

IMMEDIATELY
DANGEROUS to
LIFE or HEALTH

IDLH

VALUE PROFILE

Chlorine Trifluoride
CAS[®] No. 7790-91-2



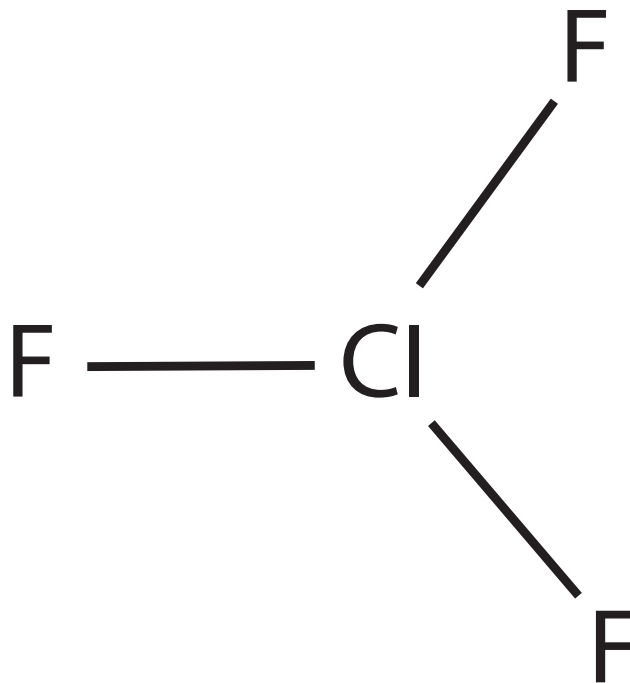
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Immediately Dangerous to Life or Health (IDLH) Value Profile

Chlorine Trifluoride

[CAS[®] No. 7790-91-2]



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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 can 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 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 (IDLH) 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.

This technical report presents the IDLH value for chlorine trifluoride (CAS[®] No. 7790-91-2). 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
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Abbreviations

ACGIH®	American Conference of Governmental Industrial Hygienists
Acute RfC	Acute reference concentration
AEGLs	Acute Exposure Guideline Levels
AIHA®	American Industrial Hygiene Association
BMC	benchmark concentration
BMD	benchmark dose
BMCL	benchmark concentration lower confidence limit
BMR	Benchmark response
°C	degrees Celsius
CAS®	Chemical Abstracts Service, a division of the American Chemical Society
CIB	Current Intelligence Bulletin
ClF ₃	Chlorine trifluoride
EPA	Environmental Protection Agency
ERPG™	Emergency Response Planning Guidelines
ET ₅₀	Effective time to 50% mortality
ECt ₅₀	median effect vapor concentration
°F	degrees Fahrenheit
HF	Hydrogen fluoride
HSDB	Hazardous Substance Data Bank
IDLH	immediately dangerous to life or health
LC	lethal concentration
LC ₅₀	median lethal concentration
LC ₀₁	lethal concentration 1%
LC _{LO}	lowest concentration that caused death in humans or animals
LEL	lower explosive limit
LD _{LO}	lowest dose that caused death in humans or animals
LOAEL	lowest observed adverse effect level
mg/m ³	milligram(s) per cubic meter
min	minutes
mmHg	millimeter(s) of mercury
MSHA	Mine Safety and Health Administration
NIOSH	National Institute for Occupational Safety and Health
NLM	National Library of Medicine
NOAEL	no observed adverse effect level
NRC	National Research Council
OEL	occupational exposure limit
OSHA	Occupational Safety and Health Administration
PEL	permissible exposure limit

POD	point of departure
ppm	parts per million
REL	recommended exposure limit
RD ₅₀	concentration of a chemical in the air estimated to cause a 50% decrease in the respiratory rate
STEL	short-term exposure limit
TERA	Toxicology Excellence for Risk Assessment
TLV®	Threshold Limit Value
TWA	time-weighted average
UEL	upper explosive limit
UF	uncertainty factor
WEEL®	Workplace Environmental Exposure Level

Glossary

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

Acute Exposure Guideline Levels (AEGs): Threshold exposure limits for the general public, applicable to emergency exposure periods ranging from 10 minutes to 8 hours. AEG-1, AEG-2, and AEG-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 [NRC 2001]. AEGs 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 [NRC 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 <https://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 2016].

