EPA Reviewer: Whang Phang, Ph.D. Signature: Why Phang
Review Section III, Toxicology Branch II Date: 9/12/93
Health Effects Division (H7509C)
EPA Section Head: James Rowe, Ph.D. Signature: James N. Rowe
Review Section III, Toxicology Branch II Date: 9/15/93
Health Effects Division (H7509C)

DATA EVALUATION REPORT

STUDY TYPE: Acute inhalation toxicity

EPA Registration No.: 057978-G

Tox Chem. No.:

MRID No.: 424845-03

PC Number: 128972

TEST MATERIAL: Suttocide A, 50% solution (Integra 44)

SYNONYM(S): Sodium hydroxymethylglycinate

SPONSOR: Sutton Laboratories, Inc., Chatham, NJ

STUDY NUMBER: T-1557

TESTING FACILITY: Product Safety Labs, East Brunswick, NJ

TITLE OF REPORT: EPA Acute Inhalation Toxicity — Defined LC_{50}: Suttocide A 50% Solution

AUTHOR: R. Shapiro

STUDY COMPLETED: June 22, 1992; amended final report submitted July 14, 1992

CONCLUSIONS: Estimated acute inhalation LC_{50} in males: 5.80 mg/L
(95% confidence interval 5.58-6.03 mg/L)
Estimated acute inhalation LC_{50} in females: 6.20 mg/L
(95% confidence interval not determined)
Estimated acute inhalation LC_{50} in sexes combined: 6.00 mg/L
(95% confidence interval 5.26-6.85 mg/L)

CORE CLASSIFICATION: Core Guideline. This study satisfies the requirements of Guideline Series 81-3 for an acute inhalation toxicity study. It is recommended, however, that future submissions include a complete description of the environmental conditions under which the test animals have been maintained.

TOXICITY CATEGORY: IV

Inert ingredient information may be entitled to confidential treatment

A. MATERIALS

Test Compound: Suttocide A, 50% solution

Identification numbers: Lot No. SA-118; PSL Code No. E20504-02
Active ingredient: Sodium hydroxymethylglycinate
Formulation: 49.8% sodium hydroxymethylglycinate, [redacted]
Purity: 49.8%
Physical description: Pale yellow solution
pH: 11.58
Receipt dates: May 4, 1992 (Limit test at 4.90 mg/L); May 8, 1992 (subsequent exposures of 5.92 and 6.91 mg/L)
Storage condition: Not reported
Stability: Not reported

Concentrations: 4.90, 5.92, and 6.91 mg/L, administered as an aerosol generated from undiluted test material as received

Controls: None

Test Animals

Species: Rat
Strain: Sprague-Dawley
Source: Hilltop Lab Animals, Scottdale, PA
Number and sex of animals: 15 males, 15 females
Age: Not reported
Weight (at initiation): Males, 206-258 g; Females, 217-244 g
Housing: 1 animal/cage
Number of animals/dose: 10 (5/sex)

Environmental conditions: Temperature: 70-74°F
Humidity: Not reported
Air changes per hour: Not reported
Photoperiod: Not reported

B. TEST PERFORMANCE

Inhalation Chamber: A 100-L rectangular perspex chamber was used for whole-body exposure of the animals. The animals were housed individually in cages within the chamber and were exposed to an aerosol generated from undiluted test material (as received, i.e., a 50% solution) for a period of 4.5 hours. At the end of the exposure period, clean air was passed through the chamber for 30 minutes prior to animal removal from the chamber.

Note: A limit test at 4.90 mg/L was conducted separately and prior to the 5.92- and 6.91-mg/L exposures.

Dose Preparation/Generation of Test Atmospheres: Aerosols of the test material were generated with a 1/4" JCO atomizer (Spraying Systems Inc.),

and were mixed with breathing grade air (Airco #300 Dry Air) supplied to the spray atomization nozzle (at a rate of 19-20 L/minute). Additional air was filtered, conditioned, and supplied directly to the exposure chamber (at a rate of 29.7-31.6 L/minute). The appropriate exposure concentrations were obtained by adjusting the rate of test material flowing through the nozzle using a Master Flex Pump (Model #7520-35).

