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

OCT 7 1985

004709

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: EPA Reg. No. 8340-15. Dermal penetration study with triphenyltin hydroxide - request for additional data.

TOX CHEM No. 896E

FROM: J.D. Doherty 10/7/85
Toxicology Branch
HED (TS-769)

TO: H.A. Jacoby 10/7/85
Product Manager #21
RD (TS-767)

The American Hoechst Co. has submitted a dermal penetration study (Wil Research Laboratories, Wil-39020, June 5, 1985) with the fungicide triphenyltin hydroxide as part of the Toxicology Branch (TB) data requirements to support registrations of this chemical. This study was referred to Dr. Robert Zendzian of TB for review. A copy of Dr. Zendzian's review is attached.

According to Dr. Zendzian this study is incommplete and additional information is required to complete the review and to determine the degree of absorption of triphenyltin hydroxide. Dr. Zendzian's conclusion is as follows:

"Dermal absorption of triphenyltin hydroxide appears to be very small under the experimental conditions, ranging from <0.01 to 0.82 percent of applied dose depending upon dose and duration of exposure. However additional information is needed for more accurate quantitation.

It is recommended that;

1. Data from the full analysis of wrap and skin be obtained in order to better quantitate the 'missing' material.

2. The remaining carcasses be analyzed, starting with the 10 hour exposures, in order to complete quantitation of the absorbed material."

The registrant should be advised of this request for additional information as soon as possible. The hard cover copy of the study will be retained in TB until receipt and review of the inforamtion as requested above.

Data Evaluation Report

004709

Compound Triphenyltin Hydroxide

Citation
A Dermal Absorption Study in Rats with ^{14}C-Triphenyltin Hydroxide, J. Laveglia, Will Research Laboratories, WIL-39020, June 5, 1985

Reviewed by Robert P. Zendzian PhD 10/7/88
Pharmacologist

Core Classification Supplimentary, Incomplete Study

Conclusion
Dermal absorption of triphenyltin hydroxide appears to be very small under the experimental conditions, ranging from <0.01 to 0.82 percent of applied dose depending upon dose and duration of exposure. However, additional information is needed for more accurate quantitation.

Materials

^{14}C-labeled tiphenyltin hydroxide, from Hoerst Aktiengesellschaft
Batch 11009 I, Specific activity 32.4 mCi/gram radiopurity 98%
Batch 11009 II, Specific activity 3.88 mCi/gram radio purity 98%

Sexually mature Sprague Dawley COBS® CD® male rats (Crl:CD(SD)BR), charles River Breeding Laboratories

Methods

Twenty rats per group were assigned to the following test groups.

Group Number	Dose mg/kg	Batch used	Amount of test material to be Administered to each rat uCi	ug
I	0.1	11009 I	1	25
II	1.0	11009 I	10	250
III	10.0	11009 II	10	2500

On the day prior to dosing the back of each rat was clipped and 30 minutes prior to dosing the clipped area was washed with acetone. A 2" by 2" application zone was marked with felt tipped pen. Dose was applied as a suspension and the application site was wrapped with a non-occlusive cover. Animals were placed in individual metabolism cages and urine and feces collected. Four animals per dose group were sacrificed at 0.5, 1, 2, 4 and 10 hours after dose application. The

wrap, blood sample and skin and muscle at the application site were collected for ^{14}C-analysis. The skin was extracted with ethanol for analysis. The remaining carcass was retained for possible analysis.

Results

Table 1, Mean actual dose applied. From tables 3, 4, 5, 6, 7, & 8 of the report.

Duration of exposure(hr)		0.5	1.0	2.0	4.0	10.0
Group #						
I	uCi	0.614	0.553	0.720	0.523	0.863
	mg/kg	0.09	0.07	0.10	0.07	0.11
II	uCi	7.045	7.150	7.281	7.820	8.295
	mg/kg	0.90	0.91	0.95	1.01	1.05
III	uCi	12.384	11.538	12.237	11.975	12.534
	mg/kg	13.02	11.99	12.72	12.37	14.01

Table 2. Mean percent of applied dose in excreta. From tables 9, 10 & 11 of the report.

Duration of exposure(hr)	0.5	1.0	2.0	4.0	10.0
Group #					
I	<0.04	<0.07	0.32	0.24	0.82
II	<0.01	<0.01	0.13	0.08	0.27
III	<0.01	<0.01	<0.01	0.01	0.20

Table 3. Mean percent of applied dose recovered from the skin after extracton with ethanol. From Table 21 of the report.

Duration of exposure(hr)	0.5	1.0	2.0	4.0	10.0
Group #					
I	ND	ND	ND	ND	16.1
II	ND	ND	ND	ND	20.5
III	ND	ND	ND	ND	26.0

ND = not determined

Table 4, Mean concentraion of material in the blood and in muscle under the application site. From tables 13, 14 & 15 of the report.

Duration of exposure(hr)	0.5	1.0	2.0	4.0	10.0
Group #	equivilants of test material (ppb)				
I blood	<1.2*	<1.2	<1.2	<1.2	<1.2
muscle	<1.2	<1.2	<1.2	<1.2	<1.2
II blood	<1.2	<1.2	1.4	<1.2	<1.2
muscle	3.0	2.8	1.5	<1.2	7.6
III blood	<10*	<10	<10	<10	<10
muscle	67	39	36	88	14

*limit of detection

Table 5. Mean percent of applied dose recovered from application site by ethanol extraction and from the wrap. From Tables 18, 19 & 20 of the report.

Duration of exposure(hr)	0.5	1.0	2.0	4.0	10.0
Group #					
I	62	71	24	116	33
II	44	76	67	81	70
III	55	53	54	51	55

Discussion

The data in Table 2, mean percent of applied dose in excreta, show that absorption of the compound follows the most common pattern observed in this type of study. Percent absorbed increases with time of exposure and decreases with increasing dose. The percent absorbed is small by this measure and the quantities found in the blood and muscle below the application site support this conclusion. The highest concentration of compound found, in the muscle, represents approximately 0.05% of the particular applied dose.

Confounding the conclusion that the precent absorbed is small is the relatively low recovery of compound from the application site. Under the protocol used in this study the absorption can be quantitated in two ways, 1) determining the amount of compound found in the animal and excreta and 2) determining the amount 'lost' from the application site.

The latter determination is relatively insensitive at low absorption rates because of the problems of obtaining quantitative recovery from the application site. In this study a large portion of each total dose is missing. Table 6 shows the apparent absorption obtained by this approach for the ten hour exposures. These values are considerably larger than those obtained from the direct absorption data and the report indicates that some of this material may be bound to the wrap. Since the carcasses were not analyzed the possibility also exists that a 'significant' portion of the missing material was absorbed and is present in the carcasses. On the other hand of the analysis shows little or no compound one may conclude that dermal absorption of small even without finding the 'missing' material from the application site.

Table 6. Mean percent of applied dose absorbed at 10 hours by subtraction from dose applied of total dose recovered from application site and wrap and recovered from the skin after extraction with ethanol.

Group #	application site and wrap	skin after extraction	total	percent absorbed
I	33	16.1	49.1	50.9
II	70	20.5	90.5	9.5
III	55	26.0	81.0	19.0

Recommendations

It is recommended that;

1. Data from the full analysis of wrap and skin be obtained in order to better quantitate the 'missing' material.

2. The remaining carcasses be analyzed, starting with the 10 hour exposures, in order to complete quantitation of the absorbed material.

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Attachments
DERs