IMMEDIATELY DANGEROUS TO LIFE OR HEALTH (IDLH) VALUE PROFILE

FOR

BROMINE TRIFLUORIDE

[CAS® NO. 7787-71-5]

Department of Health and Human Services
Centers for Disease Control and Prevention
National Institute for Occupational Safety and Health

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Foreword

Chemicals are a ubiquitous component of the modern workplace. Occupational exposures to chemicals have the potential to adversely affect the health and lives of workers. Acute or short-term exposures to high concentrations of some airborne chemicals have the ability to quickly overwhelm workers, resulting in a spectrum of undesirable health outcomes that may inhibit the ability to escape from the exposure environment (e.g., irritation of the eyes and respiratory tract or cognitive impairment), cause severe irreversible effects (e.g., damage to the respiratory tract or reproductive toxicity), and in extreme cases, cause death. Airborne concentrations of chemicals capable of causing such adverse health effects or of impeding escape from high-risk conditions may arise from a variety of non-routine workplace situations, including special work procedures (e.g., in confined spaces), industrial accidents (e.g., chemical spills or explosions), and chemical releases into the community (e.g., during transportation incidents or other uncontrolled-release scenarios).

The immediately dangerous to life or health (IDLH) air concentration values developed by the National Institute for Occupational Safety and Health (NIOSH) characterize these high-risk exposure concentrations and conditions [NIOSH 2013]. IDLH values are based on a 30-minute exposure duration and have traditionally served as a key component of the decision logic for the selection of respiratory protection devices [NIOSH 2004].

Occupational health professionals have employed these values beyond their initial purpose as a component of the *NIOSH Respirator Selection Logic* to assist in developing risk management plans for non-routine work practices governing operations in high-risk environments (e.g., confined spaces) and the development of emergency preparedness plans.

The approach used to derive IDLH values for high priority chemicals is outlined in the *NIOSH Current Intelligence Bulletin (CIB) 66: Derivation of Immediately Dangerous to Life or Health Values* [NIOSH 2013]. CIB 66 provides (1) an update on the scientific basis and risk assessment methodology used to derive IDLH values, (2) the rationale and derivation process for IDLH values, and (3) a demonstration of the derivation of scientifically credible IDLH values using available data resources.

The purpose of this technical report is to present the IDLH value for Bromine Trifluoride (CAS® No. 7787-71-5). The scientific basis, toxicologic data, and risk assessment approach used to derive the IDLH value are summarized to ensure transparency and scientific credibility.

John Howard, M.D.
Director
National Institute for Occupational Safety and Health
Centers for Disease Control and Prevention

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Abbreviations

ACGIH®	American Conference of Governmental Industrial Hygienists
AEGLs	Acute Exposure Guideline Levels
AIHA®	American Industrial Hygiene Association
BMC	benchmark concentration
BMD	benchmark dose
BMCL	benchmark concentration lower confidence limit
BrF_3	Bromine trifluoride
BrF_5	Bromine pentafluoride
°C	degrees Celsius
CAS®	Chemical Abstracts Service, a division of the American Chemical Society
CIB	Current Intelligence Bulletin
ClF_3	Chlorine trifluoride
ClF_5	Chlorine pentafluoride
ERPGs™	Emergency Response Planning Guidelines
ET_{50}	Effective time to 50% mortality
°F	degrees Fahrenheit
g/cu cm	grams per cubic centimeter
HF	Hydrogen fluoride
IDLH	immediately dangerous to life or health
LC	lethal concentration
LC_{50}	median lethal concentration
LC_{LO}	lowest concentration that caused death in humans or animals
LEL	lower explosive limit
LOAEL	lowest observed adverse effect level
mg/m^3	milligram(s) per cubic meter
min	minutes
mmHg	millimeter(s) of mercury
NAC	National Advisory Committee
NAS	National Academy of Sciences
NIOSH	National Institute for Occupational Safety and Health
NLM	National Library of Medicine
NOAEL	no observed adverse effect level
NRC	National Research Council
OSHA	Occupational Safety and Health Administration
PEL	permissible exposure limit
ppm	parts per million
RD_{50}	concentration of a chemical in the air that is estimated to cause a 50% decrease in the respiratory rate
REL	recommended exposure limit
STEL	short-term exposure limit
TLV®	Threshold Limit Value

TWA	time-weighted average
UEL	upper explosive limit
WEELs®	Workplace Environmental Exposure Levels

Glossary

Acute exposure: Exposure by the oral, dermal, or inhalation route for 24 hours or less.

Acute Exposure Guideline Levels (AEGLs): Threshold exposure limits for the general public, applicable to emergency exposure periods ranging from 10 minutes to 8 hours. AEGL-1, AEGL 2, and AEGL-3 are developed for five exposure periods (10 and 30 minutes, 1 hour, 4 hours, and 8 hours) and are distinguished by varying degrees of severity of toxic effects, ranging from transient, reversible effects to life-threatening effects [NAS 2001]. AEGLs are intended to be guideline levels used during rare events or single once-in-a-lifetime exposures to airborne concentrations of acutely toxic, high-priority chemicals [NAS 2001]. The threshold exposure limits are designed to protect the general population, including the elderly, children, and other potentially sensitive groups that are generally not considered in the development of workplace exposure recommendations (additional information available at http://www.epa.gov/oppt/aegl/).

