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IMMEDIATELY DANGEROUS TO LIFE OR HEALTH (IDLH) VALUE PROFILE

FOR

CHLOROACETYL CHLORIDE

[CAS No. 79-04-9]

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

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1 Foreword

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

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

28
29 The purpose of this technical report is to present the IDLH value for chloroacetyl chloride (CAS # 79-04-9). The
30 scientific basis, toxicologic data and risk assessment approach used to derive the IDLH value are summarized to
31 ensure transparency and scientific credibility.

32
33 John Howard, M.D.
34 Director
35 National Institute for Occupational Safety and Health

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1 Abbreviations

2		
3	ACGIH	American Conference of Governmental Industrial Hygienists
4	AEGL	Acute Exposure Guideline Levels
5	AIHA	American Industrial Hygiene Association
6	BMC	benchmark concentration
7	BMCL	benchmark concentration lower confidence limit
8	C	ceiling
9	CAS	chemical abstract service
10	ERPG	Emergency Response Planning Guidelines
11	HCl	hydrochloric acid
12	IDLH	immediately dangerous to life or health
13	LC ₅₀	median lethal concentration
14	LC _{Lo}	lowest concentration of a chemical that caused death in humans or animals
15	LEL	lower explosive limit
16	LOAEL	lowest observed adverse effect level
17	mg/m ³	milligram(s) per cubic meter
18	NAC	National Advisory Committee
19	NAS	National Academy of Sciences
20	NIOSH	National Institute for Occupational Safety and Health
21	NOAEL	no observed adverse effect level
22	OSHA	Occupational Safety and Health Administration
23	PEL	permissible exposure limit
24	ppm	parts per million
25	RD ₅₀	concentration of a chemical in the air that is estimated to cause a 50% decrease in the respiratory rate
26		
27	REL	recommended exposure limit
28	SCP	Standard Completion Program
29	STEL	short term exposure limit
30	TLV	threshold limit value
31	TWA	time weighted average
32	UEL	upper explosive limit
33	WEEL	workplace environmental exposure level

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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 or
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 (RfC):** An estimate (with uncertainty spanning perhaps an order of magnitude)
14 of a continuous inhalation exposure for an acute duration (24 hours or less) of the human population
15 (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a
16 lifetime. It can be derived from a NOAEL, LOAEL, or benchmark concentration, with uncertainty factors
17 (UFs) generally applied to reflect limitations of the data used. Generally used in USEPA noncancer health
18 assessments [USEPA 2014].
- 19 **Acute Toxicity:** Any poisonous effect produced within a short period of time following an exposure, usually 24
20 to 96 hours.
- 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
24 in response rate of an effect (called the benchmark response, or BMR) compared to background [USEPA
25 2014] (additional information available at <http://www.epa.gov/ncea/bmds/>).
- 26 **Benchmark Response (BMR):** A predetermined change in response rate of an effect. Common defaults for the
27 BMR are 10% or 5%, reflecting study design, data variability, and sensitivity limits used.
- 28 **BMCL:** A statistical lower confidence limit on the concentration at the BMC [USEPA 2014].
- 29 **Bolus Exposure:** A single, relatively large dose.
- 30 **Ceiling Value (“C”):** U.S. term in occupational exposure indicating the airborne concentration of a potentially
31 toxic substance that should never be exceeded in a worker’s breathing zone.
- 32 **Chronic Exposure:** Repeated exposure for an extended period of time. Typically exposures are more than
33 approximately 10% of life span for humans and >90 days to 2 years for laboratory species.
- 34 **Critical Study:** The study that contributes most significantly to the qualitative and quantitative assessment of risk
35 [USEPA 2014].
36
- 37 **Dose:** The amount of a substance available for interactions with metabolic processes or biologically significant
38 receptors after crossing the outer boundary of an organism [USEPA 2014].
- 39 **EC_{t50}:** A combination of the effective concentration of a substance in the air and the exposure duration that is
40 predicted to cause an effect in 50% (one half) of the experimental test subjects.

