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SCIENTIFIC DATA REVIEWS
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OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

MEMORANDUM

DATE: 11/22/05

SUBJECT: **Cloquintocet-mexyl** Acute and Chronic Dietary Exposure Assessments for the
Section 3 Registration of Wheat and Barley (4E6831).

PC Code: 700099
DP Barcode: D322951

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Executive Summary

Acute and chronic dietary risk assessments were conducted using the Dietary Exposure Evaluation Model (DEEM-FCID™, Version 2.02) which uses food consumption data from the USDA's Continuing Surveys of Food Intakes by Individuals (CSFII) from 1994-1996 and 1998. The analyses were performed to support Section 3 request for the use of cloquintocet-mexyl on wheat and barley (PP#4E6831).

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Acute Dietary Exposure Results and Characterization

An acute dietary analysis for cloquintocet-mexyl was conducted using tolerance levels and 100 %CT for all existing and proposed uses. The acute PAD for females 13-49 years was 1 mg/kg/day. For the general population, there were no appropriate toxicological effects attributable to a single exposure (dose), therefore, a dose and endpoint were not identified for this risk assessment. The results of the analysis indicate that acute risk from the dietary exposure to cloquintocet-mexyl from the requested uses did not exceed HED's level of concern for females 13-49 yrs old. The exposure to females 13-49 yrs old was <1% aPAD

Chronic Dietary Exposure Results and Characterization

A chronic dietary analysis for cloquintocet-mexyl was conducted using tolerance levels and 100 %CT for all existing and proposed uses. The chronic PAD for the U.S. population is 0.04 mg/kg/day. The exposure to the U.S. population was <1% cPAD and the most highly exposed subgroup, children 3-5 yrs old, at 1% cPAD. The results of the analysis indicate that chronic risk from the dietary exposure to cloquintocet-mexyl from the requested use did not exceed HED's level of concern for the U.S. population or any population subgroup.

Cancer Dietary Exposure Results and Characterization

The HIARC classified cloquintocet-mexyl as a "Not Likely Carcinogen" and, therefore, quantification of human cancer risk is not required.

Water Contribution

The Agency used the First Index Reservoir Screening Tool (FIRST) and the Screening Concentration in Ground Water (SCI-GROW) screening models to determine the Estimated Environmental Concentrations (EECs) of cloquintocet-mexyl in surface and ground water, respectively. The highest estimates for acute exposure, 0.186 ppb, and chronic exposure, 0.005 ppb, were used in the analysis.

I. Introduction

Dietary risk assessment incorporates both exposure and toxicity of a given pesticide. For acute and chronic assessments, the risk is expressed as a percentage of a maximum acceptable dose (i.e., the dose which HED has concluded will result in no unreasonable adverse health effects). This dose is referred to as the population adjusted dose (PAD). The PAD is equivalent to the Reference Dose (RfD) divided by the special FQPA Safety Factor.

For acute and non-cancer chronic exposures, HED is concerned when estimated dietary risk exceeds 100% of the PAD. HED is generally concerned when estimated cancer risk exceeds one

in one million (i.e., the risk exceeds 1×10^{-6}). References which discuss the acute and chronic risk assessments in more detail are available on the EPA/pesticides web site: "Available Information on Assessing Exposure from Pesticides, A User's Guide," 6/21/2000, web link: <http://www.epa.gov/fedrgstr/EPA-PEST/2000/July/Day-12/6061.pdf>; or see SOP 99.6 (8/20/99).

The most recent dietary risk assessment for cloquintocet-mexyl was conducted by M. Xue as part of a human health risk assessment in support of a Section 3 request for the use on wheat (D263506, 3/27/00).

II. Residue Information

Dietary Exposure

These acute and chronic assessments were based on the assumption of tolerance-level residues for all commodities with existing and proposed tolerances and 100% crop treated (%CT) for all commodities. The existing cloquintocet-mexyl tolerances are listed in 40 CFR §180.560. The current and proposed tolerances are listed in Table 1 for residues of cloquintocet-mexyl (acetic acid, [(5-chloro-8-quinolinyl)oxy]-, 1-methylhexyl ester) and its acid metabolite (5-chloro-8-quinlinoxyacetic acid).

Table 1. Tolerance Summary for Cloquintocet-mexyl	
Commodity	Proposed Tolerance, ppm
Wheat, forage	0.1
Wheat, straw	0.1
Wheat, hay	0.1
Wheat, grain	0.1
Barley, straw	0.1
Barley, hay	0.1
Barley, grain	0.1

Established and recommended tolerances were used in acute and chronic dietary assessments. The MARC concluded that the residues of concern for tolerances in plants and animals were cloquintocet-mexyl and its acid metabolite (5-chloro-8-quinlinoxyacetic acid).

