05
			Hay	0.14 [0.16]	6 [0]	<0.05	<0.05	<0.05
						<0.05	<0.05	<0.05
			Seed	0.14 [0.16]	31	0.08	<0.05	0.06
						0.09	<0.05	0.08
Jefferson, IA; 2005 (RCN R05122)	5	Soybean; Pioneer 93B87	Forage	0.14 [0.16]	7	<0.05	<0.05	<0.05
						<0.05	<0.05	<0.05
			Hay	0.14 [0.16]	0	<0.05	<0.05	<0.05
						<0.05	<0.05	<0.05
					7 [0]	<0.05	<0.05	<0.05
						<0.05	<0.05	<0.05
					14	<0.05	<0.05	<0.05
						<0.05	<0.05	<0.05
					21	<0.05	<0.05	<0.05
						<0.05	<0.05	<0.05
			Seed	0.14 [0.16]	23	<0.05	<0.05	0.11
						<0.05	<0.05	0.12
					30	<0.05	<0.05	0.10
						<0.05	<0.05	0.10
					37	<0.05	<0.05	0.09
						<0.05	<0.05	0.07
					44	<0.05	<0.05	0.09
						<0.05	<0.05	0.09

TABLE C.3.1.2. Residue Data for the Triazole Metabolites from Soybean Field Trials with Metconazole.

Trial ID (County, State; Year)	Zone	Crop; Variety	Matrix	Total Rate lb ai/A	PHI[1] (days)	Triazole Residues (ppm)		
						1,2,4-T	TAA	TA
Keokuk, IA; 2005 (RCN R05123)	5	Soybean; DeKalb 3451	Forage	0.14 [0.16]	8	<0.05	<0.05	<0.05
						<0.05	<0.05	<0.05
			Hay	0.14 [0.16]	8 [0]	<0.05	<0.05	<0.05
						<0.05	<0.05	<0.05
			Seed	0.14 [0.16]	30	0.07	<0.05	0.21
						0.08	<0.05	0.13
Ottawa, MI; 2005 (RCN R05124)	5	Soybean; Asgrow AG1903	Forage	0.14 [0.16]	7	<0.05	<0.05	<0.05
						<0.05	<0.05	<0.05
			Hay	0.14 [0.16]	7 [2]	<0.05	<0.05	<0.05
						<0.05	<0.05	<0.05
			Seed	0.14 [0.16]	28	0.08	<0.05	<0.05
						0.07	<0.05	0.05
St-Pie-de-Bagot, QB; 2005 (RCN R05125)	5	Soybean; 26-02R RR	Forage	0.14 [0.16]	7	<0.05	<0.05	<0.05
						<0.05	<0.05	<0.05
			Hay	0.14 [0.16]	7 [3]	<0.05	<0.05	<0.05
						<0.05	<0.05	<0.05
			Seed	0.14 [0.16]	30	0.08	<0.05	0.12
						0.10	<0.05	0.12

[1] Hay samples were cut, then allowed to dry in the field prior to collection; the drying interval is presented in brackets.

TABLE C.4.1. Summary of Residue Data for Metconazole, M11, M21, and M30 from Soybean Field Trials with Metconazole.

Commodity	Total Applic. Rate lb ai/A	PHI	Analyte	Residue Levels[1] (ppm)						
				n	Min.	Max.	HAFT[2]	Median (STMdR)	Mean (STMR)	Std. Dev.
Forage	0.14	6-8	*cis*-Metconazole	42	0.404	2.040	1.800	1.135	1.163	0.423
			trans-Metconazole	42	0.070	0.405	0.371	0.221	0.235	0.087
			Metconazole	42	0.474	2.430	2.171	1.365	1.397	0.510
			M11	30	<0.01	0.09	0.09	0.03	0.03	0.02
			M21	30	<0.01	0.03	0.03	0.01	0.02	0.01
			M30	30	<0.01	0.01	0.01	0.01	0.01	---
			Total Residues	30	0.08	2.46	2.29	1.23	1.30	0.55
Hay	0.14	6-8	*cis*-Metconazole	42	0.995	3.930	3.770	2.080	2.116	0.766
			trans-Metconazole	42	0.173	0.808	0.766	0.404	0.427	0.168
			Metconazole	42	1.168	4.738	4.536	2.484	2.543	0.930
			M11	30	0.02	0.20	0.20	0.06	0.07	0.04
			M21	30	0.01	0.08	0.08	0.04	0.04	0.02
			M30	30	<0.01	0.04	0.04	0.02	0.02	0.01
			Total Residues	30	1.21	4.89	4.69	2.70	2.72	1.06

TABLE C.4.1. Summary of Residue Data for Metconazole, M11, M21, and M30 from Soybean Field Trials with Metconazole.

Commodity	Total Applic. Rate lb ai/A	PHI	Analyte	Residue Levels[1] (ppm)						
				n	Min.	Max.	HAFT[2]	Median (STMdR)	Mean (STMR)	Std. Dev.
Seed	0.14	28-32	*cis*-Metconazole	42	<0.005	0.036	0.036	0.005	0.008	0.008
			trans-Metconazole	42	<0.005	0.090	0.051	0.005	0.007	0.013
			Metconazole	42	<0.010	0.050	0.045	0.010	0.014	0.009
			M11	30	<0.01	<0.01	0.01	0.01	0.01	---
			M21	30	<0.01	<0.01	0.01	0.01	0.01	---
			M30	30	<0.01	<0.01	0.01	0.01	0.01	---
			Total Residues	30	<0.04	0.06	0.06	0.04	0.04	0.01

[1] For calculations of median, mean, and standard deviation, the LOQ was used for any results reported as <LOQ in Table C.3.1. Data from United States and Canada trials were used in calculations.
[2] HAFT = Highest Average Field Trial.

TABLE C.4.2. Summary of Residue Data for the Triazole Metabolites from Soybean Field Trials with Metconazole.

Commodity	Total Applic. Rate lb ai/A	PHI	Analyte	Residue Levels[1] (ppm)						
				n	Min.	Max.	HAFT[2]	Median (STMdR)	Mean (STMR)	Std. Dev.
Forage	0.14	6-8	1,2,4-T	30	<0.05	<0.05	0.05	0.05	0.05	--
			TA	30	<0.05	0.23	0.23	0.05	0.06	0.04
			TAA	30	<0.05	<0.05	0.05	0.05	0.05	--
Hay	0.14	6-8	1,2,4-T	30	<0.05	0.08	0.08	0.05	0.06	0.01
			TA	30	<0.05	<0.05	0.05	0.05	0.05	--
			TAA	30	<0.05	0.08	0.08	0.05	0.05	0.01
Seed	0.14	28-32	1,2,4-T	30	<0.05	0.10	0.09	0.05	0.06	0.02
			TA	30	<0.05	0.69	0.67	0.08	0.12	0.15
			TAA	30	<0.05	<0.05	0.05	0.05	0.05	--

[1] For calculations of median, mean, and standard deviation, the LOQ was used for any results reported as <LOQ in Table C.3.2. Data from United States and Canada trials were used in calculations.
[2] HAFT = Highest Average Field Trial.

D. CONCLUSION

The submitted field trial data are adequate and reflect the use of two broadcast foliar applications of a 0.75 lb ai/gal SC/L formulation of metconazole at a total rate of ~0.14 lb ai/A, with a 9- to 11- day retreatment interval. Samples were harvested at PHIs of 6-8 days for forage and hay (dried for 0-11 days) and 28-32 days for seed. Acceptable methods were used for quantitation of residues of *cis*- and *trans*-metconazole, M11, M21, and M30, and 1,2,4-T, TA, and TAA in/on soybean samples, and the study is supported by adequate storage stability data.

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E. REFERENCES

DP#: 324541
Subject: Metconazole. Request for a Tolerance on Imported Bananas. Summary of Analytical Chemistry and Residue Data. Petition Number 9E05052.
From: N. Dodd
To: M. Waller
Date: 12/14/05
MRIDs: 44721506, 44721507, 44721508, 44721509, 44721510, and 44721511

F. DOCUMENT TRACKING

RDI: N. Dodd (2/20/08)
Petition Numbers: 6F7094 and 6F7095
DP#s: 348168 and 348206
PC Code: 125619

Template Version June 2005

Primary Evaluator	This DER was originally prepared under contract by Dynamac Corporation.
Approved by	Nancy Dodd, Chemist *Nancy Dodd* Date: 2/20/08 Registration Action Branch 3 Health Effects Division (7509P)

This DER was originally prepared under contract by Dynamac Corporation (2275 Research Boulevard, Suite 300; Rockville, MD 20850; submitted 09/17/2007). The DER has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

46902229 Leonard, R. (2005) The Magnitude of Metconazole Residues in Soybeans: Final Report. Project Number: 204640, 2004/5000755. Unpublished study prepared by BASF Agro Research, Southeast Ag Research, Inc. and Shoffner Farm Research. 113 p.

EXECUTIVE SUMMARY:

BASF has submitted data pertaining to aspirated grain fractions (AGF) for soybeans. In a single field trial conducted in IL in 2004, a 0.75 lb ai/gal soluble concentrate/liquid (SC/L) formulation of metconazole was applied as two broadcast foliar applications to soybeans at 0.07-0.08 lb ai/A/application, with a 9- to 11-day retreatment interval, for a total seasonal rate of ~0.14 lb ai/A. Applications were made in 10-11 gal/A spray volumes with a nonionic surfactant added as an adjuvant to the spray mixture. Bulk samples of soybean seed were harvested 31 days after the last application of metconazole and were processed into AGF using simulated commercial processing procedures.

Samples of soybean seed and AGF were analyzed for residues of *cis*- and *trans*-metconazole using an LC/MS/MS method, BASF Method 550/0. The validated limit of quantitation (LOQ) was 0.01 ppm for the parent metconazole (sum of *cis* and *trans* isomers at 0.005 ppm each). The method was adequate for data collection for soybean seed based on acceptable concurrent method recoveries. HED notes that no concurrent recovery or method validation data were included for soybean AGF. Samples were not analyzed for the triazole metabolites [1,2,4-triazole (1,2,4-T), triazolylalanine (TA), and triazolylacetic acid (TAA)].

Samples were stored frozen (<-10 °C) prior to extraction for 30-91 days (1-3 months) for soybean seed and 30 days (0-1 months) for soybean AGF. Adequate storage stability data are available to support the storage conditions and durations of the soybean seed samples. Because processed samples were stored for 30 days, no data are required to support the storage conditions and durations for soybean AGF commodities. No additional data are required to support the study.

Residues of *cis*- and *trans*-metconazole in soybean seed were <0.005 ppm each in two samples, for total metconazole residues (sum of *cis* and *trans* isomers) of <0.01 ppm. In two samples of soybean AGF, residues of *cis*-metconazole were 0.33 and 0.58 ppm and residues of *trans*-metconazole were 0.07 and 0.13 ppm, respectively, for total metconazole residues of 0.40 and 0.71 ppm.

The data indicate that total metconazole residues may concentrate in soybean AGF, with an average concentration factor of >56x.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the soybean AGF data are classified as scientifically acceptable.

The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document DP#s 348168 and 348206.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an impact on the validity of the study.

A. BACKGROUND INFORMATION

Metconazole [5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol] is a broad-spectrum triazole Group 3 fungicide (sterol biosynthesis inhibitors). There are currently no registered uses of metconazole in the U.S.; however, a tolerance has been established for banana, and a Section 18 emergency exemption and supporting time-limited tolerances have been granted for use on soybean. BASF Corporation has applied for registration of metconazole in the U.S. for use on barley, oats, rye, soybeans, sugar beets, triticale, and wheat.

The chemical structure and nomenclature of metconazole, and the physicochemical properties of the technical grade of metconazole are presented in Tables A.1 and A.2.

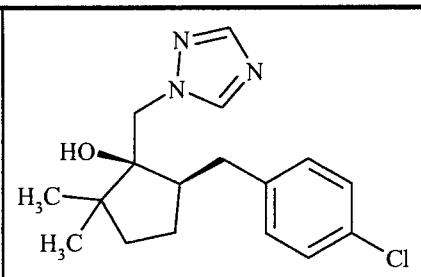
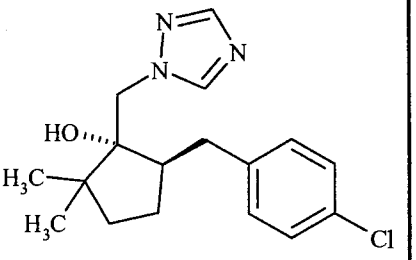
TABLE A.1. Metconazole Nomenclature.		
Chemical structure	 *cis*-isomer	 *trans*-isomer
Common name	Metconazole	
Company experimental name	KNF-S-474m (Kureha); BAS 555 F (BASF); V-10116 (Valent)	
IUPAC name	(1RS,5RS:1RS,5SR)-5-(4-chlorobenzyl)-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	
CAS name	5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	
CAS registry number	125116-23-6 (cis- and *trans*-isomers) 115850-27-6 (*cis*-isomer) 115850-28-7 (*trans*-isomer)	
End-use products (EP)	50% WDG (Metconazole 50 WDG Fungicide, EPA File Symbol 59639-RUT) 0.75 lb/gal SC/L (Caramba™ Fungicide, EPA File Symbol No. 7969-EUA) 0.67 lb/gal SC/L formulation (BAS 556 01F Fungicide, EPA File Symbol No. 7969-EUT; also contains the active ingredient pyraclostrobin at 0.83 lb/gal)	

Table A.2. Physicochemical Properties of Metconazole

Parameter	Value				References* (MRID)
Melting point/range	100.0-108.4°C (using Electrothermal Digital Melting Point Apparatus) (AC900,768 technical grade)				44721505
pH	5.81 at 25°C (1% aqueous suspension)				46808402
Relative density (20°C)	1.14 (relative density to water at 4°C, using capillary-stoppered, density-specific gravity bottle) (Lot No. AC 8879-140B)				44721505
Water solubility (20°C)	Using shake-flask method: 18.7 ± 1.0 mg/L (*cis*-isomer, WL148271, KNF-S-474m) 13.6 ± 1.7 mg/L (*trans*-isomer, WL148271, KNF-S-474m)				44721505
Solvent solubility (g/L) at 20°C	Solvent	Metconazole	*cis*	*trans*	44721505
	acetone	363	251	117	
	methanol	403	294	117	
	dichloromethane	481	343	141	
	ethyl acetate	260	173	90.0	
	propanol	132	86.6	46.7	
	toluene	103	66.2	38.0	
	Hexane	1.40	0.929	0.483	

Table A.2. Physicochemical Properties of Metconazole

Parameter	Value	References* (MRID)
Vapor pressure (20°C)	Using gas-saturation method: $< 1.23x10^{-5}$ Pa or 9.23×10^{-8} mm Hg (metconazole) $< 1.04x10^{-5}$ Pa or 7.80×10^{-8} mm Hg (*cis*-isomer) $< 1.96x10^{-6}$ Pa or 1.47×10^{-8} mm Hg (*trans*-isomer)	44721505
Dissociation constant (pK_a)	11.38±0.03 and 1.06±0.03 (in water at 29.1°C using spectrophotometric method; Lot No. AC 8879-140B)	44721505
Octanol/water partition coefficient, Log(K_{OW})	At 20 °C (using flask shaking method): K_{ow} (log K_{ow}) = 7090±989 (3.85) (Lot No. AC 8879-140B) (TGAI) K_{ow} (log K_{ow}) = 7150±803 (3.85) (*cis*-isomer, CL 354,801) K_{ow} (log K_{ow}) = 6800±1700 (3.8) (*trans*-isomer, CL 354,802)	44721505

UV/visible absorption spectrum	pH	λ	A	log ε	46808403
	cis-isomer				
	2.0	221.4	0.828	4.03	
	6.8		0.8452	4.04	
	7.0		0.9126	4.08	
	10.3		0.7226	3.98	
	trans-isomer				
	2.0	221.4	0.9053	4.07	
	7.0		0.9547	4.10	
	10.1		0.9893	4.11	

* Product Chemistry Reviews: DP #256877, Shyam Mathur, Ph.D., 9/12/2000 and DP #329168, Shyam Mathur, Ph.D., 7/13/07.

B. EXPERIMENTAL DESIGN

B.1. Application and Crop Information

In a single field trial conducted in IL in 2004, a 0.75 lb ai/gal soluble concentrate/liquid (SC/L) formulation of metconazole was applied as two broadcast foliar applications to soybeans at 0.07-0.08 lb ai/A/application, with a 9- to 11-day retreatment interval, for a total seasonal rate of ~0.14 lb ai/A. Applications were made in 10-11 gal/A spray volumes with a nonionic surfactant added as an adjuvant to the spray mixture. Bulk samples of soybean seed were harvested 31 days after the last application of metconazole. The study use pattern is detailed in Table B.1.1.

TABLE B.1. Application Rates for Soybean and Wheat.

Location (County, State; Year) Trial ID	EP[1]	Crop	Application					Tank Mix/ Adjuvants[5]
			Method; Timing	Volume[2] GPA (L/ha)	Rate lb ai/A [kg ai/ha]	RTI[3] (days)	Total Rate lb ai/A [kg ai/ha]	
Carlyle, IL; 2004 (RCN 2004197)	0.75 lb/gal SC/L	Soybean	1. Broadcast foliar; 70% pods final length	10.17 [95]	0.07 [0.08]	10	0.14 [0.16]	Lantron CS-7 (NIS)
			2. Broadcast foliar; all pods final length	10.72 [100]	0.07 [0.08]			

[1] EP = End-use Product
[2] Gallons per acre or L/ha
[3] RTI = Retreatment Interval
[4] NA = not applicable
[5] NIS = Non ionic surfactant

B.2. Sample Handling and Processing Procedures

Soybean samples were placed in coolers and stored frozen at the field sites within 5 hours of harvest. Samples remained in frozen storage at the field facilities for 25 days until shipment via ACDS freezer truck to the processing facility, Food Protein Research and Development Center (Byran, TX), where they were stored frozen (≤-23 °C) until processing. Samples were processed into aspirated grain fractions within 25 days of harvest using simulated commercial processing procedures via drying, aspiration, and classification of aspirated material.

After processing, samples were shipped via overnight courier on dry ice to BASF Agro Research for extraction and analysis. In preparation for analysis, soybean samples were homogenized in the presence of dry ice.

B.3. Analytical Methodology

Samples of soybean seed and AGF were analyzed for residues of *cis*- and *trans*-metconazole using a LC/MS/MS method, BASF Method 550/0. A brief description of the method was included in MRID 46902229.

Briefly, residues of metconazole were extracted with methanol:water:2N HCl (70:25:5 v:v:v), isolated via centrifugation, diluted with water, and partitioned with dichloromethane (DCM). The DCM phase was collected, evaporated to dryness, and redissolved in methanol:water (80:20, v:v) for LC/MS/MS analysis. The validated LOQ was 0.01 ppm for the parent metconazole (sum of *cis* and *trans* isomers at 0.005 ppm each). The limit of detection (LOD) was 0.001 ppm.

The method was validated concurrently with the analysis of field samples using samples of untreated soybean seed fortified at 0.005 and 0.5 ppm with *cis*- and *trans*-metconazole; method validation data were also submitted reflecting fortification levels of 0.005 and 0.5 ppm for both isomers.

C. RESULTS AND DISCUSSION

The storage conditions and durations for soybean seed and AGF are presented in Table C.2. Samples were stored frozen (<-10 °C) prior to extraction for 30-91 days (1-3 months) for soybean seed and for 30 days for soybean AGF. Adequate storage stability data are available indicating that residues of *cis*- and *trans*-metconazole are relatively stable under frozen storage conditions in/on soybean seed for up to 6 months (refer to 46902223.der.doc). Because soybean AGF samples were stored for 30 days, no data are required to support the storage conditions and durations for these samples. No additional data are required to support the soybean AGF study.

Concurrent method recovery data are presented in Table C.1. Samples of soybean seed and AGF were analyzed for residues of *cis*- and *trans*-metconazole using an LC/MS/MS method, BASF Method 550/0. The validated limit of quantitation (LOQ) was 0.01 ppm for the parent metconazole (sum of *cis* and *trans* isomers at 0.005 ppm each). The method was adequate for data collection based on acceptable method validation and concurrent method recoveries for soybean seed. Recoveries were within the acceptable range of 70-120%. HED notes that no concurrent recovery or method validation data were included for soybean AGF. Samples were not analyzed for the triazole metabolites, 1,2,4-triazole (1,2,4-T), triazolylalanine (TA), and triazolylacetic acid (TAA).

Residue data from the soybean AGF study are presented in Table C.3.1. Residues of *cis*- and *trans*-metconazole in soybean seed were <0.005 ppm each in two samples, for total metconazole residues (sum of *cis* and *trans* isomers) of <0.01 ppm. In two samples of soybean AGF, residues of *cis*-metconazole were 0.33 and 0.58 ppm and residues of *trans*-metconazole were 0.07 and 0.13 ppm, respectively, for total metconazole residues of 0.40 and 0.71 ppm.

The data indicate that total metconazole residues may concentrate in soybean AGF, with an average concentration factor of >56x.

TABLE C.1. Summary of Method Validation and Concurrent Recoveries of Metconazole from Soybean Seed and AGF.

Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. (%)
Concurrent Recovery					
Soybean Seed	*cis*-Metconazole	0.005	2	87, 96	92
		0.5	1	114	114
	trans-Metconazole	0.005	2	91, 92	92
		0.5	1	104	104
Method Validation					
Soybean Seed	*cis*-Metconazole	0.005	5	97, 97, 100, 102, 103	100 ± 3
		0.5	5	94, 100, 100, 106, 113	103 ± 7
	trans-Metconazole	0.005	5	92, 96, 97, 102, 103	98 ± 5
		0.5	5	94, 98, 99, 102, 109	100 ± 6
		5.000	1	100	100

TABLE C.2. Summary of Storage Conditions.

Matrix	Storage Temperature (°C)	Actual Storage Duration [1]	Interval of Demonstrated Storage Stability
Soybean Seed	< - 10	30-91 days (1-3 months)	Adequate storage stability data are available indicating that residues of *cis*- and *trans*-metconazole are relatively stable under frozen storage conditions in/on soybean seed for up to 6 months.[2]
Soybean Aspirated Grain		30 days	

[1] Storage duration from sample harvest to extraction. Samples were analyzed within 1 day of extraction.
[2] Refer to 46902223.der.doc.

TABLE C.3. Residue Data from Soybean AGF Study with Metconazole.

Trial ID (County, State; Year)	Total Rate (lb ai/A)	PHI (days)	Fraction	Residues (ppm)[2]			Processing Factor (Average)[1]
				cis-Metconazole	*trans*-Metconazole	Total Metconazole	Total Metconazole
Carlyle, IL; 2004 (RCN 2004197)	0.14	31	Seed (RAC)	<0.005 <0.005	<0.005 <0.005	<0.01 <0.01	--
			AGF	0.33 0.58	0.07 0.13	0.40 0.71	40x 71x (56x)

[1] Processing factors calculated by dividing the residue in the processed fraction by the average residue in the soybean seed (RAC).

D. CONCLUSION

Residues of total metconazole (sum of *cis* and *trans* isomers) were <0.01 ppm in/on two samples of soybean seed and 0.40 and 0.71 ppm in/on two samples of soybean AGF. The data indicate that total metconazole residues may concentrate in soybean AGF, with an average concentration factor of >56x.

An acceptable method was used for quantitation of residues of *cis*- and *trans*-metconazole in/on soybean samples, and the study is supported by adequate storage stability data.

E. REFERENCES

DP#: 324541
Subject: Metconazole. Request for a Tolerance on Imported Bananas. Summary of Analytical Chemistry and Residue Data. Petition Number 9E05052.
From: N. Dodd
To: M. Waller
Date: 12/14/05
MRIDs: 44721506, 44721507, 44721508, 44721509, 44721510, and 44721511

676

F. DOCUMENT TRACKING

RDI: N. Dodd (2/20/08)
Petition Numbers: 6F7094 and 6F7095
DP#s: 348168 and 348206
PC Code: 125619

Template Version June 2005

Primary Evaluator	This DER was originally prepared under contract by Dynamac Corporation.
Approved by	Nancy Dodd, Chemist *Nancy Dodd* Date: 2/20/08 Registration Action Branch 3 Health Effects Division (7509P)

This DER was originally prepared under contract by Dynamac Corporation (2275 Research Boulevard, Suite 300; Rockville, MD 20850; submitted 09/13/2007). The DER has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

46902230 Jordan, J.; Saha, M. (2006) The Magnitude of Residues of Metconazole (BAS 555 F) and its Metabolites in Sugar Beet: Final Report. Project Number: 137729, 2006/7006726. Unpublished study prepared by BASF Agro Research, Agresources, Inc. and Agstat. 260 p.

EXECUTIVE SUMMARY:

BASF Corporation has submitted field trial data for metconazole on sugar beets. Twelve field trials, each including two different application rates, were conducted in the United States in Zones 5 (MN, WI; 5 trials), 7 (ND; 1 trial), 8 (TX; 1 trial), 9 (MT; 1 trial), 10 (CA; 2 trials), and 11 (ID; 2 trials) during the 2005 growing season.

Each test site included one control plot and two treated plots. One of the treated plots received two broadcast foliar applications of a 0.75 lb ai/gal soluble concentrate/liquid (SC/L) formulation of metconazole at 0.10 lb ai/A/application, with a 13- to 15-day retreatment interval, for a total seasonal rate of 0.20 lb ai/A (Treatment 2). Applications were made in 18-31 gal/A spray volumes. The other treated plot received two broadcast foliar applications of metconazole at ~0.15 lb ai/A, with a 13- to 15-day retreatment interval, for a total rate of ~ 0.30 lb ai/A (Treatment 3). Applications were made in 17-30 gal/A spray volumes. A nonionic surfactant was added as a spray adjuvant for all applications.

Sugar beet roots and tops were harvested 13-15 days after the last application. Additional samples were collected from two trials 1, 7, 14-15, 21 and 27-28 days after the last application to generate residue decline data.

Samples were analyzed for residues of *cis*- and *trans*-metconazole, metabolites M11, M21, and M30, and the triazole metabolites [1,2,4-triazole (1,2,4-T), triazolylalanine (TA), and triazolyl-acetic acid (TAA)] using an LC/MS/MS method (BASF Method D0508). Residues of metabolites M11, M21, and M30 were converted to parent equivalents using molecular weight conversion factors of 0.95 for M11 and M21 and 0.96 for M30. The validated limits of quantitation (LOQs) were 0.01 ppm for the parent metconazole (sum of *cis* and *trans* isomers at 0.005 ppm each) and the metabolites M11, M21, and M30 in/on sugar beets. The validated LOQ was 0.05 ppm for 1,2,4-T, TA, and TAA. The method was adequate for data collection based on acceptable concurrent method recoveries.

Samples were stored frozen (<-10 °C) prior to extraction for 161-191 days (5.3-6.3 months) for sugar beet roots and 168-197 days (5.5-6.5 months) for sugar beet tops, and were analyzed within 0-2 days of extraction. Adequate storage stability data are available to support the storage conditions and durations of samples for the sugar beet field trials.

Following Treatment 2, maximum residues of *cis*-and *trans*-metconazole in sugar beet roots were 0.039 and 0.021 ppm, respectively; maximum total metconazole residues (sum of *cis* and *trans* isomers) were 0.048 ppm. In sugar beet tops, maximum residues of *cis*- and *trans*-metconazole were 1.077 and 0.178 ppm, respectively, and maximum total metconazole residues were 1.256 ppm. Residues of metabolites M11, M21, and M30 were <0.010 ppm in/on roots, and residues in tops were <0.010 ppm for M30 and <0.010-0.020 ppm for M11 and M21.

Following treatment 3, maximum residues of *cis*- and *trans*-metconazole in roots were 0.070 and 0.016 ppm, respectively, and maximum total metconazole residues were 0.085 ppm. In sugar beet tops, maximum residues of *cis*- and *trans*-metconazole were 2.067 and 0.426 ppm, respectively, and total metconazole residues were 2.493 ppm. Residues of metabolites M11, M21, and M30 were <0.010 ppm in/on roots, and residues in tops were <0.010 ppm for M30, <0.010-0.030 ppm for M11, and <0.010-0.020 ppm for M21.

Residues of 1,2,4-T, TA, and TAA were below the LOQ (<0.05 ppm) in/on all samples of sugar beet roots and tops following both treatments.

The submitted residue decline data indicated that total metconazole residues generally declined or did not increase in sugar beet roots and tops with increasing preharvest intervals.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the field trial residue data are classified as scientifically acceptable.

The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document DP#s 348168 and 348206.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an impact on the validity of the study.

A. BACKGROUND INFORMATION

Metconazole [5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol] is a broad-spectrum triazole Group 3 fungicide (sterol biosynthesis inhibitors). There are currently no registered uses of metconazole in the U.S.; however, a tolerance has been established for banana, and a Section 18 emergency exemption and supporting time-limited tolerances have been granted for use on soybean. BASF Corporation has applied for registration of metconazole in the U.S. for use on barley, oats, rye, soybeans, sugar beets, triticale, and wheat.

The chemical structure and nomenclature of metconazole, and the physicochemical properties of the technical grade of metconazole are presented in Tables A.1 and A.2.

TABLE A.1. Metconazole Nomenclature.

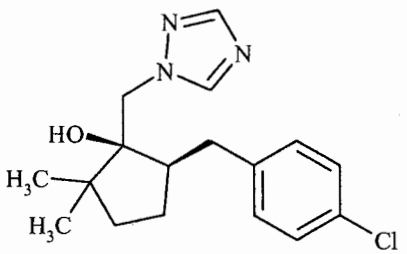
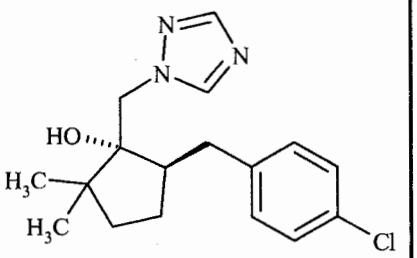
Chemical structure	 *cis*-isomer  *trans*-isomer
Common name	Metconazole
Company experimental name	KNF-S-474m (Kureha); BAS 555 F (BASF); V-10116 (Valent)
IUPAC name	(1RS,5RS:1RS,5SR)-5-(4-chlorobenzyl)-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol
CAS name	5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol
CAS registry number	125116-23-6 (cis- and *trans*-isomers) 115850-27-6 (*cis*-isomer) 115850-28-7 (*trans*-isomer)
End-use products (EP)	50% WDG (Metconazole 50 WDG Fungicide, EPA File Symbol 59639-RUT) 0.75 lb/gal SC/L (Caramba™ Fungicide, EPA File Symbol No. 7969-EUA) 0.67 lb/gal SC/L formulation (BAS 556 01F Fungicide, EPA File Symbol No. 7969-EUT; also contains the active ingredient pyraclostrobin at 0.83 lb/gal)

TABLE A.1. Metconazole Nomenclature.

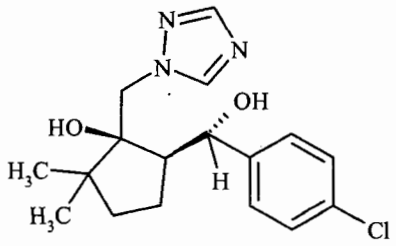
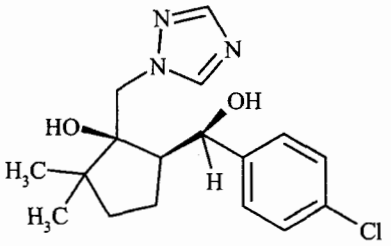
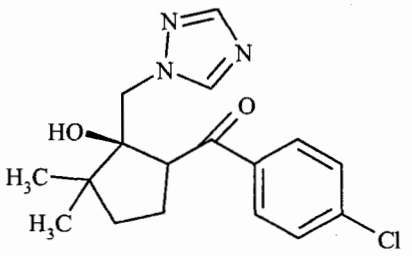
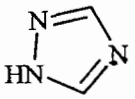
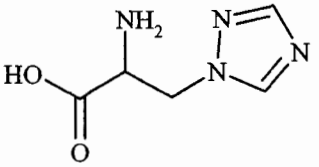
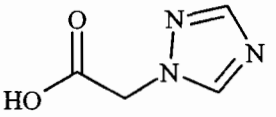
 Metconazole metabolite M11	 Metconazole metabolite M21	 Metconazole metabolite M30
 Triazole metabolite 1,2,4-triazole (1,2,4-T)	 Triazole metabolite triazolylalanine (TA)	 Triazole metabolite triazolylacetic acid (TAA)

Table A.2. Physicochemical Properties of Metconazole

Parameter	Value				References* (MRID)
Melting point/range	100.0-108.4°C (using Electrothermal Digital Melting Point Apparatus) (AC900,768 technical grade)				44721505
pH	5.81 at 25°C (1% aqueous suspension)				46808402
Relative density (20°C)	1.14 (relative density to water at 4°C, using capillary-stoppered, density-specific gravity bottle) (Lot No. AC 8879-140B)				44721505
Water solubility (20°C)	Using shake-flask method: 18.7 ± 1.0 mg/L (*cis*-isomer, WL148271, KNF-S-474m) 13.6 ± 1.7 mg/L (*trans*-isomer, WL148271, KNF-S-474m)				44721505
Solvent solubility (g/L) at 20°C	Solvent	Metconazole	*cis*	*trans*	44721505
	acetone	363	251	117	
	methanol	403	294	117	
	dichloromethane	481	343	141	
	ethyl acetate	260	173	90.0	
	propanol	132	86.6	46.7	
	toluene	103	66.2	38.0	
	Hexane	1.40	0.929	0.483	
Vapor pressure (20°C)	Using gas-saturation method: $< 1.23 \times 10^{-5}$ Pa or 9.23×10^{-8} mm Hg (metconazole) $< 1.04 \times 10^{-5}$ Pa or 7.80×10^{-8} mm Hg (*cis*-isomer) $< 1.96 \times 10^{-6}$ Pa or 1.47×10^{-8} mm Hg (*trans*-isomer)				44721505
Dissociation constant (pK_a)	11.38±0.03 and 1.06±0.03 (in water at 29.1°C using spectrophotometric method; Lot No. AC 8879-140B)				44721505

Table A.2. Physicochemical Properties of Metconazole

Parameter	Value				References* (MRID)
Octanol/water partition coefficient, Log(K_{OW})	At 20 °C (using flask shaking method): K_{ow} (log K_{ow}) = 7090±989 (3.85) (Lot No. AC 8879-140B) (TGAI) K_{ow} (log K_{ow}) = 7150±803 (3.85) (*cis*-isomer, CL 354,801) K_{ow} (log K_{ow}) = 6800±1700 (3.8) (*trans*-isomer, CL 354,802)				44721505
UV/visible absorption spectrum	pH	λ	A	log ε	46808403
	cis-isomer				
	2.0	221.4	0.828	4.03	
	6.8		0.8452	4.04	
	7.0		0.9126	4.08	
	10.3		0.7226	3.98	
	trans-isomer				
	2.0	221.4	0.9053	4.07	
	7.0		0.9547	4.10	
	10.1		0.9893	4.11	

* Product Chemistry Reviews: DP #256877, Shyam Mathur, Ph.D., 9/12/2000 and DP #329168, Shyam Mathur, Ph.D., 7/13/07.

B. EXPERIMENTAL DESIGN

B.1. Study Site Information

Twelve field trials, each including two different application rates, were conducted in the United States in Zones 5 (MN, WS; 5 trials), 7 (ND; 1 trial), 8 (TX; 1 trial), 9 (MT; 1 trial), 10 (CA; 2 trials), and 11 (ID; 2 trials) during the 2005 growing season.

One of the treated plots received two broadcast foliar applications of a 0.75 lb ai/gal soluble concentrate/liquid (SC/L) formulation of metconazole at 0.10 lb ai/A/application, with a 13- to 15-day retreatment interval, for a total seasonal rate of 0.20 lb ai/A (Treatment 2). Applications were made in spray volumes of 18-31 gal/A. The other treated plot received two broadcast foliar applications of metconazole at ~0.15 lb ai/A, with a 13- to 15-day retreatment interval, for a total rate of ~ 0.30 lb ai/A (Treatment 3). Applications were made in spray volumes of 17-30 gal/A. A nonionic surfactant was added as a spray adjuvant for all applications.

Samples of mature sugar beet root and top samples were harvested 13-15 days after the last application. Additional samples were collected from two trials at 1, 7, 14-15, 21, and 27-28 days after the last application of the 0.75 lb ai/gal SC/L formulation to evaluate residue decline.

The test crops were grown and maintained according to typical agricultural practices for each region; maintenance pesticides and fertilizers were used to produce a commercial quality crop. Irrigation was used to supplement rainfall as needed. Trial site conditions are presented in Table

B.1.1, and the study use pattern is presented in Table B.1.2. The crop varieties grown are identified in Table C.3; HED notes that the crop variety was listed as "unknown" for the Stanislaus, CA sites.

For each field trial, the petitioner presented the weather conditions at application and summarized the weather conditions for the duration of the trials. The petitioner reported that overall rainfall was generally below normal at the Dane, WI test sites (RCN R05088 and RCN R05089), resulting in drier than normal conditions and late planting. At the test site in Stutsman, ND (RCN R05090), above-average rainfall was recorded for most of the study duration from planting through harvest. These unusual weather conditions did not have an adverse effect on the sugar beet crops.

HED notes that, although the petitioner counted the two trials each conducted at Dane, WI and Stanislaus, CA, as separate trials (total of four trials for each application rate), based on the study parameters included in the data submission (site location; soil type; plant variety; application methods, timing, and dates; and harvest dates), these trials are not sufficiently different to constitute separate trials. For purposes of this submission, the Agency will count these as separate trials; however, for future submissions, the petitioner is advised to review 860.1500(e) concerning the number and location of domestic crop field trials for establishment of pesticide residue tolerances.

TABLE B.1.1. Trial Site Conditions.

Trial Identification: County, State; Year (Trial ID)	Soil characteristics			
	Type	%OM	pH	CEC (meq/g)
Wabasha, MN; 2005 (RCN R05085)	Loam	2.3	Not provided	
Wabasha, MN; 2005 (RCN R05086)	Silt Loam	3.1		
Pepin, WI; 2005 (RCN R05087)	Sandy Loam	2.6		
Dane; WI; 2005 (RCN R05088)	Silt Loam	2.4		
Dane, WI; 2005 (RCN R05089)	Silt Loam	3.3		
Stutsman, ND; 2005 (RCN R05090)	Sandy Loam	4.7		
Hockley, TX; 2005 (RCN R05091)	Sandy Loam	0.8		
Fremont, MT; 2005 (RCN R05092)	Loam	1.0		
Stanislaus, CA; 2005 (RCN R05093)	Sandy Loam	0.45		
Stanislaus, CA; 2005 (RCN R05094)	Sandy Loam	0.45		
Payette, ID; 2005 (RCN R05095)	Silty Clay Loam	0.65		
Jerome, WI; 2005 (RCN R05096)	Loam	1.2		

TABLE B.1.2. Study Use Pattern.

