UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
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OFFICE OF
PREVENTION, PESTICIDES, AND
TOXIC SUBSTANCES

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

MEMORANDUM

DATE: 18-DEC-2002

SUBJECT: **Imidacloprid.** Issues to be Presented to the Health Effects Division (HED) Metabolism Assessment Review Committee (MARC) Meeting on 12/11/02. Barcode D287025. Chemical 129099. Case 294718. Submission S609879.

FROM: Jennifer R. Tyler, Chemist
David Nixon, D.V.M., Ph.D., Toxicologist
Registration Action Branch 1 (RAB1)/HED (7509C)

THROUGH: G. Jeffrey Herndon, Branch Senior Scientist
RAB1/HED (7509C)

TO: Yan Donovan, Executive Secretary
HED MARC (7509C)

Issues to be Considered

- Residues to be included in risk assessment for drinking water.

Background

The Interregional Research Project No. 4 (IR-4), on behalf of the Agricultural Experiment Stations of several states, has submitted petitions for the establishment of permanent tolerances for the combined residues of imidacloprid (1-[(6-chloro-3-pyridinyl)methyl]-*N*-nitro-2-imidazolidinimine) and its metabolites containing the 6-chloropyridinyl moiety, all expressed as 1-[(6-chloro-3-pyridinyl)methyl]-*N*-nitro-2-imidazolidinimine, in/on several raw agricultural commodities (RACs).

Imidacloprid is an insecticide registered for uses on a variety of crops for the control of aphids, cucumber beetles and whiteflies (including Sweet potato or Silverleaf whitefly). Imidacloprid is a member of the pyridylmethylamine class of compounds. Its mode of action is the disruption of the nervous system by acting as an inhibitor at nicotinic acetylcholine receptors. Imidacloprid

blocks the signals that are induced by acetylcholine at the post-synaptic membrane, resulting in normal nerve function impairment.

Tolerances are currently established for the combined residues of imidacloprid and its metabolites containing the 6-chloropyridinyl moiety, all expressed as the parent, under 40 CFR §180.472 in/on various plant and livestock commodities. Section 18 Emergency Exemption tolerances with expiration/revocation dates are established in/on plant commodities under 40 CFR §180.472(b), and indirect or inadvertent tolerances are established as a result of application of the pesticide to growing crops and other non-food crops under 40 CFR §180.472(d).

RESIDUE CHEMISTRY DATA

Data concerning the metabolism of imidacloprid in apples, potatoes, tomatoes, eggplant, cottonseed, field corn, tobacco, ruminants, and poultry have been submitted and reviewed in conjunction with PP#3F4169/3H5655 (Memos, F. Griffith, 9/20/93, D185148; 6/8/94, D200233; and 2/29/96, D217632). The results of the aforementioned plant and livestock metabolism studies were presented to the HED Metabolism Committee on 6/22/93 (Memo, F. Griffith, 6/18/93, No Barcode). The nature of imidacloprid residues in plants and livestock is adequately understood. The residue of concern in plants and livestock is imidacloprid and its metabolites containing the 6-chloropyridinyl moiety, all expressed as the parent, as specified in 40 CFR §180.472. See Attachment 3 for the 6/18/93 document.

ENVIRONMENTAL FATE DATA

See Attachment 2 for the MARC Meeting Questionnaire provided by the Environmental Fate and Effects Division (EFED).

TOXICOLOGY DATA

The following information was taken from the HED Hazard Identification Assessment Review Committee (HIARC) document dated 10/31/02 (Memo, D. Nixon, TXR# 0051292). See Attachment 5 for the proposed metabolic pathway of imidacloprid in rats.

Rat Metabolism Study: Methylene-labeled imidacloprid was rapidly absorbed with approximately 90% of the administered dose being eliminated within 24 hours and 96% within 48 hours. There were no biologically significant differences between sexes, dose levels, or route of administration. Urinary excretion was the major route of elimination (70-80% of recovered radioactivity), with a lesser amount eliminated in feces (17-25% of recovered radioactivity). Biliary excretion was a major contributor to fecal radioactivity (36.6% vs. 4.8% of recovered radioactivity in bile-fistulated animals). Total tissue burden after 48 hours accounted for only approximately 0.5% of the recovered radioactivity, with major sites of accumulation being the liver, kidney, lung, skin, and plasma and minor sites being the brain and testes. Maximum plasma concentration occurred between 1.1 and 2.5 hours, and elimination half-lives (calculated from two exponential terms) were 3 and 26-118 hours. There were two major evident routes of biotransformation. The first included an oxidative cleavage of the parent compound to give 6-chloronicotinic acid and its glycine conjugate. Dechlorination of this metabolite formed the 6-

hydroxynicotinic acid and its mercapturic acid derivative. The second included the hydroxylation of imidazolidine followed by elimination of water of the parent compound to give NTN 35884.

In a comparison between [Methylene-^{14}C] Imidacloprid and [Imidazolidine-4,5-^{14}C] Imidacloprid, the rates of excretion were similar; however, the renal portion was higher with the imidazolidine-labeled test material (90% vs. 75% of recovered radioactivity for methylene-labeled test material. The imidazolidine-labeled test material also demonstrated higher accumulation in the tissues (approximately 1% of recovered radioactivity), with the major sites of accumulation being the liver, kidney, lung, and skin, and the minor sites being brain and muscle.

In a comparison between [Methylene-^{14}C] Imidacloprid and WAK 3839, there were no significant differences in the absorption, distribution, and excretion of the total radioactivity. More radioactivity was found in the tissues of the animals receiving imidacloprid at the 1.0 and 150.0 dose levels (respectively 0.9% and 3.4% vs. 0.2% of administered radioactivity for the WAK 3839 group). The major sites of accumulation of WAK 3839 included lung, renal fat, liver, and kidney, with minor sites being the testis and brain. WAK 3839 was formed during pretreatment (chronic oral dosing) of imidacloprid; however, the proposed metabolic pathways of the two compounds were different.

