AD-A152 230 EMERGENCY AND CONTINUOUS EXPOSURE LIMITS FOR SELECTED AIRBORNE CONTAMINAN.. (U) NATIONAL RESEARCH COUNCIL WASHINGTON DC COMMITTEE ON TOXICOLO.. OCT 84 1/1

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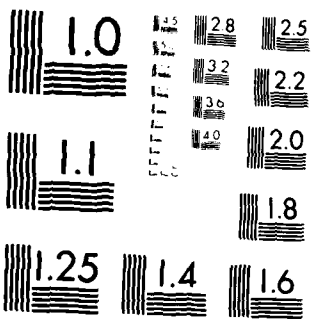

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AD-A152 230

Emergency and Continuous Exposure Limits for Selected Airborne Contaminants

Volume 3
Bromotrifluoromethane

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U.S. Government Printing Office 1978—261-647/5308

50272-101

REPORT DOCUMENTATION PAGE	1. REPORT NO.	2. AD-A152 230	3. Recipient's Accession No.
4. Title and Subtitle: Emergency and Continuous Exposure Limits for Selected Airborne Contaminants. Volume 3. Bromotrifluoromethane.			5. Report Date: October 1984
			6.
7. Author(s)			8. Performing Organization Rept. No.
9. Performing Organization Name and Address: National Research Council, Commission on Life Sciences, 2101 Constitution Ave., NW, Washington, DC 20418			10. Project/Task/Work Unit No.
			11. Contract(C) or Grant(G) No. (C) ~~N00017-C-0049~~ (G)
12. Sponsoring Organization Name and Address: Office of Naval Research			13. Type of Report & Period Covered: Final
			14.

15. Supplementary Notes

16. Abstract (Limit: 200 words)

This report contains information on the physical, chemical, and toxicologic properties of $CBrF_3$, a fire extinguishing chemical. It also contains emergency exposure limits (EELs) for 30 min and 1 hr, and contains exposure limits for 90 days.

17. Document Analysis a. Descriptors

Bromotrifluormethane, $CBrF_3$, fire extinguishing chemical.

b. Identifiers/Open-Ended Terms

c. COSATI Field/Group

18. Availability Statement: distribution is unlimited.	19. Security Class (This Report): Unclassified	21. No. of Pages: 27
	20. Security Class (This Page): Unclassified	22. Price

EMERGENCY AND CONTINUOUS EXPOSURE LIMITS FOR SELECTED AIRBORNE CONTAMINANTS

Volume 3 - BROMOTRIFLUOROMETHANE

COMMITTEE ON TOXICOLOGY

Board on Toxicology and Environmental Health Hazards
Commission on Life Sciences
National Research Council

Contract DAMD-17-82-C-3028

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National Academy Press
Washington, D.C.
October 1984

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ACKNOWLEDGMENTS

We acknowledge with thanks the assistance of the following previous committee members in the preparation of this report: Richard Bates, Health Effects Institute; Donald J. Ecobichon, McGill University; Howard I. Maibach, University of California, San Francisco; Robert Menzer, University of Maryland; Charles F. Reinhardt, E.I. duPont de Nemours and Company; Robert Snyder, Rutgers University; and Peter Spencer, Albert Einstein College of Medicine.

INTRODUCTION

The National Research Council's Committee on Toxicology recommends emergency exposure limits (EELs), short-term public limits (STPLs), and short-term public emergency limits (SPELs--formerly called public emergency limits or PELs) for a variety of chemicals of concern to its sponsoring agencies. The definitions and applicability of these limits and the criteria used to establish them were originally outlined in two documents prepared by the Committee (NRC, 1964, 1971a). In a revision of those documents (NRC, 1979a), the Committee summarized the principles used to establish exposure limits for short durations. The Committee has also recommended continuous exposure limits (CELs) in response to specific sponsor requests.

This document is one in a series prepared by the Committee that form the basis of the recommendations for EELs and CELs for selected chemicals. Since the Committee began recommending EELs and CELs for its military sponsors (U.S. Army, Navy, and Air Force), the scope of its recommendations has been expanded in response to a request by the National Aeronautics and Space Administration. The CELs, in particular, grew out of a Navy request for exposure limits for atmospheric contaminants in submarines. The EELs and CELs have been used as design criteria by the sponsors in considering the suitability of materials for particular missions (as in a submarine or a spacecraft) and in assessing the habitability of particular enclosed environments. They are recommended for narrowly defined occupational groups and are not intended for application in general industrial settings or as exposure limits for the general public.

The EEL is defined as a ceiling limit for an unpredictable single exposure, usually lasting 60 min or less, and never more than 24 h--an occurrence expected to be rare in the lifetime of any person. It reflects an acceptance of the statistical likelihood of the occurrence of a nonincapacitating, reversible effect in an exposed population. It is designed to avoid substantial decrements in performance during emergencies and might contain no uncertainty factor. The use of uncertainty factors will depend on the specific compound in question and on the type of effect produced by the compound.

The CEL is recommended in specific situations in which there may be exposure to a chemical continuously for up to 90 d. It is defined as a ceiling limit designed to avoid adverse health effects, either immediate or delayed, and to avoid degradation in crew performance that might endanger the objectives of a particular mission. Because data on continuous exposures are rarely available, uncertainty factors might be used, depending on the judgment of the Committee.