Location (County, State; Year) Trial ID	EP[1]	Application						Tank Mix/ Adjuvants[4]
		Treat-ment No.	Method; timing	Volume (GPA)[2]	Rate (lb ai/A)	RTI[3] (days)	Total Rate (lb ai/A)	
Wabasha, MN; 2005 (RCN R05085)	0.75 lb/gal SC/L	2	1. Broadcast foliar; canopy 80% closed	20.23	0.1015	14	0.20	Agridex (NIS)
			2. Broadcast foliar; crop cover complete	20.34	0.1005			

TABLE B.1.2. Study Use Pattern.

Location (County, State; Year) Trial ID	EP[1]	Application						Tank Mix/ Adjuvants[4]
		Treat-ment No.	Method; timing	Volume (GPA)[2]	Rate (lb ai/A)	RTI[3] (days)	Total Rate (lb ai/A)	
		3	1. Broadcast foliar; canopy 80% closed	20.10	0.1512	14	0.30	Agridex (NIS)
			2. Broadcast foliar; crop cover complete	20.20	0.1497			
Wabasha, MN; 2005 (RCN R05086)	0.75 lb/gal SC/L	2	1. Broadcast foliar; canopy 80% closed	20.10	0.1008	14	0.20	Agridex (NIS)
			2. Broadcast foliar; crop cover complete	20.06	0.0992			
		3	1. Broadcast foliar; canopy 80% closed	20.10	0.1512	14	0.30	Agridex (NIS)
			2. Broadcast foliar; crop cover complete	20.20	0.1497			
Pepin, WI; 2005 (RCN R05087)	0.75 lb/gal SC/L	2	1. Broadcast foliar; canopy 80% closed	19.97	0.0985	15	0.20	Agridex (NIS)
			2. Broadcast foliar; crop cover complete	19.99	0.1002			
		3	1. Broadcast foliar; canopy 80% closed	20.18	0.1494	15	0.30	Agridex (NIS)
			2. Broadcast foliar; crop cover complete	20.06	0.1507			
Dane; WI; 2005 (RCN R05088)	0.75 lb/gal SC/L	2	1. Broadcast foliar; canopy 50% closed	22.37	0.1005	15	0.20	Preference (NIS)
			2. Broadcast foliar; crop cover complete	24.15	0.0997			
		3	1. Broadcast foliar; canopy 50% closed	22.15	0.1492	15	0.30	Preference (NIS)
			2. Broadcast foliar; crop cover complete	23.56	0.1460			
Dane, WI; 2005 (RCN R05089)	0.75 lb/gal SC/L	2	1. Broadcast foliar; canopy 60% closed	23.55	0.1004	13	0.20	Preference (NIS)
			2. Broadcast foliar; crop cover complete	23.15	0.1018			
		3	1. Broadcast foliar; canopy 60% closed	23.15	0.1481	13	0.29	Preference (NIS)
			2. Broadcast foliar; crop cover complete	21.86	0.1455			
Stutsman, ND; 2005 (RCN R05090)	0.75 lb/gal SC/L	2	1. Broadcast foliar; crop cover complete	19.87	0.1016	13	0.20	Activator 90 (NIS)
			2. Broadcast foliar; roots harvestable size	19.52	0.1005			
		3	1. Broadcast foliar; crop cover complete	20.27	0.1560	13	0.31	Activator 90 (NIS)
			2. Broadcast foliar; roots harvestable size	19.82	0.1533			

TABLE B.1.2. Study Use Pattern.

Location (County, State; Year) Trial ID	EP[1]	Application						Tank Mix/ Adjuvants[4]
		Treat-ment No.	Method; timing	Volume (GPA)[2]	Rate (lb ai/A)	RTI[3] (days)	Total Rate (lb ai/A)	
Hockley, TX; 2005 (RCN R05091)	0.75 lb/gal SC/L	2	1. Broadcast foliar; beginning of crop cover	20.29	0.1000	13	0.20	Agridex (NIS)
			2. Broadcast foliar; canopy 80% closed	20.14	0.1006			
		3	1. Broadcast foliar; beginning of crop cover	20.13	0.1496	13	0.30	Agridex (NIS)
			2. Broadcast foliar; canopy 80% closed	20.24	0.1516			
Fremont, MT; 2005 (RCN R05092)	0.75 lb/gal SC/L	2	1. Broadcast foliar; crop cover complete	18.24	0.1028	14	0.20	Agridex (NIS)
			2. Broadcast foliar; full maturity	17.92	0.0999			
		3	1. Broadcast foliar; crop cover complete	16.67	0.1412	14	0.30	Agridex (NIS)
			2. Broadcast foliar; full maturity	18.40	0.1538			
Stanislaus, CA; 2005 (RCN R05093)	0.75 lb/gal SC/L	2	1. Broadcast foliar; canopy 50% closed	25.25	0.1009	14	0.20	Activator 85 (NIS)
			2. Broadcast foliar; crop cover complete	25.48	0.1019			
		3	1. Broadcast foliar; canopy 50% closed	25.08	0.1504	14	0.30	Activator 85 (NIS)
			2. Broadcast foliar; crop cover complete	25.17	0.1509			
Stanislaus, CA; 2005 (RCN R05094)	0.75 lb/gal SC/L	2	1. Broadcast foliar; canopy 50% closed	24.99	0.0999	14	0.20	Activator 85 (NIS)
			2. Broadcast foliar; crop cover complete	24.41	0.0976			
		3	1. Broadcast foliar; canopy 50% closed	25.47	0.1528	14	0.30	Activator 85 (NIS)
			2. Broadcast foliar; crop cover complete	24.56	0.1473			
Payette, ID; 2005 (RCN R05095)	0.75 lb/gal SC/L	2	1. Broadcast foliar; crop cover complete	30.56	0.1019	14	0.20	Preference (NIS)
			2. Broadcast foliar; roots harvestable size	29.76	0.0990			
		3	1. Broadcast foliar; crop cover complete	29.68	0.1481	14	0.29	Preference (NIS)
			2. Broadcast foliar; roots harvestable size	29.29	0.1461			

TABLE B.1.2. Study Use Pattern.

Location (County, State; Year) Trial ID	EP[1]	Application						Tank Mix/ Adjuvants[4]
		Treat-ment No.	Method; timing	Volume (GPA)[2]	Rate (lb ai/A)	RTI[3] (days)	Total Rate (lb ai/A)	
Jerome, WI; 2005 (RCN R05096)	0.75 lb/gal SC/L	2	1. Broadcast foliar; crop cover complete	18.88	0.1010	14	0.20	Activator 90 (NIS)
			2. Broadcast foliar; roots harvestable size	19.23	0.0993			
		3	1. Broadcast foliar; crop cover complete	19.05	0.1527	14	0.30	Activator 90 (NIS)
			2. Broadcast foliar; roots harvestable size	20.96	0.1511			

[1] EP = End-use Product
[2] Gallons per acre
[3] RTI = Retreatment Interval
[4] NIS = Nonionic surfactant

TABLE B.1.3. Trial Numbers and Geographical Locations.

NAFTA Growing Zones	Sugar Beets		
	Submitted	Requested	
		Canada	U.S.
1			
1A			
2			
3			
4			
5	5	2	5
5A			
5B			
6			
7	1		1
7A		2	
8	1		1
9	1		1
10	2		2
11	2		2
12			
13			
14		1	
15			
16			
17			
18			
19			
20			
21			
Total	12	5	12

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B.2. Sample Handling and Preparation

Sugar beet roots and tops were stored frozen at the field sites promptly after harvest. Samples remained in frozen storage at the field facilities for up to 31 days until shipment via ACDS freezer truck to the analytical laboratory, BASF Agro Research (Research Triangle Park, NC), for analysis. In preparation for analysis, sugar beet samples were homogenized in the presence of dry ice. All samples remained frozen at all times except during homogenization and subsampling for analysis.

B.3. Analytical Methodology

Sugar beet samples were analyzed for residues of metconazole, M11, M21, and M30, and the triazole metabolites (1,2,4-T, TA, and TAA) using an LC/MS/MS method (BASF Method D0508). A brief description of the method was included in the MRID. Briefly, residues of metconazole, M11, M21, and M30 were extracted with acetonitrile (ACN):water (70:30, v:v). The extracts were diluted with methanol:water (80:20, v:v), filtered, and reserved for LC/MS/MS analysis. For determination of residues of 1,2,4-T, TA, and TAA, a separate aliquot of the initial extract was evaporated to dryness, redissolved in 0.1% formic acid in water, filtered, and reserved for LC/MS/MS analysis. An optional clean-up step was used for determination of TA in sugar beet tops if needed. A separate aliquot of the initial extract was diluted with methanol/water and applied to an SPE cartridge; residues were eluted with 1% NH_4OH in methanol. The resulting eluate was evaporated to dryness and redissolved in 0.1% formic acid in water as for other extracts. Residues of metabolites M11, M21, and M30 were converted to parent equivalents using molecular weight conversion factors of 0.95 for M11 and M21 and 0.96 for M30.

The validated LOQ was 0.01 ppm for the parent metconazole (sum of *cis* and *trans* isomers at 0.005 ppm each) and the metabolites M11, M21, and M30 in/on sugar beet samples. The validated LOQ was 0.05 ppm for 1,2,4-T, TA, and TAA. The reported limit of detection was 20% LOQ.

The method was validated concurrently with the analysis of field samples using samples of untreated sugar beet roots and tops fortified at 0.005 and 0.5 ppm with *cis*- and *trans*-metconazole; at 0.01 and 1.00 ppm with M11, M21, and M30; and at 0.05 and 5.00 ppm with 1,2,4-T, TA, and TAA.

C. RESULTS AND DISCUSSION

Sample storage durations and conditions are summarized in Table C.2. Samples were stored frozen (<-10 °C) prior to extraction for 161-191 days (5.3-6.3 months) for sugar beets roots and 168-197 days (5.5-6.5 months) for sugar beet tops, and were analyzed within 0-2 days of extraction. Adequate storage stability data are available indicating that: (1) residues of *cis*- and *trans*-metconazole are relatively stable under frozen storage conditions in/on radish roots for up to 6 months and in/on carrots and lettuce for up to 12 months; (2) residues of M11, M21, and M30 are stable in/on sugar beet roots and radish tops for up to 6 months; and (3) residues of

1,2,4-T, TA, and TAA are relatively stable in/on radish roots and tops for up to 6 months (refer to 46902223.der.doc). These data are sufficient to support the storage conditions and durations for the sugar beet field trials.

The petitioner conducted a concurrent storage stability study with sugar beet tops to investigate the stability of residues in extracts stored under refrigeration. The initial (ACN/water) and final (methanol/water) extracts of selected samples of fortified sugar beet tops that had been analyzed on the day of extraction were stored refrigerated (temperature unspecified) and re-analyzed 8 days later. The results indicated that residues of *cis*- and *trans*-metconazole, M11, M21, M30, 1,2,4-T, TA, and TAA were stable in refrigerated extracts for up to 8 days.

Concurrent method recovery data are presented in Table C.1. Samples were analyzed for residues of metconazole, M11, M21, M30, 1,2,4-T, TA, and TAA using LC/MS/MS Method D0508. Residues of M11, M21, and M30 were converted to parent equivalents using molecular weight conversion factors of 0.95 for M11 and M21 and 0.96 for M30. The method was adequate for data collection based on acceptable concurrent method recovery data. Concurrent method recoveries were generally within the acceptable range of 70-120% for sugar beet roots and tops fortified at 0.005 and 0.5 ppm with *cis*- and *trans*-metconazole; at 0.01 and 1.00 ppm with M11, M21, and M30; and at 0.05 and 5.00 ppm with 1,2,4-T, TA, and TAA. Apparent residues of *cis*- and *trans*-metconazole, metabolites M11, M21, and M30, and 1,2,4-T, TA, and TAA were each below the respective LOQs in/on 12 samples each of untreated sugar beet roots and tops.

Residue data from the sugar beet field trials are reported in Table C.3. A summary of residue data for sugar beets is presented in Table C.4. Following Treatment 2, residues of *cis*- and *trans*-metconazole in sugar beet roots were <0.005-0.039 and <0.005-0.021 ppm, respectively; total metconazole residues (sum of *cis* and *trans isomers*) were <0.010-0.048 ppm. In sugar beet tops, residues of *cis*- and *trans*-metconazole were 0.010-1.077 and 0.006-0.178 ppm, respectively, and total metconazole residues were 0.037-1.256 ppm. Residues of metabolites M11, M21, and M30 were <0.010 ppm in/on roots, and residues in tops were <0.010 ppm for M30 and <0.010-0.020 ppm for M11 and M21.

Following treatment 3, residues of *cis*- and *trans*-metconazole in roots were <0.005-0.070 and <0.005-0.016 ppm, respectively, and total metconazole residues were <0.010-0.085 ppm. In sugar beet tops, residues of *cis*- and *trans*-metconazole were 0.014-2.067 and 0.005-0.426 ppm, respectively, and total metconazole residues were <0.035-2.493 ppm. Residues of metabolites M11, M21, and M30 were <0.010 ppm in/on roots, and residues in tops were <0.010 ppm for M30, <0.010-0.030 ppm for M11, and <0.010-0.020 ppm for M21.

Residues of 1,2,4-T, TA, and TAA were below the LOQ (<0.05 ppm) in/on all samples of sugar beet roots and tops following both treatments.

The submitted residue decline data indicated that total metconazole residues (sum of *cis* and *trans isomers*) generally declined or did not increase in sugar beet roots and tops with increasing preharvest intervals.

TABLE C.1. Summary of Concurrent Recoveries of Metconazole and Metabolites from Sugar Beets.

Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. (%)
Sugar beet roots	*cis*-Metconazole	0.005	6	92, 93, 94, 99, 100, 119	100 ± 10
		0.500	6	71, 83, 85, 91, 93, 99	87 ± 10
	trans-Metconazole	0.005	6	75, 87, 102, 109, 111, 125	102 ± 18
		0.500	6	64, 75, 93, 109, 114, 119	96 ± 22
	M11	0.010	6	84, 92, 99, 101, 104, 113	99 ± 10
		1.000	6	72, 73, 89, 91, 97, 104	88 ± 13
	M21	0.010	6	79, 95, 101, 104, 107, 108	99 ± 11
		1.000	6	65, 86, 90, 105, 108, 109	94 ± 17
	M30	0.010	6	74, 88, 89, 95, 99, 101	91 ± 10
		1.000	6	82, 85, 96, 98, 104, 104	95 ± 9
	1,2,4-T	0.050	6	86, 89, 91, 101, 101, 108	96 ± 9
		5.000	6	69, 87, 91, 95, 105, 110	93 ± 15
	TA	0.050	6	63, 70, 78, 79, 86, 87	77 ± 9
		5.000	6	72, 88, 97, 99, 102, 112	95 ± 14
	TAA	0.050	6	71, 73, 95, 99, 102, 107	91 ± 15
		5.000	6	77, 77, 86, 95, 95, 96	88 ± 9
Sugar beet tops	*cis*-Metconazole	0.005	6	71, 77, 88, 94, 97, 98	88 ± 11
		0.500	6	73, 81, 97, 98, 101, 106	93 ± 13
	trans-Metconazole	0.005	6	61, 70, 82, 84, 85, 93	79 ± 12
		0.500	6	66, 72, 77, 82, 104, 110	85 ± 18
	M11	0.010	6	72, 74, 77, 79, 80, 88	78 ± 6
		1.000	6	76, 80, 81, 87, 91, 104	87 ± 10
	M21	0.010	6	88, 93, 96, 100, 112, 115	101 ± 11
		1.000	6	74, 82, 87, 93, 98, 120	92 ± 16
	M30	0.010	6	72, 86, 91, 93, 103, 106	92 ± 12
		1.000	6	73, 86, 88, 92, 110, 111	93 ± 15
	1,2,4-T	0.050	6	72, 88, 88, 91, 110, 118	95 ± 17
		5.000	6	73, 77, 87, 96, 114, 117	94 ± 19
	TA	0.050	6	78, 88, 90, 92, 94, 95	90 ± 6
		5.000	6	83, 96, 97, 99, 101, 108	97 ± 8
	TAA	0.050	6	73, 81, 89, 99, 102, 112	93 ± 14
		5.000	6	76, 85, 96, 103, 110, 114	97 ± 15

TABLE C.2. Summary of Storage Conditions.

Matrix	Storage Temperature (°C)	Actual Storage Duration[1]	Interval of Demonstrated Storage Stability
Sugar beet root	< -10	161-191 days (5.3-6.3 months)	Residues of *cis*- and *trans*-metconazole were relatively stable under frozen storage conditions in/on radish roots for up to 6 months and carrots for up to 12 months. Residues of M11, M21, and M30 were relatively stable in/on sugar beet roots, and residues of 1,2,4-T, TA, and TAA were relatively stable in/on radish roots for up to 6 months.[2]

TABLE C.2. Summary of Storage Conditions.

Matrix	Storage Temperature (°C)	Actual Storage Duration[1]	Interval of Demonstrated Storage Stability
Sugar beet top	< -10	168-197 days (5.5-6.5 months)	Residues of *cis*- and *trans*-metconazole were relatively stable in/on lettuce for up to 12 months; residues of M11, M21, M30, 1,2,4-T, TA, and TAA were relatively stable in/on radish tops for up to 6 months.[2]

[1] Storage duration from harvest to extraction; samples were analyzed within 0-2 days of extraction.
[2] Refer to 46902223.der.doc.

TABLE C.3. Residue Data from Sugar Beet Field Trials with Metconazole.

Trial ID (County, State; Year)	Zone	Variety	Matrix	Total Rate (lb ai/A)	PHI (days)	Metconazole Residues (ppm parent equivalents)						
						Metconazole			Metabolites			Total[1]
						cis	*trans*	Total	M11	M21	M30	
Treatment 2												
Wabasha, MN; 2005 (RCN R05085)	5	VDH 66556 8232 Medium	Root	0.20	14	0.006	<0.005	<0.011	<0.01	<0.01	<0.01	0.04
						<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04
			Tops	0.20	14	0.997	0.167	1.163	<0.01	<0.01	<0.01	1.19
						1.077	0.178	1.256	<0.01	<0.01	<0.01	1.29
Wabasha, MN; 2005 (RCN R05086)	5	VDH 66556 8232 Medium	Root	0.20	14	<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04
						0.005	<0.005	<0.010	<0.01	<0.01	<0.01	0.04
			Tops	0.20	14	0.870	0.145	1.015	<0.01	<0.01	<0.01	1.04
						0.926	0.145	1.070	<0.01	<0.01	<0.01	1.10
Pepin, WI; 2005 (RCN R05087)	5	VDH665 56 8232 Medium	Root	0.20	1	<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04
					7	<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04
					14	<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04
					21	<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04
					28	<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04
			Tops	0.20	1	1.852	0.326	2.179	<0.01	<0.01	<0.01	2.21
						2.303	0.397	2.700	<0.01	0.01	<0.01	2.73
					7	1.428	0.246	1.674	<0.01	0.01	<0.01	1.70
						1.298	0.249	1.547	<0.01	0.01	<0.01	1.58
					14	0.724	0.112	0.835	<0.01	<0.01	<0.01	0.87
						1.064	0.148	1.212	<0.01	0.01	<0.01	1.24
					21	0.794	0.111	0.905	<0.01	<0.01	<0.01	0.94
						0.736	0.109	0.845	<0.01	0.01	<0.01	0.88
					28	0.816	0.104	0.919	<0.01	0.01	<0.01	0.95
						0.506	0.059	0.565	<0.01	<0.01	<0.01	0.60

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TABLE C.3. Residue Data from Sugar Beet Field Trials with Metconazole.

Trial ID (County, State; Year)	Zone	Variety	Matrix	Total Rate (lb ai/A)	PHI (days)	Metconazole Residues (ppm parent equivalents)						
						Metconazole			Metabolites			Total [1]
						cis	*trans*	Total	M11	M21	M30	
Dane; WI; 2005 (RCN R05088)	5	Vander-have VDH 66556	Root	0.20	13	0.031	0.008	0.039	<0.01	<0.01	<0.01	0.07
						0.018	<0.005	<0.023	<0.01	<0.01	<0.01	0.05
			Tops	0.20	13	0.014	0.116	0.130	<0.01	<0.01	<0.01	0.16
						0.015	0.138	0.153	<0.01	<0.01	<0.01	0.18
Dane, WI; 2005 (RCN R05089)	5	Vander-have VDH 66556	Root	0.20	14	0.032	0.007	0.040	<0.01	<0.01	<0.01	0.07
						0.039	0.009	0.048	<0.01	<0.01	<0.01	0.08
			Tops	0.20	14	0.034	0.006	0.040	<0.01	0.01	<0.01	0.07
						0.031	0.006	0.037	<0.01	0.01	<0.01	0.07
Stutsman, ND; 2005 (RCN R05090)	7	Vander-have 66453	Root	0.20	14	0.019	<0.005	<0.024	<0.01	<0.01	<0.01	0.05
						0.010	<0.005	<0.015	<0.01	<0.01	<0.01	0.05
			Tops	0.20	14	0.021	0.164	0.185	<0.01	<0.01	<0.01	0.22
						0.055	0.011	0.066	0.01	0.02	<0.01	0.11
Hockley, TX; 2005 (RCN R05091)	8	Eagle R	Root	0.20	14	<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04
						<0.005	0.006	<0.011	<0.01	<0.01	<0.01	0.04
			Tops	0.20	14	0.010	0.079	0.089	0.01	<0.01	<0.01	0.12
						0.010	0.082	0.092	<0.01	<0.01	<0.01	0.12
Fremont, MT; 2005 (RCN R05092)	9	Treasure	Root	0.20	14	0.009	0.014	0.023	<0.01	<0.01	<0.01	0.05
						0.006	0.008	0.014	<0.01	<0.01	<0.01	0.04
			Tops	0.20	14	0.014	0.132	0.146	<0.01	<0.01	<0.01	0.18
						0.017	0.133	0.150	<0.01	<0.01	<0.01	0.18
Stanislaus, CA; 2005 (RCN R05093)	10	Un-known	Root	0.20	14	0.010	0.016	0.026	<0.01	<0.01	<0.01	0.06
						<0.005	0.007	<0.012	<0.01	<0.01	<0.01	0.04
			Tops	0.20	14	0.012	0.098	0.110	0.01	0.01	<0.01	0.15
						0.014	0.096	0.109	0.02	0.01	<0.01	0.15
Stanislaus, CA; 2005 (RCN R05094)	10	Un-known	Root	0.20	14	0.013	0.021	0.034	<0.01	<0.01	<0.01	0.06
						0.013	<0.005	0.018	<0.01	<0.01	<0.01	0.05
			Tops	0.20	14	0.495	0.068	0.564	0.02	<0.01	<0.01	0.60
						0.522	0.075	0.597	0.02	0.01	<0.01	0.64

TABLE C.3. Residue Data from Sugar Beet Field Trials with Metconazole.

Trial ID (County, State; Year)	Zone	Variety	Matrix	Total Rate (lb ai/A)	PHI (days)	Metconazole Residues (ppm parent equivalents)						
						Metconazole			Metabolites			Total [1]
						cis	*trans*	Total	M11	M21	M30	
Payette, ID; 2005 (RCN R05095)	11	HM WS91	Root	0.20	1	0.008	<0.005	<0.013	<0.01	<0.01	<0.01	0.04
						0.007	<0.005	<0.012	<0.01	<0.01	<0.01	0.04
					7	0.025	<0.005	<0.030	<0.01	<0.01	<0.01	0.06
						0.013	<0.005	<0.018	<0.01	<0.01	<0.01	0.05
					15	0.014	<0.005	<0.019	<0.01	<0.01	<0.01	0.05
						0.009	<0.005	<0.014	<0.01	<0.01	<0.01	0.04
					21	0.006	<0.005	<0.011	<0.01	<0.01	<0.01	0.04
						<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04
					27	0.006	<0.005	<0.011	<0.01	<0.01	<0.01	0.04
						0.007	<0.005	<0.012	<0.01	<0.01	<0.01	0.04
			Tops	0.20	1	0.026	<0.005	<0.031	<0.01	<0.01	<0.01	0.06
						0.028	<0.005	<0.033	<0.01	<0.01	<0.01	0.06
					7	0.021	0.176	0.197	<0.01	<0.01	<0.01	0.23
						0.020	0.176	0.196	<0.01	<0.01	<0.01	0.23
					15	0.015	0.109	0.124	<0.01	<0.01	<0.01	0.15
						0.012	0.095	0.107	<0.01	<0.01	<0.01	0.14
					21	0.008	<0.005	<0.013	<0.01	<0.01	<0.01	0.04
						0.011	0.107	0.118	<0.01	<0.01	<0.01	0.15
					27	0.007	0.073	0.081	<0.01	<0.01	<0.01	0.11
						0.011	0.082	0.093	<0.01	<0.01	<0.01	0.12
Jerome, WI; 2005 (RCN R05096)	11	Beta 8422	Root	0.20	14	0.018	<0.005	<0.023	<0.01	<0.01	<0.01	0.05
						0.015	<0.005	<0.020	<0.01	<0.01	<0.01	0.05
			Tops	0.20	14	0.783	0.116	0.899	<0.01	<0.01	<0.01	0.93
						0.868	0.164	1.032	0.01	0.01	<0.01	1.07
Treatment 3												
Wabasha, MN; 2005 (RCN R05085)	5	VDH 66556 8232 Medium	Root	0.30	14	0.007	<0.005	<0.012	<0.01	<0.01	<0.01	0.04
						0.012	<0.005	<0.017	<0.01	<0.01	<0.01	0.05
			Tops	0.30	14	1.662	0.342	2.005	<0.01	0.01	<0.01	2.04
						2.067	0.426	2.493	<0.01	0.02	<0.01	2.53
Wabasha, MN; 2005 (RCN R05086)	5	VDH 66556 8232 Medium	Root	0.30	14	0.011	<0.005	<0.016	<0.01	<0.01	<0.01	0.05
						0.008	<0.005	<0.013	<0.01	<0.01	<0.01	0.04
			Tops	0.30	14	0.811	0.131	0.942	<0.01	<0.01	<0.01	0.97
						0.931	0.148	1.079	<0.01	<0.01	<0.01	1.11

TABLE C.3. Residue Data from Sugar Beet Field Trials with Metconazole.

Trial ID (County, State; Year)	Zone	Variety	Matrix	Total Rate (lb ai/A)	PHI (days)	Metconazole Residues (ppm parent equivalents)						
						Metconazole			Metabolites			Total [1]
						cis	*trans*	Total	M11	M21	M30	
Pepin, WI; 2005 (RCN R05087)	5	VDH665 56 8232 Medium	Root	0.30	1	<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04
					7	<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04
					14	<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04
					21	<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04
					28	<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04
			Tops	0.30	1	2.892	0.516	3.408	<0.01	0.01	<0.01	3.44
						2.450	0.467	2.917	<0.01	0.01	<0.01	2.95
					7	2.346	0.413	2.759	<0.01	0.01	<0.01	2.79
						2.788	0.485	3.273	<0.01	0.02	<0.01	3.31
					14	1.593	0.215	1.808	<0.01	0.02	<0.01	1.84
						1.792	0.324	2.116	<0.01	0.02	<0.01	2.15
					21	1.463	0.188	1.650	<0.01	0.01	<0.01	1.68
						1.263	0.152	1.415	<0.01	0.01	<0.01	1.45
					28	0.716	0.105	0.821	<0.01	<0.01	<0.01	0.85
						1.160	0.154	1.313	<0.01	<0.01	<0.01	1.32
Dane; WI; 2005 (RCN R05088)	5	Vander-have VDH 66556	Root	0.30	13	0.026	0.005	0.031	<0.01	<0.01	<0.01	0.06
						0.024	0.006	0.029	<0.01	<0.01	<0.01	0.06
			Tops	0.30	13	0.030	0.005	0.035	<0.01	0.01	<0.01	0.07
						0.026	0.203	0.229	<0.01	0.01	<0.01	0.26
Dane, WI; 2005 (RCN R05089)	5	Vander-have VDH 66556	Root	0.29	14	0.067	0.015	0.082	<0.01	<0.01	<0.01	0.11
						0.070	0.015	0.085	<0.01	<0.01	<0.01	0.11
			Tops	0.29	14	0.050	0.010	0.060	<0.01	0.01	<0.01	0.09
						0.060	0.011	0.071	<0.01	0.02	<0.01	0.11
Stutsman, ND; 2005 (RCN R05090)	7	Vander-have 66453	Root	0.31	14	0.012	<0.005	0.017	<0.01	<0.01	<0.01	0.05
						0.016	<0.005	0.021	<0.01	<0.01	<0.01	0.05
			Tops	0.31	14	0.057	0.011	0.068	0.02	0.02	<0.01	0.11
						0.024	0.194	0.218	<0.01	<0.01	<0.01	0.25
Hockley, TX; 2005 (RCN R05091)	8	Eagle R	Root	0.30	14	0.009	<0.005	<0.014	<0.01	<0.01	<0.01	0.04
						0.005	0.007	0.013	<0.01	<0.01	<0.01	0.04
			Tops	0.30	14	0.019	0.144	0.162	0.02	0.02	<0.01	0.20
						0.018	0.151	0.170	0.02	0.01	<0.01	0.21
Fremont, MT; 2005 (RCN R05092)	9	Treasure	Root	0.30	14	0.018	0.005	0.024	<0.01	<0.01	<0.01	0.05
						0.035	0.007	0.043	<0.01	<0.01	<0.01	0.07
			Tops	0.30	14	0.043	0.008	0.052	<0.01	0.02	<0.01	0.09
						0.042	0.008	0.050	<0.01	0.02	<0.01	0.09

TABLE C.3. Residue Data from Sugar Beet Field Trials with Metconazole.

Trial ID (County, State; Year)	Zone	Variety	Matrix	Total Rate (lb ai/A)	PHI (days)	Metconazole Residues (ppm parent equivalents)						
						Metconazole			Metabolites			Total [1]
						cis	*trans*	Total	M11	M21	M30	
Stanislaus, CA; 2005 (RCN R05093)	10	Unknown	Root	0.30	14	0.006	0.008	0.013	<0.01	<0.01	<0.01	0.04
						<0.005	0.007	<0.012	<0.01	<0.01	<0.01	0.04
			Tops	0.30	14	0.019	0.164	0.183	0.03	0.02	<0.01	0.24
						0.021	0.171	0.193	0.02	0.02	<0.01	0.24
Stanislaus, CA; 2005 (RCN R05094)	10	Unknown	Root	0.30	14	0.010	0.016	0.025	<0.01	<0.01	<0.01	0.06
						0.015	<0.005	<0.020	<0.01	<0.01	<0.01	0.05
			Tops	0.30	14	0.985	0.145	1.130	0.03	0.02	<0.01	1.20
						0.956	0.142	1.099	0.02	0.02	<0.01	1.15
Payette, ID; 2005 (RCN R05095)	11	HM WS91	Root	0.29	1	0.011	<0.005	<0.016	<0.01	<0.01	<0.01	0.05
						0.006	<0.005	<0.011	<0.01	<0.01	<0.01	0.04
					7	0.023	<0.005	<0.028	<0.01	<0.01	<0.01	0.06
						0.017	<0.005	<0.022	<0.01	<0.01	<0.01	0.05
					15	0.015	<0.005	<0.020	<0.01	<0.01	<0.01	0.05
						0.023	<0.005	<0.028	<0.01	<0.01	<0.01	0.06
					21	0.013	<0.005	<0.018	<0.01	<0.01	<0.01	0.05
						0.009	<0.005	<0.014	<0.01	<0.01	<0.01	0.04
					27	0.009	<0.005	<0.014	<0.01	<0.01	<0.01	0.04
						0.008	<0.005	<0.013	<0.01	<0.01	<0.01	0.04
			Tops	0.29	1	0.035	0.006	0.041	<0.01	<0.01	<0.01	0.07
						0.034	0.006	0.041	<0.01	<0.01	<0.01	0.07
					7	0.026	<0.005	<0.031	<0.01	0.01	<0.01	0.06
						0.029	0.201	0.230	<0.01	<0.01	<0.01	0.26
					15	0.014	0.135	0.149	<0.01	<0.01	<0.01	0.18
						0.017	0.137	0.154	<0.01	<0.01	<0.01	0.18
					21	0.017	0.132	0.149	<0.01	<0.01	<0.01	0.18
						0.020	0.174	0.194	<0.01	0.01	<0.01	0.23
					27	0.016	0.130	0.146	<0.01	0.01	<0.01	0.18
						0.013	0.098	0.111	<0.01	<0.01	<0.01	0.14
Jerome, WI; 2005 (RCN R05096)	11	Beta 8422	Root	0.30	14	0.032	0.007	0.039	<0.01	<0.01	<0.01	0.07
						0.034	0.007	0.041	<0.01	<0.01	<0.01	0.07
			Tops	0.30	14	1.812	0.262	2.074	0.02	0.02	<0.01	2.12
						1.471	0.218	1.689	0.01	0.02	<0.01	1.73

[1] Total = total residues; sum of *cis*- and *trans*-metconazole, M11, M21, and M30; values presented as calculated and reported by the petitioner.

TABLE C.4. Summary of Residue Data from Sugar Beet Field Trials with Metconazole.

Commodity	Total Applic. Rate (lb ai/A)	Analyte	Residue Levels[1] (ppm)						
			n	Min.	Max.	HAFT[2]	Median (STMdR)	Mean (STMR)	Std. Dev.
Treatment 02 - Two foliar applications at 0.20 lb ai/A; PHI = 13-15 days									
Sugar beet root	0.20	*cis*-Metconazole	24	<0.005	0.039	0.036	0.010	0.013	0.010
		trans-Metconazole	24	<0.005	0.021	0.012	0.005	0.007	0.004
		Metconazole	**24**	**<0.010**	**0.048**	**0.044**	**0.017**	**0.020**	**0.011**
		M11	24	<0.010	<0.010	<0.010	0.010	0.010	--
		M21	24	<0.010	<0.010	<0.010	0.010	0.010	--
		M30	24	<0.010	<0.010	<0.010	0.010	0.010	--
		Total Residues	24	<0.040	0.080	0.075	0.050	0.049	0.011
Sugar beet tops	0.20	*cis*-Metconazole	24	0.010	1.077	1.037	0.033	0.358	0.429
		trans-Metconazole	24	0.006	0.178	0.173	0.114	0.108	0.049
		Metconazole	**24**	**0.037**	**1.256**	**1.210**	**0.152**	**0.466**	**0.457**
		M11	24	<0.010	0.020	<0.010	0.010	0.010	--
		M21	24	<0.010	0.020	<0.010	0.010	0.010	--
		M30	24	<0.010	<0.010	<0.010	0.010	0.010	--
		Total Residues	24	0.070	1.290	1.240	0.180	0.4990	0.456
Treatment 03 – Two foliar applications at 0.30 lb ai/A; PHI = 13-15 days									
Sugar beet root	0.30	*cis*-Metconazole	24	<0.005	0.070	0.069	0.014	0.020	0.018
		trans-Metconazole	24	<0.005	0.016	0.015	0.005	0.007	0.003
		Metconazole	**24**	**<0.010**	**0.085**	**0.084**	**0.020**	**0.026**	**0.020**
		M11	24	<0.010	<0.010	<0.010	0.010	0.010	--
		M21	24	<0.010	<0.010	<0.010	0.010	0.010	--
		M30	24	<0.010	<0.010	<0.010	0.010	0.010	--
		Total Residues	24	<0.040	0.110	0.110	0.050	0.056	0.020
Sugar beet tops	0.30	*cis*-Metconazole	24	0.014	2.067	1.865	0.054	0.605	0.748
		trans-Metconazole	24	0.005	0.426	0.384	0.147	0.154	0.112
		Metconazole	**24**	**0.035**	**2.493**	**2.249**	**0.206**	**0.760**	**0.837**
		M11	24	<0.010	0.030	0.025	0.010	0.014	0.007
		M21	24	<0.010	0.020	0.020	0.020	0.016	0.005
		M30	24	<0.010	<0.010	<0.010	0.010	0.010	--
		Total Residues	24	0.070	2.530	2.285	0.245	0.798	0.838

[1] For calculation of median, mean, and standard deviation, the LOQ was used for any results reported as <LOQ in Table C.3.
[2] HAFT = Highest Average Field Trial.

D. CONCLUSION

The submitted field trial data are adequate and reflect the use of two broadcast foliar applications of a 0.75 lb ai/gal SC/L formulation of metconazole at a total rate of 0.20 lb ai/A (Treatment 2) or 0.29-0.31 lb ai/A (Treatment 3), with a 13- to 15-day retreatment interval. An acceptable method was used for quantitation of residues of *cis*- and *trans*-metconazole, M11, M21, and M30, and 1,2,4-T, TA, and TAA in/on sugar beet samples. The study is supported by adequate storage stability data.

E. REFERENCES

DP#:	324541
Subject:	Metconazole. Request for a Tolerance on Imported Bananas. Summary of Analytical Chemistry and Residue Data. Petition Number 9E05052.
From:	N. Dodd
To:	M. Waller
Date:	12/14/05
MRIDs:	44721506, 44721507, 44721508, 44721509, 44721510, and 44721511

F. DOCUMENT TRACKING

RDI: N. Dodd (2/20/08)
Petition Numbers: 6F7094 and 6F7095
DP#s: 348168 and 348206
PC Code: 125619

Template Version June 2005

Primary Evaluator	This DER was originally prepared under contract by Dynamac Corporation.
Approved by	Nancy Dodd, Chemist Nancy Dodd Date: 2/20/08 Registration Action Branch 3 Health Effects Division (7509P)

This DER was originally prepared under contract by Dynamac Corporation (2275 Research Boulevard, Suite 300; Rockville, MD 20850; submitted 09/17/2007). The DER has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

46902231 White, M.; Saha, M. (2006) The Magnitude of Residues of Metconazole (BAS 555 F) and its Metabolites in Wheat Processing Commodities: Final Report. Project Number: 137723, 2006/7007147. Unpublished study prepared by BASF Agro Research, Agresources, Inc. and Alvey Lab & Agr Research Services. 236 p.

