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

OCT 20 1989

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: ID:100-529; Atrazine; Assessment of risk to applicators due to carcinogenicity and cardiotoxicity.

TO: Jude Andreasen/Jack Housinger
Special Review and Reregistration Division (H-7508C)

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Marion Copley 10/18/89

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Tox. Chem. No.:63
Proj. No.:9-2280
Record No.: NA

cc: Linda Kutney
RD - FM #25

CONCLUSIONS:

The risk to M/L/A for **cardiotoxicity** is presented in terms of Margin of Safety (MOS) and ranges from <1 to 714 when actual plus potential dermal exposure and penetration are considered (see table 4). MOSs of less than 100 are considered to be of toxicologic concern. However, since this is a subchronic end point, use of the MOS for risk assessment is inappropriate for acute M/L/A exposures such as exposure for 3 or fewer days per year.

The risk to M/L/A for **carcinogenicity**, ranges from 10^{-6} to 10^{-2} when actual plus potential dermal exposure and penetration are considered (see table 4).

BACKGROUND:

The cardiac and carcinogenic risks due to applying Atrazine to sorghum have been analyzed in a similar fashion as was used in the memoranda dated 11/15/88 and 7/27/89 from Marion Copley to Jude Andreasen/Jack Housinger. Exposure values for sorghum were obtained from the memorandum dated 7/14/89 from Curt

Lunchick to J. Andreasen and the values for corn from the attached memorandum dated 7/26/89 from Steven M. Knott.

Atrazine is oncogenic (mammary tumors) in rats but not mice. A Registration Standard was completed in 1983 and a FRSTR is currently scheduled for 1989. The Scientific Advisory Panel (SAP), in September, 1988 concurred with the Toxicology Branch Peer Review Committee classifying Atrazine as a group C carcinogen however disagreed with the quantitative risk assessment ($Q_1^* = 2.2 \times 10^{-1}$).

The other endpoint of concern is cardiotoxicity. A NOEL of 0.5 mg/kg/day was obtained from a 1 year dog feeding study. Justification for use of this endpoint from a chronic study for evaluation of risk from subchronic applicator exposures is in the above mentioned 1988 memorandum.

TABLE 1 APPLICATOR EXPOSURE (not corrected for dermal absorption)

		(A) Annual exposure mg/kg/yr	(B) Day length hours	(C) Duration of exposure hours	(D) Exposure in days	(E) Exposure per day mg/kg/day	(F) Dose/day/ cm^2 skin mg/cm^2
Sorghum							
Ground Boom	M/L	3.6	5.9	7.4	2	2.9	0.07
open	A	12.00	5.9	7.4	2	9.6	0.22
closed	A	0.46	5.9	7.4	2	0.4	0.009
open/open	M/L/A	16.0	5.9	7.4	2	12.8	0.30
open/closed	M/L/A	4.1	5.9	7.4	2	3.3	0.08
Corn							
Grower open pour	M/L	5.2	4.5	8.9	2	2.6	0.06
	A	14.0	4.5	8.9	2	7.2	0.17
closed	M/L	0.084	4.5	8.9	2	0.04	0.0009
	A	0.56	4.5	8.9	2	0.3	0.007
open/open	M/L/A	20.0	4.5	8.9	2	10.0	0.23
open/closed	M/L/A	5.8	4.5	8.9	2	2.9	0.07
closed/open	M/L/A	14.0	4.5	8.9	2	7.2	0.17
closed/closed	M/L/A	0.64	4.5	8.9	2	0.3	0.007
Commercial open	M/L	160.0	5.3	80.0	15	10.7	0.25
	A	130.0	5.3	80.0	15	8.7	0.20
Commercial closed	M/L	2.6	5.3	80.0	15	0.2	0.005
	A	5.0	5.3	80.0	15	0.3	0.007
open/open	M/L/A	290.0	5.3	80.0	15	19.4	0.45
open/closed	M/L/A	165.0	5.3	80.0	15	11.0	0.26
closed/open	M/L/A	133.0	5.3	80.0	15	8.9	0.21
closed/closed	M/L/A	7.6	5.3	80.0	15	0.5	0.01
Aerial closed	M/L	2.4	0.42	6.3	15	0.16	0.004
	Pilot	0.1	0.42	6.3	15	0.007	0.0002
Sugarcane							
Ground open	M/L	80.0	5.3	79.2	15	5.33	0.12
closed	M/L	1.3	5.3	79.2	15	0.09	0.002
	A	5.2	5.3	79.2	15	0.35	0.008
Aerial closed	M/L	2.8	0.47	14.2	30	0.09	0.002
pilot	A	0.1	0.47	14.2	30	0.003	0.00007
flagger		0.7	0.47	14.2	30	0.02	0.0005
Macedonia nuts							
Ground driver	M/L	3.2	11.7	35.0*	3	1.07	0.02
Single applicator	M/L/A	70.0	11.7	35.0*	3	23.33	0.54
Split application	M/L/A	37.0	8.8	17.5*	2	18.50	0.43
Lawns							
Commercial	M/L	10.0	4.0	80.0*	20	0.50	0.01
	A	220.0	4.0	80.0*	20	11.00	0.25
Homeowner	M/L/A	0.2	1.0	1.2	2	0.10	0.002