Acute toxicity: Any poisonous effect produced within a short period of time following an exposure, usually 24 to 96 hours [U.S. EPA 2016].

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 2016] (additional information available at <https://www.epa.gov/ncea/bmds/>).

Benchmark response (BMR): A predetermined change in response rate of an effect. Common defaults for the BMR are 10% or 5%, reflecting study design, data variability, and sensitivity limits used.

Benchmark concentration lower confidence limit (BMCL): A statistical lower confidence limit on the concentration at the BMC [U.S. EPA 2016].

Bolus exposure: A single, relatively large dose.

Ceiling value ("C"): 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 2016].

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 2016].

EC₅₀: 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 2006].

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.

LC₀₁: The statistically determined concentration of a substance in the air that is estimated to cause death in 1% of the test animals.

LC₅₀: 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.

LC₁₀: The lowest lethal concentration of a substance in the air reported to cause death, usually for a small percentage of the test animals.

LD₅₀: 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.

LD₁₀: 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.

RD₅₀: 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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Division of Science Integration

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Iris Camacho, Ph.D., branch chief, Assessment Branch 1, Risk Assessment Division, Office of Pollution Prevention and Toxics, U.S. Environmental Protection Agency, Washington, DC

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

Randall Keller, Ph.D., professor; Murray State University; Jesse D. Jones College of Science, Engineering, and Technology Programs; Department of Occupational Safety and Health; Murray, Kentucky

Matthew Lloyd, CIH, New Chemicals Management Branch, Chemical Control Division, Office of Pollution Prevention and Toxics, U.S. Environmental Protection Agency, Washington, DC

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

Occupational Safety and Health Administration, Directorate of Standards and Guidance

Laurie Roszell, Ph.D., toxicologist, Army Center for Public Health, Environmental Health Risk Assessment Division, Aberdeen Proving Ground, MD

George M. Woodall, Ph.D., toxicologist, National Center for Environmental Assessment, Office of Research and Development, U.S. Environmental Protection Agency, Research Triangle Park, NC

1 Introduction

1.1 Overview of the IDLH Value for Chlorine Trifluoride

IDLH Value: 12 ppm (45 mg/m³)

Basis for IDLH Value: The IDLH value for chlorine trifluoride (ClF₃) is based on data on eye irritation in rats exposed at a concentration of 480 ppm for 5 minutes, which was determined to be escape-impairing [Horn and Weir 1955]. The duration adjusted 30-minute concentration is 121 ppm. An uncertainty factor (UF) of 10 was applied to account for interspecies variability (factor of 3) and human variability (factor of 3), resulting in a derived IDLH value of 12 ppm.

1.2 Purpose

This IDLH Value Profile presents (1) a brief summary of technical data associated with

acute inhalation exposures to ClF₃, and (2) the rationale behind the immediately dangerous to life or health (IDLH) value for ClF₃. IDLH values are developed on the basis of the 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].

1.3 Literature Search Strategy and Data Evaluation

As described in CIB 66, NIOSH performed in-depth literature searches to ensure that all relevant data from human and animal studies with acute exposures to the substance were identified. See Appendix A for further information about the literature search strategy and data evaluation methods.

1.4 General Substance Information

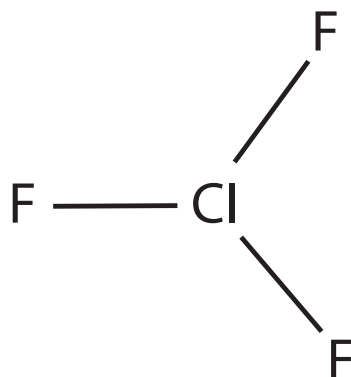
Chemical: Chlorine trifluoride

CAS No: 7790-91-2

Synonyms: Chlorine fluoride, chlorotrifluoride (ClF₃)*

Chemical category: Fluorine compounds, inorganic; chlorine compounds, inorganic[†]

Structural formula*:



References: *NRC [2007]; [†]IFA [2019]; *NLM [2019]

Table 1 highlights selected physiochemical properties of ClF₃ relevant to IDLH conditions. Table 2 provides alternative exposure

guidelines for ClF₃. Table 3 summarizes the acute exposure guideline level (AEG) values for ClF₃.