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- 1 **Emergency Response Planning Guidelines (ERPGs):** Maximum airborne concentrations below which nearly all
2 individuals can be exposed without experiencing health effects for 1-hour exposure. ERPGs are presented in a
3 tiered fashion with health effects ranging from mild or transient to serious, irreversible, or life threatening
4 (depending on the tier). ERPGs are developed by the American Industrial Hygiene Association [AIHA 2006].
- 5 **Endpoint:** An observable or measurable biological event or sign of toxicity ranging from biomarkers of initial
6 response to gross manifestations of clinical toxicity.
- 7 **Exposure:** Contact made between a chemical, physical, or biological agent and the outer boundary of an
8 organism. Exposure is quantified as the amount of an agent available at the exchange boundaries of the
9 organism (e.g., skin, lungs, gut).
- 10 **Extrapolation:** An estimate of the response at a point outside the range of the experimental data, generally
11 through the use of a mathematical model, although qualitative extrapolation may also be conducted. The
12 model may then be used to extrapolate to response levels that cannot be directly observed.
- 13 **Hazard:** A potential source of harm. Hazard is distinguished from risk, which is the probability of harm under
14 specific exposure conditions.
- 15 **Immediately Dangerous to Life or Health (IDLH) condition:** A situation that poses a threat of exposure to
16 airborne contaminants when that exposure is likely to cause death or immediate or delayed permanent adverse
17 health effects or prevent escape from such an environment [NIOSH 2004, 2013].
- 18 **IDLH value:** A maximum (airborne concentration) level above which only a highly reliable breathing apparatus
19 providing maximum worker protection is permitted [NIOSH 2004, 2013]. IDLH values are based on a 30-
20 minute exposure duration.
- 21 **LC₀₁:** The statistically determined concentration of a substance in the air that is estimated to cause death in 1% of
22 the test animals.
- 23 **LC₅₀:** The statistically determined concentration of a substance in the air that is estimated to cause death in 50%
24 (one half) of the test animals; median lethal concentration.
- 25 **LC₁₀:** The lowest lethal concentration of a substance in the air reported to cause death, usually for a small
26 percentage of the test animals.
- 27
- 28 **LD₅₀:** The statistically determined lethal dose of a substance that is estimated to cause death in 50% (one half) of
29 the test animals; median lethal concentration.
- 30 **LD₁₀:** The lowest dose of a substance that causes death, usually for a small percentage of the test animals.
- 31 **LEL:** The minimum concentration of a gas or vapor in air, below which propagation of a flame does not occur in
32 the presence of an ignition source.
- 33 **Lethality:** Pertaining to or causing death; fatal; referring to the deaths resulting from acute toxicity studies. May
34 also be used in lethality threshold to describe the point of sufficient substance concentration to begin to cause
35 death.
- 36 **Lowest Observed Adverse Effect Level (LOAEL):** The lowest tested dose or concentration of a substance that
37 has been reported to cause harmful (adverse) health effects in people or animals.
- 38 **Mode of Action:** The sequence of significant events and processes that describes how a substance causes a toxic
39 outcome. Mode of action is distinguished from the more detailed mechanism of action, which implies a more
40 detailed understanding on a molecular level.

