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

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AUG -3 1988

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Amdro® - Amdro PCO Roach Control Gel Insecticide - EPA File Symbol 241-GRG - Application for Registration of Maxforce® 2% Gel

Caswell No.: 642AB
Project No.: 8-0921
Record No.: 224436
Accession Nos.: 406582-04, -05

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William Dykstra 7/20/88

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THRU: Edwin R. Budd, Section Head
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8/2/88
8/3/88

Requested Action

Review toxicity data in support of registration and conduct risk assessment for pest control operators (PCOs) who use the product.

Conclusions and Recommendations

1. The submitted acute oral, dermal, eye, and skin toxicity data are acceptable as Core-Guideline. The dermal sensitization study in male guinea pigs is acceptable as Core-Minimum. Female guinea pigs should also be tested for dermal sensitization. The toxicity data support the registration.

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2. Amdro® has been classified as a $B_2$ carcinogen. The $Q_1^*$ is 1.1 $(mg/kg/day)^{-1}$. Additional toxicity data have been requested by TB to address the oncogenic classification of Amdro. EAB has provided an exposure estimate for PCOs who use Maxforce 2% Gel (memorandum of July 13, 1988, attached). Based on this estimation, the calculated oncogenic risk is $6.6 \times 10^{-1}$.

3. The label signal word and precautionary labeling are correct and are supported by the data for Maxforce 2% Gel.

Review

1. Acute Toxicity of Maxforce® 2% Gel; Guidelines Reference Nos. 81-1, 81-2, 81-4, and 81-5; Author: J.E. Fischer; Study Date: May 8, 1985; Performing Laboratory: American Cyanamid Company, Agricultural Research Division, P.O. Box 400, Princeton, NJ 08640; Report No. 1785-43.

   a. Rat Oral $LD_{50}$ (American Cyanamid Report No. A85-43; May 8, 1985).

      Material Tested: AC5028-31; Maxforce 2% Gel.

      Randomized groups of 5M and 5F CHRCD albino rats, 7 to 8 weeks of age and weighing between 164 to 176 g (M) and 155 to 162 g (F), were used in the study. Animals fasted for 18 hours were dosed by oral gavage with a 20% w/v aqueous dispersion of the product at a rate of 25 mL of dispersion/kg of body weight. The rats were dosed at 5000 mg/kg. All animals were observed twice daily for overt signs of toxicity during the 14-day test period.

      Results: No deaths. $LD_{50}$ > 5000 mg/kg (both sexes).

      Toxic Signs: None were observed.

      Body Weight: All animals gained weight.

      Necropsy: No compound-related lesions.

      Conclusion: Toxicity Category IV

      Classification: Core-Guideline

b. Acute Dermal $LD_{50}$ in Rabbits (American Cyanamid Report No. A85-43; May 8, 1985).

Test Material: AC5028-31; Maxforce 2% Gel.

Randomized groups of 5M and 5F NZW rabbits, 12 to 14 weeks old and weighing 2.48 to 2.99 kg, were used in the study. The rabbits were shaved 24 hours prior to exposure over 10 percent of body surface. A dose of 2000 mg/kg of test material was applied under occlusion to each animal for 24 hours. After the 24-hour exposure period, the animals were observed twice daily for 14 days for toxic signs.

Results: No deaths. $LD_{50}$ > 2000 mg/kg (both sexes).

Toxic Signs: None observed.

Body Weight: All rabbits gained weight.

Necropsy: No compound-related lesions.

Conclusion: Toxicity Category III

Classification: Core-Guideline

c. Primary Skin Irritation Study in Rabbits (American Cyanamid Report No. A85-43; May 8, 1985).

Test Material: AC5028-31; Maxforce 2% Gel.

One group of five NZW rabbits (males) were used in the study. The rabbits were shaved 24 hours prior to testing. For each test site, an amount of 0.5 g of test material was applied to an intact site and an abraded site on opposite sides of the dorsal midline of the same animal. The test material was left in contact for 24 hours under occlusion. The sites were scored at the end of the 24-hour contact period, at 72 hours postdosing, and at 144 hours postdosing.

Results: The P.I.S. = 0.043/4. One rabbit (#2630 M) had a score of 1 for erythema at 72 hours. There was no edema. All other skin sites had a zero score at 24, 72, and 144 hours.

Conclusion: Toxicity Category IV; nonirritating

Classification: Core-Guideline

d. Primary Eye Irritation in Rabbits (American Cyanamid Report No. A85-43; May 8, 1985).

Test Material: AC5028-31; Maxforce 2% Gel.

