DATE: April 11, 1980

SUBJECT: EPA File Symbol: 3876-REA
Betz ER-23; Caswell #840

FROM: Sherell A. Sterling 4-21-80
FHB/TSS E 5/5/80

TO: John H. Lee
Product Manager (31)

Applicant: Betz Laboratories, Inc.
4636 Somerton Road
Trevose, PA 19047

Active Ingredients:
3,5 - dimethyl tetrahydro - 2H - 1,3,5
thiadiazine - 2 - thione 21.0%
Inert Ingredients.....79.0%

Background: Acute Oral, Acute Dermal, Acute Inhalation, Eye and Skin Irritation studies were submitted by the applicant in support of the conditional registration of the product. All of the studies were conducted by Biosearch, Inc. of Philadelphia, Pennsylvania. The method of support is "Cite-all". Correspondence from Betz (7/30/79) states [redacted] is identical to "Betz ER - 23."

Recommendations:

1. The Acute Oral study is considered Core Supplementary Data for the following reasons:

   a. Only male subjects were used; an equal number of male and female subjects must be tested at each dose level.

   b. No necropsies were performed. All animals must be subjected to necropsies at the termination of the study.

   c. Symptoms noted during 14 day observation period were not reported. Any observations made during 14 day period must be reported.

As Supplementary Data, this study is not adequate or acceptable for conditional registration purposes.

2. The Acute Dermal study is considered Core Supplementary Data for the following reasons:

   a. Sex of animals was not reported. An equal number of male and female animals must be tested at each dose level.

   b. Autopsies must be performed on all animals.

As Core Supplementary Data, this study is not adequate or acceptable for conditional registration purposes.

3. The Acute Inhalation study is considered Core Supplementary Data for the following reasons:

   a. Animals must be observed for at least 14 days post-exposure.

   b. Only male animals were used in the study; an equal number of male and female animals must be tested.

   c. The actual atmospheric concentration must be determined and reported.

As Core Supplementary Data, this study is not adequate or acceptable for conditional registration purposes.

4. The Eye Irritation study is considered Core Supplementary Data. Please note that:

   a. The Eye Irritation study must run for at least 7 days and longer if any irritation exists.

   b. An eyewash group (minimum of 3 animals) must be tested also.

   c. The conjunctival irritation scores must be reported so that redness, chemosis and discharge scores are distinguishable.

   d. A dose of 0.1 ml must be administered in the case of liquid formulations; 0.1 mg must be used with solid formulations only.

As Core Supplementary Data, this study is not adequate or acceptable for conditional registration purposes.

5. The Skin Irritation study is adequate and acceptable for conditional registration purposes; however, the following comments are noted:

   a. A dose of 0.5 ml must be administered in the case of liquid formulations; 0.5 g must be used with solid formulations only.

   b. Four sites per animal, 2 abraded and 2 intact, must be tested.

6. Please note that whenever a range of dose levels is tested in an Acute Oral, Acute Dermal or Acute Inhalation study, dose levels must be appropriately spaced to produce test groups with mortality rates between 10% and 90%.

7. An [redacted] is registered with the following precautionary statements:

   "Harmful if swallowed. Avoid inhaling. Causes skin irritation. Do not get on skin, into eyes or on clothing. In case of contact with skin, wash well with soap and water. In case of contact with eyes, flush promptly and thoroughly with clear water. In case of ingestion or contact with eyes, secure immediate medical attention."

[redacted]

8. Based on the human hazard data submitted, FHB/TSS cannot recommend for the conditional registration of this product until additional data are submitted. The Acute Oral, Acute Dermal, Acute Inhalation and Eye Irritation studies are necessary for conditional registration, the Skin Irritation Study is adequate. FHB/TSS is not aware of any other available and acceptable data on this formulation.

9. Further labeling comments are withheld until additional data are submitted.

Note to the PM: The data under Accession #241290, Aquatic Toxicity Data, should be routed to Hazard Evaluation Division for review.