Water

The mobility of cloquintocet-mexyl (as measured by its binding to soils) varies from low in a moderate organic soil to essentially immobile in a high organic soil. The persistence of cloquintocet-mexyl in soil is also very low. Therefore, based upon the its low persistence and low mobility, the leaching potential of cloquintocet-mexyl should be negligible. The results of the aerobic aquatic metabolism studies indicate that cloquintocet-mexyl will rapidly degrade in aerobic ground and surface waters that have adequate microbial activity. The results of the direct

photolysis (DT50 of several hours) indicate that cloquintocet-mexyl is also susceptible to rapid rates of direct photolysis in clear shallow water. However, based on the results of the abiotic hydrolysis study (half-lives of 4.4 yr. at pH 5, 134 days at pH 7 and 6.6 days at pH 9), it may be substantially more persistent in aerobic waters with low microbial activity. Data are not currently available to assess its persistence in anaerobic waters.

The Agency currently lacks sufficient water-related exposure data from monitoring to complete a *quantitative* drinking water exposure analysis and risk assessment for cloquintocet-mexyl. Therefore, the Agency is presently relying on computer-generated estimated environmental concentrations (EECs). These EECs are provided by the Environmental Fate and Effects Division (EFED). GENEEC is a model used to generate EECs for *surface* water based on estimates of safener concentration. SCI-GROW is an empirical model based upon actual monitoring data collected for a number of pesticides which serve as benchmarks and has been used to predict EECs in *ground* water. Based on the environmental fate properties of cloquintocet-mexyl and the rapid degradation of the parent compound (i.e., hours to days) to the major degradate, CGA-153433 (5-chloro-8-quinolinoxyacetic acid), EFED provided HED with EECs for combined residues of cloquintocet-mexyl and CGA-153433. EFED reported that the highest EECs from the current and proposed uses were the GENEEC estimates acute (peak) and chronic (56-year mean) concentrations of cloquintocet-mexyl and CGA-153433 in water at 0.186 ppb and 0.005 ppb, respectively (DP Barcode: D323526, L. Shanaman, 11/17/05).

III Program and Consumption Information

Several reasonable peer-reviewed software packages have recently been emerging for modeling dietary exposure to pesticides. For a variety of technical, historical, and availability reasons, DEEM™ was the program generally used by EPA's Office of Pesticide Programs for conducting its dietary risk assessments. With the advent and current availability of a number of other exposure software programs, OPP, registrants, and other interested parties have available to them the option of selecting other peer-reviewed exposure software in conducting risk assessments for pesticides. Lifeline™ is one such model. Dietary Exposure assessments may also be performed with other, similar programs, and if submitted, such results will be reviewed by EPA for acceptability and comparability to existing peer-reviewed software being used by OPP.

IIIa. DEEM-FCID™ Program and Consumption Information

Cloquintocet-mexyl acute and chronic dietary exposure assessments were conducted using the Dietary Exposure Evaluation Model software with the Food Commodity Intake Database (DEEM-FCID™, Version 2.02), which incorporates consumption data from USDA's Continuing Surveys of Food Intakes by Individuals (CSFII), 1994-1996 and 1998. The 1994-96, 98 data are based on the reported consumption of more than 20,000 individuals over two non-consecutive survey days. Foods "as consumed" (e.g., apple pie) are linked to EPA-defined food commodities (e.g. apples, peeled fruit - cooked; fresh or N/S; baked; or wheat flour - cooked; fresh or N/S, baked) using publicly available recipe translation files developed jointly by USDA/ARS and EPA. For chronic exposure assessment, consumption data are averaged for the entire U.S.

population and within population subgroups, but for acute exposure assessment are retained as individual consumption events. Based on analysis of the 1994-96, 98 CSFII consumption data, which took into account dietary patterns and survey respondents, HED concluded that it is most appropriate to report risk for the following population subgroups: the general U.S. population, all infants (<1 year old), children 1-2, children 3-5, children 6-12, youth 13-19, adults 20-49, females 13-49, and adults 50+ years old.