Table 1. Physiochemical Properties of Chlorine Trifluoride (ClF₃)

Property	Value
Molecular weight	92.45
Chemical formula	ClF ₃
Description	Colorless gas; Greenish-yellow liquid (below 53°F) white solid
Odor	Sweet, suffocating
Odor Threshold	Not available
UEL	Not applicable (nonflammable gas)
LEL	Not applicable (nonflammable gas)
Vapor pressure	1064 mmHg at 20°C (68°F) (1.4 atm)
Flash point	Not applicable (nonflammable gas)
Ignition temperature	Not applicable (nonflammable gas)
Solubility	Violent hydrolysis with water

Reference: NRC [2007], NIOSH [2005]

Table 2. Alternative Exposure Values for Chlorine Trifluoride (ClF₃)

Organization	Value
NIOSH (1994) IDLH value*	20 ppm (76 mg/m ³)
NIOSH REL [†]	0.1 ppm (0.4 mg/m ³), ceiling
OSHA PEL [‡]	0.1 ppm (0.4 mg/m ³), ceiling
ACGIH [®] TLV [§]	0.1 ppm (0.4 mg/m ³), ceiling
AIHA [®] ERPGs ^{™¶}	ERPG-1: 0.1 ppm; ERPG-2: 1 ppm; ERPG-3: 10 ppm
AIHA [®] WEELS ^{®**}	Not available

References: *NIOSH [1994]; [†]NIOSH [2005]; [‡]OSHA [2019]; [§]ACGIH [2019]; [¶]AIHA [2016]; ^{**}TERA [2014]

Table 3. AEGL Values for Chlorine Trifluoride (ClF₃)

Classification	10-min	30-min	1-hour	4-hour	8-hour	End point (Reference)
AEGL-1 (Nondisabling)	0.12 ppm (0.46 mg/m ³)	0.12 ppm (0.46 mg/m ³)	0.12 ppm (0.46 mg/m ³)	0.12 ppm (0.46 mg/m ³)	0.12 ppm (0.46 mg/m ³)	Slight irritation—dog [Horn and Weir 1955]
AEGL-2 (Disabling)	8.1 ppm (31 mg/m ³)	3.5 ppm (13 mg/m ³)	2.0 ppm (7.6 mg/m ³)	0.70 ppm (2.7 mg/m ³)	0.41 ppm (1.6 mg/m ³)	Threshold, impaired ability to escape—dog [Horn and Weir 1955]
AEGL-3 (Lethal)	84 ppm (320 mg/m ³)	36 ppm (140 mg/m ³)	21 ppm (80 mg/m ³)	7.3 ppm (28 mg/m ³)	7.3 ppm (28 mg/m ³)	Threshold for lethality—monkey [MacEwen and Vernot 1970]

Reference: NRC [2007]

2 Human Data

Human toxicity studies of sufficient quality for ClF₃ were limited (see NIOSH 2013, section 3.4.1 for criteria to determine studies of sufficient quality). With moist air, or in the respiratory tract, ClF₃ disintegrates rapidly into hydrogen fluoride (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]. Studies of sufficient quality that provide acutely toxic concentration values or an odor threshold for humans were not identified, although Reed et al. [1966] and Deichmann and Gerarde [1969] reported without further detail that exposure to 50 ppm was lethal to humans within 30 minutes to 2 hours.

