

IDLH

IMMEDIATELY DANGEROUS to LIFE or HEALTH VALUE PROFILE

Acetonitrile
CAS[®] No. 75-05-8



**Centers for Disease Control
and Prevention**
National Institute for Occupational
Safety and Health

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Immediately Dangerous to Life or Health (IDLH) Value Profile

Acetonitrile

[CAS[®] No. 75-05-8]



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Suggested Citation

NIOSH [2017]. Immediately dangerous to life or health (IDLH) value profile: acetonitrile. By Dotson GS, Maier A, Parker A, Haber L. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication 2017-203.

DHHS (NIOSH) Publication No. 2017-203

October 2017

Table 2 was revised for accuracy. This revision did not affect the current IDLH value.

Foreword

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

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

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

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

The purpose of this technical report is to present the IDLH value for acetonitrile (CAS[®] No. 75-05-8). The scientific basis, toxicologic data, and risk assessment approach used to derive the IDLH value are summarized to ensure transparency and scientific credibility.

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Abbreviations

ACGIH®	American Conference of Governmental Industrial Hygienists
AEGLs	Acute Exposure Guideline Levels
AIHA®	American Industrial Hygiene Association
BMCL	benchmark concentration lower confidence limit
°C	degrees Celsius
CAS®	Chemical Abstracts Service, a division of the American Chemical Society
CI	confidence interval
CIB	Current Intelligence Bulletin
ERPGs™	Emergency Response Planning Guidelines
°F	degrees Fahrenheit
IDLH	immediately dangerous to life or health
IFA	Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung (Institute for Occupational Safety and Health of the German Social Accident Insurance)
LC	lethal concentration
LC₀₁	lethal concentration estimated to cause death in 1% of animals
LC₅₀	median lethal concentration
LC_{L0}	lowest concentration that caused death in humans or animals
LEL	lower explosive limit
LOAEL	lowest observed adverse effect level
mg/m³	milligram(s) per cubic meter
min	minutes
mmHg	millimeter(s) of mercury
NAS	National Academy of Sciences
NIOSH	National Institute for Occupational Safety and Health
NLM	National Library of Medicine
NOAEL	no observed adverse effect level
NR	not recommended
OSHA	Occupational Safety and Health Administration
PEL	permissible exposure limit
ppm	parts per million
REL	recommended exposure limit
TLV®	Threshold Limit Value
TWA	time-weighted average
UEL	upper explosive limit
WEELs®	Workplace Environmental Exposure Levels

Glossary

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

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

Acute reference concentration (Acute RfC): An estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure for an acute duration (24 hours or less) of the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. It can be derived from a NOAEL, LOAEL, or benchmark concentration, with uncertainty factors (UFs) generally applied to reflect limitations of the data used. Generally used in U.S. EPA noncancer health assessments [U.S. EPA 2016].

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

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

Benchmark dose/concentration (BMD/BMC): A dose or concentration that produces a pre-determined change in response rate of an effect (called the benchmark response, or BMR) compared to background [U.S. EPA 2016] (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 [U.S. EPA 2016].

Bolus exposure: A single, relatively large dose.

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

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

Critical study: The study that contributes most significantly to the qualitative and quantitative assessment of risk [U.S. EPA 2016].

Dose: The amount of a substance available for interactions with metabolic processes or biologically significant receptors after crossing the outer boundary of an organism [U.S. EPA 2016].

EC₅₀: A combination of the effective concentration of a substance in the air and the exposure duration that is predicted to cause an effect in 50% (one half) of the experimental test subjects.

Emergency Response Planning Guidelines (ERPGs™): Maximum airborne concentrations below which nearly all individuals can be exposed without experiencing health effects for 1-hour exposure. ERPGs are presented in a tiered fashion, with health effects ranging from mild or transient to serious, irreversible, or life threatening (depending on the tier). ERPGs are developed by the American Industrial Hygiene Association [AIHA 2006].

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

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

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

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

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

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

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

LC₅₀: The statistically determined concentration of a substance in the air that is estimated to cause death in 50% (one half) of the test animals; median lethal concentration.

LC_{L0}: The lowest lethal concentration of a substance in the air reported to cause death, usually for a small percentage of the test animals.

LD₅₀: The statistically determined lethal dose of a substance that is estimated to cause death in 50% (one half) of the test animals; median lethal concentration.

LD_{L0}: The lowest dose of a substance that causes death, usually for a small percentage of the test animals.

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

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

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

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

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

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

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

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

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

RD₅₀: The statistically determined concentration of a substance in the air that is estimated to cause a 50% (one half) decrease in the respiratory rate.

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

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

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

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

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

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

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

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

Acknowledgments

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. 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]).

The following NIOSH staff are acknowledged for providing technical and editorial review of the report:

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NIOSH acknowledges the following subject matter experts for their critical technical reviews:

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1 Introduction

1.1 Overview of the IDLH Value for Acetonitrile

IDLH value: 137 ppm (230 mg/m³)

Basis for IDLH value: The mouse LC₅₀ value of 2,693 ppm for a 60 minute exposure to acetonitrile [Willhite 1981] was selected as the basis for the IDLH value. Duration adjustment resulted in the calculation of a 30-minute equivalent LC₅₀ value of 4,120 ppm. A composite uncertainty factor of 30 was applied to account for extrapolation from a concentration that is lethal to animals, animal to human differences, and human variability, resulting in an IDLH value for acetonitrile of 137 ppm.

