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File

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Triphenyltin Hydroxide, Margin of Safety For Maternal Toxicity Utilizing Data on Exposure while Spraying Pecans and Dermal Absorption Data

TO: Betty Shackelford, PM-71RS
Registration Division (TS-767)

FROM: *[Signature]* 3/13/86
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THROUGH: Reto Engler PhD, Head
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Compound; Triphenyltin Hydroxide

Tox Chem #896E

Registration #083601

Registrant; Hoechst

Accession #N/A

Tox Project #none

Action Requested

Determine the margin of safety (MOS), for maternal toxic effects of Triphenyltin, of human exposure during airblast application to pecans.

Conclusions

Assuming that the applicator washes after applying the pesticide the MOS based on quantity absorbed data from the rat dermal absorption study ranges from 400 to 555. Based on data on the quantity remaining on the skin in the rat study and considered as possibly available for absorption, the MOS ranges from 2.5 to 2.6

Assuming that the applicator washes at the end of the work day the MOS based on the quantity absorbed from the rat dermal absorption study is approximately half that given above.

The MOS based on the quantity remaining on the skin and considered potentially absorbable remains essentially the same.

Recomendation

The recommendation of Zendzian 1986, that an additional study be performed to determine the ability of the residue of triphenyltin hydroxide on and/or in the skin to be absorbed, is repeated.

Background

Triphenyltin hydroxide (TPTH) was placed under Special Review on the basis of studies that appeared to show that the compound was teratogenic in rats. Three subsequent studies in rats, by the oral route, showed that the compound was not teratogenic. Two of the reproduction studies of TPTH in rats have shown that the most sensitive toxic effect of TPTH is maternal toxicity with a NOEL of 1.0 mg/kg/day (WIL 1985a & WIL 1985b).

Applicator exposure during airblast application of the compound to pecans is considered by EEB as producing the most applicator exposure (Jaquith 1986). Exposure is essentially all by the dermal route. A dermal absorption study in rats was submitted by the Registrant to quantitate dermal absorption (Zendzian 1986).

Discussion

Jaquith (1986) states that exposure during mixing, loading and airblast application to pecans is essentially all by the dermal route. Exposure for mixing and loading (M/L) is 0.06 mg/kg/day for a total of 4.6 minutes per day. Exposure for application (App) is low (L) 0.70 mg/kg/day and high (H) 0.73 mg/kg/day each for a total of 160 minutes per day. One individual usually mixes, loads and applies. The exposed skin area of the 70 kg applicator is given as 3000 cm².

Dermal absorption data are provided in the rat study by WIL (WIL-39020) which is reviewed in Zendzian 1986. Data used for this analysis are from tables 2 and 8 of the Zendzian review. Table 2, which presents the percent of each dose found in the excreta represents the percent TPTH absorbed, since no compound was found in blood or carcass to the limits of detection. Table 8 shows that a significant percent of each dose remains on the skin and it is concluded in the review that this material may be available for absorption.

The dermal absorption study shows that the percent of TPTH absorbed increases with time and decreases with dose, a common relationship. Therefore it is necessary to select both a dose

and time value for dermal absorption. The dose value is selected by converting the daily human dose to mg/cm² using the following equation.

$$\frac{\text{Dose mg/kg/day} \times 70 \text{ kg}}{3000 \text{ cm}^2} = \text{dose mg/cm}^2$$

The values used for dermal absorption from quantity absorbed are <0.04 % for only mixing and loading and 0.32 % for all other conditions. This assumes that the applicator washes directly after working with the pesticide. If one assumes that the applicator does not wash until the end of the working day each MOS will be halved.

An additional consideration is necessary in this evaluation. The rat dermal absorption study showed that significant quantities, in the order of 50% of the dose applied, remained on and/or in the skin and can be considered available for absorption. For the tabular dose-duration used above, 20 percent of the dose remained on and/or in the skin. Since total recovery was extremely low for this group (40%) the value of 50% of recovered dose is used for calculating potentially absorbable dose. The MOS values calculated for this condition are the same if the applicator washes after working with the pesticide or washes at the end of the day.

Table A provides the step by step calculation of the MOS for each exposure condition based on the assumption that the applicator washes after using the compound.

Table B provides MOS calculations for individuals who mix, load and apply the compound by adding the appropriate quantities absorbed from Table A. The MOSs are recalculated directly from these sums.

References

Teratology study in rats, WIL Laboratories, WIL 39011, April 1, 1985

Teratology study in rats, WIL Laboratories, WIL 39013, June 4, 1985

A Dermal Absorption Study in Rats with ¹⁴C-Triphenyltin Hydroxide, J. Laveglia, WIL Research Laboratories WIL-39020, June 5, 1985, add Ltr WIL Feb. 24, 1986

Memo Zendzian to Shackelford, Triphenyltin Hydroxide Review of Additional Data from Dermal Absorption Study
Mar 3, 1986

Memo Jaquith to Shackelford, re exposure assesment for TPTH
Mar 11, 1986

Table A. Dermal absorption of TPTH and MOS re maternal toxicity. Assuming Separate M/L and Applicator

Type exposure	Dose mg/kg/day	exposure (minutes)	Dose mg/cm ² /day	MOS Calculations based on Quantity Absorbed		MOS Calculations based on Quantity Remaining on Skin		MOS Maternal Toxicity	
				Percent ^c Absorption	Dose Absorbed mg/kg/day	Percent ^d Absorption	Dose Absorbed mg/kg/day		
Mix & Load	0.06 ^a	5(4.6)	2.0 X 10 ⁻⁵	<0.04	<2.4 X 10 ⁻⁵	>41667	49	0.03	33
	0.06 ^b	160	2.0 X 10 ⁻⁵	0.32	2 X 10 ⁻⁴	5000	50	0.03	33
Apply L	0.70	160	23.3 X 10 ⁻⁵	0.32	1.6 X 10 ⁻³	625	50	0.35	2.9
H	0.73	160	24.3 X 10 ⁻⁵	0.32	2.3 X 10 ⁻³	435	50	0.37	2.7

- a. Only mixes and loads
- b. M/L and applies. Value to be used in Table B.
- c. From Table 2 of the DER
- d. From Table 8 of the DER

Table B. Dermal absorption of TPTH and MOS re maternal toxicity. Assuming a single individual is the M/L and the Applicator

Type exposure	Dose mg/kg/day	MOS Calculations based on Quantity Absorbed		MOS Calculations Based on Quantity Remaining on Skin	
		Dose Absorbed mg/kg/day	MOS Maternal Toxicity	Dose Absorbed mg/kg/day	MOS maternal Toxicity
M/L + App L	0.76	18 X 10 ⁻⁴	555	0.38	2.6
App H	0.88	25 X 10 ⁻⁴	400	0.40	2.5