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

SEP 23 1993

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OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Kathon 886F Biocide: Evaluation of the Upper Airway Irritation Potential (RD_{50})

TO: Mr. John Lee/Ms. Karen Leavy (PM-11)
Product Manager/PM Team Reviewer
Registration Division (H7505C)

FROM: David S. Liem, Ph.D. David S. Liem 9/17/93
Toxicology Branch II, Section II
Health Effects Division (H7509C)

THROUGH: K. Clark Swentzel K. Clark Swentzel 9/20/93
Section II Head, Toxicology Branch II
Health Effects Division (H7509C)
and
Marcia van Gemert, Ph.D. Marcia van Gemert 9/20/93
Chief, Toxicology Branch II
Health Effects Division (H7509C)

TEST MATERIAL: Kathon 886F (5-chloro-2-methyl-3(2H)-isothiazolone 8.6% and 2-methyl-3(2H)-isothiazolone 2.6%)

REGISTRANT: Rohm and Haas, Spring House, PA 19477

DP BARCODE#: D193738 ID#: 00707-00130 SUBMISSION#: S445537

CHEMICAL#: 107103 & 107104 MRID#: 428380-01 CASWELL NO.: 195C

ACTION REQUESTED: Review a supplemental Respiratory Irritation (RD_{50}) study on Kathon 886F in mice.

BACKGROUND:

This study was submitted to evaluate the potential of Kathon 886F biocide to produce upper airway irritation and to provide information useful in establishing workplace exposure limits and hazard assessment. This study was not intended to satisfy a specific registration requirement. It is noted that an acute

inhalation study with Kathon 886 (5-chloro-2-methyl-4-isothiazolin-3-one 9.7% and 2-methyl-4-isothiazolin-3-one 3.4%) that was classified as core-minimum by the Toxicology Branch/HED/OPP is available. The LC_{50} was determined to be > 4.62 mg/L in rats (MRID# 244707 & 244708).

CONCLUSIONS:

Six groups of five male mice each were exposed to actual exposure concentrations of 7, 10, 38, 132, 162, and 407 µg/L of Kathon 886F, respectively.

Under the conditions of the study, the median Respiratory Depression (RD_{50}) for Kathon 886F Biocide in mice was calculated to be 69 µg/L (range 50 - 96 µg/L) (with a 95% confidence limits). Based on the American Standard Test Method (ASTM) for Estimating Sensory Irritancy for Airborne Chemicals classification, Kathon 886F biocide is considered to induce an extreme respiratory depression response in mice.

This study is a non-guideline study and the results submitted are acceptable.

Reviewed by : David S. Liem, Ph.D.
Toxicology Branch II, Section II
Secondary Reviewer: K. Clark Swentzel 11/2/93
Toxicology Branch II, Section II

DATA EVALUATION REPORT

STUDY TYPE: Upper Respiratory Irritation Study (RD_{50})
A non-guideline Study

DP#:D193738 ID#:00707-00130 CASWELL NO.:195C MRID#:428380-01

TEST MATERIAL: Kathon 886F (5-chloro-2-methyl-3(2H)-isothiazolone 8.6% and 2-methyl-3(2H)-isothiazolone 2.6%)

SYNONYMS: 5-chloro-2-methyl-3(2H)-isothiazolone (no. 107103)

STUDY NUMBER: Rohm and Haas Report No. 91RC-047; IRDC# 285-047

SPONSOR: Rohm and Haas, Spring House, PA 19477

TESTING FACILITY: IRDC, 500 N. Main St., Mattawan, Michigan 49071

TITLE OF REPORT: Kathon 886F Biocide: Evaluation of the Upper Airway Irritation Potential (RD_{50})

AUTHOR: Chris N. Papagiannis

REPORT ISSUED: April 13, 1993

CONCLUSIONS:

Under the conditions of the study, the median Respiratory Depression (RD_{50}) for Kathon 886F biocide was calculated to be 69 μg/L (range 50 - 96 μg/L) (with a 95% confidence limits). Based on the American Standard Test Method (ASTM) for Estimating Sensory Irritancy for Airborne Chemicals classification, Kathon 886F biocide is considered to induce an extreme respiratory depression response in mice.

This study is a non-guideline study and the results submitted are acceptable.

TEST MATERIAL: Kathon 885F, a mixture of 8.6% of 5-chloro-2-methyl-3(2h)-isothiazolone and 2.6% of 2-methyl-3(2H)-isothiazolone.

TEST ANIMALS: Male Swiss-Webster mice, approximately 59-61 days of age, with body weight ranging from 29 to 34 g on the day of exposure, and were acclimation for a period of 6-52 days prior to exposure.

HUSBANDRY OF TEST ANIMALS (during non-exposure periods)

Feed and Water: Certified Rodent Chow #5002, Purina Mills, Inc, St. Louis, Missouri and local tap water were provided ad libitum. Food and water were withheld during exposure period.

