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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

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FEB 28 1985

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Review of Acute Toxicity of Hyamine 3500 (The Cleaner) for Product Registration; EPA Registration No. 5741-19; Accession No. 255315; Caswell No. 16 E

TO: John Lee
Product Manager (31)
Registration Division (TS-767)

THROUGH: Theodore M. Farber, Ph.D.
Chief, Toxicology Branch
Hazard Evaluation Division (TS-769)

FROM: William Dykstra, Ph.D. *William Dykstra 2/20/85*
and
Margaret L. Jones, M.S. *Margaret L. Jones 2/20/85*
Toxicology Branch
Hazard Evaluation Division (TS-769)

Registrant: Spartan Chemical Co., Inc.
110 N. Westwood Ave.
P.O. Box 3457
Toledo, Ohio 43607

Action Requested:

The registrant has forwarded the acute toxicity package on Hyamine 3500 ("The Cleaner") for registration of their new product.

The Data Evaluation Record for the acute oral toxicity study is attached. Comments on the study appear in number 2 below.

The following comments respond to the instructions section in the Registration Division Data Review Record (green sheet).

1. The Metal Working Fluid Guidelines (ref) which require special data for this category of chemical are waived since the product is extremely caustic and its pH of 13.6 to 13.5 places it in the following toxicity categories:

Primary Eye Irritation --- I
Primary Dermal ----- I

The Acute Dermal LD₅₀ test is waived for this product due to its extremely corrosive nature.

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- b. Inhalation toxicity testing may be waived provided that the registrant can support with documentation the statement that the product is not an aerosol as claimed in the data matrix.
- c. Dermal sensitization testing can be waived if the registrant can demonstrate that it is not possible to sensitize when the product is used according to label instructions and since the product shows corrosive toxicity to skin in a primary dermal irritation.

Documentation should be provided to support the statement made in Appendix F that quaternary ammonium compounds are not sensitizers. Information with respect to the sensitizing potential of the composite product should likewise be presented, since components of the product other than the quaternary ammonium compound could cause a sensitization reaction.

Assuming the product is used as advised on the label, we can accept the statement that the product does not come into repeated contact with skin under normal conditions of use.

3. Additional Data Requirements: No further data requirements will be necessary before registration of this product provided the registrant supplies the documentation requested on the substance tested, on the sensitization issue and on the aerosolization concerns, which are detailed above.

4. Exposure Assessment Requirement: No Exposure Assessment will be required for this product assuming it is used in accordance with label instructions. The product should be applied while wearing goggles and rubber gloves, and at its advised dilution ratio.

5. Label Review: The sample label shows proper cautionary wording which warns of the corrosive nature of the product and recommends the precautions to take while using the product.

Note: This compound is not a metal-working fluid but is rather designed to clean metal-working machines. Therefore, toxicology data requirements for metal-working fluids do not apply.

Handwritten signature and date: [Signature] 5/25/85

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Data Evaluation Record

1. Chemical: Hyamine 3500, Caswell # 16E
2. Test Material: The Cleaner, Batch #7, a purple liquid. The purity of the test substance was unspecified and whether this was a technical, formulation, or use dilution was not specified.
3. Study/Action Type: Acute Oral Toxicity in Rats.
4. Study Identification: EPA Accession No. 255315; Hill Top Research Project NO. 84-0724-21, P.O. Box 42501, Cincinnati, Ohio 45242; Acute Oral Toxicity Screen in Rats of The Cleaner, Batch # 7 for Spartan Chemical Company, Toledo, Ohio, Dated July 22, 1984

5. Conclusions:

No definitive conclusions can be made until the test substance is identified and until the method of determining the dose administered to test animals is explained.

6. Recommendations:

1. The product is accorded a Supplementary status since the test substance is not clearly identified. Also, the method of calculation of the dose administered is not stated.
2. Documentation should be provided to support the claim that the test substance does not cause dermal sensitization.
3. Documentation should also be provided to support the registrant's claim that the product does not present any inhalation toxicity concerns, i.e., that the product does not aerosolize under the conditions of use.

7. Materials and Methods (Study Author):

Test Material: "The Cleaner", Hyamine 3500, a purple liquid; Batch # 7. The active ingredient is n-alkyl (C₁₄-50%, C₁₂-40%, C₁₆-10%)- dimethyl ammonium chloride.

Test Animals: Five male and five female Sprague-Dawley albino rats.

Dosage Form: The test material was administered in undiluted form in a dose of 5 g/kg.

Statistical Methods: No statistical analysis was performed on the results of this test.

Methods to Determine Exposure: Animals were observed frequently during the day of exposure and twice daily thereafter for a total of 14 days.

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Protocol:

One group of five male and five female Sprague-Dawley albino rats was selected for testing. The average weight of females at the start was 215 grams with a standard deviation of 18 grams. The average weight of males at the start was 229 with a standard deviation of 14 grams. Prior to treatment the animals were allowed to acclimate to laboratory conditions for seven days. They ate Purina Lab Chow and drank water ad libitum. Prior to dosing the animals were fasted for 18 hours. The animals were given 5.0 g/kg of the test substance by gavage administration. After dosing the animals were observed at one, 3 1/4, and 5 hours and twice daily thereafter for 11 days. The rats were weighed on days 0, 7, and 14 of the test period. One animal died during the test period and was submitted to necropsy. At 14 days, survivors were killed by administering carbon dioxide and then submitted for necropsy.

8. Reported Results: (Study Author)

The death of one male occurred on day one. Necropsy of this animal revealed pale lungs, irritated gastrointestinal lining, yellow liquid in the stomach and congested kidneys. Toxic signs in the survivors included urine and fecal stains observed at 3 1/4 hours through day three in more than five animals. Six animals showed red stains around the muzzle and eyes within three to five hours and the majority showed these symptoms for two days post-exposure. The red stains disappeared in all animals by day 5. Several animals showed hunched posture immediately following treatment but this subsided by the end of day 1. Unkempt fur was observed from days 1 through 5. Most animals returned to normal appearance and behavior by day 5 and all by day 7. Weight gain during the test period was 75 ± 11 grams for males and 48 ± 3 grams for females. At necropsy females showed congested kidneys and males showed no signs of abnormality.

9. Study Author's Conclusions/Quality Assurance Measures:

The study concluded the LD₅₀ was greater than 5 g/kg in male and female Sprague-Dawley rats and the test substance belongs in Toxicity Category IV.

Quality Assurance was affirmed by C.R. Woodiwiss, B.S., Director, Quality Assurance (signed by Warren A. Penn, 7/13/84).

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10. Reviewer's Discussion and Interpretation of Study Results:

No significant toxic effects were caused by the oral administration of The Cleaner to male and female Sprague-Dawley albino rats. The death of one male occurred on day one of the test.

Discussion:

1. From the test report it is unclear exactly which substance was tested and how the dose was determined. Batch # 7 tells nothing of the percent of active ingredient administered to the test animals. There is a discrepancy between the Confidential Statement of Formula and the label. Each lists a different percent of active ingredient present in the product. The purity of the test substance should be stated. Likewise, the method of determining the dose administered to the animals should be indicated.

2. Animals gained weight during the test period but, no comparison to normal weight gain is made.

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