

12-17-79

TOA

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

002373

DATE: November 19, 1979

SUBJECT: EPA File Symbol: 32660-1
Ametryne Technical; Caswell 12-1

FROM: Sherrell A. Sterling
FHB/TSS

TO: Robert Taylor
Product Manager (25)

12-1
12/17/79
12-1
12/17/79

Applicant: Industria Prodotti Chimici, S.p.A.
Via F.lli Beltrami, 11
21026 Novate Milanese
Italy

Active Ingredient:

Ametryne 97%

Inert Ingredients 3%

Background:

Acute Oral, Acute Dermal, Acute Inhalation, Eye and Skin Irritation studies were submitted in support of the conditional registration of this product. These studies were conducted by Consultox Laboratories Ltd. of London, England, and Hazelton Laboratories America, Inc. of Vienna, Virginia. The data are under Accession No. 232507. "Site-All" is the method of support.

Recommendations:

1. The Acute Oral, Acute Inhalation and Skin Irritation studies are adequate and acceptable for the conditional registration of this product.
2. The Acute Dermal Study is classified as Core Supplementary Data. There were no abraded skin sites and the use of rats instead of rabbits was not justified. A copy of the Proposed Guidelines for Human Health Evaluation has been enclosed for the convenience of the registrant. Section 63.83-1 outlines acceptable testing and reporting procedures for the Acute Dermal study.
3. The formulation of the test material must be further identified for the Acute Eye Irritation Study in Rabbits

189

(#915-118, 16 March 1976). A written statement that the test material was identical to 33660-I will suffice if applicable.

4. The Eye Irritation studies are Core Supplementary Data and as such are not adequate or acceptable for the conditional registration of this product. Under the "cite-all" method of support, these studies need not be repeated at this time. Section 163.81-4 of the Proposed Guidelines for Human Hazard Evaluation outlines acceptable testing and reporting procedures for the Eye Irritation studies.
5. FHB/TSS would have no objection, on the basis of hazard to humans and domestic animals, to the conditional registration of this product provided that the labeling revision noted below is made.

6. The signal word CAUTION is appropriate as proposed by the applicant.

The statement "For eyes: Get medical attention if irritation persists" should be added to the "Statement of Practical Treatment."

Comments:

1. All animals in the Acute Oral, Acute Dermal and Acute Inhalation studies should be examined for gross pathological alterations at the termination of the study.
2. LD50's for males and females should be reported separately for the Acute Oral study.
3. The atmospheric concentration should be determined in the Acute Inhalation study. Also males and females should be tested in these studies. For an outline of an acceptable test method, please consult Section 163.81-3 of the Proposed Guidelines for Human Health Evaluation.

Review:

1. Acute Oral Toxicity Determination: Consultox Laboratories Ltd., April 1974.

Procedure: Groups of 5M, 5F Wistar rats (230 +/- 2g) received oral dosages at levels of 500, 1000, 2000, 3000 and 4000 mg/kg of the test material, Ametryne, suspended in 0.5% aqueous Tween 80. Animals were observed for 14 days post-treatment.

7

Results: At 500 mg/kg, no mortalities. At 1000 mg/kg, 1/10 died. At 2000 mg/kg, 6/10 died. At 3000 mg/kg, 9/10 died. At 4000 mg/kg, 10/10 died. Symptoms included lethargy, excessive salivation, chromodacryorrhea, semi-comatose condition. Signs of toxicity occurred 30 minutes post-treatment. All survivors were asymptomatic after day 4. LD50 is 1750 mg/kg with a 95% confidence range of 1206-2538 mg/kg.

Study Classification: Core Minimum Data. No necropsies reported. M, F scores not reported separately.

Toxicity Category: III - CAUTION

2. Percutaneous Toxicity Determination; Consultox Laboratories Ltd.; April 1974.

Procedure: 5M, 5F Wistar rats (skin intact) received an application of 2000 mg/kg of Ametryne suspended in 0.5% aqueous Tween 80. Exposure was for 24 hours under occlusive wrap. Animals were observed for 14 days post-treatment.