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- 1 **No Observed Adverse Effect Level (NOAEL):** The highest tested dose or concentration of a substance that has
2 been reported to cause no harmful (adverse) health effects in people or animals.
- 3 **Occupational Exposure Limit (OEL):** Workplace exposure recommendations developed by governmental
4 agencies and non-governmental organizations. OELs are intended to represent the maximum airborne
5 concentrations of a chemical substance below which workplace exposures should not cause adverse health
6 effects. OELs may apply to ceiling, short-term (STELs), or time-weighted average (TWA) limits.
- 7 **Peak Concentration:** Highest concentration of a substance recorded during a certain period of observation.
- 8 **Permissible Exposure Limit (PEL):** Occupational exposure limits developed by OSHA (29 CFR 1910.1000) or
9 MSHA (30 CFR 57.5001) for allowable occupational airborne exposure concentrations. PELs are legally
10 enforceable and may be designated as ceiling, STEL, or TWA limits.
- 11
- 12 **Point of Departure (POD):** The point on the dose–response curve from which dose extrapolation is initiated.
13 This point can be the lower bound on dose for an estimated incidence or a change in response level from a
14 concentration-response model (BMC), or it can be a NOAEL or LOAEL for an observed effect selected from
15 a dose evaluated in a health effects or toxicology study.
- 16 **RD₅₀:** The statistically determined concentration of a substance in the air that is estimated to cause a 50% (one
17 half) decrease in the respiratory rate.
- 18 **Recommended Exposure Limit (REL):** Recommended maximum exposure limit to prevent adverse health
19 effects based on human and animal studies and established for occupational (up to 10-hour shift, 40-hour
20 week) inhalation exposure by NIOSH. RELs may be designated as ceiling, STEL, or TWA limits.
- 21 **Short-Term Exposure Limit (STEL):** A worker’s 15-minute time-weighted average exposure concentration that
22 shall not be exceeded at any time during a work day.
- 23 **Target Organ:** Organ in which the toxic injury manifests in terms of dysfunction or overt disease.
- 24 **Threshold Limit Values (TLVs®):** Recommended guidelines for occupational exposure to airborne
25 contaminants, published by the American Conference of Governmental Industrial Hygienists (ACGIH). TLVs
26 refer to airborne concentrations of chemical substances and represent conditions under which it is believed
27 that nearly all workers may be repeatedly exposed, day after day, over a working lifetime, without adverse
28 effects. TLVs may be designated as ceiling, short-term (STELs), or 8-hr TWA limits.
- 29 **Time-Weighted Average (TWA):** A worker’s 8-hour (or up to 10-hour) time-weighted average exposure
30 concentration that shall not be exceeded during an 8-hour (or up to 10-hour) work shift of a 40-hour week.
31 The average concentration is weighted to take into account the duration of different exposure concentrations.
- 32 **Toxicity:** The degree to which a substance is able to cause an adverse effect on an exposed organism.
- 33
- 34 **Uncertainty Factors (UFs):** Mathematical adjustments applied to the POD when developing IDLH values. The
35 UFs for IDLH value derivation are determined by considering the study and effect used for the POD, with
36 further modification based on the overall database.
- 37 **Workplace Environmental Exposure Levels (WEELs):** Exposure levels developed by the American Industrial
38 Hygiene Association (AIHA) that provide guidance for protecting most workers from adverse health effects
39 related to occupational chemical exposures expressed as a TWA or ceiling limit.

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1 **Acknowledgments**

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24
25
26
27

1.0 Introduction

1.1 IDLH Value for Chloroacetyl Chloride

IDLH Value: 1.3 ppm (66 mg/m³)

Basis for IDLH Value: The IDLH value for chloroacetyl chloride is based on potentially escape-impairing effects including clinical signs of severe ocular and respiratory irritation in rats exposed to 32 ppm for one hour [Dow 1986]. The equivalent 30-minute exposure duration value is 40 ppm. Applying a composite uncertainty factor of 30 to account for extrapolation from a potentially escape impairing effect in animals, animal to human differences and human variability, results in an IDLH value of 1.3 ppm.

1.2 Purpose

This *IDLH Value Profile* presents (1) a brief summary of technical data associated with acute inhalation exposures to chloroacetyl chloride and (2) the rationale behind the Immediately Dangerous to Life or Health (IDLH) value for chloroacetyl chloride. IDLH values are developed based on 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]. 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, LC₅₀ values). For chloroacetyl chloride, the in-depth literature search was conducted through February 2014.

1.3 General Substance Information

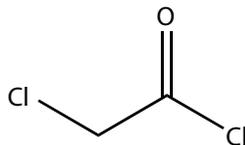
Chemical: Chloroacetyl chloride

CAS No: 79-04-9

Synonyms: Chloroacetic acid chloride; Chloroacetic chloride; Monochloroacetyl chloride*

Chemical category: Substituted carboxylic acid halides; Organic chlorine compounds[†]

1 **Structural formula:**



7 Table 1 highlights selected physiochemical properties of chloroacetyl chloride relevant to IDLH conditions. Table
8 2 provides alternative exposure guidelines for chloroacetyl chloride. Table 3 summarizes the Acute Exposure
9 Guidelines Level (AEGL) values for chloroacetyl chloride.

