UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

03/27/2000

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

Subject: Acute and Chronic Dietary Exposure Analyses for Proposed Tolerances for **Cloquintocet-mexyl** in/on Wheat Commodities.

DP Barcode: D263506 Submission: S533228
PC Code 999999

From: Manying Xue, Chemist
Registration Action Branch 3
Health Effects Division (7509C)

Through: Jennifer Rowell, Chemist
Carol Christensen, EPS
DE SAC Reviewers
Health Effects Division (7509C)

Stephen Dapson, Branch Senior Scientist
Registration Action Branch 3
Health Effects Division (7509C)
03/29/2000

To: Anna Lowit, Risk Assessor
Registration Action Branch 3
Health Effects Division (7509C)

Action Requested

Provide a Tier 1 (tolerance and 100%CT) acute and chronic dietary exposure analyses using the proposed tolerances for the combined residues of cloquintocet-mexyl (acetic acid, [(5-chloro-8-quinolinyl)oxy]-, 1-methylhexyl ester) and its metabolite 5-chloro-8-quinolinoxyacetic acid in/on wheat grain, forage, hay, and straw.

Executive Summary

The estimated risks from acute and chronic dietary exposures to cloquintocet-mexyl and its metabolite 5-chloro-8-quinolinoxyacetic acid, as represented by %PAD (Population Adjusted Dose) are below HED's level of concern for the US population and all population subgroups.

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 1.

Table 1. The doses and selected toxicological endpoints on cloquintocet-mexyl (CGA 185072)

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	

[a] 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.

Consumption Data

HED conducts dietary risk assessments using the Dietary Exposure Evaluation Model (DEEM™), which incorporates consumption data generated in USDA's Continuing Surveys of Food Intakes by Individuals (CSFII), 1989-1992. For this acute dietary risk assessment, the entire distribution of single day food consumption events is combined with a single residue level (deterministic analysis) to obtain a distribution of exposure in mg/kg. For chronic dietary risk assessment, the three-day average of consumption for each sub-population is combined with residues in commodities to determine average exposure in mg/kg/day.

Residue Information

HED has recommended for the establishment of the following tolerances for the combined residues of cloquintocet-mexyl (acetic acid, [(5-chloro-8-quinolinyl)oxy]-, 1-methylhexyl ester) and its metabolite 5-chloro-8-quinolinoxyacetic acid in/on wheat commodities:

Commodities	ppm
Wheat grain	0.1
Wheat forage	0.1
Wheat hay	0.1
Wheat straw	0.1

Acute and chronic analyses have been conducted using the recommended tolerance levels. DEEM™ default processing factors were used for the analyses.

Results

Acute Exposure Analysis The acute dietary risk estemate associated with cloquintocet-mexyl use wheat grain, forage, hay, and straw is below HED's level of concern (100% aPAD). The Tier 1 analysis estimates for females 13+ subgroups at the 95th percentile exposure are 0.03-0.04 % of the aPAD. Dietary exposure estimates at the 95th, 99th, and 99.9th percentiles for the female population subgroups are shown in Table 2. A complete listing of acute dietary exposure estimates for all DEEM™ population subgroups is included as Attachment 2.

Table 2. Acute Dietary Tier 1 Exposure Estimates

Population Subgroup	95th Percentile		99th Percentile		99.9th Percentile	
	Exposure (mg/kg/day)	% aPAD	Exposure (mg/kg/day)	% aPAD	Exposure (mg/kg/day)	% aPAD
Females (13+/preg/not nursing)	0.000310	0.03	0.000386	0.04	0.000479	0.05
Females (13+/nursing)	0.000371	0.04	0.000539	0.05	0.000646	0.06
Females (13-19 yrs/np/nn)	0.000319	0.03	0.000482	0.05	0.000846	0.08
Females (20+ years/np/nn)	0.000253	0.03	0.000366	0.04	0.000544	0.05
Females (13-50 years)	0.000284	0.03	0.000409	0.04	0.000641	0.06

Chronic Exposure Analysis The chronic dietary risk estimate associated with cloquintocet-mexyl use in/on wheat grain, forage, hay, and straw is below HED's level of concern. The Tier 1 analysis estimates are <1% of the cPAD for the U.S. population and <1% of the cPAD for all infants. Exposure estimates and associated risk, as % aPAD, are shown in Table 3 for the selected population subgroups. A complete listing of chronic exposure estimates for all DEEM™ population subgroups is included as Attachment 3.