Toxicological Doses and Endpoints: The summary of toxicological doses and endpoints for imidacloprid for use in human risk assessment is presented in Table 1.

Table 1. Toxicological Doses and Endpoints for Imidacloprid.

Exposure Scenario	Dose Used in Risk Assessment, UF	* Special FQPA SF and Level of Concern for Risk Assessment	Study and Toxicological Effects
Acute Dietary all populations	LOAEL = 42 mg/kg/day UF = 300 **Acute RfD** = 0.14 mg/kg	FQPA SF = 1X **aPAD** = acute RfD / FQPA SF = 0.14 mg/kg	Acute neurotoxicity - rat LOAEL = 42 mg/kg, based upon the decrease in motor and locomotor activities observed in females.
Chronic Dietary all populations	NOAEL= 5.7 mg/kg/day UF = 100 **Chronic RfD** = 0.057 mg/kg/day	FQPA SF = 1X **cPAD** = chr RfD / FQPA SF = 0.057 mg/kg/day	Combined chronic tox/carcinogenicity - rat LOAEL = 16.9 mg/kg/day, based upon increased incidence of mineralized particles in thyroid colloid in males.
Short-Term Oral (1-30 days)	oral study NOAEL= 10 mg/kg/day	**LOC for MOE** = 100 (Residential, includes the FQPA SF)	Developmental toxicity - rat Maternal LOAEL = 30 mg/kg/day, based upon decreased body weight gain and corrected body weight gain.
Intermediate-Term Oral (1- 6 months)	oral study NOAEL= 9.3 mg/kg/day	**LOC for MOE** = 100 (Residential, includes the FQPA SF)	Subchronic neurotoxicity - rat LOAEL = 63.3 mg/kg/day, based upon decreased body weight gain.
Short-Term Dermal (1-30 days)	oral study NOAEL= 10 mg/kg/day (dermal absorption rate = 7.2%)	**LOC for MOE** = 100 (Occupational) **LOC for MOE** = 100 (Residential, includes the FQPA SF)	Developmental toxicity - rat Maternal LOAEL = 30 mg/kg/day, based upon decreased body weight gain and corrected body weight gain.

Exposure Scenario	Dose Used in Risk Assessment, UF	* Special FQPA SF and Level of Concern for Risk Assessment	Study and Toxicological Effects
Intermediate-Term Dermal (1-6 months)	oral study NOAEL= 9.3 mg/kg/day (dermal absorption rate = 7.2%)	**LOC for MOE** = 100 (Occupational) **LOC for MOE** = 100 (Residential, includes the FQPA SF)	Subchronic neurotoxicity - rat LOAEL = 63.3 mg/kg/day, based upon decreased body weight gain.
Long-Term Dermal (> 6 months)	oral study NOAEL= 5.7 mg/kg/day (dermal absorption rate = 7.2%)	**LOC for MOE** = 100 (Occupational) **LOC for MOE** = 100 (Residential, includes the FQPA SF)	Combined chronic tox/carcinogenicity - rat LOAEL = 16.9 mg/kg/day, based upon increased incidence of mineralized particles in thyroid colloid in males.
Short-Term Inhalation (1-30 days)	oral study NOAEL= 10 mg/kg/day (inhalation absorption rate = 100%)	**LOC for MOE** = 100 (Occupational) **LOC for MOE** = 100 (Residential, includes the FQPA SF)	Developmental toxicity - rat Maternal LOAEL = 30 mg/kg/day, based upon decreased body weight gain and corrected body weight gain.
Intermediate-Term Inhalation (1- 6 months)	oral study NOAEL= 9.3 mg/kg/day (inhalation absorption rate = 100%)	**LOC for MOE** = 100 (Occupational) **LOC for MOE** = 100 (Residential, includes the FQPA SF)	Subchronic neurotoxicity - rat LOAEL = 63.3 mg/kg/day, based upon decreased body weight gain.
Long-Term Inhalation (> 6 months)	oral study NOAEL= 5.7 mg/kg/day (inhalation absorption rate = 100%)	**LOC for MOE** = 100 (Occupational) **LOC for MOE** = 100 (Residential, includes the FQPA SF)	Combined chronic tox/carcinogenicity - rat LOAEL = 16.9 mg/kg/day, based upon increased incidence of mineralized particles in thyroid colloid in males.
Cancer (oral, dermal, inhalation)	Group E	Not applicable	No evidence of carcinogenicity in rats and mice.

QUESTIONS TO THE MARC

Is there any scientific objection to conducting the drinking water assessment for imidacloprid in terms of imidacloprid *per se*? Are additional imidacloprid degradates of special toxicological concern? If so, which one(s)? Do they warrant inclusion in the drinking water assessment?

ATTACHMENTS

Attachment 1: Team Recommendation for Residues to Include in Tolerance Expression and Risk Assessment.
Attachment 2: MARC Meeting Questionnaire - EFED.
Attachment 3: Imidacloprid (Confidor®) - Issues to be Presented to the Metabolism Committee on June 22, 1993 (Available Electronically on T-drive).
Attachment 4: Proposed Metabolic Pathways of Imidacloprid in Rat (Not Available Electronically).

Cc (w/ attachments): J. Tyler, R. Forrest/S. Brothers and M. Laws/D. Daniel (RD 7505C)
RDI: G. Herndon (11/21/02)
J.Tyler: 809B: CM#2: (703)305-5564: 7509C: RAB1

ATTACHMENT 1: Team Recommendation for Residues to Include in Tolerance Expression and Risk Assessment.

