UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

TOX
UNDATED

DATE:

SUBJECT: EPA File Symbol: 201-UNO
Shell Atrazine 4L Herbicide; Caswell #63

19

Atrazine / Review #19
undated / 6 pages

FROM: S. A. Sterling
FHB/TSS

TO: Mr. Robert Taylor
Product Manager (25)

Releasable

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

Active Ingredients:

Atrazine	40.8%
Related Compounds	2.2%
Inert Ingredients	57.0%

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. (IBT) of Northbrook, Illinois. The second set of studies was conducted at Wil Research Laboratories, Inc. of Cincinnati, Ohio.

Recommendations:

1. The Acute Oral and Acute Dermal studies conducted by IBT are not acceptable for the registration of this product as no F subjects were used.

2. The Eye Irritation study conducted by IBT is acceptable and adequate for purposes of conditional registration if validated. Since the results of this study are in conflict with the Wil Eye Irritation study, the Wil study supersedes the IBT study.

3. The Primary Dermal study conducted by IBT is acceptable and adequate for conditional registration if validated.

4. The Acute Oral and Acute Dermal studies conducted by Wil are adequate and acceptable for the conditional registration of this product.

5. The Skin Irritation study conducted by Wil is adequate and acceptable for the conditional registration of this product. Please note that the Proposed Guidelines on Human Hazard Evaluation (40 CFR 163, August 22, 1978) suggest 4 sites, (2 abraded and 2 intact) per animal.

6. The Eye Irritation study conducted by Wil is adequate and acceptable for the conditional registration of this product.

7. No Acute Inhalation studies were submitted. A justification for the lack of such studies was not submitted either. Since the "cite-all" method of support is being used, such study or justification is not necessary.

8. The Dermal Sensitization study is not adequate for the registration of this product. Only 3 sensitizing doses were applied; 10 sensitizing doses are suggested. The suggested method for this type of study can be found in the Proposed Guidelines, Section 163.81-6.

9. All IRT data must be validated by the Special Pesticide Review Division (SPRD) before it can be used in support of a registration. In this case, the studies conducted at Wil Research Laboratories, Inc. sufficiently meet the acute toxicological study requirements.

10. FHB/TSS would have no objection, on the basis of adverse effects to man, domestic animals and the environment to the conditional registration under the "cite-all" method of support of this product with the label revisions indicated below, if validated.

Labeling:

1. There should be a heading "PRECAUTIONARY STATEMENTS" with subheadings "HAZARDS TO HUMANS AND DOMESTIC ANIMALS" and "ENVIRONMENTAL HAZARDS." The appropriate precautionary labeling statements should appear under the appropriate heading.

2. The statement, "It is a violation of Federal law to use this product in a manner inconsistent with its labeling," should be included immediately under the directions for use heading.

Review:

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

Procedure: Groups of 6 M Sprague-Dowley rats received oral dosages at levels of 2.025, 3.038, 4.556, 6.834 and 10.250 g/kg with 14-day observations, sacrifice of survivors, and examination of gross pathology.

Results: No mortalities at 2.025 and 4.556 g/kg. 1/6 died at 3.038 g/kg; 3/6 died at 6.834 g/kg; 6/6 died at 10.250 g/kg. Symptoms included hypoactivity, muscular weakness, labored respiration, ruffed fur, lacrimation, rhinitis, ptosis, diuresis and oily fur. Necropsy revealed red, discolored areas in lungs of 8/30 (2/8 were survivors). Hemorrhages in small intestine in 5/10 mortalities. LD_{50} for M is 6,834 mg/kg with 95% confidence range of 6,102-7,654 mg/kg.

Study Classification: Core Supplementary Data. No F subjects used in this study.

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

Procedure: Groups of 6 M (2.30-2.78 kg) New Zealand albino rabbits (3 with abraded skin, 3 with intact skin) received applications of 200 and 2,000 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 seen at day 7, day 14. No gross pathological alterations observed.

Study Classification: Core Supplementary Data. No F subjects were used in this study.

3. Eye Irritation Test - Albino Rabbits; IBT No. 601-05145; June 17, 1974.

Procedure: 0.1 ml of test material was applied into one eye of each of 6 New Zealand albino rabbits; all eyes unwashed. Draize scoring at 1, 24, 48, 72, 96 hours and 7 days.

