CASWELL FILE 481C

TECHNICAL SUPPORT SECTION Toxicology REVIEW - I

Disinfectants Branch

IN 3/5/81 OUT 4/30/81

Reviewed by James E. Wilson, Jr. Date 4/29/81

EPA Reg. No. or File Symbol 20375-ER

EPA Petition or EUP No.

Date Division Received 2/26/81

Type Product(s): I, (D), H, F, N, R, S

Data Accession No(s). 244488

Product Mgr. No. 31 (Lee)

Product Name(s) Fuel Preserve

Company Name(s) Nutmeg Chemical Company

Submission Purpose New Product

Chemical & Formulation Liquid

Active Ingredient(s):	%
Hexahydro 1,3,5-tris(2-hydroxyethyl)-3-triazine	3.1

300.0 Introduction

300.1 Uses

The product is an antioxidant, corrosion inhibitor, and bacteriostat in fuel oil.

300.2 Background

None

301.1 Data Summary

301.1 Brief Description of Studies

a. Acute Oral Toxicity in Rats. Report by Product Safety Labs, submitted to Nutmeg Chemical Co., New Haven, CT 06513, dated January 16, 1980. (Accession No. 244488).

b. Acute Oral Toxicity in Rats (Defined Oral LD_{50}). Report by Product Safety Labs, submitted to Nutmeg Chemical Co., New Haven, CT 06513, dated January 16, 1980. (Accession No. 244488).

c. Acute Dermal Toxicity in Rabbits. Report by Product Safety Labs, submitted to Nutmeg Chemical Co., New Haven, CT 06513, dated January 16, 1980. (Accession No. 244488).

d. Acute Inhalation Toxicity in Rats. Report by Product Safety Labs, submitted to Nutmeg Chemical Co., New Haven, CT 06513, dated January 16, 1980. (Accession No. 244488).

e. Primary Dermal Irritation Study. Report by Product Safety Labs, submitted to Nutmeg Chemical Co., New Haven, CT 06513, dated January 16, 1980. (Accession No. 244488).

f. Eye Irritation Study. Report by Product Safety Labs, submitted to Nutmeg Chemical Co., New Haven, CT 06513, dated January 16, 1980. (Accession No. 244488).

301.2 Study Summaries

a. Acute Oral

1. Method

Five male and five female Wistar rats were fed 5.0 ml/kg, by gavage, of the test material. The rats were observed for toxic signs and mortality for 14 days.

2. Results

Two males and four females died, all by day 3. No signs were reported. Autopsy revealed gastric corrosion and pulmonary hemorrhages.

3. Conclusion

The oral LD_{50} is less than 5.0 ml/kg.

b. Acute Oral (Defined)

1. Method

Five groups of Wistar rats, five males and five females per group, were fed doses of 2.2, 2.4, 2.6, 2.8 and 3.4 ml/kg of the test material. All animals were observed for mortality and signs for 14 days. Necropsies were performed on all mortalities. Individual body weights were recorded prior to gavage and at day 14.

2. Results

Apparent dyspnea was noted. Two females died at the 2.4 ml level, one of each sex died at 2.8, and two males and three females died at 3.4 ml. Autopsy reports showed that rats which died had pulmonary hemorrhages. Body weight gains were within normal ranges.

3. Conclusion

The oral LD_{50} of the product was calculated to be 3.3 ml/kg with 95% C.L. of 2.9-3.8 ml/kg.

c. Dermal Toxicity

1. Method

Five male and five female New Zealand albino rabbits were clipped free of dorsal fur. Of this group the skin of two males and three females was abraded. A patch containing 2.0 ml/kg of the test material was placed on the skin and secured with an elastic sleeve. After 24 hours the patches were removed and teh animals were observed for 14 days.

2. Results

No signs of toxicity were observed. Two males died during the study (days 7 and 9) with deterioration of the gastro-intestinal tract.

3. Conclusion

The dermal LD_{50} is greater than 2.0 ml/kg.

d. Inhalation Toxicity

1. Method

Five male and five female rats were placed in an inhalation chamber for one hour and exposed to a concentration of 24.9 mg/liter of the test material. Agitation was introduced to keep the mist airborne. The observation period was 14 days.

2. Results

No untoward signs or deaths were recorded.

3. Conclusion

The inhalation LC_{50}, according to this study, is greater than 24 mg/liter.

e. Skin Irritation

1. Method

Six New Zealand rabbits were clipped of dorsal hair. Each rabbit had 0.5 ml of the undiluted test material applied under a 1" square guaze patch to both an intact and abraded area. After application the area was occluded for 24 hours. The residual test material was washed from skin after 24 hours. The reactions were measured after 24 and 72 hours.

2. Results

The score for erythema and edema were 4 and 1 after 24 hours. After 72 hours the scores were 4 for erythema and 3 for edema. Marked tissue necrosis was also noted.

3. Conclusion

The product is a severe skin irritant causing skin damage.

f. Eye Irritation

1. Method

Six New Zealand albino rabbits had 0.1 ml of the test substance placed in the everted lower lid of the right eye.

The left served as the control. The lids were gently held together for one second. Readings were made at 24, 48 and 72 hours after instillation.

2. Results

Mild opacity was present in all eyes after 24 hours. After 72 hours mild opacity was found in 4/6 eyes while iritis was observed in all eyes initially and 3/6 at 72 hours. Conjunctival irritation was moderate to severe after 24 hours and decreased slightly after 72 hours.

3. Conclusion

The product causes severe moderate to severe conjunctival irritation, opacity and iritis which does not completely clear in three days.

302.0 Recommendation

302.1 Safety Supported by Data

The data submitted are adequate to support placing the chemical in the following acute toxicity categories:

Acute Oral	- 3
Acute Dermal	- 3
Skin Irritation	- 1
Eye Irritation	- 1

302.2 Safety Not Supported by Data

There were several deficiencies in the inhalation study. The rate of air flow, actual chamber concentrations, temperature and particle sizes were not reported. For these reasons the study is not acceptable to indicate the toxicity of the product.

302.3 Other Considerations

Deficiencies were found in other studies. However, they were not judged to be serious enough to affect the results significantly. Some of the shortcomings were: autopsies not performed on sacrificed animals, untoward signs not reported, eye irritation study terminated after [redacted] three days and not the recommended 14 or 21 (recently published for CRP), and washing of the residual material from the skin.

Since this reviewer can find no criteria under which inhalation data are required, it is recommended that the registrant be informed of the deficiencies and it not be required that the study be repeated unless the company feels that it is required or needed.

302.4 Additional Data Required

None

303.0 Labeling

The words "or fatal" may be removed from the statement "Harmful or fatal if swallowed."

Registrant should be made aware of our standard "Statement of Practical Treatment" for ingestion and "Note to Physician."