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5 **IMMEDIATELY DANGEROUS TO LIFE OR HEALTH (IDLH)**
6 **VALUE PROFILE**

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10 **FOR**

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17 **CHLORINE TRIFLUORIDE**

18 **[CAS[®] No. 7790-91-2]**
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28 **Department of Health and Human Services**
29 Centers for Disease Control and Prevention
30 National Institute for Occupational Safety and Health
31

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1 Foreword

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

12
13 The immediately dangerous to life or health (IDLH) air concentration values developed by the National Institute
14 for Occupational Safety and Health (NIOSH) characterize these high-risk exposure concentrations and conditions
15 [NIOSH 2013]. IDLH values are based on a 30-minute exposure duration and have traditionally served as a key
16 component of the decision logic for the selection of respiratory protection devices [NIOSH 2004].

17
18 Occupational health professionals have employed these values beyond their initial purpose as a component of the
19 *NIOSH Respirator Selection Logic* to assist in developing risk management plans for non-routine work practices
20 governing operations in high-risk environments (e.g., confined spaces) and the development of emergency
21 preparedness plans.

22
23 The approach used to derive IDLH values for high priority chemicals is outlined in the *NIOSH Current*
24 *Intelligence Bulletin (CIB) 66: Derivation of Immediately Dangerous to Life or Health Values* [NIOSH 2013].
25 CIB 66 provides (1) an update on the scientific basis and risk assessment methodology used to derive IDLH
26 values, (2) the rationale and derivation process for IDLH values, and (3) a demonstration of the derivation of
27 scientifically credible IDLH values using available data resources.

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1 The purpose of this technical report is to present the IDLH value for Chlorine trifluoride (CAS® No. 7790-91-2).
2 The scientific basis, toxicologic data, and risk assessment approach used to derive the IDLH value are
3 summarized to ensure transparency and scientific credibility.

4

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6 Director
7 National Institute for Occupational Safety and Health
8 Centers for Disease Control and Prevention

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1 Abbreviations

2		
3	ACGIH®	American Conference of Governmental Industrial Hygienists
4	AEGLs	Acute Exposure Guideline Levels
5	AIHA®	American Industrial Hygiene Association
6	BMC	benchmark concentration
7	BMD	benchmark dose
8	BMCL	benchmark concentration lower confidence limit
9	°C	degrees Celsius
10	CAS®	Chemical Abstracts Service, a division of the American Chemical Society
11	CIB	Current Intelligence Bulletin
12	ClF ₃	Chlorine trifluoride
13	ERPGs™	Emergency Response Planning Guidelines
14	ET ₅₀	Effective time to 50% mortality
15	°F	degrees Fahrenheit
16	g/cu cm	grams per cubic centimeter
17	HF	Hydrogen fluoride
18	IDLH	immediately dangerous to life or health
19	LC	lethal concentration
20	LC ₅₀	median lethal concentration
21	LC _{LO}	lowest concentration that caused death in humans or animals
22	LEL	lower explosive limit
23	LOAEL	lowest observed adverse effect level
24	mg/m ³	milligram(s) per cubic meter
25	min	minutes
26	mmHg	millimeter(s) of mercury
27	NAS	National Academy of Sciences
28	NIOSH	National Institute for Occupational Safety and Health
29	NLM	National Library of Medicine
30	NOAEL	no observed adverse effect level
31	NRC	National Research Council
32	OSHA	Occupational Safety and Health Administration
33	PEL	permissible exposure limit
34	ppm	parts per million
35	RD ₅₀	concentration of a chemical in the air that is estimated to cause a 50% decrease in the respiratory rate
36		
37	REL	recommended exposure limit
38	STEL	short-term exposure limit
39	TERA	Toxicology Excellence for Risk Assessment
40	TLV®	Threshold Limit Value
41	TWA	time-weighted average
42	UEL	upper explosive limit
43	WEELs®	Workplace Environmental Exposure Levels

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1 **Glossary**

2
3 **Acute exposure:** Exposure by the oral, dermal, or inhalation route for 24 hours or less.