Team Recommendation for Imidacloprid

Matrix	Residues included in Tolerance Expression	Residues included in Risk Assessment
Plants	Imidacloprid and its metabolites containing the 6-chloropyridinyl moiety, all expressed as the parent[1]	
Livestock	Imidacloprid and its metabolites containing the 6-chloropyridinyl moiety, all expressed as the parent[1]	
Rotational Crops	Imidacloprid and its metabolites containing the 6-chloropyridinyl moiety, all expressed as the parent[1]	
Drinking Water	NA[2]	See Attachment 2.

[1] As stated in 40 CFR §180.472.
[2] NA = Not Applicable.

ATTACHMENT 2: MARC MEETING QUESTIONNAIRE

EFED

Imidacloprid
Prepared by Michael R. Barrett (EFED)
12/04/02

In order to determine which degradates, if any, should be included in the human drinking water exposure assessment, please answer the following questions to the best of your ability and create tables using the formats provided below.

5. *What is the name of the pesticide and what uses are being considered in this assessment?*

Imidacloprid is currently registered for use on a wide variety of crops that include both preplant or at-planting soil applications and foliar applications (Appendix 1). imidacloprid is registered for direct outdoor applications on fruit, vegetable crops, and cotton . The compound is also registered as a seed treatment for several crops which do not carry a registration for direct soil or foliar application, including small grains (canola, barley, wheat), sugar beets and sorghum.

6. *Briefly describe the environmental persistence of the pesticide. What are expected to be the major routes of degradation in the environment (e.g. aerobic soil metabolism, soil photolysis, etc)? What is the expected persistence in soil and water (provide available half lives)?*

Imidacloprid is stable to hydrolysis, and typically persists for many months in soil. However, imidacloprid appears to be more rapidly transformed under anaerobic conditions and appears to be particularly photolabile in water[1]. Given that imidacloprid is mobile, and likely to be highly persistent in the subsurface, it may leach to ground water (results of the prospective ground-water monitoring studies confirm this). Imidacloprid may also pose a contamination hazard to surface waters via runoff, and may be especially persistent in surface water with high turbidity.

7. *Briefly describe the expected mobility of the pesticide. Is the pesticide volatile? Does the pesticide bind soil or sediment strongly (please provide Kd or Koc)?*

Imidacloprid is moderately mobile with measured Koc values of 132 to 256. Imidacloprid has been detected in ground water from two small-scale prospective monitoring studies at concentrations up to 3.12 ppm.

8. *Briefly describe the degradates of the pesticide. Identify major and minor degradates. Provide available information degradate stability and mobility.*

Available data do not clearly indicate that any particular degradate(s) are the most significant under most outdoor conditions. It is possible that in studies where imidacloprid was exceptionally persistent (hydrolysis, aerobic soil metabolism) major metabolites could occur over a longer term. Under anaerobic conditions Degradate 2 (NTN 38014 alias NTN 3382) did accumulate without any clear sign of further degradation over the one year period of this study.

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[1] This issue is an uncertainty as noted earlier. Therefore, EECs reflect short photolysis half-life (0.2 days) and 39 day half-life

9. *If possible, describe the effects of water treatment on the pesticide and degradates that may reach drinking water sources.*

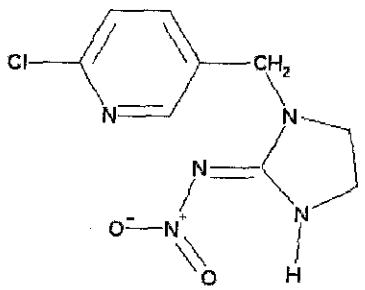
Unknown.

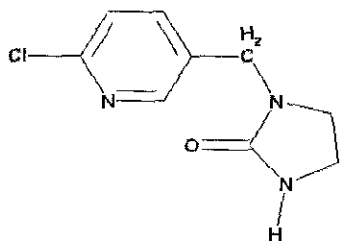
10. *Provide any other pertinent information (e.g. monitoring data).*

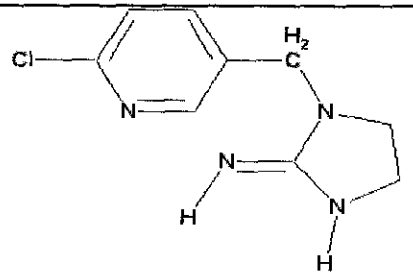
In two prospective ground-water monitoring studies and a handful of other well samples, imidacloprid was found to reach ground water.

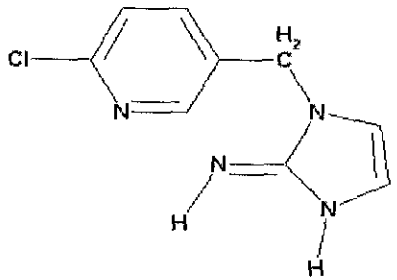
11. Complete the table for the pesticide and degradates.

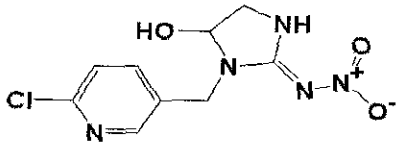
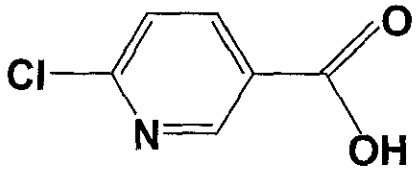
TABLE 1. IMIDACLOPRID AND ITS DEGRADATES: EXTENT OF FORMATION (OR DECLINE FOR PARENT) IN VARIOUS ENVIRONMENTAL FATE STUDIES.

