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

SEP 2 1987

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Lindane, MOS's for Selected Use Patterms

TO: Valerie M. Bael
Special Review Branch
Registration Division (TS-767)

FROM: Robert P. Zendzian PhD 9/5/87
Senior Pharmacologist
Toxicology Branch
HED (TS-769)

THROUGH: William Burnam 9/2/87
Deputy Chief
Toxicology Branch

Compound; Lindane — Tox Chem #527

Registration #009001 — Registrant; N/A

Accession #None — Tox Project #7-0965

Action Requested

Determine Margins of Safety (MOS's) for the following use patterns;

1) Forestry, Applicator, Mixer/loader & combined
2) Hardwood logs
3) Warehouses, Applicator (3 different conditions)
4) Moth spray
5) Bedbug spray

Exposures and NOELs for these uses were supplied by C. Monroe of SIS (1987, copy attached) and D. Jaquith (1987, copy attached.

Dermal absorption data is derived from the following study (DER attached);

Dermal absorption of ^{14}C-Lindane in male rats; A.L. Bosch, Hazleton Laboratories America, HLA Study No. 6188-103; Jan 13, 1987; Accession number 400561-07

Conclusion

Under all exposure conditions, except 2) Hardwood logs, the MOS's were less than 100 and mainly less than 1. The data for hardwood logs was incomplete.

Evaluation

Data utilized to determine dermal absorption is found in Table 1 of the DER. Three doses (10, 1 & 0.1 mg/rat) were used in the dermal absorption study. The percent of dose absorbed varied significantly with the dose and it is necessary to choose the dose which is closest to the field exposure in order to determine the proper dermal absorption rate. For this process all doses are converted to mg/cm^2. Since the area treated in the rat study was 4.9 cm^2, the experimental doses were 2.0, 0.2 and 0.02 mg/cm^2 respectively. The area of skin exposed in a field situation is considered, by EAB, to be 3000 cm^2. The highest individual dermal exposure, 0.9 mg/kg for a 70 kg individual, was 63 mg giving a dermal dose of 0.021 mg/cm^2. Therefore, the dermal absorption data from Group 3 (0.1 mg/rat) will be used (Table 1).

Table 1. Mean absorption of Lindane (percent of applied dose). Data from Table 1 of the DER.

Group & Dose (mg/rat)	Duration exposure (hours)	Total Absorbed	In Skin*	Total Absorbed Plus In Skin
3 (0.1)	0.5	0.60	11.39	11.99
	1	3.34	24.46	27.80
	2	4.55	31.61	36.16
	4	10.08	30.68	40.76
	10	18.07	17.55	35.62
	24	27.72	7.15	34.87

*Residue following a soap and water wash.

For the purposes of these calculations it is assumed that the workers do not wash until the end of the working day and the data for 10 hours exposure will be used. In addition it is assumed that the lindane in the washed skin is available for absorption and will be absorbed. Thus 35.6 percent of dermal dose is calculated as absorbed. This latter assumption is based on two data sets. In a previous study with a different compound it was shown that essentially all the material remaining on/in the skin after a soap and water wash was absorbed over a period of up to two weeks following washing. In this study, and the previous study, the total of absorbed and in the skin rapidly reached a maximum and essentially retained it through 24 hours exposure. During this exposure period the percent absorbed increased with time and the percent in the skin decreased proportionately.

Calculated Margins of Safety (MOS's) are shown in Table 2.

Discussion

Under all exposure conditions, except 2) Hardwood logs, the MOS's were less than 100 and mainly less than 1. The data for hardwood logs was incomplete. Two additional factors may be considered as potentially increasing the calculated MOS's, 1) the difference between dosing in the rat dermal absorption study and in the field and 2) the difference in permeability of rat and human skin.

1) In the rat study the total dose was applied at the start of the exposure period while in the field the dose would be 'applied' in small portions throughout the working day. The mathmatics of this latter process have been analyzed by Lacayo, who determined that this integration could be approximated by dividing the quantity calculated as absorbed by a factor of two. It is not certain that this correction factor can be applied to a compound of which a large percentage remains bound to the skin after washing.

