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| Document Title | | | SUPPORT: ACUTE INHALATION TOXICITY STUDY IN RATS - LIMIT TEST (FINAL REPORT), WITH 2-ETHYLHEXYL CHLOROFORMATE (2-EHCF), WITH COVER LETTER DATED 2/7/2001 (SANITIZED) | | |
| Chemical Category | | | 2-ETHYLHEXYL CHLOROFORMATE | | |

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TSCA Section 8(e) Coordinator
Office of Toxic Substances
U.S. Environmental Protection Agency
1200 Pennsylvania Ave, NW
Washington, D.C. 20460

8E HQ-01-14854
29010000 109_{st}

Re: Toxic Substances Control Act (TSCA)
Supplemental Information for January 24, 2001 Section 8(e) submission
2-Ethylhexyl chloroformate (2-EHCF)
CAS #24468-13-1

Dear Sir or Madam:

As referenced in the January 24, 2001 TSCA Section 8(e) submission for 2-EHCF, upon receipt of the final testing results by _____, a copy would be sent to your attention. A copy of the following final test results is attached as well as a sanitized version for inclusion in the public files:

Name of the Study: "Acute Inhalation Toxicity Study in Rats - Limit Test"
Chemical Studies: 2-Ethylhexyl chloroformate (2-EHCF)
Chemical Abstract Service Registry Number: CAS #24468-13-1

If you have any questions, please contact me at _____

Sincerely,

Attachments: 1

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ACUTE INHALATION TOXICITY STUDY IN RATS - LIMIT TEST**TEST METHOD NO.:****STUDY NUMBER:****SPONSOR:****TEST SUBSTANCE IDENTIFICATION:**

2-Ethylhexyl Chloroformate (2-EHCF)

TEST SUBSTANCE DESCRIPTION:

Clear colorless liquid

DATE RECEIVED:**REFERENCE NO.:****DATE OF TEST:****NOTEBOOK NO.:****1. PURPOSE**

To provide information on health hazards likely to arise from a short-term continuous exposure (4 hours) to 2-Ethylhexyl Chloroformate (2-EHCF) via the inhalation route.

2. PROCEDURE

A group of Sprague-Dawley derived, albino rats was received from .

The animals were singly housed in suspended stainless steel caging with mesh floors. Litter paper was placed beneath the cages and was changed at least three times per week. The animal room was temperature controlled and had a 12-hour light/dark cycle. The animals were fed Purina Rodent Chow #5012 and filtered tap water was supplied *ad libitum* by an automatic water dispensing system except during exposure.

Ten healthy rats (five male and five female) were selected for test. The study was terminated after 190 minutes of exposure due to complete mortality. Chamber concentration and particle size distribution of the test substance were determined periodically during the exposure period. Bodyweights were recorded prior to exposure and again after death. A gross necropsy was performed on all decedents as soon as possible after death.

3. INHALATION PROCEDURES

A. Exposure Chamber

Rectangular whole body Plexiglas[®] chamber with a volume of 150 liters, with pre-chamber, operated under slight negative pressure.

B. Air Supply

Approximately 25.1 liters per minute (Lpm) of dry filtered air was supplied by an air compressor (JUN-AIR) to the spray atomization nozzle. Approximately 20.6 Lpm of filtered conditioned room air was supplied as diluent air.

C. Atmosphere Generation

The test atmosphere was generated using a ¼ inch JCO atomizer, FC4 fluid cap and AC1502 air cap (Spraying Systems Inc.). Compressed air was supplied at 30 psi. The test substance was metered to the atomization nozzle through Size 14 Master Flex Tygon tubing, using a Master Flex Pump Model #7520-35.

D. Ambient Conditions

The room temperature and relative humidity ranges during exposure were 19-20°C and 27-39%, respectively. The temperature and relative humidity ranges within the exposure chamber during the test were 19-21°C and 40-48%, respectively. Room conditions were measured with a Dickson Temperature-Humidity Monitor Model TH550 and in-chamber measurements were made with a Taylor Humidity-Temperature Indicator 5502.

E. Nominal Chamber Concentration Measurements

The aerosolization of the test substance and total airflow into the chamber were carefully monitored during exposure. The nominal concentration is defined as follows:

$$\text{Nominal Concentration} = \frac{\text{Total Test Substance Used}}{\text{Average Airflow} \times \text{Total time}}$$

Prior to the initiation of the study, trials were conducted to determine the proper equipment and settings needed to attain the targeted exposure concentration.