Acute reference concentration (Acute RfC): An estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure for an acute duration (24 hours or less) of the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. It can be derived from a NOAEL, LOAEL, or benchmark concentration, with uncertainty factors (UFs) generally applied to reflect limitations of the data used. Generally used in U.S. EPA noncancer health assessments [U.S. EPA 2018].

Acute toxicity: Any poisonous effect produced within a short period of time following an exposure, usually 24 to 96 hours [U.S. EPA 2018].

Adverse effect: A substance-related biochemical change, functional impairment, or pathologic lesion that affects the performance of an organ or system or alters the ability to respond to additional environmental challenges.

Benchmark dose/concentration (BMD/BMC): A dose or concentration that produces a predetermined change in response rate of an effect (called the benchmark response, or BMR) compared to background [U.S. EPA 2018] (additional information available at http://www.epa.gov/ncea/bmds/).

Benchmark response (BMR): An adverse effect, used to define a benchmark dose from which a reference dose or concentration can be developed. The change in response rate over background of the BMR is usually in the range of 5-10%, which is the limit of responses typically observed in well-conducted animal experiments [EPA 2018].

BMCL: A statistical lower confidence limit on the concentration at the BMC [U.S. EPA 2018].

Bolus exposure: A single, relatively large dose.

Ceiling value ("C"): U.S. term in occupational exposure indicating the airborne concentration of a potentially toxic substance that should never be exceeded in a worker's breathing zone.

Chronic exposure: Repeated exposure for an extended period of time. Typically exposures are more than approximately 10% of life span for humans and >90 days to 2 years for laboratory species.

Critical study: The study that contributes most significantly to the qualitative and quantitative assessment of risk [U.S. EPA 2018].

Dose: The amount of a substance available for interactions with metabolic processes or biologically significant receptors after crossing the outer boundary of an organism [U.S. EPA 2018].

ECt_{50}: A combination of the effective concentration of a substance in the air and the exposure duration that is predicted to cause an effect in 50% (one half) of the experimental test subjects.

Emergency Response Planning Guidelines (ERPGs™): Maximum airborne concentrations below which nearly all individuals can be exposed without experiencing health effects for 1-hour exposure. ERPGs are presented in a tiered fashion, with health effects ranging from mild or transient to serious, irreversible, or life threatening (depending on the tier). ERPGs are developed by the American Industrial Hygiene Association [AIHA 2016].

Endpoint: An observable or measurable biological event or sign of toxicity, ranging from biomarkers of initial response to gross manifestations of clinical toxicity.

Exposure: Contact made between a chemical, physical, or biological agent and the outer boundary of an organism. Exposure is quantified as the amount of an agent available at the exchange boundaries of the organism (e.g., skin, lungs, gut).

Extrapolation: An estimate of the response at a point outside the range of the experimental data, generally through the use of a mathematical model, although qualitative extrapolation may also be conducted. The model may then be used to extrapolate to response levels that cannot be directly observed.

Hazard: A potential source of harm. Hazard is distinguished from risk, which is the probability of harm under specific exposure conditions.

Immediately dangerous to life or health (IDLH) condition: A condition that poses a threat of exposure to airborne contaminants when that exposure is likely to cause death or immediate or delayed permanent adverse health effects or prevent escape from such an environment [NIOSH 2004, 2013].

IDLH value: A maximum (airborne concentration) level above which only a highly reliable breathing apparatus providing maximum worker protection is permitted [NIOSH 2004, 2013]. IDLH values are based on a 30-minute exposure duration.

LC_{01}: The statistically determined concentration of a substance in the air that is estimated to cause death in 1% of the test animals.

LC_{50}: The statistically determined concentration of a substance in the air that is estimated to cause death in 50% (one half) of the test animals; median lethal concentration.

LC_{LO}: The lowest lethal concentration of a substance in the air reported to cause death, usually for a small percentage of the test animals.

LD_{50}: The statistically determined lethal dose of a substance that is estimated to cause death in 50% (one half) of the test animals; median lethal concentration.

LD_{LO}: The lowest dose of a substance that causes death, usually for a small percentage of the test animals.

LEL: The minimum concentration of a gas or vapor in air, below which propagation of a flame does not occur in the presence of an ignition source.

Lethality: Pertaining to or causing death; fatal; referring to the deaths resulting from acute toxicity studies. May also be used in lethality threshold to describe the point of sufficient substance concentration to begin to cause death.

Lowest observed adverse effect level (LOAEL): The lowest tested dose or concentration of a substance that has been reported to cause harmful (adverse) health effects in people or animals.

Mode of action: The sequence of significant events and processes that describes how a substance causes a toxic outcome. By contrast, the term *mechanism of action* implies a more detailed understanding on a molecular level.

