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

MAR 11 1996

OFFICE OF  
PREVENTION, PESTICIDES AND  
TOXIC SUBSTANCES

MEMORANDUM:

SUBJECT: Review Flumioxazine Exposure Assessment and Amended EUP

FROM: George Tompkins, Ph.D, Entomologist *George Tompkins*  
Special Review and Registration Section II

TO: Joanne Miller, PM #23  
Registration Division (7505C)

THRU: Mark Dow, Ph.D., Section Head *Mark Dow*  
Special Review and Registration Section II  
Larry C. Dorsey, Chief *Larry C. Dorsey*  
Occupational and Residential Exposure Branch  
Health Effects Division (7509C)

The Occupational and Residential Exposure Branch (OREB) has been requested to review a detailed PHED exposure assessment (MRID No. 43901401) and an amended EUP (MRID No.43901400) for V-53482 WP Herbicide (Flumioxazine) from Valent U.S.A. to determine if there is a need for a worker exposure study.

DP Barcode: D222276

Pesticide Chemical Code: 129034 Flumioxazine

EPA Reg. No.: 59639-EUP-RRI

MRID No.: 43901400 and 43901401

PHED: Yes, version 1.1

## I. INTRODUCTION:

### A. Background:

Valent U.S.A. Corporation has developed V-53482 WP Herbicide (active ingredient is flumioxazin, which is 7-fluoro-6-[(3,4,5,6-tetrahydro)phthalimido]-4-(2-propynyl)-1,4-benzoxazin-3(2H)-one). V-53482 is formulated as a 51% wettable powder packaged in water soluble packets and is intended for use as a preemergence low application rate herbicide on soybeans and peanuts. The application rate on soybeans will range from 1.5-2.5 oz of product per acre (0.048-0.080 lb ai/A) and for peanuts the application rate is 2.0-3.0 oz per acre (0.064-0.096 lb ai/A).

Information submitted in the exposure assessment (MRID No. 43901401) indicates that flumioxazin is a tox category III and IV for all acute toxicity studies. An official NOEL has not been established since a less than life time evaluation for endpoints has not been established for flumioxazin (personal communication with Dr. Alberto Protzel, TB II; 5 Mar 96).

### B. Purpose:

OREB has been requested to review a detailed PHED exposure assessment submitted by Valent U.S.A. Corporation. In the submitted assessment it was concluded that the results indicated that there was no need for a worker exposure study to be performed.

## II. DETAILED CONSIDERATIONS:

### A. Comments on Submitted Assessment and OREB's Assessment:

1. The acceptable minimum number of replicates per body part is 15 (Subdivision U, 231 (C) 2). Whether or not "the head and neck are a small part of the body" or that "there are significantly more observations for other body parts" is immaterial (p 4-5, MRID No. 43901401).

2. Presently there are insufficient observations in PHED Version 1.1 to adequately estimate handler exposure to wettable powders in water soluble packaging. Until EPA has adequate data, handler exposure to wettable powders in water soluble packaging is estimated under an open pour, open bag Mixer/Loader scenario.

3. The lbs ai handled for both the Mixer/Loader and Applicator runs were the closest the database could come to the projected lbs ai handled while still maintaining the required 15 replicates per body part. Further, the application rate of "less than 6" includes some observations that are significantly higher than the registrants suggested application rate. As with the lbs ai handled, this was necessary to maintain at least 15 replicates per body part. These conditions, coupled with the inclusion of "C" grade data, makes these medium confidence runs.

4. The run needs to reflect the protective clothing scenario as required by the Worker Protection Standard (in this case, both the M/L and Applicator runs need to reflect a long sleeve shirt, long pants and glove clothing scenario). Valent's applicator runs should have reflected this.

5. Unless a closed cab is specified on the label, exposure estimates need to be made under an open cab scenario.

6. In OREB's PHED run the total lb ai mixed was less than or equal to 55 lb ai/day and for the applicators calculations the total lb ai applied was less than or equal to 45 lb ai/day.