(A) - Actual annual exposure for each specific use pattern.(taken from NDEB memos 7/14/89 and 7/26/89).
(B) - Length of work day for each specific use pattern.
(C) - Actual duration of exposure per year for each specific use pattern.
(D) = Supplied from NDEB (or (C)/(B) calc. # of days of exposure per year use specific use).
(E) = Actual daily dose assuming a 70 kg person (taken from NDEB memos 7/14/89 and 7/26/89).
(F)= (70)(E)/(3000); Daily dose per cm^2; assumes a 70 kg person and 3000 cm^2 skin exposed.

TABLE 2 RATES OF DERMAL ABSORPTION

		(G) Absorption rate (%)	(H) On washed skin (%)	(I) Total potential abs. exposure (%)
Sorghum				
Ground Boom	M/L	0.54	28.45	29.00
open	A	0.54	28.45	29.00
closed	A	1.86	30.84	32.70
open/open	M/L/A	0.54	28.45	29.00
open/closed	M/L/A	0.54	28.45	29.00
Corn				
Grower open pour	M/L	0.36	18.97	19.33
	A	0.36	18.97	19.33
closed	M/L	1.24	20.56	21.80
	A	1.24	20.56	21.80
open/open	M/L/A	0.36	18.97	19.33
open/closed	M/L/A	0.36	18.97	19.33
closed/open	M/L/A	0.36	18.97	19.33
closed/closed	M/L/A	1.24	20.56	21.80
Commercial open	M/L	0.36	18.97	19.33
	A	0.36	18.97	19.33
Commercial closed	M/L	1.24	20.56	21.80
	A	1.24	20.56	21.80
open/open	M/L/A	0.36	18.97	19.33
open/closed	M/L/A	0.36	18.97	19.33
closed/open	M/L/A	0.36	18.97	19.33
closed/closed	M/L/A/	0.36	18.97	19.33
Aerial closed	M/L	0.68	23.53	24.21
	Pilot	0.68	23.53	24.21
Sugarcane				
Ground open	M/L	0.36	18.97	19.33
closed	M/L	1.24	20.56	21.80
	A	1.24	20.56	21.80
Aerial closed	M/L	0.68	23.53	24.21
pilot	A	0.68	23.53	24.21
flagger		0.68	23.53	24.21
Macedonia nuts				
Ground driver	M/L	0.53	21.10	21.63
Single applicator	M/L/A	0.26	10.49	10.75
Split application	M/L/A	0.26	10.49	10.75
Lawns				
Commercial	M/L	1.24	20.56	21.80
	A	0.36	18.97	19.33
Homeowner	M/L/A	0.68	23.53	24.21

(G) & (H) - Taken from dermal absorption data evaluation report (7/18/88), adjusted for exposure duration and dose (4 hr study exposure values adjusted for 6 hr exposure).
(I) = (G)+(H) ; Total potential rate of absorption accounting for both actual absorption and estimated potential absorption due to compound remaining of the skin after washing.