EXECUTIVE SUMMARY:

BASF Corporation has submitted a processing study with wheat. In four trials conducted in IL, ND, NE, and WI, a 0.75 lb ai/gal soluble concentrate/liquid (SC/L) formulation of metconazole was applied as two broadcast foliar sprays to wheat at 0.50-0.51 lb ai/A, with a 6- to 7-day retreatment interval, for a total rate of 1.00-1.01 lb ai/A. Applications were made in 15-20 gal/A spray volumes with a nonionic surfactant added as an adjuvant to the spray mixture. Wheat grain samples were harvested 20-22 days after the last application of metconazole, and processed into aspirated grain fractions (AGF; one site), flour, bran, middlings, shorts, and germ using simulated commercial processing procedures. In addition, cleaned grain, husk, coarse bran, low grade meal, flour type 550, whole meal flour, and whole meal bread samples were collected for analysis.

Samples were analyzed for residues of *cis*- and *trans*-metconazole, metabolites M11, M21, and M30, and the triazole metabolites 1,2,4-triazole (1,2,4-T), triazolylalanine (TA), and triazolylacetic acid (TAA) using an LC/MS/MS method (BASF Method D0508). Residues of metabolites M11, M21, and M30 were converted to parent equivalents using molecular weight conversion factors of 0.95 for M11 and M21 and 0.96 for M30. The validated limits of quantitation (LOQs) were 0.01 ppm for the parent metconazole (sum of *cis* and *trans* isomers at 0.005 ppm each), M11, M21, and M30 in/on wheat samples. The validated LOQ was 0.05 ppm for 1,2,4-T, TA, and TAA. The method was adequate for data collection based on acceptable concurrent method recoveries.

Samples were stored frozen (<-10 °C) prior to extraction for 271-328 days (8.9-10.8 months) for wheat grain, and for 22-23 days for flour and 43-71 days for bran, middlings, shorts, and germ;

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samples were analyzed within 0-6 days of extraction. Adequate storage stability data are available to support the storage conditions and durations of wheat grain samples analyzed for *cis*- and *trans*-metconazole and, by translation of available data for wheat grain, to support the storage conditions and durations of processed commodities.

Residues of *cis*-and *trans*-metconazole in/on wheat grain were 0.191-0.348 and 0.047-0.061 ppm, respectively, for total metconazole residues (sum of *cis* and *trans* isomers) of 0.238-0.409 ppm. Following processing, respective residues of *cis*-metconazole, *trans*-metconazole, and total metconazole were 0.046-0.069, 0.010-0.017, and <0.056-0.086 ppm in flour; 0.427-0.730, 0.081-0.137, and 0.508-0.867 ppm in bran; 0.275-1.038, 0.047-0.181, and 0.322-1.219 ppm in middlings; 0.475-0.890, 0.046-0.087, and 0.529-0.977 ppm in shorts; and 0.212-0.318, 0.050-0.074, and 0.262-0.392 ppm in germ. Respective residues of M11, M21, and M30 were 0.04-0.10, 0.01, and 0.01-0.03 ppm in grain; <0.01-0.01, <0.01, and <0.01 ppm in flour; 0.11-0.23, 0.03, and 0.03-0.08 ppm in bran; 0.03-0.15, 0.01-0.04, and <0.01-0.02 ppm in middlings; 0.06-0.12, 0.01-0.02, and 0.01-0.04 ppm in shorts; and 0.03-0.10, <0.01-0.02, and <0.01-0.03 ppm in germ.

The processing data indicate that residues of total metconazole may concentrate in bran, middlings, and shorts, with average processing factors of 1.9x, 2.0x, and 2.1x, respectively. Residues of total metconazole do not concentrate in flour or germ (average processing factors of 0.2x and 1.0x, respectively). Based on average processing factors for the remaining processed commodities, total metconazole residues do not concentrate in cleaned grain, low grade meal, flour type 550, whole meal flour, or whole meal bread (processing factors 0.3-1x), but may concentrate in AGF (one sample, 64.3x), husk (121.4x), and coarse bran (1.9x).

The calculated processing factors for wheat bran, flour, and shorts do not exceed the maximum theoretical concentration factor of 8x for wheat (OPPTS 860.1520, Table 1).

Residues of 1,2,4-T were <0.05 ppm in/on all samples of wheat RAC and processed commodities. Residues of TA were 0.08-0.31, <0.05-0.13, 0.15-0.58, <0.05-0.18, 0.11-0.27, and 0.20-0.45 ppm in samples of wheat grain, flour, bran, middlings, shorts, and germ, respectively. Residues of TAA were 0.05-0.10, <0.05-0.09, <0.05-0.12, <0.05-0.09, <0.05-0.10, and 0.06-0.10 ppm in/on samples of wheat grain, flour, bran, middlings, shorts, and germ, respectively.

The processing data indicate that residues of TA may concentrate in bran, shorts, and germ, with average processing factors of 2.4x, 1.2x, and 2.5x, respectively. Residues of TA do not concentrate in flour or middlings (with average processing factors of 0.5x and 0.7x, respectively). Residues of TAA may concentrate in bran and germ, with average processing factors of 1.2x, and 1.1x, respectively; residues do not concentrate in flour, middlings, and shorts (with average processing factors of 0.9x, 0.9x, and 1.0x, respectively).

HED notes that processing factors were also calculated by the petitioner using total residues of *cis*- and *trans*-metconazole, M11, M21, and M30. When processing factors were calculated using these values, average processing factors of 0.2x, 2.0x, 1.7x, 1.8x, and 0.9x were obtained

for flour, bran, middlings, shorts, and germ, respectively. A data table reflecting calculation of processing factors according to this procedure is attached as an appendix to this DER.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the processed commodity residue data are classified as scientifically acceptable.

The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP#s 348168 and 348206.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported.

A. BACKGROUND INFORMATION

Metconazole [5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol] is a broad-spectrum triazole Group 3 fungicide (sterol biosynthesis inhibitors). There are currently no registered uses of metconazole in the U.S.; however, a tolerance has been established for banana, and a Section 18 emergency exemption and supporting time-limited tolerances have been granted for use on soybean. BASF Corporation has applied for registration of metconazole in the U.S. for use on barley, oats, rye, soybeans, sugar beets, triticale, and wheat.

The chemical structure and nomenclature of metconazole, and the physicochemical properties of the technical grade of metconazole are presented in Tables A.1 and A.2.

TABLE A.1. Metconazole Nomenclature.

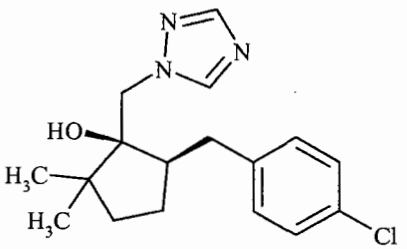
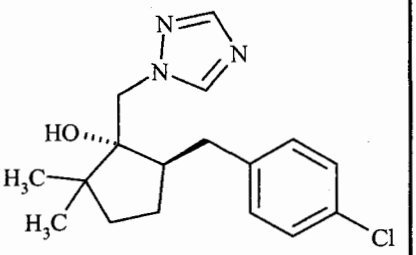
Chemical structure	 *cis*-isomer	 *trans*-isomer
Common name	Metconazole	
Company experimental name	KNF-S-474m (Kureha); BAS 555 F (BASF); V-10116 (Valent)	
IUPAC name	(1RS,5RS:1RS,5SR)-5-(4-chlorobenzyl)-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	
CAS name	5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	

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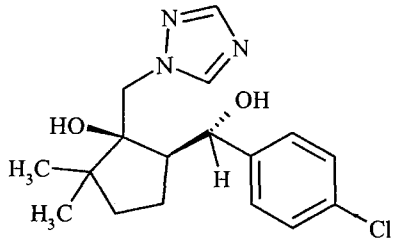
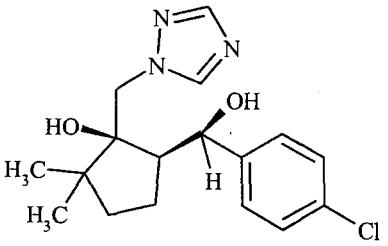
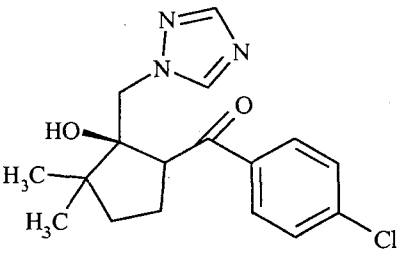
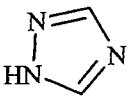
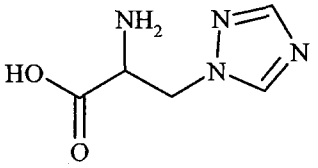
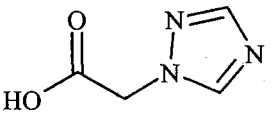
TABLE A.1. Metconazole Nomenclature.		
CAS registry number	125116-23-6 (cis- and *trans*-isomers) 115850-27-6 (*cis*-isomer) 115850-28-7 (*trans*-isomer)	
End-use products (EP)	50% WDG (Metconazole 50 WDG Fungicide, EPA File Symbol 59639-RUT) 0.75 lb/gal SC/L (Caramba™ Fungicide, EPA File Symbol No. 7969-EUA) 0.67 lb/gal SC/L formulation (BAS 556 01F Fungicide, EPA File Symbol No. 7969-EUT; also contains the active ingredient pyraclostrobin at 0.83 lb/gal)	
 Metconazole metabolite M11	 Metconazole metabolite M21	 Metconazole metabolite M30
 Triazole metabolite 1,2,4-triazole (1,2,4-T)	 Triazole metabolite trizolylalanine (TA)	 Triazole metabolite triazolylacetic acid (TAA)

Table A.2. Physicochemical Properties of Metconazole					
Parameter	Value				References* (MRID)
Melting point/range	100.0-108.4°C (using Electrothermal Digital Melting Point Apparatus) (AC900,768 technical grade)				44721505
pH	5.81 at 25°C (1% aqueous suspension)				46808402
Relative density (20°C)	1.14 (relative density to water at 4°C, using capillary-stoppered, density-specific gravity bottle) (Lot No. AC 8879-140B)				44721505
Water solubility (20°C)	Using shake-flask method: 18.7 ± 1.0 mg/L (*cis*-isomer, WL148271, KNF-S-474m) 13.6 ± 1.7 mg/L (*trans*-isomer, WL148271, KNF-S-474m)				44721505
Solvent solubility (g/L) at 20°C	Solvent	Metconazole	*cis*	*trans*	44721505
	acetone	363	251	117	
	methanol	403	294	117	
	dichloromethane	481	343	141	
	ethyl acetate	260	173	90.0	
	propanol	132	86.6	46.7	
	toluene	103	66.2	38.0	
	Hexane	1.40	0.929	0.483	

Table A.2. Physicochemical Properties of Metconazole

Parameter	Value				References* (MRID)
Vapor pressure (20°C)	Using gas-saturation method: $< 1.23x10^{-5}$ Pa or 9.23×10^{-8} mm Hg (metconazole) $< 1.04x10^{-5}$ Pa or 7.80×10^{-8} mm Hg (*cis*-isomer) $< 1.96x10^{-6}$ Pa or 1.47×10^{-8} mm Hg (*trans*-isomer)				44721505
Dissociation constant (pK_a)	11.38±0.03 and 1.06±0.03 (in water at 29.1°C using spectrophotometric method; Lot No. AC 8879-140B)				44721505
Octanol/water partition coefficient, Log(K_{OW})	At 20 °C (using flask shaking method): K_{ow} (log K_{ow}) = 7090±989 (3.85) (Lot No. AC 8879-140B) (TGAI) K_{ow} (log K_{ow}) = 7150±803 (3.85) (*cis*-isomer, CL 354,801) K_{ow} (log K_{ow}) = 6800±1700 (3.8) (*trans*-isomer, CL 354,802)				44721505
UV/visible absorption spectrum	pH	λ	A	log ε	46808403
	cis-isomer				
	2.0	221.4	0.828	4.03	
	6.8		0.8452	4.04	
	7.0		0.9126	4.08	
	10.3		0.7226	3.98	
	trans-isomer				
	2.0	221.4	0.9053	4.07	
	7.0		0.9547	4.10	
	10.1		0.9893	4.11	

* Product Chemistry Reviews: DP #256877, Shyam Mathur, Ph.D., 9/12/2000 and DP #329168, Shyam Mathur, Ph.D., 7/13/07.

B. EXPERIMENTAL DESIGN

B.1. Application and Crop Information

BASF Corporation has submitted a processing study with wheat. In four trials conducted in IL, ND, NE, and WI, a 0.75 lb ai/gal soluble concentrate/liquid (SC/L) formulation of metconazole was applied as two broadcast foliar sprays to wheat at 0.50-0.51 lb ai/A, with a 6- to 7-day retreatment interval, for a total rate of 1.00-1.01 lb ai/A. Applications were made in spray volumes of 15-20 gal/A with a nonionic surfactant added as an adjuvant to the spray mixture. Wheat grain samples were harvested 20-22 days after the last application of metconazole.

TABLE B.1.1. Study Use Pattern.

Location (County, State; Year) Trial ID	EP[1]	Application					Tank Mix/ Adjuvants[4]
		Method; Timing	Volume[2]	Rate (lb ai/A)	RTI[3] (days)	Total Rate (lb ai/A)	
Pepin, WI; 2005 (RCN R05184)	0.75 lb/gal SC/L	1. Broadcast foliar; late milk	15.04	0.5006	7	1.00	Induce (NIS)
		2. Broadcast foliar; early dough	15.10	0.4974			
Clinton, IL; 2004; (RCN R05185)	0.75 lb/gal SC/L	1. Broadcast foliar; medium milk	16.87	0.5103	7	1.01	Preference (NIS)
		2. Broadcast foliar; soft dough	17.54	0.4983			
Cass, ND; 2005; (RCN R05186)	0.75 lb/gal SC/L	1. Broadcast foliar; early milk	15.91	0.5031	6	1.01	Activator 90 (NIS)
		2. Broadcast foliar; late milk	15.58	0.5098			
York, NE; 2004; (RCN R05187)	0.75 lb/gal SC/L	1. Broadcast foliar; medium milk	19.85	0.4973	7	1.00	Activate Plus (NIS)
		2. Broadcast foliar; early dough	19.91	0.4991			

[1] EP = End-use Product
[2] Gallons per acre
[3] RTI = Retreatment Interval
[4] NIS = Non ionic surfactant

B.2. Sample Handling and Processing Procedures

Bulk samples of wheat grain (> 250 lb) were harvested from each site, and one control bulk grain sample (> 250 lb) was harvested from two sites. Samples were promptly frozen at the field facilities on the day of harvest and were shipped 6-10 days later by ACDS freezer truck to the processing facility, GLP Technologies (Navasota, TX), where they were stored frozen (≤-12 °C) prior to processing. Samples were processed, within 201-302 days of wheat grain harvest, into AGF (one site), flour, bran, middlings, shorts, and germ using simulated commercial processing procedures. In addition, cleaned grain, husk, coarse bran, low grade meal, flour type 550, whole meal flour, and whole meal bread samples were collected for analysis. A flowchart of the processing procedures is presented in Figure B.2.1 (which was copied without alteration from MRID 46902231).

Wheat grain and processed samples were shipped, within 3 days of completion of processing, overnight on dry ice to the analytical laboratory, BASF Agro Research (Research Triangle Park, NC), where samples were stored frozen (≤-10 °C) until analysis. At BASF, the wheat RAC and processed commodity samples were homogenized, if needed, in the presence of dry ice prior to analysis.

FIGURE B.2.1. Processing Flowchart for Wheat.

MATERIAL BALANCE for GENERATION, CLASSIFICATION, AND ASH CONTENT
DETERMINATION OF ASPIRATED GRAIN FRACTIONS

Sample # 5 (Trt. 2, Treated) Code # R051840002

COMMODITY 430.1 lbs.

Drying n/a lbs. (after drying)

430.1 lbs. used for generation

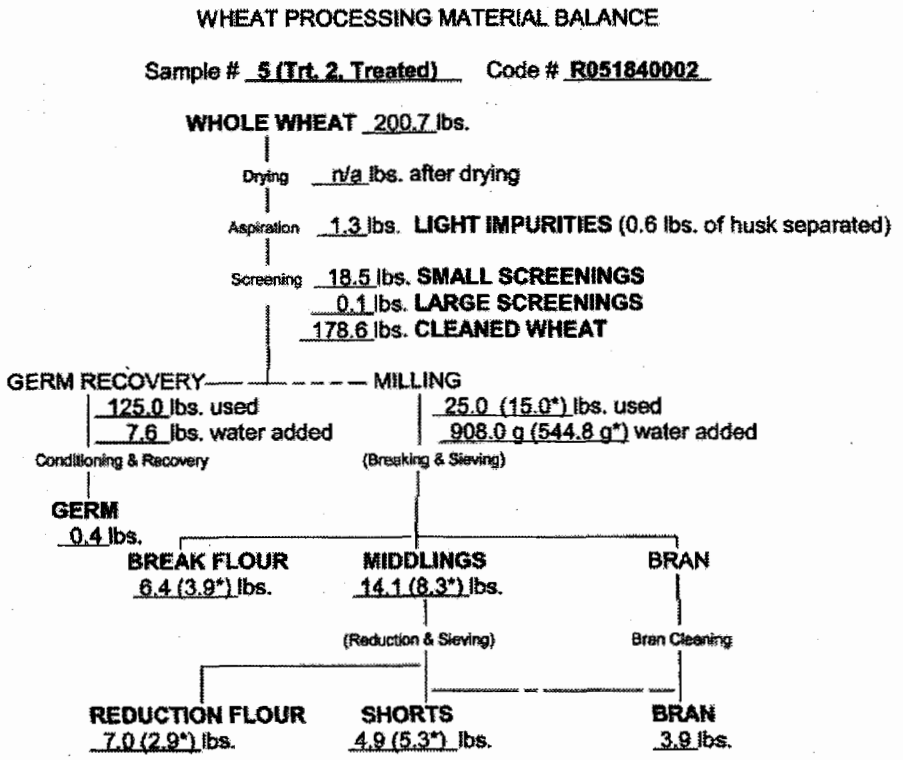
Aspiration 0.2 lbs.

Classification

- ASPIRATED GRAIN FRACTION > 2360 micron 28.8 g
- ASPIRATED GRAIN FRACTION > 2000 micron 9.4 g (Grain Dust)
- ASPIRATED GRAIN FRACTION > 1180 micron 4.0 g (Grain Dust)
- ASPIRATED GRAIN FRACTION > 850 micron 2.5 g (Grain Dust)
- ASPIRATED GRAIN FRACTION > 425 micron 7.8 g (Grain Dust)
- ASPIRATED GRAIN FRACTION < 425 micron 53.6 g (Grain Dust)

ASH CONTENT: 9.9 %

Figure 1. Processing Flowchart for Wheat (continued)



* Represents additional milling.

Note: Break and reduction flour from additional milling were combined and collected as the protocol requested "Straight Flour". Shorts from additional milling was collected and labeled "Low Grade Meal". After determining ash content of "Straight Flour" and "Low Grade Meal", the two were mixed in proportion to make the protocol requested "550 Flour".

6.0 lbs. of cleaned wheat was ground into 6.0 lbs. of Whole Meal Flour. After sampling the flour, 525.0 grams was used to produce 841.1 gram loaf of Whole Meal Bread.

B.3. Analytical Methodology

Wheat grain and processed commodities were analyzed for residues of metconazole, metabolites M11, M21, and M30, and the triazole metabolites 1,2,4-T, TA, and TAA using an LC/MS/MS method (BASF Method D0508). A brief description of the method was included in the MRID.

Briefly, residues of metconazole, M11, M21, and M30 were extracted with acetonitrile (ACN):water (70:30, v:v). The extracts were diluted with methanol:water (80:20, v:v), filtered, and reserved for LC/MS/MS analysis. For determination of residues of 1,2,4-T, TA, and TAA, a separate aliquot of the initial extract was evaporated to dryness, redissolved in 0.1% formic acid in water, filtered, and reserved for LC/MS/MS analysis. Residues of metabolites M11, M21, and M30 were converted to parent equivalents using molecular weight conversion factors of 0.95 for M11 and M21 and 0.96 for M30.

The validated LOQ was 0.01 ppm for the parent metconazole (sum of *cis* and *trans* isomers at 0.005 ppm each) and the metabolites M11, M21, and M30 in/on wheat samples. The validated LOQ was 0.05 ppm for 1,2,4-T, TA, and TAA. The reported limit of detection was 20% LOQ.

The method was validated concurrently with sample analysis using samples of untreated wheat grain and processed commodities fortified at 0.005 and 0.5 ppm with *cis*- and *trans*-metconazole; at 0.01 and 1.00 ppm with M11, M21, and M30; and at 0.05 and 5.00 ppm with 1,2,4-T, TA, and TAA.

C. RESULTS AND DISCUSSION

The storage conditions and durations for samples from the wheat processing study are presented in Table C.2. Samples were stored frozen (<-10 °C) prior to extraction for 271-328 days (8.9-10.8 months) for wheat grain, and for 22-23 days for flour and 43-71 days for bran, middlings, shorts, and germ; samples were analyzed within 0-6 days of extraction. Storage stability data are available indicating that: (1) residues of *cis*- and *trans*-metconazole are relatively stable under frozen storage conditions in wheat grain for up to 12 months (refer to 46902218.der.doc); (2) residues of M11, M21, and M30 are relatively stable in/on wheat grain for up to 6 months (refer to 4690223.der.doc); (3) residues of 1,2,4-T, TA, and TAA are stable/relatively stable in/on wheat grain for up to 6 months (refer to 46902223.der.doc); and (4) residues of TA are stable in/on wheat grain for up to 12 months (refer to 46902221.der.doc). In consideration of the nature of the processing procedures for wheat commodities (i.e., fractions are not heated or chemically treated during processing and are generally physically similar to whole grain), HED believes that the available data for wheat grain may be translated to the processed wheat commodities for purposes of this study. Adequate storage stability data for *cis*- and *trans*-metconazole are available.

Concurrent method recovery data are presented in Table C.1. Samples were analyzed for residues of metconazole, M11, M21, M30, 1,2,4-T, TA, and TAA using LC/MS/MS Method D0508. Residues of metabolites M11, M21, and M30 were converted to parent equivalents using molecular weight conversion factors of 0.95 for M11 and M21 and 0.96 for M30. The method was adequate for data collection based on acceptable concurrent method recovery data. Concurrent method recoveries were generally within the acceptable range of 70-120% for wheat RAC and processed commodities fortified at 0.005 and 0.5 ppm with *cis*- and *trans*-metconazole; at 0.01 and 1.00 ppm with M11, M21, and M30; and at 0.05 and 5.00 ppm with 1,2,4-T, TA, and TAA. Low recoveries (62-66%) were obtained for 1,2,4-T in grain (at 0.05 ppm) and for TA and TAA in flour (both at 0.05 ppm). Apparent residues of *cis*- and *trans*-metconazole, the metabolites M11, M21, and M30, and the triazole metabolites (1,2,4-T, TA, and TAA) were each below the respective LOQs in/on two samples each of untreated wheat grain, flour, bran, middlings, shorts, and germ.

Residue data from the wheat processing study are presented in Tables C.3.1 (metconazole) and C.3.2 (triazole metabolites); HED notes that results for the metabolites M11, M21, and M30 were not included in Table C.3.1 because these metabolites were not included in calculation of processing factors. Residues of *cis*-and *trans*-metconazole in/on wheat grain were 0.191-0.348

and 0.047-0.061 ppm, respectively; for total metconazole residues (sum of *cis* and *trans* isomers) of 0.238-0.409 ppm. Following processing, respective residues of *cis*-metconazole, *trans*-metconazole, and total metconazole were: 0.046-0.069, 0.010-0.017, and <0.056-0.086 ppm in flour; 0.427-0.730, 0.081-0.137, and 0.508-0.867 ppm in bran; 0.275-1.038, 0.047-0.181, and 0.322-1.219 ppm in middlings; 0.475-0.890, 0.046-0.087, and 0.529-0.977 ppm in shorts; and 0.212-0.318, 0.050-0.074, and 0.262-0.392 ppm in germ. Respective residues of M11, M21, and M30 were: 0.04-0.10, 0.01, and 0.01-0.03 ppm in grain; <0.01-0.01, <0.01, and <0.01 ppm in flour; 0.11-0.23, 0.03, and 0.03-0.08 ppm in bran; 0.03-0.15, 0.01-0.04, and <0.01-0.02 ppm in middlings; 0.06-0.12, 0.01-0.02, and 0.01-0.04 ppm in shorts; and 0.03-0.10, <0.01-0.02, and <0.01-0.03 ppm in germ.

The processing data indicate that residues of total metconazole may concentrate in bran, middlings, and shorts, with average processing factors of 1.9x, 2.0x, and 2.1x, respectively. Residues of total metconazole do not concentrate in flour or germ (average processing factors of 0.2x and 1.0x, respectively). Based on average processing factors for the remaining processed commodities, total metconazole residues do not concentrate in cleaned grain, low grade meal, flour type 550, whole meal flour, or whole meal bread (processing factors of 0.3-1x), but may concentrate in AGF (one sample, 64.3x), husk (121.4x), and coarse bran (1.9x).

Residues of 1,2,4-T were <0.05 ppm in/on all samples of wheat RAC and processed commodities. Residues of TA were 0.08-0.31, <0.05-0.13, 0.15-0.58, <0.05-0.18, 0.11-0.27, and 0.20-0.45 ppm in samples of wheat grain, flour, bran, middlings, shorts, and germ, respectively. Residues of TAA were 0.05-0.10, <0.05-0.09, <0.05-0.12, <0.05-0.09, <0.05-0.10, and 0.06-0.10 ppm in/on samples of wheat grain, flour, bran, middlings, shorts, and germ, respectively.

The processing data indicate that residues of TA may concentrate in bran, shorts, and germ, with average processing factors of 2.4x, 1.2x, and 2.5x, respectively. Residues of TA do not concentrate in flour or middlings (average processing factors of 0.5x and 0.7x, respectively). Residues of TAA may concentrate in bran and germ, with average processing factors of 1.2x, and 1.1x, respectively; residues do not concentrate in flour, middlings, and shorts (average processing factors of 0.9x, 0.9x, and 1.0x, respectively).

HED notes that processing factors were also calculated by the petitioner using total residues of *cis*- and *trans*-metconazole, M11, M21, M30. When processing factors were calculated using these values, average processing factors of 0.2x, 2.0x, 1.7x, 1.8x, and 0.9x were obtained for flour, bran, middlings, shorts, and germ, respectively. A data table reflecting calculation of processing factors according to this procedure is attached as an appendix to this DER.

TABLE C.1. Summary of Concurrent Recoveries of Metconazole, M11, M21, M30, 1,2,4-T, TA, and TAA from Wheat Grain and Processed Commodities.

Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean (%)
Grain	*cis*-Metconazole	0.005	1	85	85
		0.500	1	94	94
	trans-Metconazole	0.005	1	83	83

TABLE C.1. Summary of Concurrent Recoveries of Metconazole, M11, M21, M30, 1,2,4-T, TA, and TAA from Wheat Grain and Processed Commodities.

Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean (%)
		0.500	1	105	105
	M11	0.010	1	112	112
		1.000	1	103	103
	M21	0.010	1	97	97
		1.000	1	113	113
	M30	0.010	1	102	102
		1.000	1	115	115
	1,2,4-T	0.050	1	65	65
		5.000	1	73	73
	TA	0.050	1	75	75
		5.000	1	72	72
	TAA	0.050	1	87	87
		5.000	1	85	85
Husk	*cis*-Metconazole	0.005	1	70	70
		0.500	1	92	92
	trans-Metconazole	0.005	1	100	100
		0.500	1	105	105
	M11	0.010	1	85	85
		1.000	1	104	104
	M21	0.010	1	95	95
		1.000	1	107	107
	M30	0.010	1	109	109
		1.000	1	103	103
	1,2,4-T	0.050	1	67	67
		5.000	1	102	102
	TA	0.050	1	86	86
		5.000	1	68	68
	TAA	0.050	1	102	102
		5.000	1	75	75
Coarse Bran	*cis*-Metconazole	0.005	1	81	81
		0.500	1	110	110
	trans-Metconazole	0.005	1	104	104
		0.500	1	112	112
	M11	0.010	1	95	95
		1.000	1	96	96
	M21	0.010	1	116	116
		1.000	1	106	106
	M30	0.010	1	99	99
		1.000	1	104	104
	1,2,4-T	0.050	1	89	89
		5.000	1	90	90
	TA	0.050	1	82	82

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TABLE C.1. Summary of Concurrent Recoveries of Metconazole, M11, M21, M30, 1,2,4-T, TA, and TAA from Wheat Grain and Processed Commodities.

Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean (%)
		5.000	1	81	81
	TAA	0.050	1	83	83
		5.000	1	88	88
Flour	*cis*-Metconazole	0.005	1	104	104
		0.500	1	116	116
	trans-Metconazole	0.005	1	80	80
		0.500	1	89	89
	M11	0.010	1	90	90
		1.000	1	97	97
	M21	0.010	1	89	89
		1.000	1	103	103
	M30	0.010	1	104	104
		1.000	1	115	115
	1,2,4-T	0.050	1	75	75
		5.000	1	92	92
	TA	0.050	1	66	66
		5.000	1	74	74
	TAA	0.050	1	62	62
		5.000	1	80	80
Middlings	*cis*-Metconazole	0.005	1	96	96
		0.500	1	105	105
	trans-Metconazole	0.005	1	86	86
		0.500	1	110	110
	M11	0.010	1	107	107
		1.000	1	116	116
	M21	0.010	1	100	100
		1.000	1	105	105
	M30	0.010	1	111	111
		1.000	1	113	113
	1,2,4-T	0.050	1	83	83
		5.000	1	76	76
	TA	0.050	1	75	75
		5.000	1	72	72
	TAA	0.050	1	78	78
		5.000	1	94	94
Shorts	*cis*-Metconazole	0.005	1	92	92
		0.500	1	95	95
	trans-Metconazole	0.005	1	92	92
		0.500	1	108	108
	M11	0.010	1	92	92
		1.000	1	111	111
	M21	0.010	1	101	101

TABLE C.1. Summary of Concurrent Recoveries of Metconazole, M11, M21, M30, 1,2,4-T, TA, and TAA from Wheat Grain and Processed Commodities.

Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean (%)
		1.000	1	116	116
	M30	0.010	1	109	109
		1.000	1	112	112
	1,2,4-T	0.050	1	98	98
		5.000	1	81	81
	TA	0.050	1	100	100
		5.000	1	77	77
	TAA	0.050	1	113	113
		5.000	1	95	95
Germ	*cis*-Metconazole	0.005	1	92	92
		0.500	1	109	109
	trans-Metconazole	0.005	1	95	95
		0.500	1	111	111
	M11	0.010	1	107	107
		1.000	1	114	114
	M21	0.010	1	88	88
		1.000	1	101	101
	M30	0.010	1	100	100
		1.000	1	112	112
	1,2,4-T	0.050	1	78	78
		5.000	1	78	78
	TA	0.050	1	79	79
		5.000	1	71	71
	TAA	0.050	1	108	108
		5.000	1	100	100
Low Grade Meal	*cis*-Metconazole	0.005	1	89	89
		0.500	1	103	103
	trans-Metconazole	0.005	1	79	79
		0.500	1	103	103
	M11	0.010	1	80	80
		1.000	1	96	96
	M21	0.010	1	76	76
		1.000	1	89	89
	M30	0.010	1	76	76
		1.000	1	91	91
	1,2,4-T	0.050	1	67	67
		5.000	1	107	107
	TA	0.050	1	78	78
		5.000	1	82	82
	TAA	0.050	1	80	80
		5.000	1	92	92
Whole Meal Flour	*cis*-Metconazole	0.005	1	89	89

TABLE C.1. Summary of Concurrent Recoveries of Metconazole, M11, M21, M30, 1,2,4-T, TA, and TAA from Wheat Grain and Processed Commodities.

Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean (%)
		0.500	1	91	91
	trans-Metconazole	0.005	1	103	103
		0.500	1	103	103
	M11	0.010	1	89	89
		1.000	1	102	102
	M21	0.010	1	106	106
		1.000	1	96	96
	M30	0.010	1	97	97
		1.000	1	108	108
	1,2,4-T	0.050	1	94	94
		5.000	1	90	90
	TA	0.050	1	73	73
		5.000	1	71	71
	TAA	0.050	1	72	72
		5.000	1	88	88
Bread	*cis*-Metconazole	0.005	1	117	117
		0.500	1	112	112
	trans-Metconazole	0.005	1	117	117
		0.500	1	108	108
	M11	0.010	1	98	98
		1.000	1	109	109
	M21	0.010	1	89	89
		1.000	1	118	118
	M30	0.010	1	106	106
		1.000	1	113	113
	1,2,4-T	0.050	1	67	67
		5.000	1	131	131
	TA	0.050	1	85	85
		5.000	1	130	130
	TAA	0.050	1	102	102
		5.000	1	121	121

TABLE C.2. Summary of Storage Conditions.

Matrix	Storage Temperature (°C)	Actual Storage Duration[1] Days (Months)	Interval of Demonstrated Storage Stability
Grain RAC	< -10	272-328 (8.9-10.8)	Adequate storage stability data are available indicating that residues of *cis*- and *trans*-metconazole are relatively stable under frozen storage conditions in wheat grain for up to 12 months, residues of M11, M21, and M30 are relatively stable in/on wheat grain for up to 6 months, residues of 1,2,4-T, TA, and TAA are stable/relatively stable in/on wheat grain for up to 6 months, and residues of TA are stable in/on wheat grain for up to 12 months.[2]
AGF		34	
Cleaned grain		75-79	
Epidermis/Husk		72-76	
Coarse Bran		43-51	
Straight Flour		22-23	
Fine Bran		43-51	
Middlings		59-67	
Shorts		45-53	
Germ		65-71	
Low Grade Meal		43-44	
Flour 550		18-21	
Whole Meal Flour		25	
Whole Meal Bread		13-15	

[1] Storage duration from harvest to extraction as reported by the petitioner; the storage interval for wheat grain was recalculated by the study reviewer. Samples were analyzed within 0-6 days of extraction.

[2] Refer to 46902218.der.doc, 46902221.der.doc, and 46902223.der.doc.

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TABLE C.3.1. Residue Data for Metconazole from Wheat Processing Study with Metconazole.

Location (County, State; Year) Trial ID	Processed Commodity	Total Rate (lb ai/A)	PHI (days)	Metconazole Residues (ppm)			Processing Factor[1]	Average Processing Factor[2]
				cis-Metconazole	*trans*-Metconazole	Total Metconazole	Total Metconazole	Total Metconazole
Pepin, WI; 2005 (RCN R05184)	Grain RAC	1.00	21	0.343	0.056	0.399	--	--
	AGF			21.190	4.474	25.664	64.3x	64.3x
	Cleaned Grain			0.321	0.053	0.374	0.9x	1.0x
	Husk			8.342	3.287	11.629	29.1x	121.4x
	Coarse Bran			0.683	0.127	0.810	2.0x	1.9x
	Straight Flour			0.047	0.010	0.057	0.1x	0.2x
	Fine Bran			0.73	0.137	0.867	2.2x	1.9x
	Middlings			0.275	0.047	0.322	0.8x	2.0x
	Shorts			0.829	0.058	0.887	2.2x	2.1x
	Germ			0.316	0.053	0.369	0.9x	1.0x
	Low Grade Meal			0.236	0.027	0.263	0.7x	0.7x
	Flour Type 550			0.060	0.011	0.071	0.2x	0.3x
	Whole Meal Flour			0.321	0.042	0.363	0.9x	0.7x
	Bread			0.209	0.041	0.250	0.6x	0.6x
Clinton, IL; 2004; (RCN R05185)	Grain RAC	1.01	20	0.348	0.061	0.409	--	
	Cleaned Grain			0.393	0.070	0.463	1.1x	
	Husk			19.066	3.970	23.036	56.3x	
	Coarse Bran			0.556	0.097	0.653	1.6x	
	Straight Flour			0.046	0.010	0.056	0.1x	
	Fine Bran			0.538	0.125	0.663	1.6x	
	Middlings			0.387	0.078	0.465	1.1x	
	Shorts			0.890	0.087	0.977	2.4x	
	Germ			0.212	0.050	0.262	0.6x	
	Low Grade Meal			0.278	0.041	0.319	0.8x	
	Flour Type 550			0.070	0.016	0.086	0.2x	
	Whole Meal Flour			0.204	0.042	0.246	0.6x	
	Bread			0.147	0.032	0.179	0.4x	

TABLE C.3.1. Residue Data for Metconazole from Wheat Processing Study with Metconazole.

Location (County, State; Year) Trial ID	Processed Commodity	Total Rate (lb ai/A)	PHI (days)	Metconazole Residues (ppm)			Processing Factor[1]	Average Processing Factor[2]
				cis-Metconazole	*trans*-Metconazole	Total Metconazole	Total Metconazole	Total Metconazole
Cass, ND; 2005; (RCN R05186)	Grain RAC	1.01	22	0.191	0.047	0.238	--	
	Cleaned Grain			0.172	0.040	0.212	0.9x	
	Husk			68.748	13.941	82.689	347.4x	
	Coarse Bran			0.338	0.095	0.433	1.8x	
	Straight Flour			0.059	0.015	0.074	0.3x	
	Fine Bran			0.427	0.081	0.508	2.1x	
	Middlings			1.038	0.181	1.219	5.1x	
	Shorts			0.475	0.054	0.529	2.2x	
	Germ			0.230	0.057	0.287	1.2x	
	Low Grade Meal			0.170	0.023	0.193	0.8x	
	Flour Type 550			0.081	0.019	0.100	0.4x	
	Whole Meal Flour			0.172	0.038	0.210	0.9x	
	Bread			0.135	0.032	0.167	0.7x	
York, NE; 2004; (RCN R05187)	Grain RAC	1.00	20	0.311	0.055	0.366	--	
	Cleaned Grain			0.276	0.055	0.331	0.9x	
	Husk			16.206	3.098	19.304	52.7x	
	Coarse Bran			0.642	0.122	0.764	2.1x	
	Straight Flour			0.069	0.017	0.086	0.2x	
	Fine Bran			0.523	0.126	0.649	1.8x	
	Middlings			0.293	0.065	0.358	1.0x	
	Shorts			0.496	0.046	0.542	1.5x	
	Germ			0.318	0.074	0.392	1.1x	
	Low Grade Meal			0.179	0.026	0.205	0.6x	
	Flour Type 550			0.072	0.017	0.089	0.2x	
	Whole Meal Flour			0.105	0.039	0.144	0.4x	
	Bread			0.176	0.038	0.214	0.6x	

[1] Processing factors calculated by dividing the residue in the processed fraction by the residue in wheat grain (RAC).
[2] Average from all trials.

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TABLE C.3.2. Residue Data for the Triazole Metabolites from Wheat Processing Study with Metconazole.