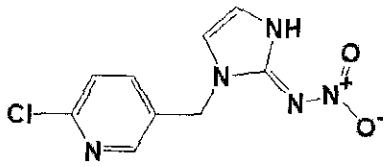
Degradate Name and Structure	Percent of Applied Dose	Study	Comments
Parent  Imidacloprid parent.	Stable at pH 5 and 7; slow degradation at pH 9 (93% @ 30 days)	MRID 42055337 *[161-1, hydrolysis]*	Half-life 355 days at pH 9 calculated from 30-day study. No degradates identified?
	Last: 28.7 @ 2 hrs	MRID 42256376 *[161-2, aqueous photolysis]*	Half Life 1 hr., "environmental" half-life = 4.2 hours (theoretical for natural sunlight).
	Last: 61.5 @ 15 days	MRID 42256377 *[161-3, soil photolysis]*	Half Life 39 days, "environmental" half-life = 171 days (theoretical for natural sunlight).
	Last 63.2 @ 100 days	MRID 45239301 *[162-1, aerobic soil]*	DT50 = 188 days. Semi-quantification of metabolites.
	Last 66.8 @ 100 days	MRID 45239302 *[162-1, aerobic soil]*	DT50 = 248 days. No metabolites were identified.
	Last 61.6 @ 366 days	MRID 42073501 *[162-1, aerobic soil]*	Half-lfe 688 days. No degradate identified at >1.7% of applied.
	<0.2 @ 249 & 358 days	MRID 42256378 *[162-3, anaerobic aquatic]*	Half Life 27 days

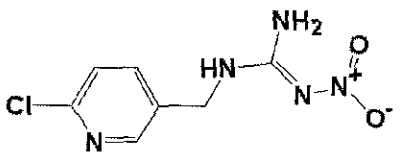
Degradate Name and Structure	Percent of Applied Dose	Study	Comments
Degradate 1: NTN 33519  Imidacloprid urea (NTN 33519)).	Maximum 10.5 @ 2 hrs (final)	MRID 42256376 *[161-2, aqueous photolysis]*	
	<2.2 (not confirmed) @ 15 days	MRID 42256377 *[161-3, soil photolysis]*	
	1.7 @ 30 days (final): pH 9 only.	MRID 42055337 *[161-1, hydroylysis]*	Another degradate represented 5.3% of applied but was not identified. 93% of the applied imidacloprid remained as parent compound.
	Not identified.	[161-3, 162-1]	

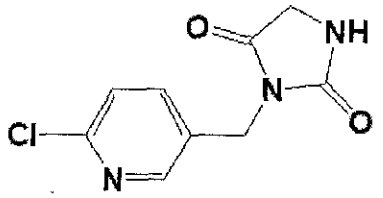
Degradate Name and Structure	Percent of Applied Dose	Study	Comments
 Imidacloprid guanidine (NTN 38014). Degradate 2: NTN 38014 alias NTN 33823	Maximum 17.5 @ 2 hrs (final)	MRID 42256376 *[161-2, aqueous photolysis]*	
	66 @ 249 & 64 @ 358 days	MRID 42256378 *[162-3, anaerobic aquatic]*	Only degradate identified.
	1.4 @ 100 days (final)	MRID 45239301 *[162-1, aerobic soil]*	63% parent remaining at close of experiment.
	1.2 @ 3 days, 1.1 @ 366 days	MRID 42073501 *[162-1, aerobic soil]*	62% parent remaining at close of experiment (366 days after treatment).
	Not identified.	[161-1, 161-3]	

Degradate Name and Structure	Percent of Applied Dose	Study	Comments
 Imidacloprid olefin (NTN 3126?). Degradate 3: NTN 3126?	Maximum 13.4 @ 2 hrs (final)	MRID 42256376 *[161-2, aqueous photolysis]*	
	Not identified.	[161-1, 161-3, 162-1, 162-3]	

Degradate Name and Structure	Percent of Applied Dose	Study	Comments
Degradate 4: WAK 4103	Maximum 6.5 @ 7 days	MRID 42256377 *[161-3, soil photolysis]*	
	Not identified.	[161-1, 161-2, 162-1, 162-3]	
Degradate 5: CPAcid	Maximum 2.3 @ 12 days	MRID 42256377 *[161-3, soil photolysis]*	
	Not identified.	[161-1, 161-2, 162-1, 162-3]	

Degradate Name and Structure	Percent of Applied Dose	Study	Comments
Degradate 6: NTN35884 (GAJ2269)	Not fully quantitated, <1.8 @ 100 days (final)	MRID 45239301 *[162-1, aerobic soil]*	63% parent remaining at close of experiment
 DEGRADATE 6: NTN35884 (GAJ2269)	Not fully quantitated, <3.7 @ 274 days	MRID 42073501 *[162-1, aerobic soil]*	62% parent remaining at close of experiment (366 days after treatment).
	Not identified.	[161-1, 161-2, 161-3, 162-3]	

Degradate Name and Structure	Percent of Applied Dose	Study	Comments
Degradate 7: DIJ11324 (WAK42301)	Not fully quantitated, <1.8 @ 100 days (final)	MRID 45239301 *[162-1, aerobic soil]*	63% parent remaining at close of experiment.
 DEGRADATE 7: DIJ11324 (WAK42301)	Not fully quantitated, <5.4 @ 274 days	MRID 42073501 *[162-1, aerobic soil]*	62% parent remaining at close of experiment (366 days after treatment).
	Not identified.	[161-1, 161-2, 161-3, 162-3]	

Degradate Name and Structure	Percent of Applied Dose	Study	Comments
Degradate 8: DIJ10048.	Not quantitated,	MRID 45239301 *[162-1, aerobic soil]*	63% parent remaining at close of experiment. Two isomers possibly present, complete separation not obtained.
	Not quantitated.	MRID 42073501 *[162-1, aerobic soil]*	62% parent remaining at close of experiment (366 days after treatment).
	Not identified.	[161-1, 161-2, 161-3, 162-3]	

ATTACHMENT 3: Imidacloprid (Confidor®) - Issues to be Presented to the Metabolism Committee on June 22, 1993
(Available Electronically on T-Drive)

MEMORANDUM

Subject: IMIDACLOPRID (CONFIDOR®) - ISSUES TO BE PRESENTED TO THE METABOLISM COMMITTEE ON JUNE 22, 1993.