For chronic dietary exposure assessment, an estimate of the residue level in each food or food-form (e.g., orange or orange juice) on the food commodity residue list is multiplied by the average daily consumption estimate for that food/food form to produce a residue intake estimate. The resulting residue intake estimate for each food/food form is summed with the residue intake estimates for all other food/food forms on the commodity residue list to arrive at the total average estimated exposure. Exposure is expressed in mg/kg body weight/day and as a percent of the cPAD. This procedure is performed for each population subgroup.

For acute exposure assessments, individual one-day food consumption data are used on an individual-by-individual basis. The reported consumption amounts of each food item can be multiplied by a residue point estimate and summed to obtain a total daily pesticide exposure for a deterministic exposure assessment, or "matched" in multiple random pairings with residue values and then summed in a probabilistic assessment. The resulting distribution of exposures is expressed as a percentage of the aPAD on both a user (i.e., only those who reported eating relevant commodities/food forms) and a per-capita (i.e., those who reported eating the relevant commodities as well as those who did not) basis. In accordance with HED policy, per capita exposure and risk are reported for all tiers of analysis. However, for tiers 1 and 2, any significant differences in user vs. per capita exposure and risk are specifically identified and noted in the risk assessment.

IV. Toxicological Information

On June 17, 1999, the HED's Hazard Identification Assessment Review Committee (HIARC) evaluated the toxicology data base on cloquintocet-mexyl, established reference doses (RfDs), and selected the toxicological endpoints for acute and chronic, as well as occupational/residential exposure, risk assessments. The HIARC also addressed the potential enhanced sensitivity of infants and children from exposure cloquintocet-mexyl as required by the Food Quality Protection Act FQPA of 1996. The doses and toxicological endpoints are summarized in Table 2.

Table 2. The Doses and Toxicological Endpoints of Cloquintocet-mexyl			
EXPOSURE SCENARIO	DOSE (mg/kg/day)	ENDPOINT	STUDY
Acute Dietary (For females 13+)	NOAEL=100 (UF=100)	Higher incidence of skeletal variants and decrease in fetal body weights in the high dose group at 400 mg/kg/day (LOAEL).	Developmental toxicity study in rats

	Acute PAD (females 13+) = 1 mg/kg/day		
Acute Dietary (For general population)	Based on available data, a suitable endpoint was not identified for general population because there were no effects observed in oral toxicity studies appropriate to this population that could be attributed to a single dose exposure. Acute PAD (general population) = Not applicable		
Chronic Dietary	NOAEL=4.3 (UF=100)	Observation of thyroid hyperplasia in females at 41.2 mg/kg/day (LOAEL).	Chronic Toxicity -Rat
		Chronic PAD = 0.04 mg/kg/day	

* use route to route extrapolation

FQPA Considerations

The HED FQPA Safety Factor Committee (SFC) met on March 6, 2000 and determined that the 10X FQPA Safety Factor for the protection of infants and children should be removed (1X). Consideration of the FQPA Safety Factor resulted in an acute PAD of 1 mg/kg and a chronic PAD of 0.04 mg/kg/day for acute and chronic risk assessment, respectively.

V. Results/Discussion

As stated above, for acute and chronic dietary assessments, HED is concerned when dietary risk exceeds 100% of the PAD. The DEEM-FCID™ analyses estimate the dietary exposure of the U.S. population and various population subgroups. The exposure results reported in Tables 3 and 4 are for the general U.S. Population, all infants (<1 year old), children 1-2, children 3-5, children 6-12, youth 13-19, females 13-49, adults 20-49, and adults 50+ years. The acute exposure results reported in Table 3 include females only at the 95th percentile females 13-49 yrs old at <1 % aPAD. The chronic dietary risk estimates in Table 4 include general US population at <1% cPAD and the most highly exposed subgroup, children 3-5 yrs old, at 1% cPAD. All the dietary risk estimates are below 100% of the PADs. A determination of cancer dietary risk was not required.

These analyses are highly conservative, Tier 1 dietary exposure assessments. Further refinement to the analyses could be made through the use of anticipated residues, incorporation of percentages of crops treated with cloquintocet-mexyl, and/or monitoring data that better reflect residues at the time of consumption. Since risk estimates are well below HED's level of concern, a more highly refined analysis is not needed at this time.