BACKGROUND INFORMATION

The Department of the Navy has requested a review of the toxicology of bromotrifluoromethane ($CBrF_3$) with recommendations for EELs and a 90-d CEL. Because $CBrF_3$ is used for firefighting aboard ships and might be used in submarines, the Navy is concerned about possible adverse health effects of its pyrolysis products.

PHYSICAL AND CHEMICAL PROPERTIES

Chemical formula:	$CBrF_3$
Molecular weight:	148.9
Common name:	Halon 1301
Synonyms:	Freon 13BI, FC-13BI, Freon 1301
CAS number:	75-63-8
Boiling point:	-57.8°C
Freezing point:	-168°C
Vapor pressure:	10,868 mm Hg (20°C)
Solubility in water:	300 ppm (25°C)
Density, liquid:	1.57 g/ml (21°C)
General characteristics:	Colorless, nonflammable, liquefied compressed gas with high density and low viscosity
Conversion factors:	1 ppm = 6.1 mg/m3 1 mg/m3 = 0.16 ppm

USES

$CBrF_3$ is used for extinguishing class A fires (of cellulosic materials, such as wood and paper), class B fires (of flammable fluids), and class C fires (of electric and electronic equipment). Most fires are extinguished in 5-10 s when the concentration of $CBrF_3$ in air is 5-7%. However, this concentration is maintained for about 10 min to avoid possible reignition. $CBrF_3$, however, is not effective in preventing the combustion or reaction of chemicals capable of oxidation without air such as cellulose nitrate and gunpowder; reactive metals such as sodium, potassium, and titanium; metal hydrides; and chemicals capable of autothermal decomposition such as organic peroxides and hydrazine (DuPont Company, undated).

On a weight basis, $CBrF_3$ is one of the more effective gaseous fire-extinguishing agents. It is up to 3 times more effective than carbon dioxide, about as effective as sodium-base dry powder, and somewhat less effective than potassium-base powder (DuPont Company, undated). $CBrF_3$ is preferred in extinguishing fires, because it causes minimal damage to equipment. The U.S. Navy has used $CBrF_3$ for shipboard firefighting and has considered its use in submarines (Farrier, 1983). However, it is unlikely to be used in submarines until ventilation problems involving removal of its pyrolysis products have been worked out.

SUMMARY OF TOXICITY INFORMATION

Several reviews have been published on the health effects of $CBrF_3$ (National Academy of Sciences, 1972; Haskell Laboratory, 1978; Van Stee, 1974).

EFFECTS ON HUMANS

No studies were found that examined the effects on humans of long-term exposures to $CBrF_3$ at low concentrations. The effects of acute exposure are summarized in Table 1.

Three subjects exposed at 7.1% were able to detect the odor of $CBrF_3$ and experienced mild ear, nose, and throat discomfort after 28 min of exposure (Stewart et al., 1978). Slight to moderate irritation of the eyes and nose and pulmonary discomfort were reported at 10% and to a lesser degree in a person exposed at 5% (Hine et al., 1968). No effects on pulmonary function have been observed.

As in studies on acute exposures of animals, the primary effects observed were cardiovascular and CNS effects. Humans exposed for 20 min at concentrations of 10% and greater had increased heart rates and a flattening of the T wave of the electrocardiogram (ECG). Cardiac arrhythmia was reported in one person who was exposed to $CBrF_3$ at 13% for 5 min (Hine et al., 1968). Normal sinus rhythm was restored within 2 min after exposure ended. No ECG changes were observed in persons exposed to $CBrF_3$ at less than 10%.

Short (30-min) exposures of three healthy men at 0.1, 4.3, 4.5, and 7.1% produced CNS effects of varied degree, such as paresthesia, light-headedness, disturbances in balance, dizziness, and euphoria. All three were able to depart safely from a well-lighted exposure chamber (Stewart et al., 1978).

Harrison et al. (1982) exposed six healthy military volunteers to 7% $CBrF_3$ for 3 h. The same volunteers were exposed on other days to sulfur hexafluoride, a placebo gas. Blood Halon concentrations were monitored to measure uptake. Each subject was given a battery of mental-performance tests to measure psychomotor, perceptual, and cognitive function. Vestibular function was examined by a balance-