From: Francis D. Griffith,Jr., Chemist
Chemistry Branch - Tolerance Support
Health Effects Division (H-7509C)

Thru: Debra F. Edwards, Ph.D., Chief
Chemistry Branch - Tolerance Support
Health Effects Division (H-7509C)

To: HED Metabolism Committee

BACKGROUND

Miles Inc., Agriculture Division proposes tolerances for residues of its new insecticide imidacloprid, trade named Confidor® (1-[(6-chloro-3-pyridinyl)methyl]-N-nitro-2-imidazolidinimine) and its metabolites containing the 6-chloropyridinyl moiety in or on the following raw agricultural commodities: apples at 1 ppm, cottonseed at 6 ppm and cotton forage at 60 ppm, potato tubers at 0.4 ppm, milk at 0.05 ppm, eggs at 0.02 ppm, meat, fat, and meat by-products of cattle, goats, hogs, horse, and sheep at 0.2 ppm, and in meat, fat, meat byproducts of poultry at 0.02 ppm. Feed additive tolerances are proposed for cottonseed meal at 9 ppm, wet apple pomace at 2 ppm, and dry apple pomace at 7 ppm. Food additive tolerances are proposed for dried potatoes at 1.5 ppm and in potato chips 0.7 ppm.

This is the first time, permanent tolerance request for imidacloprid. The petition, PP# 3F4169, passed the new chemical screen and was placed into review on December 24, 1992 (See memorandum from L. Cullen to P. Fenner-Crisp). The due date for the residue Chemistry review is September 30, 1993, per discussion between R. Schmitt (HED) and S. Irene (RD). The review is not in "expedite" status.

An extensive amount of ^{14}C-imidacloprid plant and animal metabolism data have been submitted and reviewed by the Agency. Two studies each have been submitted for ruminant and poultry metabolism. Plant metabolism studies include data for apples, corn, cotton, tomato, potato, and eggplant, plus a plant cell suspension culture. As this is a new chemical, a peer review is necessary at this time.

The chemist (D. Griffith) and the toxicologists (M. Ottley and P. Chin) responsible for the imidacloprid reviews and their Section Heads (R. Quick and M. Copley) meet on Thursday June 10 (with R. Loranger presiding) to discuss what metabolites to include in the tolerance expression and in the dietary risk assessment. We noted there are no Codex MRLs for the commodities on which tolerances are proposed and that the proposed analytical enforcement methods are common moiety procedures. The methods are currently undergoing tolerance method validations (TMVs). Additional plant and livestock metabolism studies and tox studies do not appear to be warranted at this time. The

2) reduction and loss of the nitro group on the dihydroimidazole ring to form aminoguanidine imidacloprid, then the guanidine imidacloprid and finally the urea imidacloprid,

3) opening of the dihydroimidazole ring with loss of the ethyl group and subsequent oxidation. The first step is forming the nitroguanidine imidacloprid, next the ring open guanidine which can also form both the guanidine imidacloprid and the dihydroxy guanidine imidacloprid. This metabolite can form picolylic urea, and picolylic amine which is oxidized to 6-chloronicotinic acid (6-CNA) which then can conjugate ith glycine.

The identified residues in ruminants are imidacloprid and its metabolites that contain the 6-chloropyridinyl moiety. All residues are determined as 6-CNA, then converted to imidacloprid equivalents.

POULTRY

The nature of the residue in poultry is adequately understood. Imidacloprid is metabolized by 3 pathways as follows:

1) hydroxylation of the dihydroimidazole ring of imidacloprid to form 4-hydroxy, 5-hydroxy and the dihydroxy imidacloprid followed by loss of water to form the olefin,

2) reduction and loss of the nitro group on the dihydroimidazole ring to form the dihydroxyguanidine imidacloprid, and

3) opening of the dihydroimidazole ring with the loss of the ethyl group and subsequent oxidation. The first step is forming the nitroguanidine imidacloprid, next the ring open guanidine imidacloprid which can also form from both the dihydroxy guanidine imidacloprid and the guanidine imidacloprid. This metabolite can form picolylic amine which is oxidized to 6-chloronicotinic acid (6-CNA).

The identified residues in poultry are imidacloprid and its metabolites which contain the 6-chloropyridinyl moiety. All residues are determined as 6-CNA, then converted to imidacloprid equivalents.

The attached tables summarize the imidacloprid plant and livestock metabolism data submitted to the Agency as part of PP# 3F4169. The attached figures show the structure for the parent and identified metabolites, and the proposed metabolic pathways.