Location (County, State; Year) Trial ID	Processed Commodity	Total Rate (lb ai/A)	PHI days	Triazole Compounds (ppm)						
				1,2,4-T[1]	TA	Processing Factor	Average Processing Factor[2]	TAA	Processing Factor	Average Processing Factor[2]
Pepin, WI; 2005 (RCN R05184)	Grain RAC	1.00	21	<0.05	0.08	--	--	0.05	--	--
	AGF			<0.05	<0.05	<0.6x	<0.6x	0.08	1.6x	1.6x
	Cleaned Grain			<0.05	0.07	0.9x	1.0x	<0.05	<1.0x	1.0x
	Husk			<0.05	0.09	1.1x	0.7x	<0.05	<1.0x	1.1x
	Coarse Bran			<0.05	0.15	1.9x	2.2x	<0.05	<1.0x	1.2x
	Straight Flour			<0.05	<0.05	<0.6x	0.5x	<0.05	<1.0x	0.9x
	Fine Bran			<0.05	0.15	1.9x	2.4x	<0.05	<1.0x	1.2x
	Middlings			<0.05	0.07	0.9x	0.7x	<0.05	<1.0x	0.9x
	Shorts			<0.05	0.11	1.4x	1.2x	<0.05	<1.0x	1.0x
	Germ			<0.05	0.2	2.5x	2.5x	0.06	1.2x	1.1x
	Low Grade Meal			<0.05	0.08	1.0x	1.0x	<0.05	<1.0x	1.0x
	Flour Type 550			<0.05	<0.05	<0.6x	0.6x	<0.05	<1.0x	0.9x
	Whole Meal Flour			<0.05	0.06	0.8x	0.9x	<0.05	<1.0x	0.9x
	Bread			<0.05	<0.05	0.6	0.6x	<0.05	<1.0x	0.8x
Clinton, IL; 2004; (RCN R05185)	Grain RAC	1.01	20	<0.05	0.09	--		0.06	--	
	Cleaned Grain			<0.05	0.1	1.1x		0.06	1.0x	
	Husk			<0.05	0.07	0.8x		<0.05	<0.8x	
	Coarse Bran			<0.05	0.2	2.2x		0.08	1.3x	
	Straight Flour			<0.05	<0.05	<0.6x		<0.05	<0.8x	
	Fine Bran			<0.05	0.26	2.9x		0.08	1.3x	
	Middlings			<0.05	<0.05	<0.6x		<0.05	<0.8x	
	Shorts			<0.05	0.13	1.4x		0.06	1.0x	
	Germ			<0.05	0.32	3.6x		0.07	1.2x	
	Low Grade Meal			<0.05	0.12	1.3x		0.06	1.0x	
	Flour Type 550			<0.05	<0.05	<0.6x		<0.05	<0.8x	
	Whole Meal Flour			<0.05	0.08	0.9x		<0.05	<0.8x	
	Bread			<0.05	<0.05	<0.6x		<0.05	<0.8x	

TABLE C.3.2. Residue Data for the Triazole Metabolites from Wheat Processing Study with Metconazole.

Location (County, State; Year) Trial ID	Processed Commodity	Total Rate (lb ai/A)	PHI days	Triazole Compounds (ppm)						
				1,2,4-T[1]	TA	Processing Factor	Average Processing Factor[2]	TAA	Processing Factor	Average Processing Factor[2]
Cass, ND; 2005; (RCN R05186)	Grain RAC	1.01	22	<0.05	0.31	--		0.09	--	
	Cleaned Grain			<0.05	0.28	0.9x		0.08	0.9x	
	Husk			<0.05	0.09	0.3x		0.09	1.0x	
	Coarse Bran			<0.05	0.56	1.8x		0.12	1.3x	
	Straight Flour			<0.05	0.13	0.4x		0.07	0.8x	
	Fine Bran			<0.05	0.56	1.8x		0.1	1.1x	
	Middlings			<0.05	0.18	0.6x		0.08	0.9x	
	Shorts			<0.05	0.27	0.9x		0.08	0.9x	
	Germ			<0.05	0.45	1.5x		0.09	1.0x	
	Low Grade Meal			<0.05	0.23	0.7x		0.08	0.9x	
	Flour Type 550			<0.05	0.17	0.5x		0.07	0.8x	
	Whole Meal Flour			<0.05	0.25	0.8x		0.07	0.8x	
	Bread			<0.05	0.15	0.5x		0.06	0.7x	
York, NE; 2004; (RCN R05187)	Grain RAC	1.00	20	<0.05	0.2	--		0.1	--	
	Cleaned Grain			<0.05	0.19	1.0x		0.1	1.0x	
	Husk			<0.05	0.14	0.7x		0.11	1.1x	
	Coarse Bran			<0.05	0.6	3.0x		0.11	1.1x	
	Straight Flour			<0.05	0.07	0.4x		0.09	0.9x	
	Fine Bran			<0.05	0.58	2.9x		0.12	1.2x	
	Middlings			<0.05	0.12	0.6x		0.09	0.9x	
	Shorts			<0.05	0.2	1.0x		0.1	1.0x	
	Germ			<0.05	0.44	2.2x		0.1	1.0x	
	Low Grade Meal			<0.05	0.15	0.8x		0.09	0.9x	
	Flour Type 550			<0.05	0.09	0.5x		0.09	0.9x	
	Whole Meal Flour			<0.05	0.19	1.0x		0.09	0.9x	
	Bread			<0.05	0.12	0.6x		0.07	0.7x	

[1] Processing factors were not calculated for 1,2,4-T because residues were nonquantifiable all commodities.
[2] Average from all trials for which processing factors were calculated.

D. CONCLUSION

Residues of total metconazole (sum of *cis* and *trans* isomers) in wheat grain were 0.238-0.409 ppm. Following processing, residues of total metconazole were <0.056-0.086 ppm in flour;

0.508-0.867 ppm in bran; 0.322-1.219 ppm in middlings; 0.529-0.977 ppm in shorts; and 0.262-0.392 ppm in germ.

The processing data indicate that residues of total metconazole may concentrate in bran, middlings, and shorts, with average processing factors of 1.9x, 2.0x, and 2.1x, respectively. Residues of total metconazole do not concentrate in flour or germ (with average processing factors of 0.2x and 1.0x, respectively). One sample of AGF indicated that residues of total metconazole may concentrate 64.3x in AGF.

Acceptable methods were used for quantitation of residues of *cis*- and *trans*-metconazole, M11, M21, M30, 1,2,4-T, TA, and TAA in/on wheat samples. Adequate storage stability data are available for *cis*- and *trans*-metconazole.

E. REFERENCES

DP#:	324541
Subject:	Metconazole. Request for a Tolerance on Imported Bananas. Summary of Analytical Chemistry and Residue Data. Petition Number 9E05052.
From:	N. Dodd
To:	M. Waller
Date:	12/14/05
MRIDs:	44721506, 44721507, 44721508, 44721509, 44721510, and 44721511

F. DOCUMENT TRACKING

RDI: N. Dodd (2/20/08)
Petition Numbers: 6F7094 and 6F7095
DP#s: 348168 and 348206
PC Code: 125619

Template Version June 2005

APPENDIX I. Calculation of Processing Factors for Combined Residues of cis- and trans-Metconazole, M11, M21, and M30.

TABLE C.3.1 with Metabolites. Residue Data for Metconazole, M11, M21, and M30 from Wheat Processing Study with Metconazole.

Location (County, State; Year) Trial ID	Processed Commodity	Total Rate (lb ai/A)	PHI days	Metconazole Residues (ppm)							Processing Factor [3]
				Parent metconazole			Metabolites[1]			Total[2]	
				Cis	*Trans*	Total	M11	M21	M30		
Pepin, WI; 2005 (RCN R05184)	Grain RAC	1.00	21	0.343	0.056	0.399	0.1	0.01	0.03	0.54	--
	AGF			21.19	4.474	25.664	7.15	0.71	1.44	35.98	--
	Cleaned Grain			0.321	0.053	0.374	0.1	0.02	0.03	0.52	1.0
	Husk			8.342	3.287	11.629	0.386	0.82	0.77	17.07	326
	Coarse Bran			0.683	0.127	0.81	0.23	0.03	0.07	1.14	2.1
	Straight Flour			0.047	0.01	0.057	0.01	<0.01	<0.01	0.088	0.2
	Fine Bran			0.73	0.137	0.867	0.23	0.03	0.08	1.21	2.2
	Middlings			0.275	0.047	0.322	0.08	0.01	0.02	0.43	0.8
	Shorts			0.829	0.058	0.887	0.12	0.02	0.04	1.06	2.0
	Germ			0.316	0.053	0.369	0.1	0.02	0.03	0.52	1.0
	Low Grade Meal			0.236	0.027	0.263	0.1	<0.01	0.02	0.39	0.7
	Flour Type 550			0.06	0.011	0.071	0.02	<0.01	<0.01	0.11	0.2
	Whole Meal Flour			0.321	0.042	0.363	0.09	0.01	0.03	0.5	0.9
	Bread			0.209	0.041	0.25	0.06	0.01	0.02	0.34	0.6
Clinton, IL; 2004; (RCN R05185)	Grain RAC	1.01	20	0.348	0.061	0.409	0.04	0.01	0.01	0.47	--
	Cleaned Grain			0.393	0.07	0.463	0.08	0.02	0.02	0.58	1.2
	Husk			19.066	3.97	23.036	1.22	0.56	0.21	25.02	53.2
	Coarse Bran			0.556	0.097	0.653	0.09	0.02	0.02	0.79	1.7
	Straight Flour			0.046	0.01	0.056	<0.01	<0.01	<0.01	0.09	0.2
	Fine Bran			0.538	0.125	0.663	0.11	0.03	0.03	0.83	1.8
	Middlings			0.387	0.078	0.465	0.03	0.01	<0.01	0.52	1.1
	Shorts			0.89	0.087	0.977	0.06	0.02	0.01	1.06	2.3
	Germ			0.212	0.05	0.262	0.03	<0.01	<0.01	0.31	0.7
	Low Grade Meal			0.278	0.041	0.319	0.04	0.01	0.01	0.38	0.8
	Flour Type 550			0.07	0.016	0.086	<0.01	<0.01	<0.01	0.12	0.3
	Whole Meal Flour			0.204	0.042	0.246	0.04	0.01	<0.01	0.3	0.6
	Bread			0.147	0.032	0.179	0.02	<0.01	<0.01	0.22	0.5
Cass, ND;	Grain RAC	1.01	22	0.191	0.047	0.238	0.09	0.01	0.03	0.37	--

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TABLE C.3.1 with Metabolites. Residue Data for Metconazole, M11, M21, and M30 from Wheat Processing Study with Metconazole.

Location (County, State; Year) Trial ID	Processed Commodity	Total Rate (lb ai/A)	PHI days	Metconazole Residues (ppm)							Processing Factor [3]
				Parent metconazole			Metabolites[1]			Total[2]	
				Cis	*Trans*	Total	M11	M21	M30		
	Cleaned Grain			0.172	0.04	0.212	0.07	0.01	0.02	0.32	0.9
	Husk			68.748	13.941	82.689	9.23	2.2	1.17	95.29	257
	Coarse Bran			0.338	0.095	0.433	0.2	0.03	0.07	0.73	2.0
	Straight Flour			0.059	0.015	0.074	0.01	<0.01	<0.01	0.1	0.3
	Fine Bran			0.427	0.081	0.508	0.18	0.03	0.06	0.77	2.1
	Middlings			1.038	0.181	1.219	0.15	0.04	0.02	1.43	3.9
	Shorts			0.475	0.054	0.529	0.07	0.02	0.02	0.64	1.7
	Germ			0.23	0.057	0.287	0.05	0.02	0.01	0.37	1.0
	Low Grade Meal			0.17	0.023	0.193	0.04	<0.01	0.01	0.26	0.7
	Flour Type 550			0.081	0.019	0.1	0.03	<0.01	<0.01	0.15	0.4
	Whole Meal Flour			0.172	0.038	0.21	0.07	0.01	0.02	0.31	0.8
	Bread			0.135	0.032	0.167	0.04	<0.01	0.01	0.23	0.6
York, NE; 2004; (RCN R05187)	Grain RAC	1.00	20	0.311	0.055	0.366	0.06	0.01	0.02	0.46	--
	Cleaned Grain			0.276	0.055	0.331	0.06	<0.01	0.02	0.42	0.9
	Husk			16.206	3.098	19.304	1.39	0.65	0.21	21.55	47
	Coarse Bran			0.642	0.122	0.764	0.18	0.03	0.04	1.02	2.2
	Straight Flour			0.069	0.017	0.086	<0.01	<0.01	<0.01	0.12	0.3
	Fine Bran			0.523	0.126	0.649	0.18	0.03	0.04	0.9	2.0
	Middlings			0.293	0.065	0.358	0.04	0.02	0.01	0.43	0.9
	Shorts			0.496	0.046	0.542	0.06	0.01	0.02	0.63	1.4
	Germ			0.318	0.074	0.392	0.06	0.01	0.02	0.49	1.1
	Low Grade Meal			0.179	0.026	0.205	0.03	<0.01	<0.01	0.26	0.6
	Flour Type 550			0.072	0.017	0.089	0.01	<0.01	<0.01	0.12	0.3
	Whole Meal Flour			0.105	0.039	0.144	0.06	0.01	0.02	0.23	0.5
	Bread			0.176	0.038	0.214	0.04	<0.01	<0.01	0.27	0.6

[1] Expressed in parent equivalents.
[2] Total = total residue; the sum of *cis*- and *trans*-metconazole, M11, M21, and M30; values presented as calculated and reported by the petitioner.
[3] Processing factors calculated by dividing the residue in the processed fraction by the residue in the soybean seed (RAC); values presented as calculated and reported by the petitioner

Primary Evaluator	This DER was originally prepared under contract by Dynamac Corporation.
Approved by	Nancy Dodd, Chemist Nancy Dodd Date: 2/20/08 Registration Action Branch 3 Health Effects Division (7509P)

This DER was originally prepared under contract by Dynamac Corporation (2275 Research Boulevard, Suite 300; Rockville, MD 20850; submitted 09/17/2007). The DER has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

46902232 White, M.; Saha, M. (2006) The Magnitude of Residues of Metconazole (BAS 555 F) and its Metabolites in Wheat Aspirated Grain Fractions. Project Number: 257986, 2006/7007257. Unpublished study prepared by BASF Agro Research. 131 p.

EXECUTIVE SUMMARY:

BASF has submitted data pertaining to aspirated grain fractions (AGF) for wheat. In a single field trial conducted in TX in 2004, a 1.81 lb ai/gal flowable concentrate (FlC) formulation was applied to wheat as a single broadcast foliar application at 0.69 lb ai/A. The application was made in 21 gal/A, and a nonionic surfactant was added as an adjuvant to the spray mixture. Bulk samples of wheat grain were harvested 30 days after application of metconazole and were processed into AGF using simulated commercial processing procedures. BASF noted that the wheat trial was conducted by Valent U.S.A., and that wheat grain samples were obtained by BASF for the sole purpose of generating AGF samples for analysis. Samples of wheat grain were not analyzed in the submitted study.

Samples of wheat AGF were analyzed for residues of *cis*- and *trans*-metconazole, metabolites M11, M21, and M30, and the triazole metabolites [triazole (1,2,4-T), triazolylalanine (TA), and triazolylacetic acid (TAA)] using an LC/MS/MS method (BASF Method D0508). Residues of metabolites M11, M21, and M30 were converted to parent equivalents using molecular weight conversion factors of 0.95 for M11 and M21 and 0.96 for M30. The validated limits of quantitation (LOQs) were 0.01 ppm for the parent metconazole (sum of *cis* and *trans* isomers at 0.005 ppm each) and the metabolites M11, M21, and M30 in wheat AGF. The validated LOQ was 0.05 ppm for 1,2,4-T, TA, and TAA. The method was adequate for data collection based on acceptable concurrent method recoveries for wheat AGF. The petitioner noted that one of the two treated samples of AGF was too small to be analyzed.

Samples of wheat AGF were generated within 42 days of harvest and were stored frozen (<-8 °C) from sample generation to extraction for 683 days (22.5 months). The available storage stability data for wheat grain are not adequate to support the storage conditions and durations of

the AGF samples, as the data represent much shorter storage intervals (6 months for metabolites M11, M21, M30, 1,2,4-T, and TAA, and 12 months for *cis*- and *trans*-metconazole and TA).

Residues of *cis*- and *trans*-metconazole in/on a single sample of wheat AGF were 3.305 and 0.668 ppm, respectively, and total metconazole residues (sum of *cis* and *trans* isomers) were 3.97 ppm. Residues of metabolites M11, M21, and M30 were 0.03, 0.04, and 0.01 ppm, respectively, and residues of the triazole metabolites were below the LOQ (<0.05 ppm). A processing factor for wheat AGF could not be calculated in this study because residues in the wheat grain RAC were not determined.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the data depicting residues in wheat AGF are classified as incomplete because 1) adequate storage stability data are not available to support the study (i.e., the storage stability data do not represent the storage duration of the AGF sample (22.5 months); and 2) the wheat grain samples used to generate the AGF fractions were not analyzed; thus, a processing factor based on the residue level in wheat grain could not be calculated.

The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document DP# 348168 and 348206.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an impact on the validity of the study.

A. BACKGROUND INFORMATION

Metconazole [5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol] is a broad-spectrum triazole Group 3 fungicide (sterol biosynthesis inhibitors). There are currently no registered uses of metconazole in the U.S.; however, a tolerance has been established for banana, and a Section 18 emergency exemption and supporting time-limited tolerances have been granted for use on soybean. BASF Corporation has applied for registration of metconazole in the U.S. for use on barley, oats, rye, soybeans, sugar beets, triticale, and wheat.

The chemical structure and nomenclature of metconazole, and the physicochemical properties of the technical grade of metconazole are presented in Tables A.1 and A.2.

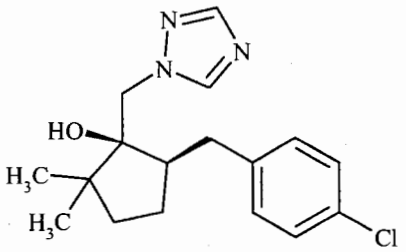
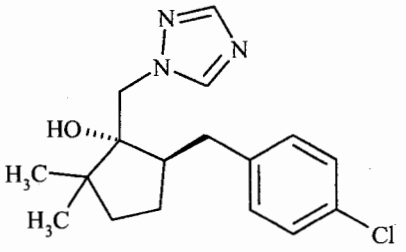
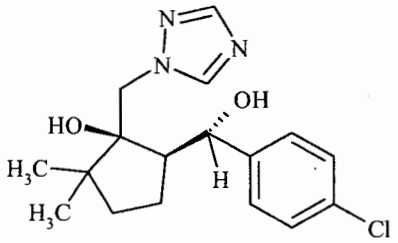
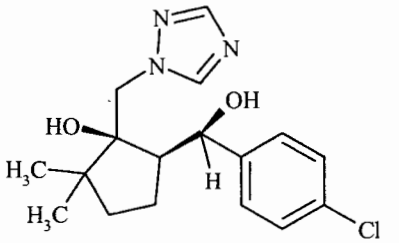
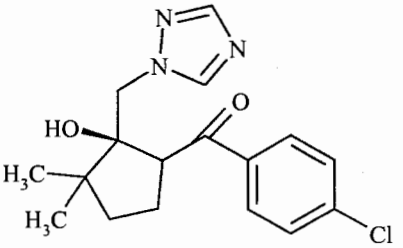
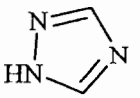
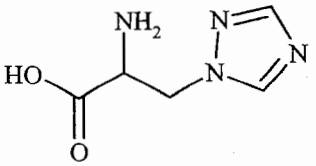
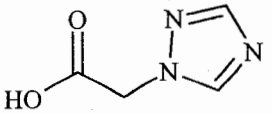
TABLE A.1. Metconazole Nomenclature.		
Chemical structure	 *cis*-isomer	 *trans*-isomer
Common name	Metconazole	
Company experimental name	KNF-S-474m (Kureha); BAS 555 F (BASF); V-10116 (Valent)	
IUPAC name	(1RS,5RS:1RS,5SR)-5-(4-chlorobenzyl)-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	
CAS name	5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	
CAS registry number	125116-23-6 (cis- and *trans*-isomers) 115850-27-6 (*cis*-isomer) 115850-28-7 (*trans*-isomer)	
End-use products (EP)	50% WDG (Metconazole 50 WDG Fungicide, EPA File Symbol 59639-RUT) 0.75 lb/gal SC/L (Caramba™ Fungicide, EPA File Symbol No. 7969-EUA) 0.67 lb/gal SC/L formulation (BAS 556 01F Fungicide, EPA File Symbol No. 7969-EUT; also contains the active ingredient pyraclostrobin at 0.83 lb/gal)	
 Metconazole metabolite M11	 Metconazole metabolite M21	 Metconazole metabolite M30
 Triazole metabolite 1,2,4-triazole (1,2,4-T)	 Triazole metabolite triazolylalanine (TA)	 Triazole metabolite triazolylacetic acid (TAA)

Table A.2. Physicochemical Properties of Metconazole		
Parameter	Value	References* (MRID)
Melting point/range	100.0-108.4°C (using Electrothermal Digital Melting Point Apparatus) (AC900,768 technical grade)	44721505
pH	5.81 at 25°C (1% aqueous suspension)	46808402

Table A.2. Physicochemical Properties of Metconazole

Parameter	Value	References* (MRID)
Relative density (20°C)	1.14 (relative density to water at 4°C, using capillary-stoppered, density-specific gravity bottle) (Lot No. AC 8879-140B)	44721505
Water solubility (20°C)	Using shake-flask method: 18.7 ± 1.0 mg/L (*cis*-isomer, WL148271, KNF-S-474m) 13.6 ± 1.7 mg/L (*trans*-isomer, WL148271, KNF-S-474m)	44721505

Solvent solubility (g/L) at 20°C — 44721505

Solvent	Metconazole	*cis*	*trans*
acetone	363	251	117
methanol	403	294	117
dichloromethane	481	343	141
ethyl acetate	260	173	90.0
propanol	132	86.6	46.7
toluene	103	66.2	38.0
Hexane	1.40	0.929	0.483

Vapor pressure (20°C)	Using gas-saturation method: $< 1.23 \times 10^{-5}$ Pa or 9.23×10^{-8} mm Hg (metconazole) $< 1.04 \times 10^{-5}$ Pa or 7.80×10^{-8} mm Hg (*cis*-isomer) $< 1.96 \times 10^{-6}$ Pa or 1.47×10^{-8} mm Hg (*trans*-isomer)	44721505
Dissociation constant (pK_a)	11.38±0.03 and 1.06±0.03 (in water at 29.1°C using spectrophotometric method; Lot No. AC 8879-140B)	44721505
Octanol/water partition coefficient, Log(K_{OW})	At 20 °C (using flask shaking method): K_{ow} (log K_{ow}) = 7090±989 (3.85) (Lot No. AC 8879-140B) (TGAI) K_{ow} (log K_{ow}) = 7150±803 (3.85) (*cis*-isomer, CL 354,801) K_{ow} (log K_{ow}) = 6800±1700 (3.8) (*trans*-isomer, CL 354,802)	44721505

UV/visible absorption spectrum — 46808403

pH	λ	A	log ε
cis-isomer			
2.0	221.4	0.828	4.03
6.8		0.8452	4.04
7.0		0.9126	4.08
10.3		0.7226	3.98
trans-isomer			
2.0	221.4	0.9053	4.07
7.0		0.9547	4.10
10.1		0.9893	4.11

* Product Chemistry Reviews: DP #256877, Shyam Mathur, Ph.D., 9/12/2000 and DP #329168, Shyam Mathur, Ph.D., 7/13/07.

B. EXPERIMENTAL DESIGN

B.1. Application and Crop Information

In a single field trial conducted in TX in 2004, a 1.81 lb ai/gal flowable concentrate (FlC) formulation was applied as a single broadcast foliar application to wheat at 0.69 lb ai/A. The application was made in 21 gal/A, and a nonionic surfactant was added as an adjuvant to the spray mixture. Bulk samples of wheat grain were harvested 30 days after application of metconazole.

BASF noted that the wheat trial was conducted by Valent U.S.A., and that wheat grain samples were obtained by BASF for the sole purpose of generating AGF samples for analysis.

TABLE B.1. Application Rates for Soybean and Wheat.

Location (County, State; Year) Trial ID	EP[1]	Crop	Application					Tank Mix/ Adjuvants[4]
			Method; Timing	Volume[2] GPA (L/ha)	Rate lb ai/A [kg ai/ha]	RTI[3] (days)	Total Rate lb ai/A [kg ai/ha]	
Hockley, TX; 2004 (V-25697-04-V)	1.81 lb/gal FlC	Wheat	1. Broadcast foliar; maturing grain	21.3 [199]	0.69 [0.77]	NA	0.69 [0.77]	R-11 (NIS)

[1] EP = End-use Product
[2] Gallons per acre or L/ha
[3] RTI = Retreatment Interval; NA = not applicable
[4] NIS = Non ionic surfactant

B.2. Sample Handling and Processing Procedures

Wheat grain samples were transferred to freezers at the field facility promptly after harvest. Samples remained in frozen storage at the field facility for 21 days until shipment via ACDS freezer truck to the processing facility, Food Protein Research and Development Center (Bryan, TX), where they were stored frozen (≤-8 °C) until processing. Samples were processed into aspirated grain fractions within 20 days of receipt at the facility using simulated commercial processing procedures via drying, aspiration, and classification of aspirated material.

Processed samples were shipped to Valent Technical Center (Dublin, CA) within 4 days of processing by overnight courier on dry ice and were stored frozen at Valent for 436 days. Samples were then shipped by ACDS freezer truck to BASF Agro Research (Research Triangle, NC), where they were stored frozen (≤-10 °C) until extraction and analysis.

B.3. Analytical Methodology

Wheat AGF samples were analyzed for residues of metconazole, metabolites M11, M21, and M30, and the triazole metabolites 1,2,4-T, TA, and TAA using an LC/MS/MS method (BASF Method D0508). The petitioner noted that one of the two treated samples of AGF was too small to be analyzed. A brief description of the method was included in the MRID.

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Briefly, residues of metconazole, M11, M21, and M30 were extracted with acetonitrile (ACN):water (70:30, v:v). The extracts were diluted with methanol:water (80:20, v:v), filtered, and reserved for LC/MS/MS analysis. For determination of residues of 1,2,4-T, TA, and TAA, a separate aliquot of the initial extract was evaporated to dryness, redissolved in 0.1% formic acid in water, filtered, and reserved for LC/MS/MS analysis. Residues of metabolites M11, M21, and M30 were converted to parent equivalents using molecular weight conversion factors of 0.95 for M11 and M21 and 0.96 for M30.

The validated LOQ was 0.01 ppm for the parent metconazole (sum of *cis* and *trans* isomers at 0.005 ppm each), M11, M21, and M30 in/on wheat samples. The validated LOQ was 0.05 ppm for 1,2,4-T, TA, and TAA. The reported limit of detection was 20% LOQ.

The method was validated concurrently with the analysis of samples using samples of wheat AGF fortified at 0.005 and 0.5 ppm with *cis*- and *trans*-metconazole; at 0.01 and 1.00 ppm with M11, M21, and M30; and at 0.05 and 5.00 ppm with 1,2,4-T, TA, and TAA.

C. RESULTS AND DISCUSSION

The storage conditions and duration for the wheat AGF are presented in Table C.2. Samples were generated within 42 days of harvest and were stored frozen (<-8 °C) from sample generation to analysis for 683 days (22.5 months). Storage stability data are available for wheat grain indicating that: (1) residues of *cis*- and *trans*-metconazole are stable under frozen storage conditions in/on wheat grain for up to 12 months (refer to 46902218.der.doc; (2) residues of M11, M21, M30, 1,2,4-T, and TAA are stable in/on wheat grain for up to 6 months (refer to 46902223.der.doc; and (3) residues of TA are stable in/on wheat grain for up to 12 months (refer to 46902221.der.doc). Although storage stability data for wheat grain may be translated to support wheat AGF, the available storage stability data are not adequate to support the storage conditions and durations of the AGF samples, as the storage stability data do not represent the storage duration of the AGF samples (22.5 months).

Concurrent method recovery data are presented in Table C.1. Samples of wheat AGF were analyzed for residues of *cis*- and *trans*-metconazole, metabolites M11, M21, and M30, and the triazole metabolites 1,2,4-T, TA, and TAA using LC/MS/MS Method D0508. Residues of metabolites M11, M21, and M30 were converted to parent equivalents using molecular weight conversion factors of 0.95 for M11 and M21 and 0.96 for M30. The method was adequate for data collection based on acceptable concurrent method recovery data. Concurrent method recoveries were generally within the acceptable range of 70-120% for wheat AGF fortified at 0.005 and 0.5 ppm with *cis*- and *trans*-metconazole; at 0.01 and 1.00 ppm with M11, M21, and M30; and at 0.05 and 5.00 ppm with 1,2,4-T, TA, and TAA. A low recovery of 63% was obtained for M30 in a single sample of AGF (at 0.010 ppm). Apparent residues were below the respective LOQs for all analytes in/on two samples of untreated AGF. The petitioner noted that one of the two treated samples of AGF was too small to be analyzed.

Residue data from the wheat AGF study are presented in Table C.3.1. Residues of *cis*- and *trans*-metconazole in/on aspirated grain fraction samples were 3.305 and 0.668 ppm,

respectively, and total metconazole residues were 3.97 ppm. Residues of metabolite M11, M21, and M30 were 0.03, 0.04, and 0.01 ppm, respectively, and residues of the triazole metabolites were below the LOQ (<0.05 ppm). A processing factor for wheat AGF could not be calculated in this study because residues in the wheat grain RAC were not determined.

TABLE C.1. Summary of Concurrent Recoveries of Metconazole and Metabolites from Wheat AGF.

Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. (%)
Wheat AGF	*cis*-Metconazole	0.005	1	76	76
		0.500	1	93	93
	trans-Metconazole	0.005	1	73	73
		0.500	1	91	91
	M11	0.010	1	77	77
		1.000	1	101	101
	M21	0.010	1	73	73
		1.000	1	89	89
	M30	0.010	1	63	63
		1.000	1	98	98
	1,2,4-T	0.050	1	67	67
		5.000	1	109	109
	TA	0.050	1	81	81
		5.000	1	80	80
	TAA	0.050	1	102	102
		5.000	1	100	100

TABLE C.2. Summary of Storage Conditions.

Matrix	Storage Temperature (°C)	Actual Storage Duration [1]	Interval of Demonstrated Storage Stability
Wheat AGF	≤-8 °C	683 days (22.5 months)	The available storage stability data indicate that residues of *cis*- and *trans*-metconazole are stable in/on wheat grain for up to 12 months; residues of M11, M21, M30, 1,2,4-T, and TAA are stable in/on wheat grain for up to 6 months; and residues of TA are stable in/on wheat grain for up to 12 months.[2]

[1] Interval from sample generation to analysis; samples were analyzed on the day of extraction.
[2] Refer to 46902218.der.doc, 46902221.der.doc, and 46902223.der.doc.

TABLE C.3. Residue Data from Wheat AGF Study with Metconazole.

Trial ID (County, State; Year)	Total Rate (lb ai/A)	PHI (days)	Fraction	Residues (ppm)			Processing Factor
				cis-Metconazole	*trans*-Metconazole	Total Metconazole	Total Metconazole
Hockley, TX; 2004 (V-25697-04-V)	0.69	30	AGF	3.305	0.668	3.97	Not calculated because residues in the wheat grain RAC were not determined.

D. CONCLUSION

Total metconazole residues (sum of *cis* and *trans* isomers) in wheat AGF were 3.97 ppm. Residues of metabolites M11, M21, and M30 were 0.03, 0.04, and 0.01 ppm, respectively, and residues of the triazole metabolites were below the LOQ (<0.05 ppm). A processing factor for wheat AGF could not be calculated because residues in the wheat grain RAC were not determined.

An acceptable method was used for the quantitation of residues of *cis*- and *trans*-metconazole, M11, M21, M30, 1,2,4-T, TA, and TAA in wheat AGF. Adequate storage stability data are not available to support the study since the AGF sample was stored for 22.5 months.

E. REFERENCES

DP Barcode:	324541
Subject:	Metconazole. Request for a Tolerance on Imported Bananas. Summary of Analytical Chemistry and Residue Data. Petition Number 9E05052.
From:	N. Dodd
To:	M. Waller
Date:	12/14/05
MRIDs:	44721506, 44721507, 44721508, 44721509, 44721510, and 44721511

F. DOCUMENT TRACKING

RDI: N. Dodd (2/20/08)
Petition Numbers: 6F7094 and 6F7095
DP#s: 348168 and 348206
PC Code: 125619

Template Version June 2005

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Primary Evaluator	This DER was originally prepared under contract by Dynamac Corporation.
Approved by	Nancy Dodd, Chemist *Nancy Dodd* Date: 2/20/08 Registration Action Branch 3 Health Effects Division (7509P)

This DER was originally prepared under contract by Dynamac Corporation (2275 Research Boulevard, Suite 300; Rockville, MD 20850; submitted 09/17/2007). The DER has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

46902301 White, M.; Saha, M. (2006) The Magnitude of Residues of Metconazole (BAS 555 F) and its Metabolites in Soybean Processing Commodities: Final Report. Project Number: 137732, 2006/7006996. Unpublished study prepared by BASF Corporation, Agresources, Inc. and Midwest Research, Inc. 208 p.

EXECUTIVE SUMMARY:

BASF Corporation has submitted a processing study with soybeans. In four trials conducted in IL, ND, NE, and WI, a 0.75 lb ai/gal soluble concentrate/liquid (SC/L) formulation of metconazole was applied as two broadcast foliar sprays to soybeans at 0.35-0.36 lb ai/A, with 8- to 11-day retreatment intervals, for a total rate of 0.70-0.71 lb ai/A. Applications were made in 15-20 gal/A spray volumes with a nonionic surfactant added as an adjuvant to the spray mixture. Samples of soybean seed were harvested 27-31 days after the last application of metconazole, and were processed into hulls, meal, crude oil, and refined oil using simulated commercial processing procedures.

Samples were analyzed for residues of *cis*- and *trans*-metconazole, metabolites M11, M21, and M30, and the triazole metabolites [1,2,4-triazole (1,2,4-T), triazolylalanine (TA), and triazolylacetic acid (TAA)] using an LC/MS/MS method (BASF Method D0508). Residues of metabolites M11, M21, and M30 were converted to parent equivalents using molecular weight conversion factors of 0.95 for M11 and M21 and 0.96 for M30. The validated limits of quantitation (LOQs) were 0.01 ppm for the parent metconazole (sum of *cis* and *trans* isomers at 0.005 ppm each), M11, M21, and M30 in/on soybean seed and processed samples. The validated LOQ was 0.05 ppm for 1,2,4-T, TA, and TAA. The method was adequate for data collection based on acceptable concurrent method recoveries.

Samples were stored frozen (<-10 °C) prior to extraction for 125-147 days (4.1-4.8 months) for soybean seeds, 85-86 days (2.8 months) for hulls, 76-77 days (2.5 months) for meal, 62 days (2.0 months) for crude oil, and 58-59 days (1.9 months) for refined oil, and were analyzed within 0-2 days of extraction. Adequate storage stability data are available to support the storage conditions

and durations of the soybean seed samples. To support sample storage conditions and durations for the processed commodities, the petitioner conducted a concurrent storage stability study which indicated that residues of *cis*- and *trans*-metconazole, M11, M21, M30, 1,2,4-T, TA, and TAA were reasonably stable during frozen storage for 63-66 days in/on soybean hulls, meal, and oil. These data are adequate to support the soybean processing study.

Residues of *cis*-and *trans*-metconazole in soybean seed were <0.005-0.016 and <0.005 ppm, respectively, for total metconazole residues (sum of *cis* and *trans* isomers) of <0.01-<0.021 ppm. Following processing, respective residues of *cis*-metconazole, *trans*-metconazole, and total metconazole were 0.013-0.42, <0.005-0.007, and <0.016-0.049 ppm in hulls; <0.005-0.006, <0.005, and <0.01-<0.011 ppm in meal; <0.005-0.011, <0.005, and <0.01-<0.016 ppm in crude oil; and <0.005-0.006, <0.005, and <0.01-0.011 ppm in refined oil. Residues of metabolites M11, M21, and M30 were <0.010 ppm in/on all samples of soybean seed and processed commodities.

The processing data indicate that residues of total metconazole may concentrate in hulls (average processing factor of 1.7x), but do not concentrate in meal, crude oil, or refined oil (respective processing factors of 0.6x, 0.9x, and 0.6x).

The calculated processing factors for hulls do not exceed the maximum theoretical concentration factor of 12x for soybean (OPPTS 860.1520, Table 1).

Residues of 1,2,4-T and TAA were <0.05 ppm in/on all samples of soybean seed and processed commodities. Residues of TA were <0.05-0.16 ppm in soybean seed, <0.05-0.15 ppm in hulls, 0.05-0.21 ppm in meal, and <0.05 ppm in crude and refined oil.

Because residues of 1,2,4-T and TAA were below the LOQ in all soybean samples, processing factors were not calculated. The processing data indicate that residues of TA may concentrate in hulls and meal, with average processing factors of 1.3x. Residues of TA do not concentrate in crude or refined oil (averaging processing factors of <0.4x). The petitioner noted that a reliable estimate of the concentration factor for TA could not be made because apparent residues of TA were found in samples of untreated seed (0.06 ppm), hulls (0.07 ppm) and meal (0.11 ppm) and because triazole-related compounds are naturally abundant in soybean seeds.

HED notes that processing factors were also calculated by the petitioner using total residues of *cis*- and *trans*-metconazole, M11, M21, and M30. When processing factors were calculated using these values, an average processing factor of 1.2x was obtained for hulls, and processing factors of 0.9x, 1.0x, and 0.9x, respectively, were obtained for meal, crude oil, and refined oil. A data table reflecting calculation of processing factors according to this procedure is attached as an appendix to this DER.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the processed commodity residue data are classified as scientifically acceptable.

The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP#s 348168 and 348206.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported.

A. BACKGROUND INFORMATION

[Metconazole [5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol] is a broad-spectrum triazole Group 3 fungicide (sterol biosynthesis inhibitors). There are currently no registered uses of metconazole in the U.S.; however, a tolerance has been established for banana, and a Section 18 emergency exemption and supporting time-limited tolerances have been granted for use on soybean. BASF Corporation has applied for registration of metconazole in the U.S. for use on barley, oats, rye, soybeans, sugar beets, triticale, and wheat.

The chemical structure and nomenclature of metconazole, and the physicochemical properties of the technical grade of metconazole are presented in Tables A.1 and A.2.