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

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

19 **Acute toxicity:** Any poisonous effect produced within a short period of time following an exposure, usually 24 to
20 96 hours [U.S. EPA 2018].

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

23 **Benchmark dose/concentration (BMD/BMC):** A dose or concentration that produces a predetermined change in
24 response rate of an effect (called the benchmark response, or BMR) compared to background [U.S. EPA
25 2018] (additional information available at <http://www.epa.gov/ncea/bmds/>).

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

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

31 **Bolus exposure:** A single, relatively large dose.

32 **Ceiling value (“C”):** U.S. term in occupational exposure indicating the airborne concentration of a potentially
33 toxic substance that should never be exceeded in a worker’s breathing zone.

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

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

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- 1
2 **Dose:** The amount of a substance available for interactions with metabolic processes or biologically significant
3 receptors after crossing the outer boundary of an organism [U.S. EPA 2018].
- 4 **EC₅₀:** A combination of the effective concentration of a substance in the air and the exposure duration that is
5 predicted to cause an effect in 50% (one half) of the experimental test subjects.
- 6 **Emergency Response Planning Guidelines (ERPGsTM):** Maximum airborne concentrations below which nearly
7 all individuals can be exposed without experiencing health effects for 1-hour exposure. ERPGs are presented
8 in a tiered fashion, with health effects ranging from mild or transient to serious, irreversible, or life
9 threatening (depending on the tier). ERPGs are developed by the American Industrial Hygiene Association
10 [AIHA 2016].
- 11 **Endpoint:** An observable or measurable biological event or sign of toxicity, ranging from biomarkers of initial
12 response to gross manifestations of clinical toxicity.
- 13 **Exposure:** Contact made between a chemical, physical, or biological agent and the outer boundary of an
14 organism. Exposure is quantified as the amount of an agent available at the exchange boundaries of the
15 organism (e.g., skin, lungs, gut).
- 16 **Extrapolation:** An estimate of the response at a point outside the range of the experimental data, generally
17 through the use of a mathematical model, although qualitative extrapolation may also be conducted. The
18 model may then be used to extrapolate to response levels that cannot be directly observed.
- 19 **Hazard:** A potential source of harm. Hazard is distinguished from risk, which is the probability of harm under
20 specific exposure conditions.
- 21 **Immediately dangerous to life or health (IDLH) condition:** A condition that poses a threat of exposure to
22 airborne contaminants when that exposure is likely to cause death or immediate or delayed permanent adverse
23 health effects or prevent escape from such an environment [NIOSH 2004, 2013].
- 24 **IDLH value:** A maximum (airborne concentration) level above which only a highly reliable breathing apparatus
25 providing maximum worker protection is permitted [NIOSH 2004, 2013]. IDLH values are based on a 30-
26 minute exposure duration.
- 27 **LC₀₁:** The statistically determined concentration of a substance in the air that is estimated to cause death in 1% of
28 the test animals.
- 29 **LC₅₀:** The statistically determined concentration of a substance in the air that is estimated to cause death in 50%
30 (one half) of the test animals; median lethal concentration.
- 31 **LC_{LO}:** The lowest lethal concentration of a substance in the air reported to cause death, usually for a small
32 percentage of the test animals.
- 33
- 34 **LD₅₀:** The statistically determined lethal dose of a substance that is estimated to cause death in 50% (one half) of
35 the test animals; median lethal concentration.
- 36 **LD_{LO}:** The lowest dose of a substance that causes death, usually for a small percentage of the test animals.

