EB-#47
TAB-8145

Memorandum

003145

Date: 15 August 1983

Subject: EPA Reg. No. 279-1830 THIODAN 50 WP
Caswell #420
In 6-15-83; record no. 99296

From: B. T. Backus
IRB/TSS

To: Mr. George LaRocca
Product Manager 15

Registrant: FMC Corp.
Agricultural Chemical Group
2000 Market St.
Philadelphia, PA 19103

Active Ingredient:
Endosulfan (Hexachlorohexahydromethano-2,4,3-benzodioxathiepin oxide).....50%
Inert Ingredients:.....50%

Background:

Acute oral LD_{50}, acute dermal LD_{50}, acute inhalation LC_{50}, primary eye and dermal irritation studies have been received for this formulation with proposed labeling incorporating appropriate revisions. This material has been sent in for reregistration purposes.

Comments and Recommendations:

1. The acute oral LD_{50}, dermal LD_{50}, primary eye and dermal irritation studies are acceptable. This formulation is in toxicity category I on the basis of potential oral hazard.

2. In the inhalation LC_{50} study, there is a considerable difference between analytically (0.08 mg/L) and gravimetrically (1.26 mg/L) determined concentrations in the one exposure for which both values are given. There is also a relatively poor fit of mortality to gravimetrically determined concentration values in this study. According to page 7 of the report analytical sampling was discontinued after the exposure for which the two concentration values are given. However, there were two exposures (02-18-83 and 02-24-83) prior to this for which gravimetric concentrations (6.06 and 2.02 mg/L respectively) are reported with no analytical values. Were analytical concentrations determined for these two runs, and if so, how do they compare with gravimetric values? The deaths of 5/5 females at 0.08 mg/L suggest near-toxicity category I hazard, as does the run in which a gravimetrically-determined concentration of 0.05 mg/L resulted in 2/6 exposed females rats dying. Given the data, as presented, there is uncertainty as to whether this formulation is in toxicity category I or II with respect to inhalation hazard.

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Labeling:

Since there is some question as to whether this formulation is in toxicity category I or II with respect to inhalation hazard, comments regarding the proposed precautionary and first aid labeling will be deferred at this time.

Review:

The following studies were conducted by the FMC Corp. Chemical Research & Development Center, Box 8, Princeton, NJ 08540. Studies were received 6-1-83 and are in Acc. 250424.

1. Acute oral LD_{50} - rat. FMC reference A82-793; dated 3-14-83.

Procedure: Groups of 10F SD rats received orally dosage levels of 25, 32.9, 43.3 or 75 mg/kg. Groups of 10 or 20M rats received dosage levels of 250, 387 or 600 mg/kg. There was subsequent 14-day observation, necropsies of mortalities and necropsies of survivors following sacrifice at 14 days.

Results:

Mortalities (female):

Dosage Level (mg/kg)	Deaths/Animals Dosed
25	1/10
32.9	0/10
43.3	7/10
75	9/10

Mortalities (male):

Dosage Level (mg/kg)	Deaths/Animals Dosed
250	3/10
387	9/20
600	8/10

Oral LD_{50}(F) = 41.2 (32.6-49.9) mg/kg
Oral LD_{50}(M) = 376 (267-485) mg/kg

Symptoms: Clonic convulsions, tremors, ataxia, decreased locomotion, chromorhinorrhea and oral discharge. Recovery complete in survivors by day 4. Some animals which died had blood in their intestines. Post-sacrifice necropsies of survivors were unremarkable.

Study Classification: Core Guidelines Data

Product Classification: Tox. Cat. I (on basis of oral LD_{50} in females)

2. Acute Dermal LD_{50} - rabbit. FMC reference A82-794; dated 3-14-83.

Procedure: 5M, 5F NZ white rabbits received 24-hr occluded dermal exposure to a dosage level of 2000 mg/kg. Material was moistened with physiological saline solution. Subjects were observed for 14 days following exposure.

Results: No mortalities. Diarrhea, lacrimation and nasal discharge noted in some subjects throughout observation period. Desquamation noted in 9/10 on day 14. Dermal LD_{50} > 2000 mg/kg. Post-sacrifice necropsies were unremarkable.

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Study Classification: Core Minimum Data

Product Classification: Tox. Cat. III

3. Primary Eye Irritation - rabbit. FMC reference A82-796; dated 2-16-83.

Procedure: 0.1 g was applied to one eye of each of 9 rabbits. Three eyes were flushed with water starting 20-30 seconds after instillation. The remaining 6 eyes were unwashed.