F. Gravimetric Chamber Concentration Measurements

Gravimetric samples were withdrawn on 4 occasions from the breathing zone of the animals. Samples were collected using 25 mm glass fiber filters (GF/B Whatman) in a filter holder attached by 1/4 inch tygon tubing to an Emerson Electric vacuum pump Model #S55NXMLD-6711. Filter papers were weighed before and after collection to determine the mass collected. This value was divided by the total volume of air sampled to determine the chamber concentration. The collections were carried out for 3 minutes at airflows of 4 Lpm.

G. Analytical Chamber Concentration Measurements

As part of the original design of the study, attempts were made to assess the analytical concentration of the chamber atmosphere during pre-test trials as well as during the animal exposure. A MicroFID meter (PE Photovac) was used in an attempt to determine the levels of 2-EHCF in the chamber atmosphere. The device was calibrated according to manufacturer's instructions and tested during pre-exposure trials on December 18, 2000. Results at that time indicated that the probe's readings were similar but generally lower than the gravimetric measurements. It was therefore decided that the animal exposure would be based on the gravimetric measurements. On the date of the animal exposure, the probe was again calibrated according to the manufacturer's instructions but during the test, the probe proved unreliable by failing to respond at all.

H. Particle Size Distribution

An eight-stage Anderson cascade impactor was used to assess the particle size distribution of the test atmosphere. Samples were withdrawn from the breathing zone of the animals at two intervals during the exposure. The filter paper collection stages were weighed before and after sampling to determine the mass collected at each stage. The aerodynamic mass median diameter and geometric standard deviation were determined graphically using two-cycle logarithmic probit axes.

I. Exposure Period

The exposure period was shortened to 190 minutes due to complete mortality. The exposure period was extended beyond 190 minutes to allow the chamber to reach equilibrium (T_{99}). The times for 90 and 99% equilibration of the atmosphere were 7.5 and 15.1 minutes, respectively. At the end of the exposure period, the generation was terminated and the chamber was operated for a further 10 minutes with clean air. At the end of this period the animals were removed from the chamber.

4. RESULTS

Nominal and gravimetric chamber concentrations are shown in Table 1. Particle size sampling results are presented in Table 2. Individual bodyweights and mortalities are presented in Table 3. Cage-side and necropsy observations are shown in Tables 4 and 5.

All animals died as a result of exposure to the test atmosphere. The gravimetric chamber concentration was 2.02 mg/L. The mass median aerodynamic diameter was estimated to be 3.6 microns based on the particle size distribution as measured with an Anderson Cascade Impactor.

All animals died within 190 minutes of exposure to the test atmosphere. In-chamber animal observations noted prior to death included ocular and nasal discharge, irregular respiration, dyspnea, gasping, hunched posture and/or hypoactivity. Gross necropsy of the decedents revealed corneal opacity, edema of the lungs and/or discoloration of the lungs and intestines.

5. CONCLUSION

The acute inhalation LC_{50} of 2-Ethylhexyl Chloroformate (2-EHCF) is less than 2.02 mg/L (gravimetric). Additional testing would be required to establish an LC_{50} for this compound.

SIGNATURES

We the undersigned declare that the methods, results and data contained in this report faithfully reflect the procedures used and raw data collected during the study.

D

TABLE 1: NOMINAL CHAMBER CONCENTRATION

| Target Exposure Level (mg/L) | Total Test Substance Used(g) | Average Total Airflow (Lpm) | Total Time of Exposure (min) | Nominal Concentration¹ (mg/L) |
|-------------------------------------|-------------------------------------|------------------------------------|-------------------------------------|---|
| 2.0 | 209.6 | 45.7 | 190 | 24.14 |

GRAVIMETRIC CHAMBER CONCENTRATIONS

| Sample Number | Time of Sampling (hour) | Mass Collected (mg) | Airflow Sampled (Lpm) | Collection Time (min) | Chamber Concentration (mg/L) |
|-------------------------------------|--------------------------------|----------------------------|------------------------------|------------------------------|-------------------------------------|
| 1 | 0.5 | 25.0 | 4 | 3 | 2.08 |
| 2 | 1 | 25.6 | 4 | 3 | 2.13 |
| 3 | 2 | 22.8 | 4 | 3 | 1.90 |
| 4 | 2.5 | 23.8 | 4 | 3 | 1.98 |
| Average ± Standard Deviation | | | | | 2.02 ± 0.10 |