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- 1 **LEL:** The minimum concentration of a gas or vapor in air, below which propagation of a flame does not occur in
2 the presence of an ignition source.
- 3 **Lethality:** Pertaining to or causing death; fatal; referring to the deaths resulting from acute toxicity studies. May
4 also be used in lethality threshold to describe the point of sufficient substance concentration to begin to cause
5 death.
- 6 **Lowest observed adverse effect level (LOAEL):** The lowest tested dose or concentration of a substance that has
7 been reported to cause harmful (adverse) health effects in people or animals.
- 8 **Mode of action:** The sequence of significant events and processes that describes how a substance causes a toxic
9 outcome. By contrast, the term *mechanism of action* implies a more detailed understanding on a molecular
10 level.
- 11 **No observed adverse effect level (NOAEL):** The highest tested dose or concentration of a substance that has
12 been reported to cause no harmful (adverse) health effects in people or animals.
- 13 **Occupational exposure limit (OEL):** Workplace exposure recommendations developed by governmental
14 agencies and nongovernmental organizations. OELs are intended to represent the maximum airborne
15 concentrations of a chemical substance below which workplace exposures should not cause adverse health
16 effects. OELs may apply to ceiling limits, STELs, or TWA limits.
- 17 **Peak concentration:** Highest concentration of a substance recorded during a certain period of observation.
- 18 **Permissible exposure limits (PELs):** Occupational exposure limits developed by OSHA (29 CFR 1910.1000) or
19 MSHA (30 CFR 57.5001) for allowable occupational airborne exposure concentrations. PELs are legally
20 enforceable and may be designated as ceiling limits, STELs, or TWA limits.
- 21
- 22 **Point of departure (POD):** The point on the dose–response curve from which dose extrapolation is initiated. This
23 point can be the lower bound on dose for an estimated incidence or a change in response level from a
24 concentration–response model (BMC), or it can be a NOAEL or LOAEL for an observed effect selected from
25 a dose evaluated in a health effects or toxicology study.
- 26 **RD₅₀:** The statistically determined concentration of a substance in the air that is estimated to cause a 50% (one
27 half) decrease in the respiratory rate.
- 28 **Recommended exposure limit (REL):** Recommended maximum exposure limit to prevent adverse health
29 effects, based on human and animal studies and established for occupational (up to 10-hour shift, 40-hour
30 week) inhalation exposure by NIOSH. RELs may be designated as ceiling limits, STELs, or TWA limits.
- 31 **Short-term exposure limit (STEL):** A worker’s 15-minute time-weighted average exposure concentration that
32 shall not be exceeded at any time during a work day.
- 33 **Target organ:** Organ in which the toxic injury manifests in terms of dysfunction or overt disease.
- 34 **Threshold Limit Values (TLVs®):** Recommended guidelines for occupational exposure to airborne
35 contaminants, published by the American Conference of Governmental Industrial Hygienists (ACGIH®).
36 TLVs refer to airborne concentrations of chemical substances and represent conditions under which it is

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1 believed that nearly all workers may be repeatedly exposed, day after day, over a working lifetime, without
2 adverse effects. TLVs may be designated as ceiling limits, STELs, or 8-hr TWA limits.

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

6 **Toxicity:** The degree to which a substance is able to cause an adverse effect on an exposed organism.
7

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

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

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2
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1.0 Introduction

1.1 Overview of the IDLH Value for Chlorine Trifluoride

IDLH Value: 10 ppm (38 mg/m³)

Basis for IDLH Value: The IDLH value for chlorine trifluoride is based on an LC₅₀ of 178 ppm in mice exposed for 60 minutes [Darmer et al. 1972]. The duration adjusted 30-minute LC₅₀ 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 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 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 LC₅₀ values). For ClF₃, the in-depth literature search was conducted through November 2017.

1.3 General Substance Information

Chemical: Chlorine trifluoride

CAS No: 7790-91-2

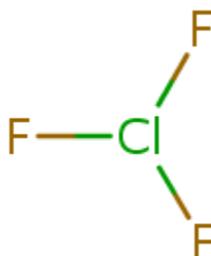
Synonyms: Chlorine fluoride, chlorotrifluoride (ClF₃)*

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1 **Chemical category:** Fluorine compounds, inorganic; chlorine compounds, inorganic †

2 **References:** * NAS [2007]; † IFA [2018]

3 **Structural formula*:**



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8
9 Table 1 highlights selected physiochemical properties of ClF₃ relevant to IDLH conditions. Table 2 provides
10 alternative exposure guidelines for ClF₃. Table 3 summarizes the Acute Exposure Guideline Level (AEGL) values
11 for ClF₃.

