UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

Tox

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Releasable

DATE: October 1, 1979

SUBJECT: EPA File Symbol: 201-URN
Shell Atrazine 80 W Herbicide; Caswell #63

FROM: S.A. Sterling
FHB/TSS

TO: Mr. Robert Taylor
Product Manager (25)

Applicant: Shell Oil Company
Suite 200
1025 Connecticut Ave., NW
Washington, D.C. 20036

Active Ingredients:
Atrazine.....76%
Related Compounds..... 4%
Inert Ingredients.....20%

Background : Two sets of studies were submitted in support of this registration. The first set of studies was done by the Industrial Bio-Test Laboratories, Inc., of Northbrook, Illinois. The second set of studies was conducted at Wil Research Laboratories, Inc., in Cincinnati, Ohio. These studies are contained in Accession No. 240852.

Recommendations :

1. The Acute Oral and Acute Dermal studies conducted by IBT are not acceptable to support the registration of this product. There were no F subjects in these studies.

2. The Eye Irritation study conductewd by IBT would be acceptable and adequate for conditional registration if it were validated.

3. The Acute Inhalation study conducted by IBT is considered supplementary data. The actual concentration within the test chamber is not known.

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4. The Dermal Sensitization study is considered supplementary data. The animals received only 3 sensitizing exposures before being challenged; 10 exposures are more appropriate. The Proposed Guidelines for Evaluation of Human Hazard (40 CFR 163; August 22, 1978) outline are an acceptable method for this type of study in 163.81-6. In light of the "cite all" method of support, this study will not be required.

5. The Acute Oral, Acute Dermal, Eye Irritation and Primary Dermal Irritation studies by Wil Laboratories are adequate and acceptable to support the conditional registration of this product.

6. The IBT data submitted in support of this product have not been validated. Before the IBT studies can be considered acceptable for support of a registration, they must be validated by the Special Pesticide Review Division (SPRD). However, the Wil studies meet the acute toxicological data requirements for the conditional registration of this product.

7. FHB/TSS would have no objection, on the basis of adverse effects to man, domestic animals and the environment, to the conditional registration of this product with the label revisions indicated below, *if validated.*

Labeling :

1. Based on the Eye Irritation study, the appropriate signal word is "Warning." The precautionary statements should be changed to read something like:

> "Causes eye and skin irritation.
> Do not get in eyes, on skin, or on
> clothing. Avoid inhalation of
> dust and contamination of food and
> feed. Harmful if swallowed."

2. There should be a heading "PRECAUTIONARY STATEMENTS," with subheadings "HAZARDS TO HUMANS AND DOMESTIC ANIMALS" and "ENVIRONMENTAL HAZARDS."

3. A statement like the following should appear under the "Hazards to Humans and Domestic Animals" section:

> IN CASE OF CONTACT WITH EYES,
> immediately flush eyes with plenty
> of water for at least 15 minutes.
> Call a physician.

4. The statement "It is a violation of Federal law to use this product in a manner inconsistent with its labeling" must appear under the directions for use heading [40 CFR 162.10(i)(2)(ii)].

Review :

1. Acute Oral Toxicity Study - Male Albino Rats ; IBT No.: 601-05145; June 17, 1974.

   Procedure : Groups of 6 M Sprague-Dawley rats received oral dosages at levels of 0.9, 1.350, 2.025, 3.038, 4.556 and 6.834 g/kg with 14-days observations, sacrifice of survivors, and examination of gross pathology.

   Results : No mortalities at 0.9, 1.350, 2.025 g/kg. 4/6 died at 3.038 g/kg, 6/6 died at 4.556 and 6.834 g/kg. Symptoms included hypoactivity, ruffed fur, labored respiration, muscular weakness, ptosis, diarrhea, lacrimation, salivation and death. Necropsy of mortalities showed that 4/6 had gastroenteritis. Body weights of survivors increased from initial to terminal day. LD50 for M is 2825 mg/kg with a 95% confidence range of 2,394-3,333 mg/kg.

   Study Classification : Core Supplementary Data; F subjects were not included in the study.

2. Acute Dermal Toxicity Study - Male Albino Rabbits ; IBT No.: 601-05145; June 17, 1974.

   Procedure : Groups of 6 M New Zealand albino rabbits (3 with abraded sites, 3 with intact sites) received an application of 200 and 2000 mg/kg of test material with 24 hours occluded exposure. Animals were observed for 14 days after exposure, sacrificed and examined for gross pathological changes.

   Results : No mortalities. Very slight desquamation observed on day 7 and day 14. 3/12 body weights went down from initial to terminal day; 1/12 appeared emaciated. Necropsy showed no gross pathological alterations. LD50 is greater than 2 g/kg for M.

   Study Classification : Core supplementary Data. F were not tested.

3. Eye Irritation Test - Albino Rabbits ; IBT No.: 601-05154; June 17, 1974.

   Procedure : 100 mg of test material was applied into one eye of each of 6 rabbits; all eyes unwashed. Scoring at

1,24,48,72 and 96 hours and at 7 days.

Results : Corneal opacity in 6/6 at 24 hours, iris and conjunctival irritation at 24 hours. Epithelial sloughing 3/6 at 1 hour. All scores are zero by day 7.

Study Classification : Core Guideline Data if validated.

Product Classification : Tox. Cat. II.

4. Primary Skin Irritation Test - Albino Rabbits ; IBT No.: 601-05154; June 17, 1974.

Procedure : 0.5 ml of test material was applied to each of 2 sites (1 abraded, 1 intact) on each of 6 New Zealand albino rabbits with 24 hour exposure under occlusive wrap. Scoring at 24 and 72 hours.