TABLE 1

Effects on Humans of Short-Term Exposure to $CBrF_3$

$CBrF_3$ Conc., % in air	Exposure Duration	Cardiovascular Effects	Central Nervous System Effects	Reference
10-17	15-25 min	Flattening of T wave, premature ventricular contractions, tachycardia	Paresthesia, light-headedness, buzzing in ears, numbness, confusion, fear of impending unconsciousness at concentrations above 14%	Hine et al., 1968
12-15	1 min	Increased heart rate, depressed T wave	Paresthesia, severe dizziness, fear of impending unconsciousness	Reinhardt and Reinke, 1972
10	20-25 min	--	Drowsiness, light-headedness, decreases in judgment, alertness, neuromuscular skill	Hine et al., 1968
10	3-3.5 min	No ECG changes	Light-headedness, disturbances in balance and ability to respond to visual stimulus	Reinhardt and Reinke, 1972
10	1 min	Increased heart rate and blood pressure, depressed T wave	Slight paresthesia, dizziness	Reinhardt and Reinke, 1972
9	2 min	Increased heart rate, no ECG changes	Dizziness	Reinhardt and Reinke, 1972
7.1	30 min	No changes in ECG, blood pressure, or heart rate	Dizziness, light-headedness, euphoria; disturbances in equilibrium and coordination; increased EEG activity	Stewart et al., 1978
7	3 h	No changes in cardiac function	Decrement in mental performance tests	Harrison et al., 1982
7	3-3.5 min	No ECG changes	Light-headedness, disturbance in balance and ability to respond to visual stimulus	Reinhardt and Reinke, 1972
7	3 min	No ECG changes	Dizziness, faintness, or drowsiness in 6 of 8 men; increased reaction time; no effect on maze tracking tests	Call, 1973
6	3 min	Increased heart rate	Slight paresthesia, dizziness	Reinhardt and Reinke, 1972

Table 1 (continued)

$CBrF_3$ Conc., % in Air	Exposure Duration	Cardiovascular Effects	Central Nervous System Effects	Reference
5	20-25 min	No ECG changes	Drowsiness, light-headedness, slight effect on judgment	Hine et al., 1968
5	3-3.5 min	No ECG changes	None observed	Reinhardt and Reinke, 1972
4.3-4.5	30 min	No changes in ECG, blood pressure, or heart rate	Dizziness, light-headedness, euphoria, disturbances in equilibrium and coordination	Stewart et al., 1978
4	3 min	No ECG changes	Dizziness, faintness, or drowsiness in 3 of 8 men; increased reaction time; no effect on maze tracking tests	Call, 1973
3	3-3.5 min	No ECG changes	None observed	Reinhardt and Reinke, 1972
1	3-3.5 min	No ECG changes	None observed	Reinhardt and Reinke, 1972
0.1%	30 min	No changes in ECG, blood pressure, or heart rate	None observed	Stewart et al., 1978

board test. The authors stated that no changes in hepatic function, cardiac function according to ECG, or vestibular function could be correlated with exposure to 7% $CBrF_3$ for 3 h. They also reported significant decrements in each mental-function test during the exposure period. These ranged from 11% to 17% mean reduction in function in the individual tests. Mental performance returned to normal within 0.5 h after exposure stopped. The authors reported that the extent of decreased mental performance was roughly comparable with that on waking at 3-5 a.m. or that associated with a blood alcohol concentration of 90 mg/100 ml (Harrison et al., 1982).

EFFECTS ON ANIMALS

The effects of short-term and prolonged exposures of animals to $CBrF_3$ are summarized in Tables 2 and 3, respectively. $CBrF_3$ is only slightly toxic in acute exposures. Underwriter's Laboratories, Inc., classified $CBrF_3$ among the least toxic fluorocarbons (Reinhardt and Reinke, 1972). A 2-h exposure at 85% in air was lethal to mice and guinea pigs (Paulet, 1962), and a 15-min exposure at 83.2% in air was lethal to rats (Reinhardt and Reinke, 1972). Oxygen deficiency was very likely a contributory cause of death in these cases. Clark and Tinston (1982) reported that a 10-min LC_{50} of $CBrF_3$ mixed with oxygen was above 80% in rats. Mice, rats, guinea pigs, and rabbits all survived 2-h exposures to $CBrF_3$ at 50-80% mixed with 20% oxygen (Paulet, 1962). Longer exposures to $CBrF_3$ have reportedly resulted in deaths at lower concentrations (Haskell Laboratory, 1978). When one cat, six guinea pigs, four rabbits, ten mice, and ten rats were exposed at 37% for 7 h, all the animals except two mice and six rats died. The lowest reported concentration of $CBrF_3$ resulting in fatalities was 18%; one of four rabbits exposead for 7 h died (Haskell Laboratory, 1978).

Cardiovascular and CNS effects of exposures to $CBrF_3$ are discussed below.

CENTRAL NERVOUS SYSTEM EFFECTS

In addition to observation of gross behavioral changes in test animals, CNS effects have been studied by measuring changes in electroencephalograms (EEGs) and by using behavioral tests. In monkeys exposed to $CBrF_3$ at 70-80%, increased activation of EEGs coincided with an auditory or visual stimulus (Van Stee et al., 1970). Monkeys exposed at 20-50% had decrements in continuous and discrete avoidance-performance tests, and higher concentrations caused some animals to cease performance entirely, although there were no signs of general CNS depression or analgesia (Carter et al., 1970). $CBrF_3$ at 10.5-20% did not impair performance during the tests. In general, CNS effects have not been observed in animals exposed for less than 7 h to $CBrF_3$ at concentrations below 20%. Clark and