TABLE 3 APPLICATOR EXPOSURE ADJUSTED FOR ACTUAL AND POTENTIAL DERMAL PENETRATION

		(J)	(K)	(L) Adjusted for lifetime exposure	(M) Adjusted for lifetime exposure
		Actual absorbed mg/kg/day	Total potential absorption mg/kg/day	Actual absorbed mg/kg/day	Total potential absorption mg/kg/day
Sorghum					
Ground boom	M/L	.015	0.85	.0000266	.00143
open	A	.05	2.78	.000261	.01403 .0048
closed	A	.007	0.13	.0000117	.000206
open/open	M/L/A	.07	3.71	.000118	.00636
open/closed	M/L/A	.018	0.01	.0000303	.00163
Corn					
Grower open pour	M/L	.009	0.50	.0000256	.00138
	A	.03	1.39	.000069	.00371
closed	M/L	.00005	0.008	.0000014	.00025 .000025
	A	.004	0.06	.0000095	.000167
open/open	M/L/A	.036	1.93	.0000986	.00530
open/closed	M/L/A	.01	0.56	.0000286	.00154
closed/open	M/L/A	.03	1.39	.000069	.00371
closed/closed	M/L/A	.003	0.06	.0000108	.000191
Commercial open	M/L	.04	2.07	.000789	.0424
	A	.03	1.68	.0000641	.0344
Commercial closed	M/L	.002	0.04	.0000441	.000754
	A	.004	0.06	.0000849	.00149
open/open	M/L/A	.07	3.75	.00143	.0768
open/closed	M/L/A	.31	2.13	.000814	.0437
closed/open	M/L/A	.03	1.72	.000656	.0352
closed/closed	M/L/A	.002	0.01	.0000374	.00201
Aerial closed	M/L	.001	0.04	.0000224	.00130 .000796
	Pilot	.00005	0.002	.00000093	.0000331
Sugarcane					
Ground open	M/L	.02	1.01	.000395	.0212
closed	M/L	.001	0.02	.0000221	.000388
	A	.004	0.08	.0000883	.00155
Aerial closed	M/L	.0006	0.02	.0000261	.000929
pilot	A	.00002	0.0007	.0000631	.0000331
flagger		.0001	0.005	.00000652	.000232
Macedonia nuts					
Ground driver	M/L	.006	0.23	.000394	.000948
Single applicator	M/L/A	.06	2.52	.000249	.0103
Split application	M/L/A	.05	2.00	.000132	.00545
Lawns					
Commercial	M/L	.006	0.11	.000170	.00299
	A	.04	2.12	.00108	.0583
Homeowner	M/L/A	.0007	0.02	.00000186	.0000663

(J) = (E)(G) ; Actual absorbed compound on a workday.
(K) = (E)(I) ; Actual plus potential absorbed compound on a workday.
(L) = 35(A)(G)/[(70)(365)] ; Daily lifetime exposure (based on actual absorption), assumes 35 working years, and 70 years lifespan, 365 days/year.
(M) = 35(A)(I))/[(70)(365)] ; Daily lifetime exposure (based on actual plus potential absorption), assumes 35 working years, and 70 years lifespan, 365 days/year.