10
11 **Table 1: Physiochemical Properties of Chloroacetyl Chloride**

12

Property	Value
Molecular weight	112.94 [‡]
Chemical formula	C ₂ H ₂ Cl ₂ O
Description	Colorless to yellow liquid
Odor	Pungent
Odor Threshold	Strongly detectable at 0.140 ppm; barely detectable at 0.023 ppm; undetectable at 0.011 ppm, [‡]
UEL	Not available [§]
LEL	Not available [§]
Vapor pressure	25.2 mmHg at 25°C (77°F) [‡]
Flash point	Non-combustible [†]
Ignition temperature	Non-combustible [†]
Solubility	Violent decomposition in water [†]

13 **Abbreviation:** °C – Celsius; °F – Fahrenheit; mmHg – millimeter mercury; LEL – lower explosive limit; UEL – upper explosive limit

14 ^{*} NLM [2014]

15 [†] IFA [2014]

16 [‡] HSDB [2014]

17 [§] OSHA [2014]

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Table 2: Alternative Exposure Guidelines for Chloroacetyl Chloride

Organization	Value
Original (SCP) IDLH value [NIOSH 2014]	None
NIOSH REL [2014]	0.05 ppm (0.23 mg/m ³), TWA
OSHA PEL [2014]	0.05 ppm (0.23 mg/m ³), TWA 8-hour
ACGIH TLV [2014]	0.05 ppm (0.23 mg/m ³), TWA 0.15 ppm (0.69 mg/m ³) STEL
AIHA ERPG [2010]	ERPG-1: 0.05 ppm ERPG-2: 0.5 ppm ERPG-3: 10 ppm
AIHA WEEL [2010]	Not available

Abbreviation: ACGIH – American Conference of Governmental Industrial Hygienists; AIHA – American Industrial Hygiene Association; ERPG – Emergency Response Preparedness Guidelines; IDLH – immediately dangerous to life or health; NIOSH – National Institute for Occupational Safety and Health; OSHA – Occupational Safety and Health Administration; PEL – permissible exposure limit; REL – recommended exposure limit; SCP – Standards Completion Program; STEL – short-term exposure limit; TWA – time-weighted average; WEEL – workplace environmental exposure level

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1 **Table 3: AEGL Values for Chloroacetyl Chloride**

2

Classification	10-min	30-min	1-hour	4-hour	8-hour	Endpoint [reference]
AEGL-1	0.04 ppm 0.19 mg/m ³	0.04 ppm 0.19 mg/m ³	0.040 ppm 0.19 mg/m ³	0.04 ppm 0.19 mg/m ³	0.04 ppm 0.19 mg/m ³	NOEL for conjunctivitis in rats [Dow 1982]
AEGL-2	2.9 ppm 13.0 mg/m ³	2.0 ppm 9.2 mg/m ³	1.6 ppm 7.4 mg/m ³	0.40ppm 1.8 mg/m ³	0.20 ppm 0.92 mg/m ³	NOEL for inability to escape due to eye irritation in rats [Dow 1986]
AEGL-3	95.0 ppm 440.0 mg/m ³	66.0 ppm 300.0 mg/m ³	52.0 ppm 240.0 mg/m ³	13.0 ppm 60.0 mg/m ³	6.5 ppm 30.0 mg/m ³	Threshold for lethality in male rats [Dow 1986]

3 **Abbreviation:** AEGL – acute exposure guideline levels; mg/m³ – milligrams per cubic meter; min – minute; ppm – parts per million

4 ***References:** NAS [2007]

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2.0 Animal Toxicity Data

Chloroacetyl chloride decomposes in water to produce chloroacetic acid and hydrochloric acid (HCl), releasing heat in the process. Both chloroacetyl chloride and its hydrolysis products are irritants. Several modern studies [Dow 1982, 1986] reported analytical concentrations substantially lower than nominal concentrations (analytical concentrations about 25-50% of nominal). This difference has been attributed to both hydrolysis and incomplete volatilization of the test chemical. Since the total concentration of irritant chemicals in the air (including HCl) may have been higher than the analytical concentration of chloroacetyl chloride, use of the analytical concentration is a conservative approach. In light of the difference between nominal and analytical concentrations, the true concentrations (and associated LC₅₀ values) in some of the older acute studies may have been lower than the reported nominal concentrations.