TABLE A.1. Metconazole Nomenclature.

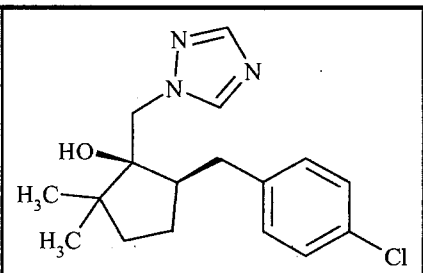
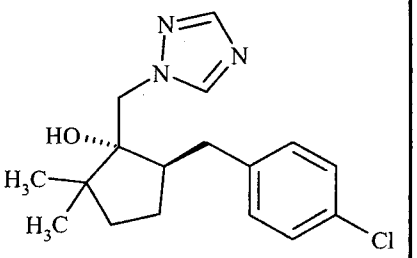
Chemical structure	 *cis*-isomer	 *trans*-isomer
Common name	Metconazole	
Company experimental name	KNF-S-474m (Kureha); BAS 555 F (BASF); V-10116 (Valent)	
IUPAC name	(1RS,5RS:1RS,5SR)-5-(4-chlorobenzyl)-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	
CAS name	5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	
CAS registry number	125116-23-6 (cis- and *trans*-isomers) 115850-27-6 (*cis*-isomer) 115850-28-7 (*trans*-isomer)	

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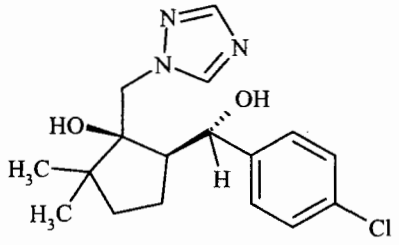
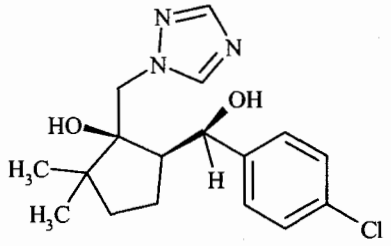
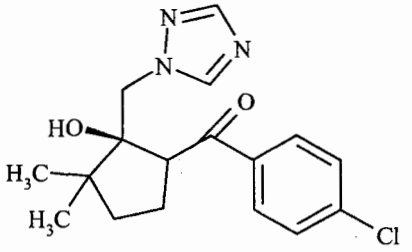
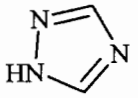
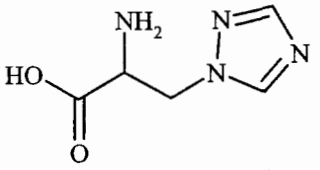
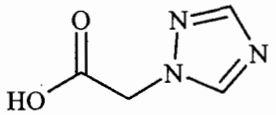
TABLE A.1. Metconazole Nomenclature.		
End-use products (EP)	50% WDG (Metconazole 50 WDG Fungicide, EPA File Symbol 59639-RUT) 0.75 lb/gal SC/L (Caramba™ Fungicide, EPA File Symbol No. 7969-EUA) 0.67 lb/gal SC/L formulation (BAS 556 01F Fungicide, EPA File Symbol No. 7969-EUT; also contains the active ingredient pyraclostrobin at 0.83 lb/gal)	
 Metconazole metabolite M11	 Metconazole metabolite M21	 Metconazole metabolite M30
 Triazole metabolite 1,2,4-triazole (1,2,4-T)	 Triazole metabolite triazolylalanine (TA)	 Triazole metabolite triazolylacetic acid (TAA)

Table A.2. Physicochemical Properties of Metconazole					
Parameter	Value				References* (MRID)
Melting point/range	100.0-108.4°C (using Electrothermal Digital Melting Point Apparatus) (AC900,768 technical grade)				44721505
pH	5.81 at 25°C (1% aqueous suspension)				46808402
Relative density (20°C)	1.14 (relative density to water at 4°C, using capillary-stoppered, density-specific gravity bottle) (Lot No. AC 8879-140B)				44721505
Water solubility (20°C)	Using shake-flask method: 18.7 ± 1.0 mg/L (*cis*-isomer, WL148271, KNF-S-474m) 13.6 ± 1.7 mg/L (*trans*-isomer, WL148271, KNF-S-474m)				44721505
Solvent solubility (g/L) at 20°C	Solvent	Metconazole	*cis*	*trans*	44721505
	acetone	363	251	117	
	methanol	403	294	117	
	dichloromethane	481	343	141	
	ethyl acetate	260	173	90.0	
	propanol	132	86.6	46.7	
	toluene	103	66.2	38.0	
	Hexane	1.40	0.929	0.483	

Table A.2. Physicochemical Properties of Metconazole

Parameter	Value	References* (MRID)
Vapor pressure (20°C)	Using gas-saturation method: $< 1.23x10^{-5}$ Pa or 9.23 x 10^{-8} mm Hg (metconazole) $< 1.04x10^{-5}$ Pa or 7.80 x 10^{-8} mm Hg (*cis*-isomer) $< 1.96x10^{-6}$ Pa or 1.47 x 10^{-8} mm Hg (*trans*-isomer)	44721505
Dissociation constant (pK_a)	11.38±0.03 and 1.06±0.03 (in water at 29.1°C using spectrophotometric method; Lot No. AC 8879-140B)	44721505
Octanol/water partition coefficient, Log(K_{OW})	At 20 °C (using flask shaking method): K_{ow} (log K_{ow}) = 7090±989 (3.85) (Lot No. AC 8879-140B) (TGAI) K_{ow} (log K_{ow}) = 7150±803 (3.85) (*cis*-isomer, CL 354,801) K_{ow} (log K_{ow}) = 6800±1700 (3.8) (*trans*-isomer, CL 354,802)	44721505
UV/visible absorption spectrum	pH / Λ / A / log ε	46808403
	cis-isomer	
	2.0 / 221.4 / 0.828 / 4.03	
	6.8 / 0.8452 / 4.04	
	7.0 / 0.9126 / 4.08	
	10.3 / 0.7226 / 3.98	
	trans-isomer	
	2.0 / 221.4 / 0.9053 / 4.07	
	7.0 / 0.9547 / 4.10	
	10.1 / 0.9893 / 4.11	

* Product Chemistry Reviews: DP #256877, Shyam Mathur, Ph.D., 9/12/2000 and DP #329168, Shyam Mathur, Ph.D., 7/13/07.

B. EXPERIMENTAL DESIGN

B.1. Application and Crop Information

In four trials conducted in IL, ND, NE, and WI, a 0.75 lb ai/gal soluble concentrate/liquid (SC/L) formulation of metconazole was applied as two broadcast foliar sprays to soybeans at 0.35-0.36 lb ai/A, with 8- to 11-day retreatment intervals, for a total rate of 0.70-0.71 lb ai/A. Applications were made in 15-20 gal/A spray volumes with a nonionic surfactant added as an adjuvant to the spray mixture. Samples of soybean seed were harvested 27-31 days after the last application of metconazole. The study use pattern is detailed in Table B.1.1.

TABLE B.1.1. Study Use Pattern.

Location (County, State; Year) Trial ID	EP[1]	Application					Tank Mix/ Adjuvants[4]
		Method; Timing	Volume[2]	Rate (lb ai/A)	RTI[3] (days)	Total Rate (lb ai/A)	
Pepin, WI; 2005 (RCN R05188)	0.75 lb/gal	1. Broadcast foliar; 50% pods final length	20.00	0.3511	8	0.70	Agri-Dex (NIS)

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TABLE B.1.1. Study Use Pattern.

Location (County, State; Year) Trial ID	EP[1]	Application					Tank Mix/ Adjuvants[4]
		Method; Timing	Volume[2]	Rate (lb ai/A)	RTI[3] (days)	Total Rate (lb ai/A)	
	SC/L	2. Broadcast foliar; 70% pods final length	19.92	0.3497			
York, NE; 2005 (RCN R05189)	0.75 lb/gal SC/L	1. Broadcast foliar; 50% pods final length	20.31	0.3551	10	0.71	Activate Plus (NIS)
		2. Broadcast foliar; 70% pods final length	20.04	0.3511			
Cass, ND; 2005 (RCN R05190)	0.75 lb/gal SC/L	1. Broadcast foliar; all pods final length	15.38	0.3517	11	0.70	Activator-90 (NIS)
		2. Broadcast foliar; 1st pods ripe, beans final color, dry and hard	19.81	0.3455			
Clinton, IL; 2005 (RCN R05191)	0.75 lb/gal SC/L	1. Broadcast foliar; 70% pods final length	18.67	0.3547	11	0.70	Preference (NIS)
		2. Broadcast foliar; all pods final length	19.37	0.345			

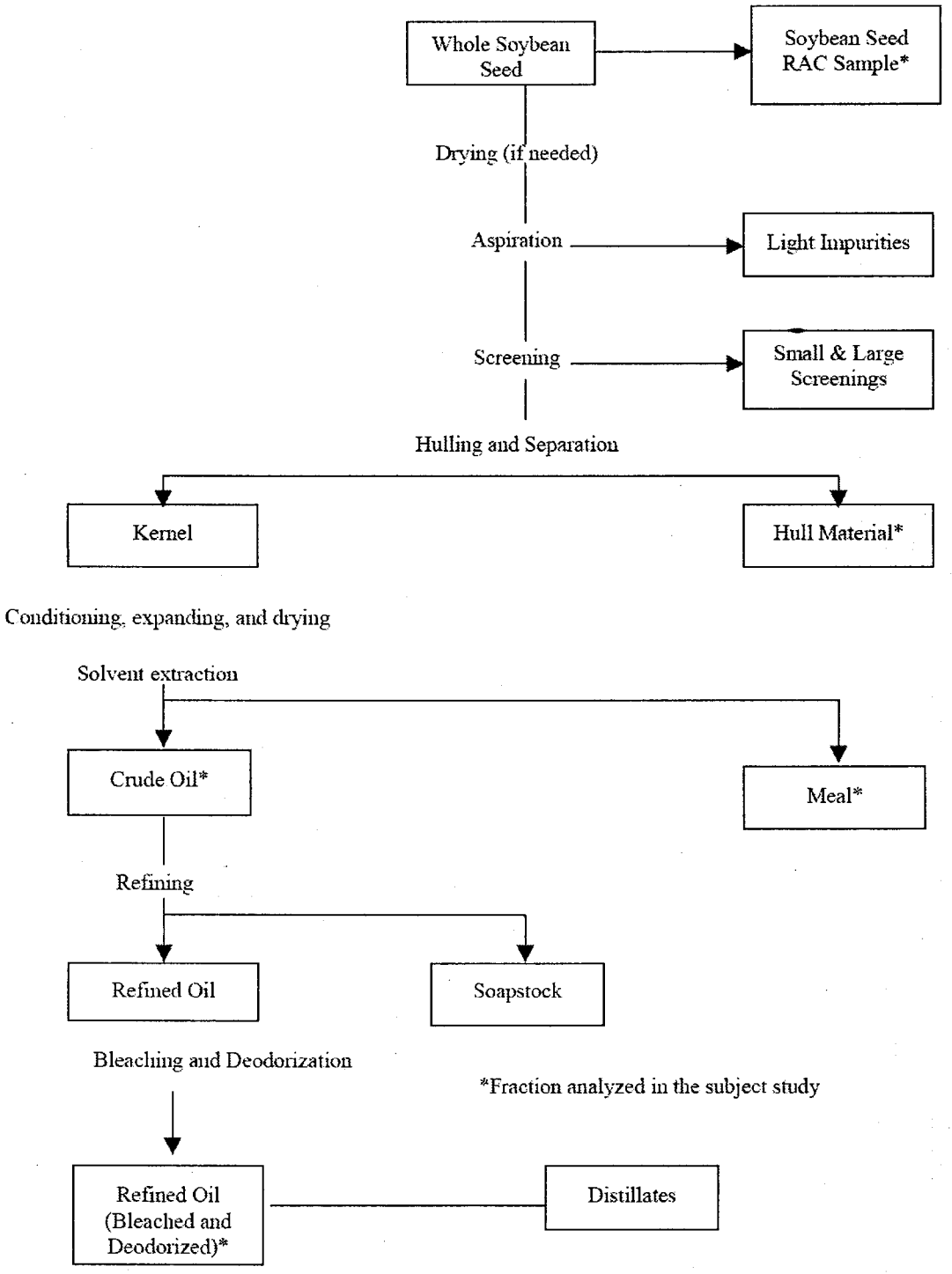
[1] EP = End-use Product
[2] Gallons per acre
[3] RTI = Retreatment Interval
[4] NIS = Non ionic surfactant

B.2. Sample Handling and Processing Procedures

Bulk samples of soybean seed (>65 lb) were harvested 27-31 days after last application from each site, and one control bulk seed sample (>65 lb) was harvested from two sites. Samples were frozen promptly at the field facilities on the day of harvest and were shipped 7-13 days later by ACDS freezer truck to the processing facility, GLP Technologies (Navasota, TX), where they were stored frozen (≤-12 °C) until processing. Samples were processed within 42 days of receipt at the facility into hulls, meal, and crude and refined oil using simulated commercial processing procedures. A flowchart of the processing procedures is presented in Figure B.2.1 (which was copied without alteration from MRID 46902301).

Soybean seed and processed samples were shipped frozen to the analytical laboratory, BASF Agro Sciences (Research Triangle Park, NC). At BASF, samples were stored frozen (≤-10 °C) until analysis.

FIGURE B.2.1. Processing Flowchart for Soybean Seed.



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B.3. Analytical Methodology

Soybean seed and processed commodities were analyzed for residues of metconazole, metabolites M11, M21, and M30, and the triazole metabolites (1,2,4-T, TA, and TAA) using an LC/MS/MS method (BASF Method D0508). A brief description of the method was included in the MRID.

Briefly, for all commodities except crude and refined oil, residues of metconazole, M11, M21, and M30 were extracted with acetonitrile (ACN):water (70:30, v:v). The extracts were diluted with methanol:water (80:20, v:v), filtered, and reserved for LC/MS/MS analysis. For determination of residues of 1,2,4-T, TA, and TAA, a separate aliquot of the initial extract was evaporated to dryness, redissolved in 0.1% formic acid in water, filtered, and reserved for LC/MS/MS analysis. An optional clean-up step was used for determination of TA in soybean seed if needed. A separate aliquot of the ACN/water extract was diluted with methanol/water and applied to an SPE cartridge; residues were eluted with 1% NH_4OH in methanol. The resulting eluate was evaporated to dryness and redissolved in 0.1% formic acid in water as for other extracts. For refined and crude oils, samples were first combined with ACN/0.1% formic acid and partitioned with hexane. The resulting ACN/water layer was diluted with ACN, and aliquots were processed as for the other commodities.

Residues of metabolites M11, M21, and M30 were converted to parent equivalents using molecular weight conversion factors of 0.95 for M11 and M21 and 0.96 for M30.
The validated LOQ was 0.01 ppm for the parent metconazole (sum of *cis* and *trans* isomers at 0.005 ppm each), M11, M21, and M30 in/on soybean samples. The validated LOQ was 0.05 ppm for 1,2,4-T, TA, and TAA. The reported limit of detection was 20% LOQ.

The method was validated concurrently with the analysis of field samples using samples of untreated soybean seed and processed commodities fortified at 0.005 and 0.5 ppm with *cis*- and *trans*-metconazole; at 0.01 and 1.00 ppm with M11, M21, and M30; and at 0.05 and 5.00 ppm with 1,2,4-T, TA, and TAA.

C. RESULTS AND DISCUSSION

The storage conditions and durations for samples from the soybean processing study are presented in Table C.2. Samples were stored frozen (<-10 °C) prior to extraction for 125-147 days (4.1-4.8 months) for soybean seeds, 85-86 days (2.8 months) for hulls, 76-77 days (2.5 months) for meal, 62 days (2.0 months) for crude oil, and 58-59 days (1.9 months) for refined oil, and were analyzed within 0-2 days of extraction. Acceptable storage stability data are available indicating that residues of all analytes are stable/relatively stable under frozen storage conditions in/on soybean seed for up to 6 months (refer to 46902223.der.doc). To support sample storage conditions and durations for processed commodities, the petitioner conducted a concurrent storage stability study which indicated that residues of *cis*- and *trans*-metconazole, M11, M21, M30, 1,2,4-T, TA, and TAA were reasonably stable during frozen storage 63- 66 days in/on soybean hulls, meal, and oil. These data are adequate to support the soybean processing study.

Concurrent method recovery data are presented in Table C.1. Samples were analyzed for residues of metconazole, metabolites M11, M21, and M30, 1,2,4-T, TA, and TAA using LC/MS/MS Method D0508. Residues of metabolites M11, M21, and M30 were converted to parent equivalents using molecular weight conversion factors of 0.95 for M11 and M21 and 0.96 for M30. The method was adequate for data collection based on acceptable concurrent method recovery data. Concurrent method recoveries were generally within the acceptable range of 70-120% for soybean RAC and processed commodities fortified at 0.005 and 0.5 ppm with *cis*- and *trans*-metconazole; at 0.01 and 1.00 ppm with M11, M21, and M30; and at 0.05 and 5.00 ppm with 1,2,4-T, TA, and TAA. Apparent residues of *cis*- and *trans*-metconazole, metabolites M11, M21, and M30, and 1,2,4-T, and TAA were each below the respective LOQs in/on all samples of untreated soybean seed, hull, meal, crude oil, and refined oil, except that detectable residues of TA were observed in/on one sample each of untreated seed (0.06 ppm), hulls (0.07 ppm), and meal (0.11 ppm) from the NE trial.

Residue data from the soybean processing study are presented in Tables C.3.1 (metconazole) and C.3.2 (triazole metabolites); HED notes that results for the metabolites M11, M21, and M30 were not included in Table C.3.1 because residues were nonquantifiable in all samples and because these metabolites were not included in calculation of processing factors. Residues of *cis*-and *trans*-metconazole in soybean seed were <0.005-0.016 and <0.005 ppm, respectively, for total metconazole residues (sum of *cis* and *trans* isomers) of <0.01-<0.021 ppm. Following processing, respective residues of *cis*-metconazole, *trans*-metconazole, and total metconazole were 0.013-0.42, <0.005-0.007, and <0.016-0.049 ppm in hulls; <0.005-0.006, <0.005, and <0.01-<0.011 ppm in meal; <0.005-0.011, <0.005, and <0.01-<0.016 ppm in crude oil; and <0.005-0.006, <0.005, and <0.01-0.011 ppm in refined oil. Residues of metabolites M11, M21, and M30 were <0.010 ppm in/on all samples of soybean seed and processed commodities.

The processing data indicate that residues of total metconazole may concentrate in hulls (average processing factor of 1.7x), but do not concentrate in meal, crude oil, or refined oil (respective processing factors of 0.6x, 0.9x, and 0.6x).

Residues of 1,2,4-T and TAA were <0.05 ppm in/on all samples of soybean seed and processed commodities. Residues of TA were <0.05-0.16 ppm in soybean seed, <0.05-0.15 ppm in hulls, 0.05-0.21 ppm in meal, and <0.05 ppm in crude and refined oil.

Because residues of 1,2,4-T and TAA were below the LOQ in all soybean samples, processing factors were not calculated. The processing data indicate that residues of TA may concentrate in hulls and meal, with average processing factors of 1.3x. Residues of TA do not concentrate in crude or refined oil (averaging processing factors of <0.4x). The petitioner noted that a reliable estimate of the concentration factor for TA could not be made because apparent residues of TA were found in samples of untreated seed (0.06 ppm), hulls (0.07 ppm) and meal (0.11 ppm) and because triazole-related compounds are naturally abundant in soybean seeds.

HED notes that processing factors were also calculated by the petitioner using total residues of *cis*- and *trans*-metconazole, M11, M21, M30. When processing factors were calculated using these values, an average processing factor of 1.2x was obtained for hulls, and processing factors

of 0.9x, 1.0x, and 0.9x, respectively were obtained for meal, crude oil, and refined oil. A data table reflecting calculation of processing factors according to this procedure is attached as an appendix to this DER.

TABLE C.1. Summary of Concurrent Recoveries of Metconazole and Metabolites from Soybean Seed and Processed Commodities.

Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean
Seed	*trans*-Metconazole	0.005	1	74	74
		0.500	1	86	86
	cis-Metconazole	0.005	1	75	75
		0.500	1	93	93
	M11	0.010	1	71	71
		1.000	1	94	94
	M21	0.010	1	81	81
		1.000	1	78	78
	M30	0.010	1	84	84
		1.000	1	95	95
	1,2,4-T	0.050	1	103	103
		5.000	1	83	83
	TA	0.050	1	77	77
		5.000	1	86	86
	TAA	0.050	1	86	86
		5.000	1	88	88
Hulls	*trans*-Metconazole	0.005	1	84	84
		0.500	1	89	89
	cis-Metconazole	0.005	1	88	88
		0.500	1	102	102
	M11	0.010	1	86	86
		1.000	1	115	115
	M21	0.010	1	82	82
		1.000	1	91	91
	M30	0.010	1	89	89
		1.000	1	104	104
	1,2,4-T	0.050	1	97	97
		5.000	1	84	84
	TA	0.050	1	84	84
		5.000	1	75	75
	TAA	0.050	1	96	96
		5.000	1	94	94
Meal	*trans*-Metconazole	0.005	1	70	70
		0.500	1	96	96
	cis-Metconazole	0.005	1	70	70
		0.500	1	87	87
	M11	0.010	1	70	70
		1.000	1	112	112

TABLE C.1. Summary of Concurrent Recoveries of Metconazole and Metabolites from Soybean Seed and Processed Commodities.

Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean
	M21	0.010	1	73	73
		1.000	1	90	90
	M30	0.010	1	67	67
		1.000	1	104	104
	1,2,4-T	0.050	1	99	99
		5.000	1	81	81
	TA	0.050	1	82	82
		5.000	1	67	67
	TAA	0.050	1	98	98
		5.000	1	99	99
Crude Oil	*trans*-Metconazole	0.005	1	103	103
		0.500	1	98	98
	cis-Metconazole	0.005	1	94	94
		0.500	1	84	84
	M11	0.010	1	91	91
		1.000	1	99	99
	M21	0.010	1	109	109
		1.000	1	93	93
	M30	0.010	1	102	102
		1.000	1	89	89
	1,2,4-T	0.050	1	80	80
		5.000	1	68	68
	TA	0.050	1	76	76
		5.000	1	97	97
	TAA	0.050	1	88	88
		5.000	1	93	93
Refined Oil	*trans*-Metconazole	0.005	1	101	101
	cis-Metconazole	0.005	1	94	94
	M11	0.010	1	98	98
	M21	0.010	1	89	89
	M30	0.010	1	101	101
	1,2,4-T	0.050	1	83	83
	TA	0.050	1	71	71
	TAA	0.050	1	99	99

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TABLE C.2. Summary of Storage Conditions.

Matrix	Storage Temperature (°C)	Actual Storage Duration[1] Days (Months)	Interval of Demonstrated Storage Stability
Whole Seed RAC	< -10	125-147 (4.1-4.8)	Acceptable storage stability data are available indicating that residues of all analytes are stable/relatively stable under frozen storage conditions in/on soybean seed for up to 6 months.[2] Residues of metconazole, M11, M21, M30, 1,2,4-T, TA, and TAA are relatively stable in/on soybean processed commodities for at least 2 months. (See Table C.2.2.)
Hulls		85-86 (2.8)	
Meal		76-77 (2.5)	
Crude Oil		62 (2.0)	
Refined Oil		58-59 (1.9)	

[1] Storage duration from harvest/processing to extraction; samples were analyzed within 0-2 days of extraction.
[2] Refer to 46902223.der.doc.

TABLE C.2.2 Stability of Metconazole, M11, M21, M30, 1,2,4-T, TA, and TAA in/on Soybean Processed Commodities Stored Frozen.

Matrix	Analyte	Spike Level (ppm)	Storage Interval (Days)[1]	Freshly fortified Recovery (%) [Average]	Stored Sample Residues (%) [Average]	Average Corrected Stored Recovery[2] (%)
Hulls	*trans*-Metconazole	0.05	63	96, 107 [102]	84, 102 [93]	91
	cis-Metconazole	0.05		111, 120 [116]	114, 116 [115]	99
	M11	0.1		113, 127 [120]	103, 111 [107]	89
	M21	0.1		93, 104 [98]	121, 126 [124]	126
	M30	0.1		97, 124 [111]	104, 117 [111]	100
	1,2,4-T	0.5		100 [100]	75, 109 [92]	92
	TA	0.5		75 [75]	65, 71 [68]	91
	TAA	0.5		92 [92]	74, 94 [84]	91
Meal	*trans*-Metconazole	0.05	63	87, 97 [92]	98, 108 [103]	112
	cis-Metconazole	0.05		97, 103 [100]	97, 106 [102]	102
	M11	0.1		116, 117 [117]	105 [105]	90
	M21	0.1		99, 120 [110]	141 [141]	128
	M30	0.1		114, 130 [122]	96, 118 [107]	88
	1,2,4-T	0.5		74, 108 [91]	94, 97 [96]	105

TABLE C.2.2 Stability of Metconazole, M11, M21, M30, 1,2,4-T, TA, and TAA in/on Soybean Processed Commodities Stored Frozen.

Matrix	Analyte	Spike Level (ppm)	Storage Interval (Days)[1]	Freshly fortified Recovery (%) [Average]	Stored Sample Residues (%) [Average]	Average Corrected Stored Recovery[2] (%)
	TA	0.5		70, 74 [72]	49, 63 [56]	78
	TAA	0.5		84, 94 [89]	65, 80 [73]	81
Oil	*trans*-Metconazole	0.05	66	82, 83 [82]	74, 81 [78]	95
	cis-Metconazole	0.05		85, 90 [87]	93, 100 [97]	111
	M11	0.1		84, 95 [90]	101, 107 [104]	116
	M21	0.1		91, 94 [93]	102, 106 [104]	112
	M30	0.1		97, 100 [99]	98, 100 [99]	100
	1,2,4-T	0.5		60, 74 [67]	63, 78 [71]	105
	TA	0.5		96, 102 [99]	77, 97 [87]	88
	TAA	0.5		102, 102 [102]	89, 98 [94]	92

[1] Interval from fortification to extraction
[2] Residues were corrected for concurrent recovery in freshly fortified samples.

TABLE C.3.1. Residue Data for Metconazole from Soybean Processing Study with Metconazole.

Location (County, State; Year) Trial ID	Processed Commodity	Total Rate (lb ai/A)	PHI (days)	Metconazole Residues (ppm)			Processing Factor[1]	Average Processing Factor[2]
				cis-Metconazole	*trans*-Metconazole	Total Metconazole	Total Metconazole	Total Metconazole
Pepin, WI; 2005 (RCN R05188)	Seed RAC	0.70	31	<0.005	<0.005	<0.010	--	--
	Hulls			0.017	<0.005	<0.022	2.2x	1.7x
	Meal			<0.005	<0.005	<0.010	NC	0.6x
	Crude Oil			<0.005	<0.005	<0.010	NC	0.9x
	Refined Oil			<0.005	<0.005	<0.010	NC	0.6x
York, NE; 2005 (RCN R05189)	Seed RAC	0.71	31	0.016	<0.005	<0.021	--	
	Hulls			0.013	<0.005	<0.018	0.9x	
	Meal			0.005	<0.005	<0.010	0.5x	
	Crude Oil			0.011	<0.005	<0.016	0.8x	
	Refined Oil			<0.005	<0.005	<0.010	0.5x	
Cass, ND; 2005 (RCN R05190)	Seed RAC	0.70	27	0.014	<0.005	<0.019	--	
	Hulls			0.042	0.007	<0.049	2.6x	
	Meal			<0.005	<0.005	<0.010	0.5x	
	Crude Oil			0.011	<0.005	<0.016	0.8x	
	Refined Oil			0.005	<0.005	<0.010	0.5x	

TABLE C.3.1. Residue Data for Metconazole from Soybean Processing Study with Metconazole.

Location (County, State; Year) Trial ID	Processed Commodity	Total Rate (lb ai/A)	PHI (days)	Metconazole Residues (ppm)			Processing Factor[1]	Average Processing Factor[2]
				cis-Metconazole	*trans*-Metconazole	Total Metconazole	Total Metconazole	Total Metconazole
Clinton, IL; 2005 (RCN R05191)	Seed RAC	0.70	29	0.011	<0.005	<0.016	--	
	Hulls			0.015	<0.005	<0.020	1.2x	
	Meal			0.006	<0.005	<0.011	0.7x	
	Crude Oil			0.011	<0.005	<0.016	1.0x	
	Refined Oil			0.006	<0.005	<0.011	0.7x	

[1] Processing factors calculated by dividing the residue in the processed fraction by the residue in the soybean seed (RAC). NC = Not calculated because residues were nonquantifiable in both the RAC and the processed commodity.
[2] Average from all trials for which processing factors were calculated.

TABLE C.3.2 Residue Data for the Triazole Metabolites from Soybean Processing Study with Metconazole.

Location (County, State; Year) Trial ID	Processed Commodity	Total Rate (lb ai/A)	PHI (days)	Triazole-Related Compounds (ppm)						
				1,2,4-T	Processing Factor[1]	TA	Processing Factor[1]	Average Processing Factor[2]	TAA	Processing Factor[1]
Pepin, WI; 2005 (RCN R05188)	Seed RAC	0.70	31	<0.05	--	<0.05	--	--	<0.05	--
	Hulls			<0.05	NC	0.15	3.0x	1.3x	<0.05	NC
	Meal			<0.05	NC	0.05	1.0x	1.3x	<0.05	NC
	Crude Oil			<0.05	NC	<0.05	NC	<0.4x	<0.05	NC
	Refined Oil			<0.05	NC	<0.05	NC	<0.4x	<0.05	NC
York, NE; 2005 (RCN R05189)	Seed RAC	0.71	31	<0.05	--	0.12	--		<0.05	--
	Hulls			<0.05	NC	<0.05	<0.4x		<0.05	NC
	Meal			<0.05	NC	0.21	1.8x		<0.05	NC
	Crude Oil			<0.05	NC	<0.05	<0.4x		<0.05	NC
	Refined Oil			<0.05	NC	<0.05	<0.4x		<0.05	NC
Cass, ND; 2005 (RCN R05190)	Seed RAC	0.70	27	<0.05	--	0.10	--		<0.05	--
	Hulls			<0.05	NC	0.13	1.3x		<0.05	NC
	Meal			<0.05	NC	0.12	1.2x		<0.05	NC
	Crude Oil			<0.05	NC	<0.05	<0.5x		<0.05	NC
	Refined Oil			<0.05	NC	<0.05	<0.5x		<0.05	NC
Clinton, IL; 2005 (RCN R05191)	Seed RAC	0.70	29	<0.05	--	0.16	--		<0.05	--
	Hulls			<0.05	NC	0.08	0.5x		<0.05	NC
	Meal			<0.05	NC	0.17	1.1x		<0.05	NC
	Crude Oil			<0.05	NC	<0.05	<0.3x		<0.05	NC
	Refined Oil			<0.05	NC	<0.05	<0.3x		<0.05	NC

[1] Processing factors calculated by dividing the residue in the processed fraction by the residue in the soybean seed (RAC). NC = Not calculated.
[2] Average from all trials for which processing factors were calculated.

D. CONCLUSION

Total metconazole residues (sum of *cis* and *trans* isomers) were <0.01-<0.021 ppm in/on soybean seed, and <0.016-0.049 ppm in hulls, <0.01-<0.011 ppm in meal, <0.01-0.016 ppm in crude oil, and <0.01-0.011 ppm in refined oil. Residues of metabolites M11, M21, and M30 were <0.010 ppm in/on all samples of soybean RAC and processed commodities.

The processing data indicate that residues of total metconazole may concentrate in hulls (average processing factor of 1.7x), but do not concentrate in meal, crude oil, or refined oil (respective processing factors of 0.6x, 0.9x, and 0.6x). The processing data also suggest that residues of TA may concentrate in hulls and meal, with average processing factors of 1.3x; however, this estimate is complicated by the observation of apparent detectable residues of TA in samples of untreated seed, hulls, and meal and the natural occurrence of triazole-related compounds in soybean seed.

Acceptable methods were used for quantitation of residues of *cis*- and *trans*-metconazole, M11, M21, M30, 1,2,4-T, TA, and TAA in/on soybean samples, and the study is supported by adequate storage stability data.

E. REFERENCES

DP#:	324541
Subject:	Metconazole. Request for a Tolerance on Imported Bananas. Summary of Analytical Chemistry and Residue Data. Petition Number 9E05052.
From:	N. Dodd
To:	M. Waller
Date:	12/14/05
MRIDs:	44721506, 44721507, 44721508, 44721509, 44721510, and 44721511

F. DOCUMENT TRACKING

RDI: N. Dodd (2/20/08)
Petition Numbers: 6F7094 and 6F7095
DP#s: 348168 and 348206
PC Code: 125619

Template Version June 2005

APPENDIX I. Calculation of Processing Factors for Combined Residues of cis- and trans-Metconazole, M11, M21, and M30.

Residue Data for Metconazole, M11, M21, M30 from Processing Study with Metconazole.

Location (County, State; Year) Trial ID	Processed Commodity	Total Rate (lb ai/A)	PHI (days)	Metconazole Residues (ppm)							Processing Factor[3]
				Parent metconazole			Metabolites[1]			Total[2]	
				Cis	Trans	Total	M11	M21	M30		
Pepin, WI; 2005 (RCN R05188)	Seed RAC	0.70	31	<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04	--
	Hulls			0.017	<0.005	<0.022	<0.01	<0.01	<0.01	0.05	1.2x
	Meal			<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04	1.0x
	Crude Oil			<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04	1.0x
	Refined Oil			<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04	1.0x
York, NE; 2005 (RCN R05189)	Seed RAC	0.71	31	0.016	<0.005	<0.021	<0.01	<0.01	<0.01	0.05	--
	Hulls			0.013	<0.005	<0.018	<0.01	<0.01	<0.01	0.05	1.0x
	Meal			0.005	<0.005	<0.010	<0.01	<0.01	<0.01	0.04	0.8x
	Crude Oil			0.011	<0.005	<0.016	<0.01	<0.01	<0.01	0.05	1.0x
	Refined Oil			<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04	0.8x
Cass, ND; 2005 (RCN R05190)	Seed RAC	0.70	27	0.014	<0.005	<0.019	<0.01	<0.01	<0.01	0.05	--
	Hulls			0.042	0.007	<0.049	<0.01	<0.01	<0.01	0.08	1.6x
	Meal			<0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04	0.8x
	Crude Oil			0.011	<0.005	<0.016	<0.01	<0.01	<0.01	0.05	1.0x
	Refined Oil			0.005	<0.005	<0.010	<0.01	<0.01	<0.01	<0.04	0.8x
Clinton, IL; 2005 (RCN R05191)	Seed RAC	0.70	29	0.011	<0.005	<0.016	<0.01	<0.01	<0.01	0.05	--
	Hulls			0.015	<0.005	<0.020	<0.01	<0.01	<0.01	0.05	1.0x
	Meal			0.006	<0.005	<0.011	<0.01	<0.01	<0.01	0.04	0.8x
	Crude Oil			0.11	<0.005	<0.115	<0.01	<0.01	<0.01	0.05	1.0x
	Refined Oil			0.006	<0.005	<0.011	<0.01	<0.01	<0.01	0.04	0.8x

[1] Expressed in parent equivalents.
[2] Total = total residue; the sum of *cis*- and *trans*-metconazole, M11, M21, and M30; values presented as calculated and reported by the petitioner.
[3] Processing factors calculated by dividing the residue in the processed fraction by the residue in the soybean seed (RAC); values presented as calculated and reported by the petitioner.

Primary Evaluator	This DER was originally prepared under contract by Dynamac Corporation.
Approved by	Nancy Dodd, Chemist *Nancy Dodd* Date: 2/20/08 Registration Action Branch 3 Health Effects Division (7509P)

This DER was originally prepared under contract by Dynamac Corporation (2275 Research Boulevard, Suite 300; Rockville, MD 20850; submitted 09/17/2007). The DER has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

46902302 Jordan, J.; Saha, M. (2006) Magnitude of Residues of Metconazole (BAS 555 F) and its Metabolites in Sugar Beets and Sugar Beet Processed Fractions Following Applications of BAS 555 01F: Final Report. Project Number: 137735, 2006/7006727. Unpublished study prepared by BASF Corporation, Agresources, Inc. and Prairie Agricultural Research, Inc. 206 p.

EXECUTIVE SUMMARY:

BASF Corporation has submitted a processing study with sugar beets. In four trials conducted in CA, ID, SD, and WI, a 0.75 lb ai/gal soluble concentrate/liquid (SC/L) formulation of metconazole was applied as two broadcast foliar sprays to sugar beets at ~0.50 lb ai/A, with ~14 day retreatment intervals, for a total rate of ~1.00 lb ai/A. Applications were made in ~25 gal/A spray volumes with a nonionic surfactant added as an adjuvant to the spray mixture. Sugar beet root samples were harvested 14-15 days after the last application of metconazole, and processed into refined sugar, dried pulp, and molasses using simulated commercial processing procedures. In addition, extracted pulp, pressed water, raw juice, lime sludge, thin juice, thick juice, and raw sugar were collected for analysis.

Samples of sugar beet root and processed commodities were analyzed for residues of *cis*- and *trans*-metconazole, metabolites M11, M21, and M30, and the triazole metabolites [1,2,4-triazole (1,2,4-T), triazolylalanine (TA), and triazolylacetic acid (TAA)] using an LC/MS/MS method (BASF Method D0508). Residues of metabolites M11, M21, and M30 were converted to parent equivalents using molecular weight conversion factors of 0.95 for M11 and M21 and 0.96 for M30. The validated limit of quantitation (LOQ) was 0.01 ppm each for parent metconazole (sum of *cis*- and *trans*-isomer at 0.005 ppm each), M11, M21, and M30 in/on sugar beet root and processed commodities. The LOQ was 0.05 ppm for 1,2,4-T, TA, and TAA. The method was adequate for data collection based on acceptable concurrent method recovery data.

Samples of sugar beet root were stored frozen (<-10 °C) prior to analysis for 161-202 days (5.3-6.6 months); sugar beet processed commodities were stored for 21-45 days (0.7-1.5 months). Adequate storage stability data are available to support the storage conditions and durations of

the sugar beet root samples. Because processed samples were stored for just over one month, no data are required to support the storage conditions and durations for sugar beet processed commodities. No additional data are required to support the sugar beet processing study.