Environmental Parameters: Maintained under controlled environment; a 12-hour light/dark cycle; temperature range = 18-26°C; relative humidity range = 40-70%. Mice were housed in groups of five in polycarbonate shoe box type cages with beta chip bedding material.

PROCEDURES

Selection of Test Animals: Five male mice, free from disease, with body weight ranging from 29-34 gms were selected for each group. The mean body weights (in grams) of each group prior to dosing were as follows:

Group 8	Group 9	Group 10	Group 11	Group 15	Group 16
30± 0.96	32 ± 1.8	33 ± 0.96	29 ± 1.7	31 ± 1	31 ± 1.3

Generation of Exposure Atmospheres: Kathon liquid solution is pumped into an atomizer which generates vapor/aerosol atmospheres. Twenty liters per minute of vapor/aerosol atmosphere was drawn from the atomization chamber to the exposure chamber.

Determination of Exposure Concentrations: The nominal exposure concentration for each dose group was calculated by dividing the amount of test material solution used during the exposure by the total volume of air passed through the atomization chamber. The actual exposure concentrations were determined by sampling the exposure atmosphere for 7 or 9 minutes and collected in a 50 ml of a 75% aqueous methanol solution using a double fritted bubblers. The samples were then analyzed using a reverse phase high performance liquid chromatography for the two components of the test material formulation. The exposure concentrations were monitored with a Sibita Light Scattering Aerosol Photometer to ensure that the exposure concentrations were stable during the exposure periods.

Particle Size Determination: The particle size distribution of aerosol in the atomization chamber was determined with an Anderson 8-stage cascade impactor. The chamber was sampled at 28.3 L/min. for a suitable duration and the amount of aerosol collected on each stage was determined by HPLC analysis. The cumulative percentage, by weight, of particles with aerodynamic diameters smaller than the cutoffs for the individual stages were derived and plotted by a computer. The mass median aerodynamic diameter and geometric standard deviations were then calculated.

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Animal Exposure Method: The test article was administered using a head only exposure apparatus. Each mouse was held in an individual body plethysmograph. The plethysmograph was then inserted into matching joints on the exposure chamber.

Respiratory Rate Determination: The respiratory rate was recorded for a 5-minute control period, followed by a 10-minute exposure to the test atmosphere, and a 15-minute post-exposure period.

Respiratory Depression Response Classification: Classification for respiratory depression responses was based on the American Standard Test Method (ASTM) for Estimating Sensory Irritancy for Airborne Chemicals as follows:

- Slight response: 12 - 20% respiratory depression
- Moderate response: 20 - 50% respiratory depression
- Extreme response: 50 - 85% respiratory depression

Sacrifice: All animals were sacrificed by CO_2 asphyxiation and discarded after the post-exposure period.

RESULTS

Exposure Concentrations: The nominal and actual exposure concentrations for each group are as follows:

Treated Group	Nominal Concentration (μ/L)	Actual Concentration (μg/L)	Weight of Kathon Used During Exposure (g)
8	910	407	16.169
9	440	162	7.763
10	190	132	6.518
11	40	38	7.396
15	21	7	7.470
16	25	10	8.635

Particle Size Determination: The particle size distribution is summarized as follows:

Analytical Concentration(μg/L)	Mass Median Aero-dynamic Diameter(μm)	Geometric Standard Deviation
407	2.5	1.91
162,132	2.6	1.93
38	1.6	2.61
7,10	1.8	2.67

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Respiratory Rates: The respiratory rates for each treated group are summarized as follows:

Group	Analytical Conc. (µg/L)	Breaths per Minute		% Decrease in Respiratory Rate
		No Exposure	Exposure	
8	407	255	80	69%
9	162	245	80	67%
10	132	250	110	56%
11	38	280	160	43%
15	7	310	225	27%
16	10	235	185	21%

The median Respiratory Depression (RD_{50}) of mice exposed to Kathon 886F biocide was calculated to be 69 µg/L (range 50-96µg/L), with a 95% confidence limits.

DISCUSSIONS AND CONCLUSIONS

Under the conditions of the study the median Respiratory Depression (RD_{50}) for Kathon 886F Biocide was calculated to be 69 µg/L (range 50 - 96 µg/L) (with a 95% confidence limits). Based on the American Standard Test Method (ASTM) for Estimating Sensory Irritancy for Airborne Chemicals classification, Kathon 886F biocide is considered to induce an extreme respiratory depression response in mice.

This study was submitted to evaluate the potential of Kathon 886F biocide to produce upper airway irritation and to provide information useful in establishing workplace exposure limits and hazard assessment. This study was not intended to satisfy a specific registration requirement.

A FIFRA GLP Compliance Statement and a Quality Assurance Statement were provided, signed and dated.

This study is a non-guideline study and the results submitted are acceptable.