No observed adverse effect level (NOAEL): The highest tested dose or concentration of a substance that has been reported to cause no harmful (adverse) health effects in people or animals.

Occupational exposure limit (OEL): Workplace exposure recommendations developed by governmental agencies and nongovernmental organizations. OELs are intended to represent the maximum airborne concentrations of a chemical substance below which workplace exposures should not cause adverse health effects. OELs may apply to ceiling limits, STELs, or TWA limits.

Peak concentration: Highest concentration of a substance recorded during a certain period of observation.

Permissible exposure limits (PELs): Occupational exposure limits developed by OSHA (29 CFR 1910.1000) or MSHA (30 CFR 57.5001) for allowable occupational airborne exposure concentrations. PELs are legally enforceable and may be designated as ceiling limits, STELs, or TWA limits.

Point of departure (POD): The point on the dose–response curve from which dose extrapolation is initiated. This point can be the lower bound on dose for an estimated incidence or a change in response level from a concentration-response model (BMC), or it can be a NOAEL or LOAEL for an observed effect selected from a dose evaluated in a health effects or toxicology study.

RD_{50}: The statistically determined concentration of a substance in the air that is estimated to cause a 50% (one half) decrease in the respiratory rate.

Recommended exposure limit (REL): Recommended maximum exposure limit to prevent adverse health effects, based on human and animal studies and established for occupational (up to 10-hour shift, 40-hour week) inhalation exposure by NIOSH. RELs may be designated as ceiling limits, STELs, or TWA limits.

Short-term exposure limit (STEL): A worker's 15-minute time-weighted average exposure concentration that shall not be exceeded at any time during a work day.

Target organ: Organ in which the toxic injury manifests in terms of dysfunction or overt disease.

Threshold Limit Values (TLVs®): Recommended guidelines for occupational exposure to airborne contaminants, published by the American Conference of Governmental Industrial Hygienists (ACGIH®). TLVs refer to airborne concentrations of chemical substances and represent conditions under which it is believed that nearly all workers may be repeatedly exposed, day after day, over a working lifetime, without adverse effects. TLVs may be designated as ceiling limits, STELs, or 8-hr TWA limits.

Time-weighted average (TWA): A worker's 8-hour (or up to 10-hour) time-weighted average exposure concentration that shall not be exceeded during an 8-hour (or up to 10-hour) work shift of a 40-hour week. The average concentration is weighted to take into account the duration of different exposure concentrations.

Toxicity: The degree to which a substance is able to cause an adverse effect on an exposed organism.

Uncertainty factors (UFs): Mathematical adjustments applied to the POD when developing IDLH values. The UFs for IDLH value derivation are determined by considering the study and effect used for the POD, with further modification based on the overall database.

Workplace Environmental Exposure Levels (WEELs®): Exposure levels developed by the American Industrial Hygiene Association (AIHA®) that provide guidance for protecting most workers from adverse health effects related to occupational chemical exposures, expressed as TWA or ceiling limits.

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Education and Information Division

Devin Baker, M.Ed.
Charles L. Geraci, Ph.D.
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Michael S. Bisesi, Ph.D., R.E.H.S., C.I.H., Senior Associate Dean for Academic Affairs; Director, Center for Public Health Practice; Interim Chair and Associate Professor, Division of Environmental Health Science, College of Public Health, Ohio State University, Columbus, OH

Mary A. Fox, Ph.D., Assistant Professor; Co-Director, Risk Sciences and Public Policy Institute; Department of Health Policy and Management, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD

Bill Luttrell, Ph.D., Chair and Professor, Department of Chemistry and Physics, College of Natural and Health Sciences, Oklahoma Christian University, Edmond, OK

Richard B. Schlesinger, Ph.D., Fellow A.T.S., Senior Associate Dean for Academic Affairs and Research and Professor of Biology, Dyson College of Arts and Sciences, Pace University, New York, NY

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1.0 Introduction

1.1 Overview of the IDLH Value for Bromine Trifluoride

IDLH Value: 10 ppm (56 mg/m^3)

Basis for IDLH Value: Data were inadequate to directly derive an IDLH value for bromine trifluoride (BrF_3). For this reason, data from studies with chlorine trifluoride (ClF_3) were used to develop an IDLH value for BrF_3 because their structures, reaction mechanisms, and potencies are assumed to be similar. Therefore, deriving an IDLH value based on the toxicity data for ClF_3 is appropriately health-protective. The mouse LC_{50} of 178 ppm of ClF_3 is used as the basis for the IDLH value since it is the most protective [Darmer et al. 1972]. The duration adjusted 30-minute LC_{50} is 303 ppm. An uncertainty factor of 30 was applied to account for extrapolation from a concentration that is lethal to animals, animal to human differences, and human variability, resulting in a derived IDLH value of 10 ppm.

