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

MEMORANDUM

APR 25 1984

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: Alachlor, EPA Reg. No. 524-316. Quantitative Risk Assessment based on Feeding/Oncogenicity Study in Rats, Monsanto R.D. #520, Special Report #MSL-3382, Feb. 27, 1984; Report compiled by Robert W. Street, Volumes 1, 2 and 3. Accession Nos.: 252496, -7 and 8 CASWELL #11

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Volume 3 of Special Report MSL 3382 contains the company (Monsanto) cancer risk assessment (see Section II of subject report) based on the female rat nasal turbinate tumor rates and rat dosage in mg/kg/day reported in volumes 1 and 2 of the subject report. We have ascertained that the company estimates of Extra Risk and the upper 95% Confidence Bound on that MLE estimation are numerically in agreement with our own estimates when we apply Monsanto mg/kg/day estimates of human exposure and rat nasal turbinate tumor rates and dose levels unadjusted for interspecies sensitively. The linearized-multistage model seems to be preferable in this instance because the history of testing this compound has consistently reduced the level at which cancer and nasal tumors in particular have been detected.

If we were to use the female data suggested by the Registrant the cancer risk could be estimated from Q_1^* of 2.01×10^{-2}. When the surface area correction is applied i.e., $(2.01 \times 10^{-2}) \times (5)$, one obtains a Q_1^* estimate of potency of 1×10^{-1} . The EPA utilizes a surface area adjustment to estimate the increased sensitivity expected in humans compared to experimental rodent species.

However, we observe that the female data are quite similar to the findings reported for the male rats (see Table 1 of Section II):

	0 mg/kg/d	0.5	2.5	15.0
males	0/48	0/48	0/45	11/45
females	0/42	0/44	1/47	9/48

When it is clear that both sexes have approximately the same sensitivity to a chemical, EPA uses the total data set to estimate the dose response and risk levels. When all 8 rates are used in the Global 79 Program, the multistage model yields a Q_1^* 1.19×10^{-2} for the unadjusted data and a Q_1^* of 5.95×10^{-2} for the data adjusted by surface area correction to human equivalents.

The best available estimate of Alachlor's potential potency may be expressed by Q_1^* of 5.95×10^{-2}. This estimator may be used to obtain an upper 95% Bound on the expected cancer rates associated with specific human exposures. The examples following are taken from the residues and tolerances shown in the TOX Branch dietary exposure data for Alachlor as obtained from printout dated 4/10/84 and 1/14/83 respectively. Residues tolerances and TMRCs are expressed in mg/day (1.5 kg diet) divided by 60 to obtain mg/kg/day for dietary risks. Worker exposures in mg/day are divided by 70 kg for estimating exposure to workers. The dietary estimates are shown in Table 1 for both the tolerance assumption (worst case) and using Residue Levels where available. In Table 2 the additional increments of risk for agricultural workers are shown for a variety of assumptions using a 100% dermal absorption estimate recommended by EAB. However, TOX Branch has determined that 50% of the alachlor actually penetrates the skin. Since there is only an inconsequential increment associated with inhalation; the Table 2 data should be used dividing all values by 2.

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Table I

Quantitative Assessment of Dietary Risks for Alachlor

Crop for Dietary Exposure	Worst Case Estimate		Best Available Estimate	
	Tolerance Level (mg/kg/d)	Upper 95% Bound on Added Risk	Residue Level or tolerance (mg/kg/d)	Upper 95% Bound on Added Risk
corn (3)	1.255×10^{-4}	7.5×10^{-6}	3.13×10^{-5}	1.9×10^{-6}
soybeans (148)	4.58×10^{-5}	2.7×10^{-6}	2.07×10^{-5}	1.2×10^{-6}
Beans, dry edible (10)	7.83×10^{-6}	4.7×10^{-7}	7.00×10^{-6}	4.2×10^{-7}
beans, Lima (11)	4.83×10^{-6}	2.9×10^{-7}	3.83×10^{-6}	2.3×10^{-7}
Peas (117)	1.73×10^{-5}	1.0×10^{-6}	1.73×10^{-5}	1.0×10^{-6}
Potatoes (127)	1.36×10^{-6}	8.1×10^{-6}	1.09×10^{-4}	6.5×10^{-6}
Cottonseed (oil) (41)	1.83×10^{-6}	1.1×10^{-7}	6.67×10^{-7}	4.0×10^{-8}
Peanuts (115)	4.50×10^{-6}	2.7×10^{-7}	4.5×10^{-6}	2.7×10^{-7}
Sorghum (147)	8.33×10^{-7}	5.0×10^{-8}	8.33×10^{-7}	5.0×10^{-8}
Sunflower (156)	1.83×10^{-6}	1.1×10^{-7}	1.83×10^{-6}	1.1×10^{-7}
Milk & Dairy (93)	1.43×10^{-4}	8.5×10^{-6}	1.43×10^{-4}	8.5×10^{-6}
Meat & Poultry (89)	6.92×10^{-5}	4.1×10^{-6}	6.92×10^{-5}	4.1×10^{-6}
Eggs (54)	1.38×10^{-6}	8.2×10^{-7}	1.38×10^{-6}	8.2×10^{-7}
TMRC	5.72×10^{-4}	3.4×10^{-5}	4.23×10^{-4}	2.5×10^{-5}