Table 3. Chronic Dietary Tier 1 Exposure Estimates

Population Subgroup	Exposure, mg/kg/day	% cPAD
U.S. Population (total)	0.000148	0.4
All infants (< 1 year)	0.000052	0.1
Children 1-6 yrs	0.000338	0.8
Children 7-12 yrs	0.000237	0.6
Females 13-50 yrs	0.000115	0.3

List of Attachments

Attachment 1: Cloquintocet-mexyl Dietary Residue Inputs
Attachment 2: Acute Dietary Exposure Estimates
Attachment 3: Chronic Dietary Exposure Estimates

cc: Petition file, M. Xue (RAB3)
RDI: Dietary Exposure SAC: 03/27/00
7509C:RAB3: CM-2: Rm 810F: 703 305-6198

Attchment 1: Cloquintocet-mexyl Dietary Residue Inputs

Filename: C:\deem\cloqui.R96 Chemical name: Cloquintocet-mexyl
Date created/last modified: 02-23-2000/14:07:26/8 Program ver. 6.77

Food Code	Crop Grp	Food Name	RESIDUE (ppm)	RDF #	Adj.Factors #1	Adj.Factors #2	Comment
278	15	Wheat-bran	0.100000	0	1.000	1.000	
279	15	Wheat-flour	0.100000	0	1.000	1.000	
277	15	Wheat-germ	0.100000	0	1.000	1.000	
437	15	Wheat-germ oil	0.100000	0	1.000	1.000	
276	15	Wheat-rough	0.100000	0	1.000	1.000	

Attachment 2: Acute Dietary Exposure Estimates

U.S. Environmental Protection Agency Ver. 6.78
DEEM ACUTE analysis for (1989-92 data)
Residue file: cloqui.R96 Adjustment factor #2 NOT used.
Analysis Date: 02-23-2000/14:10:43 Residue file dated: 02-23-2000/14:07:26/8
Acute Reference Dose (aRfD) = 1.000000 mg/kg body-wt/day
NOEL (Acute) = 100.000000 mg/kg body-wt/day

Summary calculations:

	5th Percentile			1st Percentile			0.1st Percentile	
Exposure	% aRfD	MOE	Exposure	% aRfD	MOE	Exposure	% aRfD	MOE
Females (13+/preg/not nsg):								
0.000310	0.03	322542	0.000386	0.04	259309	0.000479	0.05	208821
Females (13+/nursing):								
0.000371	0.04	269558	0.000539	0.05	185519	0.000646	0.06	154764
Females (13-19 yrs/np/nn):								
0.000319	0.03	313667	0.000482	0.05	207380	0.000846	0.08	118235
Females (20+ years/np/nn):								
0.000253	0.03	395942	0.000366	0.04	273000	0.000544	0.05	183825
Females (13-50 years):								
0.000284	0.03	352285	0.000409	0.04	244634	0.000641	0.06	155965

U.S. Environmental Protection Agency Ver. 6.78
DEEM ACUTE analysis for (1989-92 data)
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Analysis Date: 02-23-2000/14:10:43 Residue file dated: 02-23-2000/14:07:26/8
Acute Reference Dose (aRfD) = 1.000000 mg/kg body-wt/day
NOEL (Acute) = 100.000000 mg/kg body-wt/day

Females (13+/preg/not nsg)

Daily Exposure Analysis (mg/kg body-weight/day)	per Capita	per User
Mean	0.000127	0.000131
Standard Deviation	0.000089	0.000087
Standard Error	0.000004	0.000005
Margin of Exposure	786,788	760,551
Percent of aRfD	0.01	0.01

Percent of Person-Days that are User-Days = 96.67%

Estimated percentile of user-days exceeding calculated exposure in mg/kg body-wt/day and corresponding

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
90.00	0.000040	0.00	>1,000,000	10.00	0.000260	0.03	384,209
80.00	0.000058	0.01	>1,000,000	5.00	0.000312	0.03	320,703
70.00	0.000081	0.01	>1,000,000	2.50	0.000363	0.04	275,687
60.00	0.000097	0.01	>1,000,000	1.00	0.000386	0.04	258,947
50.00	0.000112	0.01	896,448	0.50	0.000427	0.04	234,136
40.00	0.000129	0.01	773,071	0.25	0.000466	0.05	214,613
30.00	0.000156	0.02	641,241	0.10	0.000479	0.05	208,689
20.00	0.000189	0.02	529,203				

