

7YI-94000976

FYI

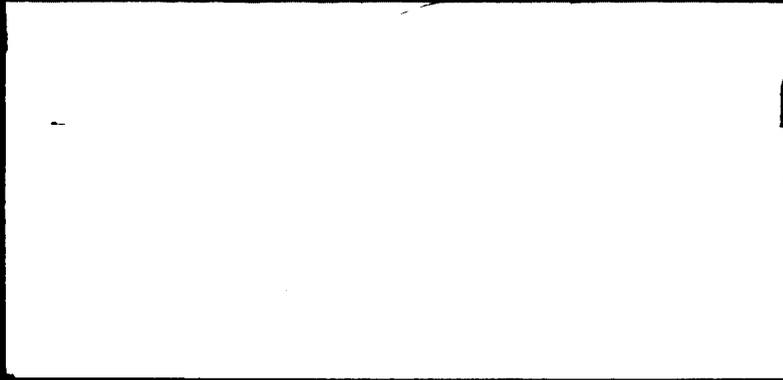


84940000076/0

ATTACHMENT III

RECEIVED
24 JUL 25 01 24 47

3



HASKELL
LABORATORY

TOXICITY REVIEW

HALON 1301

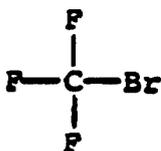


HASKELL LABORATORY

LIMITED DISTRIBUTION

This review reflects the available toxicity literature, both published and unpublished. Studies have not been evaluated for scientific merit. Contact Haskell Laboratory if you have questions.

Common Name: Halon 1301
Chemical Name: Methane, bromotrifluoro-
Synonyms: Freon® 13B1, FC-13B1
CAS Registry No.: 75-63-8
Chemical Structure:



Physical and Chemical Properties:

Description:	Colorless gas
Molecular Weight:	148.9
Boiling Point:	-57.8°C @ 760 mm Hg
Melting Point:	-168°C
Density/Specific Gravity:	1.57 g/cc (liquid at 70°F)
Vapor Pressure:	56.5 psig @ 0°F 199 psig @ 70°F 300 psig @ 100°F
Flash Point/Flammability:	Nonflammable
Solubility:	300 ppm in water @ 77°F
Conversion Factors:	1 mg/L = 164 ppm ₃ 1 ppm = 6.1 mg/m ³

Exposure Standards:

TLV® = 1000 ppm; STEL = 1200 ppm (1).
OSHA 8-hour TWA = 1000 ppm (2).
See Related Reference 52 for additional information.

DOT Classification:

Nonflammable gas; DOT shipping name monobromotrifluoromethane (44).

EPA RCRA Status

None.

FDA Status:

None.

TSCA Inventory:

Yes.

TOXICITY

A. Acute

1. Oral

- Not applicable.

2. Skin and Eyes

- Liquid Halon 1301 may freeze the skin (frostbite) on contact. Such contact should be avoided by wearing protective clothing and eye protection (3).

3. Inhalation

a) Animal Studies

<u>Concentration (ppm)</u>	<u>Duration of Exposure</u>	<u>Animal Species</u>	<u>Effect(s)</u>	<u>Refer- ence</u>
850,000	2 hours	Mice Guinea pigs	Lethal	4
832,000	15 minutes	Rats	Lethal	5
800,000	4 hours	Rats	3/70 deaths	40
800,000	2 hours	Rats Rabbits Mice Guinea pigs	No deaths Toxic effects: drowsiness, tremors, ataxia and convulsions	4

<u>Concentration (ppm)</u>	<u>Duration of Exposure</u>	<u>Animal Species</u>	<u>Effect(s)</u>	<u>Refer- ence</u>
800,000	30 minutes	Rats, Mice	Lethal	10
770,000	1 hour	Rats	No deaths	6
600,000	2 hours	Mice, Rats, Guinea Pigs, Rabbits	No deaths Hypoactivity Slow and deep respiration	4
560,000	1 hour	Rats	No deaths	6
500,000	2 hours	Rats, Mice, Guinea Pigs, Rabbits	Slight initial CNS, depression Normal behavior thereafter	4
500,000	26 minutes	Rats	Drowsiness	7
400,000	2 hours	Mice, Rats, Guinea Pigs, Rabbits	No effect	4
370,000	7 hours	Cats Guinea Pigs Mice Rats Rabbits	Lethal (1/1) Lethal (6/6) Survived Survived Survived	8
370,000	7 hours	Guinea Pigs	No deaths	11
360,000	3.5 hours	Cats Guinea Pigs Mice Rats Rabbits	Survived Lethal (5/6) Survived Survived Survived	8
360,000	1.33 hours	Cats Guinea Pigs Mice Rats Rabbits	Survived Survived Survived Survived Survived	8
300,000	2 hours	Mice, Rats Guinea Pigs Rabbits	No effect	4

