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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

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DATE: August 22, 1978

SUBJECT: Vitavax-200 [Active Ingredients: Carboxin (5,6-dihydro-2-methyl -1,4-oxathiin -3- carboxanilide) and Thiram (tetramethylthiuram disulfide)]- Amendment (Label Revision) EPA Reg. No. 400-112 Caswell No. 165A,856 Shaughnessy No. 090201

FROM: Toxicology Branch
Hazard Evaluation Division

TO: Eugene Wilson
Product Manager #21

Recommendations

Acute dermal LD_{50}, acute oral LD_{50}, acute inhalation LC_{50}, eye irritation, and skin irritation studies are adequate. Although the results of the 2 acute dermal LD_{50} studies reviewed herein are somewhat inconsistent, the relative acute dermal toxicity of the formulation is considered to be sufficiently defined. Replacement of DANGER with CAUTION as the label signal word is acceptable. The label proposed by the registrant is adequate; however, the following change in the First Aid statements is required:

First Aid:
In case of contact, immediately flush eyes or skin with plenty of water for at least 15 minutes.

* No FIFRA criteria have been exceeded.

Review

A. Acute Dermal LD_{50} Study of Vitavax-200 in Rabbits (Cannon Laboratories, Inc., Lab. No. 7E-8114, 11/1/77, submitted by Uniroyal Chemical, 6/29/78).

1. Procedure

Four New Zealand albino rabbits (2 males and 2 females), 2.3-3.0 kg, received dermal applications of 2.0 g/kg of test material under occlusive dressing. Test sites of ½ of the animals were abraded. Dressing and residual test material were removed at 24 hours after treatment. Observtions of toxic signs, mortality, and body weight changes were made during 14 days post-application.

2. Results

a). Mortality: None LD 50 > 20 g/kg

b). Toxic Signs: Decreased locomotor activity, erythema and edema at test sites.

c). Body Weight Changes: Gain of 0.1-0.2 kg.

175

EPA FORM 1320-6 (REV. 3-76)

3. Conclusions

a). Classification: Core Minimum Data

(i). Although only 2 animals/sex were used, the results, i.e., no deaths, adequately show the relative toxicity of the test material.

(ii). Body weights in conjunction with food intake were not determined daily.

(iii). Necropsies were not performed

b). TOX. Cat. IV

B. Acute Inhalation LC_{50} Study of Vitavax-200 in Rats (Food and Drug Research Laboratories, Inc., Lab. No. 5480 b, 9/15/77, submitted by Uniroyal Chemical, 6/29/78).

1. Procedure

Ten (5 males and 5 females) albino rats (Blu: Sprague-Dawley), 200-300 g, were placed into a 75 L inhalation chamber and were exposed to a mist of 20 mg of test material/L of air for 1 hour. Animals were observed for mortality and toxic signs during 14 days following exposure.

2. Results

a). Mortality: None LC 50 > 20 mg/L (1 hour)

b). Toxic Signs: Decreased activity

3. Conclusions

a). Classification: Core Minimum Data

i). Body weight data were not submitted
ii). Necropsies were not done

b). TOX. Cat.: IV

C. Acute Oral LD 50 Study of Vitavax-200 in Rats (Pharmaleon Laboratories, 5/30/73, submitted by Uniroyal Chemical, 6/29/78).

1. Procedure

Seventy Long Evans rats, 150-250 g, were divided into 7 groups of 10 animals each (5 males and 5 females) which were administered 3, 4, 5, 6,7, 9 or 10 g/kg of test material orally. Observations of mortality and toxic signs were conducted over 14 days post-treatment. Necropsies were done.

2. Results

a). Mortality: LD 50 =6.25 (4.88-8.00) g/kg

b). Toxic Signs: Decreased body tone, prostration, chromaturia

c). Necropsy: Test compound present in the stomach, irritation and hemorrhage of the gastrointestinal tract.

3. Conclusions

a). Classification: Core Minimum Data

i). Body weight data were not reported in conjunction with food intake daily.

b). TOX. Cat.: IV

D. Eye Irritation Study of Vitavax-200 in Rabbits (Food and Drug Research Laboratories, Inc., Lab. No. 5241c, 11/18/76, submitted by Uniroyal Chemical 6/29/78).

1. Procedure

Six young adult albino rabbits were used. The study was conducted according to the method described in 16 CFR 1500.42. Injuries were scored according to Draize et al. (1944) at 24, 48 and 72 hours and 7 days following treatment.

2. Results

Eye Injuries: Conjunctivitis was observed throughout 72 hours post-treatment. No corneal opacities were evident.

3. Conclusions

a). Classification: Core Minimum Data

i). Although the procedure is referenced and, therefore, is not fully described, the results adequately define the eye irritation potential of the test material.

ii). The effect of washing eyes after treatment was not done

b). TOX. Cat.: III

E. Skin Irritation Study of Vitavax-200 in Rabbits (Food and Drug Research Laboratories, Inc., Lab. No. 5241c, 11/30/76, submitted by Uniroyal Chemical 6/29/78).

000753

1. Procedure

Six adult albino rabbits, sex and weights not stated, were used. Onto both intact and abraded test sites was applied 0.5 mg of test material under occlusive dressing. Dressing was removed at 24 hours after application. Irritation was scored according to Draize et al. (1944) at 24 and 72 hours post-treatment.

2. Results

P.I. Index = 1.96/8.0

3. Conclusions

a). Classification: Core Guidelines

b). TOX. Cat. III (Erring on the side of safety).

F. Acute Dermal LD 50 Study in Rabbits (Food and Drug Research Laboratories, Inc., Lab. No. 5522, 7/26/77, submitted by Uniroyal Chemical, 6/29/78).

1. Procedure

Ten rabbits, sex and weights unspecified, received dermal applications of 20 g/kg of test material according to the method described in 16 CFR 1500.40. Observation for mortality and toxic signs were made during 14 days after treatment. Necropsies were done.

2. Results

a). Mortality: Five deaths. LD 50 = 20 g/kg

b). Toxic Signs: Decreased activity, anorexia

c). Necropsy: Dark, mottled liver, vascularized gastrointestinal tract.

3. Conclusions

a). Classification: Core Minimum Data

i). The procedure was referenced and, hence, was not completely described, However, enough information is provided to allow an adequate evaluation of the acute dermal toxicity of the test compound, considering the high dosage level used and the results of a similar study discussed in part A of this review.

ii). Body weights in conjunction with food intake were not reported.

iii). The sex of the animals was not stated.

iv). Use of abraded test sites was not reported.

b). TOX. Cat. : III

6. Final Conclusions

Use of the signal word CAUTION proposed by the registrant is supported by the following hazard indicators:

Hazard Indicator	TOX. Cat.
Acute Dermal LD 50	IV
Acute Inhalation LC 50	IV
Acute oral LD 50	IV
Eye irritation	III
Skin irritation	III
Acute dermal LD 50	III

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5