



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

JUL 27 1989

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: ID:100-529; Use of Atrazine on Sorghum: Assessment of risk to mixer/loader/applicators for oncogenicity and cardiotoxicity.

TO: Jude Andreasen/Jack Housinger
Special Review and Reregistration Division (H7508C)

FROM: Marion P. Copley, D.V.M., Section Head
Section 2, Toxicology Branch I (IRS)
Health Effects Division (H7509C)

THRU: Edwin Budd, Acting Branch Chief
Toxicology Branch I (IRS)
Health Effects Division (H7509C)

Tox. Chem. No.:63
Proj. No.:none assigned
Record No.: NA

cc: Quest
Caswell file

CONCLUSIONS:

The risk to M/L/A for **cardiotoxicity** is presented in terms of Margin of Safety (MOS) and ranges from 1 to 3 when actual plus potential dermal exposure and penetration are considered (see table 4). MOSs of less than 100 are usually considered to be of toxicologic concern. However, for this use, the concern is diminished since the applicators are only exposed for only 2 days per year.

The risk to M/L/A for **oncogenicity**, ranges from 10^{-5} to 10^{-4} when actual plus potential dermal exposure and penetration are considered (see table 4).

BACKGROUND:

The cardiac and oncogenic risks due to applying Atrazine to sorghum have been analyzed in a similar fashion as was used in the memorandum dated 11/15/88 from Marion Copley to Jude Andreasen/Jack Housinger. The primary change is the incorporation of an oncogenic risk assessment using the Q,* rather than an extra 10 fold safety factor. Exposure values for sorghum were obtained from the attached memorandum dated 7/14/89 from Curt Lunchick to J. Andreasen.

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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 C oncogen however disagreed with the quantitative risk assessment ($Q_{1*} = 2.2 \times 10^{-1}$).

The other endpoint of concern was cardiotoxicity in the dog. 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	(E) Exposure in days	(F) Exposure per day mg/kg/day	(F1) Dose/day/ cm ² skin mg/cm ²
Sorghum							
Ground Boom	M/L	3.6	5.9	7.4	2	2.80	0.07
	A	0.97	5.9	7.4	2	0.78	0.02
	M/L/A	4.6	5.9	7.4	2	3.60	0.08

- (A) - Actual annual exposure for each specific use pattern. (taken from NDEB memo 7/14/89).
 (B) - Length of work day for each specific use pattern.
 (C) - Actual duration of exposure per year for each specific use pattern.
 (D) = (C)/(B) ; Calculated # of days of exposure per year for each specific use pattern.
 (E) = (A)/(D) ; Calculated exposure per work day for each specific use pattern.
 (F) = Actual daily dose assuming a 70 kg person (taken from NDEB memo 7/14/89).
 (F1) = (70)(F)(3000); Daily dose per cm²; assumes a 70 kg person and 3000 cm² 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	18.97	19.51
	A	1.86	20.56	22.42
	M/L/A	0.54	18.97	19.51

- (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)	(M)
		Actual <u>absorbed</u> mg/kg/day	Total potential <u>absorption</u> mg/kg/day	<u>Adjusted for lifetime exposure</u> Actual <u>absorbed</u> mg/kg/day	Total potential <u>absorption</u> mg/kg/day
Sorghum					
Ground boom	M/L	.015	0.55	.0000266	.000962
	A	.015	0.17	.0000247	.000298
	M/L/A	.019	0.70	.0000340	.00123

(J) = (F)(G) ; Actual absorbed compound on a workday.