Cloyd and Murphy [1965] reported that “odorously detectable concentrations” of ClF₃ cause gasping, ocular irritation with lacrimation, cloudiness of the cornea, severe salivation, coughing and dyspnea, skin burns, and convulsions after a few minutes of exposure. Fatigue may last some time beyond the end of exposure, the corneal damage may be permanent, and skin damage may

heal poorly [Cloyd and Murphy 1965]. The National Research Council (NRC) cited an incident report in which one worker was exposed for 1–2 minutes to an unknown concentration of ClF₃ [Longley et al. 1965]. 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]. The acute symptoms of ClF₃ poisoning resemble those caused by HF [Darmer et al. 1972; MacEwen and Vernot 1970]. Also similar to HF, more severe respiratory effects (e.g., lung congestion, edema, emphysema, and diffuse hemorrhagic changes) of ClF₃ exposure may develop in a delayed fashion [HSDB 2019; MacEwen and Vernot 1970].

The weight of evidence suggests that irritative and toxic effects occur with human exposure to ClF₃; however, quantitative data to derive a point of departure (POD) for derivation of an IDLH value on human data were not identified.

3 Animal Toxicity Data

Multiple animal studies of sufficient quality for derivation of an IDLH value for ClF₃ were identified. These included lethality studies [Darmer et al. 1972; Dost et al. 1967, 1974; Horn and Weir 1955; MacEwen and Vernot 1970; Vernot et al. 1977] and two nonlethal concentration studies [Horn and Weir 1955; MacEwen and Vernot 1970]. Some of the limited data on nonlethal effects of ClF₃ were taken from clinical observations

of irritative effects in the lethality studies at concentrations or time periods less than the LC₅₀ or ET₅₀ derived values.

Twenty rats exposed to 5.15 ppm ClF₃ 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 severity

of the effects seen in dogs was not reported, so a determination of whether they were escape-impairing could not be made. 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 began preening shortly after a 10-minute period of exposure. The authors reported rhinorrhea and lacrimation after the first exposure period; however, no information was provided as to the severity of these effects. It was also reported that both dogs began experiencing rhinorrhea and lacrimation within 10 minutes of the exposure starting. Additionally, it was 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]. Additional data from two studies on irritative effects observed in monkeys, dogs, rats, and mice during lethal concentration studies were also identified [Horn and Weir 1955; MacEwen and Vernot 1970]. Twenty rats exposed to 480 ppm for 5 minutes experienced “considerable” lacrimation and had their eyelids closed. Some animals were observed to have swollen and raw eyelids, while other animals had considerable crusting of their eyelids [Horn and Weir 1955]. In a group of 20 rats exposed to 96 ppm for 65 minutes, one rat was in acute distress with marked gasping respiration; the other 19 rats were observed to be lying on the floor with their eyes tightly closed [Horn and Weir 1955]. In the same study, at 120 minutes, the rats were observed to have considerable exudate around the eyes, swollen and raw eyelids, crusting around the mouth and nose, and bubbling rhinorrhea [Horn and Weir 1955]. Eight rats exposed to 200 ppm for 60 minutes and 15 mice exposed to 125 ppm for 60 minutes were observed to have lacrimation, salivation, dyspnea, and rhinorrhea during the exposures [MacEwen and Vernot 1970]. Four monkeys exposed to 127 ppm for 60 minutes were observed to have signs of bronchotracheal/gastrointestinal irritation, which included sneezing, coughing, and a gagging reflex [MacEwen and Vernot 1970]. Table 4 summarizes nonlethal data reported in animal studies with 30-minute equivalent derived values for ClF_3 . Information in these

tables includes species of test animals, toxicological metrics (i.e., LC, BMCL, NOAEL, LOAEL), and adjusted 30-minute concentration.

Median lethal concentration (LC_{50}) and the effective median lethal time to 50% of the animal (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 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. [1967, 1974] reported that ClF_3 caused severe inflammation in all exposed tissues, lacrimation, and shallow breathing in male rats. High concentrations made hair appear “singled,” 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

ClF₃; 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. NRC [2007, 2014] provided an estimated 1-hour LC₅₀ value of 222 ppm based on these data but indicated that this value may be an underestimate because post-exposure observations were not completed [NRC 2007, 2014]. Table 5 summarizes the LC data identified in animal studies and provides 30-minute equivalent derived values for ClF₃. Information in this table includes species of test animals, toxicological metrics (i.e., LC, BMCL, NOAEL, LOAEL), and adjusted 30-minute concentration.