<u>Concentration (ppm)</u>	<u>Duration of Exposure</u>	<u>Animal Species</u>	<u>Effect(s)</u>	<u>Refer- ence</u>
300,000	40 minutes	Rats	No effect Pathology normal	40
200,000	2 hours	Monkeys Rabbits Guinea Pigs Rats	Glassy eyes (1/2) Restlessness (4/4) Lacrimation (1/6) Restlessness (10/10) Normal recovery	40
200,000	2 hours	Guinea Pigs	No effect Normal Pathology	9
200,000	2 hours	Rats	No effects Normal Pathology	40
180,000	7 hours	Rabbits Cats Mice Rats Guinea Pigs	Lethal (1/4) Survived Survived Survived Survived	8
150,000	2 hours	Monkeys Rabbits Guinea Pigs Rats	Glassy eyes (1/2) No effect No effect No effect	40
90,000	7 hours	Cats, Mice Rats, Rabbits, Guinea Pigs	No effect	8
46,000-50,000	2 hours	Guinea Pigs	No effect	9
44,000	2 hours	Guinea Pigs	No effect	8
24,000-28,000	2 hours	Guinea Pigs	No effect	9
9,000-13,000	2 hours	Guinea Pigs	No effect	9

- Pathological examination of animals killed by Halon 1301 exposure revealed edema and hemorrhage in the lungs, severe pneumonitis and tracheitis and congestion of the liver, spleen and kidneys. No cellular changes were seen in these organs (5). Examination of other animals which survived Halon 1301 exposures failed to reveal any significant changes (40).

- Hematological examination of the monkeys exposed to 10 or 20% Halon 1301 failed to reveal any significant changes (40).
- Seven monkeys trained on continuous and discrete avoidance performance tasks were exposed to Halon 1301 concentrations ranging from 10.5 to 42%. . Significant performance decrements were observed in all monkeys during 20-25% exposures. Higher concentrations resulted in impaired performance to the point of complete disruption of operant behavior in some monkeys. No visible signs of CNS depression or analgesia accompanied this loss of ability to perform conditioned performance tasks (12).
- See Related References 45, 47, 49 and 50 for more information.

b) Human Exposures

<u>Concentration (percent)</u>	<u>Duration of Exposure</u>	<u>Effect(s)</u>	<u>Reference</u>
15	1 minute	Severe dizziness and marked paresthesia. Increased heart rate and T-wave depression (EKG). Recovery was rapid and complete within 5 minutes.	13
12	1 minute	Severe dizziness and mild paresthesia in 1/2 subjects. T-wave depression and increased heart rate.	13
10	1 minute	No effect for the first 30 second followed by slight dizziness and paresthesia (1/2). Heart rate increased and T-wave was depressed in 1/2 subjects.	13
10	3-3.5 minutes	Light headedness increasing to near unconsciousness. Slight disturbance tests (balance and reaction time). No EKG changes were observed.	40

10	20 minutes	Euphoria (2/6) Light-headedness (3/6) Paresthesia (1/6) Tinnitus (1/6) Slight to moderate eye/ nose irritation (2/6) Pulmonary discomfort (2/6)	14
9	2 minutes	After 1 minute of exposure dizziness was felt which increased in intensity. Increased heart rate, no EKG changes.	13
7	3 minutes	Exposure was during flight at 5,000-20,000 feet. No adverse subjective biomedical or EKG effects were reported.	16
7	3 minutes	Dizziness, faintness and drowsiness (6/8). Dif- ferent altitudes had no effect on subjective symptoms. No compound- related EKG changes.	15
7	3-3.5 minutes	Light-headedness. No EKG changes.	40
6	3 minutes	Slight paresthesia, dizziness. No EKG changes. Increased heart rate.	13
5	3-3.5 minutes	No effects observed. EKGs normal.	40
5	20 minutes	Euphoria (2/4) Light headedness (2/4) Pressure in the ears (1/4) or in the head (1/4) Slight eye and nose irritation (1/4) Slight pulmonary discomfort (1/4)	14

4	3 minutes	Dizziness, faintness and drowsiness (3/8). Changes in altitude had no effect on symptoms. No compound-related EKG changes.	15
4	3 minutes	Exposure was during flight at 5,000-20,000 feet. No adverse subjective biomedical or EKG effects were reported.	16
3	3-3.5 minutes	No effects observed. EKGs normal.	40
1	3-3.5 minutes	No effects observed. EKGs normal.	40

- Ten volunteers were exposed to inhalation of CBrF_3 from an anesthesia machine. These experiments consisted of a series of relatively short exposures to different concentrations of CBrF_3 . Heart rate, blood pressure and electrocardiographic tracings were monitored. Cardiac arrhythmias were not observed to develop during exposure of 5 subjects for a total of 10 to 17 minutes to 4-6.7% nor during the additional exposures of 5 subjects to 7-9.6% for 5 to 7 minutes. These subjects reported reactions including dizziness, tingling of extremities, light-headedness and a fear of imminent loss of consciousness. Five subjects were exposed to 8.2-15.7% for total exposure times of 10-31 minutes. Only one of these subjects developed a serious cardiac arrhythmia. The subjective sensations which were reported to have developed during these serial exposures to CBrF_3 were on the central nervous system. These sensations ranged from an increased awareness of sound, visual disturbances (e.g. flashing before eyes), tingling of extremities and numbness of body to the sensation of the room rocking back and forth or spinning, drowsiness, and the fear of impending unconsciousness (14).
- Three volunteers, one visually handicapped, were exposed to 0.1, 4.3, 4.5 and 7.1% of Halon 1301 for up to 30 minutes. The subjects' health and feelings were monitored before, during, and up to 2 hours after exposure. Included before each exposure were