TABLE 4 MARGIN OF SAFETY AND CARCINOGENIC RISK FOR APPLICATORS

		(N) Margin of Safety (MOS)	(O) Carcinogenic risk
Sorghum			
Ground Boom	M/L	1 **	3.1×10^{-4}
open	A	0.2**	3.1×10^{-3}
closed	A	3 **	4.5×10^{-5}
open/open	M/L/A	0.1**	1.4×10^{-3}
open/closed	M/L/A	50 **	3.6×10^{-4}
Corn			
Grower open pour	M/L	1 **	3.0×10^{-4}
	A	0.4 **	8.2×10^{-4}
closed	M/L	56 **	5.5×10^{-5}
	A	7 **	3.7×10^{-5}
open/open	M/L/A	0.3**	1.2×10^{-3}
open/closed	M/L/A	1 **	3.4×10^{-4}
closed/open	M/L/A	0.4**	8.2×10^{-4}
closed/closed	M/L/A	7 **	4.2×10^{-5}
Commercial open	M/L	0.2	9.3×10^{-3}
	A	0.3	7.6×10^{-3}
Commercial closed	M/L	12	1.7×10^{-4}
	A	7	3.3×10^{-4}
open/open	M/L/A	0.1	1.7×10^{-2}
open/closed	M/L/A	0.2	9.6×10^{-3}
closed/open	M/L/A	0.3	7.7×10^{-3}
closed/closed	M/L/A	50	4.4×10^{-4}
Aerial closed	M/L	12	2.9×10^{-4}
	Pilot	25	7.2×10^{-6}
Sugarcane			
Ground open	M/L	0.5	4.7×10^{-3}
closed	M/L	25	8.5×10^{-5}
	A	6	3.4×10^{-4}
Aerial closed	M/L	25	2.0×10^{-4}
pilot	A	714	7.2×10^{-6}
flagger		100	5.1×10^{-5}
Macedonia nuts			
Ground driver	M/L	2 **	2.1×10^{-4}
Single applicator	M/L/A	0.2**	2.3×10^{-3}
Split application	M/L/A	0.2**	1.2×10^{-3}
Lawns			
Commercial	M/L	5	6.6×10^{-4}
	A	0.2	1.3×10^{-2}
Homeowner	M/L/A	25 **	1.5×10^{-5}

1.0×10^{-3}

5.5×10^{-6}

1.8×10^{-4}

(N) = NOEL/(K) ; The NOEL is 0.5 mg/kg/day
(O) = (M)(Q_1*) where the Q_1* = 2.2×10^{-1} $(mg/kg/day)^{-1}$
** - MARGINS ARE LESS THAN 100 BUT EXPOSURE IS ONLY 1 TO 3 DAYS/YEAR

COPLEY, PC6\ATRAZINE\APL-EXP3.266, Proj 9-2280, #63, 10/16/89

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

26 JUL 1989

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: NON-DIETARY EXPOSURE ASSESSMENT FOR THE APPLICATION OF ATRAZINE USING AN OPEN CAB VERSUS A CLOSED CAB TRACTOR (No HED Project Number)

TO: Jude Andresean
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A. INTRODUCTION

As per SRB's 19 July 1989 oral request, the assessment of atrazine exposure via a ground-boom applicator (Lunchick, EAB# 80077, January 6, 1988) has been expanded to include open cab and closed cab tractors.

B. CONCLUSION

NDEB has assessd applicator exposure to Atrazine for applicators within a closed cab versus on open cab tractor. The exposure estimates assume a 70 kg individual and have not been, adjusted for dermal absorption. NDEB defers to Toxicology Branch 1-IRS the adjustment of the dermal exposure estimates for the dermal absorption of Atrazine. The results of the exposure assessment are as follows:

			Estimated Annual Exposure (mg/kg/yr)
CORN			
	Grower	Open Cab/Open Pour	20
		Closed Cab/Open Pour	5.8
	Commercial	Open Cab/Open Pour	290
		Open Cab/Closed Pour	133
		Closed Cab/Open Pour	165
		Closed Cab/Closed Pour	7.6
SORGHUM			
	Grower	Open Cab/Open Pour	16
		Closed Cab/Open Pour	4.1

A M/L

C. DETAILED CONSIDERATIONS

1.0 ASSESSMENT OF UNIT EXPOSURE

The triazine herbicide, Atrazine, has previously been the subject of an exposure assessment to estimate nondietary risk to mixer-loaders and applicators. In the original assessment (Lunchick, EAB # 80077, January 6, 1988), exposure was assessed for ground-boom applicators using the following studies:

Study	Replicates	Exposure (mg/hr)	Clothing
Abbott	18	40	Long-Sleeved Shirt, Long Pants
Maitlen	21	0.7	Short-Sleeved Shirt, Long Pants
Dubelman	12	0.93	Long-Sleeved Shirt, Long Pants
Wojeck	23	72	Long-Sleeved Shirt, Long Pants
Staiff	20	0.4	Short-Sleeved Shirt, Long Pants
Wolfe	7	9.4	Short-Sleeved Shirt, Long Pants

These data were integrated to produce a weighted geometric mean of 4.6 mg/hr, at an application rate of 1.0 lb ai/acre. From these data, it was estimated that, for corn, a grower doing his/her own application may be exposed to an average of 1.2 mg/kg/yr. If the grower also acts as the mixer-loader, his/her combined exposure would average 6.4 mg/kg/yr. For a commercial applicator treating corn, the applicator's annual exposure would be 11 mg/kg/yr and, if the applicator mixes or loads the pesticide, the annual exposure may be 170 mg/kg/yr for open pour, or 14 mg/kg/yr for closed pour systems.

Data from these studies were also used to estimate exposure from applying Atrazine to sorghum. The annual exposure was calculated to be 0.97 mg/kg/yr with a combined exposure of 4.6 mg/kg/yr.

A large range exists in the data from the original six studies (0.4 mg/hr - 72 mg/hr). This has been attributed to variability in equipment, weather conditions, and the personal habits of the applicator.

In an attempt to further refine NDEB's prior assessment, ground-boom applicator exposure has been reevaluated to distinguish exposure to applicators within an open cab from those within a closed cab. Only a few of the original six studies identify tractor cab type. These are listed below:

OPEN CAB

Study	Replicates	Exposure (mg/hr)	Clothing
Abbott	18	39.9	Long Sleeved Shirt, Long Pants
Wojeck	21	76.7	Long Sleeved Shirt, Long Pants

CLOSED CAB

Study	Replicates	Exposure (mg/hr)	Clothing
Wojeck	2	28.4	Long Sleeved Shirt, Long Pants
Dubelman	6	0.93	Long Sleeved Shirt, Long Pants

In the open cab exposure studies, the total of 39 replicates yields a weighted, geometric mean of 56.7 mg/hr. A geometric mean was calculated because the full data set, used in the original assessment (EAB # 80077) consisted of a broad range of values which in general, have been assumed to follow a log normal distribution. Although a data sub-set (closed cabs) of 2 data points has no true distribution, it is assumed to have the same frequency distribution as the parent data set. Therefore, the geometric rather than the arithmetic mean was calculated. The influence of weather conditions and the personal habits of the applicator can still be observed in the difference between the two studies (39.3 vs. 76.7).

In the closed cab exposure study, the total of 8 replicates yields a weighted geometric mean of 2.2 mg/hr. Again, the range in data (0.93 vs. 28.4) indicates some variability in the factors discussed above.

Other equipment factors such as boom length, shielded booms and tractor size and design will also influence applicator exposure. The surrogate data do not contain sufficient identified replications of these subsets to quantify these effects on exposure.

2.0 ANNUAL NONDIETARY EXPOSURE TO ATRAZINE, CORN

Use information, discussed below, was obtained from a SSB/BUD (now BAB/BEAD) memorandum dated December 11, 1987. Atrazine is applied to corn at 2.0 lb ai/acre. A grower will handle 390 lb ai in treating 195 acres annually. The required spray time is 8.9 hours. The commercial applicator will treat 6000 acres annually, over an 80 hour period. The mixer-loader will handle 12000 lb of Atrazine.