The weight of evidence suggests that ClF₃ irritates the respiratory and ocular systems in the four animal species tested, and the effects occurred in concentrations as low as 5.15 ppm. Lethal concentrations were also available for three animal species as well, but they were higher than the irritative effects and were excluded from consideration as a POD for the IDLH value. The most

sensitive species appears to be rats in which irritative ocular effects, determined to be escape impairing, began to occur at 480 ppm at a 5-minute exposure period, resulting in a 30-minute time adjusted concentration of 121 ppm [Horn and Weir 1955]. This endpoint was selected as the POD for the derivation of the IDLH value. Similar irritative effects were observed at similar 30-minute time-adjusted concentrations in multiple animal species and ranged from 142–341 ppm. One study identified irritative effects at a lower concentration than the chosen POD [Horn and Weir 1955]. In this study, dogs exposed at concentrations of 5.15 ppm over a 360-minute exposure period experienced irritation, lacrimation, rhinorrhea, and coughing and sneezing; however, the severity of these effects was not provided. The authors concluded that at the end of the first exposure period the dogs were not markedly affected. This concentration was not considered to be escape-impairing, so it was not considered as the POD for the derivation of the IDLH value. See Section 4 for information regarding the derivation of the IDLH for ClF₃, including additional information on the study selected as the POD and the UFs applied to derive a final IDLH value.

Table 4. Nonlethal Concentration Data for Chlorine Trifluoride (ClF₃)

Reference	Species	Critical nonlethal effect	Number of animals	Dose (ppm)	Time (min)	Adjusted 30-min Concentration* (ppm)
Horn and Weir [1955]	Dog	Salivation, lacrimation, rhinorrhea, severe coughing, sneezing.	2	5.15	360**	35
		Rhinorrhea, lacrimation, continuous eye blinking, kept eyes closed tightly	2	21	360**	142
Horn and Weir [1955]	Rat	None reported	20	5.15	360**	35
		Rhinorrhea and lacrimation	20	21	360**	142
		Considerable lacrimation and eyelids closed, some animals had swollen and raw eyelids, some animals had considerable crusting of eyelids	20	480	5 ^s	121
		1 of 20 rats in acute distress with marked gasping respiration, lacrimation, salivation, and rhinorrhea. 19 of 20 rats lying on cage floor with eyes tightly closed	20	96	65 ^t	174
MacEwen and Vernot [1970]	Monkey	Considerable exudate around eyes with swollen and raw eyelids, crusting around mouth and nose, bubbling rhinorrhea	20	96	120 ^t	279
		Bronchotracheal/gastrointestinal irritation (sneezing, coughing, and gagging reflex)	4	127	60**	217

(Continued)

Table 4 (Continued). Nonlethal Concentration Data for Chlorine Trifluoride (ClF₃)

Reference	Species	Critical nonlethal effect	Number of animals	Dose (ppm)	Time (min)	Adjusted 30-min Concentration* (ppm)
MacEwen and Vernot [1970]	Rat	Lacrimation, salivation, dyspnea, rhinorrhea during exposures.	8	200	60**	341
	Mouse	Lacrimation, salivation, dyspnea, rhinorrhea during exposures.	15	125	60**	213

*For exposures other than 30 minutes, the ten Berge et al. [1986] relationship is used for duration adjustment ($C_n \times t = k$), where C = concentration, t = time, k = constant, n = time scaling value; NRC [2007] 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].

†The exposure time and symptoms noted were from the first daily exposure of a 6 week, 6-hour-per-day, 5-day-per-week inhalation study.

‡The exposure time and symptoms noted were from the first daily exposure of a 2 day, 6-hour-per-day inhalation study.

§The exposure time and symptoms noted were from an ET₅₀ acute inhalation study at a concentration of 480 ppm.

¶The exposure time and symptoms noted were from an ET₅₀ acute inhalation study at a concentration of 96 ppm.

