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SCIENTIFIC DATA REVIEWS
EPA SERIES 361

OFFICE OF
PREVENTION, PESTICIDES, AND
TOXIC SUBSTANCES

MEMORANDUM

DATE: 10-MAY-1999

SUBJECT: **Pyridate - Corrected Acute and Chronic Dietary Exposure Analyses.** PP#: 99MT0012. Chemical#: 128834. DP Barcode: D255654. Case #: 291638. Submission #: S558560.

FROM: Jennifer E. Rowell, Chemist
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TO: George F. Kramer, Ph.D., Chemist
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Action Requested

Provide an estimate of the dietary exposure and associated risk for pyridate resulting from existing tolerances and proposed tolerance level for residues on mint (PP# 99MT0012). The petitioner proposes the establishment of time-limited tolerances for the residues of pyridate in or on the following raw agricultural commodities (RACs):

Peppermint, tops (leaves and stems)	-	0.3 ppm
Spearmint, tops (leaves and stems)	-	0.3 ppm

Tolerances have been established for the residues of pyridate (40 CFR §180.462) in or on cabbage at 0.03 ppm; chickpeas at 0.1 ppm; corn, fodder at 0.03 ppm; corn, forage at 0.03 ppm; corn, grain at 0.03 ppm; corn, silage at 0.03 ppm; and peanut, nutmeat at 0.03 ppm.

Note: The previous dietary exposure estimate was performed in conjunction with this Section 18 (Memo, J.

Rowell 4/14/99; Barcode D254602) without considering the following RACs: peppermint, peppermint oil, spearmint, and spearmint oil. These commodities have been included in the this dietary exposure estimate.

Executive Summary

Acute and chronic dietary exposure analyses for pyridate were performed using the Dietary Exposure Evaluation Model (DEEM™). Acute and chronic dietary exposure analyses were performed using tolerance level residues and 100% crop treated (CT) information for all commodities. All dietary risk estimates are below the Agency's level of concern for the U.S. population and sub-populations (including infants and children).

Toxicological Endpoints

On October 21, 1997, the Health Effects Division's Hazard Identification Review Committee (HIARC) met to evaluate the toxicology data base of pyridate with special reference to the reproductive, developmental and neurotoxicity data. These data were re-reviewed specifically to address the sensitivity of infants and children from exposure to pyridate as required by the Food Quality Protection Act (FQPA). In addition, the Committee also re-assessed the doses and endpoints selected for acute dietary, chronic dietary (RfD) as well as occupational and residential exposure risk assessments (Memo, J. Rowland 11/3/97). A summary of the toxicological endpoints chosen by HIARC is listed in Table 1.

Acute
Acute RfD = 0.20 mg/kg/day. For acute dietary risk assessment, the HIARC recommended use of the systemic NOAEL of 20 mg/kg/day based on neurotoxic effects (ataxia and emesis) seen at 60 mg/kg/day (LOAEL) in the 90-day feeding study in dogs (MRID# 40101604). An uncertainty factor of 100 (10x for interspecies differences and 10x for intraspecies variations) was used to determine the acute RfD of 0.20 mg/kg/day.

Chronic
Chronic RfD = 0.11 mg/kg/day. For chronic dietary risk assessment, a NOAEL of 10.8 mg/kg/day was used based on decreased body weight gain in males seen at 67.5 mg/kg/day (LOAEL) in a 2-year feeding study in rats (MRID# 00137289, -90, 00138638). An uncertainty factor of 100 (10x for interspecies differences and 10x for intraspecies variations) was incorporated. This was supported by the parental systemic toxicity NOAEL and LOAEL established in the three-generation reproduction study in rats (MRID# 0072347). In that study the NOAEL was 10.8 mg/kg/day and the LOAEL was 67.5 mg/kg/day based on decreased pup weight gain (at post natal days 14 and 21 in the first litters of both generations).