1.2 Purpose

This *IDLH Value Profile* presents (1) a brief summary of technical data associated with acute inhalation exposures to BrF_3 and (2) the rationale behind the immediately dangerous to life or health (IDLH) value for BrF_3. IDLH values are developed on the basis of scientific rationale and logic outlined in the *NIOSH Current Intelligence Bulletin (CIB) 66: Derivation of Immediately Dangerous to Life or Health (IDLH) Values* [NIOSH 2013]. As described in CIB 66, NIOSH performs in-depth literature searches to ensure that all relevant data from human and animal studies with acute exposures to the substance are identified. Information included in CIB 66 on the literature search includes pertinent databases, key terms, and guides for evaluating data quality and relevance for the establishment of an IDLH value. The information that is identified in the in-depth literature search is evaluated with general considerations that include description of studies (i.e., species, study protocol, exposure concentration and duration), health endpoint evaluated, and critical effect levels (e.g., NOAELs, LOAELs, and LC_{50} values). For BrF_3, the in-depth literature search was conducted through November 2017.

1.3 General Substance Information

Chemical: Bromine trifluoride

CAS No: 7787-71-5

Synonyms: Bromine fluoride (BrF_3)*

Chemical category: Not available

Reference: * NAS [2014]

Structural formula*:

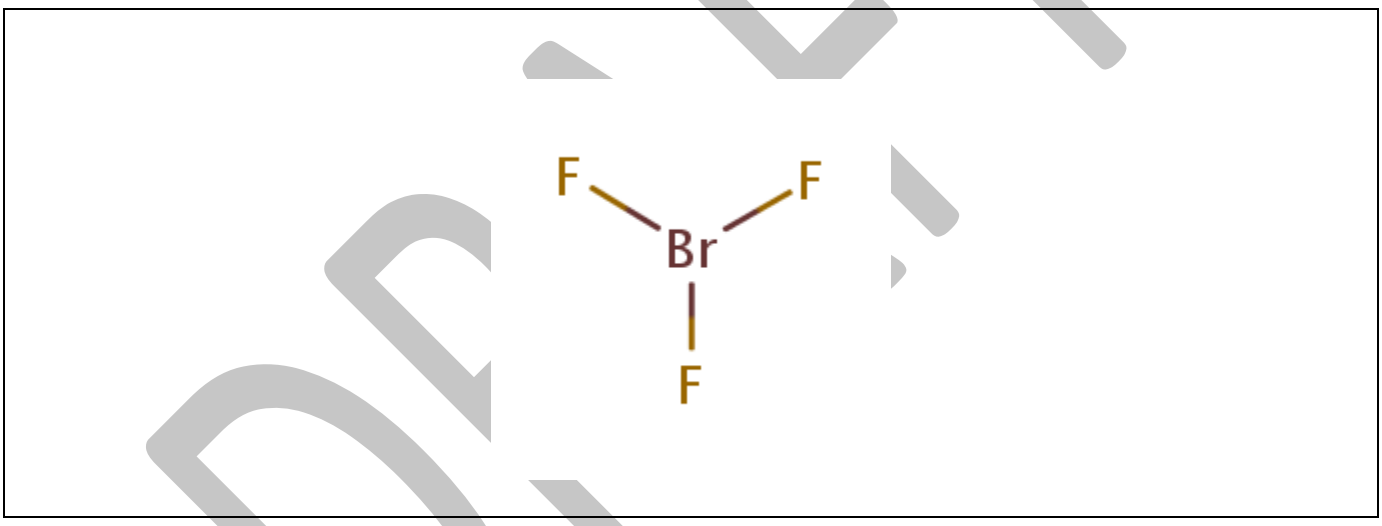

Table 1 highlights selected physiochemical properties of BrF_3 relevant to IDLH conditions. Table 2 provides alternative exposure guidelines for BrF_3. Table 3 summarizes the Acute Exposure Guideline Level (AEGL) values for BrF_3.

Reference: *NLM [2018]

Table 1: Physiochemical Properties of Bromine Trifluoride

Property	Value*
Molecular weight	136.91
Chemical formula	BrF_3
Description	Colorless to pale yellow liquid
Odor	Not available
Odor Threshold	Not available
UEL	Not flammable
LEL	Not flammable
Vapor pressure	2.803 g/cu cm at 25°C (77°F)
Flash point	Not flammable
Ignition temperature	Not flammable
Solubility	Reacts with water

Reference: * NAS [2014]

Table 2: Alternative Exposure Values for Bromine Trifluoride

Organization	Value
NIOSH (1994) IDLH value*	None
NIOSH REL†	None
OSHA PEL‡	None
ACGIH® TLV®§	None
AIHA® ERPGs™¶	None
AIHA® WEELs®**	None

References: *NIOSH [1994]; †NIOSH [2005]; ‡OSHA [2018]; §ACGIH [2016]; ¶AIHA [2016]; ** TERA [2014]