¹ Nominal Concentration (mg/L) = $\frac{\text{Total Test Substance Used (mg)}}{\text{Average Airflow (Lpm) X Total Time (min)}}$

TABLE 2: PARTICLE SIZE DISTRIBUTION

| Stage | Effective Cutoff Diameter (μm) | % of Total Particles Captured (by weight) | Cumulative (%) ¹ |
|-----------------|---|---|-----------------------------|
| Sample 1 | | | |
| 0 | 9.0 | 6.6 | 93.4 |
| 1 | 5.8 | 16.5 | 76.8 |
| 2 | 4.7 | 11.7 | 65.1 |
| 3 | 3.3 | 28.5 | 36.6 |
| 4 | 2.1 | 17.6 | 19.1 |
| 5 | 1.1 | 10.7 | 8.4 |
| 6 | 0.7 | 5.9 | 2.5 |
| 7 | 0.4 | 2.0 | 0.5 |
| F | 0.0 | 0.5 | 0.0 |
| Sample 2 | | | |
| 0 | 9.0 | 4.7 | 95.3 |
| 1 | 5.8 | 16.6 | 78.7 |
| 2 | 4.7 | 12.8 | 66.0 |
| 3 | 3.3 | 28.6 | 37.4 |
| 4 | 2.1 | 20.4 | 17.0 |
| 5 | 1.1 | 10.1 | 6.9 |
| 6 | 0.7 | 4.7 | 2.2 |
| 7 | 0.4 | 1.8 | 0.4 |
| F | 0.0 | 0.4 | 0.0 |

SUMMARY OF PARTICLE SIZE DISTRIBUTION

| Time of Sample (hour) | Collection Time (minutes) | Mass Median Aerodynamics Diameter (μm) | Geometric Standard Deviation |
|-----------------------|---------------------------|---|------------------------------|
| 1.5 | 4 | 3.7 | 2.35 |
| 3 | 4 | 3.5 | 2.06 |

¹ Percent of particles smaller than corresponding effective cutoff diameter.

TABLE 3: INDIVIDUAL BODYWEIGHTS AND MORTALITY

| Animal No. | Sex | Bodyweight (g) | | | Mortality | |
|------------|-----|----------------|-------|--------|------------------|--------|
| | | Initial | Day 7 | Day 14 | Day ¹ | Weight |
| 9774 | M | 300 | - | - | 0 | 288 |
| 9775 | M | 285 | - | - | 0 | 278 |
| 9776 | M | 280 | - | - | 0 | 271 |
| 9777 | M | 291 | - | - | 0 | 280 |
| 9778 | M | 281 | - | - | 0 | 275 |
| 9779 | F | 225 | - | - | 0 | 219 |
| 9780 | F | 225 | - | - | 0 | 220 |
| 9781 | F | 198 | - | - | 0 | 194 |
| 9782 | F | 210 | - | - | 0 | 205 |
| 9783 | F | 196 | - | - | 0 | 192 |

¹ All animals died during exposure to the test atmosphere.

TABLE 4: INDIVIDUAL CAGE-SIDE OBSERVATIONS

| <u>Animal Number</u> | <u>Findings</u> | <u>Day of Occurrence</u> |
|----------------------|-----------------|--------------------------|
| <u>MALES</u> | | |
| 9774-9778 | Dead | During exposure |
| <u>FEMALES</u> | | |
| 9779-9783 | Dead | During exposure |

TABLE 5: INDIVIDUAL NECROPSY OBSERVATIONS

| <u>Animal Number</u> | <u>Tissue</u> | <u>Findings</u> |
|-------------------------|----------------------------|--|
| <u>MALES</u> | | |
| 9774, 9777 | Eye Lungs Intestines | Corneal opacity Extreme edema, dark red Moderately red |
| 9775, 9776, 9778 | Lungs Intestines | Extreme edema, dark red Moderately red |
| <u>FEMALES</u> | | |
| 9779, 9780, 9781, 9782, | Lungs Intestines | Extreme edema, dark red Moderately red |
| 9783 | Eye Lungs Intestines | Corneal opacity Extreme edema, dark red Moderately red |