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IMMEDIATELY DANGEROUS TO LIFE OR HEALTH (IDLH) VALUE PROFILE

FOR

ACRYLONITRILE

[CAS No. 107-13-1]

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

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Foreword

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

The “immediately dangerous to life or health air concentration values (IDLH values)” developed by the National Institute for Occupational Safety and Health (NIOSH) characterize these high-risk exposure concentrations and conditions [NIOSH 2013]. IDLH values are based on a 30-minute exposure duration and have traditionally served as a key component of the decision logic for the selection of respiratory protection devices [NIOSH 2004]. Occupational health professionals have employed these values beyond their initial purpose as a component of the NIOSH Respirator Selection Logic to assist in developing Risk Management Plans for non-routine work practices governing operations in high-risk environments (e.g., confined spaces) and the development of Emergency Preparedness Plans.

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

The purpose of this technical report is to present the IDLH value for acrylonitrile (CAS # 107-13-1). The scientific basis, toxicologic data and risk assessment approach used to derive the IDLH value are summarized to ensure transparency and scientific credibility.

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

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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	°C	degree Celsius
10	CAS	chemical abstract service
11	CEO	cyanooethylene oxide
12	ERPG	Emergency Response Planning Guidelines
13	°F	degree Fahrenheit
14	IDLH	immediately dangerous to life or health
15	LC ₅₀	median lethal concentration
16	LEL	lower explosive limit
17	LOAEL	lowest observed adverse effect level
18	mg/m ³	milligram(s) per cubic meter
19	NAC	National Advisory Committee
20	NAS	National Academy of Sciences
21	NIOSH	National Institute for Occupational Safety and Health
22	NOAEL	no observed adverse effect level
23	OSHA	Occupational Safety and Health Administration
24	PEL	permissible exposure limit
25	ppm	parts per million
26	RD ₅₀	concentration of a chemical in the air that is estimated to cause a 50% decrease in the respiratory
27		rate
28	REL	recommend exposure limit
29	SCP	Standard Completion Program
30	STEL	short-term exposure limit
31	TLV	threshold limit value
32	TWA	time weighted average
33	UEL	upper explosive limit
34	WEEL	workplace environmental exposure level

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Glossary

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

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

Acute Reference Concentration (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 USEPA noncancer health assessments [USEPA 2014].

Acute Toxicity: Any poisonous effect produced within a short period of time following an exposure, usually 24 to 96 hours.

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 [USEPA 2014] (additional information available at <http://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.

BMCL: A statistical lower confidence limit on the concentration at the BMC [USEPA 2014].

Bolus Exposure: A single, relatively large dose.

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

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

Critical Study: The study that contributes most significantly to the qualitative and quantitative assessment of risk [USEPA 2014].

Dose: The amount of a substance available for interactions with metabolic processes or biologically significant receptors after crossing the outer boundary of an organism [USEPA 2014].

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.

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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.
- 40
- 41

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1 **Acknowledgments**

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This document was developed by the Education and Information Division (Paul Schulte, Ph.D., Director). G. Scott Dotson, Ph.D., was the project officer and lead NIOSH author for this technical report. The basis for this document was a report contracted by NIOSH and prepared by Andrew Maier, Ph.D., Ann Parker, and Lynn Haber, Ph.D. (Toxicology Excellence for Risk Assessment [TERA]).

8 **Education and Information Division**

9 Devin Baker, M.Ed.
10 Charles L. Geraci, Ph.D.
11 Thomas J. Lentz, Ph.D.
12 Richard Niemeier, Ph.D.
13 Chris Sofge, Ph.D.

14
15 NIOSH would like to acknowledge the contribution of the following subject matter experts for their critical
16 technical review of this report.

17
18 Michael S. Bisesi, Ph.D., R.E.H.S., C.I.H., Senior Associate Dean for Academic Affairs; Director, Center
19 for Public Health Practice; Interim Chair & Associate Professor, Division of Environmental Health
20 Science, College of Public Health, Ohio State University

21
22 Richard B. Schlesinger, Ph.D., Fellow A.T.S., Senior Associate Dean for Academic Affairs and Research
23 Professor of Biology, Dyson College of Arts and Sciences, Pace University

24
25
26
27

1.0 Introduction

1.1 Overview of the IDLH Value for Acrylonitrile

IDLH Value: 60 ppm

The IDLH value for acrylonitrile is based on a BMCL₀₅ for lethality of 1,784 ppm in rats exposed for 30 minutes [Appel et al. 1981]. A composite uncertainty factor of 30 was applied to account for extrapolation from a lethal concentration threshold in animals, interspecies differences and human variability. The IDLH value for acrylonitrile is set at **60 ppm**.