Table 3: AEGL Values for Bromine Trifluoride

Classification	10-min	30-min	1-hour	4-hour	8-hour	End point (Reference)
AEGL-1	0.12 ppm 0.67 mg/m^3	0.12 ppm 0.67 mg/m^3	0.12 ppm 0.67 mg/m^3	0.12 ppm 0.67 mg/m^3	0.12 ppm 0.67 mg/m^3	Set equal to AEGL-1 values for chlorine trifluoride [NAS 2007]
AEGL-2	8.1 ppm 45 mg/m^3	3.5 ppm 20 mg/m^3	2 ppm 11 mg/m^3	0.7 ppm 3.9 mg/m^3	0.41 ppm 2.3 mg/m^3	Set equal to AEGL-2 values for chlorine trifluoride [NAS 2007]
AEGL-3	84.0 ppm 470 mg/m^3	36 ppm 200 mg/m^3	21 ppm 120 mg/m^3	7.3 ppm 41 mg/m^3	7.3 ppm 41 mg/m^3	Set equal to AEGL-3 values for chlorine trifluoride [NAS 2007]

Reference: NAS [2014]

2.0 Human Data

No reliable toxicity data were available for BrF_3. Human toxicity information is limited to a statement that concentrations of 50 ppm or more may be fatal in 30 minutes to 2 hours [Braker and Mossman 1980] but insufficient details were available to use this as the basis for an IDLH value. However, based on the chemical and physical properties, as well as data from animal studies (Section 3.0), $B3F_3$ is likely irritating and corrosive to skin, eyes, mucous membranes and respiratory tract. Hydrogen fluoride (HF) is the principle hydrolysis product of both BrF_3 and chlorine trifluoride (ClF_3) (3 moles of HF formed per mole of BrF_3/ ClF_3). Braker and Mossman [1980] reported that the toxic effects of BrF_3 are comparable to those of ClF_3 since the toxicity of halogen fluorides is consistent with their relative reactivity. Limited data indicate that bromine pentafluoride (BrF5) is less toxic than chlorine pentafluoride (ClF_5) (consistent with their relative reactivity); BrF_3 is similarly predicted to be less toxic than ClF_3 [Braker and Mossman 1980; NIOSH 2016a, b]. The NAS used a similar strategy for development of the AEGL values for BrF_3 [NAS 2014]. In this case, the AEGL-1, AEGL-2, and AEGL-3 values for BrF_3 were based on ClF_3, due to their similarities in structural activity with halogen fluorides. In addition, NAS chose to set the AEGL values for BrF_3 to the more toxic analogue, ClF_3, and did not apply any modifying factors since BrF_3 was considered to be less toxic [NAS 2007, 2014]. NAS indicated that the use of the ClF_3 AEGL values for BrF_3 would be "reasonably protective" [NAS 2014]. In the absence of human and animal data for BrF_3, ClF_3 data were used to derive an IDLH value for BrF_3.

Reliable human toxicity data for ClF_3 were limited as well. ClF_3 is used as a fluorinator in uranium enrichment and as an igniter in rocket propellants. Depending on ambient temperature it exists as a liquid or gas (boiling point 12°C/53°F) that reacts violently with water and organic or siliceous materials. With moist air or in the respiratory tract ClF_3 disintegrates rapidly into HF, chlorine, chlorine dioxide, and other highly reactive compounds [Dost et al. 1974]. Consequently, the chemical is a potent irritant of mucous membranes, eyes, and skin [Teitelbaum 2001]. Reliable acutely toxic concentration values or an odor threshold for humans were not identified, although Reed et al. [1966] reported without further detail that 50 ppm were lethal to humans within 30 minutes to 2 hours.

At sufficiently high concentrations, ClF_3 causes gasping, ocular irritation with lacrimation, cloudiness of the cornea, severe salivation, coughing and dyspnea, skin burns, headache, abdominal pain, and convulsions after a few minutes of exposure. Fatigue may last some time beyond the end of exposure, the corneal damage may remain permanent, and skin damage may heal poorly [Cloyd and Murphy 1965]. The National Resource Council (NRC) cited an accident report in which one worker was exposed for 1–2 minutes to unknown concentration of ClF_3 [Longley et al. 1965 (as cited in NRC 1984)]. The worker complained of headache, abdominal pain, and breathing difficulty that lasted for approximately 2 hours, however no local or systemic effects were observed. The report indicated that the worker reported to work the day following exposure "with no apparent after-effects except fatigue [Longley et al. 1965 (as cited in NRC 1984)]." The acute symptoms of ClF_3 poisoning resemble those caused by HF [Darmer et al. 1972; MacEwen and Vernot 1970]. Also similar to HF, more severe respiratory effects of ClF_3 exposure may develop in a delayed fashion [HSDB 2017; MacEwen and Vernot 1970].

3.0 Animal Toxicity Data

BrF_3 is irritating and corrosive to the skin, eyes, mucous membranes, and respiratory tract. Because of the absence of empirical data for BrF_3, this assessment uses ClF_3 as a surrogate because of chemical and toxicological similarities [Braker and Mossman 1980; NAS 2014] (see Section 2.0 for full explanation of read-across).