The annual grower exposure, when atrazine is applied to corn is as follows:

Mixer-Loader Open Pour	0.93 mg/lb x 390 lb/yr x 1/70 kg = 5.2 mg/kg/yr
Mixer-Loader Closed	0.015 mg/lb x 390 lb/yr x 1/70 kg = 0.084 mg/kg/yr
Ground-Boom Applicators	
Open cab	56.7 mg/hr x 2 x 8.9 hr/yr x 1/70 kg = 14 mg/kg/yr
Closed cab	2.2 mg/yr x 2 x 8.9 hr/yr x 1/70 kg = 0.56 mg/kg/yr
Combined	
Open pour / Open cab	5.2 mg/kg/yr + 14.4 mg/kg/yr = 20 mg/kg/yr
Open pour / Closed cab	5.2 mg/kg/yr + 0.56 mg/kg/yr = 5.8 mg/kg/yr

If the commercial mixer-loader open pours Atrazine, the annual exposure is estimated to be 160 mg/kg/yr (0.93 mg/lb ai x 12000 lb/yr x 1/70 kg). If the mixer-loader uses a closed loading system, the annual exposure would be reduced to 2.6 mg/kg/yr (0.015 mg/lb ai x 12000 lb/yr x 1/70 kg). The annual commercial applicator exposure is as follows:

Combined

Closed pour / Open Cab 0.084 mg/kg/yr + 14 mg/kg/yr = 14 mg/kg/yr

Ground-Boom applicator

Open cab - 56.7 mg/hr x 2 x 80 hr/yr x 1/70 kg = 130 mg/kg/yr

Closed cab - 2.2 mg/hr x 2 x 80 hr/yr x 1/70 kg = 5.0 mg/kg/yr

Combined exposure

Open cab/open pour - 160 mg/kg/yr + 130 mg/kg/yr = 290 mg/kg/yr

Open cab/closed pour - 2.6 mg/kg/yr + 130 mg/kg/yr = 133 mg/kg/yr

Closed cab/open pour - 5.0 mg/kg/yr + 160 mg/kg/yr = 165 mg/kg/yr

Closed cab/closed pour - 5.0 mg/kg/yr +2.6 mg/kg/yr = 7.6 mg/kg/yr

4.0 GROUND-BOOM APPLICATOR EXPOSURE, SORGHUM

The assessment of the ground-boom application of Atrazine to sorghum has also been further divided into an assessment of open cab versus closed cab exposure. Use information obtained from a BAB/BEAD memorandum dated July 3, 1989, indicated that 135 acres would be the typical annual acreage treated and would require 7.4 hours, spread over two days. Based on the average application rate of 2 lb ai/acre, a mixer-loader would handle 270 lb ai/yr.

Surrogate data was used in the assessment of the application of Atrazine to corn. Using these data, the dermal exposure to mixer-loaders wearing long pants, long-sleeved shirts and chemical resistant goggles, was estimated to be 0.93 mg/lb ai for open pour loading. For the ground boom applicator in an open cab, dermal exposure was estimated to average 56.7 mg/hr at an application rate of 1 lb ai/acre. For the ground boom applicator in a closed cab, dermal exposure was estimated to average 2.2 mg/hr. The applicator is assumed to be wearing long pants and long sleeved shirts. Inhalation exposure is negligible compared to dermal exposure. These data can be applied to sorghum as follows:

Annual dermal exposure during mixing and loading:
0.93 mg/lb ai x 270 lb ai/yr x 1/70 kg = 3.6 mg/kg/yr

The annual exposure to applicator in an open cab:
56.7 mg/hr x 2 x 7.4 hrs/yr x 1/70 kg = 12 mg/kg/yr

The annual exposure to applicator in a closed cab:
2.2 mg/hr x 2 x 7.4 hrs/yr x 1/70 kg = 0.46 mg/kg/yr

Typically, the private farmer will do both the mixing-loading and application of Atrazine to sorghum. The combined annual exposure to an applicator in an open cab would be 16 mg/kg/yr. That for an applicator in a closed cab would be 4.1 mg/kg/yr.

cc: SACB
Circulation
Correspondence File
Atrazine File