TABLE 2

Effects on Animals of Short-Term Exposure to $CBrF_3$

$CBrF_3$ Conc., %	Exposure Duration	Animal	Cardiovasacular Effects	Central Nervous System Effects	Other Observations	Reference
85[a]	2 h	Mouse, guinea pig	--	--	Approximate lethal concentration	Paulet, 1962
83.2[b]	15 min	Rat	--	--	Approximate lethal concentration	Reinhardt and Reinke, 1972
42[b]	10 min	Rat	Ventricular tachycardia	Tremors, ataxia	--	Clark and Tinston, 1982
80[a]	2 h	Rat, guinea pig	--	Depression	--	Paulet, 1962
		Mouse	--	Hyperactivity	--	Paulet, 1962
		Rabbit	--	Convulsions, depression	--	Paulet, 1962
80[c]	Up to 40 min	Dog	Spontaneous arrhythmias, cardiac arrest and ventricular fibrillation after iv injection of epinephrine, decreased blood pressure	Agitation, convulsions	--	Van Stee and Back, 1969
70-80[c]	Up to 60 min	Monkey	--	Activation of EEG, particularly in presence of sensory stimuli	Suggested that $CBrF_3$ affects "higher" CNS functions to greater degree than "lower" functions	Van Stee *et al.*, 1970
20-80[c]	10-60 min	Monkey, baboon	Arrhythmias induced within 5-40 s, increased heart rate	Cortical depression	Epinephrine had less pressor effect than in dog	Van Stee and Back, 1969
60[a]	2 h	Rat, guinea pig, mouse, rabbit	--	Hypoactivity	Slow, deep respiration	Paulet, 1962
60[c]	3 min	Dog	T-wave alterations in ECG, arrhythmias	Convulsions	--	Van Stee and Back, 1969
50[a]	2 h	Rat, guinea pig, mouse, rabbit	--	Initial slight depression	--	Paulet, 1962
50[c]	40 min	Dog	ECG changes after injection of epinephrine	Convulsions	--	Van Stee and Back, 1969

Table 2 (continued)

$CBrF_3$ Conc., %	Exposure Duration	Animal	Cardiovasacular Effects	Central Nervous System Effects	Other Observations	Reference
20–42[c]	15 min	Monkey	--	Decrements in avoidance - performance tests, higher concentrations caused animals to cease performance entirely	--	Carter et al., 1970
20–40[c]	Up to 40 min	Dog	Increased heart rate	--	--	Van Stee and Back, 1969
37[b]	7 h	Cat	--	--	1 of 1 died	Graham, 1978
		Guinea pig	--	--	6 of 6 died	
		Mouse	--	--	8 of 10 died	
		Rat	--	--	4 of 10 died	
		Rabbit	--	--	4 of 4 died	
37[b]	7 h	Guinea pig	--	--	No deaths	Graham, 1978
30[b]	2 h	Rabbit, guinea pig, rat, mouse	--	--	No effect seen	Paulet, 1962
20[b]	2 h	Monkey	--	--	Glassy eyes	Graham, 1978
		Rabbit	--	--	Restlessness	
		Guinea pig	--	--	Lacrimation	
		Rat	--	--	Restlessness	
20[b]	2 h	Guinea pig	--	--	No signs of toxicity observed	Reinhardt and Reinke, 1972
20[b]	5 min	Dog	Arrhythmias in 8 of 13 after injection of epinephrine	--	--	Mullin et al., 1978
10.5–20[c]	15 min	Monkey	--	No decrements in avoidance - performance tests	--	Carter et al., 1970
10–20[b]	2 h	Monkey, rabbit, guinea pig	--	--	No change in physical appearance or blood chemistry	Reinhardt and Reinke, 1972
18[b]	7 h	Rabbit	--	--	1 of 4 died	Graham, 1978
		Cat, mouse, guinea pig	--	--	No deaths	
15[b]	2 h	Monkey	--	--	Glassy eyes	Graham, 1978
		Rabbit, guinea pig, rat	--	--	No effects	

Table 2 (continued)

$CBrF_3$ Conc., %	Exposure Duration	Animal	Cardiovasacular Effects	Central Nervous System Effects	Other Observations	Reference
15[b]	5 min	Dog	Arrhythmias in 2 of 7 after injection of epinephrine	--	--	Mullin et al., 1978
10[b]	30 min	Dog	Arrhythmias in 2 of 12 after injection of epinephrine	--	--	Mullin et al., 1978
10[b]	5 min	Dog	Arrhythmias in 8 of 69 after injection of epinephrine	--	--	Mullin et al., 1978
9[b]	7 h	Cat, mouse, rat, rabbit, guinea pig	--	--	No effects	Graham, 1978
7.5[b]	60 min	Dog	Arrhythmias in 1 of 12 after injection of epinephrine	--	--	Mullin et al., 1978
7.5[b]	30 min	Dog	Arrhythmias in 2 of 12 after injection of epinephrine	--	--	Mullin et al., 1978
7.5[b]	5 min	Dog	Arrhythmias in 1 of 18 after injection of epinephrine	--	--	Mullin et al., 1978
5	60 min	Dog	No arrhythmias in 12 after injection of epinephrine	--	--	Mullin et al., 1978
5[b]	5 min	Dog	No arrhythmias in 16 after injection of epinephrine	--	--	Mullin et al., 1978
0.9-5[b]	2 h	Guinea pig	--	--	No effects	Graham, 1978.

[a] In air enriched with oxygen.
[b] In air.
[c] In oxygen.

