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

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OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

APR 1 1992

MEMORANDUM:

Subject: EPA ID # 099901-000707: Octhilinone. Review of Skane M-8 Technical, HQ: Evaluation of the Upper Airway Irritation Potential (RD_{50}) in Mice (MRID # 420911-01)

EPA Record No. S380416
Caswell No. 613C
HED Project No. 2-1490

From: Guruva B. Reddy, D.V.M., Ph. D. 3/31/92
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To: Barbara Briscoe/Franklin Rubis
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Thru: Marion P. Copley, D.V.M., D.A.B.T.
Section Head
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Health Effects Division (H7509C)

The Toxicology Branch I has reviewed the study submitted by Rohm & Haas Company regarding the evaluation of the upper airway irritation potential (RD_{50}) of octhilinone in mice. Following are our conclusions:

CONCLUSIONS: The study meets the objectivity of demonstrating the irritability of the compound in comparison to formaldehyde, however, failed the criteria set forth in Subdivision, F Series 81-3 for Acute Inhalation Study.

CLASSIFICATION: core-Supplementary

ACTION REQUESTED: Under cover letter November 7, 1991, the Rohm

& Haas Company submitted a study entitled " Skane M-8 Technical, HQ: Evaluation of the Upper Airway Irritation Potential (RD_{50})" for review.

STUDY CONCLUSIONS:

The RD_{50} was 19.9 μg/L (0.0199 ppm) in comparison to 5.4 ppm for formaldehyde. Doses tested 3.2, 3.9, 6.1, 6.5, 7.1, 7.5 and 9.4 μg/L in Swiss-Webster CFW mice. The MMAD (mass median aerodynamic diameter) was 1.8 μ and GSD (geometric standard deviation) was 2.97 μ. Particles <1 μ was ≈ 27 %.

Reviewed by: Guruva B. Reddy, DVM, PHD 3/30/92
Section 4, Tox. Branch 1 (H7509C)
Secondary reviewer: Marion P. Copley, DVM, DABT
Section 4, Tox. Branch 1 (H7509C) 3/30/92

DATA EVALUATION REPORT

STUDY TYPE: Acute Inhalation (81-3)/Mice

TOX. CHEM NO: 613C

MRID NO.: 420911-01

TEST MATERIAL: Skane M-8 Technical, HQ

SYNONYMS: Kathon® 893T Industrial Microbicide and Octhilinone

STUDY NUMBER: Rohm & Haas Report No. 90RC-180

SPONSOR: Rohm & Haas Company
Philadelphia, PA

TESTING FACILITY: International Research and Development Corp.
Mattawan, MI

TITLE OF REPORT: Skane M-8 Technical, HQ: Evaluation of the Upper Airway Irritation Potential (RD_{50})

AUTHOR(S): Charles E. Ulriach

REPORT ISSUED: June 14, 1991

CONCLUSION: The RD_{50} was 19.9 μg/L (0.0199 ppm) in comparison to 5.4 ppm for formaldehyde. Doses tested 3.2, 3.9, 6.1, 6.5, 7.1, 7.5 and 9.4 μg/L in Swiss-Webster CFW mice. The MMAD (mass median aerodynamic diameter) was 1.8 μ and GSD (geometric standard deviation) was 2.97 μ. Particles < 1 μ was ≈ 27 %.

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The study meets the objectivity of demonstrating the irritability of the compound in comparison to formaldehyde, however, failed the criteria set forth in Subdivision, F Series 81-3 for Acute Inhalation Study.

A. **MATERIALS:**

1. **Test compound:** Skane M-8 Technical, HQ. Description - Amber liquid, Batch # - 3192, Lot # - ON 1760, Purity - > 95 %. Positive control - Formaldehyde, Lot # 09507EX, Purity - 37 % (v/v) in water; Source - Aldrich Chemical Company. Vehicle

- Propylene glycol from Sigma Chemical Co.

2. **Test animals:** Species: Mice, Strain: Swiss-Webster CFW, Age: 61 - 70 days, Weight: 26 - 34 grams, Source: Charles River Labs., Portage, MI.