In a static-exposure study, Carpenter et al. [1949] reported an approximate 4-hour LC₅₀ value of 1,000 ppm in rats. No further experimental results were provided. Younger Labs [1969] exposed rats to “concentrated” chloroacetyl chloride; all died within two hours. The exposure concentration was not specified, although information suggested a saturated atmosphere (25,000 ppm at 20°C) [AIHA 2000]. Immediately upon exposure, the rats showed signs of irritation including pawing at the face and mouth, and tightly shut eyes. Within 10 minutes, rats had reddened eyes with nasal and salivary excretion and gasping, and within 30 minutes they had opaque corneas, and death occurred after 90 (3/4 rats) or 120 (4/4) minutes. Severely hemorrhaged lungs were seen at necropsy [Younger Labs 1969].

Studies conducted by Dow Chemical Company in rats [Dow 1986] provide the most informative data for deriving the IDLH value. F344 rats were exposed whole-body to 32, 208, 522, or 747 ppm chloroacetyl chloride for 1 hour, followed by observation for 14 days. Clinical signs observed during exposure included squinting and lacrimation at all concentrations (32 to 747 ppm), and shallow or labored breathing at 208 ppm and higher. Stress-related clinical signs were also observed at the higher concentrations; these included lethargy (≥208 ppm), salivation, and stained eyes and face. Gross pathological examination of the rats that died during the 2-week post exposure period showed lung and nasal tissue congestion. Death occurred only at 747 ppm, in 5/6 males and 1/6 females, yielding an LC₅₀ value of 645 ppm for males. The LC₅₀ value for females could not be calculated, but was greater than 747 ppm. The effects at 32 ppm were considered potentially escape impairing. Results in mice and guinea pigs [Herzog 1959] support the determination that respiratory tract irritation is the key effect from exposure to chloroacetyl chloride, but the results are limited by the use of a static exposure protocol and the

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1 absence of monitoring of analytical concentrations. Results from a 2-minute exposure study by Herzog [1959]
2 support the conclusion that the onset of irritation is rapid.

3

4 Table 4 summarizes the LC data identified in animal studies and provides 30-minute equivalent derived values for
5 chloroacetyl chloride. Table 5 provides non-lethal data reported in animal studies with 30-minute equivalent
6 derived values. Information included in these tables includes species of test animals, toxicological metrics (i.e.,
7 LC, BMCL, NOAEL, LOAEL), adjusted 30-minute concentration, and the justification for the composite
8 uncertainty factors applied to calculate the derived values.

9

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1 **Table 4: Lethal Concentration Data for Chloroacetyl Chloride**
2

Reference	Species (sex)	LC ₅₀ (ppm)	LC _{Lo} (ppm)	Time (min)	Adjusted 30-min Concentration* (ppm)	Composite Uncertainty Factor	Derived Value (ppm) [†]
Herzog [1959]	Mouse	1,066	--	120	1,692	30 [‡]	56
Dow [1986]	Rat (female)	--	747	60	941	10 [‡]	94
Dow [1986]	Rat (male)	645	--	60	813	30 [‡]	27

3
4 **Abbreviation:** LC – lethal concentration; LC₅₀ – median lethal concentration; LC_{Lo} – lowest concentration of a chemical that caused death in humans or animals; min – minute; ppm – parts
5 per million
6

7 * For exposures other than 30 minutes the ten Berge et al. [1986] relationship is used for duration adjustment ($C^n \times t = k$); no empirically estimated n values were available, therefore the
8 default values were used, n = 3 for exposures greater than 30 minutes and n = 1 for exposures less than 30 minutes.

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

10 [‡]Composite uncertainty factor to account for adjustment of LC₅₀ values to LC₀₁ values, use of lethal concentration threshold in animals, interspecies differences and human variability.

11 [‡]Composite uncertainty factor to account for lethal concentration threshold in animals, interspecies differences and human variability.
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1 **Table 5: Non-lethal Concentration Data for Chloroacetyl Chloride**

2

Reference	Species (reference)	NOAEL (ppm)	LOAEL (ppm)	Time (min)	Adjusted 30-min Concentration* (ppm)	Composite Uncertainty Factor	Derived Value (ppm) [†]
Dow [1986] [‡]	Rat	--	32	60	40	30 [±]	1.3

3 **Abbreviation:** NOAEL – no observed adverse effect level; min – minute; LOAEL – lowest observed adverse effect level; ppm – parts per million

4
5 * For exposures other than 30 minutes the ten Berge et al. [1986] relationship is used for duration adjustment ($C_n \times t = k$); no empirically estimated n values were available, therefore the
6 default values were used, n = 3 for exposures greater than 30 minutes and n = 1 for exposures less than 30 minutes.