TABLE 3

Effects on Animals of Prolonged Exposure to $CBrF_3$

$CBrF_3$ Conc., %	Exposure Duration	Animal	Effects	Reference
20-60[a]	Up to 70 h	Rat (3), guinea pig (3), dog (1), cat (3)	None observed	Scholz and Weigand, 1964
50[b]	2 h/d, 15 d	Mouse (20), rat (10), guinea pig (10)	None observed	Paulet, 1962
18[c]	7 h twice	Cat (1) Guinea pig (5) Rabbit (4) Rat (10) Mouse (10) Dog (1)	None observed 5 died 1 died None observed None observed None observed	Graham, 1978
9[c]	7 h twice	Dog (1)	None observed	Graham, 1978
8.7[c]	7 h twice	Guinea pig (6)	4 died	Graham, 1978
5[c]	24 h/d, 10 d	Rat (20), guinea pig (20)	No signs of toxicity or blood and cellular changes observed	McHale, 1974
5[a]	23 h/d, 30 d	Rat	No hematologic or gross pathologic changes observed	Griffin et al., 1972
2.3[c]	6 h/d, 5 d/wk, 18 wk	Rat (30), dog (2)	No signs of toxicity observed, pulmonary congestion	Comstock et al., 1953
2.8[c]	29 d	Monkey	Blood content 100-300 µg/ml	Geller et al., 1981

Tinston (1982) reported that $CBrF_3$ at 42% resulted in gross CNS effects (tremors, ataxia, or loss of righting reflex) in 50% of rats in 10 min.

Four baboons were used in a behavioral study involving a match-to-sample discrimination task, and six cynomolgus monkeys were studied for conditioned emotional response and cardiac arrhythmias (Geller et al., 1981). Each species was exposed continuously to $CBrF_3$ at 2.8% for 30 d. The monkeys were under severe stress during the study, and two had to be sacrificed before its completion. The baboons served as their own controls; behavioral tests were done before, during, and after the exposure period. Some prolongation of reaction time was found during the exposure period, and it was significant in two of the four animals.

CARDIOVASCULAR EFFECTS

Like many other halogenated hydrocarbons, $CBrF_3$ sensitizes the heart to the effects of epinephrine. Cardiac arrhythmias and ventricular fibrillation have been produced in animals exposed to $CBrF_3$ with or without the injection of epinephrine. The 10 min EC_{50} of $CBrF_3$ for ventricular tachycardia or arrhythmia in dogs given epinephrine was 20% (Clark and Tinston, 1982).

Anesthetized dogs exposed to $CBrF_3$ at 80% in oxygen for up to 40 min developed ventricular fibrillation and cardiac arrest after intravenous injection of epinephrine (5-10 µg/kg) (Van Stee and Back, 1969). Monkeys and baboons developed spontaneous arrhythmias within 40 s of exposure to $CBrF_3$ at 20-90% (Van Stee and Back, 1969). Dogs were not quite as sensitive; arrhythmias began within 2 min of exposure at concentrations of 40% or greater. In another study, however, half the dogs exposed to $CBrF_3$ at 20% for 5 min and given injections of epinephrine (5 µg/kg) during the last 10 s developed arrhythmias (Clark and Tinston, 1973).

Mullin et al. (1978) exposed dogs to $CBrF_3$ at 5-20% after injection of epinephrine at 8-10 µg/kg. Arrhythmias considered to pose "a serious threat to life" were tabulated. These were defined as multiple consecutive ventricular beats or ventricular fibrillation. None of the dogs exposed to $CBrF_3$ at 5% had serious arryhthmias. One of 18 at 7.5% and an increasing proportion of dogs at higher concentrations (8 of 13 at 20%) were so affected.

Trochimowicz et al. (1976) exposed dogs that had recovered from experimentally induced myocardial infarctions to $CBrF_3$ at 5, 7.5, and 10% and then gave them intravenous injections of epinephrine. They found no greater potential for cardiac sensitization in dogs that had recovered from myocardial infarction than in normal animals.

$CBrF_3$ at 10-80% caused a decrease of 10-60 mm Hg in mean arterial blood pressure in dogs; the magnitude of the decrease was generally related to the concentration of the gas (Van Stee and Back,

1969). Some dogs exposed to $CBrF_3$ also had increases in heart rate at concentrations of 20-30%, and all had increases of 10-15% at concentrations of 40% or greater. Monkeys also exhibited increases in heart rate of 10-15% associated with exposure to $CBrF_3$ at over 20% during the first minute of exposure and before ventricular premature beats appeared. Back and Van Stee (1979) exposed five dogs to $CBrF_3$ at 50 and 75%. The mean peak dp/dt - p (rate of change of intraventricular pressure) during the $CBrF_3$ exposures differed significantly ($P < 0.01$) from those measured during before exposure and 10 min after exposure.

EFFECTS OF PROLONGED EXPOSURE

Studies of animals exposed to $CBrF_3$ for long periods have been limited to investigating gross signs of toxicity. No effects were observed in three rats, three guinea pigs, three cats and one dog exposed at 20-60% for up to 70 h (Scholz and Weigand, 1964) or in 20 mice, 10 rats and 10 guinea pigs exposed at 50% for 2 h/d for 15 d (Paulet, 1962). All five guinea pigs and one of four rabbits died after two 7-h exposures to $CBrF_3$ at 18% (Haskell Laboratory, 1978). Cats, dogs, rats, and mice were unaffected. Continuous exposure for 10 d at 5% produced no observable signs of toxicity or any histologic or hematologic changes in rats and guinea pigs (McHale, 1974). Similar results were obtained in rats exposed at 5% for 23 h/d for 30 d (Griffin et al., 1972). In rats and dogs exposed at 2.3% for 6 h/d, 5 d/wk, for 18 wk, the only effect seen was some pulmonary congestion (Comstock et al., 1953).