Table 1. Summary of Toxicological Endpoint Selection

EXPOSURE SCENARIO	DOSE (mg/kg/day)	ENDPOINT	STUDY
Acute Dietary	NOAEL= 20 UF = 100	Clinical signs indicative of neurotoxicity characterized as ataxia and emesis were observed within 1-3 hours post-dosing on the first day and persisted for duration of study. LOAEL = 60 mg/kg/day.	90-Day Feeding Study - Dog
		Acute RfD = 0.20	
Chronic Dietary	NOAEL = 10.8 UF = 100	Based on decreased body weight gain in males seen at 67.5 mg/kg/day (LOAEL) in a 2-year feeding study in rats. (This was supported by the parental systemic toxicity NOAEL and LOAEL established in the three-generation reproduction study in rats. In that study the NOAEL was 10.8 mg/kg/day and the LOAEL was 67.5 mg/kg/day based on decreased pup weight gain (at post natal days 14 and 21 in the first litters of both generations)).	Chronic Toxicity/Carcinogenicity Study - Rat
		Chronic RfD = 0.11	
Short-Term (Dermal)	NOAEL= 20	See Acute Dietary.	90-Day Feeding Study - Dog
Intermediate-Term (Dermal)	NOAEL= 20	See Acute Dietary.	90-Day Feeding Study - Dog
Long-Term (Dermal)	NOAEL= 10.8	See Chronic Dietary.	Chronic Toxicity/Carcinogenicity Study - Rat
Short Term (Inhalation)	NOAEL= 20	See Acute Dietary.	90-Day Feeding- Dog
Intermediate Term (Inhalation)	NOAEL= 20	See Acute Dietary.	90-Day Feeding- Dog
Long Term (Inhalation)	NOAEL= 10.8	See Chronic Dietary.	Chronic Toxicity/Carcinogenicity-Rat

FQPA Recommendation

On April 5,1999, the FQPA Safety Factor Committee (SFC) met and determined that the 10x factor to account for enhanced sensitivity of infants and children should be removed. **Please note: the decisions made at this meeting for this chemical are applicable only to this Section 18 request** (Memo, B. Tarplee 4/8/99).

The Population Adjusted Dose (PAD) is a modification of the acute or chronic RfD to accommodate the

FQPA Safety Factor. The PAD is equal to the acute or chronic RfD divided by the FQPA Safety Factor. **Since the HED FQPA SFC determined to remove the 10x safety factor, the RfD is identical to the PAD.**

Cancer
Pyridate has not been evaluated by the Cancer Peer Review Committee. However, the DERs for the mouse and rat oncogenicity studies indicate that pyridate was negative in both species for carcinogenic effects (Memo, A. Kocialski, et. al. 7/11/97).

Residue Information

Tolerances for pyridate are published in 40 CFR §180.462. For the acute and chronic analyses, tolerance level residues and 100% CT information were used for all commodities. Default processing factors were used for both the acute and chronic analyses. A summary of the residue information used in the acute and chronic analyses is attached (Attachment 1).

Results/Discussion

The DEEM™ analysis evaluated the individual food consumption as reported by respondents in the USDA 1989-91 Nationwide Continuing Surveys of Food Intake by Individuals (CSFII) and accumulated exposure to the chemical for each commodity.

Acute Dietary Exposure Analysis
The acute dietary exposure analysis estimates the distribution of single-day exposures for the U.S. population and certain subgroups and accumulates exposure to the chemical for each commodity. Each analysis assumes uniform distribution of pyridate for the commodities on which pyridate is used.

A Tier 1 acute analysis was performed using published and proposed tolerance levels and 100% CT information for all commodities (Attachment 1). For acute dietary risk, HED's level of concern is >100% aPAD. Dietary exposures and associated acute risk at the 95th percentile are shown in Table 2. The other subgroups included in Table 2 represent the highest dietary exposures for their respective subgroups (i.e., children, females, and the other general population subgroups higher than U.S. population). A full listing of dietary exposures is attached (Attachment 2).

Table 2- Summary of Results of Acute DEEM Analysis for Pyridate at the 95th Percentile.

Subgroups	Exposure (mg/kg/day)	% aPAD
U.S. Population (48 states)	0.000139	0.1
Non-Hispanic Blacks	0.000159	0.1
Non-nursing Infants (<1 yr)	0.000278	0.1
Children (1-6 years)	0.000269	0.1
Females (13+/nursing)	0.000124	0.1

The results of the acute analysis indicate that the acute dietary risk associated with the existing and proposed uses of pyridate is well below the Agency's current level of concern.

Chronic Dietary Exposure Analysis

The chronic dietary exposure analysis used mean consumption (3-day average) data. A Tier 1 analysis was performed using published and proposed tolerance level residues and 100% CT information for all commodities. For chronic dietary risk, HED's level of concern is 100% cPAD. Dietary exposures for the General Population and other subgroups are presented in Table 3. The other subgroups included in Table 3 represent the highest dietary exposures for their respective subgroups (i.e., children, females, and the other general population subgroups higher than U.S. population). A full listing of chronic dietary exposures is attached (Attachment 3).

Table 3. Summary of Results from Chronic DEEM Analysis of Pyridate.