1.2 Purpose

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

1.3 General Substance Information

Chemical: Acrylonitrile

CAS No: 107-13-1

Synonyms: 2-Propenenitrile; Cyanoethylene; Vinyl cyanide; Fumigrain; Ventox*

Chemical category: Nitriles[†]

Structural formula:

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

Table 1: Physiochemical Properties of Acrylonitrile

Property	Value
Molecular weight	53.06 [‡]
Chemical formula	C ₃ H ₃ N
Description	Colorless to pale-yellow liquid
Odor	Sharp onion-garlic odor
Odor Threshold	1.6 ppm [§]
UEL	28% [*]
LEL	2.8% [†]
Vapor pressure	109 mmHg at 25°C (77°F) [‡]
Flash point	-5°C (23°F) [†] - closed cup
Ignition temperature	480°C (896°F) [†]
Solubility	Soluble in water [†]

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

References: ^{*} NLM [2014]; [†] IFA [2014]; [‡] HSDB [2014]; [§] AIHA [1989]

Table 2: Alternative Exposure Guidelines for Acrylonitrile

Organization	Value
Revised (1994) IDLH value [*]	85 ppm
NIOSH REL [†]	1 ppm, TWA cancer; 10 ppm, 15-minute ceiling, skin
OSHA PEL[2014] [^]	2 ppm, TWA; 10 ppm, 15-minute ceiling, skin
ACGIH TLV [2014] [‡]	2 ppm, TWA
AIHA ERPG [2010] ⁺	ERPG-1: 10 ppm; ERPG-2: 35 ppm; ERPG-3: 75 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; TWA – time-weighted average; WEEL – workplace environmental exposure level

References: ^{*}NIOSH [1994]; [^]OSHA [2014]; [†]NIOSH [2014]; [‡]ACGIH [2014]; AIHA [2010a]+; [§]AIHA [2010b]

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1 **Table 3: AEGL Values for Acrylonitrile***
2

Classification	10-min	30-min	1-hour	4-hour	8-hour	End Point [reference]
AEGL-1	1.5 ppm (3.3 mg/m ³)	1.5 ppm (3.3 mg/m ³)	NR	NR	NR	No-effect level for notable discomfort (ocular irritation) in human subjects, 4.6 ppm for 8 hour [Sakurai et al. 1978; Jakubowski et al. 1987].
AEGL-2	8.6 ppm (19 mg/m ³)	3.2 ppm (6.9 mg/m ³)	1.7 ppm (3.7 mg/m ³)	0.48 ppm (1.0 mg/m ³)	0.26 ppm (0.56 mg/m ³)	No-effect level for fetal toxicity (fetal body weight) in rats, 12 ppm for 6 hour [Saillenfait et al. 1993].
AEGL-3	130 ppm (280 mg/m ³)	50 ppm (110 mg/m ³)	28 ppm (61 mg/m ³)	9.7 ppm (21 mg/m ³)	5.2 ppm (11 mg/m ³)	No-effect level for lethality (30-minute, 1-hour, and 8-hour BMCL05) in rats [Dudley and Neal 1942; Appel et al. 1981].

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

4 **References:** * NAS [2014]

2.0 Animal Toxicity Data

Following acute inhalation exposure to acrylonitrile, the most reported effect is ocular and respiratory irritation, with convulsions and tremors occurring at higher concentrations. The mechanism by which irritation is caused is unknown. Central nervous system (CNS) effects are likely a result of the metabolism of acrylonitrile to the cyanide metabolite, cyanoethylene oxide (CEO). While early seizures are likely due to cyanide formation metabolism of acrylonitrile, the later severe clonic convulsions prior to death are speculated to be due to acrylonitrile itself [Ghanayem et al. 1991; Nerland et al. 1989; Benz and Nerland 2005]. Following the formation of cyanide, it is detoxified to thiocyanate via a rhodanese-mediated pathway. Rhodanese is a mitochondrial enzyme and identified as mediating one of the primary pathways for the detoxification of cyanide [Cipollone et al. 2008].