7. On page 5 of the Section G for the EUP (MRID No. 43901400) it was specified that for soybeans a total of 480 acres was to be treated. The maximum application rate was to be 43.4 grams ai/A per EUP treated acre in a single growing season. However, on page 2 of the use information (MRID No. 43901401, III, Use Information) it was stated that the maximum application rate on soybeans was to be 0.08 lb ai/A, but for peanuts it was to be 0.096 lb ai/A. If 0.08 lb ai/A is the maximum application rate for soybeans, then the total ai used per year in the proposed EUP should be 38.4 lb/year (17418 grams).

B. OREB's tentative exposure assessment is based on the following assumptions (TABLE ONE).

TABLE ONE ASSUMPTIONS	
Mixer/loader weight	60 kg
Applicator weight	60 kg
Acres treated/day: peanuts-	100 acres
soybeans-	150 acres
Mixer/loader unit of exposure, PHED <sup>1</sup>	220.0355 ug/lb ai
Applicator unit of exposure	60.6565 ug/lb ai
Combined exposure <sup>2</sup>	280.6920 ug/lb ai

<sup>1</sup> PHED run with protective clothing consisting of long pants, long sleeved shirt, and gloves for both mixer/loader and for applicator. The daily total lb ai mixed was less than or equal to 55 lb ai/day and the total lb ai applied was less than or equal to 45 lb ai/day.

<sup>2</sup> The combined exposure was calculated because it was mentioned on p 5 of Valent's exposure assessment that "a grower is likely to do both the mixing/loading and application".

### III. CONCLUSIONS:

OREB tentatively concludes that the following worker exposure results from the use of V-53482 WP utilizing the data generated from the PHED.

TABLE TWO. V-53482 WP WORKER EXPOSURE		
	Daily Exposure (ADD)	Annual Average Daily Exppsure (AADD)
Mixer/loader: peanuts- soybeans-	35.206 ug/kg bw/day 44.0 ug/kg bw /day	0.096 ug/kg bw/day 0.121 ug/kg bw/day
Applicator: peanuts soybeans	9.705 ug/kg bw/day 12.131 ug/kg bw/day	0.027 ug/kg bw/day 0.033 ug/kg bw/day
Combined Exposure <sup>1</sup> : peanuts- soybeans-	44.911 ug/kg bw/day 56.131 ug/kg bw/day	0.123 ug/kg bw/day 0.154 ug/kg bw/day

<sup>1</sup> If the same person both mixes and applies the compound.

It can be concluded that if the values of 100 mg/kg/day or 30 mg/kg/day for dermal rat NOEL are used, then the tentative calculated MOE for a peanut grower would range from 668.003 to 2226.676 times less than the dermal rat NOEL. The MOE for a soybean grower would range from 534.47 to 1781.578 times less than the NOEL.

If these calculations based on open mixing of wettable powder formulations are not acceptable for comparison to that submitted for a wettable powder in a water soluble package, then OREB welcomes the submission of a detailed mixer/loader/applicator study utilizing the packaging of V-53482 in water soluble bags.

Attachment (1)

cc: RCAB  
G. Tompkins  
Chemical File, 129034 (Flumioxazine)

APPENDIX I. Exposure Calculations

Total ai handled per day and per farm:

Peanuts:  $0.096 \text{ lb ai/A} \times 100 \text{ acres/day} = 9.6 \text{ lb ai/day}$

Soybeans:  $0.080 \text{ lb ai/A} \times 150 \text{ A/day} = 12.0 \text{ lb ai/day}$

Mixer/Loader Daily Exposure (DE) or Absorbed Daily Dose:

Peanuts:  $220.0355 \text{ ug/lb ai} \times 9.6 \text{ lb ai/day} \div 60 \text{ kg} =$   
 $35.206 \text{ ug/kg bw/day}$

Soybeans:  $220.0355 \text{ ug/lb ai} \times 12 \text{ lb ai/day} \div 60 \text{ kg} =$   
 $44.0 \text{ ug/kg bw/day}$

Mixer/Loader Annual Average Daily Dose (AADD):

Peanuts:  $35.206 \text{ ug/kg/day} \times 1 \text{ treatment/yr} \div 365 \text{ days} =$   
 $0.096 \text{ ug/kg bw/day}$

Soybeans:  $44.0 \text{ ug/kg/day} \times 1 \text{ treatment/yr} \div 365 \text{ days} =$   
 $0.121 \text{ ug/kg bw/day}$