Results: No corneal involvement. 5/6 unwashed eyes, 0/3 washed eyes showed some conjunctival irritation at 24 hours. All eyes scored zero by day 4.

Study Classification: Core Guidelines Data

Product Classification: Tox. Cat. III

4. Primary Dermal Irritation - Rabbit. FMC reference A82-795; dated 2-9-83.

Procedure: 0.5 g test material moistened with physiological saline solution was applied to each of 2 sites, one intact, one abraded, on each of 6 rabbits with 4-hr occluded exposure.

Results: All sites scored zero at 4-1/2, 24, 48 and 72 hrs. PDIS = 0.

Study Classification: Core Minimum Data

Product Classification: Tox. Cat. IV

The following study was conducted by Stillmeadow, Inc. Biological Testing Laboratory, 9525 Town Park Drive, Houston, TX 77036.

5. Acute Inhalation LC_{50} - rat. Project No. 2879-83; dated March 28, 1983.

Procedure: Groups of from 5-8M were exposed to gravimetrically determined concentration levels of 0.20, 0.37, 0.58, 0.84, 0.93, 0.96, 1.06, 1.16, 1.26, 1.66 and 6.06 mg/L. Groups of 5-8F were exposed to gravimetrically determined concentrations of 0.05, 0.20, 0.38, 0.48, 0.59, 0.66, 0.74, 0.75, 1.06, 1.26, and 2.02 mg/L. Exposures were for 4 hours, with particle sizes usually measured twice during this exposure period. The analytically determined concentration of the exposure which was gravimetrically found to be 1.26 mg/L was only 0.08 mg/L. There was an additional exposure in which the analytical concentration was found to be 0.44 mg/L, but no gravimetric concentration could be determined.

Results: Run Sequence	Date	Nominal Conc. (mg/L)	Grav. Conc. (mg/L)	Anal. Conc. (mg/L)	Mass Med. Aer. Dia. (um)	Geom. S.D.	Mortalities/Exposed M	F
15	03-11-83	0.018	0.05	-	12.196 8.565	3.911 3.911	-	2/6
5	02-28-83	0.475	0.20	-	8.050	5.229	0/5	0/5
13	03-10-83	0.694	0.37	-	2.345 6.842	4.722 2.355	1/5	-
14	03-11-83	0.549	0.38	-	4.783 4.143	1.783 2.767	-	3/6
16	03-12-83	2.39	0.48	-	9.561 10.207	2.139 3.210	-	6/6
19	03-14-83	1.66	0.58	-	4.572 4.580	2.295 1.985	3/7	-
11	03-09-83	0.955	0.59	-	5.433 5.660	3.518 3.454	-	4/6
20	03-15-83	0.405	0.66	-	4.506 5.749	1.971 2.071	-	6/6
10	03-09-83	1.28	0.74	-	5.561 6.443	4.018 2.506	-	5/6
8	03-04-83	1.98	0.75	-	5.394 5.298	1.825 1.878	-	8/8
12	03-10-83	3.13	0.84	-	6.217 11.171	2.177 2.557	3/5	-
9	03-08-83	2.22	0.93	-	7.369 5.769	2.356 2.269	2/7	-
17	03-13-83	2.58	0.96	-	4.537 4.668	2.692 2.894	3/7	-
6	03-02-83	3.19	1.06	-	5.341 4.791	3.244 2.847	0/6	0/6
7	03-03-83	10.3	1.16	-	10.581 6.848	3.429 2.318	8/8	-
4	02-26-83	4.04	1.26	0.08	4.519 4.053	2.650 3.873	0/5	5/5
18	03-14-83	0.812	1.66	-	3.907 5.067	2.064 3.207	1/7	-
3	02-24-83	14.4	2.02	-	8.537 6.133	2.990 2.534	-	5/5
2	02-18-83	33.8	6.06	-	10.039 5.361	2.777 2.609	5/5	-
1	02-16-83	6.28	-	0.44	4.185 3.784	1.489 2.511	2/5	5/5

By throwing out some of the exposure levels an LC_{50} (M) of 0.693(0.510-0.942) mg/L and an LC_{50} (F) of 0.231 (0.120-0.445) mg/L were obtained. By using most of above figures an LC_{50} (M) of 1.48 (0.675-3.24) mg/L and an LC_{50} (F) of 0.212 (0.0743-C.602) mg/L.

Symptoms: Included piloerection, epistaxis, salivation, dilated pupils, body tremors. Many of animals which died had mucoid material in intestine, mottled lungs.

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Study Classification: Core Supplementary Data

Product Classification: (possibility of toxicity category I)

Byron T Backus 08/15/:3

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