Residues of *cis*-and *trans*-metconazole in/on sugar beet root were <0.005-0.0128 and <0.005 ppm, respectively, for total metconazole residues (sum of *cis* and *trans* isomers) of <0.01-<0.0232 ppm. Following processing, respective residues of *cis*-metconazole, *trans*-metconazole, and total metconazole were 0.0089-0.7951, <0.005-0.1181, and <0.0139-0.9131 ppm in dried pulp; 0.0101-0.0722, <0.005-0.0110, and <0.0151-0.0832 ppm in molasses; and <0.005-0.0216, <0.005, and <0.01-<0.266 ppm in refined sugar. Residues of metabolites M11, M21, and M30 were <0.010 ppm in/on all samples of sugar beet root and processed commodities, except that residues of M21 were detected in one sample of dried pulp at 0.0137 ppm.

The processing data indicate that residues of total metconazole may concentrate in dried pulp (average processing factor of 14x), and molasses (average processing factor of 1.9x), but do not concentrate in refined sugar (average processing factor of 0.8x). Based on average processing factors for the remaining processed commodities, total metconazole residues do not concentrate in water, raw juice, lime sludge, or thin juice (processing factors 0.6-1x), but may concentrate in pulp, thick juice, and raw sugar (processing factors of 1.3-2.2x).

The calculated processing factors for dried pulp, molasses and sugar do not exceed the maximum theoretical concentration factor of >20x for sugar beets (OPPTS 860.1520, Table 1).

Residues of 1,2,4-T, TA, and TAA were below the LOQ (<0.05 ppm) in/on all samples of sugar beet root, and in most processed commodities. Residues of TA were <0.05-0.17 ppm in molasses and <0.05-0.14 ppm in raw sugar.

The processing data indicate that residues of TA may concentrate in molasses and raw sugar (processing factors of >2.3x for both).

HED notes that processing factors were also calculated by the petitioner using total residues of *cis*- and *trans*-metconazole, M11, M21, and M30. When processing factors were calculated using these values, an average processing factor of 6.8x was obtained for dried pulp, and a processing factor of 1.4x was obtained for molasses. A data table reflecting calculation of processing factors according to this procedure is attached as an appendix to this DER.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the processed commodity residue data are classified as scientifically acceptable.

The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP#s 348168 and 348206.

COMPLIANCE:

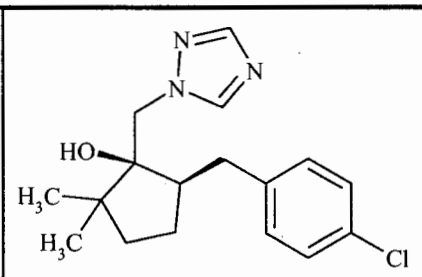
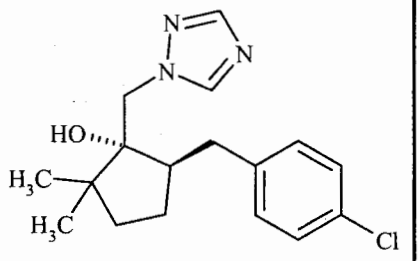
Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported.

A. BACKGROUND INFORMATION

Metconazole [5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol] is a broad-spectrum triazole Group 3 fungicide (sterol biosynthesis inhibitors). There are currently no registered uses of metconazole in the U.S.; however, a tolerance has been established for banana, and a Section 18 emergency exemption and supporting time-limited tolerances have been granted for use on soybean. BASF Corporation has applied for registration of metconazole in the U.S. for use on barley, oats, rye, soybeans, sugar beets, triticale, and wheat.

The chemical structure and nomenclature of metconazole, and the physicochemical properties of the technical grade of metconazole are presented in Tables A.1 and A.2.

TABLE A.1. Metconazole Nomenclature.

Chemical structure	 *cis*-isomer  *trans*-isomer
Common name	Metconazole
Company experimental name	KNF-S-474m (Kureha); BAS 555 F (BASF); V-10116 (Valent)
IUPAC name	(1RS,5RS:1RS,5SR)-5-(4-chlorobenzyl)-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol
CAS name	5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol
CAS registry number	125116-23-6 (cis- and *trans*-isomers) 115850-27-6 (*cis*-isomer) 115850-28-7 (*trans*-isomer)
End-use products (EP)	50% WDG (Metconazole 50 WDG Fungicide, EPA File Symbol 59639-RUT) 0.75 lb/gal SC/L (Caramba™ Fungicide, EPA File Symbol No. 7969-EUA) 0.67 lb/gal SC/L formulation (BAS 556 01F Fungicide, EPA File Symbol No. 7969-EUT; also contains the active ingredient pyraclostrobin at 0.83 lb/gal)

750

TABLE A.1. Metconazole Nomenclature.

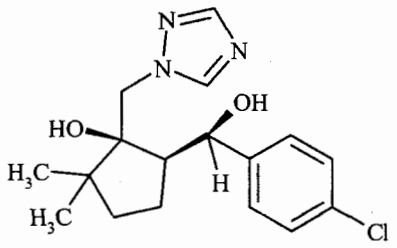
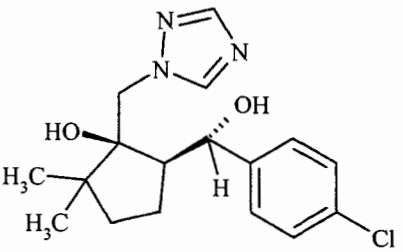
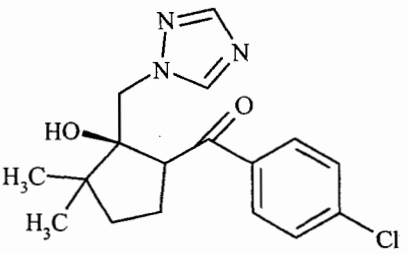
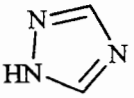
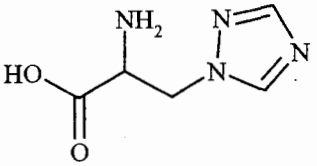
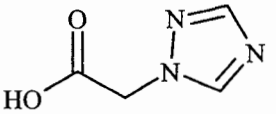
 Metconazole metabolite M11	 Metconazole metabolite M21	 Metconazole metabolite M30
 Triazole metabolite 1,2,4-triazole (1,2,4-T)	 Triazole metabolite trizolylalanine (TA)	 Triazole metabolite triazolylacetic acid (TAA)

Table A.2. Physicochemical Properties of Metconazole

Parameter	Value				References* (MRID)
Melting point/range	100.0-108.4°C (using Electrothermal Digital Melting Point Apparatus) (AC900,768 technical grade)				44721505
pH	5.81 at 25°C (1% aqueous suspension)				46808402
Relative density (20°C)	1.14 (relative density to water at 4°C, using capillary-stoppered, density-specific gravity bottle) (Lot No. AC 8879-140B)				44721505
Water solubility (20°C)	Using shake-flask method: 18.7 ± 1.0 mg/L (*cis*-isomer, WL148271, KNF-S-474m) 13.6 ± 1.7 mg/L (*trans*-isomer, WL148271, KNF-S-474m)				44721505
Solvent solubility (g/L) at 20°C	Solvent	Metconazole	*cis*	*trans*	44721505
	acetone	363	251	117	
	methanol	403	294	117	
	dichloromethane	481	343	141	
	ethyl acetate	260	173	90.0	
	propanol	132	86.6	46.7	
	toluene	103	66.2	38.0	
	Hexane	1.40	0.929	0.483	
Vapor pressure (20°C)	Using gas-saturation method: $< 1.23 \times 10^{-5}$ Pa or 9.23×10^{-8} mm Hg (metconazole) $< 1.04 \times 10^{-5}$ Pa or 7.80×10^{-8} mm Hg (*cis*-isomer) $< 1.96 \times 10^{-6}$ Pa or 1.47×10^{-8} mm Hg (*trans*-isomer)				44721505
Dissociation constant (pK_a)	11.38±0.03 and 1.06±0.03 (in water at 29.1°C using spectrophotometric method; Lot No. AC 8879-140B)				44721505

Table A.2. Physicochemical Properties of Metconazole					
Parameter	Value				References* (MRID)
Octanol/water partition coefficient, Log(K_{OW})	At 20 °C (using flask shaking method): K_{ow} (log K_{ow}) = 7090±989 (3.85) (Lot No. AC 8879-140B) (TGAI) K_{ow} (log K_{ow}) = 7150±803 (3.85) (*cis*-isomer, CL 354,801) K_{ow} (log K_{ow}) = 6800±1700 (3.8) (*trans*-isomer, CL 354,802)				44721505
UV/visible absorption spectrum	pH	λ	A	log ε	46808403
	cis-isomer				
	2.0	221.4	0.828	4.03	
	6.8		0.8452	4.04	
	7.0		0.9126	4.08	
	10.3		0.7226	3.98	
	trans-isomer				
	2.0	221.4	0.9053	4.07	
	7.0		0.9547	4.10	
	10.1		0.9893	4.11	

* Product Chemistry Reviews: DP #256877, Shyam Mathur, Ph.D., 9/12/2000 and DP #329168, Shyam Mathur, Ph.D., 7/13/07.

B. EXPERIMENTAL DESIGN

B.1. Application and Crop Information

In four trials conducted in CA, ID, SD, and WI, a 0.75 lb ai/gal soluble concentrate/liquid (SC/L) formulation of metconazole was applied as two broadcast foliar sprays to sugar beets at ~0.50 lb ai/A, with ~14 day retreatment intervals, for a total rate of ~1.00 lb ai/A. Applications were made in ~25 gal/A spray volumes with a nonionic surfactant added as an adjuvant to the spray mixture. Sugar beet root samples were harvested 14-15 days after the last application of metconazole. The study use pattern is detailed in Table B.1.1.

TABLE B.1.1. Study Use Pattern.							
Location (County, State; Year) Trial ID	EP[1]	Application					Tank Mix/ Adjuvants[4]
		Method; Timing	Volume[2]	Rate (lb ai/A)	RTI[3] (days)	Total Rate (lb ai/A)	
Pepin, WI; 2005 (RCN R05097)	0.75 lb/gal SC/L	1. Broadcast foliar; contact of 80% of plants in adjacent rows	20.04	0.4941	15	0.99	AgriDex (NIS)
		2. Broadcast foliar; crop cover complete	19.99	0.5005			AgriDex (NIS)
Brown, SD; 2005 (RCN R05098)	0.75 lb/gal SC/L	1. Broadcast foliar; contact of 80% of plants in adjacent rows	20.02	0.5002	14	1.00	Preference (NIS)
		2. Broadcast foliar; crop cover complete	20.03	0.5002			Preference (NIS)

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TABLE B.1.1. Study Use Pattern.

Location (County, State; Year) Trial ID	EP[1]	Application					Tank Mix/ Adjuvants[4]
		Method; Timing	Volume[2]	Rate (lb ai/A)	RTI[3] (days)	Total Rate (lb ai/A)	
Fresno, CA; 2005 (RCN R05099)	0.75 lb/gal SC/L	1. Broadcast foliar; beet root harvestable size	20.30	0.5090	13	1.01	AgriDex (NIS)
		2. Broadcast foliar; contact between 70% of plants in adjacent rows	19.93	0.4988			AgriDex (NIS)
Payette, ID; 2005 (RCN R05100)	0.75 lb/gal SC/L	1. Broadcast foliar; crop cover complete	29.96	0.4984	14	1.00	Preference (NIS)
		2. Broadcast foliar; beet root harvestable size	29.85	0.4967			Preference (NIS)

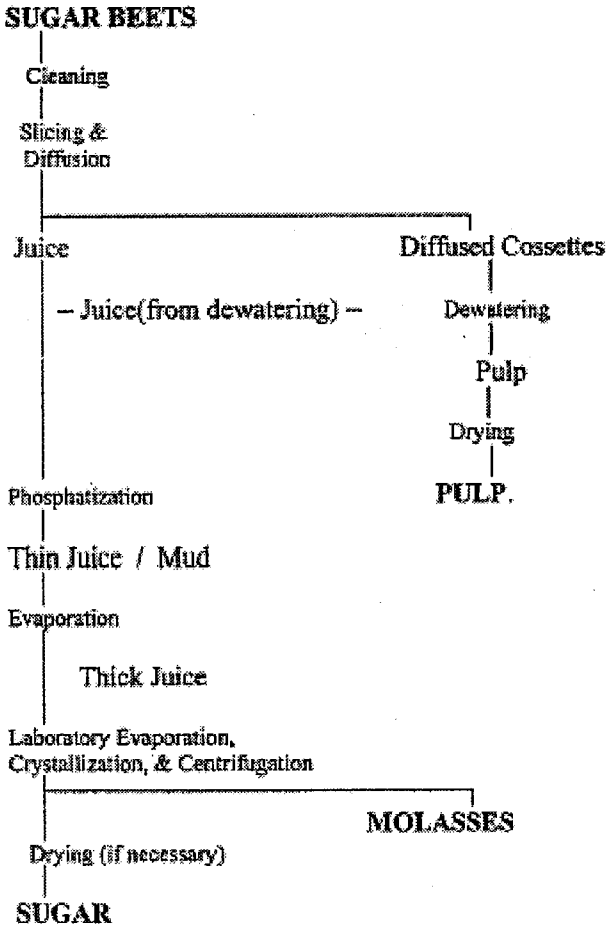
[1] EP = End-use Product
[2] Gallons per acre
[3] RTI = Retreatment Interval
[4] NIS= nonionic surfactant

B.2. Sample Handling and Processing Procedures

Sugar beet root samples were shipped overnight to the processing facility, GLP Technologies (Navasota, TX), under ambient temperatures within 0-1 day of harvest or were promptly transferred to freezers on the day of harvest and shipped 14 days later by ACDS freezer truck to GLP Technologies, where they were stored frozen (≤-12 °C) prior to processing. Samples were processed, within 125-167 days of receipt, into dried pulp, molasses, and refined sugar using simulated commercial processing procedures. In addition, extracted pulp, pressed water, raw juice, lime sludge, thin juice, thick juice, and raw sugar were collected for analysis. The petitioner noted that isolated rises in temperature (up to 58 °F) occurred prior to processing due to freezer malfunctions, but that there was no evidence of samples having thawed during this incident. A flowchart of the processing procedures is presented in Figure B.2.1 (which was copied without alteration from MRID 46902302).

Sugar beet root and processed samples were shipped, within 1-15 days of completion of processing, overnight on dry ice to the analytical laboratory, BASF Agro Research (Research Triangle Park, NC), where samples were stored frozen (≤-10 °C) until analysis.

FIGURE B.2.1. Processing Flowchart for Sugar beets.



B.3. Analytical Methodology

Samples of sugar beet root and processed commodities were analyzed for residues of *cis*- and *trans*-metconazole, metabolites M11, M21, and M30, and the triazole metabolites 1,2,4-T, TA, and TAA using LC/MS/MS Method D0508. A description of the method was included with the MRID.

Briefly, for all commodities except molasses and sugar, residues of metconazole, M11, M21, and M30 were extracted with acetonitrile (ACN):water (70:30, v:v). The extracts were diluted with methanol:water (80:20, v:v), filtered, and reserved for LC/MS/MS analysis. For determination of residues of 1,2,4-T, TA, and TAA, a separate aliquot of the initial extract was evaporated to dryness, redissolved in 0.1% formic acid in water, filtered, and reserved for LC/MS/MS analysis. Residues of metabolites M11, M21, and M30 were converted to parent equivalents using molecular weight conversion factors of 0.95 for M11 and M21 and 0.96 for M30.

For determination of residues in molasses and sugar, samples were extracted with ACN:water (50:50, v:v) and centrifuged. The extract was evaporated to dryness, and redissolved in methanol/water for analysis for metconazole, M21, M11, and M30, or mixed with water, concentrated, and diluted with 0.1% formic acid for analysis of the triazole metabolites. For determination of residues of TA in molasses and sugar, an aliquot of the original extract was cleaned up on an SPE column; residues were eluted with NH_4OH in methanol.

The validated limit of quantitation (LOQ) was 0.01 ppm each for parent metconazole (sum of *cis*- and *trans*-isomer at 0.005 ppm each), M11, M21, and M30 in/on sugar beet root and processed commodities. The LOQ was 0.05 ppm for 1,2,4-T, TA, and TAA.

The method was validated concurrently with the analysis of field samples, using samples of untreated sugar beet root, juice, molasses, dried pulp, raw sugar, and water fortified at 0.005 and 0.5 ppm with *cis*- and *trans*-metconazole; at 0.01 and 1.00 ppm with M11, M21, and M30; and at 0.05 and 5.00 ppm with 1,2,4-T, TA, and TAA.

C. RESULTS AND DISCUSSION

The storage conditions and durations for samples from the sugar beet processing study are presented in Table C.2. Samples of sugar beet root were stored frozen (<-10 °C) prior to analysis for 161-202 days (5.3-6.6 months); sugar beet processed commodities were stored for 21-45 days (0.7-1.5 months). For sugar beet root, adequate storage stability data are available indicating that: (1) residues of *cis*- and *trans*-metconazole are relatively stable under frozen storage conditions in/on radish roots for up to 6 months; (2) residues of M11, M21, and M30 are stable in/on sugar beet root for up to 6 months; and (3) residues of 1,2,4-T, TA, and TAA are stable in/on radish roots for up to 6 months (refer to 46902223.der.doc). Because processed samples were stored for just over one month, no data are required to support the storage conditions and durations for sugar beet processed commodities. No additional data are required to support the sugar beet processing study.

Concurrent method recovery data are presented in Table C.1. Samples were analyzed for residues of metconazole, M11, M21, M30, 1,2,4-T, TA, and TAA using LC/MS/MS Method D0508. Residues of metabolites M11, M21, and M30 were converted to parent equivalents using molecular weight conversion factors of 0.95 for M11 and M21 and 0.96 for M30. The method was adequate for data collection based on acceptable concurrent method recovery data. Concurrent method recoveries were generally within the acceptable range of 70-120% for sugar beet root, juice, molasses, dried pulp, raw sugar, and water fortified at 0.005 and 0.5 ppm with *cis*- and *trans*-metconazole; at 0.01 and 1.00 ppm with M11, M21, and M30; and at 0.05 and 5.00 ppm with 1,2,4-T, TA, and TAA. Low recoveries (61-66%) were obtained for M30 in raw sugar (at both fortifications) and molasses (at 1.0 ppm), for 1,2,4-T in dried pulp (at 0.05 ppm), and for TA in root (at 0.05 ppm).

Residue data from the sugar beet processing study are presented in Tables C.3.1 (metconazole) and C.3.2 (triazole metabolites). HED notes that results for the metabolites M11, M21, and M30 were not included in Table C.3.1 because residues were nonquantifiable in all but one sample

(i.e., except in one sample of dried pulp) and because these metabolites were not included in calculation of processing factors. Residues of *cis*-and *trans*-metconazole in sugar beet root were <0.005-0.0128 and <0.005 ppm, respectively, for total metconazole residues (sum of *cis* and *trans* isomers) of <0.01-<0.0232 ppm. Following processing, respective residues of *cis*-metconazole, *trans*-metconazole, and total metconazole were: 0.0089-0.7951, <0.005-0.1181, and <0.0139-0.9131 ppm in dried pulp; 0.0101-0.0722, <0.005-0.0110, and <0.0151-0.0832 in molasses; and <0.005-0.0216, <0.005, and <0.01-<0.266 ppm in refined sugar. Residues of metabolites M11, M21, and M30 were <0.010 ppm in/on all samples of sugar beet root and processed commodities, except that residues of M21 were detected in one sample of dried pulp at 0.0137 ppm.

The processing data indicate that residues of total metconazole may concentrate in dried pulp (average processing factor of 14x) and molasses (average processing factor of 1.9x), but do not concentrate in refined sugar (average processing factor of 0.8x). Based on average processing factors for the remaining processed commodities, total metconazole residues do not concentrate in water, raw juice, lime sludge and thin juice (processing factors 0.6-1x), but may concentrate in pulp, thick juice, and raw sugar (processing factors of 1.3-2.2x).

Residues of 1,2,4-T, TA, and TAA were below the LOQ (<0.05 ppm) in/on all samples of sugar beet root and in most processed commodities. Residues of TA were <0.05-0.17 ppm in molasses and <0.05-0.14 ppm in raw sugar.

The processing data indicate that residues of TA may concentrate in molasses and raw sugar (processing factors of >2.3x for both).

HED notes that processing factors were also calculated by the petitioner using total residues of *cis*- and *trans*-metconazole, M11, M21, and M30. When processing factors were calculated using these values, an average processing factor of 6.8x was obtained for dried pulp, and a processing factor of 1.4x was obtained for molasses. A data table reflecting calculation of processing factors according to this procedure is attached as an appendix to this DER.

TABLE C.1. Summary of Concurrent Recoveries of Metconazole and Metabolites from Sugar Beet Root and Processed Commodities.

Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean (%)
Root	*trans*-Metconazole	0.005	1	68	68
		0.50	1	67	67
	cis-Metconazole	0.005	1	93	93
		0.50	1	75	75
	M11	0.01	1	98	98
		1.0	1	78	78
	M21	0.01	1	100	100
		1.0	1	78	78
	M30	0.01	1	88	88
		1.0	1	84	84
	1,2,4-T	0.05	1	104	104

TABLE C.1. Summary of Concurrent Recoveries of Metconazole and Metabolites from Sugar Beet Root and Processed Commodities.

Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean (%)
		5.0	1	73	73
	TA	0.05	1	61	61
		5.0	1	104	104
	TAA	0.05	1	75	75
		5.0	1	89	89
Juice	*trans*-Metconazole	0.005	1	88	88
		0.50	1	89	89
	cis-Metconazole	0.005	1	103	103
		0.50	1	95	95
	M11	0.01	1	95	95
		1.0	1	99	99
	M21	0.01	1	88	88
		1.0	1	81	81
	M30	0.01	1	92	92
		1.0	1	85	85
	1,2,4-T	0.05	1	79	79
		5.0	1	102	102
	TA	0.05	1	86	86
		5.0	1	97	97
	TAA	0.05	1	93	93
		5.0	1	85	85
Molasses	*trans*-Metconazole	0.005	1	80	80
		0.50	1	108	108
	cis-Metconazole	0.005	1	97	97
		0.50	1	76	76
	M11	0.01	1	89	89
		1.0	1	91	91
	M21	0.01	1	93	93
		1.0	1	93	93
	M30	0.01	1	68	68
		1.0	1	63	63
	1,2,4-T	0.05	1	94	94
		5.0	1	105	105
	TA	0.05	1	90	90
		5.0	1	95	95
	TAA	0.05	1	111	111
		5.0	1	118	118
Dried pulp	*trans*-Metconazole	0.005	2	75, 88	82
		0.50	2	70, 101	86
	cis-Metconazole	0.005	2	87, 87	87
		0.50	2	80, 102	91
	M11	0.01	2	94, 97	96

TABLE C.1. Summary of Concurrent Recoveries of Metconazole and Metabolites from Sugar Beet Root and Processed Commodities.

Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean (%)
		1.0	2	95, 113	104
	M21	0.01	2	80, 92	86
		1.0	2	90, 105	98
	M30	0.01	2	91, 103	97
		1.0	2	94, 116	105
	1,2,4-T	0.05	1	65	65
		5.0	1	69	69
	TA	0.05	1	96	96
		5.0	1	99	99
	TAA	0.05	1	93	93
		5.0	1	89	89
Raw sugar	*trans*-Metconazole	0.005	1	74	74
		0.50	1	120	120
	cis-Metconazole	0.005	1	95	95
		0.50	1	81	81
	M11	0.01	1	83	83
		1.0	1	89	89
	M21	0.01	1	87	87
		1.0	1	94	94
	M30	0.01	1	61	61
		1.0	1	66	66
	1,2,4-T	0.05	1	85	85
		5.0	1	103	103
	TA	0.05	1	107	107
		5.0	1	88	88
	TAA	0.05	1	101	101
		5.0	1	93	93
Water	*trans*-Metconazole	0.005	1	92	92
		0.50	1	92	92
	cis-Metconazole	0.005	1	90	90
		0.50	1	94	94
	M11	0.01	1	114	114
		1.0	1	101	101
	M21	0.01	1	114	114
		1.0	1	77	77
	M30	0.01	1	112	112
		1.0	1	103	103
	1,2,4-T	0.05	1	72	72
		5.0	1	91	91
	TA	0.05	1	80	80
		5.0	1	91	91
	TAA	0.05	1	84	84

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TABLE C.1. Summary of Concurrent Recoveries of Metconazole and Metabolites from Sugar Beet Root and Processed Commodities.

Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean (%)
		5.0	1	87	87

TABLE C.2. Summary of Storage Conditions.

Matrix	Storage Temperature (°C)	Actual Storage Duration[1] Days (Months)	Interval of Demonstrated Storage Stability
Root (RAC)	< -10	161-202 (5.3-6.6)	Storage stability data are available indicating that residues of *cis*- and *trans*-metconazole are relatively stable under frozen storage conditions in/on radish roots, residues of M11, M21, and M30 are stable in/on sugar beet root, and residues of 1,2,4-T, TA, and TAA are stable in/on radish roots for up to 6 months. [2] Because processed samples were stored for just over one month, no data are required to support the storage conditions and durations for sugar beet processed commodities.
Pulp (extracted)		28-41 (0.9-1.3)	
Pressed (dried) pulp		29-45 (1.0-1.5)	
Pressed water		25-39 (0.8-1.3)	
Raw juice		25-39 (0.8-1.3)	
Mud (lime sludge)		25-39 (0.8-1.3)	
Thin juice		25-38 (0.8-1.3)	
Thick juice		25-38 (0.8-1.3)	
Molasses		21-39 (0.7-1.3)	
Raw sugar		21-39 (0.7-1.3)	
Refined sugar		21-39 (0.7-1.3)	

[1] Storage duration from harvest/processing to analysis. Samples were analyzed within 0-4 days of extraction.
[2] Refer 46902223.der.doc.

TABLE C.3.1. Residue Data for Metconazole from Sugar Beet Processing Study with Metconazole.

Location (County, State; Year) Trial ID	Processed Commodity	Total Rate (lb ai/A)	PHI (days)	Metconazole Residues (ppm)			Processing Factor[1]	Average Processing Factor[2]
				cis-Metconazole	*trans*-Metconazole	Total Metconazole	Total Metconazole	Total Metconazole
Pepin, WI; 2005 (RCN R05097)	Root (RAC)	0.99	14	0.0128	<0.005	<0.0178	--	--
	Pulp			0.0079	<0.005	<0.0129	0.7x	1.9x
	Dried pulp			0.0672	0.0110	0.0781	>4.4x	14x
	Water			<0.005	<0.005	<0.01	0.6x	0.8x
	Raw juice			<0.005	<0.005	<0.01	0.6x	0.9x
	Lime sludge			<0.005	<0.005	<0.01	0.6x	0.6x
	Thin Juice			<0.005	<0.005	<0.01	0.6x	1.0x
	Thick Juice			<0.005	<0.005	<0.01	0.6x	1.3x
	Molasses			0.0136	<0.005	<0.0186	1.0x	1.9x
	Raw sugar			0.0116	<0.005	<0.0166	0.9x	2.2x
	Refined sugar			<0.005	<0.005	<0.01	0.6x	0.8x

TABLE C.3.1. Residue Data for Metconazole from Sugar Beet Processing Study with Metconazole.

Location (County, State; Year) Trial ID	Processed Commodity	Total Rate (lb ai/A)	PHI (days)	Metconazole Residues (ppm)			Processing Factor[1]	Average Processing Factor[2]
				cis-Metconazole	*trans*-Metconazole	Total Metconazole	Total Metconazole	Total Metconazole
Brown, SD; 2005 (RCN R05098)	Root (RAC)	1.00	14	<0.005	<0.005	<0.01	--	
	Pulp			<0.005	<0.005	<0.01	NC	
	Dried pulp			0.0089	<0.005	<0.0139	1.4x	
	Water			<0.005	<0.005	<0.01	NC	
	Raw juice			<0.005	<0.005	<0.01	NC	
	Lime sludge			<0.005	<0.005	<0.01	NC	
	Thin Juice			<0.005	<0.005	<0.01	NC	
	Thick Juice			<0.005	<0.005	<0.01	NC	
	Molasses			0.0101	<0.005	<0.0151	1.5x	
	Raw sugar			<0.005	<0.005	<0.01	NC	
	Refined sugar			<0.005	<0.005	<0.01	NC	
Fresno, CA; 2005 (RCN R05099)	Root (RAC)	1.01	14	0.0166	<0.005	<0.0216	--	
	Pulp			0.0700	0.0148	0.0848	>3.9x	
	Dried pulp			0.7951	0.1181	0.9131	>42x	
	Water			0.0253	<0.005	<0.0303	1.4x	
	Raw juice			0.0270	<0.005	<0.0320	1.5x	
	Lime sludge			0.0132	<0.005	<0.0182	0.8x	
	Thin Juice			0.0400	0.0055	0.0454	>2.1x	
	Thick Juice			0.0488	<0.005	<0.0538	2.5x	
	Molasses			0.0722	0.0110	0.0832	>3.9x	
	Raw sugar			0.0786	0.0154	0.0940	>4.4x	
	Refined sugar			0.0216	<0.005	<0.0266	1.2x	
Payette, ID; 2005 (RCN R05100)	Root (RAC)	1.00	15	0.0182	<0.005	<0.0232	--	
	Pulp			0.0179	<0.005	<0.0229	1.0x	
	Dried pulp			0.1822	0.0320	0.2142	>9.2x	
	Water			<0.005	<0.005	<0.01	0.4x	
	Raw juice			0.0055	<0.005	<0.0105	0.5x	
	Lime sludge			0.0056	<0.005	<0.0106	0.5x	
	Thin Juice			<0.005	<0.005	<0.01	0.4x	
	Thick Juice			0.0131	<0.005	<0.0181	0.8x	
	Molasses			0.0253	<0.005	<0.0303	1.3x	
	Raw sugar			0.0223	<0.005	<0.0273	1.2x	
	Refined sugar			0.0074	<0.005	<0.0124	0.5x	

[1] Processing factors were calculated by dividing the residue in the processed fraction by the residue in the soybean seed (RAC).
NC = Not calculated because residues were nonquantifiable in both the RAC and the processed commodity.
[2] Average from all trials for which processing factors were calculated.

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TABLE C.3.2. Residue Data from Sugar Beet Processing Study with Triazole-Related Compounds.

Location (County, State; Year) Trial ID	Processed Commodity	Total Rate (lb ai/A)	PHI days	Triazole-Related Compounds (ppm)						
				1,2,4-T	1,2,4-T Proc. Factor [1]	TA	TA Proc. Factor [1]	Average Proc. Factor[2]	TAA	TAA Proc. Factor [1]
Pepin, WI; 2005 (RCN R05097)	Root (RAC)	0.99	14	<0.05	---	<0.05	---		<0.05	---
	Pulp			<0.05	NC	<0.05	NC	--	<0.05	NC
	Dried pulp			<0.05	NC	<0.05	NC	--	<0.05	NC
	Water			<0.05	NC	<0.05	NC	--	<0.05	NC
	Raw juice			<0.05	NC	<0.05	NC	--	<0.05	NC
	Lime sludge			<0.05	NC	<0.05	NC	--	<0.05	NC
	Thin Juice			<0.05	NC	<0.05	NC	--	<0.05	NC
	Thick Juice			<0.05	NC	<0.05	NC	--	<0.05	NC
	Molasses			<0.05	NC	0.06	>1.2x	>2.3x	<0.05	NC
	Raw sugar			<0.05	NC	<0.05	NC	>2.3x	<0.05	NC
	Refined sugar			<0.05	NC	<0.05	NC	--	<0.05	NC
Brown, SD; 2005 (RCN R05098)	Root (RAC)	1.00	14	<0.05	---	<0.05	---		<0.05	---
	Pulp			<0.05	NC	<0.05	NC		<0.05	NC
	Dried pulp			<0.05	NC	<0.05	NC		<0.05	NC
	Water			<0.05	NC	<0.05	NC		<0.05	NC
	Raw juice			<0.05	NC	<0.05	NC		<0.05	NC
	Lime sludge			<0.05	NC	<0.05	NC		<0.05	NC
	Thin Juice			<0.05	NC	<0.05	NC		<0.05	NC
	Thick Juice			<0.05	NC	<0.05	NC		<0.05	NC
	Molasses			<0.05	NC	<0.05	NC		<0.05	NC
	Raw sugar			<0.05	NC	<0.05	NC		<0.05	NC
	Refined sugar			<0.05	NC	<0.05	NC		<0.05	NC
Fresno, CA; 2005 (RCN R05099)	Root (RAC)	1.01	14	<0.05	---	<0.05	---		<0.05	---
	Pulp			<0.05	NC	<0.05	NC		<0.05	NC
	Dried pulp			<0.05	NC	<0.05	NC		<0.05	NC
	Water			<0.05	NC	<0.05	NC		<0.05	NC
	Raw juice			<0.05	NC	<0.05	NC		<0.05	NC
	Lime sludge			<0.05	NC	<0.05	NC		<0.05	NC
	Thin Juice			<0.05	NC	<0.05	NC		<0.05	NC
	Thick Juice			<0.05	NC	<0.05	NC		<0.05	NC
	Molasses			<0.05	NC	0.17	>3.4x		<0.05	NC
	Raw sugar			<0.05	NC	0.14	>2.8x		<0.05	NC
	Refined sugar			<0.05	NC	<0.05	NC		<0.05	NC

TABLE C.3.2. Residue Data from Sugar Beet Processing Study with Triazole-Related Compounds.

Location (County, State; Year) Trial ID	Processed Commodity	Total Rate (lb ai/A)	PHI days	Triazole-Related Compounds (ppm)						
				1,2,4-T	1,2,4-T Proc. Factor [1]	TA	TA Proc. Factor [1]	Average Proc. Factor[2]	TAA	TAA Proc. Factor [1]
Payette, ID; 2005 (RCN R05100)	Root (RAC)	1.00	15	<0.05	---	<0.05	---		<0.05	---
	Pulp			<0.05	NC	<0.05	NC		<0.05	NC
	Dried pulp			<0.05	NC	<0.05	NC		<0.05	NC
	Water			<0.05	NC	<0.05	NC		<0.05	NC
	Raw juice			<0.05	NC	<0.05	NC		<0.05	NC
	Lime sludge			<0.05	NC	<0.05	NC		<0.05	NC
	Thin Juice			<0.05	NC	<0.05	NC		<0.05	NC
	Thick Juice			<0.05	NC	<0.05	NC		<0.05	NC
	Molasses			<0.05	NC	0.11	>2.2x		<0.05	NC
	Raw sugar			<0.05	NC	0.09	>1.8		<0.05	NC
	Refined sugar			<0.05	NC	<0.05	NC		<0.05	NC

[1] The processing factor was calculated by dividing the residue in the processed commodity by the residue in the associated RAC sample.
[2] Average from all trials for which processing factors were calculated.

D. CONCLUSION

Total metconazole residues (sum of *cis* and *trans* isomers) were <0.01-<0.0232 ppm in/on sugar beet root, <0.0139-0.9131 ppm in dried pulp, <0.0151-0.0832 in molasses, and <0.01-<0.266 ppm in refined sugar. Residues of metabolites M11, M21, and M30 were <0.010 ppm in/on all samples of sugar beet root and processed commodities, except that residues of M21 were detected in one sample of dried pulp at 0.0137 ppm.

The processing data indicate that residues of total metconazole may concentrate in dried pulp (average processing factor of 14x), and molasses (average processing factor of 1.9x), but do not concentrate in refined sugar (average processing factor of 0.8x).

Residues of 1,2,4-T, TA, and TAA were below the LOQ (<0.05 ppm) in/on all samples of sugar beet root and in most processed commodities. Residues of TA were <0.05-0.17 ppm in molasses and <0.05-0.14 ppm in raw sugar. The processing data indicate that residues of TA may concentrate in molasses and raw sugar (processing factors of >2.3x for both).

E. REFERENCES

DP#: 324541
Subject: Metconazole. Request for a Tolerance on Imported Bananas. Summary of Analytical Chemistry and Residue Data. Petition Number 9E05052.
From: N. Dodd
To: M. Waller
Date: 12/14/05
MRIDs: 44721506, 44721507, 44721508, 44721509, 44721510, and 44721511

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F. DOCUMENT TRACKING

RDI: N. Dodd (2/20/08)
Petition Numbers: 6F7094 and 6F7095
DP#s: 348168 and 348206
PC Code: 125619

Template Version June 2005

APPENDIX I. Calculation of Processing Factors for Combined Residues of cis- and trans-Metconazole, M11, M21, and M30.

Residue Data for Metconazole, M11, M21, and M30 from Sugar Beet Processing Study with Metconazole.

Location (County, State; Year) Trial ID	Processed Commodity	Total Rate (lb ai/A)	PHI days	Metconazole Residues (ppm)							Processing Factor [3]
				Parent metconazole			Metabolites[1]			Total[2]	
				Trans	Cis	Total	M11	M21	M30		
Pepin, WI; 2005 (RCN R05097)	Root (RAC)	0.99	14	<0.005	0.0128	0.0178	<0.01	<0.01	<0.01	0.05	---
	Pulp			<0.005	0.0079	0.0129	<0.01	<0.01	<0.01	0.04	0.8x
	Dried pulp			0.0110	0.0672	0.0781	<0.01	<0.01	<0.01	0.11	2.2x
	Water			<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04	0.8x
	Raw juice			<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04	0.8x
	Lime sludge			<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04	0.8x
	Thin Juice			<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04	0.8x
	Thick Juice			<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04	0.8x
	Molasses			<0.005	0.0136	0.0186	<0.01	<0.01	<0.01	0.05	1.0x
	Raw sugar			<0.005	0.0116	0.0166	<0.01	<0.01	<0.01	0.05	1.0x
	Refined sugar			<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04	0.8x
Brown, SD; 2005 (RCN R05098)	Root (RAC)	1.00	14	<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04	---
	Pulp			<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04	1.0x
	Dried pulp			<0.005	0.0089	0.0139	<0.01	<0.01	<0.01	0.04	1.0x
	Water			<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04	1.0x
	Raw juice			<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04	1.0x
	Lime sludge			<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04	1.0x
	Thin Juice			<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04	1.0x
	Thick Juice			<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04	1.0x
	Molasses			<0.005	0.0101	0.0151	<0.01	<0.01	<0.01	0.05	1.3x
	Raw sugar			<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04	1.0x
	Refined sugar			<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04	1.0x

Residue Data for Metconazole, M11, M21, and M30 from Sugar Beet Processing Study with Metconazole.