Applicator Daily Exposure (ADD):

Peanuts:  $60.6565 \text{ ug/lb ai} \times 9.6 \text{ lb ai/day} \div 60 \text{ kg} =$   
 $9.705 \text{ ug/kg bw/day}$

Soybeans:  $60.6565 \text{ ug/lb ai} \times 12.0 \text{ lb ai/day} \div 60 \text{ kg} =$   
 $12.131 \text{ ug/kg bw/day}$

Applicator Annual Average Daily Dose (AADD):

Peanuts:  $9.705 \text{ ug/kg/day} \times 1 \text{ day} \div 365 \text{ days} = 0.027 \text{ ug/kg/day}$

Soybeans:  $12.131 \text{ ug/kg/day} \times 1 \div 365 \text{ days} = 0.033 \text{ ug/kg/day}$

Combined Mixer/Loader Daily Exposure:

Peanuts:  $35.206 \text{ ug/kg/day} + 9.705 \text{ ug/kg/day} = 44.911 \text{ ug/kg/day}$

Soybeans:  $44.0 \text{ ug/kg/day} + 12.131 \text{ ug/kg/day} = 56.131 \text{ ug/kg/day}$

An Official EPA rat dermal NOEL has not yet been established. However, for purposes of comparison in this review the dermal rat NOEL of 100 mg/kg/day and 30 mg/kg/day will be used as cited on p 4 and 9 of MRID No. 43901401 to estimate tentative risk. These values may have to be recalculated when an official NOEL has been established. Using 100 mg/kg/day as the NOEL would yield:

$$\text{MOE} = \frac{\text{NOEL}}{\text{Dose}}$$

The combined daily exposure for a soybean grower was 56.131 ug/kg/day, which is equal to 0.056131 mg/kg/day.

The combined daily exposure for a peanut grower was 44.911 ug/kg/day, which is equal to 0.04491 mg/kg/day.

$$\text{Soybean Grower MOE: } \frac{100 \text{ mg/kg/day}}{0.056131 \text{ mg/kg/day}} = 1781.578$$

$$\text{Peanut grower MOE: } \frac{100 \text{ mg/kg/day}}{0.04491 \text{ mg/kg/day}} = 2226.676$$

By using 30 mg/kg/day as the dermal rat NOEL would yield:

$$\text{Soybean grower MOE: } \frac{30 \text{ mg/kg/day}}{0.05613 \text{ mg/kg/day}} = 534.47$$

$$\text{Peanut grower MOE: } \frac{30 \text{ mg/kg/day}}{0.04491 \text{ mg/kg/day}} = 668.003$$

DP Barcode D222276  
 Case: 285019  
 Submission: S499257

SUMMARY STATISTICS FOR CALCULATED DERMAL EXPOSURES

SCENARIO: Long pants, long sleeves, gloves \*\* Wettable Powder/Open Mixing

PATCH LOCATION	DISTRIB. TYPE	MICROGRAMS PER LB AI MIXED				
		Median	Mean	Coef of Var	Geo. Mean	Obs.
HEAD (ALL)	Lognormal	48.88	71.9206	95.938	37.7966	17
NECK.FRONT	Lognormal	25.74	68.7909	191.2033	30.1274	17
NECK.BACK	Lognormal	11.605	45.7335	214.8491	13.817	17
UPPER ARMS	Lognormal	11.64	140.5391	449.9592	18.4796	42
CHEST	Lognormal	17.75	162.3501	431.3388	23.7833	37
BACK	Other	17.75	166.5814	427.5597	22.3832	37
FOREARMS	Other	6.2315	30.365	256.0991	8.2374	40
HIGHS	Lognormal	14.134	21.9377	128.203	10.3663	35
LOWER LEGS	Lognormal	7.378	11.7017	94.6598	7.4052	30
FEET						0
HANDS	Lognormal	8.3194	29.4415	120.5115	11.2572	12
TOTAL DERM:	177.0141	169.4279	749.3615		183.6532	

95% C.I. on Mean: Dermal: [-11433.2082, 12931.9312]