B. **STUDY DESIGN:**

1. **Animal assignment**

Animals were acclimated for 19 days to the controlled temperature, humidity and light (12/12 hours, light and dark cycles). Animals were assigned 4/group to the following test groups:

Test Group	Exposure Concentration (mcg/L)	Number of Animals male
28	3.9	4
29	6.1	4
33	7.5	4
34	9.4	4
35	3.2	4
36	6.5	4
37	7.1	4

The objectivity of the study was to evaluate the upper airway irritation potential of a test material.

Preliminary studies (group 1 to 27) established the suitability of formaldehyde as the positive control and the RD_{50} (respiratory depression) was 5.4 ppm. At exposure levels above 10 ppm both upper and lower respiratory tract irritation occurred. Therefore, for RD_{50} calculation only data with exposure concentration below 10 ppm was used. During the exposure with Skane M-8, a number of groups (30, 31, 32 and 38) presented both upper and lower respiratory tract irritation, therefore, these data were excluded from analysis.

2. **Inhalation Conditions**

Exposure was by head only method based on the procedures of Alarie (1966 and 1973). The plethysmograph consisted of a large, glass, standard taper-joint which would fit the matching joint in the exposure chamber. The head of the mouse protruded through a hole in the rubber seal of the plethysmograph into the exposure chamber. After a acclimation period of 10 minutes, respiratory rate was recorded for 5 minute control period, followed by 10-minute

exposure to the test material and a 10-minute post-exposure period. The respiratory rates for the four mice were continuously monitored electronically and recorded on strip chart. The average respiration rate for the control and the exposure period was estimated visually from the recording strip.

3. **Statistics** - The data was analyzed using Bliss (The determination of dosage-mortality curve from small numbers; Quart. J. Pharm. Pharmacol., 11, 1938) for RD_{50}.

4. A signed quality assurance statement was enclosed.

C. **METHODS AND RESULTS:**

A concentration of test material in the vehicle was aerosolized using Dautrebande nebulizer and fed into the exposure chamber.Exposure concentrations of the chamber atmosphere was collected on 25 mm glass fiber filter at the rate of 0.96 L/min. for 9 minutes, then extracted, diluted and the concentrations determined using reverse-phase HPLC at 275 nm. Linearity of the detector response ranged from 1 to 60 μg/ml and had a correlation of coefficient of 0.999. The recovery ranges of the test material from glass fiber filters ranged from 83 to 122 % of the added amounts.

Aerosol particle size was determined analytically, two times during the development phase, using an Anderson® 8-stage cascade impactor on filters, at a rate of 28.3 L/min for 20 minutes. The cumulative percentages, by weight, of particles with aerodynamic diameters smaller than the cutoffs for the individual stages were derived and plotted. The mass median aerodynamic diameter (MMAD) and geometric standard deviations (GSD) were calculated according to that of Raabe (1978).

The RD_{50} was calculated using a method based on Bliss (1938).

Results - The actual aerosol concentrations achieved are reported under experimental design. Aerosol particles ranged in size from 0.44 to 9 μ; % of particles < 1 μ were $\approx$ 27. The mass median aerodynamic diameter of 1.8 μ and geometric standard deviation of 2.97 μ was reported. The % difference in respiratory rate at various concentrations were as follows:

Group #	% Difference	Concentration (μg/L)
28	22	3.9
29	30	6.1
33	38	7.5
34	37	9.4
35	27	3.2
36	38	6.5
37	33	7.1

The data generally follows a dose-related decrease in the respiratory rate. Based on the above data, the author concluded that the RD_{50} for Skane M-8 Technical was 19.9 μg/L (0.0199 ppm).

D. **DISCUSSION:**

The data was generated to test the irritation potential of Skane M-8 Technical in comparison to formaldehyde. The RD_{50} for positive control formaldehyde was 5.4 ppm. The RD_{50} of the test material was 19.9 μg/L (0.0199 ppm). The particle size $< 1\ \mu$ comprised $\approx$ 27 % of the aerosol concentration of the chamber and is adequate. There were no deaths. No other clinical signs associated with the exposure to the compound was reported. The study as presented adequately satisfies the objective of the study, however, it does not satisfy the requirements set forth in Subdivision F Guideline, 81-3, for Acute Inhalation Study.