Location (County, State; Year) Trial ID	Processed Commodity	Total Rate (lb ai/A)	PHI days	Metconazole Residues (ppm)							Processing Factor [3]
				Parent metconazole			Metabolites[1]			Total[2]	
				Trans	Cis	Total	M11	M21	M30		
Fresno, CA; 2005 (RCN R05099)	Root (RAC)	1.01	14	<0.005	0.0166	0.0216	<0.01	<0.01	<0.01	0.05	---
	Pulp			0.0148	0.0700	0.0848	<0.01	<0.01	<0.01	0.11	2.2x
	Dried pulp			0.1181	0.7951	0.9131	<0.01	0.0137	<0.01	0.95	19x
	Water			<0.005	0.0253	0.0303	<0.01	<0.01	<0.01	0.06	1.2x
	Raw juice			<0.005	0.0270	0.0320	<0.01	<0.01	<0.01	0.06	1.2x
	Lime sludge			<0.005	0.0132	0.0182	<0.01	<0.01	<0.01	0.05	1.0x
	Thin Juice			0.0055	0.0400	0.0454	<0.01	<0.01	<0.01	0.08	1.6x
	Thick Juice			<0.005	0.0488	0.0538	<0.01	<0.01	<0.01	0.08	1.6x
	Molasses			0.0110	0.0722	0.0832	<0.01	<0.01	<0.01	0.11	2.2x
	Raw sugar			0.0154	0.0786	0.0940	<0.01	<0.01	<0.01	0.12	2.4x
	Refined sugar			<0.005	0.0216	0.0266	<0.01	<0.01	<0.01	0.06	1.2x
Payette, ID; 2005 (RCN R05100)	Root (RAC)	1.00	15	<0.005	0.0182	0.0232	<0.01	<0.01	<0.01	0.05	---
	Pulp			<0.005	0.0179	0.0229	<0.01	<0.01	<0.01	0.05	1.0x
	Dried pulp			0.0320	0.1822	0.2142	<0.01	<0.01	<0.01	0.24	4.8x
	Water			<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04	0.8x
	Raw juice			<0.005	0.0055	0.0105	<0.01	<0.01	<0.01	0.04	0.8x
	Lime sludge			<0.005	0.0056	0.0106	<0.01	<0.01	<0.01	0.04	0.8x
	Thin Juice			<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04	0.8x
	Thick Juice			<0.005	0.0131	0.0181	<0.01	<0.01	<0.01	0.05	1.0x
	Molasses			<0.005	0.0253	0.0303	<0.01	<0.01	<0.01	0.06	1.2x
	Raw sugar			<0.005	0.0223	0.0273	<0.01	<0.01	<0.01	0.06	1.2x
	Refined sugar			<0.005	0.0074	0.0124	<0.01	<0.01	<0.01	0.04	0.8x

[1] Expressed in parent equivalents.
[2] Total = total residue; the sum of *cis*- and *trans*-metconazole, M11, M21, and M30; values presented as calculated and reported by the petitioner.
[3] Processing factors calculated by dividing the residue in the processed fraction by the residue in the soybean seed (RAC); values presented as calculated and reported by the petitioner.

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Primary Evaluator	This DER was originally prepared under contract by Dynamac Corporation.
Approved by	Nancy Dodd, Chemist *Nancy Dodd* Date: 2/20/08 Registration Action Branch 3 Health Effects Division (7509P)

This DER was originally prepared under contract by Dynamac Corporation (2275 Research Boulevard, Suite 300; Rockville, MD 20850; submitted 09/13/2007). The DER has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

46902303 White, M.; Saha, M. (2006) Field Accumulation of Residues of Metconazole (BAS 555 F) and its Metabolites in Rotational Crops from Limited Field Trials in Mississippi: Final Report. Project Number: V/04/27131, 2006/7007130. Unpublished study prepared by BASF Corporation. 156 p.

EXECUTIVE SUMMARY:

BASF Corporation has submitted a limited field rotational crop study for metconazole on radish (root and tuber vegetable) and spinach (leafy vegetable). Two limited field rotational crop trials were conducted on radish and spinach (one trial each) during the 2004-2006 growing seasons in the U.S. in Zone 4 (MS).

Each trial consisted of one untreated plot and one treated plot, with soybeans planted as the primary crop. Soybeans received two broadcast foliar applications of a 1.81 lb ai/gal flowable concentrate (FlC) formulation at 0.25 lb ai/A/application with a 13-day retreatment interval, for a total seasonal rate of 0.50 lb ai/A. The applications were made in spray volumes of ~20 gal/A of water without an adjuvant using ground equipment.

The primary crop was destroyed and tilled into the soil ~2 weeks after the last application, and the ground was prepared for planting according to area-typical practices. Radish and spinach were grown at plantback intervals of 35, 129, 157, and 366 days after last application of metconazole to soybean crops. The petitioner noted that the first plantback interval was 35 days instead of 30 days due to wet weather, and that the second plantback interval was 129 days instead of 90 days because the first crops were destroyed by cold wet weather, and new crops had to be planted.

Radish tops and roots were harvested at maturity, 33-83 days after planting. Spinach was collected at maturity, 60-177 days after planting.

Samples were analyzed for residues of *cis*- and *trans*-metconazole, metabolites M11, M21, and M30, and the triazole metabolites [triazole (1,2,4-T), triazolylalanine (TA), and triazolylacetic acid (TAA)] using an LC/MS/MS method (BASF Method D0508). Residues of metconazole metabolites M11, M21, and M30 were converted to parent equivalents using molecular weight conversion factors of 0.95 for M11 and M21 and 0.96 for M30. The validated limit of quantitation (LOQ) was 0.01 ppm for the parent metconazole (sum of *cis* and *trans* isomers at 0.005 ppm each), M11, M21, and M30 in wheat samples. The validated LOQ was 0.05 ppm for 1,2,4-T, TA, and TAA. The reported limit of detection was 20% of the LOQ. The method was adequate for data collection based on acceptable concurrent method recoveries.

Radish tops and root samples were stored frozen (≤-10 °C) from harvest to extraction for 225-531 days (7.4-17.5 months), and spinach samples were stored for 79-406 days (2.6-13.3 months). All samples were analyzed within 0-7 days of extraction. Adequate storage stability data are available to support the storage conditions and duration of spinach samples analyzed for *cis*- and *trans*-metconazole. Additional data are required reflecting the stability of *cis*- and *trans*-metconazole following frozen storage in/on radish tops and roots for up to 18 months.

At the 35-day PBI, one sample of radish tops bore quantifiable residues of *cis*-metconazole at 0.006 ppm; residues of trans-metconazole were <LOQ for total metconazole residues of <0.011 ppm. Residues of metconazole (*cis* and *trans* isomers), M11, M21, and M30 in remaining samples of radish tops, radish roots, and spinach from the 35-, 129-, 157-, and 366-day PBIs were below the LOQ.

Residues of 1,2,4-T in all samples of radish roots, tops and spinach at all PBIs were below the LOQ. One spinach sample from the 35-day PBI bore residues of TAA at 0.06 ppm; residues were <LOQ in all other samples of radish commodities and spinach. Quantifiable residues of TA were observed in all matrices from PBIs. Residues of TA generally declined from the 35-day PBI to the 366-day PBI in radish tops (from 0.19 ppm to 0.08 ppm) and spinach (from 0.89 ppm to 0.05 ppm), and increased in radish roots (from 0.10 ppm at the 35-day PBI to 0.13 ppm at the 366-day PBI).

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the data depicting residues in rotational radish and spinach are tentatively classified as scientifically acceptable pending submission of additional storage stability data. Additional data are required reflecting the stability of *cis*- and *trans*-metconazole following frozen storage in radish tops and roots for up to 18 months.

The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP#s 348168 and 348206.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported.

A. BACKGROUND INFORMATION

Metconazole [5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol] is a broad-spectrum triazole Group 3 fungicide (sterol biosynthesis inhibitors). There are currently no registered uses of metconazole in the U.S.; however, a tolerance has been established for banana, and a Section 18 emergency exemption and supporting time-limited tolerances have been granted for use on soybean. BASF Corporation has applied for registration of metconazole in the U.S. for use on barley, oats, rye, soybeans, sugar beets, triticale, and wheat.

The chemical structure and nomenclature of metconazole, and the physicochemical properties of the technical grade of metconazole are presented in Tables A.1 and A.2.

TABLE A.1. Metconazole Nomenclature.

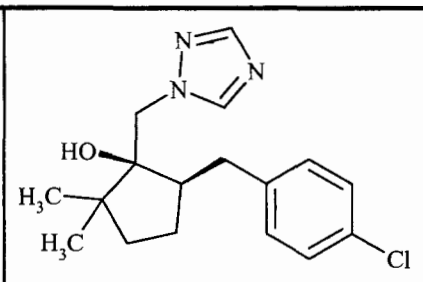
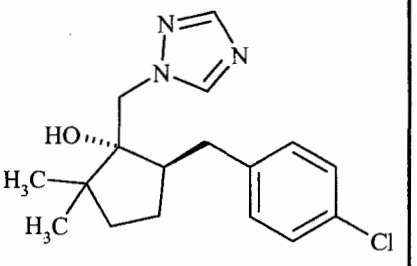
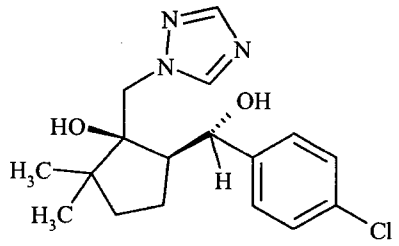
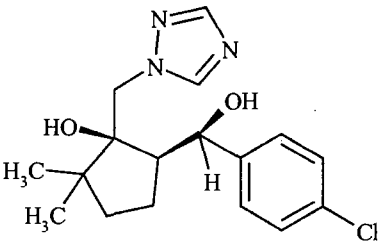
Chemical structure	 *cis*-isomer  *trans*-isomer
Common name	Metconazole
Company experimental name	KNF-S-474m (Kureha); BAS 555 F (BASF); V-10116 (Valent)
IUPAC name	(1RS,5RS:1RS,5SR)-5-(4-chlorobenzyl)-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol
CAS name	5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol
CAS registry number	125116-23-6 (cis- and *trans*-isomers) 115850-27-6 (*cis*-isomer) 115850-28-7 (*trans*-isomer)
End-use products (EP)	50% WDG (Metconazole 50 WDG Fungicide, EPA File Symbol 59639-RUT) 0.75 lb/gal SC/L (Caramba™ Fungicide, EPA File Symbol No. 7969-EUA) 0.67 lb/gal SC/L formulation (BAS 556 01F Fungicide, EPA File Symbol No. 7969-EUT; also contains the active ingredient pyraclostrobin at 0.83 lb/gal)

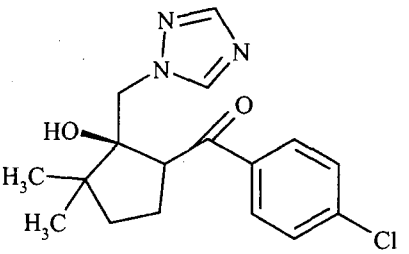
TABLE A.1. Metconazole Nomenclature.



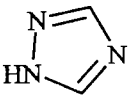
Metconazole metabolite M11



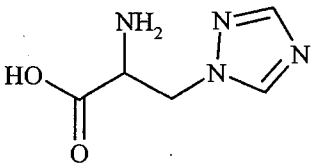
Metconazole metabolite M21



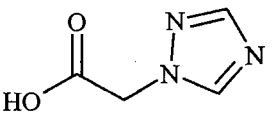
Metconazole metabolite M30



Triazole metabolite 1,2,4-triazole (1,2,4-T)



Triazole metabolite triazolylalanine (TA)



Triazole metabolite triazolylacetic acid (TAA)

Table A.2. Physicochemical Properties of Metconazole

Parameter	Value				References* (MRID)
Melting point/range	100.0-108.4°C (using Electrothermal Digital Melting Point Apparatus) (AC900,768 technical grade)				44721505
pH	5.81 at 25°C (1% aqueous suspension)				46808402
Relative density (20°C)	1.14 (relative density to water at 4°C, using capillary-stoppered, density-specific gravity bottle) (Lot No. AC 8879-140B)				44721505
Water solubility (20°C)	Using shake-flask method: 18.7 ± 1.0 mg/L (*cis*-isomer, WL148271, KNF-S-474m) 13.6 ± 1.7 mg/L (*trans*-isomer, WL148271, KNF-S-474m)				44721505
Solvent solubility (g/L) at 20°C	Solvent	Metconazole	*cis*	*trans*	44721505
	acetone	363	251	117	
	methanol	403	294	117	
	dichloromethane	481	343	141	
	ethyl acetate	260	173	90.0	
	propanol	132	86.6	46.7	
	toluene	103	66.2	38.0	
	Hexane	1.40	0.929	0.483	
Vapor pressure (20°C)	Using gas-saturation method: $< 1.23 \times 10^{-5}$ Pa or 9.23×10^{-8} mm Hg (metconazole) $< 1.04 \times 10^{-5}$ Pa or 7.80×10^{-8} mm Hg (*cis*-isomer) $< 1.96 \times 10^{-6}$ Pa or 1.47×10^{-8} mm Hg (*trans*-isomer)				44721505
Dissociation constant (pK_a)	11.38±0.03 and 1.06±0.03 (in water at 29.1°C using spectrophotometric method; Lot No. AC 8879-140B)				44721505

Table A.2. Physicochemical Properties of Metconazole

Parameter	Value				References* (MRID)
Octanol/water partition coefficient, Log(K_{OW})	At 20 °C (using flask shaking method): K_{ow} (log K_{ow}) = 7090±989 (3.85) (Lot No. AC 8879-140B) (TGAI) K_{ow} (log K_{ow}) = 7150±803 (3.85) (*cis*-isomer, CL 354,801) K_{ow} (log K_{ow}) = 6800±1700 (3.8) (*trans*-isomer, CL 354,802)				44721505
UV/visible absorption spectrum	pH	λ	A	log ε	46808403
	cis-isomer				
	2.0	221.4	0.828	4.03	
	6.8		0.8452	4.04	
	7.0		0.9126	4.08	
	10.3		0.7226	3.98	
	trans-isomer				
	2.0	221.4	0.9053	4.07	
	7.0		0.9547	4.10	
	10.1		0.9893	4.11	

* Product Chemistry Reviews: DP #256877, Shyam Mathur, Ph.D., 9/12/2000 and DP #329168, Shyam Mathur, Ph.D., 7/13/07.

B. EXPERIMENTAL DESIGN

B.1. Study Site Information

Two limited field rotational crop trials were conducted on radish and spinach (one trial each) during the 2004-2006 growing seasons in the U.S. in Zone 4 (MS).

The study use pattern is detailed in Table B.1.2. Each trial consisted of one untreated plot and one treated plot, with soybeans planted as the primary crop. Soybeans received two broadcast foliar applications of a 1.81 lb ai/gal flowable concentrate (FlC) formulation at 0.25 lb ai/A/application with a 13-day retreatment interval, for a total seasonal rate of 0.50 lb ai/A. The applications were made in spray volumes of ~20 gal/A of water without an adjuvant using ground equipment.

The primary crop was destroyed and tilled into the soil ~2 weeks after the last application of metconazole and the ground was prepared for planting according to area-typical practices. The representative crops of radish and spinach were grown at plantback intervals of 35, 129, 157, and 366 days after the last application of metconazole to soybean crops. Typical agricultural practices were used to grow and maintain the test crops. The first plantback interval was 35 days instead of 30 days due to wet weather. The second plantback interval was 129 days instead of 90 days because the first crops were destroyed by cold wet weather, and a new crop had to be planted.

Trial site conditions are presented in Table B.1.1. Crop varieties are listed in Table C.3.1. Data regarding the use of maintenance pesticides applied during the trials were provided. The weather conditions for each application and for the field trial duration, along with historical comparative data, were reported for each field trial. Irrigation supplemented rainfall as needed.

Radish tops and roots were harvested at maturity, 33-83 days after planting. Spinach was collected at maturity, 60-177 days after planting.

TABLE B.1.1 Trial Site Conditions.

Trial Identification: County, State; Year (Trial ID)	Soil characteristics				Meteorological Data	
	Type	%OM	pH	CEC meq/g	Overall Rainfall Range	Overall Temperature
Washington, MS; 2004 (V-27131-04-A)	Silt loam	0.6	6.3	10.5	Above normal in 2004. Below normal in January and December 2005. Above normal in January, February, and March 2006.	Generally normal

TABLE B.1.2. Study Use Pattern.

Trial Identification: County, State; Year (Trial ID)	EP[1]	Application					Tank Mix/ Adjuvant
		Method; Timing	Volume (GPA)[2] [L/ha]	Rate (lb ai/A) [kg ai/ha]	RTI[3] (days)	Total Rate (lb ai/A) [kg ai/ha]	
Washington, MS; 2004 (V-27131-04-A)	1.81 lb/gal FlC	1. Broadcast foliar to soybeans; blooming	20.1 [188]	0.25 [0.28]	13	0.50 [0.56]	None
		2.Broadcast foliar to soybeans; pod set and formation	19.8 [185]	0.25 [0.28]			

[1] EP = End-use Product
[2] GPA = Gallons per Acre
3 RTI = Retreatment Interval

B.2. Sample Handling and Preparation

Samples were stored frozen at the field site <2 hours after sampling. Samples were shipped initially within 1-210 days to Valent Technical Center (Dublin, CA) via ACDS freezer truck or overnight courier on dry ice. Samples were stored frozen at Valent for 7-218 days, then shipped by ACDS freezer truck to the analytical laboratory, BASF Agro Research (Research Triangle Park, NC). At BASF samples were homogenized in the presence of dry ice and stored frozen (~ -10 °C) until extraction and analysis.

B.3. Analytical Methodology

Samples of rotational radish tops and roots and spinach were analyzed for residues of metconazole, metabolites M11, M21, and M30, and the triazole metabolites (1,2,4-T, TA, and TAA) using an HPLC/MS/MS method (BASF Method D0508). A brief description of the method was included in the MRID.

Briefly, residues of metconazole and its metabolites (M11, M21, and M30) were extracted with acetonitrile (ACN):water (70:30, v:v). The extracts were diluted with methanol:water (80:20, v:v), filtered, and reserved for LC/MS/MS analysis. For determination of residues of 1,2,4-T, TA, and TAA, a separate aliquot of the initial extract was evaporated to dryness, redissolved in 0.1% formic acid in water, filtered, and reserved for LC/MS/MS analysis. Residues of metabolites M11, M21, and M30 were converted to parent equivalents using molecular weight conversion factors of 0.95 for M11 and M21 and 0.96 for M30.

The validated LOQ was 0.01 ppm for the parent metconazole (sum of *cis* and *trans* isomers at 0.005 ppm each), M11, M21, and M30 in wheat samples. The validated LOQ was 0.05 ppm for 1,2,4-T, TA, and TAA. The reported limit of detection was 20% of the LOQ.

The method was validated concurrently with the analysis of field samples using untreated radish tops and roots and spinach fortified at 0.005 and 0.5 ppm with *cis*- and *trans*-metconazole; at 0.01 and 1.0 ppm with M11, M21, and M30; and at 0.05 and 5.0 ppm with 1,2,4-T, TA, and TAA.

C. RESULTS AND DISCUSSION

Sample storage conditions and intervals are summarized in Table C.2. Radish tops and root samples were stored frozen (≤-10 °C) prior to extraction for 225-531 days (7.4-17.5 months), and spinach samples were stored for 79-406 days (2.6-13.3 months). All samples were analyzed within 0-7 days of extraction. Acceptable storage stability data are available indicating that: (1) residues of *cis*- and *trans*-metconazole are relatively stable under frozen storage conditions in/on carrots and lettuce for up to 12 months (refer to 46902218.der.doc); (2) residues of M11, M21, and M30 are stable in/on radish top and sugar beet root for up to 6 months (refer to 46902223.der.doc); and (3) residues of 1,2,4-T, TA, and TAA are stable/relatively stable in/on radish root and radish top for up to 6 months (refer to 46902223.der.doc). Additional data are required reflecting the stability of *cis*- and *trans*-metconazole following frozen storage in/on radish tops and roots for up to 18 months.

Concurrent method recovery data are presented in Table C.1. Samples of rotational crop commodities were analyzed for residues of metconazole (*cis* and *trans* isomers), metabolites M11, M21, and M30, and the triazole metabolites (1,2,4-T, TA, and TAA) using LC/MS/MS Method D0508. Residues of metabolites M11, M21, and M30 were converted to parent equivalents using molecular weight conversion factors of 0.95 for M11 and M21, and 0.96 for M30. The method was adequate for data collection based on acceptable concurrent method recovery data. Concurrent method recoveries were generally within the acceptable range of 70-120% for radish roots and tops and spinach samples fortified at 0.005 and 0.5 ppm with *cis* and *trans*-metconazole; at 0.01 and 1.00 ppm with M11, M21 and M30; and at 0.05 and 5.00 ppm with 1,2,4-T, TA, and TAA. Low recoveries (61-63%) were obtained for 1,2,4-T in radish tops at both fortification levels.

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Apparent residues of *cis*- and *trans*-metconazole, its metabolites M11, M21, and M30, and 1,2,4-T, TA, and TAA were each below the respective LOQs in two untreated samples each of radish (roots and tops) and spinach.

Metconazole residue data from the field rotational crop study are presented in Tables C.3.1 (metconazole, M11, M21, and M30) and C.3.2 (triazole metabolites). A summary of residue data for rotated radish and spinach commodities is presented in Table C.4. At the 35-day PBI, one sample of radish tops bore quantifiable residues of *cis*-metconazole at 0.006 ppm; residues of trans-metconazole were <LOQ for total metconazole residues of 0.011 ppm. Residues of metconazole (*cis* and *trans* isomers), M11, M21, and M30 in the remaining samples of radish tops, radish roots, and spinach from the 35-, 129-, 157-, and 366-day PBIs were below the LOQ.

Residues of 1,2,4-T in all samples of radish roots, tops and spinach at all PBIs were below the LOQ. One spinach sample from the 35-day PBI bore residues of TAA at 0.06 ppm; residues were <LOQ in all other samples of radish commodities and spinach. Quantifiable residues of TA were observed in all matrices from PBIs. Residues of TA generally declined from the 35-day PBI to the 366-day PBI in radish tops (from 0.19 ppm to 0.08 ppm) and spinach (from 0.89 ppm to 0.05 ppm), and increased in radish roots (from 0.10 ppm at the 35-day PBI to 0.13 ppm at 366-day PBI).

TABLE C.1. Summary of Concurrent Recoveries of Metconazole, M11, M21, M30, and the Triazole Metabolites from Radish Roots and Tops and Spinach.

Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean (%)
Radish root	*trans*-Metconazole	0.005	1	84	84
		0.5	1	97	97
	cis-Metconazole	0.005	1	95	95
		0.5	1	91	91
	M11	0.01	1	95	95
		1.0	1	91	91
	M21	0.01	1	87	87
		1.0	1	88	88
	M30	0.01	1	85	85
		1.0	1	90	90
	1,2,4-T	0.05	1	70	70
		5.0	1	69	69
	TA	0.05	1	75	75
		5.0	1	79	79
	TAA	0.05	1	93	93
		5.0	1	80	80
Radish tops	*trans*-Metconazole	0.005	1	93	93
		0.5	1	106	106
	cis-Metconazole	0.005	1	104	104
		0.5	1	104	104
	M11	0.01	1	81	81
		1.0	1	95	95

TABLE C.1. Summary of Concurrent Recoveries of Metconazole, M11, M21, M30, and the Triazole Metabolites from Radish Roots and Tops and Spinach.

Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean (%)
	M21	0.01	1	86	86
		1.0	1	93	93
	M30	0.01	1	81	81
		1.0	1	93	93
	1,2,4-T	0.05	1	63	63
		5.0	1	61	61
	TA	0.05	1	91	91
		5.0	1	88	88
	TAA	0.05	1	101	101
		5.0	1	104	104
Spinach	*trans*-Metconazole	0.005	1	83	83
		0.5	1	98	98
	cis-Metconazole	0.005	1	93	93
		0.5	1	83	83
	M11	0.01	1	83	83
		1.0	1	90	90
	M21	0.01	1	93	93
		1.0	1	83	83
	M30	0.01	1	82	82
		1.0	1	97	97
	1,2,4-T	0.05	1	70	70
		5.0	1	78	78
	TA	0.05	1	90	90
		5.0	1	91	91
	TAA	0.05	1	91	91
		5.0	1	97	97

TABLE C.2. Summary of Storage Conditions.

Matrix	Storage Temperature (°C)	Actual Storage Duration[1] Days (Months)	Interval of Demonstrated Storage Stability[2]
Radish tops	≤ -10	225-531 (7.4-17.5)	Adequate storage stability data are available indicating that residues of *cis*- and *trans*-metconazole are relatively stable under frozen storage conditions in/on carrots and lettuce for up to 12 months; M11, M21, and M30 are stable in/on radish top and sugar beet root for up to 6 months; and 1,2,4-T, TA, and TAA are stable/relatively stable in/on radish root and radish top for up to 6 months.
Radish root		225-531 (7.4-17.5)	
Spinach		79-406 (2.6-13.3)	

[2] Refer to 46902218.der.doc and 46902223.der.doc.

TABLE C.3.1. Residues of Metconazole, M11, M21, and M30 in Rotational Crops.

Trial Identification: County, State; Year (Trial ID)	Crop; Variety	Matrix	Total Rate (lb ai/A)	Harvest DAP[1]	PBI [2]	Metconazole Residues (ppm parent equivalents)						
						Metconazole			Metabolites			Total[3]
						cis	*trans*	Total	M11	M21	M30	
Washington, MS; 2004 (V-27131-04-A) Zone 4	Radish, Sparkler White Top	Tops	0.50	58	35	0.006	<0.005	<0.011	<0.01	<0.01	<0.01	<0.041
						<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
				83	129	<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
				60	157	<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
				33	366	<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
		Roots	0.50	58	35	<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
				83	129	<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
				60	157	<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
				33	366	<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
Washington, MS; 2004 (V-27131-04-A) Zone 4	Spinach, Blooms-dale	Leaves	0.50	177	35	<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
				88	129	<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
				60	157	<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
				173	366	<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04

[1] DAP = Days After Planting.
[2] PBI = Plantback Interval.
[3] Total = total residues; sum of *cis*- and *trans*-metconazole, M11, M21, and M30; values presented as calculated and reported by the petitioner.

TABLE C.3.2. Residues of the Triazole Metabolites in Rotational Crops.

Trial Identification: County, State; Year (Trial ID)	Crop; Variety	Matrix	Total Rate (lb ai/A)	Harvest DAP[1]	PBI[2]	Triazole Residues (ppm)		
						1,2,4-T	TA	TAA
Washington, MS; 2004 (V-27131-04-A) Zone 4	Radish, Sparkler White Top	Tops	0.50	58	35	<0.05	0.19	<0.05
						<0.05	0.17	<0.05
				83	129	<0.05	0.10	<0.05
						<0.05	0.10	<0.05
				60	157	<0.05	0.08	<0.05
						<0.05	0.08	<0.05
				33	366	<0.05	0.06	<0.05
						<0.05	0.08	<0.05
		Roots	0.05	58	35	<0.05	0.10	<0.05
						<0.05	0.12	<0.05
				83	129	<0.05	0.07	<0.05
						<0.05	0.07	<0.05
				60	157	<0.05	0.10	<0.05
						<0.05	0.10	<0.05
				33	366	<0.05	0.11	<0.05
						<0.05	0.13	<0.05
Washington, MS; 2004 (V-27131-04-A) Zone 4	Spinach, Bloomsdale	Leaves	0.50	177	35	<0.05	0.89	0.06
						<0.05	0.71	<0.05
				88	129	<0.05	0.39	<0.05
						<0.05	0.42	<0.05
				60	157	<0.05	0.25	<0.05
						<0.05	0.21	<0.05
				173	366	<0.05	0.05	<0.05
						<0.05	0.05	<0.05

[1] DAP = Days After Planting
[2] PBI = Plantback Interval.

TABLE C.4. Summary of Residue Data in Rotational Crops Following Treatment of a Primary Crop with Metconazole.

Commodity	Total Applic. Rate (lb ai/A)	Analyte	PBI (days)	Residue Levels [1] (ppm)						
				n	Min.	Max.	HAFT[2]	Median (STMdR)	Mean (STMR)	Std. Dev.
35-Day plantback interval										
Radish tops	0.50	*cis*-Metconazole	35	2	<0.005	0.006	0.006	0.006	0.006	--
		trans-Metconazole		2	<0.005	<0.005	0.005	0.005	0.005	--
		Metconazole		**2**	**<0.01**	**0.011**	**0.011**	**0.011**	**0.011**	**--**
		M11		2	<0.01	<0.01	0.01	0.01	0.01	--
		M21		2	<0.01	<0.01	0.01	0.01	0.01	--
		M30		2	<0.01	<0.01	0.01	0.01	0.01	--
		Total Residues		2	<0.04	<0.041	0.041	0.041	0.041	--

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TABLE C.4. Summary of Residue Data in Rotational Crops Following Treatment of a Primary Crop with Metconazole.

Commodity	Total Applic. Rate (lb ai/A)	Analyte	PBI (days)	Residue Levels [1] (ppm)						
				n	Min.	Max.	HAFT[2]	Median (STMdR)	Mean (STMR)	Std. Dev.
Radish roots	0.50	*cis*-Metconazole	35	2	<0.005	<0.005	0.005	0.005	0.005	--
		trans-Metconazole		2	<0.005	<0.005	<0.005	0.005	0.005	--
		Metconazole		**2**	**<0.01**	**<0.01**	**0.01**	**0.01**	**0.01**	**--**
		M11		2	<0.01	<0.01	0.01	0.01	0.01	--
		M21		2	<0.01	<0.01	0.01	0.01	0.01	--
		M30		2	<0.01	<0.01	0.01	0.01	0.01	--
		Total Residues		2	<0.04	<0.04	0.04	0.04	0.04	--
Spinach	0.50	*cis*-Metconazole	35	2	<0.005	<0.005	0.005	0.005	0.005	--
		trans-Metconazole		2	<0.005	<0.005	0.005	0.005	0.005	--
		Metconazole		**2**	**<0.01**	**<0.01**	**0.01**	**0.01**	**0.01**	**--**
		M11		2	<0.01	<0.01	0.01	0.01	0.01	--
		M21		2	<0.01	<0.01	0.01	0.01	0.01	--
		M30		2	<0.01	<0.01	0.01	0.01	0.01	--
		Total residues		2	<0.04	<0.04	0.04	0.04	0.04	--
Radish tops	0.50	*cis*-Metconazole	129	2	<0.005	<0.005	0.005	0.005	0.005	--
		trans-Metconazole		2	<0.005	<0.005	0.005	0.005	0.005	--
		Metconazole		**2**	**<0.01**	**<0.01**	**0.01**	**0.01**	**0.01**	**--**
		M11		2	<0.01	<0.01	0.01	0.01	0.01	--
		M21		2	<0.01	<0.01	0.01	0.01	0.01	--
		M30		2	<0.01	<0.01	0.01	0.01	0.01	--
		Total Residues		2	<0.04	<0.04	0.04	0.04	0.04	--
Radish roots	0.50	*cis*-Metconazole	129	2	<0.005	<0.005	0.005	0.005	0.005	--
		trans-Metconazole		2	<0.005	<0.005	0.005	0.005	0.005	--
		Metconazole		**2**	**<0.01**	**<0.01**	**0.01**	**0.01**	**0.01**	**--**
		M11		2	<0.01	<0.01	0.01	0.01	0.01	--
		M21		2	<0.01	<0.01	0.01	0.01	0.01	--
		M30		2	<0.01	<0.01	0.01	0.01	0.01	--
		Total Residues		2	<0.04	<0.04	0.04	0.04	0.04	--

TABLE C.4. Summary of Residue Data in Rotational Crops Following Treatment of a Primary Crop with Metconazole.

Commodity	Total Applic. Rate (lb ai/A)	Analyte	PBI (days)	Residue Levels [1] (ppm)						
				n	Min.	Max.	HAFT[2]	Median (STMdR)	Mean (STMR)	Std. Dev.
Spinach	0.50	*cis*-Metconazole	129	2	<0.005	<0.005	0.005	0.005	0.005	--
		trans-Metconazole		2	<0.005	<0.005	0.005	0.005	0.005	--
		Metconazole		**2**	**<0.01**	**<0.01**	**0.01**	**0.01**	**0.01**	--
		M11		2	<0.01	<0.01	0.01	0.01	0.01	--
		M21		2	<0.01	<0.01	0.01	0.01	0.01	--
		M30		2	<0.01	<0.01	0.01	0.01	0.01	--
		Total residues		2	<0.04	<0.04	0.04	0.04	0.04	--
Radish tops	0.50	*cis*-Metconazole	157	2	<0.005	<0.005	0.005	0.005	0.005	--
		trans-Metconazole		2	<0.005	<0.005	0.005	0.005	0.005	--
		Metconazole		**2**	**<0.01**	**<0.01**	**0.01**	**0.01**	**0.01**	--
		M11		2	<0.01	<0.01	0.01	0.01	0.01	--
		M21		2	<0.01	<0.01	0.01	0.01	0.01	--
		M30		2	<0.01	<0.01	0.01	0.01	0.01	--
		Total Residues		2	<0.04	<0.04	0.04	0.04	0.04	--
Radish roots	0.50	*cis*-Metconazole	157	2	<0.005	<0.005	0.005	0.005	0.005	--
		trans-Metconazole		2	<0.005	<0.005	0.005	0.005	0.005	--
		Metconazole		**2**	**<0.01**	**<0.01**	**0.01**	**0.01**	**0.01**	--
		M11		2	<0.01	<0.01	0.01	0.01	0.01	--
		M21		2	<0.01	<0.01	0.01	0.01	0.01	--
		M30		2	<0.01	<0.01	0.01	0.01	0.01	--
		Total Residues		2	<0.04	<0.04	0.04	0.04	0.04	--
Spinach	0.50	*cis*-Metconazole	157	2	<0.005	<0.005	0.005	0.005	0.005	--
		trans-Metconazole		2	<0.005	<0.005	0.005	0.005	0.005	--
		Metconazole		**2**	**<0.01**	**<0.01**	**0.01**	**0.01**	**0.01**	--
		M11		2	<0.01	<0.01	0.01	0.01	0.01	--
		M21		2	<0.01	<0.01	0.01	0.01	0.01	--
		M30		2	<0.01	<0.01	0.01	0.01	0.01	--
		Total residues		2	<0.04	<0.04	0.04	0.04	0.04	--

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TABLE C.4. Summary of Residue Data in Rotational Crops Following Treatment of a Primary Crop with Metconazole.

Commodity	Total Applic. Rate (lb ai/A)	Analyte	PBI (days)	Residue Levels [1] (ppm)						
				n	Min.	Max.	HAFT[2]	Median (STMdR)	Mean (STMR)	Std. Dev.
Radish tops	0.50	*cis*-Metconazole	366	2	<0.005	<0.005	0.005	0.005	0.005	--
		trans-Metconazole		2	<0.005	<0.005	0.005	0.005	0.005	--
		Metconazole		**2**	**<0.01**	**<0.01**	**0.01**	**0.01**	**0.01**	**--**
		M11		2	<0.01	<0.01	0.01	0.01	0.01	--
		M21		2	<0.01	<0.01	0.01	0.01	0.01	--
		M30		2	<0.01	<0.01	0.01	0.01	0.01	--
		Total Residues		2	<0.04	<0.04	0.04	0.04	0.04	--
Radish roots	0.50	*cis*-Metconazole	366	2	<0.005	<0.005	0.005	0.005	0.005	--
		trans-Metconazole		2	<0.005	<0.005	0.005	0.005	0.005	--
		Metconazole		**2**	**<0.01**	**<0.01**	**0.01**	**0.01**	**0.01**	**--**
		M11		2	<0.01	<0.01	0.01	0.01	0.01	--
		M21		2	<0.01	<0.01	0.01	0.01	0.01	--
		M30		2	<0.01	<0.01	0.01	0.01	0.01	--
		Total Residues		2	<0.04	<0.04	0.04	0.04	0.04	--
Spinach	0.50	*cis*-Metconazole	366	2	<0.005	<0.005	0.005	0.005	0.005	--
		trans-Metconazole		2	<0.005	<0.005	0.005	0.005	0.005	--
		Metconazole		**2**	**<0.01**	**<0.01**	**0.01**	**0.01**	**0.01**	**--**
		M11		2	<0.01	<0.01	0.01	0.01	0.01	--
		M21		2	<0.01	<0.01	0.01	0.01	0.01	--
		M30		2	<0.01	<0.01	0.01	0.01	0.01	--
		Total residues		2	<0.04	<0.04	0.04	0.04	0.04	--

[1] For calculation of the mean and median, the LOQ was used for any results reported as <LOQ in Table C.3.
[2] HAFT = Highest Average Field Trial.

D. CONCLUSION

In limited field rotational crop trials conducted on the representative crops of radish and spinach, a primary crop of soybeans received two broadcast foliar applications of a 1.81 lb ai/gal FlC formulation of metconazole at 0.25 lb ai/A at a 13-day retreatment interval, for a total seasonal rate of 0.50 lb ai/A. The primary crop was destroyed and tilled into the soil, and rotational radish and spinach crops were planted 32, 90, 150, and 365 days after the last application. Samples of radish tops and roots, and spinach were harvested at maturity. An acceptable method was used for quantitation of residues of *cis*- and *trans*-metconazole, M11, M21, M30, and the triazole metabolites (1,2,4-T, TA, and TAA) in radish and spinach matrices. Additional data are required reflecting the stability of *cis*- and *trans*-metconazole following frozen storage in/on radish tops and roots for up to 18 months.

E. REFERENCES

DP#: 324541
Subject: Metconazole. Request for a Tolerance on Imported Bananas. Summary of Analytical Chemistry and Residue Data. Petition Number 9E05052.
From: N. Dodd
To: M. Waller
Date: 12/14/05
MRIDs: 44721506, 44721507, 44721508, 44721509, 44721510, and 44721511

F. DOCUMENT TRACKING

RDI: N. Dodd (2/20/08)
Petition Numbers: 6F7094 and 6F7095
DP#s: 348168 and 348206
PC Code: 125619

Template Version June 2005

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Primary Evaluator	This DER was originally prepared under contract by Dynamac Corporation.
Approved by	Nancy Dodd, Chemist *Nancy Dodd* Date: 2/20/08 Registration Action Branch 3 Health Effects Division (7509P)

This DER was originally prepared under contract by Dynamac Corporation (2275 Research Boulevard, Suite 300; Rockville, MD 20850; submitted 09/13/2007). The DER has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

46902304 White, M.; Saha, M. (2006) Field Accumulation of Residues of Metconazole (BAS 555 F) and its Metabolites in Rotational Crops from Limited Field Trials in Ohio: Final Report. Project Number: V/04/27115, 2006/7007127. Unpublished study prepared by BASF Corporation and Ag. Consultants Inc. 150 p.