Number of Records: 45  
 Subset Name: WP1.OPN.MLOD

Data File: MIXER/LOADER

ADD INHALATION                      CHANGE HEAD                      LB AI TO KG AI                      EXIT

<< Specifications >>                      Page 1 of 1  
 Subset Specifications for WP1.OPN.MLOD

With Dermal Grade Uncovered Equal to "A" "B" "C"  
 Subset originated from WP.OPN.MLOD  
 With Solid Type Equal to 1 and (wetable powder)  
 With Packaging Type Equal to 1 and (open pour bag)  
 With Mixing Procedures Equal to 1 and (open mixing)  
 With Total lb ai Mixed Less than or Equal to 55 *lb ai mixed*  
 Subset originated from MLOD.FILE



DP Barcode D222276  
 Case: 285019  
 Submission: S499257

SUMMARY STATISTICS FOR CALCULATED DERMAL EXPOSURES

SCENARIO: Long pants, long sleeves, gloves

PATCH LOCATION	DISTRIB. TYPE	MICROGRAMS PER LB AI MIXED				Obs.
		Median	Mean	Coef of Var	Geo. Mean	
HEAD (ALL)	Lognormal	71.695	79.7364	90.8245	42.1942	14
NECK FRONT	Lognormal	24.87	77.9571	184.8654	31.3567	14
NECK BACK	Lognormal	13.101	53.493	200.5681	15.3491	14
UPPER ARMS	Lognormal	36.8115	321.1731	316.2777	35.9645	16
CHEST	Lognormal	52.895	461.3709	275.3911	71.0953	11
BACK	Lognormal	29.465	475.6032	271.3597	57.9708	11
FOREARMS	Lognormal	13.31	64.0695	192.8687	20.0622	14
HIGHS	Lognormal	31.706	36.8842	73.2555	30.8864	9
LOWER LEGS	Other	19.754	19.754	0	19.754	4
FEET						0
HANDS	Lognormal	10.3298	25.6902	113.3884	12.4574	19
TOTAL DERM:		337.0906	303.9373	1615.7316	337.0906	

95% C.I. on Mean: Dermal: [-35910.3905, 39141.8537]

Data File: MIXER/LOADER

Number of Records: 26  
 Subset Name: WP2.OPN.MLOD

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ADD INHALATION                      CHANGE HEAD                      LB AI TO KG AI                      EXIT

<< Specifications >>                      Page 1 of 1  
 Subset Specifications for WP2.OPN.MLOD

With Hand Grade Equal to "A" "B" "C"  
 Subset originated from WP.OPN.MLOD  
 With Solid Type Equal to 1 and (wettable powder)  
 With Packaging Type Equal to 1 and (open pour bag)  
 With Mixing Procedures Equal to 1 and (open mixing)  
 With Total lb ai Mixed Less than or Equal to 55  
 Subset originated from MLOD.FILE

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DP Barcode D222276  
Case: 285019  
Submission: S499257

SUMMARY STATISTICS FOR INHALATION EXPOSURES

EXPOSURE	DISTRIB.	NANOGRAMS PER LB AI MIXED				Obs.
	TYPE	Median	Mean	Coef of Var	Geo. Mean	
	Lognormal	39529.6246	101286.2878	147.5458	41821.2557	40

95% C.I. on Geo. Mean: [2873.6808, 608633.1529]

Number of Records: 42

Data File: MIXER/LOADER

Subset Name: WP3.OPN.MLOD

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Subset Specifications for WP3.OPN.MLOD

With Airborne Grade Equal to "A" "B" "C"  
Subset originated from WP.OPN.MLOD  
With Solid Type Equal to 1 and (wetttable powder)  
With Packaging Type Equal to 1 and (open pour bag)  
With Mixing Procedures Equal to 1 and (open mixing)  
With Total lb ai Mixed Less than or Equal to 55  
Subset originated from MLOD.FILE

EXPOSURE

\*BASED ON A LONG PANTS, LONG SLEEVE SHIRT, GLOVE CLOTHING SCENARIO

\*Presently there are insufficient observations in PHED VERSION 1.1 to adequately estimate handler exposure to wetttable powders in water soluble packaging. Until EPA has adequate data, handler exposure to wetttable powders in water soluble packaging is estimated under an open pour, open bag M/L scenario. EPA welcomes registrants who find the resulting exposure value to be inordinately high to submit a study.