12 **Reference:** *NLM [2018]

13
14
15 **Table 1: Physiochemical Properties of Chlorine Trifluoride**

Property	Value
Molecular weight	92.45
Chemical formula	ClF ₃
Description	Colorless gas; Yellowish-green liquid; White solid
Odor	Sweetish, suffocating
Odor Threshold	Not available
UEL	Not flammable
LEL	Not flammable
Vapor pressure	1064 mmHg at 20°C (68°F)
Flash point	Not flammable
Ignition temperature	Not flammable
Solubility	Violent hydrolysis with water

17
18 **Reference:** NAS [2007]

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1 **Table 2: Alternative Exposure Values for Chlorine Trifluoride**

Organization	Value
NIOSH (1994) IDLH value [*]	20 ppm (76 mg/m ³)
NIOSH REL [†]	0.1 ppm (0.38 mg/m ³), ceiling
OSHA PEL [‡]	0.1 ppm (0.38 mg/m ³), ceiling
ACGIH [®] TLV ^{®§}	0.1 ppm (0.38 mg/m ³), ceiling
AIHA [®] ERPGs ^{TM¶}	ERPG-1: 0.1 ppm; ERPG-2: 1 ppm; ERPG-3: 10 ppm
AIHA [®] WEELs ^{®**}	Not available

2
3 **References:** ^{*}NIOSH [1994]; [†]NIOSH [2005]; [‡]OSHA [2018]; [§]ACGIH [2017]; [¶]AIHA [2016]; ^{**} TERA [2014]
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1 **Table 3: AEGL Values for Chlorine Trifluoride**
2

Classification	10-min	30-min	1-hour	4-hour	8-hour	End point (Reference)
AEGL-1	0.12 ppm (0.46 mg/m ³)	Slight irritation- dog [Horn and Weir 1956]				
AEGL-2	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 [Horn and Weir 1956]
AEGL-3	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]

3
4 **Reference:** NAS [2007]

2.0 Human Data

Reliable human toxicity data for ClF_3 were limited. 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 $12^\circ\text{C}/53^\circ\text{F}$) 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 2018; MacEwen and Vernot 1970].

3.0 Animal Toxicity Data

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

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1 after the first exposure period, however no information was provided as to the severity of these effects. It was
2 reported that both dogs began experiencing rhinorrhea and lacrimation within 10 minutes of the exposure starting.
3 It was also reported that the dogs “blinked continuously at first and later kept their eyes tightly closed,” however,
4 the time that these symptoms began was not noted [Horn and Weir 1955]. These effects were considered escape-
5 impairing in the dogs. Table 4 summarizes non-lethal data reported in animal studies with 30-minute equivalent
6 derived values for ClF₃. Information included in these tables includes species of test animals, toxicological
7 metrics (i.e., LC, BMCL, NOAEL, LOAEL), adjusted 30-minute concentration, and the justification for the
8 composite uncertainty factors applied to calculate the derived values.

9
10 Median lethal concentration (LC₅₀) and the effective median lethal time to 50% of the animals (ET₅₀) values for
11 ClF₃ were evaluated in several animal species. MacEwen and Vernot [1970] exposed mice, rats, and monkeys to
12 ClF₃ for 60 minutes and observed lacrimation, salivation, rhinorrhea, and dyspnea that, within a few hours after
13 exposure, turned into bloody discharges if the animals survived. Monkeys also showed signs typical of bronchial
14 and gastrointestinal irritation. Death occurred with delays as long as 36 hours after exposure. Upon death,
15 massive alveolar and interstitial hemorrhage were noted. Near-fatal concentrations resulted in concentration-
16 dependent pulmonary congestion, edema, emphysema, and hemorrhage. The 60-minute LC₅₀ values were 178
17 ppm for mice, 299 ppm for rats, and 230 ppm for monkeys (also reported in Darmer et al. [1972]).