QUESTIONS TO THE METABOLISM COMMITTEE

1. Are any additional imidacloprid plant and animal (livestock, rat) metabolism studies needed?

TABLE 1

DISTRIBUTION AND IDENTIFICATION OF ^{14}C-IMIDACLOPRID RESIDUES IN/ON PLANTS FOR WHICH TOLERANCES ARE PROPOSED

Commodity	Apples		Cottonseed		Cotton Forage		Potato Leaves		Potato Tubers	
Use in ^{14}C-Metabolism Studies	3 X 0.3 mg/apple 1 month apart		Seed treatment @ 0.5 mg/100 kg, plus Soil drench @ 2 X 15 mg ai 11 & 145 days after planting **(No foliar applications)**				1.52 g/1000'row, in-furrow, at planting, and a separate 1 X 0.12 lb ai/A or 30 mg/plant foliar (0.2% spray)			
PHI (Days)	0, **14**		**85**				**129** (soil) & 7, 28, **64** (foliar)			
Proposed Use	5 X 0.1 lb ai/A/appl., foliar, 0.5 lb ai max. 10 day repeat, 7 PHI		0.325 oz ai/1000' row in-furrow at planting,plus 0.05 lb ai X 4 foliar, 0.5 lb ai max./season 7 day repeat, 7 PHI **(No seed treatment use)**				0.325 oz or 9.2 gm/1000'row, in-furrow, at planting; plus 0.05 lb ai X 4 foliar applications. 0.3 lb ai max/season, 7 day repeat, 7 PHI			
	PPM	%TRR	PPM	%TRR	PPM	%TRR	PPM	%TRR	PPM	%TRR
Total Radioactive Residues (TRR)	1.445	100.	seed+drench 9.35	100.0	seed treat. 0.11	100.0	5.76 (s) 1.35 (f)	100.0 (s)	0.09 (f) 0.009 (s)	100.0 (s)
Imidacloprid	0.996	69.	0.08	0.8	0.003	2.9	1.53 s/0.51 f	26.7 (s)	0.044s/0.001	48.3 (s)
4-Hydroxy/ 5-Hydroxy	0.039	2.7	-	-	-	-	0.26 (s) 0.095 (f)	4.6 (s)	0.007 (s)	8.0 (s)
Dihydroxy	0.016	1.1	-	-	-	-	0.02 s/0.036f	0.3 (s)	-	-
Olefin	0.082	5.7	-	-	0.002	1.5	0.19 s/0.034f	3.3 (s)	0.003 (s)	3.1 (s)
Guanidine	0.038	2.4	-	-	0.011	9.8	0.48 s/0.17f	8.3 (s)	0.01 (s)	11.3 (s)
Nitrosimino	0.01	0.7	-	-	0.002	1.4	0.015 s/0.03f	2.6 (s)	-	-
Urea	-	-	-	-	-	-	-	-	-	-
6-CPA & Gluc.	0.031	2.2	-	-	0.002	1.9	0.08 s/0.025f	1.4 (s)	-	-
6-CNA	-	-	3.96	43.5	0.002	2.2	0.048 (s)	8.3 (s)	0.009s/0.003	9.4 (s)
6-CNA Gluc.	-	-	-	-	0.019	17.6	-	-	-	-
Triazinone	-	-	-	-	-	-	0.014 (f)		-	-
Ring open guanidine	-	-	-	-	-	-	-	-	-	-
Unidentified Residues Ext. & Recovered by Method	0.16		3.03		0.011		0.93 (s) 0.25 (f)		0.012 (s) 0.005 (f)	
Total Identified Residue	1.236	85.5	3.96	43.5	0.041	37.3	3.2s/0.9f	55.4s/67f	0.073 (s)	80.1 (s)

TABLE 3

DISTRIBUTION AND IDENTIFICATION OF ^{14}C-IMIDACLOPRID RESIDUES IN GOATS

DOSE	Oral intubation for 3 days at 10 mg/kg-body weight equivalent to 200 ppm in the diet									
TISSUES	LIVER		KIDNEY		SC FAT		LOIN MUSCLE		MILK	
	PPM	%TRR	PPM	%TRR	PPM	%TRR	PPM	%TRR	PPM	%TRR
Total Radioactive Residues	17.12	100.	13.54	100.	2.20	100.	3.80	100.	4.10	100.
Imidacloprid	0.13*		0.838	6.19	1.54	73.5	2.65	69.8	2.27	55.3
4-Hydroxy	-	-	0.265 combined, 1.904 as Glucuronides	1.06 combined, 14.06 as Glucuronides	0.12	5.8	0.27	7.1	0.40	9.7
5-hydroxy	-	-			0.07	3.1	0.12	3.2	0.29	7.0
Dihydroxy	-	-			-	-	-	-	-	-
Olefin	0.543	3.17	2.398	17.70	0.17	7.7	0.23	6.1	0.23	5.6
Nitrosimino	-	-	-	-	0.01	0.6	0.01	0.6	0.014	0.3
Aminoguanidine	0.260	1.52	-	-	-	-	-	-	-	-
Guanidine	2.805	16.39	0.793	5.86	-	-	-	-	-	-
Urea	0.336	1.96	0.990	0.73	-	-	-	-	-	-
Nitroguanidine	0.060	0.35	0.110	0.81	-	-	-	-	-	-
Ring open guanidine	1.238	7.23	0.567	4.19	-	-	-	-	-	-
Picolylic urea	0.216	1.26	0.026	0.19	-	-	-	-	-	-
Picolylic amine	0.740	0.43	0.219	1.84	-	-	-	-	-	-
6-CNA	0.25*		0.043	0.32	-	-	-	-	-	-
Glycine 6-CNA	0.164	0.96	2.272	16.78	-	-	-	-	0.13	3.1
Dihydroxy guanidine	0.103	0.60	0.083	0.6	-	-	-	-	-	-
Unidentified Residues ext. & Recovered by method	6.0		0.9		-	-		-	-	
Total identified residue	5.8	33.9	9.7	71.6	1.91	90.7	3.29	86.8	3.334	81.0

ATTACHMENT 4: Proposed Metabolic Pathways of Imidacloprid in Rats
(Not Available Electronically)

Figure 3.