Estimated percentile of per-capita days exceeding calculated exposure in mg/kg body-wt/day and corresponding

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
90.00	0.000028	0.00	>1,000,000	10.00	0.000258	0.03	387,875
80.00	0.000053	0.01	>1,000,000	5.00	0.000310	0.03	322,542
70.00	0.000076	0.01	>1,000,000	2.50	0.000361	0.04	277,029
60.00	0.000093	0.01	>1,000,000	1.00	0.000386	0.04	259,309
50.00	0.000109	0.01	917,641	0.50	0.000426	0.04	234,912
40.00	0.000127	0.01	788,037	0.25	0.000465	0.05	215,232
30.00	0.000153	0.02	652,761	0.10	0.000479	0.05	208,821
20.00	0.000187	0.02	535,660				

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DEEM ACUTE analysis for (1989-92 data)
Residue file: cloqui.R96 Adjustment factor #2 NOT used.
Analysis Date: 02-23-2000/14:10:43 Residue file dated: 02-23-2000/14:07:26/8
Acute Reference Dose (aRfD) = 1.000000 mg/kg body-wt/day
NOEL (Acute) = 100.000000 mg/kg body-wt/day

Females (13+/nursing)

Daily Exposure Analysis (mg/kg body-weight/day)	per Capita	per User
Mean	0.000150	0.000160
Standard Deviation	0.000121	0.000118
Standard Error	0.000008	0.000008
Margin of Exposure	666,269	625,620
Percent of aRfD	0.02	0.02

Percent of Person-Days that are User-Days = 93.90%

Estimated percentile of user-days exceeding calculated exposure in mg/kg body-wt/day and corresponding

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
90.00	0.000037	0.00	>1,000,000	10.00	0.000328	0.03	304,596
80.00	0.000054	0.01	>1,000,000	5.00	0.000374	0.04	267,421
70.00	0.000077	0.01	>1,000,000	2.50	0.000453	0.05	220,808
60.00	0.000108	0.01	928,978	1.00	0.000543	0.05	184,187
50.00	0.000137	0.01	730,027	0.50	0.000623	0.06	160,462
40.00	0.000160	0.02	625,057	0.25	0.000641	0.06	156,008
30.00	0.000197	0.02	508,165	0.10	0.000646	0.06	154,708
20.00	0.000267	0.03	373,960				

Estimated percentile of per-capita days exceeding calculated exposure in mg/kg body-wt/day and corresponding

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
90.00	0.000015	0.00	>1,000,000	10.00	0.000324	0.03	308,311
80.00	0.000045	0.00	>1,000,000	5.00	0.000371	0.04	269,558
70.00	0.000066	0.01	>1,000,000	2.50	0.000448	0.04	223,338
60.00	0.000096	0.01	>1,000,000	1.00	0.000539	0.05	185,519
50.00	0.000127	0.01	784,616	0.50	0.000618	0.06	161,817
40.00	0.000154	0.02	649,322	0.25	0.000640	0.06	156,290
30.00	0.000190	0.02	527,389	0.10	0.000646	0.06	154,764
20.00	0.000258	0.03	387,250				

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Residue file: cloqui.R96 Adjustment factor #2 NOT used.
Analysis Date: 02-23-2000/14:10:43 Residue file dated: 02-23-2000/14:07:26/8
Acute Reference Dose (aRfD) = 1.000000 mg/kg body-wt/day
NOEL (Acute) = 100.000000 mg/kg body-wt/day

Females (13-19 yrs/np/nn)

Daily Exposure Analysis (mg/kg body-weight/day)	per Capita	per User
Mean	0.000137	0.000140
Standard Deviation	0.000100	0.000099
Standard Error	0.000002	0.000002
Margin of Exposure	732,280	713,211
Percent of aRfD	0.01	0.01

Percent of Person-Days that are User-Days = 97.40%

Estimated percentile of user-days exceeding calculated exposure in mg/kg body-wt/day and corresponding