18
19 Horn and Weir [1955] exposed rats to two concentrations of ClF₃ and determined ET₅₀. In rats, the ET₅₀ at 480
20 ppm was 40 minutes (all dead within 70 minutes), at 96 ppm it was 3.7 hours (observation time after the end of
21 the 4.5-hour exposure to 96 ppm was not stated). Clinical signs appeared within minutes of exposure and
22 included increased activity, nasal flow and salivation, respiratory difficulty, eye irritation, and convulsions and
23 coma shortly before death. Dost et al. [1974, 1967] reported that ClF₃ caused severe inflammation in all exposed
24 tissues, lacrimation, and shallow breathing in male rats. High concentrations made hair appear “singled,” caused
25 skin burns, and produced corneal ulceration. These authors also observed that rats surviving ClF₃ exposure for
26 4 hours did not eat for several days thereafter. Time to death was tested in presence of 400 and 800 ppm ClF₃; all
27 animals died within 45–90 minutes of exposure to 800 ppm for 15 minutes; at longer exposure times, up to 30
28 minutes, the earliest deaths occurred within 20 minutes but some animals survived as long as 160 minutes. At
29 400 ppm, death occurred after 55–140 minutes with ≥30 minutes exposure but no deaths were observed at
30 ≤25 minutes exposure. NAS [2007] provided an estimated 1-hour LC₅₀ value of 222 ppm based on these data but

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1 indicated that this value may be an underestimate since post-exposure observations were not completed [NAS
2 2007]. Table 5 summarizes the LC data identified in animal studies and provides 30-minute equivalent derived
3 values for ClF₃. Information in this table includes species of test animals, toxicological metrics (i.e., LC, BMCL,
4 NOAEL, LOAEL), adjusted 30-minute concentration, and the justification for the composite uncertainty factors
5 applied to calculate the derived values.

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Table 4: Non-lethal Concentration Data for Chlorine Trifluoride (ClF₃)

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

*For exposures other than 30 minutes the ten Berge et al. [1986] relationship is used for duration adjustment ($C^n \times t = k$); NAS [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 derived value is the result of the adjusted 30-minute concentration divided by the composite uncertainty factor.

[‡]Values rounded to the appropriate significant figure.

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

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

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

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1 *For exposures other than 30 minutes the ten Berge et al. [1986] relationship is used for duration adjustment ($C^n \times t = k$); NAS [2007] provided an empirically estimated n
2 of 1.3 for all time-scaling. Additional information on the calculation of duration adjusted concentrations can be found in NIOSH [2013].

3 †The derived value is the result of the adjusted 30-minute concentration divided by the composite uncertainty factor.

4 ‡Values rounded to the appropriate significant figure.

5 §Composite uncertainty factor to account for adjustment of LC₅₀ values to LC₀₁ values, use of lethal concentration threshold in animals, interspecies differences and
6 human variability.

7 ¶Estimated value based on NAS [2007] extrapolation of Dost [1974] data.

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1 **4.0 Summary**

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3 Several acute toxicity studies with exposure to ClF_3 were identified. After adjustment to a 30-minute exposure
4 duration, LC_{50} values in experimental animals range from 303 to 599 ppm [Darmer 1972; MacEwen and Vernot
5 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
6 value since it results in the most protective adjusted 30 minute LC_{50} value [Darmer et al. 1972; MacEwen and
7 Vernot 1970]. The adjusted 30-minute LC_{50} is 303 ppm. An uncertainty factor of 30 was applied to account for
8 extrapolation from a concentration that is lethal to animals, animal to human differences, and human variability,
9 resulting in an IDLH value of 10 ppm.