Results: No mortalities. 2/10 showed slight chromodacryorrhea day 2-4. All asymptomatic after day 4. LD50 is greater than 2g/kg.

Study Classification: Core Supplementary Data. Rats, not rabbits, were used without justification. No abraded skin sites.

3. Acute Inhalation Toxicity Study in Rats; Hazelton Project # M915-103; April 10, 1975.

Procedure: 10M albino rats (243-280g) were confined to an enclosed chamber for one hour and exposed to the dust of the test material, Ametrina Tecnica. The concentration was 200.4 mg/l of air. Animals were observed for 14 days post-treatment. At termination of study, survivors were sacrificed and all animals were subjected to gross pathological examinations.

Results: No mortalities. Animals were hypoactive then hyperactive. Discharge from eyes, nose and mouth observed in animals during exposure. Slight to moderate red exudate from muzzle and eyes observed after exposure. Day 1 post-treatment red discolored areas under muzzle and on forelegs, discoloration around eyes and urogenital area. All appeared normal days 2-14.

3

Study Classification: Core Minimum Data. Only
M subjects used. Atmospheric concentration not determined.
Since all males survived a nominal concentration of 200.4
mg/l, it is dubious that females would be 10X as susceptible,
particularly as oral LD50's between the sexes were similar.
Additionally, applicant has proposed the toxicity Category
III statement "Avoid breathing dust." In lieu of a study on
females, it is probably appropriate to retain this statement.

Toxicity Category: III - CAUTION

4. Acute Eye Irritation Potential Study in Rabbits -
Ametrina Tecnica; Hazelton Project No. 915-104; April 1,
1975.

Procedure: 38 mg of test material, Ametrina Tecnica, was
applied into one eye of each of 6 New Zealand white rabbits;
all eyes unrinsed. Scoring at 24, 48 and 72 hours.

Results: No corneal, iris irritation noted. At 24 hours
5/6 showed slight conjunctival redness, 2/6 at 48 hours; all
normal by 72 hours.

Study Classification: Core Supplementary Data.

Dose is too small to determine appropriate toxicity category.

5. Acute Eye Irritation Study in Rabbits - Ametryne; Hazelton
Project No. 915-118; April 13, 1975.

Procedure: 0.1 ml (150 mg) of test material, Ametryne,
was applied into one eye of each of 3 New Zealand white
rabbits. Treated eyes were washed with 200 ml. of tap water
20 seconds post-treatment. Scoring at 24, 48 and 72 hours.

Results: No corneal, iris irritation noted. At 24 hours
3/3 showed conjunctival redness (score = 1). All scores
were zero by 48 hours.

Study Classification: Core Supplementary Data.

The "Ametryn" formulation is not specified. Once
identified, we could consider upgrading the classification
to Core Minimum Data.

6. Primary Skin Irritation Study in Rabbits - Ametrina
Tecnica; Hazelton Project = 915-105; April 1, 1975.

002373

-5-

Procedure: 0.5. g of Emetrina Technica moistened with distilled water was applied to each of 2 sites (1 abraded, 1 intact) on each of 6 New Zealand white rabbits. Exposure was under occlusive wrap for 24 hours. Draize scoring at 24 and 72 hours.

Results: All scores were zero.

Study Classification: Core Minimum Data.

Toxicity Category: IV

5

Ametryne
RIN 4236-96

Page is not included in this copy.

Pages 6 through 9 are not included.

The material not included contains the following type of information:

- ☐ Identity of product inert ingredients.
 - ☐ Identity of product impurities.
 - ☐ Description of the product manufacturing process.
 - ☐ Description of quality control procedures.
 - ☐ Identity of the source of product ingredients.
 - ☐ Sales or other commercial/financial information.
 - ☒ A draft product label.
 - ☐ The product confidential statement of formula.
 - ☐ Information about a pending registration action.
 - ☐ FIFRA registration data.
 - ☐ The document is a duplicate of page(s) .
 - ☐ The document is not responsive to the request.
-

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.