a complete physical examination (blood pressure, body temperature, electrocardiogram [ECG], pulmonary function, urinalysis, clinical blood chemistry & symptoms) and mood evaluation. During and after each exposure, the subjects performed various tasks to measure effects of exposure on eye-hand coordination, short-term memory, reaction time, depth perception, balance, ability to walk on a treadmill, write, and speak. Finally, spontaneous electroencephalograms (EEGs) were made immediately after exposure on each subject. At 0.1% Halon 1301, no significant deviations from normal were detected in any of the subjects. At 4.3 and 4.5%, subjects experienced sensations of light-headedness, dizziness, and euphoria 2 minutes into exposure. At 9 minutes into exposure at 4.5%, only the visually handicapped subject showed signs of impaired balance; at 30 minutes after exposure, his response was normal. A second subject showed mild impairment in balance at 30 minutes. At 7.1%, one subject showed mild changes in tests of balance during exposure, while the visually handicapped subject performed unsatisfactorily in the balance and eye-hand coordination tests. Sensations of light-headedness, dizziness, and euphoria also were noted, persisting up to 60 minutes after exposure. Analysis of ECG tracings did not show any abnormalities caused by the exposures. One of the subjects showed slight changes in brain wave activity (EEG) at 7.1%, with a pattern representative of slight anesthesia. All untoward physiological and subjective responses were reversible shortly after exposure. Results of the other health tests were within normal limits (40)

B. Extended Inhalation Studies

- A single cat survived two 7-hour exposures to 18% Halon 1301. Guinea pigs exposed to the same concentration died after 2 exposures as did 1/4 rabbits. All of the 10 rats and 10 mice similarly exposed survived. Five 7-hour exposures to 8.72% killed 4/6 guinea pigs. Mice, rats, cats and rabbits were not killed except for 2 natural deaths. Five 7-hour exposures to 4.44% was responsible for the death of 1/10 mice, but no other deaths were attributable to the Halon 1301 exposure. Dogs exposed to either 9 or 18% for 7 hours on each of 2 consecutive days developed no signs of intoxication. Acute hemorrhagic pneumonitis and degeneration of

the liver and kidneys were found among animals that died as the result of exposure (8).

- Exposure of groups of 3 rats, 3 guinea pigs, 1 dog and 3 cats to 20-60% Halon 1301 for up to 70 hours did not produce symptoms of toxicity (17).
- A group of 20 rats and 20 guinea pigs was exposed to 5.1% Halon 1301 continuously for 10 days. No toxic effects or pathologic or histopathologic changes were observed. Hematologic determinations also failed to reveal any adverse compound-related changes (6).
- A group of 20 mice, 10 rats and 10 guinea pigs was exposed to 50% of Halon 1301 in air, 2 hours daily for 15 days. No significant effects were observed (4).
- Rats were exposed to 5% of Halon 1301, 23 hours daily for 30 days. Studies of blood did not reveal any accumulation of Halon 1301. There was no elevation in the rate of excretion of fluoride ion in the urine. No gross pathological changes were found (18).
- Rats and dogs were exposed to 2.3% of Halon 1301 in air for 6 hours daily, 5 days per week for up to 18 weeks. At no time did the animals show any signs of intoxication. Upon autopsy the animals showed no evidence of pulmonary edema or necrosis as had been seen in acute lethal studies. There was a moderate diffuse congestion of the entire respiratory tract but no other significant changes. All other organs appeared normal (19).

Halon 1301 Blood Levels

- Beagle dogs with cannulas surgically implanted in the common carotid artery and external jugular vein were exposed to 5%, 7.5%, and 10% Halon 1301 for 60 minutes. Blood samples were withdrawn from the cannulas before, during, and after exposure and analyzed for the Halon 1301 concentration. Blood levels of Halon 1301 increased rapidly during the first ten minutes of exposure, plateaued within twenty minutes, and declined rapidly after exposure. The mean blood concentrations at equilibrium were directly proportional to inspired levels: at an inspired concentration of 5% - arterial 19.2 ug/mL,

venous 14.6 ug/mL; at an inspired concentration of 7.5% - arterial 30.6 ug/mL, venous 28.4 ug; and at an inspired concentration of 10% - arterial 40.2 ug/mL, venous 32.1 ug/mL. During exposure arterial concentration was greater than venous concentration, but after exposure the venous concentration slightly exceeded the arterial concentration (40 , 41).