10
11 Even though information on sublethal endpoints was available [Horn and Weir 1955], the resulting calculated
12 IDLH value was less protective than the LC_{50} data that was used to derive the final IDLH value. In addition, the
13 sub-lethal endpoint data presented by Horn and Weir [1955] did not provide sufficient documentation of time to
14 relevant health effects and there was additional uncertainty with the low number of animals tested.

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References

- 1
2
3 ACGIH (American Conference of Governmental Industrial Hygienists) [2017]. Annual TLVs® (Threshold Limit
4 Values) and BEIs® (Biological Exposure Indices) booklet. Cincinnati, OH: ACGIH Signature Publications.
5
6 AIHA (American Industrial Hygiene Association) [2014]. AIHA Emergency Response Planning (ERP)
7 Committee procedures and responsibilities. Fairfax, VA: American Industrial Hygiene Association.
8
9 AIHA (American Industrial Hygiene Association) [2016]. Emergency response planning guidelines (ERPG) and
10 workplace environmental exposure levels (WEEL) handbook. Fairfax, VA: American Industrial Hygiene
11 Association Press.
12
13 Cloyd DR, Murphy WJ [1965]. Handling hazardous materials. Washington, DC: National Aeronautics and Space
14 Administration, NASA SP-5032.
15
16 Darmer KI, Haun CC, MacEwen JD [1972]. The acute inhalation toxicity of chlorine pentafluoride. Am Ind Hyg
17 Assoc J 33:661–668.
18
19 Dost FN, Reed DJ, Smith VN, Wang CH [1974]. Toxic properties of chlorine trifluoride. Toxicol Appl
20 Pharmacol 27:527–536.
21
22 Dost FN, Reed DJ, Smith VN, Wang CH [1967]. Metabolism and pharmacology of inorganic and fluorine
23 containing compounds. Wright-Patterson Air Force Base, OH: Aerospace Medical Research Laboratories,
24 Aerospace Medical Division, Air Force Systems Command, AMRL-TR-67-224.
25
26 EPA [2018]. Integrated Risk Information System (IRIS): glossary
27 [[https://ofmpub.epa.gov/sor_internet/registry/termreg/searchandretrieve/glossariesandkeywordlists/search.do?det
28 ils=&glossaryName=IRIS%20Glossary#formTop](https://ofmpub.epa.gov/sor_internet/registry/termreg/searchandretrieve/glossariesandkeywordlists/search.do?details=&glossaryName=IRIS%20Glossary#formTop)]. Accessed February 1, 2018
29
30 Horn HJ, Weir RJ [1955]. Inhalation toxicity of chloride trifluoride. I. Acute and subacute toxicity. AMA Arch
31 Ind Health 12:515–521.
32
33 HSDB [2018]. Hazardous Substances Data Bank [<http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB>] CAS No.
34 7790-91-2. Date accessed: January 10, 2018.
35
36 IFA (Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung) [2018]. GESTIS: database on
37 hazardous substances, [http://gestis-
en.itrust.de/nxt/gateway.dll?f=templates&fn=default.htm&vid=gestiseng:sdbeng](http://gestis-en.itrust.de/nxt/gateway.dll?f=templates&fn=default.htm&vid=gestiseng:sdbeng).
38
39 Longley MY, Pierce JF, Griesemer EC [1965]. A toxic hazard study of selected missile propellants. AMRL-TR-
40 65-99. Wright-Patterson Air Force Base, OH: Aerospace Medical Research Laboratories (as cited in NRC 1984).