Table 3. Results of Acute Dietary Exposure Analysis							
Population Subgroup	aPAD (mg/kg/day)	95 th Percentile		99 th Percentile		99.9 th Percentile	
		Exposure (mg/kg/day)	% aPAD	Exposure (mg/kg/day)	% aPAD	Exposure (mg/kg/day)	% aPAD
Females 13-49 years old	1	0.000347	<1	0.000503	<1	0.000769	<1

Table 4. Results of Chronic Dietary Exposure Analysis			
Population Subgroup	cPAD (mg/kg/day)	Exposure (mg/kg/day)	% cPAD
General U.S. Population	0.04	0.000180	<1
All Infants (< 1 year old)	0.04	0.000077	<1
Children 1-2 years old	0.04	0.000403	1
Children 3-5 years old	0.04	0.000411	1
Children 6-12 years old	0.04	0.000289	<1
Youth 13-19 years old	0.04	0.000176	<1
Adults 20-49 years old	0.04	0.000153	<1
Adults 50+ years old	0.04	0.000120	<1
Females 13-49 years old	0.04	0.000137	<1

VI. Conclusions

These Tier 1 analyses demonstrate that the requested uses for cloquintocet-mexyl will not result in dietary risk estimates that exceed HED's level of concern for any of the regulated population subgroups, including those comprised of infants and children.

A summary of the dietary exposure analyses is given in Table 5. Cloquintocet-mexyl does not possess cancer dietary endpoints; therefore, the results of only the acute and chronic analyses are given in the table.

Table 5. Summary of Dietary Exposure and Risk for Cloquintocet-mexyl.						
Population Subgroup*	Acute Dietary (95th Percentile)		Chronic Dietary		Cancer	
	Dietary Exposure (mg/kg/day)	% aPAD	Dietary Exposure (mg/kg/day)	% cPAD	Dietary Exposure (mg/kg/day)	Risk
General U.S. Population	NA		0.000180	<1	N/A	
All Infants (< 1 year old)			0.000077	<1		
Children 1-2 years old			0.000403	1		
Children 3-5 years old			0.000411	1		
Children 6-12 years old			0.000289	<1		
Youth 13-19 years old			0.000176	<1		

Table 5. Summary of Dietary Exposure and Risk for Cloquintocet-mexyl.

Population Subgroup*	Acute Dietary (95th Percentile)		Chronic Dietary		Cancer	
	Dietary Exposure (mg/kg/day)	% aPAD	Dietary Exposure (mg/kg/day)	% cPAD	Dietary Exposure (mg/kg/day)	Risk
Adults 20-49 years old			0.000153	<1		
Adults 50+ years old			0.000120	<1		
Females 13-49 years old	0.000347	<1	0.000137	<1		

VII. List of Attachments

- Attachment 1. Acute Food plus Water Residue Input file.
- Attachment 2. Acute Results file.
- Attachment 3. Chronic Food plus Water Residue Input file.
- Attachment 4. Chronic Results file.

Attachment I. Acute Food plus Water Residue Input file.

Filename: K:\working\C-mexyl\700099a.r98 Chemical: C-Mexyl
RfD(Chronic): .04 mg/kg bw/day NOEL(Chronic): 0 mg/kg bw/day
RfD(Acute): 1 mg/kg bw/day NOEL(Acute): 0 mg/kg bw/day
Date created/last modified: 11-14-2005/08:09:34/8 Program ver. 2.03

EPA Code	Crop Grp	Commodity Name	Def Res (ppm)	Adj. Factors #1 #2	Comment
15000250	15	Barley, pearled barley	0.100000	1.000 1.000	
15000251	15	Barley, pearled barley-babyfood	0.100000	1.000 1.000	
15000260	15	Barley, flour	0.100000	1.000 1.000	
15000261	15	Barley, flour-babyfood	0.100000	1.000 1.000	
15000270	15	Barley, bran	0.100000	1.000 1.000	
86010000	0	Water, direct, all sources	0.000186	1.000 1.000	
86020000	0	Water, indirect, all sources	0.000186	1.000 1.000	
15004010	15	Wheat, grain	0.100000	1.000 1.000	
15004011	15	Wheat, grain-babyfood	0.100000	1.000 1.000	
15004020	15	Wheat, flour	0.100000	1.000 1.000	
15004021	15	Wheat, flour-babyfood	0.100000	1.000 1.000	
15004030	15	Wheat, germ	0.100000	1.000 1.000	
15004040	15	Wheat, bran	0.100000	1.000 1.000	

Attachment 2. Acute Results file.

U.S. Environmental Protection Agency
DEEM-FCID ACUTE Analysis for C-MEXYL
Residue file: 700099a.r98
Analysis Date: 11-21-2005/09:25:11
Run Comment: ""
=====

Ver. 2.02
(1994-98 data)

Adjustment factor #2 NOT used.