- Anesthetized rats were exposed to 5% of Halon 1301 for 30 minutes and blood levels of Halon 1301 determined. The following blood levels were found at the indicated post-exposure times:

<u>Time</u>	<u>Level</u>
0	5.6 ug/g
15 minutes	0.62 ug/g
1 hour	0.35 ug/g
2 hour	0.05 ug/g
4 hour	0.07 ug/g

(18)

- Groups of 15 rats were exposed for 1-5 minutes to 70% Halon 1301. Rats were removed at various times for collection of brain tissue, heart and intracardiac blood samples. During the first minutes of exposure, the Halon 1301 concentration in the brain and heart rose rapidly. Following the end of exposure, the concentrations in brain and heart fell rapidly. The Halon 1301 concentrations in the samples of intracardiac blood were similar to those of the hearts obtained at the corresponding time intervals (20).

Cardiac Studies

a) Cardiac Arrhythmias

- It has been known for some time that inhalation of vapors from certain organic materials, which include such compounds as carbon tetrachloride and gasoline, can make the heart muscle abnormally reactive to elevated adrenalin levels with resulting cardiac arrhythmias. These arrhythmias are frequently ventricular in origin and may result in sudden death. This phenomenon is commonly referred to as cardiac sensitization. Since Halon 1301 is used as a fire extinguishing agent and fire is a life-threatening emergency which can be expected to result in high circulating levels of adrenalin in persons attempting to extinguish the fire or those

whose escape may be blocked, several investigators have studied the effects of adrenalin plus Halon 1301 exposure on the cardiovascular system.

- EC50* (dogs) = 200,000 ppm (23).
- Development of spontaneous cardiac arrhythmias were not observed in the electrocardiographic tracings obtained during exposure of 1 dog to 10% (100,000 ppm) CBrF₃ for 20 minutes, exposure of 4 dogs to 20% (200,000 ppm) for 15 minutes, and exposure of 5 dogs to 30% (300,000 ppm) for 15 minutes. Salivation and whole body trembling occurred during exposures to 30% and to a lesser extent during exposures to 20%. Weakness and inability to stand was reported only for those dogs exposed to 20%. Recovery following exposure to 30% occurred within 1-2 minutes after exposure was ended. The author does not report whether the CBrF₃ was mixed with air or with oxygen. Cardiac sensitization to intravenously injected epinephrine during 5-minute exposures to 10% or to 20% CBrF₃ was evidenced by increases in the number of ectopic beats in 2/2 exposed to 10% and in 1/2 exposed to 20% and by ventricular tachycardia in 1/2 exposed to 20% (13).
- Dogs were exposed to 5, 7.5 and 10% of Halon 1301 for 30-60 minutes. The test animals received an injection of epinephrine both before and after the exposure. None of the dogs exposed to 5.0% developed cardiac arrhythmias. Two of 12 dogs exposed to 7.5% showed a marked response after a 30-minute exposure. Following a 30-minute exposure to 10% Halon 1301 there was one definite and one questionable response in 12 dogs (40).
- A dog was exposed to 10% Halon 1301 for a few minutes following an injection of epinephrine. A challenge injection followed the exposure. Some effect on the heart was seen (40).
- Halon 1301 did not cause cardiac sensitization of the beagle heart below a concentration of 10% in air (40). Further experimentation showed that the minimum effect level is closer to 7.5% than 10% (40).

* EC50 is the concentration causing cardiac arrhythmias in 50% of the animals. Exposure was for 5 minutes followed by an exogenous dose of epinephrine.

- Groups of 8 dogs were exposed to 10, 20 or 40% Halon 1301 in air. Exposure times were 15, 27 and 55 minutes, respectively. During exposure the chambers were darkened and the dogs subject for 5 minutes to fright-inducing stimuli. Those dogs exposed to 10% Halon 1301 demonstrated increased alertness, those exposed to 20% developed tremors without increased alertness and those exposed to 40% howled, salivated and developed dyspnea and tremors (14).
- Spontaneous cardiac arrhythmias developed within 1-3 minutes of exposure to 40% Halon 1301. Arrhythmias could be produced in those animals not developing spontaneous arrhythmias by the intravenous injection of a pressor dose of epinephrine. Larger doses caused ventricular fibrillation with cardiac arrest in dogs and, commonly, spontaneous defibrillation in monkeys (21).
- Anesthetized guinea pigs, cats and dogs were exposed to 20% Halon 1301. This exposure increased the arrhythmogenic effect of i.v. infusion of epinephrine (24).
- Five anesthetized monkeys were exposed, successively, for 10 minutes each, to 10-80% Halon 1301. spontaneous ventricular arrhythmias developed during the first 5 minutes of exposure to 30% and higher. Cardiac arrhythmias spontaneously appearing in monkeys exposed to CBrF_3 required a minimal blood pressure threshold for their production. The blood pressure threshold varied as an inverse function of the log of the CBrF_3 concentration to which monkeys in acid-base balance were exposed. Acidosis decreased the threshold and alkalosis increased the threshold at concentrations of 10 and 20% CBrF_3 but were without effect at 30% or greater concentrations. Epinephrine decreased the blood pressure threshold required to trigger arrhythmias but was not necessary for their production as it is in the case of cyclopropane (25).
- No significant difference in the percentage of marked responses was seen when dogs with myocardial infarctions were used instead of healthy dogs (40, 42).