There are notable species differences in the metabolism of acrylonitrile. Dogs are more susceptible to acrylonitrile than other species following inhalation exposures [Dudley and Neal 1942]. For example, inhalation exposures to 65 or 100 ppm acrylonitrile for 4 hours caused effects including coma and death in dogs, while exposures to acrylonitrile at airborne concentrations between 65 to 100 ppm exposures for 4 hours caused minimal irritation and respiratory change in monkeys, cats or rabbits. Higher airborne concentrations in species more tolerant did lead to coma, convulsions and death. This difference in toxic susceptibility is thought to be due to dogs having lower levels of a rhodanese [Drawbaugh and Marrs 1987].

In a lethality study, the LC₅₀ value of rats exposed to acrylonitrile for 4 hours was calculated to be 333 ppm; deaths occurred within 2-4 hours [Haskell Laboratories 1942]. Reported effects included irregular respiration, hyperemia, lacrimation, tremors, convulsions and death. Dudley and Neal [1942] investigated the effects of single acute exposure to acrylonitrile in rats, dogs, cats, monkeys, rabbits and guinea pigs. The reported effects varied between species and exposure scenarios (i.e., exposure duration and concentration). For example, female monkeys treated at 65 ppm for 4 hours experienced slight increased respiratory rates. In comparison, dogs exposed at 65 ppm for 4 hours exhibited severe salivation, weakness, comas and 50% mortality. At 315 ppm acrylonitrile for 4 hours, rats experienced marked effects and 25% mortality during exposure. Rats treated with 665 ppm acrylonitrile for 30 minutes had moderate transitory effects of ocular and nasal irritation with no mortality reported [Dudley and Neal 1942]. In a study of rats exposed to 1080 ppm for 1 hour, there were no deaths, but clinical signs of toxicity included rapid shallow breathing, decreased activity, salivation, lacrimation [Vernon et al. 1990]. Three of ten animals became comatose, but all of the rats recovered within 5 minutes of

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1 exposure termination. Species differences in metabolism can be observed between rodents and humans. Rats and
2 mice are reported to form CEO at greater rates than humans [Roberts et al. 1991]. Humans also detoxify CEO
3 more efficiently than do rodents [Kedderis et al. 1995]. However, evaluation of metabolism and physiologically
4 based pharmacokinetic modeling results suggest that rats are better than mice as an animal model of human
5 acrylonitrile inhalation exposure [Appel et al. 1981; NAS 2014].

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

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1 **Table 4: Lethal Concentration Data for Acrylonitrile**
2

Reference	Species	LC ₅₀ (ppm)	BMCL ₀₅ (ppm)	Time (min)	Adjusted 30-min Concentration* (ppm)	Composite Uncertainty Factor	Derived Value [†] (ppm)
Haskell Laboratory [1942, 1968]	Rat	333	--	240	2,205	30‡	74
Dudley and Neal [1942]	Rat	--	1,024	60	1,924	30‡	64
WIL Research Laboratories [2005]	Rat	946	--	240	6,264	30‡	209
Appel et al. [1981]⁺	Rat	--	1,784	30	1,784	30‡	60

3
4 **Abbreviation:** LC – lethal concentration; LC₅₀ – median lethal concentration; BMCL₀₅ – benchmark concentration lower-bound confidence limit that corresponds with
5 the estimated 95% lower confidence bound on the concentration associated with a 5% increased lethality response above controls; min – minute; ppm – parts per million
6 *For exposures other than 30 minutes the ten Berge et al. [1986] relationship is used for duration adjustment ($C^n \times t = k$); ten Berge et al. [1986] provided an empirically
7 estimated $n = 1.1$ for all time-scaling.

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

9 ‡Composite uncertainty factor to account for the use of lethal concentration threshold in animals, interspecies differences and human variability.