These data on prolonged exposure indicate that a $CBrF_3$ concentration of 5% in air produces no effect on blood chemistry and does not cause pathologic changes. Specifically, none of these studies found histopathologic damage to CNS or cardiovascular tissue. However, none of them investigated the possibility of functional CNS or cardiovascular changes (as measured by psychomotor or electrophysiologic tests), which acute exposures to $CBrF_3$ are known to produce. Detailed studies of that kind are needed before the Committee can completely assess the risks of prolonged exposure to $CBrF_3$.

CARCINOGENICITY, MUTAGENICITY, AND TERATOGENICITY

No evidence of a carcinogenic potential has been found. However, the longest study conducted was an 18-wk inhalation study (Comstock et al., 1953)

$CBrF_3$ was tested in Salmonella typhimurium strains TA 1535, TA 1537, TA 1538, TA 98, and TA 100 at up to 40%. The gas was not mutagenic either in the presence or in the absence of a liver microsomal system (Haskell Laboratory, undated).

Groups of 27 pregnant rats were exposed to $CBrF_3$ at 962 ± 57, $10,196 \pm 1514$ or $49,505 \pm 4753$ ppm for 6 h/d on days 6-15 of

gestation. 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 -- was not adversely affected by the exposure. Exposure did not affect fetal development as measured by fetal weight and crown-rump length. Three fetuses were found with malformations; all three were from dams exposed at the intermediate level, but, these effects were not considered compound-related. Under the conditions of this test, $CBrF_3$ was not embryotoxic or teratogenic (Haskell Laboratory, undated).

PHARMACOKINETICS

Blood concentrations of $CBrF_3$ in dogs and humans after brief exposure appear to be roughly comparable. In dogs exposed at 5, 7.5, and 10%, arterial and venous concentrations rose rapidly during the first 5 - 10 min of exposure and then fluctuated about a plateau until exposure was stopped after 60 min (Mullin et al., 1978). By 5 min after exposure, blood concentrations had decreased to about one-third of the plateau value in venous blood and one-fourth to one-tenth in arterial blood. The mean concentrations between 20 and 60 min of exposure are shown in Table 4.

Van Stee et al. (1971) exposed 30 mice to $CBrF_3$ at 80% for 5 h/d for 3 consecutive days. The hexabarbital sleeping times and zoxazolamine paralysis times were not found to be different between $CBrF_3$-exposed mice and control animals.

Mean venous concentrations in six human volunteers exposed to $CBrF_3$ at 7% were between 26 and 28 μg/g of blood between 30 min and 3 h after onset of exposure (Harrison et al., 1982). Postexposure blood concentrations were not reported. The concentration in alveolar air decreased rapidly during the first 2 h after cessation of exposure, but measurable amounts were still found after 19 h. Serum bromine, a possible indicator of the breakdown of $CBrF_3$, was undetectable.

Van Stee and Back (1971) studied tissue concentrations in rats acutely exposed to $CBrF_3$ at 70-75% in oxygen for 5 min. At the end of the 5-min exposure, the brain concentration was approximately 50% greater than the heart concentration. The heart concentration did not differ significantly from the blood concentration. The postexposure rates of decrease in tissue concentrations of $CBrF_3$ were approximately equal. Only trace amounts of $CBrF_3$ were detectable beyond 10 min after exposure.

In the study of Geller et al. (1981) on cynomolgus monkeys discussed earlier, the amount of $CBrF_3$ in venous blood of three monkeys was examined after 29 d of exposure at 2.8%. The concentrations were between 100 and 300 μg/ml in individual animals. No data were given on short exposures. These blood concentrations are at least 10 times those expected from results in dogs and humans after short exposures. Whether the difference is related to species,

TABLE 4

Blood Concentrations of CBrF3 in Dogs at Equilibrium (20-60 Minutes)[a]

Exposure Concentration, %	Mean Arterial Blood Concentration, μg/ml	Mean Venous Blood Concentration, μg/ml
5%	19.2	14.6
7.5%	30.6	28.4
10%	40.2	32.1

[a]Data from Mullin et al. (1978).

longer exposure time, or the physical condition of the animals used cannot be determined.

HEALTH EFFECTS OF BROMOTRIFLUOROMETHANE DECOMPOSITION PRODUCTS

The relatively slight acute toxicity of $CBrF_3$, compared with that of other halogenated fire-extinguishing agents, and its general effectiveness in fighting some kinds of fires have led to its widespread acceptance. Because of the likelihood of decomposition during use, the toxicity of its decomposition products must also be considered in evaluating its appropriateness as a fire-extinguishing agent.