Only limited data on non-lethal effects of ClF_3 were available. Twenty rats exposed to 5.15 ppm ClF_3 for 6 hours appeared unaffected [Horn and Weir 1955]. Two of two dogs exposed to this concentration for 6 hours exhibited salivation, lacrimation, rhinorrhea and blinking of the eyes [Horn and Weir 1955]. The effects seen in dogs were not considered escape-impairing. In the same study, a group of 20 rats and 2 dogs were exposed to 21 ppm ClF_3 for 6 hours per day for 2 consecutive days [Horn and Weir 1955]. Rats experienced rhinorrhea and lacrimation after the first exposure period, however no information was provided as to the severity of these effects. It was reported that both dogs began experiencing rhinorrhea and lacrimation within 10 minutes of the start of exposure. It was also reported that the dogs "blinked continuously at first and later kept their eyes tightly closed," however, the time that these symptoms began was not noted [Horn and Weir 1955]. These effects were considered escape-impairing in the dogs. Table 4 summarizes non-lethal data reported in animal studies with 30-minute equivalent

derived values for ClF_3. Information included in these tables includes species of test animals, toxicological metrics (i.e., LC, BMCL, NOAEL, LOAEL), adjusted 30-minute concentration, and the justification for the composite uncertainty factors applied to calculate the derived values.

Median lethal concentration (LC_{50}) and lethal time (ET_{50}) values for ClF_3 were evaluated in several animal species. MacEwen and Vernot [1970] exposed mice, rats, and monkeys to ClF_3 for 60 minutes and observed lacrimation, salivation, rhinorrhea, and dyspnea that, within a few hours after exposure, turned into bloody discharges if the animals survived. Monkeys also showed signs typical of bronchial and gastrointestinal irritation. Death occurred with delays as long as 36 hours after exposure. Upon death, massive alveolar and interstitial hemorrhage were noted. Near-fatal concentrations resulted in concentration-dependent pulmonary congestion, edema, emphysema, and hemorrhage. The 60-minute LC_{50} values were 178 ppm for mice, 299 ppm for rats, and 230 ppm for monkeys (also reported in Darmer et al. [1972]).

Horn and Weir [1955] exposed rats to two concentrations of ClF_3 and determined the effective median time to death of 50% of the animals (ET_{50}). In rats, the ET_{50} at 480 ppm was 40 minutes (all dead within 70 minutes), at 96 ppm it was 3.7 hours (observation time after the end of the 4.5-hour exposure to 96 ppm was not stated). Clinical signs appeared within minutes of exposure and included increased activity, nasal flow and salivation, respiratory difficulty, eye irritation, and convulsions and coma shortly before death. Dost et al. [1974, 1967] reported that ClF_3 caused severe inflammation in all exposed tissues, lacrimation, and shallow breathing in male rats. High concentrations made hair appear "singed," caused skin burns, and produced corneal ulceration. These authors also observed that rats surviving ClF_3 exposure for 4 hours did not eat for several days thereafter. Time to death was tested in presence of 400 and 800 ppm ClF_3; all animals died within 45–90 minutes of exposure to 800 ppm for 15 minutes; at longer exposure times, up to 30 minutes, the earliest deaths occurred within 20 minutes but some animals survived as long as 160 minutes. At 400 ppm, death occurred after 55–140 minutes with ≥30 minutes exposure but no deaths were observed at ≤25 minutes exposure. NAS [2014] provided an estimated 1-hour LC_{50} value of 222 ppm based on these data but indicated that this value may be an underestimate since post-exposure observations were not completed [NAS 2014]. Table 5 summarizes the LC data identified in animal studies and provides 30-minute equivalent derived values for ClF_3. Information in this table includes

species of test animals, toxicological metrics (i.e., LC, BMCL, NOAEL, LOAEL), adjusted 30-minute concentration, and the justification for the composite uncertainty factors applied to calculate the derived values.

Table 4: Non-lethal Concentration Data for Chlorine Trifluoride (ClF_3)[*]

Reference	Species	Critical non-lethal effect	LOAEL (ppm)	Time (min)	Adjusted 30-min Concentration[†] (ppm)	Composite Uncertainty Factor[‡]	30-min Equivalent Derived Value (ppm)[§]	Final Value (ppm)[¶]
Horn and Weir [1955]	Dog	Severe lacrimation	21	360	142	10	14.2	14

[*] Data for ClF_3 data is used as a surrogate for derivation of an IDLH value for BrF_3

[†]For exposures other than 30 minutes the ten Berge et al. [1986] relationship is used for duration adjustment ($C^n \times t = k$); NAS [2014] provided an empirically estimated n of 1.3 for all time-scaling. Additional information on the calculation of duration adjusted concentrations can be found in NIOSH [2013].

[‡]Composite uncertainty factor to account for interspecies differences, human variability, and extrapolation from a LOAEL to NOAEL.

[§]The derived value is the result of the adjusted 30-minute concentration divided by the composite uncertainty factor.

[¶]Values rounded to the appropriate significant figure.