Chamber Monitoring: Temperature and relative humidity within the exposure chamber were monitored continuously during each treatment and chamber air flow was monitored frequently. Air changes per hour, as calculated by our reviewers, are based on the total air flow into the 100-L chamber for each exposure level.

Chamber Environmental Conditions:
Temperature: 69-71°F
Relative humidity:
4.90-mg/L exposure: 33-35%
5.92- and 6.92-mg/L exposures: 55-88%
Air flow: 49.0-50.9 L/min
Air changes per hour: 29.4-30.5
% O_2: Not reported
Chamber equilibrium (T_{99}): 9.2 minutes

Analytical Determinations: The achieved chamber concentrations were determined gravimetrically from six breathing-zone samples (drawn at a rate of 4 L/minute for 3 minutes, sampled at half-hour intervals), and collected onto 25 mm glass fiber filters. Nominal chamber concentrations were calculated by the performing laboratory based on the amount of test substance "used" (i.e., the starting weight minus final weight of test material) divided by the total volume of air passing through the chamber during the experiment. The results from these determinations are shown below:

Target Exposure Concentration (mg/L)	Chamber Concentration Mean ± S.D. (mg/L)	Nominal Concentration (mg/L)
5.0	4.90 ± 0.20	72.65
6.0	5.92 ± 0.09	87.96
7.0	6.91 ± 0.18	105.86

Particle Size Determination: In order to determine the size distribution of particles in the test material aerosol at each exposure level, two 5-10-minute samples (at approximately 1.5 and 3 hours) were drawn from the chamber using an Andersen cascade impactor. The mass median aerodynamic diameter (MMAD) and geometric standard deviation (GSD) were calculated by the performing laboratory using two-cycle logarithmic probit axes. Results from two samples per exposure level were as follows:

Exposure Concentration (mg/L)	Cumulative % Particles <1.1 µm	Cumulative % Particles <3.3 µm	MMAD[a] (µm)
4.90	5.7	58.4	2.5 ± 1.77
	5.9	63.0	2.5 ± 1.67
5.92	6.0	61.9	2.6 ± 1.77
	6.5	63.3	2.4 ± 1.71
6.91	6.9	62.8	2.4 ± 1.80
	6.9	66.9	2.4 ± 1.82

[a]Mass median aerodynamic diameter ± geometric standard deviation

Exposure Period: 4.5 hours

Observation Period: 14 days

Observation Frequency: In-chamber observations were conducted every 15 minutes during the first hour, and every half hour thereafter for the duration of the exposure. Animals were observed postexposure at least once daily for 14 days.

Body Weight Interval: Days 0, 1, 2, 4, 7, 10, and 14

Gross Pathology: YES X ; NO ____

Histopathology: YES ____; NO X

C. REPORTED RESULTS:

Mortality: Mortality results are summarized below.

Concentration (mg/L)	Number Dead/Number Tested		
	Males	Females	Combined
4.90	0/5	1/5	1/10
5.92	4/5	3/5	7/10
6.91	5/5	2/5	7/10

In the limit test at 4.90 mg/L, one female died on day 4. Following exposure to higher concentrations (5.92 and 6.91 mg/L), seven males and two females died during the exposure period (prior to chamber removal); the remaining early deaths in these two dose groups occurred during the first 24 hours postexposure.

Clinical Observations: Upon removal from the exposure chamber, all treated animals were reported to have irregular or labored breathing and hunched posture; in addition, all treated animals were observed to have test substance on their fur up to 6 days postexposure. Other signs of toxicity frequently observed in animals that died prior to sacrifice included lethargy, reduced or absent feces, ocular discharge or irritation and rales; less frequently reported signs included lateral recumbency, abnormal gait and loss of balance. Similar signs of toxicity, including rales, ocular discharge, and reduced or absent feces, were reported in animals that survived treatment; all surviving animals appeared normal from day 10 through study termination on day 14.