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

8 [‡]Identified study is the primary basis of the IDLH value for chloroacetyl chloride.

9 [±]Composite uncertainty factor assigned to account for adjusting from a LOAEL to NOAEL, interspecies differences, human variability and extrapolation to an escape-impairing effect.

3.0 Human Data

No reports of human deaths resulting from inhalation of chloroacetyl chloride were located. Exposure for an undefined time period (likely a few minutes) to an air concentration of 0.011 ppm chloroacetyl chloride was undetectable by odor; 0.023 ppm was “barely detectable,” and 0.14 ppm was considered a “strong” odor to an industrial hygienist [Dow 1988a]. Ocular irritation was not experienced at these concentrations, but 0.91 ppm was painful to the eyes and caused lacrimation [Dow 1988a]. This study is not appropriate as the basis for an IDLH value because insufficient information was provided about the exposure conditions, but the study does provide information on the range of exposure levels that are irritating.

The medical department of a chemical company reported that six workers who received “mild” inhalation exposures of chloroacetyl chloride (exposures not stated) experienced dyspnea and cough, and that three workers that received “moderate” inhalation exposures had cyanosis and cough [Dow 1988b].

4.0 Summary

Available human and animal data demonstrated the ability of chloroacetyl chloride to act as a potent irritant, causing ocular and respiratory tract irritation, respiratory tract pathology and death depending on the exposure concentration and duration. Concentrations that induce potentially escape-impairing and significant irritant effects appear to be well below the estimated LC₅₀ values summarized in Table 4. Studies reporting non-lethal effects, such as Dow [1988a], provide evidence that painful eye irritation and lacrimation occurred in humans exposed to 0.91 ppm for an undisclosed duration. Dow [1986] reported significant irritation at 32 ppm as a LOAEL in rats. Taking into account the potential for significant irritant effects at concentrations well below reported LC₅₀ values, the LOAEL of 32 ppm in rats is an appropriate basis for deriving the IDLH value. Duration adjustment to a 30-minute equivalent concentration yields a concentration of 40 ppm. Application of a composite uncertainty factor to account for extrapolation from a potentially escape-impairing effect in animals, animal to human differences and human variability results in an IDLH value for chloroacetyl chloride of 1.3 ppm. This value is expected to protect against both lethality and severe ocular and respiratory irritation that might impair escape.

