UNITED STATES ENVIRONMENTAL PROTECTION AGENCY 6-16-80

DATE: June 16, 1980

SUBJECT: Lysoff Pour-On For Lice
EPA Registration No. 11556-48
Caswell # 456F

FROM: Cheryl Ann Peterson Cheryl Ann Peterson
IRB/TSS

TO: Mr. George La Rocca
Product Manager (15)

Applicant: BAYVET Division Cutter Labs, Inc.
P.O. Box 390
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Active Ingredient:

Fenthian (0,0-dimethyl 0-[3-methyl-4-(methylthio)phenyl] phosphorothioate).....7.6%
petroleum distillate.....56.7%
Xylene.....20.0%

Inert Ingredients.....15.7%

Background:

This product is registered for use against lice and hornflies on beef and non-lactating dairy cattle. It was agreed at the time of registration that an acute oral LD_{50} in rats, an acute dermal LD_{50} in rabbits, an eye irritation study in rabbits, and a cholinesterase inhibition study in cattle would be submitted no later than July 10, 1980.

Recommendations:

1. The primary eye irritation, skin irritation, oral LD_{50} and cattle cholinesterase inhibition studies are acceptable.

2. The acute dermal study has been classified Core Supplementary Data and is not adequate to satisfy the requirement imposed

in our letter of July 10, 1979. The study must be repeated, using at least 5 subjects of each sex and using the protocols indicated in FR 43, #163 (August 22, 1978).

Labeling:

1. The subheading GENERAL CLASSIFICATION should be deleted.

2. There should be a statement on the label similar to the following:

> Use particular care when applying this product to Brahmin cattle, as they tend to be more suceptible to cholinesterase inhibition than are other breeds.

Review:

The following studies were performed by the Chemgro Division of Baychem Corp., Research and Development on material identified as TIGUVON 7.6% Pour-on Concentrate (Formula 1730, Batch 3050456). They were received by EPA on 5-2-80, and are in Acc. No. 242427.

1. Acute Oral LD_{50} - Rat. Dated: July 24, 1974. Report No. 41200.

Procedure:

4 groups of 4M, 4F fasted Sprague-Dawley rats received 1143, 1600, 2240 and 3136 mg/kg. Formulation (diluted with a 20% ethanol - 80% propylene glycol solution) via oral intubation. There was a 14-day observation period.

Results:

No mortalities at 1143 and 1600 mg/kg. 2/4 M & 4/4F died 2 to 5 days at 2240 mg/kg and 4/4M & 4/4F died 2 days at 3136 mg/kg. Oral LD_{50} for M = 22440 mg/kg (1831-2728 mg/kg C.L.) and Oral LD_{50} for F = 1895 mg/kg (no C.L.)

Study Classification:

Core Minimum Data (No individual body weight data; presumably, symptoms were those of a cholinesterase inhibitor.)
Product Classification: Tox. Cat. III.

2. Acute Dermal LD_{50} - Rabbit. Dated: July 24, 1974.

Procedure:

2M & 2F received 2000 mg/kg test material on abraded and nonabroaded skin with 24-hour exposure. There was a 14-day observation period.

Result: No mortalities.

Study Classification:

Core Supplementary Data (Only 4 animals exposed, it is not indicated that there was occluded exposure, no body weight data were given.)

The following study was done by the Bayuet Division of Cutter Labs, Inc., Pharmaceutical Research & Dev., Toxicology. Bayvet Rpt. No. 71614; dated 3-24-80. Study was received by EPA on 5-2-80 and is in Acc. No. 242427.

3. Safety Evaluation - Cattle.

Procedure:

9M, 9F were used; 6 serving as controls (group I), 6 receiving recommended label dosage (group II), and 6 receiving 5X volume treatments (group III). Exposures to test material were via backline dipper applicatons at 0,14 and 28 days. Cholinesterase activity determinations (modified Michel method) were made at -6, 0, 3, 7, 14, 17, 21, 28, 31, 35, 42, 56, 70, and 84 days. Animals were housed under a roof for the first 24 hours after each application to prevent possible loss due to rainfall. Observations were made every 7 days for signs of dermal irritation and/or systemic photosensitization through 14 days after the 3rd treatment; then at 14-day intervals through Day 84.

Results:

Most subjects exposed to the Formulation had either slight superficial epidermal flaking or moderate epidermal cracking at 7 & 14 days following product application, but there were no permanent effects. Animals in group II (IX application) reached lowest percentage cholinesterase activity (ave. 61%) 7 days following the 3rd application. One subject was at 16% pretreatment cholinesterase activity at that time. Animals in group III (5X application) reached the lowest percentage cholinesterase activity (ave. 26%) also at 7 days after the 3rd application; one animal was at 16%, other at 18% pretreatment activity level. All animals remained normal throughout study so apparently no physical or behavioral symptoms were noted.

Study Classification:

Core Minimum Data (as a cholinesterase study).

4. Primary Eye Irritation - Rabbit. Dated September 29, 1978.

Procedure:

9F NZ White rabbits received 0.1 ml. of test material in one eye. 3/9 had eyes washed for 1 min. Starting 30 sec, after treatment. Observations were made at 24, 48, 72 hours and 4 & 7 days.

Results:

No corneal opacity. 6/6 rabbits with unwashed eyes showed conjunctivitis which cleared by 4 days after application. 3/3 rabbits with unwashed eyes showed conjunctivitis which cleared by 4 days after application. 3/3 rabbits with unwashed eyes showed conjunctivitis which cleared by 2 days.

Study Classification: Core Guideline Data.

Product Classification: Tox. Cat. III.

5. Primary Dermal Irritation - Rabbit. Dated October 30, 1978.

Procedure:

6 F NZ Albino rabbits dermally received 0.5 ml. test material at both a clipped, abraded skin site and a nonabraded skin site with 24 hour occluded exposure. Observations were made at 24 and 72 hours.

Results:

Abraded skin areas showed minor erythema (score = 1) in 4/6 rabbits up through 72 hours. Primary dermal irritation index 0.79 (calculated from scores as presented).

Study Classification: Core Minimum Data (No M rabbits were used).

Product Classificaiton: Tox. Cat. IV.

Cheryl Ann Peterson