Dermal Exposure = 178.2143  $\mu\text{g}/\text{lb ai M/L}$

Inhalation Exposure = 41.8212  $\mu\text{g}/\text{lb ai M/L}$

TOTAL EXPOSURE = 220.0355  $\mu\text{g}/\text{lb ai M/L}$   
(Combined Dermal and Inhalation)

PHED VERSION 1.1

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DP Barcode D222276  
 Case: 285019  
 Submission: S499257

SUMMARY STATISTICS FOR CALCULATED DERMAL EXPOSURES

SCENARIO: Long pants, long sleeves, gloves

PATCH LOCATION	DISTRIB. TYPE	MICROGRAMS PER LB AI SPRAYED				Obs.
		Median	Mean	Coef of Var	Geo. Mean	
HEAD (ALL)	Lognormal	3.51	13.07	218.303	3.7811	39
NECK.FRONT	Lognormal	.87	1.7555	127.5591	.794	32
NECK.BACK	Lognormal	.594	1.3003	136.9299	.5341	34
UPPER ARMS	Lognormal	2.1825	2.4735	64.7301	2.0787	12
CHEST	Lognormal	2.84	8.6601	157.1033	3.436	38
BACK	Lognormal	2.84	7.8287	171.257	3.2828	38
FOREARMS	Lognormal	1.331	5.5621	217.7559	2.0628	31
HIGHS	Lognormal	.764	6.0301	303.6086	1.097	14
LOWER LEGS	Lognormal	1.19	2.9882	133.0065	1.3425	27
FEET	Lognormal	24.497	59.7797	104.1312	42.1309	3
HANDS	Lognormal	9.3022	28.6537	167.4723	3.069	15
TOTAL DERM:		63.6089	49.9207	138.1019	63.6089	

95% C.I. on Mean: Dermal: [-2266.7266, 2542.9304]

Data File: APPLICATOR

Number of Records: 44  
 Subset Name: GBM2.OPN.APPL

ADD INHALATION                      CHANGE HEAD                      LB AI TO KG AI                      EXIT

<< Specifications >>  
 Subset Specifications for GBM2.OPN.APPL

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With Hand Grade Equal to "A" "B" "C"  
 Subset originated from GBM.OPN.APPL  
 With Application Method Equal to 2 and (Groundboom Tractor)  
 With Cab Type Equal to 1 2 and (Open Cab)  
 With Rate (lb ai/acre) Less than 6 and  
 With Total lb ai Applied Less than or Equal to 45  
 Subset originated from APPL.FILE

DP Barcode D222276  
Case: 285019  
Submission: S499257

SUMMARY STATISTICS FOR INHALATION EXPOSURES

EXPOSURE	DISTRIB.	NANOGRAMS PER LB AI SPRAYED				Obs.
	TYPE	Median	Mean	Coef of Var	Geo. Mean	
	Lognormal	1035.7895	2101.2639	146.9486	666.9355	15

95% C.I. on Geo. Mean: [18.6574, 23840.613]

Number of Records: 15

Data File: APPLICATOR

Subset Name: GBM3.OPN.APPL

<< Specifications >>

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Subset Specifications for GBM3.OPN.APPL

With Airborne Grade Equal to "A" "B"  
Subset originated from GBM.OPN.APPL  
With Application Method Equal to 2 and (Groundboom Tractor)  
With Cab Type Equal to 1 2 and (Open Cab)  
With Rate (lb ai/acre) Less than 6 and  
With Total lb ai Applied Less than or Equal to 45  
Subset originated from APPL.FILE

EXPOSURE

BASED ON A LONG PANTS, LONG SLEEVE SHIRT, GLOVE CLOTHING SCENARIO

Dermal Exposure = 59.9892  $\mu\text{g}/\text{lb ai}$  Applied

Inhalation Exposure = 0.6669  $\mu\text{g}/\text{lb ai}$  Applied

TOTAL EXPOSURE = 60.6565  $\mu\text{g}/\text{lb ai}$  Applied  
(Combined Dermal and Inhalation)