Table II

Quantitative Assessment of Risk Increments for Workers

Work Exposure Setting	Canadian Estimate (No protective clothing except for Gloves)		EPA Estimate (Protective Clothing except for Face, neck and Gloves)	
	Exposure in mg/kg/day*	Upper 95% Bound on Added Risk	Exposure in mg/kg/day*	Upper 95% Bound on Added Risk
Ground Open-Tank Fill				
Worst Case = mg/kg/d	.38	2.3×10^{-2}	2.4×10^{-2}	1.4×10^{-3}
Avg Daily lifetime: 1 d	6.1×10^{-4}	3.6×10^{-5}	3.8×10^{-5}	2.3×10^{-6}
" " 5 d	3.0×10^{-3}	1.8×10^{-4}	1.9×10^{-4}	1.1×10^{-5}
" " 6 d	3.6×10^{-3}	2.1×10^{-4}	2.2×10^{-4}	1.3×10^{-5}
" " 30 d	1.8×10^{-2}	1.1×10^{-3}	1.2×10^{-3}	7.1×10^{-5}
Ground Application				
Worst Case	1.8×10^{-2}	1.1×10^{-3}	4.7×10^{-3}	2.8×10^{-4}
Avg Daily lifetime: 1 d	2.9×10^{-5}	1.7×10^{-6}	7.5×10^{-6}	4.5×10^{-7}
" " 5 d	1.4×10^{-4}	8.3×10^{-6}	3.8×10^{-5}	2.3×10^{-6}
" " 6 d	1.8×10^{-4}	1.1×10^{-5}	4.5×10^{-5}	2.7×10^{-6}
" " 30 d	8.6×10^{-4}	5.1×10^{-5}	2.2×10^{-4}	1.3×10^{-5}
Ground Probe Transfer (5 gal)				
Worst Case	2×10^{-2}	1.2×10^{-3}	5.5×10^{-3}	3.3×10^{-4}
Avg Daily lifetime: 1 d	3.2×10^{-5}	1.9×10^{-6}	8.5×10^{-6}	5.1×10^{-7}
" " 5 d	1.6×10^{-4}	9.5×10^{-6}	4.5×10^{-5}	2.7×10^{-6}
" " 6 d	1.9×10^{-4}	1.1×10^{-5}	5.3×10^{-5}	3.2×10^{-6}
" " 30 d	9.6×10^{-4}	5.7×10^{-5}	2.6×10^{-4}	1.5×10^{-5}
(Note: for 55 gal. multiply 5 gal. estimates by 11)				
Aerial: Tank Fill				
Worst Case	18.3	1.1	2.4×10^{-1}	1.4×10^{-2}
Avg Daily lifetime: 5 d	1.4×10^{-1}	8.3×10^{-3}	1.9×10^{-3}	1.1×10^{-4}
" " 10 d	2.9×10^{-1}	1.7×10^{-2}	3.8×10^{-3}	2.3×10^{-4}
Aerial: Pilot				
Worst Case	8.4×10^{-1}	5.0×10^{-2}	5.3×10^{-2}	3.2×10^{-3}
Avg. Daily lifetime: 5 d	6.7×10^{-3}	3.9×10^{-4}	4.2×10^{-4}	2.5×10^{-5}
" " 10 d	1.3×10^{-2}	7.7×10^{-4}	8.5×10^{-4}	5.1×10^{-5}
Aerial: Flagman				
Worst Case	25.2	1.5	2.2	1.3×10^{-1}
Avg Daily lifetime: 5 d	0.2	1.2×10^{-2}	1.8×10^{-2}	1.1×10^{-3}
" " 10 d	0.4	2.4×10^{-2}	3.5×10^{-2}	2.1×10^{-3}

(Vales for Exposure Extracted from Creeger, EAB, memo to Taylor; 4/4/84)

*The EAB exposure estimates are based on the assumption of 100% Dermal Absorption, however, TOX Branch has determined that Dermal Absorption = 50%. Because the inhaled exposure levels are inconsequential this table may be adjusted to the TOX Branch requirements by dividing all values by 2.