$CBrF_3$ begins to decompose on contact with a flame or hot surface at approximately 540°C (Haskell Laboratory, 1978). Decomposition products of $CBrF_3$ that have been identified include hydrogen fluoride (HF), hydrogen bromide (HBr), bromine gas (Br_2), and carbonyl halides (COF_2 and $COBr_2$). In one study, rats were exposed for 15 min to the products of $CBrF_3$ pyrolyzed in a hydrogen-oxygen flame at 800°C (Haun et al., 1969). The concentrations of $CBrF_3$ before and after ignition of the material were measured, and the difference represented the concentration of pyrolyzed $CBrF_3$. When $CBrF_3$ was originally at 3,400-7,900 ppm (0.34-0.79%), it was found that 49-50% was pyrolyzed. HF was by far the most prevalent decomposition product; HBr and Br_2 were also detected. The rats were observed for 14 d after exposure. The LC_{50} for pyrolyzed $CBrF_3$ for a 15 min exposure was 2,300 ppm (0.23%). Autopsies showed pulmonary congestion, edema, and hemorrhage, which were of increased severity at the higher concentrations of pyrolysis products. Severe eye and nose irritation occurred in rats exposed at or above the LC_{50}. The toxic effects of pyrolyzed $CBrF_3$ were attributed to the formation of HF. It was found that prolysis of $CBrF_3$ at 3,920 ppm (0.39%) resulted in an HF concentration of 2,280 ppm (0.23%), which is similar to the LC_{50} for HF and for pyrolyzed $CBrF_3$ (Haun et al., 1969).

The approximate lethal concentration of $CBrF_3$ in rats for a 15-min exposure was found to be 14,000 ppm (1.4%) for pyrolysis in an iron tube at 800°C and 17,000 ppm (1.7%) for pyrolysis in an Inconel tube at 1,090°C (Chambers et al., 1950; Haun et al., 1969).

McHale (1974) measured the rate of formation of pyrolysis products. Liquid- and solid-fuel fires were set in a 3.75-in-diameter pan in a 16-ft^3 chamber. About 3% $CBrF_3$ was needed to extinguish the fire, and it was found that HF was formed at the rate of 30 ppm/s. The author stated that that was equivalent to a 1-ft-diameter fire in a 1,000-ft^3 enclosure producing HF at 5 ppm/s of discharge time. To examine the effects of $CBrF_3$ under fire conditions, male rats were exposed for 1 h to room air, to the vapors from a 30-s acetone fire, or to the vapors produced by extinguishing an acetone fire in 7.5 s with $CBrF_3$. The rats were observed for 72 h, and the

only adverse effect seen was labored breathing in the rats exposed to the vapors of the $CBrF_3$-extinguished fire (McHale, 1974).

When mice and rats were exposed to the vapors from a gasoline fire extinguished with $CBrF_3$ in 15-60 s, the highest mortality rate observed was 6% (Comstock and Oberst, 1953). The concentration of $CBrF_3$ ranged from 0.18-0.27%, and the temperature in the chamber, from 28 to 51°C. Adverse effects included incoordination, increased respiration, and congestion of the trachea and lungs. The only decomposition products detected were carbonyl halides in trace amounts.

Pyrolysis temperature has been observed to affect the toxicity of $CBrF_3$ dramatically (Paulet, 1962). $CBrF_3$ (400,000-800,000 ppm) (40-80%) was heated to 800°C in an iron tube. All rats, mice, and guinea pigs exposed to its pyrolysis products survived after exposure for 30 min. Some animals became prostrate and had labored breathing. When the pyrolysis temperature was raised to 1,000°C, all animals exposed at 10,000 ppm (1%) died, and half those exposed at 5,000 ppm (0.5%) died. Toxic effects included irritation of the eyes, nose, and throat and pulmonary edema.

At high temperatures or when $CBrF_3$ is used to extinguish large fires in enclosed spaces, HF is the most important toxic decomposition product, because of the amount formed and its inherent toxicity, in comparison with other decomposition products (Vernot, 1967). At the LC_{50} value of pyrolyzed $CBrF_3$ (2,300 ppm), 2,480 ppm of HF were formed (Vernot, 1967).

When fires are extinguished rapidly and completely, as is the case when discharge time is short and $CBrF_3$ concentration is 6-7%, the formation of decomposition products is so small as to be of no concern with regard to toxicity and corrosivity. Contact time with flame and hot surfaces appears to be the critical factor.

The DuPont Company has reported that under most fire situations where $CBrF_3$ is used in automatic protection systems, the HF concentration is usually less than 20 ppm -- often barely detectable to the nose. However, severe fire tests indicate that larger amounts of HF (200-300 ppm) and HBr (40-50 ppm) are produced when $CBrF_3$ decomposes in the extinguishing of a large, hot fire (DuPont, undated). Such concentrations are noxious and irritating and may be harmful if exposure is prolonged. Even in very low concentrations, however, these gases have a characteristic sharp, acrid odor, which constitutes a built-in warning system.

The U.S. Coast Guard (1972) conducted several fire tests to determine the efficacy of $CBrF_3$ and the production of its decomposition products. Its conclusion was that, in most cases when the $CBrF_3$ concentration was above 5% and discharge time was 10 s or less, HF and HBr were produced at below 5 ppm and 1 ppm, respectively, and that the discharge time was very important (the smaller the

discharge time, the smaller the amounts of decomposition product). By comparison, the emergency and continuous exposure limits for HF recommended by the National Research Council (1971b) were as follows: 10 min, 20 ppm; 30 min, 10 ppm; 60 min, 8 ppm; 24 h, 2 ppm; and 90 d, 1 ppm.