(K) = (F)(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 ONCOGENIC RISK FOR APPLICATORS**

		(N)	(O)
		Margin of Safety (MOS)	Oncogenic risk
Sorghum			
Ground Boom	M/L	1**	2.1×10^{-4}
	A	3**	6.6×10^{-5}
	M/L/A	1**	2.7×10^{-4}

(N) = $NOEL/(K)$; The NOEL is 0.5 mg/kg/day

(O) = $(M)(Q_*)$ where the $Q_* = 2.2 \times 10^{-4} \text{ (mg/kg/day)}^{-1}$

** - MARGINS ARE LESS THAN 100 BUT EXPOSURE IS ONLY 1 OR 2 DAYS/YEAR



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MEMORANDUM

SUBJECT: EXPOSURE ASSESSMENT FOR THE APPLICATION OF ATRAZINE
TO SORGHUM

TO: J. Andreasen
Special Review Branch
Special Review and Reregistration Division (H7505C)

FROM: Curt Lunchick *Curt Lunchick*
Environmental Chemistry Review Section
Non-Dietary Exposure Branch
Health Effects Division (H7509C)

THRU: *Al Nielsen Jr*
Michael Firestone, Section Head
Environmental Chemistry Review Section
Non-Dietary Exposure Branch
Health Effects Division (H7509C)

THRU: Charles L. Trichilo, PhD., Chief
Non-Dietary Exposure Branch
Health Effects Division (H7509C) *Trichilo*

Please find below the NDEB review of

HED Project #: 9-1762

RD or SRRD Record #: 247831

Caswell #: 63

Date Received: 07/12/89 Review Time: 2 days

Date Returned: 07/14/89

Deferral to: Biological Analysis Branch/BEAD

 X Science Analysis & Coordination Branch

 X TB - Insecticide/Rodenticide Support Section

 TB - Herbicide/Fungicide/Antimicrobial Support
Section

As per your request, the Non-Dietary Exposure Branch has conducted an exposure assessment for the use of atrazine on sorghum. Based on usage information provided by the Biological Analysis Branch/BEAD (Use Data for Exposure Analysis for the Application of Atrazine to Sorghum, Dennis Szuhay, 3 July 1989), atrazine may be applied to sorghum by ground boom application at 1.6 to 3.0 lbs a.i./acre. One application per year may occur to treated acreage. The average boom width is 30 ft and the typical acreage for sorghum is 135 acres per farm. BEAD estimated that 107 acres would be the typical daily acreage treated and would require 5.9 hours. The time required to treat 135 acres would be 7.4 hours and would be spread over two days. Based on the average application rate of 2.0 lbs a.i./acre, a mixer/loader would handle 214 lbs a.i./day and 270 lbs. a.i./yr.

The Non-Dietary Exposure Branch conducted an exposure assessment for ground boom application of atrazine to corn in January 1988 (EAB# 80077). Surrogate data were utilized in that assessment and as described the dermal exposure to mixer/loaders wearing long pants, long sleeved shirts, and chemical resistant gloves was estimated to be 0.93 mg/lb a.i. for open pour loading. Ground boom applicator dermal exposure was estimated to average 4.6 mg/hr at an application rate of 1.0 lbs a.i./acre. The applicator was assumed to be wearing long pants and long sleeved shirts. Inhalation exposure is negligible compared to dermal exposure.

Daily dermal exposure during mixing and loading would be:
 $0.93 \text{ mg/lb a.i.} \times 214 \text{ lb a.i./day} \times 1/70 \text{ kg} = 2.8 \text{ mg/kg/day}$

Annual dermal exposure during mixing and loading would be:
 $0.93 \text{ mg/lb a.i.} \times 270 \text{ lb a.i./yr} \times 1/70 \text{ kg} = 3.6 \text{ mg/kg/yr}$

The average daily exposure during application would be:
 $4.6 \text{ mg/hr} \times 2 \times 5.9 \text{ hrs/day} \times 1/70 \text{ kg} = 0.78 \text{ mg/kg/day}$

The average annual exposure during application would be:
 $4.6 \text{ mg/hr} \times 2 \times 7.4 \text{ hrs/yr} \times 1/70 \text{ kg} = 0.97 \text{ mg/kg/yr}$

Typically the private farmer will do both the mixing/loading and application of atrazine to sorghum. The combined daily and annual exposure to atrazine are estimated to be 3.6 mg/kg/day and 4.6 mg/kg/yr. The exposure estimates assume a 70 kg individual and have not been adjusted for dermal absorption. NDEB defers to Toxicology Branch I the adjustment of the dermal exposure estimates for the dermal absorption of atrazine.

cc: M. Copley/TB I
E. Saito/SACB
Correspondence File
Atrazine File