Subgroups	Exposure (mg/kg/day)	% cPAD
U.S. Population (48 states)	0.000044	0.0
Non-Hispanic Blacks	0.000050	0.0
Non-nursing Infants	0.000121	0.1
Females 13-19 (not preg or nursing)	0.000043	0.0
Males 13-19 yrs	0.000054	0.0

The results of the chronic analysis indicate that the chronic dietary risk associated with the existing and proposed uses of pyridate is well below the Agency's current level of concern.

Cancer Dietary Exposure Analysis

Pyridate has not been evaluated by the Cancer Peer Review Committee. However, the DERs for the mouse and rat oncogenicity studies indicate that pyridate was negative in both species for carcinogenic effects (Memo, A. Kocialski, et. al. 7/11/97). Therefore, no cancer dietary exposure analysis was performed.

Conclusions

The acute analysis was performed using published and proposed tolerance levels and 100% CT information for all commodities (Attachment 1). The %aPADs were <100%, and the highest was 0.14% for non-nursing infants (<1 year). For acute dietary risk, HED's level of concern is 100% aPAD. The results of the acute analysis indicate that the acute dietary risk associated with the existing and proposed uses of pyridate is well below the Agency's current level of concern.

For the chronic analysis, a Tier 1 analysis was performed using published and proposed tolerance level residues and 100% CT information for all commodities. The %cPADs for all subgroups were <100%, and the highest was 0.1% for non-nursing infants. The results of the chronic analysis indicate that the chronic dietary risk associated with the existing and proposed uses of pyridate is well below the Agency's current level of concern.

Pyridate has not been evaluated by the Cancer Peer Review Committee. However, the DERs for the mouse and rat oncogenicity studies indicate that pyridate was negative in both species for carcinogenic effects (Memo, A. Kocialski, et. al. 7/11/97). Therefore, no cancer dietary exposure analysis was performed.

Attachment 1: Pyridate Residue File for Acute and Chronic DEEM™ Analyses.
Attachment 2: Pyridate Acute DEEM™ Analysis (J. Rowell, 30-APR-1999).
Attachment 3: Pyridate Chronic DEEM™ Analysis (J. Rowell, 30-APR-1999).

cc (w/attachments): J.Rowell (RAB1); M.Sahafeyen (CEB1)
RDI: DRES Team [W. Donovan (5/6/99), D. Soderberg (4/30/99)]; M.Morrow (5/10/99)
J.Rowell:806W:CM#2:(703)305-5564:7509C:RAB1

Attachment 1: Pyridate Residue File for Acute and Chronic DEEM™ Analyses.

Filename: C:\JRDeem\Pyridate\128834.r96
Chemical name: Pyridate
RfD(Chronic): .11 mg/kg bw/day NOEL(Chronic): 10.8 mg/kg bw/day
RfD(Acute): .2 mg/kg bw/day NOEL(Acute): 20 mg/kg bw/day
Date created/last modified: 04-30-1999/11:02:38/8 Program ver. 6.73
Comment: Pyridate on mint - G. Kramer. The FQPA Safety Factor was removed, therefore the PAD and RfD are the same.

Food Code	Crop Grp	Food Name	RESIDUE (ppm)	RDF #	Adj.Factors #1	#2	Comment
259	6C	Beans-dry-garbanzo/chick pea	0.100000	0	1.000	1.000	
170	5A	Cabbage-green and red	0.030000	0	1.000	1.000	
383	5B	Cabbage-savoy	0.030000	0	1.000	1.000	
267	15	Corn grain-bran	0.030000	0	1.000	1.000	
266	15	Corn grain-endosperm	0.030000	0	1.000	1.000	
289	15	Corn grain-oil	0.030000	0	1.000	1.000	
268	15	Corn grain/sugar/hfcs	0.030000	0	1.500	1.000	
388	15	Corn grain/sugar-molasses	0.030000	0	1.500	1.000	
403	O	Peanuts-butter	0.030000	0	1.890	1.000	
940	O	Peanuts-hulled	0.030000	0	1.000	1.000	
293	O	Peanuts-oil	0.030000	0	1.000	1.000	
310	O	Peppermint	0.300000	0	1.000	1.000	
311	O	Peppermint-oil	0.300000	0	1.000	1.000	
312	O	Spearmint	0.300000	0	1.000	1.000	
313	O	Spearmint-oil	0.300000	0	1.000	1.000	

Attachment 2: Pyridate Acute DEEM™ Analysis (J. Rowell, 30-APR-1999).