Residue file dated: 11-21-2005/09:23:48/8

Daily totals for food and foodform consumption used.

Summary calculations (per capita):

	95th Percentile Exposure	% aRfD	99th Percentile Exposure	% aRfD	99.9th Percentile Exposure	% aRfD
Females 13-49 yrs:	0.000347	0.03	0.000503	0.05	0.000769	0.08

Attachment 3. Chronic Food plus Water Residue Input file.

Filename: K:\working\C-mexyl\700099c.r98 Chemical: C-Mexyl
RfD(Chronic): .04 mg/kg bw/day NOEL(Chronic): 0 mg/kg bw/day
RfD(Acute): 1 mg/kg bw/day NOEL(Acute): 0 mg/kg bw/day
Date created/last modified: 11-09-2005/14:51:24/8 Program ver. 2.03

EPA Code	Crop Grp	Commodity Name	Def Res (ppm)	Adj.Factors #1	Adj.Factors #2	Comment
15000250	15	Barley, pearled barley	0.100000	1.000	1.000	
15000251	15	Barley, pearled barley-babyfood	0.100000	1.000	1.000	
15000260	15	Barley, flour	0.100000	1.000	1.000	
15000261	15	Barley, flour-babyfood	0.100000	1.000	1.000	
15000270	15	Barley, bran	0.100000	1.000	1.000	
86010000	0	Water, direct, all sources	0.000005	1.000	1.000	
86020000	0	Water, indirect, all sources	0.000005	1.000	1.000	
15004010	15	Wheat, grain	0.100000	1.000	1.000	
15004011	15	Wheat, grain-babyfood	0.100000	1.000	1.000	
15004020	15	Wheat, flour	0.100000	1.000	1.000	
15004021	15	Wheat, flour-babyfood	0.100000	1.000	1.000	
15004030	15	Wheat, germ	0.100000	1.000	1.000	
15004040	15	Wheat, bran	0.100000	1.000	1.000	

Attachment 4. Chronic Results file.

U.S. Environmental Protection Agency Ver. 2.00
DEEM-FCID Chronic analysis for C-MEXYL (1994-98 data)
Residue file name: K:\working\C-mexyl\700099c.r98 Adjustment factor #2 NOT used.
Analysis Date 11-14-2005/08:12:07 Residue file dated: 11-14-2005/08:10:45/8
Reference dose (RfD, Chronic) = .04 mg/kg bw/day

Total exposure by population subgroup

Population Subgroup	Total Exposure	
	mg/kg body wt/day	Percent of Rfd
U.S. Population (total)	0.000180	0.4%
U.S. Population (spring season)	0.000184	0.5%
U.S. Population (summer season)	0.000175	0.4%
U.S. Population (autumn season)	0.000179	0.4%
U.S. Population (winter season)	0.000182	0.5%
Northeast region	0.000190	0.5%
Midwest region	0.000192	0.5%
Southern region	0.000167	0.4%
Western region	0.000178	0.4%
Hispanics	0.000162	0.4%
Non-hispanic whites	0.000186	0.5%
Non-hispanic blacks	0.000166	0.4%
Non-hisp/non-white/non-black	0.000168	0.4%
All infants (< 1 year)	0.000077	0.2%
Nursing infants	0.000043	0.1%
Non-nursing infants	0.000091	0.2%
Children 1-6 yrs	0.000401	1.0%
Children 7-12 yrs	0.000275	0.7%
Females 13-19 (not preg or nursing)	0.000154	0.4%
Females 20+ (not preg or nursing)	0.000124	0.3%
Females 13-50 yrs	0.000142	0.4%
Females 13+ (preg/not nursing)	0.000146	0.4%
Females 13+ (nursing)	0.000167	0.4%
Males 13-19 yrs	0.000196	0.5%
Males 20+ yrs	0.000159	0.4%
Seniors 55+	0.000118	0.3%
Children 1-2 yrs	0.000403	1.0%
Children 3-5 yrs	0.000411	1.0%
Children 6-12 yrs	0.000289	0.7%
Youth 13-19 yrs	0.000176	0.4%
Adults 20-49 yrs	0.000153	0.4%
Adults 50+ yrs	0.000120	0.3%
Females 13-49 yrs	0.000137	0.3%



13544

R118474

Chemical: Acetic acid, {(5-chloro-8-quinolinyl)oxy}-, 1-methylhexyl ester

PC Code:
700099

HED File Code: 11000 Chemistry Reviews

Memo Date: 11/22/2005

File ID:

Accession #: 412-06-0009

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