***The exposure time and symptoms noted were from an LC₅₀ acute inhalation study.

Table 5. Lethal Concentration Data for Chlorine Trifluoride (ClF₃)

Reference	Species	Number of animals	Dose(s) (ppm)	LC ₅₀ (ppm)	ET ₅₀ (ppm)	Time (min)	30-min Concentration*	Adjusted (ppm)
Darmer et al. [1972]; MacEwen and Vernot [1970]	Monkey	5/dose	127, 150, 200, 300, 400	230	-	60		392
Darmer et al. [1972]; MacEwen and Vernot [1970]; Vernot et al. [1977]	Rat	8/dose	200, 400	299	-	60		510
	Mouse	15/dose	125, 150, 175, 200, 400	178	-	60		303
Horn and Weir [1955]	Rat	20/dose	480	-	480	40		599
			96	-	96	222		448
Dost et al. [1967, 1974]	Rat	34	400	222 [†]		20-40		378
		46	800			10-30		

*For exposures other than 30 minutes, the ten Berge et al. [1986] relationship is used for duration adjustment ($C^t \times t = k$), where C = concentration, t = time, k = constant, n = time scaling value; NRC [2007] 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].

[†]Estimated value based on NRC [2007] extrapolation of Dost et al. [1974] data.

4 Summary

Several acute toxicity studies with exposure to ClF_3 were identified. After adjustment to a 30 minute exposure duration, nonlethal concentrations corresponding to escape-impairing health effects ranged from 121 to 341 ppm. These concentrations were time-concentration adjusted to 30-minute exposure durations using the ten Berge methodology with $n = 1.3$ [ten Berge et al. 1986, NRC 2007]. It was determined appropriate to use a time-concentration factor for the irritative endpoint because these tissue damage effects caused by a direct-contact irritant appeared to be along a continuum [NRC 2007]. In one lower concentration (30-minute equivalent of 35 ppm), irritative symptoms were observed in dogs but insufficient information was presented on the severity of the effects, so a determination whether that concentration was escape-impairing could not be made [Horn and Weir 1955]. Some of the exposure and symptom data were collected during lethal concentration studies; however, the symptoms reported were useful in the identification of irritative effects that may be escape impairing. LC_{50} values in experimental animals range from 303 to 599 ppm [Darmer et al. 1972; MacEwen and Vernot 1970; Horn and Weir 1955; Dost et al. 1967, 1974].

These values were higher than the irritative effects, would require the application of additional UFs, and thus were excluded from consideration as a POD for the IDLH value. Additionally, because the irritative effects for ClF_3 appear at lower concentrations in the cascade of adverse effects, the irritation endpoint was chosen as the POD. However, if the lethality endpoint was chosen as the POD, the final IDLH values would have been within a factor of 4 after the application of appropriate UF (UFs = 30–100). The

most sensitive endpoint appeared to be in 20 rats exposed to 480 ppm as part of a lethal concentration study. As part of this study, it was observed that after 5 minutes of exposure the rats experienced considerable lacrimation; kept their eyelids closed; and had swollen, raw, and crusting eyelids [Horn and Weir 1955]. These effects were judged by NIOSH to be a severe ocular irritation that would be escape-impairing and thus were used as the POD for the IDLH derivation. An adjusted 30-minute concentration was calculated from 5 minutes of exposure with a final POD of 121 ppm. A composite UF of 10 was applied to account for extrapolation from interspecies variability (animal to human); characterized by a factor of 3; and human variability, characterized by a factor of 3; resulting in a POD of 121 ppm divided by an UF of 10 or an IDLH value of 12 ppm. The justification for the underlying component UFs is as follows:

- Interspecies UF (=3)

This value was selected because rats were the most sensitive animal species tested when comparing the 30-minute time-adjusted concentrations, and interspecies differences are not as pronounced for direct-acting irritative effects as with other endpoints.

- Intraspecies UF (=3)

This value was selected because the difference in sensitivity to irritants among workers is typically less than other endpoints.