U.S. Environmental Protection Agency Ver. 6.73
DEEM ACUTE analysis for PYRIDATE (1989-92 data)
Residue file: 128834.r96 Adjustment factor #2 NOT used.
Analysis Date: 04-30-1999/11:10:15 Residue file dated: 04-30-1999/11:02:38/8
Acute Reference Dose (aRfD) = 0.200000 mg/kg body-wt/day
NOEL (Acute) = 20.000000 mg/kg body-wt/day
Run Comment: Pyridate on mint - G. Kramer. The FQPA Safety Factor was removed, therefore the PAD and RfD are the same.

Summary calculations:

	95th Percentile Exposure	95th Percentile % aRfD	99th Percentile Exposure	99th Percentile % aRfD	99.9th Percentile Exposure	99.9th Percentile % aRfD
U.S. pop - all seasons:	0.000139	0.07	0.000244	0.12	0.000407	0.20
Hispanics:	0.000149	0.07	0.000250	0.13	0.000422	0.21
Non-hispanic whites:	0.000135	0.07	0.000234	0.12	0.000410	0.20
Non-hispanic blacks:	0.000159	0.08	0.000279	0.14	0.000379	0.19
Non-hispanic other:	0.000128	0.06	0.000250	0.13	0.000594	0.30
All infants (<1 year):	0.000277	0.14	0.000411	0.21	0.000657	0.33
Nursing infants (<1 year):	0.000095	0.05	0.000142	0.07	0.000186	0.09
Non-nursing infants (<1 yr):	0.000278	0.14	0.000442	0.22	0.000682	0.34
Children (1-6 years):	0.000269	0.13	0.000392	0.20	0.000726	0.36
Children (7-12 years):	0.000180	0.09	0.000249	0.12	0.000356	0.18
Females (13+/preg/not nsg):	0.000082	0.04	0.000121	0.06	0.000200	0.10
Females (13+/nursing):	0.000124	0.06	0.000177	0.09	0.000194	0.10
Females (13-19 yrs/np/nn):	0.000109	0.05	0.000147	0.07	0.000320	0.16
Females (20+ years/np/nn):	0.000081	0.04	0.000130	0.07	0.000238	0.12
Females (13-50 years):	0.000092	0.05	0.000137	0.07	0.000268	0.13
Males (13-19 years):	0.000134	0.07	0.000209	0.10	0.000308	0.15
Males (20+ years):	0.000085	0.04	0.000132	0.07	0.000211	0.11
Seniors (55+):	0.000074	0.04	0.000117	0.06	0.000212	0.11

Attachment 3: Pyridate Chronic DEEM™ Analysis (J. Rowell, 30-APR-1999).

U.S. Environmental Protection Agency Ver. 6.74
DEEM Chronic analysis for PYRIDATE (1989-92 data)
Residue file name: C:\JRDeem\Pyridate\128834.r96 Adjustment factor #2 NOT used.
Analysis Date 04-30-1999/11:04:58 Residue file dated: 04-30-1999/11:02:38/8
Reference dose (RfD, CHRONIC) = .11 mg/kg bw/day
COMMENT 1: Pyridate on mint - G. Kramer. The FQPA Safety Factor was removed, therefore the PAD and RfD are the same.

Total exposure by population subgroup

Population Subgroup	Total Exposure mg/kg body wt/day	Total Exposure Percent of Rfd
U.S. Population (total)	0.000044	0.0%
U.S. Population (spring season)	0.000043	0.0%
U.S. Population (summer season)	0.000046	0.0%
U.S. Population (autumn season)	0.000045	0.0%
U.S. Population (winter season)	0.000042	0.0%
Northeast region	0.000041	0.0%
Midwest region	0.000045	0.0%
Southern region	0.000046	0.0%
Western region	0.000043	0.0%
Hispanics	0.000044	0.0%
Non-hispanic whites	0.000043	0.0%
Non-hispanic blacks	0.000050	0.0%
Non-hisp/non-white/non-black)	0.000041	0.0%
All infants (< 1 year)	0.000092	0.1%
Nursing infants	0.000023	0.0%
Non-nursing infants	0.000121	0.1%
Children 1-6 yrs	0.000105	0.1%
Children 7-12 yrs	0.000076	0.1%
Females 13-19(not preg or nursing)	0.000043	0.0%
Females 20+ (not preg or nursing)	0.000028	0.0%
Females 13-50 yrs	0.000032	0.0%
Females 13+ (preg/not nursing)	0.000031	0.0%
Females 13+ (nursing)	0.000036	0.0%
Males 13-19 yrs	0.000054	0.0%
Males 20+ yrs	0.000032	0.0%
Seniors 55+	0.000026	0.0%
Pacific Region	0.000041	0.0%

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Chemical:	**Pyridate**
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