STUDY TITLE

1,1,1,3,3,3-Hexafluoro-2-methoxypropane (HFMOP):
Acute Dermal Toxicity in Rats

DATA REQUIREMENT

U.S. EPA Health Effects Test Guidelines, OPPTS 870.1200 (1998)

AUTHOR

Melissa Slonina, BS

STUDY COMPLETED ON

October 10, 2017

PERFORMING LABORATORY

Product Safety Labs

LABORATORY STUDY NUMBER

46319

SPONSOR

Halocarbon Products Corporation
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GOOD LABORATORY PRACTICE COMPLIANCE STATEMENT

1,1,1,3,3,3-Hexafluoro-2-methoxypropane (HFMOP)

This study meets the requirements of U.S. EPA GLP (TSCA): 40 CFR Part 792, 1989. Specific information related to the characterization of the test substance as received and tested is the responsibility of the study Sponsor (see Test Substance section).

Study Director: M. Slonina Date: 10/10/17

Name of Signer: Melissa Slonina, BS

Name of Company: Product Safety Labs

Sponsor: _____ Date: _____

Name of Signer: _____

Name of Company: Halocarbon Products Corporation

Submitter: _____ Date: _____

Name of Signer: _____

Name of Company: Halocarbon Products Corporation

QUALITY ASSURANCE STATEMENT

The Product Safety Labs' Quality Assurance Unit has reviewed this final study report to assure the report accurately describes the methods and standard operating procedures, and that the reported results accurately reflect the raw data of the study.

QA activities for this study:

QA Activity	Performed By	Date Conducted	Date Findings Reported To Study Director And Management
Protocol review	A. Adamiec; A. Villagran	Oct 1, 2013[1]; Sep 15, 2017	Oct 1, 2013; Sep 18, 2017
In-process inspection: *Initiation of dosing*	B. Simms	Aug 23, 2017	Aug 23, 2017
Raw data audit	A. Villagran	Sep 15, 2017	Sep 18, 2017
Draft report review	A. Villagran	Sep 15, 2017	Sep 18, 2017

Final report reviewed by:

Alicia Villagran

Alicia Villagran, RQAP-GLP
Quality Assurance Auditor
Product Safety Labs

Oct. 10, 2017
Date

[1] PSL's "generic" protocol used for this study was reviewed by the Quality Assurance group on this date.

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1,1,1,3,3,3-HEXAFLUORO-2-METHOXYPROPANE (HFMOP): ACUTE DERMAL TOXICITY IN RATS

PROTOCOL NO.:	P322.RAT
STUDY NUMBER:	46319
SPONSOR:	Halocarbon Products Corporation 1100 Dittman Court North Augusta, SC 29861
TEST SUBSTANCE IDENTIFICATION:	1,1,1,3,3,3-Hexafluoro-2-methoxypropane (HFMOP) Lot #: HFMOP17004
DATE RECEIVED:	August 18, 2017
PSL REFERENCE NO.:	170818-3R
STUDY INITIATION DATE:	August 21, 2017
DATES OF TEST:	August 23 - September 6, 2017
NOTEBOOK NO.:	46319: pages 1-23

1. PURPOSE

To provide information on health hazards likely to arise from a short-term exposure to 1,1,1,3,3,3-Hexafluoro-2-methoxypropane (HFMOP) by the dermal route.

2. SUMMARY

An acute dermal toxicity test was conducted with rats to determine the potential for 1,1,1,3,3,3-Hexafluoro-2-methoxypropane (HFMOP) to produce toxicity from a single topical application. Under the conditions of this study, the single dose acute dermal LD_{50} of the test substance is greater than 5000 mg/kg of body weight in male and female rats.

Five thousand milligrams of the test substance per kilogram of body weight was applied to the skin of ten healthy rats for 24 hours. The animals were observed for mortality, signs of gross toxicity, and behavioral changes at least once daily for 14 days. Body weights were recorded prior to application (initial) and again on Days 7 and 14 (terminal). Necropsies were performed on all animals at terminal sacrifice.

All animals survived test substance administration, gained body weight, and appeared active and healthy during the study. There were no signs of gross toxicity, dermal irritation, adverse clinical effects, or abnormal behavior. No gross abnormalities were noted for any of the animals when necropsied at the conclusion of the 14-day observation period.

3. MATERIALS

A. Test Substance

The test substance, identified as 1,1,1,3,3,3-Hexafluoro-2-methoxypropane (HFMOP), Lot #: HFMOP17004, was received on August 18, 2017, and was further identified with PSL Reference Number 170818-3R. The test substance was stored at room temperature. Documentation of the methods of synthesis, fabrication, or derivation of the test substance is retained by the Sponsor.