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May 2018**

- 1 MacEwen JD, Vernot EH [1970]. Toxic Hazards Research Unit. Annual Technical Report: 1970. Wright-
2 Patterson Air Force Base, OH: Aerospace Medical Research Laboratories, Aerospace Medical Division, Air Force
3 Systems Command, AMRL-TR-70-77.
4
- 5 NAS [2001]. Standing operating procedures for developing Acute Exposure Guidelines Levels for hazardous
6 chemicals. National Academy of Sciences, National Research Council (NRC), Committee on Toxicology,
7 Subcommittee on Acute Exposure Guide-line Levels. Washington, DC: National Academy Press, ISBN: 0-309-
8 07553-X [[http://www.epa.gov/sites/production/files/2015-09/documents/sop_final_stand-](http://www.epa.gov/sites/production/files/2015-09/documents/sop_final_standing_operating_procedures_2001.pdf)
9 [ing_operating_procedures_2001.pdf](http://www.epa.gov/sites/production/files/2015-09/documents/sop_final_standing_operating_procedures_2001.pdf)]. Date accessed: January 10, 2018
10
- 11 NAS (National Academy of Science) [2007]. Acute Exposure Guideline Levels (AEGLs) for selected airborne
12 chemicals, Volume 5: chlorine trifluoride [[https://www.epa.gov/sites/production/files/2014-](https://www.epa.gov/sites/production/files/2014-11/documents/chlorinetrifluoride_final_volume5_2007.pdf)
13 [11/documents/chlorinetrifluoride_final_volume5_2007.pdf](https://www.epa.gov/sites/production/files/2014-11/documents/chlorinetrifluoride_final_volume5_2007.pdf)]. Date accessed: January 10, 2018.
14
- 15 NIOSH [1994]. Documentation for Immediately Dangerous to Life or Health Concentrations (IDLHs): Chlorine
16 trifluoride [<http://www.cdc.gov/niosh/idlh/7790912.html>]. Date accessed: January 10, 2018.
17
- 18 NIOSH [2004]. NIOSH Respirator Selection Logic. By: Bollinger N. Cincinnati, OH: U.S. Department of Health
19 and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and
20 Health, DHHS (NIOSH) Publication No. 2005-100.
21
- 22 NIOSH [2005]. NIOSH pocket guide to chemical hazards. Barsan ME, ed. Cincinnati, OH: U.S. Department of
23 Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational
24 Safety and Health, DHHS (NIOSH) Publication No. 2005-149.
25
- 26 NIOSH [2013]. Current Intelligence Bulletin #66: Derivation of Immediately Dangerous to Life or Health
27 (IDLH) Values. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control
28 and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2014-
29 100.
30
- 31 NLM (National Library of Medicine) [2018]. ChemIDplus lite
32 [<http://chem.sis.nlm.nih.gov/chemidplus/chemidlite.jsp>]. Date accessed: January 10, 2018.
33
- 34 NRC (National Research Council) [1984]. Emergency and continuous exposure limits for
35 selected airborne contaminants, Volume 2. Washington, DC: The National Academies.
36
- 37 OSHA (Occupational Safety and Health Administration) [2018]. Occupational Safety and Health Standards. 29
38 CFR 1910. Subpart Z -- Toxic and Hazardous Substances. OSHA; Washington, DC
39 [http://www.osha.gov/pls/oshaweb/owadisp.show_document?p_table=standards&p_id=9992]. Date accessed:
40 January 10, 2018.
41
- 42 Reed DJ, Dost FN, Wang CH [1966]. Inorganic fluoride propellant oxidizers, Volume I: their effects upon seed
43 germination and plant growth. Wright-Patterson Air Force Base, OH: Aerospace Medical Research Laboratories,
44 Aerospace Medical Division, Air Force Systems Command.

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- 1
2 ten Berge WF, Zwart A, Appelman LM [1986]. Concentration-time mortality response relationship of irritant and
3 systematically acting vapors and gases. *J Haz Mat* 13:301–309.
4
5 Teitelbaum DT [2001]. The halogens. In: Bingham E, Cohrssen B, Powell CH (eds.), *Patty's toxicology*, Vol. 3.
6 New York: John Wiley & Sons, Inc., pp. 731–825.
7
8 TERA [2014]. Occupational Alliance for Risk Science-Workplace Environmental Exposure Levels (WEEL)TM
9 [<http://www.tera.org/OARS/WEELs.pdf>]. Date accessed: January 10, 2018.
10

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