Results : All scores were zero.

Study Classification : Core Guideline Data if validated.

Product Classification : Toxx. Cat. IV.

5. Acute Dust Inhalation Toxicity Study with SD 12011 - 80% Wettable Powder in Albino Rats ; IBT No.: 663-05239; June 13, 1974.

Procedure : One group of 5M, 5F Charles River strain albino rats were exposed to test material for one hour in a specially designed Plexiglas inhalation chamber. Animals were observed for 14 days post-treatment, sacrificed and examined for gross pathological changes.

Results : No mortalities, M rats lost weight, F rats gained weight. The average concentration was calculated to be 0.2 mg/l; 5.8% of the particles were calculated to be between 1-5 microns.

Study Classification : Core Supplementary Data. The exposure level was calculated to be 0.2 mg/l which means that the test substance is no worse than toxicity category II; however, a higher exposure level would be necessary to determine the appropriate toxicity category.

6. Acute Oral Toxicity Study in Rats with SD 12011 (Atrazine 80% WP) ; Wil-1173-78; August 24, 1978.

Procedure : Groups of 5M (203.3-276.5g), 5F (200.0-226.8g) Sprague-Dawley CD albino rats received oral dosages at levels

of 0.6, 0.9, 1.35, 2.025, 3.038 g/kg with 14-days observations, sacrifice of survivors and examination of gross pathology.

Results : No mortalities for M at 0.6, 0.9 and 1.35 g/kg. No mortalities for F at 0.6 g/kg. 2/5 F died at 0.9 g/kg, 1/5F died at 1.35 g/kg. At 2.025 g/kg 2/5 M, 1/5 F died. At 3.038 g/kg 3/5 F, 4/5 M died. Symptomology included depression, diarrhea, decreased eating, unkempt coats, depressed righting and placement reflexes, labored respiration, excessive salivation, blood stains around muzzle, emaciation and death. LD50 was not calculated; estimated to be between 2000-2500 mg/kg.

Study Classification : Core Minimum Data.

Product Classification : Tox, Cat. III.

7. Acute Dermal Toxicity Study in Rabbits with SD 12011 Atrazine 80 WP ; Wil-1173-78; July 13, 1978.

Procedure : 3M, 3F New Zealand albino rabbits received an application of 2g/kg of test material with 24 hour occluded exposure; skin was not abraded. Animals were observed for 14 days after exposure, sacrificed and examined for gross pathological alterations.

Results : No mortalities. No observable signs of toxicity. At necropsy, all viscera appeared normal. Study shows that LD50 is greater than 2,000 mg/kg.

Study Classification : Core Minimum Data.

Product Classification : Tox. Cat. III.

8. Acute Eye Irritation Study in Rabbits with SD 12011 Atrazine 80 WP ; Wil-1173-78; July 5, 1978.

Procedure : 100 mg of test material was applied into one eye of each of 6 New Zealand albino rabbits. Scoring at 1,24,72 hours and at 7 days.

Results : At 24 hours corneal opacity seen in 3/6; iris irritation in 1/6; conjunctival irritation in 6/6. By day 7 all scores were zero.

Study Classification : Core Guideline Data.

Product Classification : Tox. Cat. II.

9. Acute Eye Irritation Study in Rabbits with SD 12011 Atrazine 80 WP ; Wil-1173-78; July 21, 1978.

Procedure : 100 mg of test material was applied into one eye of each of 3 New Zealand albino rabbits. Treated eyes were flushed with 300 ml of warm tap water 30 seconds after exposure. Scoring at 1,24,72 hours and at 7 days.

Results : 2/3 showed corneal opacity at 1 hour. No corneal opacity seen at 24 hours, slight conjunctival irritation. All scores are zero by day 7. Those with rinsed eyes showed less severe irritation than those unrinsed in previous study (see above #8).

Study Classification : Combined with the Eye Irritation study of July 5, 1978 (see above): Core Guideline Data.

10. Primary Skin Irritation and Corrosivity Study in Rabbits with SD 12011 Atrazine 80 WP; Wil-1173-78; July 5, 1978.

Procedure : 0.5 g of the test material was applied to each of 2 sites (1 abraded, 1 intact) on New Zealand albino rabbits (3M, 3F) with 24 hour exposure under occlusive wrap. Scoring at 24 and 72 hours.

Results : All scores zero.

Study Classification : Core Guideline Data.

Product Classification : Tox. Cat. IV.

11. Delayed Contact Hypersensitivity Study in Guinea Pigs with SD 12011 (Atrazine) 80 WP ; Wil-1173-78; August 21, 1978.

Procedure : 3 groups of 10(5M,5F) Hartley albino guinea pigs were exposed to 3 sensitizing doses of 0.5 ml for 6hours. One group was exposed to diethylether (vehicle control); one group was exposed to 0.1% 2,4-dinitrochlorobenzene in diethylether (positive control); and one group was exposed to the test substance. Animals were exposed to one dose per week for 3 weeks. Two weeks passed and animals were exposed to challenge dosage. Observations made at 24 and 48 hours after exposures.

Results : Animals exposed to test substance exhibited minimal erythema 24 hours after first sensitizing dose; no response to challenge exposure.

Study Classification : Core Supplementary Data. Not enough sensitizing exposures before animals were challenged. Positive control group, on challenge, showed relatively mild reaction (2 had slight erythema, remaining 8 had moderate erythema with slight edema).