Table 5: Lethal Concentration Data for Chlorine Trifluoride (ClF_3) [*]

Reference	Species	LC_{50} (ppm)	ET_{50} (ppm)	Time (min)	Adjusted 30-min Concentration[†] (ppm)	Composite Uncertainty Factor[‡]	30-min Equivalent Derived Value (ppm) [§]	Final Value (ppm) [¶]
Darmer et al. [1972]; MacEwen and Vernot [1970]	Mouse	178		60	303	30	10.1	10
Darmer et al. [1972]; MacEwen and Vernot [1970]	Monkey	230		60	392	30	13.1	13
Darmer et al. [1972]; MacEwen and Vernot [1970]	Rat	299		60	510	30	17.0	17
Horn and Weir [1955]	Monkey		480	40	599	30	19.9	20
Horn and Weir [1955]	Monkey		96	222	448	30	14.9	15
Dost [1974]	Rat	222[**]		60	378	30	12.6	13

[*] Data for ClF_3 data is used as a surrogate for derivation of an IDLH value for BrF_3
[†]For exposures other than 30 minutes the ten Berge et al. [1986] relationship is used for duration adjustment ($C^n \times t = k$); NAS [2014] provided an empirically estimated n of 1.3 for all time-scaling. Additional information on the calculation of duration adjusted concentrations can be found in NIOSH [2013].
[‡]Composite uncertainty factor to account for adjustment of LC_{50} values to LC_{01} values, use of lethal concentration threshold in animals, interspecies differences and human variability.
[§]The derived value is the result of the adjusted 30-minute concentration divided by the composite uncertainty factor.
[¶]Values rounded to the appropriate significant figure.
[**]Estimated value based on NAS [2014] extrapolation of Dost [1974] data.

4.0 Summary

Inadequate toxicity data were available for BrF_3. The data on ClF_3 are used to derive an IDLH for BrF_3 because their structures, reaction mechanisms, and potencies are assumed to be similar. Therefore deriving an IDLH value based on the toxicity data for ClF_3 is appropriately health-protective [NIOSH 2018]. Braker and Mossman [1980] reported that the toxic effects of BrF_3 are comparable to those of ClF_3 since the toxicity of halogen fluorides is consistent with their relative reactivity. In the absence of such data for BrF_3, ClF_3 was used as a surrogate to derive an IDLH value for BrF_3. The NAS used a similar strategy for development of the AEGL values for BrF_3 [NAS 2014].

After adjustment to a 30-minute exposure duration, LC_{50} values in experimental animals range from 303 to 599 ppm [Darmer 1972; MacEwen and Vernot 1970; Horn and Weir 1955; Dost et al. 1974, 1967].The mouse LC_{50} of 178 ppm is used as the basis for the IDLH value since it results in the most protective adjusted 30 minute LC_{50} value[Darmer et al. 1972; MacEwen and Vernot 1970]. The adjusted 30-minute LC_{50} is 303 ppm. An uncertainty factor of 30 was applied to account for extrapolation from a concentration that is lethal to animals, animal to human differences, and human variability, resulting in an IDLH value of 10 ppm.

Even though information on sublethal endpoints was available [Horn and Weir 1955], the resulting calculated IDLH value was less protective than the LC_{50} data that were used to derive the final IDLH value. In addition, the sub-lethal endpoint data presented by Horn and Weir [1955] did not provide sufficient documentation of time to relevant health effects and there was additional uncertainty with the low number of animals tested.

References

ACGIH (American Conference of Governmental Industrial Hygienists) [2017]. Annual TLVs® (Threshold Limit Values) and BEIs® (Biological Exposure Indices) booklet. Cincinnati, OH: ACGIH Signature Publications.

AIHA (American Industrial Hygiene Association) [2014]. AIHA Emergency Response Planning (ERP) Committee procedures and responsibilities. Fairfax, VA: American Industrial Hygiene Association.

AIHA (American Industrial Hygiene Association) [2016]. Emergency response planning guidelines (ERPG) and workplace environmental exposure levels (WEEL) handbook. Fairfax, VA: American Industrial Hygiene Association Press.

Braker W, Mossman AL [1980]. Bromine pentafluoride. In: Matheson gas data book. 6th ed. Lyndhurst, NJ: Matheson.

Cloyd DR, Murphy WJ [1965]. Handling hazardous materials. Washington, DC: National Aeronautics and Space Administration, NASA SP-5032.

Darmer KI, Haun CC, MacEwen JD [1972]. The acute inhalation toxicity of chlorine pentafluoride. Am Ind Hyg Assoc J *33*:661–668.

Dost FN, Reed DJ, Smith VN, Wang CH [1974]. Toxic properties of chlorine trifluoride. Toxicol Appl Pharmacol *27*:527–536.

Dost FN, Reed DJ, Smith VN, Wang CH [1967]. Metabolism and pharmacology of inorganic and fluorine containing compounds. Wright-Patterson Air Force Base, OH: Aerospace Medical Research Laboratories, Aerospace Medical Division, Air Force Systems Command, AMRL-TR-67-224.

EPA [2018]. Integrated Risk Information System (IRIS): glossary [https://ofmpub.epa.gov/sor_internet/registry/termreg/searchandretrieve/glossariesandkeywordlists/search.do?details=&glossaryName=IRIS%20Glossary#formTop]. Date accessed: February 1, 2018.