- Groups of rats were exposed to one of the following conditions:
 - 1) simulated altitude with added Halon 1301 (27 rats);
 - 2) simulated altitude without Halon 1301 (9 rats);
 - 3) simulated altitude with added Halon 1301 and injected epinephrine (27 rats);
 - 4) simulated altitude without Halon 1301 but with injected epinephrine (9 rats).

No rats died during any chamber exposure. Three animals developed cardiac arrhythmias during inhalation of Halon 1301. One rat breathing 24 percent Halon 1301 at a simulated altitude of 5,000 feet, and one exposed to 16 percent CBrF_3 at 389 mm Hg, developed premature atrial contractions about one minute after the Halon 1301 was admitted to the chamber. Indications of bundle branch blocks appeared as the exposure continued. In both cases, these changes disappeared when the CBrF_3 -air mixture was replaced with room air during the chamber descents. Premature atrial contractions were also noted in the electrocardiogram of one rat breathing 24 percent Halon 1301 at 632 mm Hg. This animal had received an epinephrine injection before the exposure. Normal EKG tracings reappeared when the rat was returned to ambient conditions. No other prolonged cardiac arrhythmias were noted on the electrocardiograms from any other rats. Histological examination of the lungs from rats sacrificed immediately after exposure showed no pathologic changes which could be directly related to breathing Halon 1301 or exposure to hypobaric conditions. In this experiment epinephrine was administered intramuscularly to rats rather than the usual intravenous route. The use of i.m. administration would be expected to produce much lower blood levels of epinephrine than i.v. injection. The observation of only 1/27 premature atrial contractions after exposure to 24% Halon 1301 at 632 mm Hg may reflect the low dose of epinephrine rather than any species different (22).

- Rats were subjected to 79% Halon 1301 plus 21% oxygen and challenged with subtoxic doses of epinephrine. CNS effects were the major

observations in rats, 17/20 showed respiratory arrest within 40 minutes and several exhibited erratic convulsive behavior prior to exhibiting respiratory difficulties (26).

b) Heart Rate And Blood Pressure

- Inhalation of 80% Halon 1301 caused blood pressure falls in many cases and a marked elevated diastolic pressure in rhesus monkeys. Inhalation of 70 percent Halon 1301 triggered cardiac arrhythmias. These arrhythmias were dependent on the maintenance of a minimum blood pressure. Halon 1301 (80%) inhalation in dogs which had undergone a left lumbar sympathectomy caused a large increase in right femoral artery blood flow. Concurrently, mean arterial blood pressure, peak systolic blood pressure fell while left ventricular and diastolic pressure rose (27).
- Dogs were exposed to 50 and 75% Halon 1301 for 10-minute periods. Recordings were made and arterial and coronary sinus blood samples were obtained before, during and after the exposures. A small decrease in the vigor of myocardial contraction, decreases in vasoconstrictor tone and mean arterial blood pressure, an increase in aortic blood flow, an increase in myocardial lactate utilization and a decrease in myocardial oxygen consumption were observed as functions of the Halon 1301 concentration. Conclusions were that under the conditions of this experiment (1), a decrease in pressure-volume work done by the left ventricular myocardium during Halon 1301 exposure resulted in a decrease in myocardial oxygen consumption; (2) myocardial metabolism was little affected; and (3) decreased peripheral vascular flow resistance was accompanied by increased cardiac output (28).
- To investigate the effect of Halon 1301 on blood pressure 10 anesthetized dogs were exposed to air or 70% Halon 1301 for 50 minutes. The blood pressure of the treated dogs was significantly lower than pre- and postexposure levels and also lower than for air treated controls. No significant differences were seen for cardiac output. Heart rate was significantly lower (29).
- Halon 1301 was administered to dogs and the following parameters recorded: pulmonary

resistance, pulmonary compliance, respiratory minute volume, heart rate and aortic blood pressure. Halon 1301 was shown to produce an increase in pulmonary resistance a decrease in compliance an increase in respiratory minute volume, very little effect on heart rate even at concentrations up to 20%, and a mild hypertensive effect (4% increase at 20% concentration). Heart-lung experiments in surgically prepared dogs showed little change in myocardial contraction even at high concentrations. Experiments with rats showed Halon 1301 capable of producing apnea with atrioventricular conduction blocks occurring during this period of apnea. Halon 1301 also produced a rise in pulmonary resistance and fall in compliance as it did in the dog experiments (40).

- Exposure of dogs and monkeys to 10-80% of Halon 1301 caused cardiovascular and CNS effects which increased in severity with increasing concentration. An initial fall in blood pressure of 10-20 mm Hg at the lower concentrations and 40-60 mm Hg at the higher concentrations was observed. Epileptiform convulsions were seen in about 50% of the dogs exposed to 50-80% Halon 1301 while conscious. Conscious monkeys, on the other hand, became lethargic, and no convulsions were seen (21).
- The mechanism of the decrease in mean arterial blood pressure in the dog during Halon 1301 exposure was a decrease vasomotor tone resulting from ganglionic blockade. No direct vascular smooth muscle effect of CBrF_3 was observed. When arterial blood from one dog was perfused through the hind leg at constant flow rate through a hind limb of another dog, exposure of the donor to 67-70% CBrF_3 was accompanied by a reversible decrease in the donor's mean arterial blood pressure, but the perfusion pressure was unaltered (30).
- When anesthetized dogs were exposed to Halon 1301 the animals myocardial contractility decreased inversely with the concentration of Halon 1301 (31).
- Halon 1301 significantly decreased total peripheral resistance and myocardial contractility in anesthetized open-chested dogs and monkeys resulting in a reversible hypotension during exposure (32).