SAS
4-21-80

Review:

1. Acute Oral Toxicity - Rats; December 27, 1972; Accession No. 241285

Procedure: Groups of 5M Sherman - Wistar rats (125-150 g) received oral dosages of 0.5, 1.0, 2.0, 4.0 and 8.0 ml/kg of Slime - Trol RX - 28. Animals were observed for 14 days.

Results: No deaths occurred at 0.5 and 1.0 ml/kg; all animals died at 2.0, 4.0, 8.0 ml/kg. LD_{50} for males was 1.4 ml/kg (1.28 g/kg) with a 95% confidence range of 1.0 to 2.0 ml/kg.

Study Classification: Core Supplementary Data. No necropsies reported. Only M animals tested. No symptoms reported. Poor selection of dosage range; either 0% or 100% mortality.

2. Acute Dermal Toxicity - Rabbits; December 27, 1972; Accession No. 241286

Procedure: Groups of 4 albino rabbits (2.0 - 2.5 kg) received applications of 1.0, 2.0, 4.0 and 8.0 ml/kg of Slime - Trol RX - 28. Exposure was for 24 hours under occlusive wrap. Animals were observed for 14 days. The animals which died were subjected to necropsies.

Results: No mortalities. LD_{50} was greater than 8.0 ml/kg (7.336 g/kg).

Study Classification: Core Supplementary Data. Animals were not sexed. All test animals must be autopsied.

3. Acute Inhalation Toxicity - Rats; December 27, 1972; Accession No. 241287

Procedure: 10 M albino rats were subjected to an aerosol of Slime - Trol RX-28 for one hour. Exposure was in a 70 liter chamber with a rate of flow of 8.48 l/min. Aerosol particles were 3 to 5 microns in diameter. Concentration was calculated at 20,268 ppm by differential weighing.

Results: No mortalities. During exposure rats showed labored breathing and were sluggish.

Study Classification: Core Supplementary Data. Only M tested. Actual concentration not determined. Calculated concentration appeared extremely high. No post-exposure observations made.

4. Primary Eye Irritation Study - Rabbits;
December 27, 1972; Accession No. 241288

Procedure: 0.1 gm of Slime - Trol RX-28 was applied into one eye or each of 6 albino rabbits; all eyes remained unwashed. Scoring at 24, 48 and 72 hours.

Results: At 24 hours corneal opacity observed in 1/6 = 40, 4/6 = 60 and 1/6 = 80; iris irritation of 5 in 6/6; conjunctival irritation in 1/6 = 12, 1/6 = 14 and 4/6 = 18. By 72 hours corneal opacity exhibited in 2/6 = 40, 2/6 = 60 and 2/6 = 80; iris irritation in 4/6 = 5 and 2/6 = 10; conjunctival irritation in 1/6 = 10, 1/6 = 14, 2/6 = 18 and 2/6 = 20.

Study Classification: Core Supplementary Data. Animals only observed for 3 days. Dose was 0.1 g. No "washed" group tested. Conjunctival irritation not described.

5. Primary Skin Irritation Study - Rabbits;
December 27, 1972; Accession No. 241289

Procedure: 0.5 g of Slime - Trol RX-28 was applied to each of 2 sites (1 abraded, 1 intact) on each of 6 M albino rabbits. Exposure was for 24 hours under occlusive wrap. Draize scoring at 24, 72 hours.

Results: At 24 hours intact sites showed erythema in 3/6 = 1; abraded sites showed erythema in 4/6 = 1 and 2/6 = 2. At 72 hours intact sites exhibited no erythema: abraded sites showed erythema in 2/6 = 1, 4/6 = 2. No edema observed during study. Primary Irritation Index was 0.88.

Study Classification: Core Minimum Data. Only 2 sites per animal.

Toxicity Category: IV-CAUTION

DAZOMET SCIENTIFIC REVIEWS

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