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
90.00	0.000041	0.00	>1,000,000	10.00	0.000260	0.03	384,358
80.00	0.000062	0.01	>1,000,000	5.00	0.000320	0.03	312,090
70.00	0.000082	0.01	>1,000,000	2.50	0.000386	0.04	259,335
60.00	0.000101	0.01	992,101	1.00	0.000484	0.05	206,629
50.00	0.000122	0.01	819,064	0.50	0.000545	0.05	183,435
40.00	0.000144	0.01	694,900	0.25	0.000696	0.07	143,752
30.00	0.000168	0.02	594,339	0.10	0.000848	0.08	117,856
20.00	0.000200	0.02	500,977				

Estimated percentile of per-capita days exceeding calculated exposure in mg/kg body-wt/day and corresponding

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
90.00	0.000031	0.00	>1,000,000	10.00	0.000259	0.03	386,765
80.00	0.000057	0.01	>1,000,000	5.00	0.000319	0.03	313,667
70.00	0.000078	0.01	>1,000,000	2.50	0.000384	0.04	260,513
60.00	0.000098	0.01	>1,000,000	1.00	0.000482	0.05	207,380
50.00	0.000119	0.01	838,617	0.50	0.000544	0.05	183,987
40.00	0.000142	0.01	706,351	0.25	0.000692	0.07	144,588
30.00	0.000166	0.02	601,318	0.10	0.000846	0.08	118,235
20.00	0.000198	0.02	505,221				

U.S. Environmental Protection Agency Ver. 6.78
DEEM ACUTE analysis for (1989-92 data)
Residue file: cloqui.R96 Adjustment factor #2 NOT used.
Analysis Date: 02-23-2000/14:10:43 Residue file dated: 02-23-2000/14:07:26/8
Acute Reference Dose (aRfD) = 1.000000 mg/kg body-wt/day
NOEL (Acute) = 100.000000 mg/kg body-wt/day

Females (20+ years/np/nn)

Daily Exposure Analysis (mg/kg body-weight/day)	per Capita	per User
Mean	0.000104	0.000109
Standard Deviation	0.000078	0.000077
Standard Error	0.000001	0.000001
Margin of Exposure	961,544	920,309
Percent of aRfD	0.01	0.01

Percent of Person-Days that are User-Days = 95.71%

Estimated percentile of user-days exceeding calculated exposure in mg/kg body-wt/day and corresponding

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
90.00	0.000030	0.00	>1,000,000	10.00	0.000209	0.02	478,932
80.00	0.000048	0.00	>1,000,000	5.00	0.000255	0.03	392,749
70.00	0.000061	0.01	>1,000,000	2.50	0.000303	0.03	330,299
60.00	0.000077	0.01	>1,000,000	1.00	0.000368	0.04	271,550
50.00	0.000092	0.01	>1,000,000	0.50	0.000420	0.04	238,101
40.00	0.000110	0.01	907,141	0.25	0.000475	0.05	210,507
30.00	0.000132	0.01	759,487	0.10	0.000546	0.05	183,110
20.00	0.000159	0.02	627,518				

Estimated percentile of per-capita days exceeding calculated exposure in mg/kg body-wt/day and corresponding

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
90.00	0.000018	0.00	>1,000,000	10.00	0.000207	0.02	484,068
80.00	0.000041	0.00	>1,000,000	5.00	0.000253	0.03	395,942
70.00	0.000057	0.01	>1,000,000	2.50	0.000301	0.03	332,669
60.00	0.000072	0.01	>1,000,000	1.00	0.000366	0.04	273,000
50.00	0.000089	0.01	>1,000,000	0.50	0.000418	0.04	239,422
40.00	0.000107	0.01	934,345	0.25	0.000473	0.05	211,605
30.00	0.000129	0.01	776,475	0.10	0.000544	0.05	183,825
20.00	0.000157	0.02	637,443				

U.S. Environmental Protection Agency Ver. 6.78
DEEM ACUTE analysis for (1989-92 data)
Residue file: cloqui.R96 Adjustment factor #2 NOT used.
Analysis Date: 02-23-2000/14:10:43 Residue file dated: 02-23-2000/14:07:26/8
Acute Reference Dose (aRfD) = 1.000000 mg/kg body-wt/day
NOEL (Acute) = 100.000000 mg/kg body-wt/day

Females (13-50 years)

Daily Exposure Analysis (mg/kg body-weight/day)	per Capita	per User
Mean	0.000115	0.000120
Standard Deviation	0.000088	0.000087
Standard Error	0.000001	0.000001
Margin of Exposure	868,659	831,981
Percent of aRfD	0.01	0.01