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Appendix A—Literature Search Strategy and Data Evaluation

As described in CIB 66 [NIOSH 2013], NIOSH performed in-depth literature searches to ensure that all relevant data from human and animal studies with acute exposures to the substance were identified. This search was conducted in June 2019 and included available literature to June 2019. The process included reviewing toxicity summaries and acute exposure guidelines during an initial screening approach, including the AEGL documentation [NRC 2007], ACGIH TLV[®] documentation [ACGIH 2020], NIOSH 1994 IDLH documentation [NIOSH 1994], and the Emergency and Continuous Exposure Limits for Selected Airborne Contaminants documentation [NRC 1984].

Studies were identified from these summaries and additional database queries were conducted in the databases listed Table A-1.

Search terms used in these databases are provided in Table A-2. For ClF₃, the chemical identifiers used in the database searches were “chlorine trifluoride,” “chlorotrifluoride,” “chlorine fluoride,” and “CAS Registry Number: 7790-91-2.” For ClF₃, the in-depth literature search was conducted through June 2019. The information identified in the in-depth literature search was evaluated with general considerations that included description of studies (i.e., species, study protocol, exposure concentration, and duration), health endpoint evaluated, and critical effect levels (e.g., NOAELs, LOAELs, and LC₅₀ values). Eighteen references were identified in the literature search, and 10 of these were cited in the IDLH document. These references included both peer-reviewed literature and scientific reports. The eight references that were not cited did not provide primary data on ClF₃.

Table A-1. Literature search sources

Database and Databases	Link
Centers for Disease Control and Prevention (CDC)/ Agency for Toxic Substance and Disease Registry (ATSDR) ToxProfiles	https://www.atsdr.cdc.gov/toxprofiles/index.asp
ChemIDplus	https://chem.sis.nlm.nih.gov/chemidplus/chemidlite.jsp
EU, European INventory of Existing Commercial chemical Substances (EINECS)	https://ihcp.jrc.ec.europa.eu/our_labs/predictive_toxicology/information-sources/ec_inventory
EMBASE	https://www.embase.com/
Hazardous Substance Data Bank (HSDB)	https://www.nlm.nih.gov/databases/download/hsdb.html
Haz-map	https://haz-map.com/
National Library of Medicine (NLM)	https://pubchem.ncbi.nlm.nih.gov/
International Agency for Research on Cancer (IARC)	https://www.iarc.fr/
Environmental Protection Agency (EPA) Toxic Substance Control Act (TSCA) Section 8(e) Notices	https://www.epa.gov/chemicals-under-tsca
World Health Organization (WHO)/IPCS International Chemical Safety Card (ICSC)	https://www.ilo.org/safework/lang--en/index.htm
International Toxicity Estimates for Risk (ITER)	https://tera.org/iter/
New Jersey Hazardous Substance Fact Sheets (NJ-HSFS)	https://web.doh.state.nj.us/rtkhsfs/indexfs.aspx
NIOSHTIC-2	https://www2a.cdc.gov/nioshtic-2/default.asp
NLM, PUBMED	https://pubmed.ncbi.nlm.nih.gov/
National Institute for Occupational Safety and Health (NIOSH)/Registry of Toxic Effects of Chemical Substances (RTECS)	https://www.cdc.gov/niosh/rtecs/
NLM, Toxicology Literature Online (TOXLINE)	https://www.ncbi.nlm.nih.gov/pubmed?term=tox%20%5Bsubset%5D%20AND%20
Scopus	https://www.scopus.com/search/form.uri?display=basic

Table A-2. Literature search terms

Search terms		
Acute	Fatal	Threshold
Inhalation	Fatality	Case study
Lethal	Irritation	Poisoning
Lethal concentration	Respiratory	Chemical identifiers
LC	RD	

References

ACGIH (American Conference of Governmental Industrial Hygienists) [2020]. Documentation of the threshold limit values and biological exposure indices, 7th edition - 2020 supplement. Cincinnati, OH: American Conference of Governmental Industrial Hygienists, <https://www.acgih.org/forms/store/ProductFormPublic/documentation-of-the-threshold-limit-values-and-biological-exposure-indices-7th-ed-2020-supplement>. Date accessed: January 8, 2020.

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