EXECUTIVE SUMMARY:

BASF Corporation has submitted a limited field rotational crop study for metconazole on wheat (small grain). One rotational crop trial was conducted on wheat during the 2004-2005 growing season in the U.S. in Zone 5 (OH).

The trial consisted of one untreated plot and three treated plots, with wheat planted as the primary crop. The primary wheat crop received two broadcast foliar applications of the 1.81 lb ai/gal flowable concentrate (FlC) formulation of metconazole at 0.25-0.26 lb ai/A/application, at a 14- to 15-day retreatment interval, for a total seasonal rate of 0.50-0.52 lb ai/A. Applications were made using ground equipment in spray volumes of ~15-19 gal/A of water without an adjuvant.

The primary crop was destroyed and tilled into the soil, and the ground was prepared for planting according to area-typical agricultural practices. Rotational wheat was grown at the plantback intervals (PBIs) of 32, 90, 150, and 365 days after the last application of metconazole to the primary wheat crop.

Samples of wheat forage, hay, straw and grain were collected at the appropriate crop growth stage, 36-203 days after planting for forage, 55-247 days after planting for hay, and 84-266 days after planting for grain and straw.

Samples were analyzed for residues of metconazole (*cis* and *trans* isomers), metabolites M11, M21, M30, and the triazole metabolites [triazole (1,2,4-T), triazolylanine (TA), and triazolylacetic acid (TAA)] using an LC/MS/MS method (BASF Method D0508). Wheat hay

and straw were not analyzed for the triazole metabolites. Residues of metabolites M11, M21, and M30 were converted to parent equivalents using molecular weight conversion factors of 0.95 for M11 and M21 and 0.96 for M30. The validated limit of quantitation (LOQ) was 0.01 ppm for the parent metconazole (sum of *cis* and *trans* isomers at 0.005 ppm each), M11, M21, and M30 in wheat matrices. The validated LOQ was 0.05 ppm for 1,2,4-T, TA, and TAA. The method was adequate for data collection based on generally acceptable concurrent method recoveries.

Samples were stored frozen (~-10 °C) from harvest to extraction for 336-382 days (11.0-12.6 months) for forage samples, 316-348 days (10.4-11.4 months) for hay samples, 286-328 days (9.4-10.8 months) for grain samples, and 287-329 days (9.4-10.8 months) for straw samples. All samples were analyzed within 0-6 days of extraction. Adequate storage stability data are available to support the storage conditions and duration of wheat commodities analyzed for *cis*- and *trans*-metconazole.

Residues of metconazole (*cis* and *trans* isomers), M11, M21, and M30 were below the LOQ (<0.01 ppm) in samples of wheat forage, hay, straw, and grain from the 32-, 90-, 150-, and 365-day PBIs.

Residues of 1,2,4-T were below the LOQ s (<0.05 ppm) in samples of wheat forage and grain from all PBIs. Quantifiable residues of TA and TAA were found in wheat forage and grain from all PBIs, and residues of both analytes generally declined from the 32-day PBI to the 365-day PBI (i.e., from 0.52 to 0.05 ppm for TA and from 0.19 to <0.05 ppm for TAA in wheat forage; and from 0.69 to 0.33 ppm for TA and from 1.00 to 0.22 ppm for TAA in wheat grain).

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the data depicting residues in rotational crops are classified as scientifically acceptable.

The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document, DP#s 348168 and 348206.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an impact on the validity of the study.

A. BACKGROUND INFORMATION

Metconazole [5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol] is a broad-spectrum triazole Group 3 fungicide (sterol biosynthesis inhibitors). There are currently no registered uses of metconazole in the U.S.; however, a tolerance has been established for banana, and a Section 18 emergency exemption and

supporting time-limited tolerances have been granted for use on soybean. BASF Corporation has applied for registration of metconazole in the U.S. for use on barley, oats, rye, soybeans, sugar beets, triticale, and wheat.

The chemical structure and nomenclature of metconazole, and the physicochemical properties of the technical grade of metconazole are presented in Tables A.1 and A.2.

TABLE A.1. Metconazole Nomenclature.

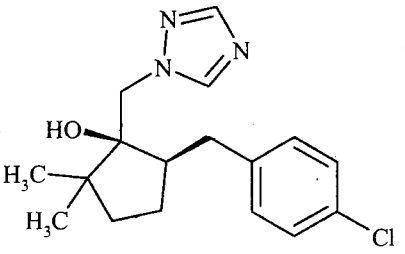
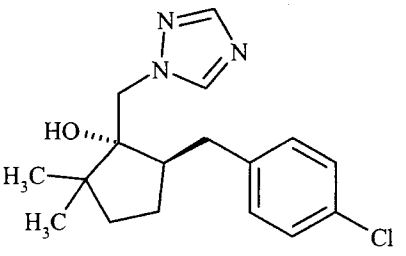
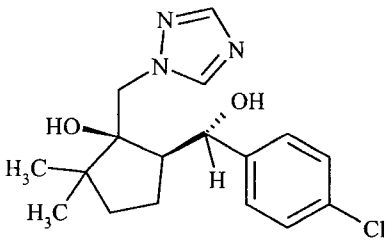
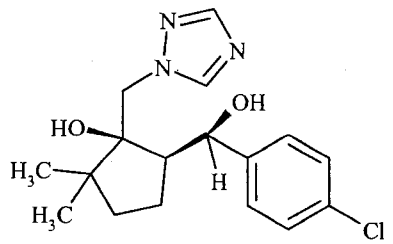
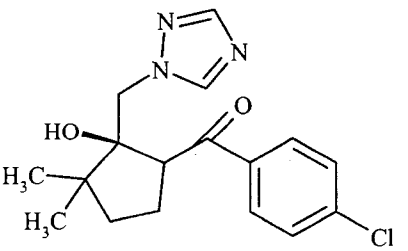
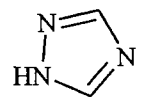
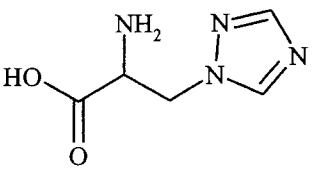
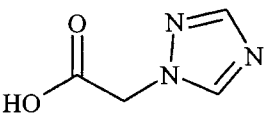
Chemical structure	 *cis*-isomer	 *trans*-isomer
Common name	Metconazole	
Company experimental name	KNF-S-474m (Kureha); BAS 555 F (BASF); V-10116 (Valent)	
IUPAC name	(1RS,5RS:1RS,5SR)-5-(4-chlorobenzyl)-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	
CAS name	5-[(4-chlorophenyl)methyl]-2,2-dimethyl-1-(1*H*-1,2,4-triazol-1-ylmethyl)cyclopentanol	
CAS registry number	125116-23-6 (cis- and *trans*-isomers) 115850-27-6 (*cis*-isomer) 115850-28-7 (*trans*-isomer)	
End-use products (EP)	50% WDG (Metconazole 50 WDG Fungicide, EPA File Symbol 59639-RUT) 0.75 lb/gal SC/L (Caramba™ Fungicide, EPA File Symbol No. 7969-EUA) 0.67 lb/gal SC/L formulation (BAS 556 01F Fungicide, EPA File Symbol No. 7969-EUT; also contains the active ingredient pyraclostrobin at 0.83 lb/gal)	
 Metconazole metabolite M11	 Metconazole metabolite M21	 Metconazole metabolite M30
 Triazole metabolite 1,2,4-triazole (1,2,4-T)	 Triazole metabolite triazolylalanine (TA)	 Triazole metabolite triazolylacetic acid (TAA)

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Table A.2. Physicochemical Properties of Metconazole

Parameter	Value	References* (MRID)
Melting point/range	100.0-108.4°C (using Electrothermal Digital Melting Point Apparatus) (AC900,768 technical grade)	44721505
pH	5.81 at 25°C (1% aqueous suspension)	46808402
Relative density (20°C)	1.14 (relative density to water at 4°C, using capillary-stoppered, density-specific gravity bottle) (Lot No. AC 8879-140B)	44721505
Water solubility (20°C)	Using shake-flask method: 18.7 ± 1.0 mg/L (*cis*-isomer, WL148271, KNF-S-474m) 13.6 ± 1.7 mg/L (*trans*-isomer, WL148271, KNF-S-474m)	44721505

Solvent solubility (g/L) at 20°C — 44721505

Solvent	Metconazole	*cis*	*trans*
acetone	363	251	117
methanol	403	294	117
dichloromethane	481	343	141
ethyl acetate	260	173	90.0
propanol	132	86.6	46.7
toluene	103	66.2	38.0
Hexane	1.40	0.929	0.483

Vapor pressure (20°C)	Using gas-saturation method: $< 1.23 \times 10^{-5}$ Pa or 9.23×10^{-8} mm Hg (metconazole) $< 1.04 \times 10^{-5}$ Pa or 7.80×10^{-8} mm Hg (*cis*-isomer) $< 1.96 \times 10^{-6}$ Pa or 1.47×10^{-8} mm Hg (*trans*-isomer)			44721505
Dissociation constant (pK_a)	11.38±0.03 and 1.06±0.03 (in water at 29.1°C using spectrophotometric method; Lot No. AC 8879-140B)			44721505
Octanol/water partition coefficient, Log(K_{OW})	At 20 °C (using flask shaking method): K_{ow} (log K_{ow}) = 7090±989 (3.85) (Lot No. AC 8879-140B) (TGAI) K_{ow} (log K_{ow}) = 7150±803 (3.85) (*cis*-isomer, CL 354,801) K_{ow} (log K_{ow}) = 6800±1700 (3.8) (*trans*-isomer, CL 354,802)			44721505

UV/visible absorption spectrum — 46808403

pH	λ	A	log ε
cis-isomer			
2.0	221.4	0.828	4.03
6.8		0.8452	4.04
7.0		0.9126	4.08
10.3		0.7226	3.98
trans-isomer			
2.0	221.4	0.9053	4.07
7.0		0.9547	4.10
10.1		0.9893	4.11

* Product Chemistry Reviews: DP #256877, Shyam Mathur, Ph.D., 9/12/2000 and DP #329168, Shyam Mathur, Ph.D., 7/13/07.

B. EXPERIMENTAL DESIGN

B.1. Study Site Information

One rotational crop trial was conducted on wheat during the 2004-2005 growing season in the U.S. in Zone 5 (OH).

The study use pattern is detailed in Table B.1.2. The trial consisted of one untreated plot and three treated plots, with wheat planted as the primary crop. The primary wheat crop received two broadcast foliar applications of the 1.81 lb ai/gal flowable concentrate (FlC) formulation of metconazole at 0.25-0.26 lb ai/A/application, at a 14- to 15-day retreatment interval, for a total seasonal rate of 0.50-0.52 lb ai/A. Applications were made using ground equipment in spray volumes of ~15-19 gal/A of water without an adjuvant.

The treated primary wheat crop was destroyed and tilled into the soil, and the ground was prepared for planting according to area-typical agricultural practices. The representative rotational crops were grown at the plantback intervals of 32, 90, 150, and 365 days after the last application of metconazole to the primary wheat crop. Typical agricultural practices were used to grow and maintain the test crops. At each treatment plot, samples of wheat forage, hay, straw and grain were collected at the appropriate crop growth stage.

Trial site conditions are presented in Table B.1.1. Crop varieties are listed in Table C.3.1. The registrant reported that no maintenance pesticides were applied during the experimental period.

The weather conditions at each application and for the field trial duration, along with historical comparative data, were reported for the field trial. Rainfall was supplemented with irrigation as needed. The petitioner reported that in 2004, the temperatures were slightly cooler than average and during July and August of 2005 the temperatures were slightly higher than normal. Rainfall was normal during 2004 and below normal in 2005. No variations in weather conditions were reported which would adversely affect the growth of the crops.

One control and two treated samples of each rotational crop commodity were collected from each trial. Forage samples were collected 36-203 days after planting by cutting whole, immature green plants 2-3 inches above the soil at the 6-8 inch to jointing stage. Hay samples were similarly harvested 55-247 days after planting at early flower to soft dough stage and allowed to dry in the field for up to three days prior to collection. Grain and straw were collected 84-266 days after planting at crop maturity. Grain was separated from the straw by means of a mechanical thresher.

TABLE B.1.1 Trial Site Conditions.

Trial Identification: County, State; Year (Trial ID)	Soil characteristics				Meteorological data	
	Type	%OM	pH	CEC meq/g	Rainfall	Temperature
Fayette, OH; 2004 (V-27115-04-A)	Loam	3.8	6.6	23	For 2004, above normal. For 2005, below normal. The period June to August well below normal	For 2004, slightly cooler than normal in general. For 2005, above normal in July and August.

TABLE B.1.2. Study Use Pattern.

Trial Identification: County, State; Year (Trial ID)	EP[1]	Application					Tank Mix/ Adjuvants
		Method; Timing	Volume GPA[2]	Rate lb ai/A	RTI[3] (days)	Total Rate lb ai/A	
Fayette, OH; 2004 (V-27115-04-A)	1.81 lb ai/gal FlC	1. Broadcast foliar to wheat; Feekes Stage 8	19	0.26	14	0.52	None
		2. Broadcast foliar to wheat; Feekes stage 10.51	19	0.26			
	1.81 lb ai/gal FlC	1. Broadcast foliar to wheat; Feekes stage 11.4	15.5	0.25	14	0.50	None
		2. Broadcast foliar to wheat; Feekes stage 11.4 mature	14.9	0.25			
	1.81 lb ai/gal FlC	1. Broadcast foliar to wheat; Feekes stage 2	15.6	0.25	15	0.51	None
		2. Broadcast foliar to wheat; Feekes stage 2	15.9	0.25			

[1] EP = End-use Product
[2] GPA = Gallons per Acre
[3] RTI = Retreatment Interval

B.2. Sample Handling and Preparation

Samples were stored frozen at the field site immediately after harvest or collection. Samples were shipped initially by ACDS freezer truck to Valent Technical Center (Dublin, CA) 3-38 days after collection. Samples were stored frozen at Valent for 85-145 days, and then shipped to the analytical laboratory, BASF Agro Research (Research Triangle Park, NC). At BASF, samples were homogenized in the presence of dry ice and stored frozen (~-10 °C) until extraction and analysis.

B.3. Analytical Methodology

Samples of rotational wheat crop commodities were analyzed for residues of metconazole, metabolites M11, M21, and M30, and the triazole metabolites (1,2,4-T, TA, and TAA) using an LC/MS/MS method (BASF Method D0508). Wheat hay and straw were not analyzed for the triazole metabolites. A brief description of the method was included in the MRID.

Briefly, residues of metconazole and its metabolites (M11, M21, and M30) were extracted with acetonitrile (ACN):water (70:30, v:v). The extracts were diluted with methanol:water (80:20, v:v), filtered, and reserved for LC/MS/MS analysis. For determination of residues of 1,2,4-T, TA, and TAA, a separate aliquot of the initial extract was evaporated to dryness, redissolved in 0.1% formic acid in water, filtered, and reserved for LC/MS/MS analysis. Residues of metabolites M11, M21, and M30 were converted to parent equivalents using molecular weight conversion factors of 0.95 for M11 and M21 and 0.96 for M30.

The validated LOQ was 0.01 ppm for the parent metconazole (sum of *cis* and *trans* isomers at 0.005 ppm each), M11, M21, and M30 in wheat samples. The validated LOQ was 0.05 ppm for 1,2,4-T, TA, and TAA. The reported limit of detection was 20% of the LOQ.

The method was validated concurrently with the analysis of field samples using untreated wheat forage, hay, grain, and straw samples fortified at 0.005 and 0.5 ppm with *cis* and *trans*-metconazole; 0.01 and 1.0 ppm with M11, M21, and M30; and at 0.05 and 5.0 ppm with 1,2,4-T, TA, and TAA.

C. RESULTS AND DISCUSSION

Sample storage conditions and intervals are summarized in Table C.2. Samples were stored frozen (<-10 °C) from harvest to extraction for 336-382 days (11.0-12.6 months) for forage samples, 316-348 days (10.4-11.4 months) for hay samples, 286-328 days (9.4-10.8 months) for grain samples , and 287-329 days (9.4-10.8 months) for straw samples. All samples were analyzed within 0-6 days of extraction. Acceptable storage stability data are available indicating that: (1) residues of *cis*- and *trans*-metconazole are relatively stable under frozen storage conditions in/on wheat grain, rye forage, and wheat straw for up to 12 months (refer to 46902218.der.doc); (2) residues of M11, M21, and M30 are stable in/on wheat hay, grain, and straw for up to 6 months (refer to 46902223.der.doc); (3) residues of the triazole metabolites are stable/relatively stable in/on wheat grain for up to 6 months (refer to 46902223.der.doc); and (4) residues of TA are stable in/on wheat grain for up to 12 months (refer to 46902221.der.doc). Adequate storage stability data are available to support the storage conditions and duration of wheat commodities analyzed for *cis*- and *trans*-metconazole.

Concurrent method recovery data are presented in Table C.1. Samples of rotational wheat commodities were analyzed for residues of *cis*- and *trans*-metconazole, metabolites M11, M21, and M30 and the triazole metabolites (1,2,4-T, TA, and TAA) using LC/MS/MS Method D0508. Wheat hay and straw were not analyzed for the triazole metabolites. Residues of metabolites M11, M21, and M30 were converted to parent equivalents using molecular weight conversion

factors of 0.95 for M11 and M21 and 0.96 for M30. The method was adequate for data collection based on acceptable concurrent method recovery data. Concurrent method recoveries were generally within the acceptable range of 70-120% for wheat forage, grain, hay, and straw samples fortified at 0.005 and 0.5 ppm with *cis* and *trans*-metconazole, at 0.01 and 1.00 ppm with M11, M21 and M30, and at 0.05 and 5.00 ppm with 1,2,4-T, TA, and TAA. Low recoveries (64-65%) were obtained for M11 and M30 in wheat straw at 0.01 ppm each; for 1,2,4-T in forage at 0.05 ppm; and for TA in forage and grain at 0.05 and 5.0 ppm, respectively.

Apparent residues of *cis*- and *trans*-metconazole, its metabolites M11, M21, and M30, and 1,2,4-T, TA, and TAA were each below the respective LOQs in two samples of untreated wheat forage, hay, grain, and straw, with the exception of one grain sample which bore TAA residues of 0.06 ppm.

Metconazole residue data from the field rotational crop study are presented in Tables C.3.1 (metconazole, M11, M21, and M30) and C.3.2 (triazole metabolites). A summary of residue data for rotated wheat commodities is presented in Table C.4. Residues of metconazole (*cis* and *trans* isomers), M11, M21, and M30 were below the LOQ (<0.01 ppm) in samples of wheat forage, hay, straw, and grain from the 32-, 90-, 150-, and 365-day PBIs.

Residues of 1,2,4-T were below the LOQ s (<0.05 ppm) in samples of wheat forage and grain from all PBIs. Quantifiable residues of TA and TAA were found in wheat forage and grain from all PBIs, and residues of both analytes generally declined from the 32-day PBI to the 365-day PBI (i.e., from 0.52 to 0.05 ppm for TA and from 0.19 to <0.05 ppm for TAA in wheat forage; and from 0.69 to 0.33 ppm for TA and from 1.00 to 0.22 ppm for TAA in wheat grain).

TABLE C.1. Summary of Concurrent Recoveries of Metconazole and Metabolites from Rotated Wheat Commodities.

Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean (%)
Forage	*trans*-Metconazole	0.005	1	77	77
		0.50	1	101	101
	cis-Metconazole	0.005	1	93	93
		0.50	1	97	97
	M11	0.01	1	75	75
		1.00	1	87	87
	M21	0.01	1	93	93
		1.00	1	81	81
	M30	0.01	1	80	80
		1.00	1	91	91
	1,2,4-T	0.05	1	64	64
		5.00	1	77	77
	TA	0.05	1	64	64
		5.00	1	72	72
	TAA	0.05	1	90	90
		5.00	1	99	99
Grain	*trans*-	0.005	1	81	81

TABLE C.1. Summary of Concurrent Recoveries of Metconazole and Metabolites from Rotated Wheat Commodities.

Matrix	Analyte	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean (%)
	Metconazole	0.50	1	97	97
	cis-Metconazole	0.005	1	105	105
		0.50	1	86	86
	M11	0.01	1	93	93
		1.00	1	85	85
	M21	0.01	1	113	113
		1.00	1	99	99
	M30	0.01	1	109	109
		1.00	1	91	91
	1,2,4-T	0.05	1	89	89
		5.00	1	72	72
	TA	0.05	1	84	84
		5.00	1	65	65
	TAA	0.05	1	100	100
		5.00	1	83	83
Hay	*trans*-Metconazole	0.005	1	94	94
		0.50	1	98	98
	cis-Metconazole	0.005	1	86	86
		0.50	1	100	100
	M11	0.01	1	87	87
		1.00	1	102	102
	M21	0.01	1	105	105
		1.00	1	103	103
	M30	0.01	1	88	88
		1.00	1	92	92
Straw	*trans*-Metconazole	0.005	1	71	71
		0.50	1	112	112
	cis-Metconazole	0.005	1	73	73
		0.50	1	94	94
	M11	0.01	1	64	64
		1.00	1	99	99
	M21	0.01	1	72	72
		1.00	1	115	115
	M30	0.01	1	64	64
		1.00	1	95	95

TABLE C.2. Summary of Storage Conditions.

Matrix	Storage Temperature (°C)	Actual Storage Duration [1] Days (Months)	Interval of Demonstrated Storage Stability
Forage	≤-10	336-382 (11.0-12.6)	Acceptable storage stability data are available indicating that residues of *cis*- and *trans*-metconazole are relatively stable in/on wheat grain, rye forage, and wheat straw for up to 12 months; residues of M11, M21, and M30 are stable in/on wheat hay, grain, and straw for up to 6 months; residues of the triazole metabolites are stable/relatively stable in/on wheat grain for up to 6 months; and residues of TA are stable in/on wheat grain stored frozen for up to 12 months.[2]
Hay		316-348 (10.4-11.4)	
Grain		286-328 (9.4-10.8)	
Straw		287-329 (9.4-10.8)	

[1] Storage duration from harvest to extraction; samples analyzed within 1-6 days of extraction.
[2] Refer to 46902218.der.doc, 46902221.der.doc, and 46902223.der.doc.

TABLE C.3.1. Residues of Metconazole, M11, M21, and M30 in Rotated Wheat Commodities.

Trial ID: County, State; Year	Crop; Variety	Matrix	Total Rate (lb ai/A)	Harvest DAP[1]	PBI[2]	Metconazole Residues (ppm parent equivalents)						Total [3]
						Metconazole			Metabolites			
						cis	*trans*	Total	M11	M21	M30	
Fayette, OH; 2004 (V-27115-04-A) Zone 5	Winter wheat; Crop Plan 569W	Forage	0.51	212	32	<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
			0.50	212	90	<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
			0.52	203	150	<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
	Spring wheat; Garinger HRS		0.52	36	365	<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
Fayette, OH; 2004 (V-27115-04-A) Zone 5	Winter wheat; Crop Plan 569W	Grain	0.51	266	32	<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
			0.50	266	90	<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
			0.52	257	150	<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
	Spring wheat; Garinger HRS		0.52	84	365	<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
Fayette, OH; 2004 (V-27115-04-A) Zone 5	Winter wheat; Crop Plan 569W	Hay	0.51	247	32	<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
			0.50	247	90	<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
			0.52	238	150	<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
	Spring wheat; Garinger HRS		0.52	55	365	<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04

TABLE C.3.1. Residues of Metconazole, M11, M21, and M30 in Rotated Wheat Commodities.

Trial ID: County, State; Year	Crop; Variety	Matrix	Total Rate (lb ai/A)	Harvest DAP[1]	PBI[2]	Metconazole Residues (ppm parent equivalents)						Total[3]
						Metconazole			Metabolites			
						cis	*trans*	Total	M11	M21	M30	
Fayette, OH; 2004 (V-27115-04-A) Zone 5	Winter wheat; Crop Plan 569W	Straw	0.51	266	32	<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
			0.50	266	90	<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
			0.52	257	150	<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
	Spring wheat; Garinger HRS		0.52	84	365	<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04
						<0.005	<0.005	<0.01	<0.01	<0.01	<0.01	<0.04

[1] DAP = Days After Planting
[2] PBI = Plantback Interval (days).
[3] Total = total residues; sum of *cis*- and *trans*-metconazole, M11, M21, and M30; values presented as calculated and reported by the petitioner.

TABLE C.3.2. Residues of the Triazole Metabolites in Rotated Wheat Commodities.

Trial Identification: County, State; Year (Trial ID)	Zone	Crop; Variety	Matrix	Total Rate (lb ai/A)	Harvest DAP[1]	PBI[2]	Triazole Residues (ppm)[3]		
							1,2,4-T	TA	TAA
Fayette, OH; 2004 (V-27115-04-A)	5	Wheat	Forage	0.51	212	32	<0.05	0.52	0.19
							<0.05	0.48	0.17
				0.50	212	90	<0.05	0.29	0.11
							<0.05	0.29	0.12
				0.52	203	150	<0.05	0.31	0.12
							<0.05	0.35	0.12
				0.52	36	365	<0.05	0.05	<0.05
							<0.05	0.05	<0.05
Fayette, OH; 2004 (V-27115-04-A)	5	Wheat	Grain	0.51	266	32	<0.05	0.69	1.00
							<0.05	0.45	0.75
				0.50	266	90	<0.05	0.37	0.45
							<0.05	0.43	0.54
				0.52	257	150	<0.05	0.40	0.49
							<0.05	0.51	0.67
				0.52	84	365	<0.05	0.33	0.22
							<0.05	0.30	0.21
							NA	NA	NA

[1] DAP = Days After Planting
[2] PBI = Plantback Interval.
[3] NA = Not analyzed

TABLE C.4. Summary of Residue Data in Rotational Crops Following Treatment of a Primary Crop with Metconazole.

Commodity	Total Applic. Rate (lb ai/A)	Analyte	PBI	Residue Levels (ppm) [1]						
				n	Min.	Max.	HAFT[2]	Median (STMdR)	Mean (STMR)	Std. Dev.
Wheat, forage	0.50-0.52	*cis*-metconazole	32	2	<0.005	<0.005	0.005	0.005	0.005	--
		trans-metconazole		2	<0.005	<0.005	0.005	0.005	0.005	--
		Metconazole		**2**	**<0.01**	**<0.01**	**0.01**	**0.01**	**0.01**	**--**
		M11		2	<0.01	<0.01	0.01	0.01	0.01	--
		M12		2	<0.01	<0.01	0.01	0.01	0.01	--
		M30		2	<0.01	<0.01	0.01	0.01	0.01	--
		Total Residues		2	<0.04	<0.04	0.04	0.04	0.04	--
Wheat, hay	0.50-0.52	*cis*-metconazole	32	2	<0.005	<0.005	0.005	0.005	0.005	--
		trans-metconazole		2	<0.005	<0.005	0.005	0.005	0.005	--
		Metconazole		**2**	**<0.01**	**<0.01**	**0.01**	**0.01**	**0.01**	**--**
		M11		2	<0.01	<0.01	0.01	0.01	0.01	--
		M21		2	<0.01	<0.01	0.01	0.01	0.01	--
		M30		2	<0.01	<0.01	0.01	0.01	0.01	--
		Total Residues		2	<0.04	<0.04	0.04	0.04	0.04	--
Wheat, grain	0.50-0.52	*cis*-metconazole	32	2	<0.005	<0.005	0.005	0.005	0.005	--
		trans-metconazole		2	<0.005	<0.005	0.005	0.005	0.005	--
		Metconazole		**2**	**<0.01**	**<0.01**	**0.01**	**0.01**	**0.01**	**--**
		M11		2	<0.01	<0.01	0.01	0.01	0.01	--
		M21		2	<0.01	<0.01	0.01	0.01	0.01	--
		M30		2	<0.01	<0.01	0.01	0.01	0.01	--
		Total Residues		2	<0.04	<0.04	0.04	0.04	0.04	--
Wheat, straw	0.50-0.52	*cis*-metconazole	32	2	<0.005	<0.005	0.005	0.005	0.005	--
		trans-metconazole		2	<0.005	<0.005	0.005	0.005	0.005	--
		Metconazole		**2**	**<0.01**	**<0.01**	**0.01**	**0.01**	**0.01**	**--**
		M11		2	<0.01	<0.01	0.01	0.01	0.01	--
		M21		2	<0.01	<0.01	0.01	0.01	0.01	--
		M30		2	<0.01	<0.01	0.01	0.01	0.01	--
		Total Residues		2	<0.04	<0.04	0.04	0.04	0.04	--
Wheat, forage	0.50-0.52	*cis*-metconazole	90	2	<0.005	<0.005	0.005	0.005	0.005	--
		trans-metconazole		2	<0.005	<0.005	0.005	0.005	0.005	--
		Metconazole		**2**	**<0.01**	**<0.01**	**0.01**	**0.01**	**0.01**	**--**
		M11		2	<0.01	<0.01	0.01	0.01	0.01	--
		M21		2	<0.01	<0.01	0.01	0.01	0.01	--
		M30		2	<0.01	<0.01	0.01	0.01	0.01	--
		Total Residues		2	<0.04	<0.04	0.04	0.04	0.04	--

TABLE C.4. Summary of Residue Data in Rotational Crops Following Treatment of a Primary Crop with Metconazole.

Commodity	Total Applic. Rate (lb ai/A)	Analyte	PBI	Residue Levels (ppm) [1]						
				n	Min.	Max.	HAFT[2]	Median (STMdR)	Mean (STMR)	Std. Dev.
Wheat, hay	0.50-0.52	*cis*-metconazole	90	2	<0.005	<0.005	0.005	0.005	0.005	--
		trans-metconazole		2	<0.005	<0.005	0.005	0.005	0.005	--
		Metconazole		**2**	**<0.01**	**<0.01**	**0.01**	**0.01**	**0.01**	**--**
		M11		2	<0.01	<0.01	0.01	0.01	0.01	--
		M21		2	<0.01	<0.01	0.01	0.01	0.01	--
		M30		2	<0.01	<0.01	0.01	0.01	0.01	--
		Total Residues		2	<0.04	<0.04	0.04	0.04	0.04	--
Wheat, grain	0.50-0.52	*cis*-metconazole	90	2	<0.005	<0.005	0.005	0.005	0.005	--
		trans-metconazole		2	<0.005	<0.005	0.005	0.005	0.005	--
		Metconazole		**2**	**<0.01**	**<0.01**	**0.01**	**0.01**	**0.01**	**--**
		M11		2	<0.01	<0.01	0.01	0.01	0.01	--
		M21		2	<0.01	<0.01	0.01	0.01	0.01	--
		M30		2	<0.01	<0.01	0.01	0.01	0.01	--
		Total Residues		2	<0.04	<0.04	0.04	0.04	0.04	--
Wheat, straw	0.50-0.52	*cis*-metconazole	90	2	<0.005	<0.005	0.005	0.005	0.005	--
		trans-metconazole		2	<0.005	<0.005	0.005	0.005	0.005	--
		Metconazole		**2**	**<0.01**	**<0.01**	**0.01**	**0.01**	**0.01**	**--**
		M11		2	<0.01	<0.01	0.01	0.01	0.01	--
		M21		2	<0.01	<0.01	0.01	0.01	0.01	--
		M30		2	<0.01	<0.01	0.01	0.01	0.01	--
		Total Residues		2	<0.04	<0.04	0.04	0.04	0.04	--
Wheat, forage	0.50-0.52	*cis*-metconazole	150	2	<0.005	<0.005	0.005	0.005	0.005	--
		trans-metconazole		2	<0.005	<0.005	0.005	0.005	0.005	--
		Metconazole		**2**	**<0.01**	**<0.01**	**0.01**	**0.01**	**0.01**	**--**
		M11		2	<0.01	<0.01	0.01	0.01	0.01	--
		M21		2	<0.01	<0.01	0.01	0.01	0.01	--
		M30		2	<0.01	<0.01	0.01	0.01	0.01	--
		Total Residues		2	<0.04	<0.04	0.04	0.04	0.04	--
Wheat, hay	0.50-0.52	*cis*-metconazole	150	2	<0.005	<0.005	0.005	0.005	0.005	--
		trans-metconazole		2	<0.005	<0.005	0.005	0.005	0.005	--
		Metconazole		**2**	**<0.01**	**<0.01**	**0.01**	**0.01**	**0.01**	**--**
		M11		2	<0.01	<0.01	0.01	0.01	0.01	--
		M21		2	<0.01	<0.01	0.01	0.01	0.01	--
		M30		2	<0.01	<0.01	0.01	0.01	0.01	--
		Total Residues		2	<0.04	<0.04	0.04	0.04	0.04	--

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TABLE C.4. Summary of Residue Data in Rotational Crops Following Treatment of a Primary Crop with Metconazole.

Commodity	Total Applic. Rate (lb ai/A)	Analyte	PBI	Residue Levels (ppm) [1]						
				n	Min.	Max.	HAFT[2]	Median (STMdR)	Mean (STMR)	Std. Dev.
Wheat, grain	0.50-0.52	*cis*-metconazole	150	2	<0.005	<0.005	0.005	0.005	0.005	--
		trans-metconazole		2	<0.005	<0.005	0.005	0.005	0.005	--
		Metconazole		**2**	**<0.01**	**<0.01**	**0.01**	**0.01**	**0.01**	**--**
		M11		2	<0.01	<0.01	0.01	0.01	0.01	--
		M21		2	<0.01	<0.01	0.01	0.01	0.01	--
		M30		2	<0.01	<0.01	0.01	0.01	0.01	--
		Total Residues		2	<0.04	<0.04	0.04	0.04	0.04	--
Wheat, straw	0.50-0.52	*cis*-metconazole	150	2	<0.005	<0.005	0.005	0.005	0.005	--
		trans-metconazole		2	<0.005	<0.005	0.005	0.005	0.005	--
		Metconazole		**2**	**<0.01**	**<0.01**	**0.01**	**0.01**	**0.01**	**--**
		M11		2	<0.01	<0.01	0.01	0.01	0.01	--
		M21		2	<0.01	<0.01	0.01	0.01	0.01	--
		M30		2	<0.01	<0.01	0.01	0.01	0.01	--
		Total Residues		2	<0.04	<0.04	0.04	0.04	0.04	--
Wheat, forage	0.50-0.52	*cis*-metconazole	365	2	<0.005	<0.005	0.005	0.005	0.005	--
		trans-metconazole		2	<0.005	<0.005	0.005	0.005	0.005	--
		Metconazole		**2**	**<0.01**	**<0.01**	**0.01**	**0.01**	**0.01**	**--**
		M11		2	<0.01	<0.01	0.01	0.01	0.01	--
		M21		2	<0.01	<0.01	0.01	0.01	0.01	--
		M30		2	<0.01	<0.01	0.01	0.01	0.01	--
		Total Residues		2	<0.04	<0.04	0.04	0.04	0.04	--
Wheat, hay	0.50-0.52	*cis*-metconazole	365	2	<0.005	<0.005	0.005	0.005	0.005	--
		trans-metconazole		2	<0.005	<0.005	0.005	0.005	0.005	--
		Metconazole		**2**	**<0.01**	**<0.01**	**0.01**	**0.01**	**0.01**	**--**
		M11		2	<0.01	<0.01	0.01	0.01	0.01	--
		M21		2	<0.01	<0.01	0.01	0.01	0.01	--
		M30		2	<0.01	<0.01	0.01	0.01	0.01	--
		Total Residues		2	<0.04	<0.04	0.04	0.04	0.04	--
Wheat, grain	0.50-0.52	*cis*-metconazole	365	2	<0.005	<0.005	0.005	0.005	0.005	--
		trans-metconazole		2	<0.005	<0.005	0.005	0.005	0.005	--
		Metconazole		**2**	**<0.01**	**<0.01**	**0.01**	**0.01**	**0.01**	**--**
		M11		2	<0.01	<0.01	0.01	0.01	0.01	--
		M21		2	<0.01	<0.01	0.01	0.01	0.01	--
		M30		2	<0.01	<0.01	0.01	0.01	0.01	--
		Total Residues		2	<0.04	<0.04	0.04	0.04	0.04	--

TABLE C.4. Summary of Residue Data in Rotational Crops Following Treatment of a Primary Crop with Metconazole.

Commodity	Total Applic. Rate (lb ai/A)	Analyte	PBI	Residue Levels (ppm) [1]						
				n	Min.	Max.	HAFT[2]	Median (STMdR)	Mean (STMR)	Std. Dev.
Wheat, straw	0.50-0.52	*cis*-metconazole	365	2	<0.005	<0.005	0.005	0.005	0.005	--
		trans-metconazole		2	<0.005	<0.005	0.005	0.005	0.005	--
		Metconazole		**2**	**<0.01**	**<0.01**	**0.01**	**0.01**	**0.01**	**--**
		M11		2	<0.01	<0.01	0.01	0.01	0.01	--
		M21		2	<0.01	<0.01	0.01	0.01	0.01	--
		M30		2	<0.01	<0.01	0.01	0.01	0.01	--
		Total Residues		2	<0.04	<0.04	0.04	0.04	0.04	--

[1] For calculation of the mean and median, the LOQ was used for any results reported as <LOQ in Table C.3.
[2] HAFT = Highest Average Field Trial.

D. CONCLUSION

In limited field rotational crop trials conducted on wheat, a primary crop of wheat received two broadcast foliar applications of a 1.81 lb/gal FlC formulation of metconazole at a 14- to 15-day retreatment interval for a total rate of ~0.52 lb ai/A. The primary crop was destroyed and tilled into the soil, and rotational wheat was grown at plantback intervals of 32, 90, 150, and 365 days after the last application of metconazole to the primary wheat crop. An acceptable method was used for quantitation of residues of *cis*- and *trans*- metconazole, M11, M21, M30, 1,2,4-T, TA, and TAA in/on wheat matrices. Adequate storage stability data are available to support the storage conditions and duration of wheat commodities analyzed for *cis*- and *trans*-metconazole.

E. REFERENCES

DP#: 324541
Subject: Metconazole. Request for a Tolerance on Imported Bananas. Summary of Analytical Chemistry and Residue Data. Petition Number 9E05052.
From: N. Dodd
To: M. Waller
Date: 12/14/05
MRIDs: 44721506, 44721507, 44721508, 44721509, 44721510, and 44721511

F. DOCUMENT TRACKING

RDI: N. Dodd (2/20/08)
Petition Numbers: 6F7094 and 6F7095
DP#s: 348168 and 348206
PC Code: 125619

Template Version June 2005

13544

R157862

Chemical: Metconazole

PC Code:
125619

HED File Code: 11500 Petition Files Chemistry
Memo Date: 2/20/2008
File ID: DPD348168
DPD348206
DPD324541
DPD348234
DPD339992
DPD339994
DPD339995
Accession #: 000-00-0124

HED Records Reference Center
3/31/2008