The following information related to the characterization of the test substance was provided by the Sponsor:

Composition: 1,1,1,3,3,3-hexafluoro-2-methoxypropane - >99.99%, CAS #13171-18-1

Physical Description: Clear liquid

pH: Neutral molecule

Stability: Test substance was expected to be stable for the duration of testing.

Expiration Date: Not applicable

B. Animals

3.B.1 Number of Animals: 10

3.B.2 Sex: 5 Males and 5 Females. Females assigned to test were nulliparous and non-pregnant.

3.B.3 Species/Strain: Rats/Sprague-Dawley derived, albino

3.B.4 Age/Body Weight: Young adult (8-9 weeks)/males 261-280 grams and females 173-205 grams at experimental start.

3.B.5 Source: Received from SAGE® Labs on August 16, 2017.

4. METHODS

A. Husbandry

4.A.1 Housing: The animals were singly housed in suspended stainless steel caging, which conforms to the size recommendations in the most recent *Guide for the Care and Use of Laboratory Animals* (Natl. Res. Council, 2011). Enrichment (e.g., toy) was placed in each cage. Litter paper was placed beneath the cage and was changed at least three times per week.

4.A.2 Animal Room Temperature and Relative Humidity Ranges: 19-23°C and 45-60%, respectively.

4.A.3 Animal Room Air Changes/Hour: 12. Airflow measurements are evaluated regularly and the records are kept on file at Product Safety Labs.

4.A.4 Photoperiod: 12-hour light/dark cycle

4.A.5 Acclimation Period: 7 days

4.A.6 Food: Envigo Teklad Global 16% Protein Rodent Diet® #2016. The diet was available *ad libitum*.

4.A.7 Water: Filtered tap water was supplied *ad libitum*.

4.A.8 Contaminants: There were no known contaminants reasonably expected to be found in the food or water at levels which would have interfered with the results of this study. Analyses of the food and water are conducted regularly and the records are kept on file at Product Safety Labs.

B. Identification

4.B.1 Cage: Each cage was identified with a cage card indicating at least the study number and identification and sex of the animal.

4.B.2 Animal: A number was allocated to each rat on receipt and a stainless steel ear tag bearing this number was attached to the animal. This number, together with a sequential animal number assigned to study 46319, constituted unique identification. Only the sequential animal number is presented in this report.

5. PROCEDURE

A. Preparation and Selection of Animals

On the day prior to application, a group of animals was prepared by clipping the dorsal area and the trunk. After clipping and prior to application, the animals were examined for health, weighed (initial) and the skin checked for any abnormalities. Ten healthy, naive rats (five males and five females; not previously tested) were selected for test.

B. Preparation of Test Substance

The test substance was applied as received and mixed well prior to use.

C. Dose Calculations

Individual doses were calculated based on the initial body weights, taking into account the density (determined by PSL) of the test substance.

D. Application of Test Substance

Five thousand milligrams of the test substance per kilogram of body weight was applied evenly over a dose area of approximately 2 inches x 3 inches (approximately 10% of the body surface) and covered with a 2-inch x 3-inch, 4-ply gauze pad. The gauze pad and entire trunk of each animal were then wrapped with 3-inch Durapore tape to avoid dislocation of the pad and to minimize loss of the test substance. The rats were then returned to their designated cages. The day of application was considered Day 0 of the study.

After 24 hours of exposure to the test substance, the pads were removed and the test sites were gently cleansed with a 3% soap solution followed by tap water and a clean paper towel to remove any residual test substance.

E. Cage-Side Observations

The animals were observed for mortality, signs of gross toxicity, and behavioral changes during the first several hours after application, after patch removal, and then at least once daily thereafter for 14 days. Observations included gross evaluation of skin and fur, eyes and mucous membranes, respiratory, circulatory, autonomic and central nervous systems, somatomotor activity and behavior pattern. Particular attention was directed to observation of tremors, convulsions, salivation, diarrhea, and coma.

F. Body Weights

Individual body weights of the animals were recorded prior to test substance application (initial) and again on Days 7 and 14 (terminal).

G. Necropsy

All rats were euthanized via CO_2 inhalation at the end of the 14-day observation period. Gross necropsies were performed on all animals. Tissues and organs of the thoracic and abdominal cavities were examined.

6. STATISTICAL ANALYSIS

Statistical analysis was limited to the calculation of the mean density value for dosing.