- Groups of dogs were exposed to 27-75% Halon 1301 in oxygen or 27-75% mixture of O₂ and N₂. Exposure to Halon 1301 may result in disturbances of myocardial energy metabolism that are connected to myocardial performance. The exposure resulted in a progressive rise of plasma glucose concentrations that persisted for at least 30 minutes post exposure (33).
- Exposure of dogs to 27, 51 or 75% Halon 1301 produced no myocardial tissue hypoxia, slight metabolic acidosis, normal pyruvate, lactate, and coronary sinus blood glucose, decreased mean arterial blood pressure and myocardial contraction strength and elevated arterial blood glucose (34).
- Twelve anesthetized cats were subjected under hyperbarbic conditions to 5-minute inhalation of 5% Halon 1301. This exposure was associated with:
 - 1) Cardiac arrhythmias in 10/12 cats;
 - 2) Fall in systolic blood pressure (average decrease -18.4 mm Hg) in 10/10 cats and a fall in diastolic pressure (average decrease - 19 mm Hg) in 9/10 cats (35).
- A anesthetized cat was exposed to 80% Halon 1301 and 20% oxygen. This exposure did not materially modify the physiologic equilibrium of the cat. The following changes were observed:
 - Slight activation of respiration;
 - Decreased arterial blood pressure (1 mm Hg);
 - Slight decrease in oxygen consumption;
 - CNS depression (hypnotic). (4)
- Anesthetized dogs and monkeys were exposed to 70 or 80% of Halon 1301 and EEGs recorded. The most significant findings were (1) dominance of the EEGs by 6-9 Hz waves beginning 2-3 minutes after beginning exposure to CBrF₃ and (2) a nearly normal susceptibility of the EEG to activation by auditory and photic stimuli during exposure to CBrF₃. Several lines of evidence were explored which suggested that the central nervous system effects of CBrF₃ may be the result of the induction of functional changes at the rhinencephalic level (36).

- To determine if the negative inotropic effect of Halon 1301 was accompanied by altered myocardial metabolism, urethane anesthetized-guinea pigs were exposed for 30 minutes and myocardial ATP, ADP, AMP and creatine phosphate levels were determined. A concentration of 75% Halon 1301, produced a 34% decrease in contractibility. Blood levels stabilized within 2.5 minutes. Blood pressure and heart rate were decreased. High energy phosphate levels were not altered in a fashion commensurate with the theory that a block in energy metabolism was responsible for the production of the induced negative inotropic effect (43).
- See Related References 46, 48 and 51 for more information.

C. Carcinogenic Potential

- No evidence of a carcinogenic potential has been found. However, the longest study conducted was an 18-week inhalation study (19).

D. Mutagenic Potential

- Halon 1301 was tested in Salmonella typhimurium strains TA 1535, TA 1537, TA 1538, TA 98 and TA 100 at levels up to 40%. The gas was not mutagenic either in the presence or absence of a liver microsomal system (40).

E. Embryotoxic Potential

- Groups of 27 pregnant rats were exposed 6 hours a day on days 6-15 of gestation to 962 + 57, 10,196 + 1514 or 49,505 + 4753 ppm of Halon 1301. No compound-related clinical signs of toxicity or changes in behavior were noted. The outcome of pregnancy, measured by the number of implantation sites, resorptions and live fetuses, were not adversely affected by the exposure. Exposure did not affect embryonal development as measured by weight and crown-rump length of the fetuses. Three fetuses were found with malformations. All three were from dams exposed at the intermediate level, however, these effects were not considered compound-related. Under the conditions of this test, Halon 1301 was not embryotoxic or teratogenic (40).

F. Other Reproduction Studies

- None.

G. Aquatic

- None.

H. Human Exposure

- See Section A.2.b. for details of controlled inhalation experiments in human volunteers.

I. Epidemiology

- No information available.

J. Metabolism

- See Related References 53-55.