A comparison of the acute toxicity of nondecomposed $CBrF_3$ vapor with that of decomposed vapor shows that, in a fire, the toxicity of $CBrF_3$ can be greatly increased, depending primarily on the temperature of the fire. Whereas the approximate lethal concentration of nondecomposed $CBrF_3$ is greater than 80% in rats and mice, during pyrolysis the approximate lethal concentration has been reported to be as low as 1%. However, wide variations in the lethal concentration of $CBrF_3$ from pyrolysis have been reported. The differences are due to the lack of uniformity of method, and to differences in temperature, type of fuel burned, and oxygen availability. All can produce differences in the quantities and types of pyrolysis products. Therefore it is difficult to make valid comparisons from these studies.

INHALATION EXPOSURE LIMITS

The American Conference of Governmental Industrial Hygienists (1980, 1983) has recommended a threshold limit value (TLV) of 1,000 ppm (0.1%) for $CBrF_3$ as a time-weighted average (TLV-TWA) concentration for an 8-h workday and a 40-h workweek. That value was selected because "it represents the maximal limit hygienically desirable for any contaminant." A 15-min short-term exposure limit (STEL) of 1,200 ppm was also recommended by the ACGIH. The Occupational Safety and Health Administration (1983) proposed 1,000 ppm as the standard for an 8-h time-weighted average concentration.

COMMITTEE RECOMMENDATIONS

The Committee on Toxicology of the National Research Council has responded to prior requests from its sponsoring agencies to review the literature concerning $CBrF_3$. Inhalation exposure limits were recommended in 1967, 1973, and 1979.

In 1967, the Committee evaluated the toxicity of $CBrF_3$ for the National Aeronautics and Space Administration (NASA). On the basis of human and animal toxicity data, the Committee concluded that personnel can be exposed without substantial hazard for a maximum of 5 min to normal air at 1 atm admixed with $CBrF_3$ at a mean concentration of up to 60,000 ppm (6%) by volume. That conclusion was based on the assumption that the fire would be extinguished promptly by $CBrF_3$ and that pyrolysis would be minimized.

In 1973, the Navy asked the Committee to recommend 1-, 8-, and 24-h exposure limits for $CBrF_3$, because it would be carried on submarines. Because $CBrF_3$ would not be removed by the air purification system of a submarine, the crew might be exposed

during its entire mission and in the absence of information on the effects of long-term exposure to $CBrF_3$, the Committee elected not to recommend maximal exposure limits. The Committee later approved a 10-min exposure limit for $CBrF_3$ of 70,000 ppm (7%) in shipboard machinery spaces, provided that a ventilation system could begin operating immediately on the release of $CBrF_3$ at an air-exchange rate of 2-4 min and continue operating for 20 min.

NASA asked the Committee in 1979 to recommend exposure limits for $CBrF_3$, which was to be used in the fire-extinguishing systems of the shuttles Orbiter and Spacelab. The Committee (NRC, 1979b) recommended a 1-h EEL of 25,000 ppm (2.5%), on the basis of minor reversible CNS effects in humans exposed at 4.5% for up to 30 min, an absence of effects in humans exposed at 3% for 30 min or less, and an absence of effects in several species of animals exposed at 9% for up to 7 h. (Tables 1 and 2).

Studies on $CBrF_3$ issued or published since the last report of the Committee on Toxicology (1979b) are compatible with its conclusions on short-term toxic effects. They reinforce the conclusion that, for short-term exposures, the pyrolysis products of $CBrF_3$ are much more toxic than the parent compound. Intense fires in enclosed spaces could produce concentrations of HF, in particular, that far exceed recommended human exposure limits proposed by the Committee (1971b). Protection against these exposures and rapid exchange of air after fires in enclosed spaces that humans must occupy are needed. The Committee therefore recommends a 1-h EEL of 25,000 ppm (2.5%) and a 30-min EEL of 40,000 ppm (4.0%). Some decrements, such as in reasoning and equilibrium, may be experienced by some persons at these concentrations.

Portable monitoring devices are available for $CBrF_3$ and HF and should be used before one enters areas where CBr_3 was used for extinguishing fires.

The Committee also recommends a 90-d CEL of 100 ppm. That is based on the study of Comstock et al. (1953), who showed that rats and dogs exposed at 23,000 ppm (vol/vol) for 6 h/d, 5 d/wk, for 18 wk showed no substantial adverse effects. However, no chronic-exposure studies have included carcinogenicity. On the basis of its low biologic reactivity, negative in vitro mutagenicity results, and similarity to other fluorocarbons, it is unlikely to be carcinogenic. The CEL of 100 ppm is in agreement with the CEL established for FC-11, FC-12, FC-113 and FC-114--all closely related to $CBrF_3$ (NRC, 1984).

The present Committee's recommended EELs and CEL for bromotrifluoromethane and the limits proposed previously are shown below.

	1967	1973	1979	1984
5-min EEL	60,000 ppm	--	--	--
10-min EEL	--	70,000 ppm	--	--
30-min EEL	--	--	--	40,000 ppm
1-h EEL	--	--	25,000 ppm	25,000 ppm
90-d CEL	--	--	--	100 ppm

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