One group of six NZW rabbits (5M and 1F) were used in the study. One-tenth milliliter (0.1 mL) of test material was instilled into the conjunctival sac of the right eye of each rabbit. The left eye served as a control. The lids were held together for 5 seconds. At the end of 24 hours, the treated eyes were rinsed with tap water and examined for irritation with the aid of ultraviolet light and fluorescein. The eyes were examined at postdosing, and 1 and 24 hours according to Draize.

Results: No irritation. The cornea, iris, and conjunctivae of each rabbit did not display any irritation. The scores were zero.

Conclusion: Toxicity Category IV

Classification: Core-Guideline

e. Dermal Sensitization Study with Maxforce® Gel (Lot No. AC5560-75) in Guinea Pigs (Biosearch, Incorporated Project No. 87-596212; February 3, 1988).

Test Material: Maxforce 2% Gel; Lot No. AC5560-75.

Positive Control: 1-chloro-2,4-dinitrobenzene

Thirty male Hartley guinea pigs were used in the study. They were tested as shown below by the Buehler method.

| Group | Number of Animals |
|---|---|
| Test | 10 |
| Naive Control | 10 |
| Positive Control | 10 |

Test Group: Each guinea pig in the test group received a 0.4 g portion of test material (Maxforce 2% Gel) on the clipped intact skin under a patch occlusion for 6 hours. After a 6-hour contact period, the patch was removed and the site was

examined for irritation at 24 and 48 hours according to Draize. This sequence was repeated three times weekly until a total of nine (9) applications were made to the same test site. After the ninth application, the animals were rested for a 2-week period before being challenged. The challenge application was applied to a clipped area on the right flank for a contact period of 6 hours. The site was examined for dermal irritation at 24 and 48 hours.

Positive Control Group: A group of 10 male guinea pigs was used as the positive control. The positive control material, 1-chloro-2,4-dinitrobenzene, was freshly prepared for each of the 10 applications as a 0.1% w/v suspension in a 50% ethanol:0.9% saline solution. These animals were tested employing the same procedure as in the test group.

Naive Control Group: A group of 10 male guinea pigs was maintained in the same manner as the above two groups; however, they remained untreated during the induction phase. These animals were treated with the test material (Maxforce 2% Gel), at the same time the test animals were challenged.

All animals in each group were observed daily for toxic signs. Body weights were taken 2 days prior to initiation of the study and at weekly intervals during the study and at study termination. All animals were sacrificed at study termination.

Results: The irritation scores for erythema and edema were zero for all test group (Maxforce 2% Gel) guinea pigs at 24 and 48 hours at each of the nine induction periods except for the 48-hour observation period of the third induction treatment only, which showed erythema scores of 2, 1, 2, 2, 0, 0, 0, 1, 1 and 1 for each of the 10 guinea pigs. No edema was observed at any time. The erythema scores were zero at each of the other induction treatments. The 24- and 48-hour challenge scores were also zero for each of the 10 guinea pigs of the test group (Maxforce 2% Gel).

In the positive control group, erythema was produced during the induction phase, and the grade was increased slightly in severity (scores

of 2 in challenge vs. 0 and 1 in ninth induction treatment) in the challenge phase. Edema was only slightly observed in the guinea pigs of the positive control. The positive control was considered to have produced a skin sensitization effect in the male guinea pigs.

The naive control group did not show any irritation (scores of zero) during challenge phase in any guinea pig.

There were no toxic signs in any guinea pig in any of the three groups. Body weight gains were comparable among groups.

Conclusion: Maxforce 2% Gel was not a skin sensitizer in male guinea pigs by the Buehler method.

Classification: Core-~~Guideline~~ Minimum Data
[Female guinea pigs not tested.]

2. Calculation of Oncogenic Risk for PCO Users of Maxforce 2% Gel.

In the July 13, 1988 memorandum from M. Firestone of EAB, the "rough-cut" estimate of PCO exposure was 0.6 mg/kg bwt/day. Since the $Q_1^*$ for Amdro is 1.1 $(mg/kg/day)^{-1}$, the calculated oncogenic risk is shown below:

$$\text{Risk} = Q_1^* \times \text{Exposure}$$

$$\text{Risk} = 1.1\ (mg/kg/day)^{-1} \times 0.6\ mg/kg/day$$

$$\text{Risk} = 6.6 \times 10^{-1}$$

~~The level of acceptability of worker oncogenic risks has been less than $10^{-4}$. Therefore,~~ The PCO risk based on the Amdro data is significantly greater than the level of acceptability.

Attachment

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