2) The rat skin is considered to be five times more permeable then the human skin.

Combining these factors one can increase the MOS's by a factor of ten. This correction is meaningful only if one were to use the NOEL of 0.3 mg/kg rather than the NOEL of 0.01 mg/kg.

Attachments

Memo Monroe, Lindane Exposures for Calculating MOSs as a Followup to SRB's Request, Aug 26, 1987

Memo Jaquith, Exposure Assesment for Lindane Use on Bedbugs and for Control of Clothes Moths, Aug 28, 1987.

DER Zendzian, re Dermal Absorption of ^{14}C-Lindane in male rats. 7/27/87

cc Monroe SIS

Table 2. Dermal Absorption of lindane for selected exposures.

Use	Exposure (mg/kg/day)[f]		Absorbed Dermally(mg/kg) (10 hr=35.6%[h])	Total dose[g] (mg/kg/day)	Margin of Safety (MOS)	
	Dermal	Inhalation			NOEL 0.01 mg/kg	NOEL 0.3 mg/kg
1) Forestry						
Applicator	0.1	1.8×10^{-3}	0.04	0.042	0.25	7.14
mixer/loader	0.15	Negligible	0.05	0.05	0.20	6.00
	-0.9[e]		0.32	0.32	0.03	0.94
combined	0.25	1.8×10^{-3}	0.09	0.092	0.11	3.26
2) Hardwood logs	no data	1.8×10^{-3}	----	>1.8×10^{-3}	<5.56	<166.67
3) Warehouses[a]						
applicator[b]	0.17	7×10^{-4}	0.06	0.0607	0.16	4.48
applicator[c]	0.034	7×10^{-4}	0.01	0.0107	0.93	28.04
applicator[d]	0.034	7×10^{-5}	0.01	0.01007	0.93	28.04
4) Moth spray[h]	0.078	8.2×10^{-4}	0.03	0.03082	0.32	7.85
5) Bedbug spray[h]	0.016	1.7×10^{-4}	0.006	0.00617	1.62	48.62

a) Uninhabited buildings & empty storage Bins.
b) Based on current label without protective clothing.
c) Based on additional protective clothing, no respirator.
d) Based on additional protective clothing, respirator.
e) Range refers to a mixer/loader servicing one to six applicators.
f) Using protective clothing required by current labels.
g) Inhalation dose assumed 100% absorbed.
h) Total of percent absorbed at 10 hours plus percent of dose remaining in skin after soap and water wash.
i) Mg/kg/treatment. Number of applications per day not stated.

Note: [illegible] Exposures [illegible]
Followup to SRB's Request

From: Carol L. Moore
SIS/HED

AUG 26 1997

To: Bob Zendzian
Tox/HED

The following are the exposures to use to calculate MOEs per SRB's request. They are not take into account dermal absorption. I got them from the Reg. Std. Tox will have to decide which NOEL to use: either the one from the 90 day feeding study of 0.3 mg/kg/day or the one from the German 90 day inhalation study of 0.01 mg/kg/day. Also, please indicate which dermal absorption rate is used.

Use	Exposure in mg/kg/day using protective clothing required by current labels: Dermal	Respiratory
① Forestry		
applicator	0.10	1.8x10-3
mixer/loader	0.15 - 0.9 [1]	Negligible
combined	0.25	1.8 x 10-3
② Hardwood logs	no data	1.8 x10-3
③ Warehouses (Uninhabited buildings + empty storage bins)		
applicator [2]	0.17	7x10-4
applicator [3]	3.4x10-2	7x10-4
applicator [4]	3.4 x10-2	7x10-5
④ Moths Spray	EAB to provide	EAB to provide
⑤ Bedbug Spray	EAB to provide	EAB to provide

1/ Range refers to mixer/loader servicing one to six applicators
2/ Based on current label without any protective clothing requirements
3/ Based on additional protective clothing, no respirator.
4/ Based on additional protective clothing plus respirator.