K. Pyrolysis Studies

- Halon 1301 decomposes upon contact with flames or hot surfaces above 1000°F. While this action appears necessary for the product to function effectively as a fire extinguishing agent, it also results in the formation of several new compounds whose properties are considerably different from Halon 1301. The common decomposition products of Halon 1301 are: HF, HBr, Br₂, carbonyl halides, consisting of carbonyl fluoride (COF₂) and carbonyl bromide (COBr₂). The quantities of these materials in the post-extinguishment atmosphere depend upon several factors, such as the size of the fire, type of fuel, enclosure size, degree of ventilation, and rapidity of flame extinguishment. In practical fire tests, the predominant decomposition products are HF and HBr. Free bromine and carbonyl halides have not been detected in significant quantities and post-extinguishment atmospheres.
- ALC (15-minute exposure, rats) = 14,000 ppm (5).
- The toxicity of pyrolyzed Halon 1301 appears to be due to the HF formed. The 15-minute LC50 for HF is 2700 ppm. At the LC50 determined for pyrolyzed Halon 1301 (2300 ppm), 2480 ppm of HF is formed.
(37)

- The passage of Halon 1301 through an Inconel tube heated to 482°C did not result in any detectable decomposition of the compound, nor did the exposure of the animals to the effluent material result in any deviation in the mortality rates seen with undecomposed material. When the tube is heated to 593°C, some decomposition of the compound and an increase in mortality was seen. The incidence of mortality was dependent on the Halon 1301 concentration. Mild degrees of pneumonitis were found in all exposed species, except rats, which were exposed to 482°C fumes. Acute chemical pneumonitis and degeneration of the liver, kidneys and brain were found in all species exposed to fumes generated at temperatures greater than 482°C (8).
- Deaths as the result of inhalation of pyrolysis products of Halon 1301 characteristically resulted from pulmonary hemorrhage and edema. The 15-minute LC50 value for pyrolyzed Halon 1301 calculated from these experiments was 2300 ppm. The pathologic response and delayed death patterns are similar to those seen from HF (38).
- Groups of animals were exposed for 30 minutes to atmospheres containing the pyrolysis products of Halon 1301. None of the animals died after being exposed at concentrations up to 80% of 800°C pyrolysis products. Signs of toxicity included dyspnea and prostration. When exposed to vapor products at 1000°C, all of the animals were killed at concentrations greater than 1%. At 0.75% approximately 20% of the exposed rats and 90% of the mice were killed. At 0.5%, none of the rats and 50% of the mice died (4).
- When Halon 1301 is applied to ordinary fires such as gasoline or wood, the resulting decomposition products may include HF, HBr, carbonyl halides and in some cases free bromine in concentrations depending on the quantity used. When applied in quantities of 2.3 pounds in a 720 cubic foot room for durations of the order of 5 to 30 minutes Halon 1301 caused some injury to guinea pigs, but was not lethal (9).
- With the exception of initial excitement, no symptoms indicative of a toxic action were observed during exposure of 20 mice and 40 rats to 1.07% Halon 1301 in air for 15 minutes. Very few deaths occurred during gasoline fires, however, the trachea and lungs were found to be congested (39).

REFERENCES

1. "ACGIH TLV® Booklet" (1981).
2. Code of Federal Regulations, Title 29 Section 1910.1000.
3. Du Pont Bulletin B-29D, "Du Pont Halon 1301 Fire Extinguishment" (1977) (C-1205).
4. Paulet, G., Arch. Mal. Prof., 23, 341-347 (1962) (J-2142).
5. Comstock, C. C. et al., Army Chemical Center, Report No. 23 (1950) (J-31).
6. Unpublished Data, Hazleton Laboratories, Reported by McHale, E. T., Atlantic Research Corporation, U. S. Army Res. Office Contract DAHC 19-71-C-0026 (J-1638).
7. Unpublished Data, ICI Ltd. (1954) (J-102).
8. Treon, J. F. et al., Unpublished Data, Kettering Laboratory (1957) (J-1868).
9. Dufour, R. E., Underwriters' Laboratories, Inc., Report NC 445 (J-1493).
10. Caujolle, F., Bull. Ins., Ind du Froid, 21 (1964) (J-1683).
11. Engibous, D. L. and T. R. Torkelson, Dow Chemical Company. Data reported in U.S.N.T.I.S. Report PB 161942.
12. Carter, V. L. Jr., et al., Tox. Appl. Pharmacol., 17(3), 648-655 (1970).
13. Clark, D. G., Unpublished Data, ICI Ltd. (1970) (J-4064).
14. Hine, C. H. et al., Proc. 4th Ann. Conf. Atmospheric Cont. Conf. Spaces, AMRL-TR-68-175, 127-144 (1968) (J-2418).
15. Call, D. W., Aerosp. Med., 44, 202-204 (1973) (J-2409).
16. Smith, D. G. and D. J. Harris, Ibid., 198-201 (J-2408).
17. Scholz, J. and W. Weigand, Z. Arbeitsmed. Arbeitsschutz, 14(6), 129-131 (1964) (CA 62:2166h). (J-2439).
18. Griffin, T. B. et al., Appr. Halogenated Fire Ext. Agents, Proc. Symp., 136-147 (1972) (J-2383).

REFERENCES (Cont'd.)