Results: Only conjunctival irritation at 1 hour. All other scores were zero.

Study Classification: Core Minimum Data if validated.

Product Classification: Data suggest Toxicology Category IV; however, this study is superseded by the Wil study showing product is in Toxicology Category III.

4. Primary Skin Irritation Test - Albino Rabbits; IBT No.: 601-05145; 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. Draize scoring at 24 and 72 hours.

Results: 4/12 sites exhibited irritation at 24 hours. All scores were zero by 72 hours. Primary Irritation Index = 0.2.

Study Classification: Core Guideline Data if validated.

Product Classification: Toxicology Category IV.

5. 102 Acute Oral Toxicity Study in Rats with SD 12011 Atrazine 4L; WIL-1174-78; August 16, 1978.

Procedure: One group of 5 M, 5 F Sprague-Dawley CD strain rats received oral dosages at levels of 0.3, 1.0, 3.0, 5.0 and 10.0 ml/kg; with 14-day observations, sacrifice of survivors, and examination of gross pathology.

Results: No mortalities at 0.3 mg/kg; 0/5 M, 3/5 F died at 1.0 mg/kg; 5/5 M, 4/5 F died at 3.0 ml/kg; all subjects died at 5.0 and 10.0 ml/kg. Symptoms included depression, diarrhea, unkempt coats, excessive salivation, decreased appetite, depressed righting and placement reflexes, blood-colored stains around muzzle, emaciation, labored breathing and death. Mortalities exhibited redness in lungs, kidneys and adrenals; darkened spleens, wrinkled and red peritoneal walls; redness in gastrointestinal tract, pale and mottled liver. M exhibited retracted testicles with external blood vessels dilated. No gross pathological alterations. LD_{50} for M is 1.69 ml/kg and for F is 1.06 ml/kg. 95% confidence limits could not be calculated for M; for F, the range is 0.5 ml/kg - 2.20 ml/kg.

Study Classification: Core Guideline Data

Product Classification: Toxicology Category III.

6. Acute Dermal Toxicity in Rabbits with SD 12011 Atrazine 4L; WIL-1174-78; July 13, 1978.

Procedure: 3 M, 3 F New Zealand albino rabbits received an application of 2 ml/kg of test material with 24-hour occluded exposure; no abraded skin sites. Animals were observed for 14 days, sacrificed and examined for changes.

Results: No mortalities. On day 1, 5/6 showed irritation; all other scores were zero.

Study Classification: Core Minimum Data.

Product Classification: Toxicology Category III.

7. Primary Skin Irritation and Corrosivity Study in Rabbits with SD 12011 Atrazine 4L; WIL-1174-78; July 5, 1978.

Procedure: 0.5 ml of the test material was applied to each of 2 sites (1 abraded, 1 intact) on 6 New Zealand albino rabbits, with 24-hour occluded exposure. Draize scoring at 24 and 72 hours.

Results: 2/12 showed slight irritation at 24 hours. All scores were zero by 72 hours. Primary Irritation Index is 0.085.

Study Classification: Core Guideline Data

Product Classification: Toxicology Category IV.

8. Acute Eye Irritation Study in Rabbits with SD 12011 Atrazine 4L; WIL-1174-78; July 5, 1978.

Procedure: 0.1 ml of test material was applied into one eye of each of 6 New Zealand albino rabbits; treated eyes were not rinsed. Draize scoring at 1, 24, 72 hours and at 7 days.

Results: 1/6 showed slight corneal opacity at 24 hours. By day 7, all scores were zero.

Study Classification: Core Guideline Data.

Product Classification: Toxicology Category III.

9. Delayed Contact Hypersensitivity Study in Guinea Pigs with SD 12011 Atrazine 4L; WIL-1174-78; August 15, 1978.

Procedure: Three groups of 10 (5 M, 5 F) Huntley albino strain guinea pigs were exposed to 3 sensitizing doses of 0.5 ml for 6 hours. 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 exposure.

Results: After challenge all scores for vehicle control were zero; all scores for the test material were zero; slight to moderate irritation scores for positive control.

Study Classification: Core Supplementary Data. When using guinea pigs as the test organism for this type of study, all subjects should be M. Not enough sensitizing exposures before animals were challenged; this was indicated by the moderate positive control irritation.