7. STUDY CONDUCT

This study was conducted at Product Safety Labs' (PSL) test facility at 2394 US Highway 130, Dayton, New Jersey 08810. The Study Director for this study was Melissa Slonina, BS. The primary scientist for this study was Matthew Sorber, BS, with contributions from Monika Abraham, BA, Mark Schooley, and Katherine Sibley, BS. This study was conducted to comply with the Good Laboratory Practice (GLP) regulations as defined in:

- U.S. EPA GLP: Toxic Substances Control Act (TSCA): 40 CFR Part 792, 1989

and based on the following testing guideline:

- U.S. EPA Health Effects Test Guidelines, OPPTS 870.1200 (1998)

8. QUALITY ASSURANCE

The final report was audited for agreement with the raw data records and for compliance with the protocol, Product Safety Labs Standard Operating Procedures and appropriate Good Laboratory Practice Standards. Dates of inspections and audits performed during the study and the dates of reporting of the inspection and audit findings to the Study Director and Facility Management are presented in the Quality Assurance Statement.

9. AMENDMENTS TO THE PROTOCOL

None.

10. DEVIATIONS FROM THE PROTOCOL

None.

11. FINAL REPORT AND RECORDS TO BE MAINTAINED

Information on care of the test system, equipment maintenance and calibration, storage, usage, and disposition of the test substance, and all other records that would demonstrate adherence to the protocol will be maintained. Facility records which are not specific to the subject study will be maintained by the testing facility and archived according to PSL SOP.

The original, signed final report will be forwarded to the Sponsor. A copy of this signed report, together with the protocol and all raw data generated at PSL, is maintained in the PSL Archives. PSL will maintain these records for a period of at least five years. After this time, the Sponsor will be offered the opportunity to take possession of the records or may request continued archiving by PSL.

12. RESULTS

Individual body weights and doses are presented in Table 1. Individual cage-side and necropsy observations are presented in Tables 2 and 3, respectively.

All animals survived test substance administration, gained body weight, and appeared active and healthy during the study. There were no signs of gross toxicity, dermal irritation, adverse clinical effects, or abnormal behavior. No gross abnormalities were noted for any of the animals when necropsied at the conclusion of the 14-day observation period.

13. CONCLUSION

Under the conditions of this study, the single dose acute dermal LD_{50} of 1,1,1,3,3,3-Hexafluoro-2-methoxypropane (HFMOP) is greater than 5000 mg/kg of body weight in male and female rats.

14. REFERENCES

National Research Council. (2011). *Guide for the Care and Use of Laboratory Animals (8th ed.)*. Washington, DC: The National Academies Press.

SIGNATURE

1,1,1,3,3,3-Hexafluoro-2-methoxypropane (HFMOP)

I, 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.

M. Slonina
Melissa Slonina, BS
Study Director
Product Safety Labs

10/10/17
Date

TABLE 1: INDIVIDUAL BODY WEIGHTS AND DOSES

Animal No.	Sex	Body Weight (g)			Dose[1]
		Initial	Day 7	Day 14	mL
3201	M	261	291	328	0.95
3202	M	272	310	344	0.99
3203	M	263	302	337	0.96
3204	M	280	317	351	1.0
3205	M	276	297	333	1.0
3206	F	173	188	213	0.63
3207	F	179	192	213	0.65
3208	F	178	200	222	0.65
3209	F	177	183	197	0.65
3210	F	205	221	248	0.75

[1] The test substance was applied as received. Density - 1.371 g/mL.

TABLE 2: INDIVIDUAL CAGE-SIDE OBSERVATIONS

Animal Number	Animal Sex	Dose Level (mg/kg)	Observation	Day of Observation (x=observation is present)															
				0(1 hr)	0(4 hrs)	1	2	3	4	5	6	7	8	9	10	11	12	13	14
3201	M	5000	Active and healthy	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
3202	M	5000	Active and healthy	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
3203	M	5000	Active and healthy	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
3204	M	5000	Active and healthy	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
3205	M	5000	Active and healthy	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
3206	F	5000	Active and healthy	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
3207	F	5000	Active and healthy	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
3208	F	5000	Active and healthy	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
3209	F	5000	Active and healthy	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
3210	F	5000	Active and healthy	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x

TABLE 3: INDIVIDUAL NECROPSY OBSERVATIONS

Animal Number	Animal Sex	Dose Level (mg/kg)	Organ / Tissue	Observation
3201	M	5000	All tissues and organs	No gross abnormalities
3202	M	5000	All tissues and organs	No gross abnormalities
3203	M	5000	All tissues and organs	No gross abnormalities
3204	M	5000	All tissues and organs	No gross abnormalities
3205	M	5000	All tissues and organs	No gross abnormalities
3206	F	5000	All tissues and organs	No gross abnormalities
3207	F	5000	All tissues and organs	No gross abnormalities
3208	F	5000	All tissues and organs	No gross abnormalities
3209	F	5000	All tissues and organs	No gross abnormalities
3210	F	5000	All tissues and organs	No gross abnormalities