19. Comstock, C. C. et al., U. S. Army Chemical Corps, Med. Div. Report No. 5030-180 (1953) (J-476).
20. Van Stee, E. W. and K. C. Back, Aerosp. Res. Lab., Wright-Patterson Air Force Base, AMRL-TR-70-139 (1970) (CA 75:74289).
21. Van Stee, E. W. and K. C. Back, Tox. Appl. Pharmacol., 15, 164-174 (1969).
22. Call, D. W., Appr. Halogenated Fire Ext. Agents, Proc. Symp., 127-135 (1972) (J-2383).
23. Clark, D. G. and D. J. Tinston, Brit. J. Pharmacol., 49(2), 355-357 (1973).
24. Wills, J. H. et al., Tox. Appl. Pharmacol., 22, 305-306 (1972).
25. Van Stee, E. W. and K. C. Back, Aerospace Med. Res. Lab., AMRL-TR-68-188 (J-2370).
26. Rhoden, R. A. and K. L. Gabriel, Tox. Appl. Pharmacol., 25, 469 (1973).
27. Van Stee, E. W. et al., Proc. Annu. Conf. Environ. Toxicol., 5th, AMRL-TR-74-125, 155-167 (1974) (J-2836).
28. Back, K. C. and E. W. Van Stee, Tox. Appl. Pharmacol., 25, 469 (1973).
29. Van Stee, E. W. et al., Proc. 4th Ann. Conf. Atmos. Cont. Conf. Spaces, AMRL-TR-68-175, 113-126 (1968).
30. Van Stee, E. W. and K. C. Back, Tox. Appl. Pharmacol., 23(3), 428-442 (1972).
31. Van Stee, E. W. et al., Ibid., 26(4), 549-558 (1973).
32. Van Stee, E. W. and K. C. Back, Aerosp. Med. Res. Lab, Wright-Patterson Air Force Base, AMRL-TDR-68-182 (1971) (J-2369).
33. Van Stee, E. W. et al., Tox. Appl. Pharmacol., 34(1), 62-71 (1975).
34. Van Stee, E. W. et al., Proc. Annu. Conf. Environ. Toxicol., 4th, 65-83 (1973) (J-5247).

RELATED REFERENCES

Inhalation

45. Dimov, D., Arh. Hig. Rada Toksikol., 23(2), 153-5 (1972) (CA 79:944).
"Toxicology of bromotrifluoromethane"
46. Back, K. C. and E. W. Van Stee, Wright-Patterson Air Force Base, AGARD Rep. R-599 (CA 78:132355) (J-5248).
"Cardiovascular and nervous system effects of bromotrifluoromethane" A review.
47. Van Stee, E. W., Wright-Patterson AFB, U.S.N.T.I.S. Report No. AD-A011538 (1974) (CA 84:26504).
"Review of the toxicology of halogenated fire extinguishing agents"
48. Toy, P. A. et al., Tox. Appl. Pharmacol., 38(1), 7-17 (1976).
"The effects of three halogenated alkanes on excitation and contraction in the isolated, perfused rabbit heart"
49. Kappus, H., et al., Funct. Glutathione Liver Kidney, [Pap. Konf. Ges. Biol. Chem], 25th, 176-182 (1978) (CA 91:118086).
"Lipid peroxidation induced by ethanol and halogenated hydrocarbons in vivo as measured by ethane exhalation"
50. Karpov, B. D., Tr. Leningr. Sanit.-Gig. Med. Inst., 111, 10-14 (1975) (CA 89:79501).
"Materials for the toxicology of some bromofluorohydrocarbons of the methane and ethane series"
51. Back, K. C. and E. W. Van Stee, Int. Encycl. Pharmacol. Ther., Section 102 (Pharmacol. Methods Toxicol.), 103-113 (1979) (CA 92:70440) (J-).
"Various techniques for evaluating cardiodynamic function using chronically instrumented canine models"

RELATED REFERENCES (Cont'd.)

Industrial Hygiene

52. Bales, R. E., NIOSH Pub. No. 79-101 (1978) (CA 90:209347)
(J-).

"Fluorocarbons. An industrial hygiene survey of worker exposure in four facilities"

Metabolism/Biochemical

53. Wolf, C. R. et al., Mol. Pharmacol., 13(4), 698-705 (1977)
(CA 87:63685).

"The reduction of polyhalogenated methanes by liver microsomal cytochrome P450"

54. Van Stee, E. W. et al., Wright-Patterson AFB, U.S.N.T.I.S.
Report AD-751428 (1971) (CA 78:132421).

"Halogenated hydrocarbons and drug metabolism. Effect of fluorocarbons on hexobarbital sleeping and zoxazolamine paralysis times in mice"

55. Young, W. and J. A. Parker, Combust. Toxicol., 2(4), 286-97
(1975) (CA 84:100431).

"Effect of fluorocarbon on acetylcholinesterase activity and some counter measures"

Richard C. Graham:md
March 6, 1978

Updated:
Richard C. Graham:jrg
November 18, 1981

R. C. Graham

THIS REPORT HAS BEEN MADE AVAILABLE TO YOU FREE OF CHARGE AND AT YOUR REQUEST. WE BELIEVE THE INFORMATION CONTAINED HEREIN IS RELIABLE. HOWEVER, WE MAKE NO WARRANTY, EXPRESSED OR IMPLIED, AND ASSUME NO LIABILITY IN CONNECTION WITH ANY USE OF THIS INFORMATION.