10 [†]Identified study is the primary basis of the IDLH value for acrylonitrile.
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1 **Table 5: Non-lethal Concentration Data for Acrylonitrile**

2

Reference	Species	NOAEL (ppm)	LOAEL (ppm)	Time (min)	Adjusted 30-min Concentration*	Composite Uncertainty Factor	Derived Value [†] (ppm)
Dudley and Neal [1942]	Monkey	65	--	240	430	3 [‡]	143
Dudley and Neal [1942]	Dog		65	240	430	10 [±]	43
Dudley and Neal [1942]	Rat	665	--	30	665	3 [‡]	222
Vernon et al. [1990]	Rat	--	1,080	60	2,028	10 [±]	203
Wilson et al. [1948]	Humans	--	100	45	145	1	145
Jakubowski et al. [1987]	Humans	4.5	--	480	56	1	56

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

4 *For exposures other than 30 minutes the ten Berge et al. [1986] relationship is used for duration adjustment ($C_n \times t = k$); ten Berge et al. [1986] provided an empirically
5 estimated $n = 1.1$ for all time-scaling.

6 [†]The derived value is the result of the adjusted 30-min value divided by the composite uncertainty factor.

7 [‡]Composite uncertainty factor assigned to account for interspecies differences and human variability.

8 [±]Composite uncertainty factor assigned to account for adjusting from a LOAEL to NOAEL, interspecies differences and human variability.

3.0 Human Data

Case studies of fatal acute exposures to airborne acrylonitrile are reported. However, because concentrations and exposure durations were not indicated, no adequate quantitative data for human lethality are available. Quantitative data are available, however, for non-lethal inhalation exposure to acrylonitrile. Workers exposed to 16-100 ppm acrylonitrile for 20-45 minutes were reported to experience dull headaches, nasal and ocular irritation, discomfort in the chest, nervousness and irritability [Wilson et al. 1948]. These mild effects were reversible upon removal from exposure and are not considered escape-impairing. In another study, exposure to 4.6 ppm acrylonitrile for 8 hours resulted in no reported signs or symptoms of toxicity [Jakubowski et al. 1987]. NAS [2014] cited a personal communication reporting that occupational exposure to 12-15 ppm resulted in ocular irritation and headache. These effects were not considered escape-impairing.

NAS [2014] noted various inhalation cancer assessments for acrylonitrile, and IARC downgraded acrylonitrile from category 2A - *Probably carcinogenic to humans* to 2B - *Possibly Carcinogenic to Humans*, noting that data relative to human carcinogenicity are inadequate and no causal association exists. NAS [2014] stated that it is very unlikely that a single acute once-in-a-lifetime exposure to acrylonitrile could cause cancer in humans.

4.0 Summary

The IDLH value for acrylonitrile is based on a lethality study by Appel et al. [1981] reported a BMCL₀₅ of 1,784 ppm in rats exposed for 30 minutes. Application of a composite uncertainty factor of 30 to account for extrapolation from a lethal concentration threshold in animals, animal to human differences and human variability, yielded an IDLH value for acrylonitrile of **60 ppm**. This value is believed to be protective of escape-impairing, irreversible adverse health effects and deaths associated with exposures to acrylonitrile for 30 minutes or less.

It should be noted that the IDLH value for acrylonitrile differs by more than an order of magnitude from the AEGL-2 30-minute value, which is intended to represent an airborne concentration of a substance above which it is predicted that the general population, including susceptible individuals, could experience irreversible or other serious, long-lasting adverse health effects or an impaired ability to escape [NAS 2001]. The AEGL-2 value for acrylonitrile is based upon transient effects in rats exposed to 305 ppm for 2 hours [Dudley and Heal 1942; NAS 2014]. NIOSH based the IDLH value for acrylonitrile on the 30-minute BMCL₀₅ value of 1748 ppm from Appel

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1 et al. [1981]. The use of this value as the basis of the IDLH value prevented the need for time duration
2 adjustment and allowed for the use of a lower uncertainty factor. Additionally, the IDLH value aligns closely
3 with the AEGL-3 30 minute value for acrylonitrile, which is intended to represent an airborne concentration of a
4 substance above which it is predicted that the general population, including susceptible individuals, could
5 experience life-threatening health effects or death [NAS 2001].
6

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