Proposed degradation pathway of Imidacloprid

Source: MRID No 422563-73

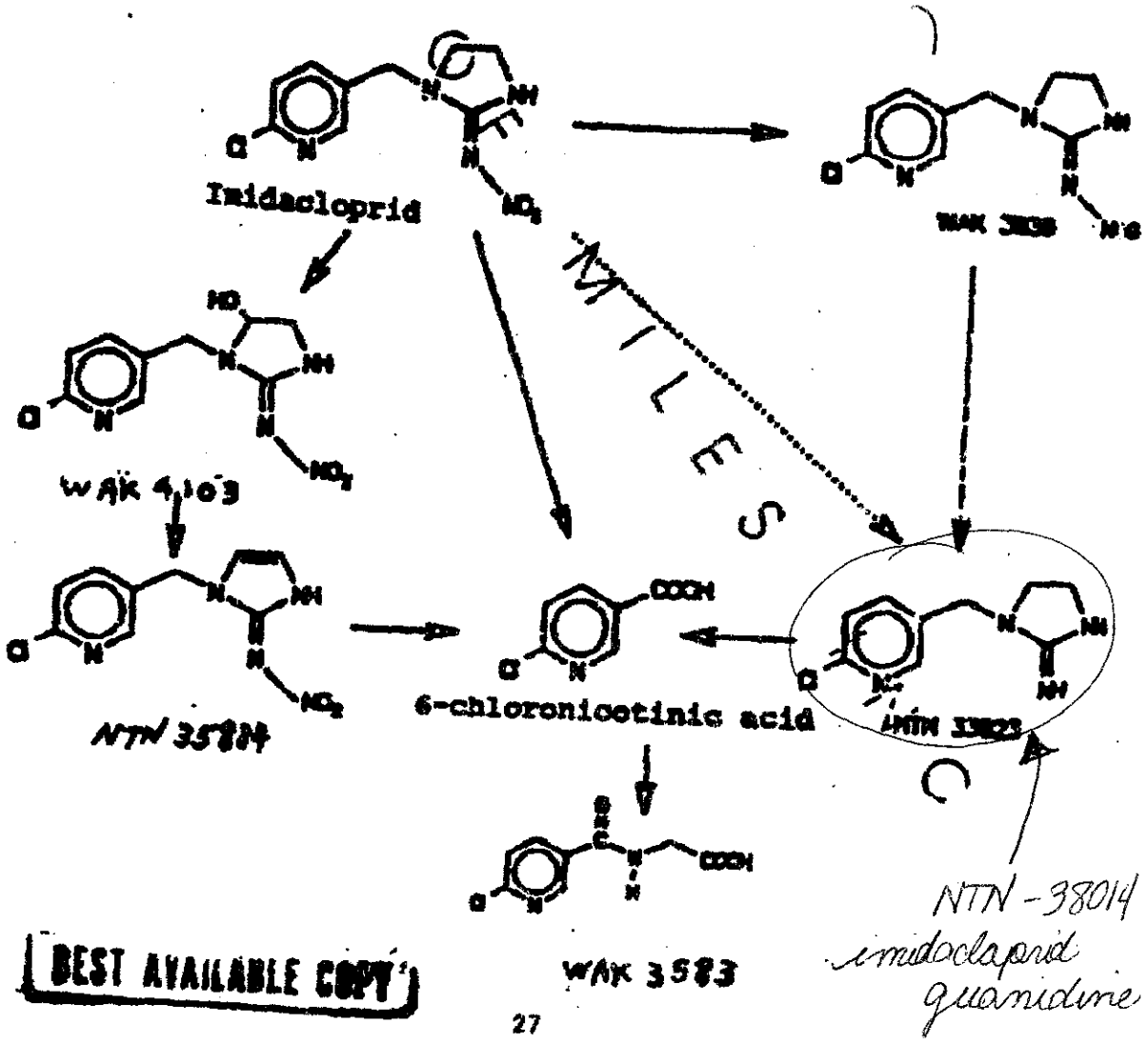


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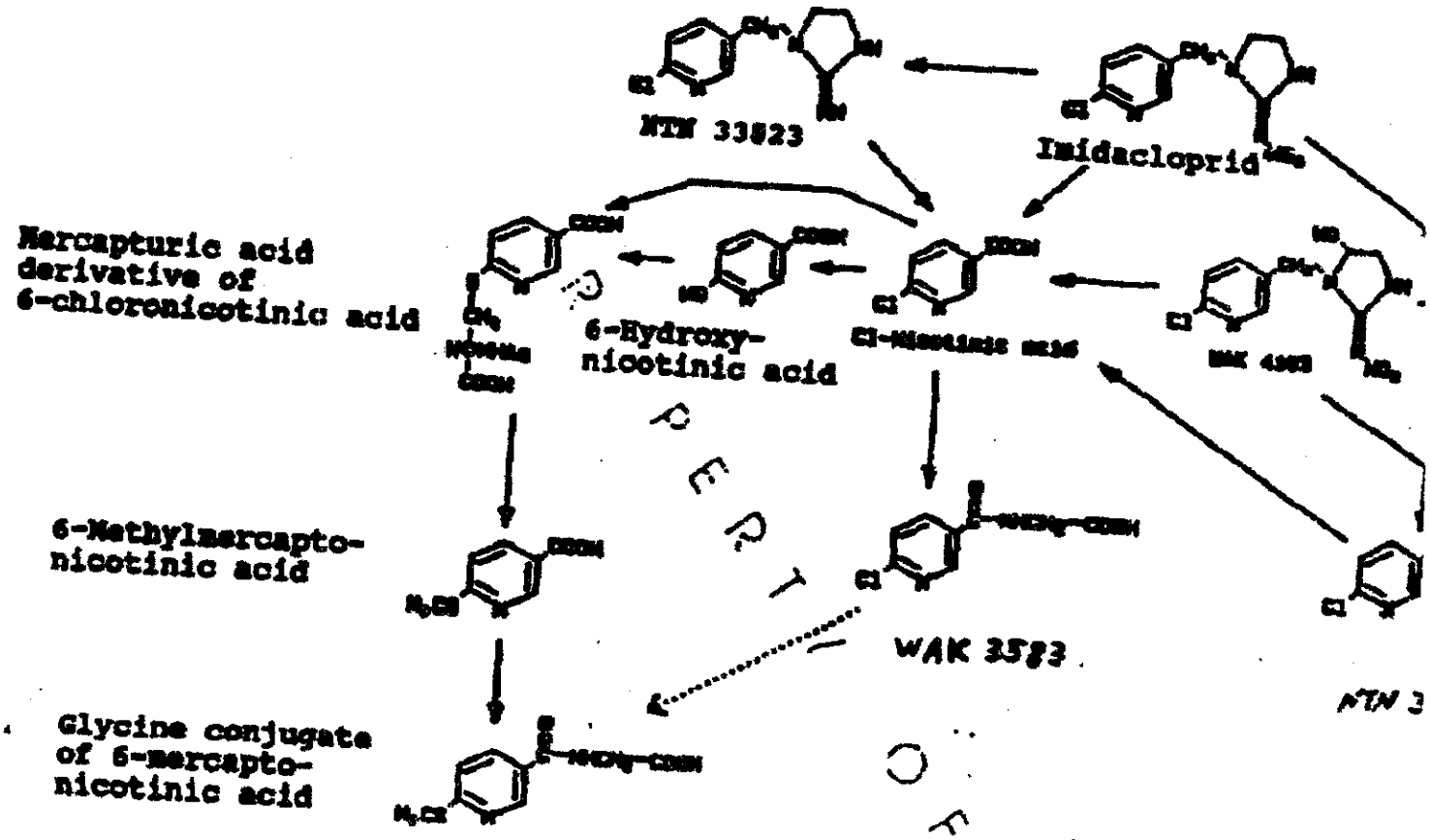
Figure 1.