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References

- 1
2
3 ACGIH (American Conference of Governmental Industrial Hygienists) [2014]. Annual TLVs® (Threshold Limit
4 Values) and BEIs® (Biological Exposure Indices) booklet. Cincinnati, OH: ACGIH Signature Publications.
5
6 AIHA (American Industrial Hygiene Association) [2009]. AIHA Emergency Response Planning (ERP)
7 Committee procedures and responsibilities. Fairfax, VA: American Industrial Hygiene Association.
8
9 AIHA (American Industrial Hygiene Association) [2010]. Emergency response planning guidelines (ERPG) and
10 workplace environmental exposure levels (WEEL) handbook. Fairfax, VA: American Industrial Hygiene
11 Association Press.
12
13 Carpenter CP, Smyth HF Jr., Pozzani UC [1949]. The assay of acute vapor toxicity and the grading and
14 interpretation of results on 96 chemical compounds. *J Ind Hyg Toxicol* 31:343–346.
15
16 Dow (Dow Chemical Company) [1982]. Dow Chemical Company initial submission: chloroacetyl chloride: a
17 four-week inhalation toxicity study in rats, mice, and hamsters with cover sheet & letter dated 04/21/92
18 (sanitized). Study report written by Henck JW, Nitschke KD, Jersey GC, et al., issued 6/28/82. Midland, MI:
19 Dow Chemical Company, NTIS/OTS 0536493, EPA Doc. #88-920002593S.
20
21 Dow (Dow Chemical Company) [1986]. Chloroacetyl chloride: an acute vapor inhalation study with rats. Final
22 report by Streeter CM, Battjes JE, Zimmer MA. Midland, MI: Dow Chemical Company, Mammalian and
23 Environmental Toxicology Research Laboratory.
24
25 Dow (Dow Chemical Company) [1988a]. Subjective response to chloroacetyl chloride. February 18, 1988 memo
26 by Vaccaro JR, Industrial Hygienist. Midland, MI: Dow Chemical Company.
27
28 Dow (Dow Chemical Company) [1988b]. Human exposure to chloroacetyl chloride. Compilation by McCarty LP,
29 January 19, 1988. Midland, MI: Dow Chemical Company, Medical Division.
30
31 Herzog S [1959]. Experimental studies on the toxicity of chloro-acetyl chloride. *Igiena Bucharest* 8:135 144.
32 Translated into English from Romanian.
33
34 HSDB (Hazardous Substances Data Bank) [2014]. Chloroacetyl chloride (CAS No. 79-04-9).
35 [<http://toxnet.nlm.nih.gov/cgi-bin/sis/search2/p?.temp/~9uunNY:1>]. Date accessed: March 21, 2014.
36
37 IFA (Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung) [2014]. GESTIS: database on
38 hazardous substances [<http://www.dguv.de/ifa/en/gestis/stoffdb/index.jsp>]. Date accessed: March 21, 2014.
39
40 NAS (National Academy of Science) [2007]. Interim Acute Exposure Guideline Levels (AEGs) for
41 Chloroacetyl Chloride, CAS No. 79-04-9. Washington, DC: National Research Council, Commission of Life
42 Sciences.
43 [http://www.epa.gov/oppt/aegl/pubs/chloroacetylchloride_and_dichloroacetylchloride_tsd_interimversion1_8_28_07.pdf]. Date accessed: March 21, 2014.
44
45
46 NIOSH (National Institute for Occupational Safety and Health) [2004]. NIOSH respirator selection logic.
47 Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention,

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- 1 National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2005-100.
2 [<http://www.cdc.gov/niosh/docs/2005-100/pdfs/2005-100.pdf>]. Date accessed: March 21, 2014.
3
- 4 NIOSH [2013]. NIOSH Current Intelligence Bulletin 66: Derivation of Immediately Dangerous to Life or Health
5 (IDLH) values. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and
6 Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2014-100.
7 [<http://www.cdc.gov/niosh/docs/2014-100/pdfs/2014-100.pdf>]. Date accessed: March 21, 2014.
8
- 9 NIOSH [2014]. NIOSH pocket guide to chemical hazards. Cincinnati, OH: U.S. Department of Health and
10 Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and
11 Health, DHHS (NIOSH) Publication No. 2005-149. [<http://www.cdc.gov/niosh/npg/>]. Date accessed: March 17,
12 2014.
13
- 14 NLM (National Library of Medicine) [2014]. ChemIDplus lite . [<http://chem.sis.nlm.nih.gov/chemidplus/>]. Date
15 accessed: March 17, 2014.
16
- 17 OSHA (Occupational Safety and Health Administration) [2014]. OSHA occupational chemical database:
18 chloroacetyl chloride. [<https://www.osha.gov/chemicaldata/chemResult.html?recNo=685>]. Date accessed: March
19 21, 2014.
20
- 21 ten Berge WF, Zwart A, Appelman LM [1986]. Concentration-time mortality response relationship of irritant and
22 systematically acting vapours and gases. *J Haz Mat* 13:301–309.
23
- 24 USEPA (U.S. Environmental Protection Agency) [2014]. Integrated Risk Information System (IRIS).
25 [<http://www.epa.gov/iris/>]. Date accessed: March 17, 2014.
26
- 27 Younger Labs (Younger Laboratories, Inc.) [1969]. Monsanto Company initial submission: toxicological
28 investigation of chloroacetyl chloride with cover letter dated 06/10/92. Report by Birch MD, Study No. Y-69-105,
29 October 6, 1969. St. Louis, MO: Younger Laboratories Inc., NTIS/OTS 0536760; EPA Doc. #88-920003911.