Body Weights: Many animals surviving treatment lost weight during the first 24-48 hours postexposure (1-24% of initial weight). By the end of the 13-day observation period, however, all surviving animals had gained weight, with similar gains across dose groups for each sex. Males gained an average of 43% (range 29-71%) and females gained an average of 12% (range 4-18%).

Gross Necropsy: The lungs of animals that died prior to sacrifice were reported to be extremely red and frequently mottled or edematous. Other gross changes that were reported frequently in the animals that died prior to sacrifice included discolored liver and intestines (red, pink, yellow, or tan), and gaseous distention of the gastrointestinal tract. Changes that occurred less frequently among the animals that died prior to sacrifice included corneal opacity and bladder filled with black fluid. With the exception of discolored lungs (moderately red, occasionally with an uneven surface), there were no other macroscopic abnormalities in animals that survived treatment. This discoloration was considered a typical finding in animals euthanized by ether inhalation.

LC_{50} Determination: The estimated acute inhalation LC_{50}, calculated by probit analysis, was approximately 5.80 mg/L (95% confidence interval 5.58-6.03 mg/L) in males, and, in both sexes combined, approximately 6.00 mg/L (95% confidence interval 5.26-6.85 mg/L); the estimated acute inhalation LC_{50} in females, estimated graphically because the data did not allow probit analysis, was approximately 6.20 mg/L. These values correspond to Toxicity Category: IV.

D. REVIEWERS' COMMENTS: The reviewers agree with the study author's interpretation of the reported findings. Rats were exposed to Suttocide A, 50% solution near or above the limit concentration (5 mg/L), and the estimated acute inhalation LC_{50} was approximately 6.00 mg/L for both sexes combined. Signs of toxicity reported in treated animals included irregular or labored breathing, hunched posture, and lethargy. The presence of the test material on the fur of the study animals for as long as 6 days postexposure raises concern that the route of exposure in this study was not limited to the intended inhalation route, but also included oral and dermal absorption. The test material's toxicity from inhalation exposure may have, therefore, been overestimated. However, 14 of the 15 unscheduled deaths occurred during the first 24 hours after

exposure, including nine deaths prior to removal from the exposure chamber. In addition, the estimated acute oral LD_{50} in rats (both sexes combined) was approximately 2100 mg/kg (see DER 2-99/274; MRID No. 424845-01 in this submission). Therefore, the estimated acute inhalation LC_{50} is most likely a reasonable approximation.

In addition, the following technical and reporting deficiencies were noted, but were judged not to have affected the outcome of the study:

- The relative humidity in the exposure chamber during the various exposures was outside of the recommended range of 40-60%. During the mid- and high-dose exposures, the relative humidity in the chamber was 55-88%; this finding is not surprising, given the nature of the test material (i.e., 50% water). During the 4.92-mg/L exposure, however, relative humidity in the chamber was only 33-35%; no explanation was provided for this deviation.

- The percentage of oxygen in the chamber atmosphere was not reported. However, the total air flow into the chamber (49.0-50.9 L/min) was sufficient to ensure that adequate oxygen was available to the test animals during the exposure period.

- The age of the study animals was not reported; however, based on the body weights of the animals, it appears that the animals were young adults.

- A full description of the environmental conditions in the animal room, including the humidity, number of air changes per hour and photo-period, was not provided.

- Data for the in-chamber observations were presented only in the study report's summary, and not in the results section or in tabular form. Without individual animal data, it was not possible to verify the accuracy of the clinical signs as reported in the summary.

E. QUALITY ASSURANCE MEASURES: Was the test performed under GLPs? Yes. (A quality assurance statement, signed and dated June 22, 1992, was included in the report.)