Proposed degradation pathway of methylene-^{14}C-labeled Imidacloprid

Source: MRID No 422563-54



REPORT OF

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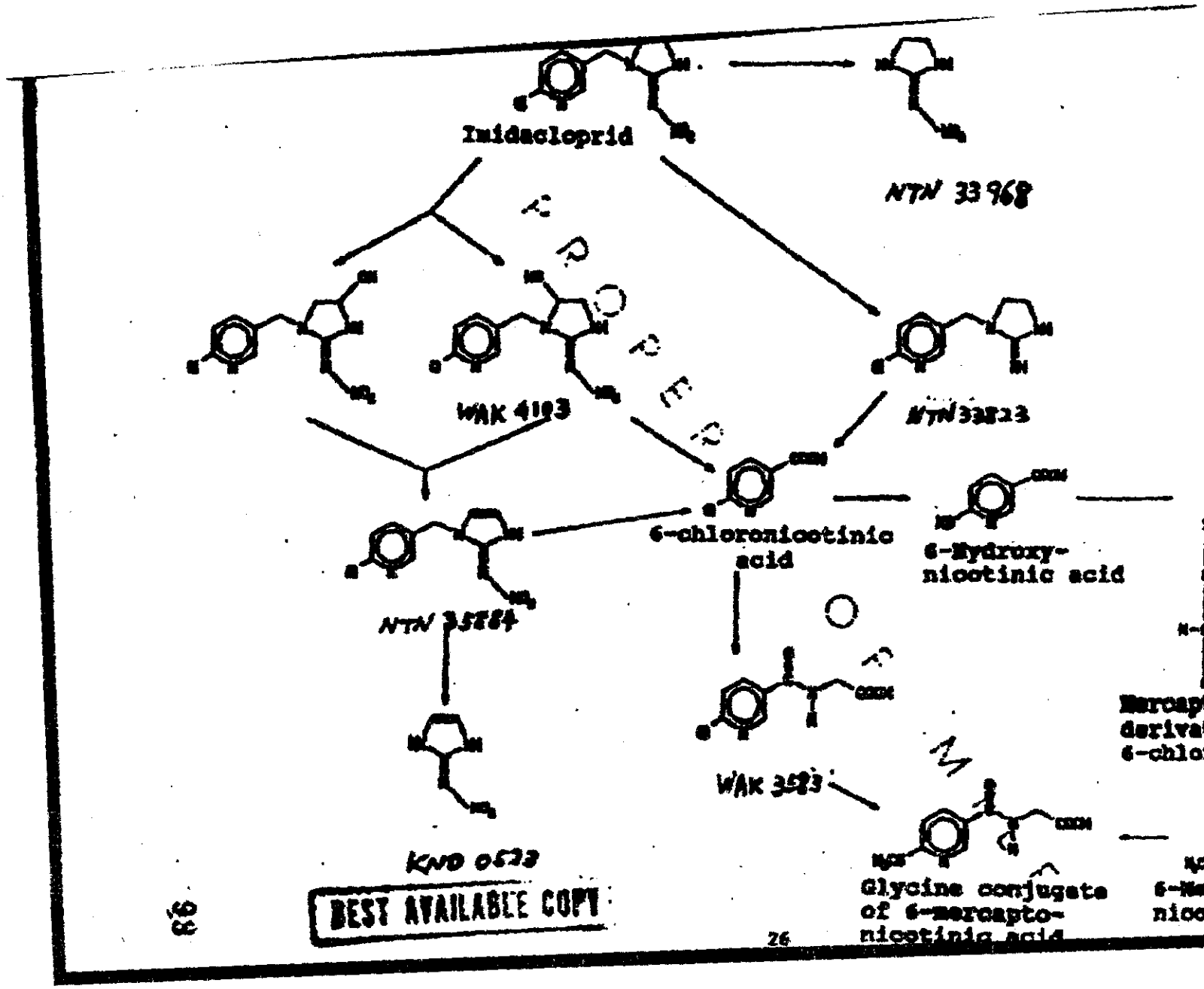
Imidacloprid
NTN 33968
WAK 4193
NTN 33823
6-chloronicotinic acid
6-Hydroxy-nicotinic acid
NTN 35884
WAK 3583
KWD 0523
Glycine conjugate of 6-mercapto-nicotinic acid
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13544

R058972

Chemical:	**Imidacloprid**
PC Code:	**129099**
HED File Code	**11000 Chemistry Reviews**
Memo Date:	**12/18/2002 12:00:00 AM**
File ID:	**DPD287025**
Accession Number:	**412-04-0047**

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