Horn HJ, Weir RJ [1955]. Inhalation toxicity of chloride trifluoride. I. Acute and subacute toxicity. AMA Arch Ind Health *12*:515–521.

HSDB [2017]. Hazardous Substances Data Bank [http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB] CAS No. 7790-91-2. Date accessed: November 6, 2017.

Longley MY, Pierce JF, Griesemer EC [1965]. A toxic hazard study of selected missile propellants. AMRL-TR-65-99. Wright-Patterson Air Force Base, OH: Aerospace Medical Research Laboratories (as cited in NRC 1984).

MacEwen JD, Vernot EH [1970]. Toxic Hazards Research Unit. Annual Technical Report: 1970. Wright-Patterson Air Force Base, OH: Aerospace Medical Research Laboratories, Aerospace Medical Division, Air Force Systems Command, AMRL-TR-70-77.

NAS [2001]. Standing operating procedures for developing Acute Exposure Guidelines Levels for hazardous chemicals. National Academy of Sciences, National Research Council (NRC), Committee on Toxicology, Subcommittee on Acute Exposure Guide-line Levels. Washington, DC: National Academy Press, IBSN: 0-309-07553-X [http://www.epa.gov/sites/production/ files/2015-09/documents/sop_final_standing_operating_procedures_2001.pdf]. Date accessed: January 10, 2018

NAS (National Academy of Science) [2014]. Acute Exposure Guideline Levels (AEGLs) for selected airborne chemicals, Volume 18: selected halogen fluorides [https://www.epa.gov/sites/production/files/2015-09/documents/halogen_fluorides_final_volume-18_aug-2014.pdf]. Date accessed January 10, 2018.

NAS (National Academy of Science) [2007]. Acute Exposure Guideline Levels (AEGLs) for selected airborne chemicals, Volume 5: chlorine trifluoride [http://www.epa.gov/oppt/aegl/pubs/chlorinetrifluoride_final_volume5_2007.pdf]. Date accessed January 10, 2018.

NIOSH [1994]. Documentation for Immediately Dangerous To Life or Health Concentrations (IDLHs): Chlorine trifluroide [http://www.cdc.gov/niosh/idlh/7790912.html]. Date accessed: January 10, 2018.

NIOSH [2004]. NIOSH Respirator Selection Logic. By: Bollinger N. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2005-100.

NIOSH [2005]. NIOSH pocket guide to chemical hazards. Barsan ME, ed. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2005-149.

NIOSH [2013]. Current intelligence bulletin #66: Derivation of Immediately Dangerous to Life or Health (IDLH) Values. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2014-100.

NIOSH [2016a]. Immediately dangerous to life or health (IDLH) value profile: Bromine pentafluoride. By Dotson GS, Maier A, Parker A, Haber L. Cincinnati, OH: US Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication 2017-106.

NIOSH [2016b]. Immediately dangerous to life or health (IDLH) value profile: Chlorine pentafluoride. By Dotson GS, Maier A, Parker A, Haber L. Cincinnati, OH: US Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication 2016-170.

NIOSH [2018]. Immediately dangerous to life or health (IDLH) value profile: Chlorine trifluoride (DRAFT). By Niemeier RT, Dotson GS, Maier A, Parker A, Haber L. Cincinnati, OH: US Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication 2018-xxx

NLM (National Library of Medicine) [2018]. ChemIDplus lite [http://chem.sis.nlm.nih.gov/chemidplus/chemidlite.jsp]. Date accessed: January 10, 2018.

NRC (National Research Council) [1984]. Emergency and continuous exposure limits for selected airborne contaminants, Volume 2. Washington, DC: The National Academies.

OSHA (Occupational Safety and Health Administration) [2018]. Occupational Safety and Health Standards. 29 CFR 1910. Subpart Z -- Toxic and Hazardous Substances. OSHA; Washington, DC [http://www.osha.gov/pls/oshaweb/owadisp.show_document?p_table=standards&p_id=9992]. Date accessed: January 10, 2018.

Reed DJ, Dost FN, Wang CH [1966]. Inorganic fluoride propellant oxidizers, Volume I: their effects upon seed germination and plant growth. Wright-Patterson Air Force Base, OH: Aerospace Medical Research Laboratories, Aerospace Medical Division, Air Force Systems Command.

ten Berge WF, Zwart A, Appelman LM [1986]. Concentration-time mortality response relationship of irritant and systematically acting vapors and gases. J Haz Mat *13*:301–309.

Teitelbaum DT [2001]. The halogens. In: Bingham E, Cohrssen B, Powell CH (eds.), Patty's toxicology, Vol. 3. New York: John Wiley & Sons, Inc., pp. 731–825.

TERA [2014]. Occupational Alliance for Risk Science-Workplace Environmental Exposure Levels (WEEL)™ [http://www.tera.org/OARS/WEELs.pdf]. Date accessed: January 10, 2018.