Percent of Person-Days that are User-Days = 95.78%

Estimated percentile of user-days exceeding calculated exposure in mg/kg body-wt/day and corresponding

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
90.00	0.000033	0.00	>1,000,000	10.00	0.000232	0.02	431,797
80.00	0.000051	0.01	>1,000,000	5.00	0.000286	0.03	349,319
70.00	0.000066	0.01	>1,000,000	2.50	0.000342	0.03	292,080
60.00	0.000084	0.01	>1,000,000	1.00	0.000411	0.04	243,436
50.00	0.000102	0.01	977,597	0.50	0.000483	0.05	206,888
40.00	0.000122	0.01	818,970	0.25	0.000537	0.05	186,182
30.00	0.000145	0.01	688,859	0.10	0.000644	0.06	155,202
20.00	0.000175	0.02	570,991				

Estimated percentile of per-capita days exceeding calculated exposure in mg/kg body-wt/day and corresponding

Perc.	Exposure	% aRfD	MOE	Perc.	Exposure	% aRfD	MOE
90.00	0.000020	0.00	>1,000,000	10.00	0.000229	0.02	436,488
80.00	0.000045	0.00	>1,000,000	5.00	0.000284	0.03	352,285
70.00	0.000062	0.01	>1,000,000	2.50	0.000340	0.03	294,205
60.00	0.000079	0.01	>1,000,000	1.00	0.000409	0.04	244,634
50.00	0.000098	0.01	>1,000,000	0.50	0.000480	0.05	208,266
40.00	0.000119	0.01	843,094	0.25	0.000535	0.05	187,007
30.00	0.000142	0.01	703,643	0.10	0.000641	0.06	155,965
20.00	0.000172	0.02	579,737				

Attachment 3: Chronic Dietary Exposure Estimates

U.S. Environmental Protection Agency Ver. 6.76
DEEM Chronic analysis for (1989-92 data)
Residue file name: C:\deem\cloqui.R96 Adjustment factor #2 NOT used.
Analysis Date 02-23-2000/14:13:57 Residue file dated: 02-23-2000/14:07:26/8
Reference dose (RfD, CHRONIC) = .04 mg/kg bw/day
NOEL (CHRONIC) = 4.3 mg/kg bw/day

Total exposure by population subgroup

Population Subgroup	Total Exposure mg/kg body wt/day	Margin of Exposure 1/	Percent of RfD
U.S. Population (total)	0.000148	29,141	0.4%
U.S. Population (spring season)	0.000142	30,181	0.4%
U.S. Population (summer season)	0.000148	29,104	0.4%
U.S. Population (autumn season)	0.000157	27,446	0.4%
U.S. Population (winter season)	0.000143	30,136	0.4%
Northeast region	0.000153	28,015	0.4%
Midwest region	0.000151	28,476	0.4%
Southern region	0.000143	30,166	0.4%
Western region	0.000146	29,473	0.4%
Hispanics	0.000126	34,044	0.3%
Non-hispanic whites	0.000152	28,374	0.4%
Non-hispanic blacks	0.000133	32,309	0.3%
Non-hisp/non-white/non-black)	0.000166	25,971	0.4%
All infants (< 1 year)	0.000052	82,863	0.1%
Nursing infants	0.000022	193,160	0.1%
Non-nursing infants	0.000064	66,808	0.2%
Children 1-6 yrs	0.000338	12,720	0.8%
Children 7-12 yrs	0.000237	18,139	0.6%
Females 13-19(not preg or nursing)	0.000137	31,490	0.3%
Females 20+ (not preg or nursing)	0.000104	41,349	0.3%
Females 13-50 yrs	0.000115	37,355	0.3%
Females 13+ (preg/not nursing)	0.000127	33,834	0.3%
Females 13+ (nursing)	0.000150	28,652	0.4%
Males 13-19 yrs	0.000166	25,834	0.4%
Males 20+ yrs	0.000119	36,194	0.3%
Seniors 55+	0.000099	43,446	0.2%
Pacific Region	0.000143	30,119	0.4%

13544

002782

Chemical:	**Inert ingredient undetermined**
PC Code:	**999999**
HED File Code	**11000 Chemistry Reviews**
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