1.2 Purpose

This *IDLH Value Profile* presents (1) a brief summary of technical data associated with acute inhalation exposures to acetonitrile and (2) the rationale behind the immediately dangerous to life or health (IDLH) value for acetonitrile. 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 acetonitrile, the in-depth literature search was conducted through July 2017.

1.3 General Substance Information

Chemical: Acetonitrile

CAS No: 75-05-8

Synonyms: Cyanomethane; ethanenitrile; nitrile of acetic acid; methyl cyanide; ethyl nitrile; methanecarbonitrile*

Chemical category: Nitriles[†]

Structural formula:



References: *NAS [2014], †IFA [2017]

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

Table 1: Physiochemical properties of acetonitrile

Property	Value
Molecular weight	41.05*
Chemical formula	CH ₃ CN*
Description	Colorless liquid*
Odor	Pungent
Odor threshold	Not available
UEL	Not available
LEL	Not available
Vapor pressure	88.8 mmHg at 25°C (77°F)*
Flash point	5.6°C (42.1°F) open cup*
Ignition temperature	Not available
Solubility	Infinitely soluble in water; readily miscible with ethanol, ether, acetone, chloroform, carbon tetrachloride, and ethylene chloride; immiscible with saturated hydrocarbons (petroleum fractions)*

Reference: *NAS [2014]

Table 2: Alternative exposure guidelines for acetonitrile

Organization	Value
NIOSH (1994) IDLH value*	500 ppm
NIOSH REL†	20 ppm (33 mg/m ³), 8-hr TWA
OSHA PEL‡	40 ppm (66 mg/m ³), 8-hr TWA
ACGIH TLV®§	20 ppm (33 mg/m ³), 8-hr TWA
AIHA ERPGs™¶	None
AIHA WEELS®¶	None

References: *NIOSH [1994]; †NIOSH [2017]; ‡OSHA [2017]; §ACGIH [2016]; ¶AIHA [2014]

Table 3: A EGL values for acetonitrile

Classification	10-min	30-min	1-hour	4-hour	8-hour	Endpoint [reference]
A EGL-1	13 ppm	13 ppm	13 ppm	13 ppm	NR*	Slight chest tightness and cooling sensation in lung [Pozzani et al. 1959]
	22 mg/m ³	22 mg/m ³	22 mg/m ³	22 mg/m ³		
A EGL-2	80 ppm	80 ppm	50 ppm	21 ppm	14 ppm	One-third of A EGL-3 values
	130 mg/m ³	130 mg/m ³	84 mg/m ³	35 mg/m ³	24 mg/m ³	
A EGL-3	240 ppm	240 ppm	150 ppm	64 ppm	42 ppm	No-effect level for maternal and fetal lethality in rats [Saillenfait et al. 1993]
	74 mg/m ³	400 mg/m ³	250 mg/m ³	110 mg/m ³	71 mg/m ³	

Reference: NAS [2014]

*Not recommended. Absence of an A EGL-1 value does not imply that exposure below the A EGL-2 value is without adverse effects.

2 Animal Toxicity Data

LC₅₀ data and information on the nonlethal effects of acetonitrile are available in multiple species, with pulmonary effects increasing with progression to lethality as the exposure concentration increased [Monsanto 1986; Ponzani et al. 1959; Willhite 1981]. A study performed in rats reported a LOAEL of 10,100 ppm and a LC₅₀ value of 19,950 ppm for a 4-hour exposure, suggesting a potentially steep dose-response curve following inhalation of acetonitrile [Monsanto 1986]. Ponzani et al. [1959] investigated the effects of inhalation exposures to acetonitrile in multiple species, including rats, dogs, and guinea pigs. Male and female rats were exposed to concentrations ranging from 1,000 to 32,000 ppm for either 1 or 2 hours. The 4-hour LC₅₀ value for both sexes was calculated at 16,000 ppm [NAS 2014]. The 8-hour LC₅₀ values for male and female rats were 7,551 and 12,435 ppm, respectively [NAS 2014]. In another experiment, dogs were treated for 4 hours at concentrations ranging from 2,000–32,000 ppm. No LC₅₀ value was calculated, but Ponzani et al. [1959] reported that all animals treated at 16,000 and 32,000 ppm died. Ponzani et al. [1959] exposed guinea pigs to acetonitrile at concentrations ranging from 4,000–16,000 ppm for 4 hours. The 4-hour LC₅₀ value was calculated at 5,655 ppm [NAS 2014]. Pathological investigations revealed that exposed animals experienced prostration, convulsive seizures, and death with pathological examination revealing pulmonary effects including congestion and hemorrhaging.

Willhite [1981] investigated the relative toxicity of the following aliphatic nitrile compounds: acetonitrile, propionitrile, and n-butyronitrile. Mice were exposed via the inhalation route to 1 of 5 or 6 concentrations of the test compound for 60 minutes. All deaths occurred within 3 days of the cessation of exposure. Animals that survived past 3 days were observed for 14 days with gross pathology conducted following termination. Willhite [1981] stated that all

animals experienced similar signs regardless of the aliphatic nitrile compound to which they were exposed. These signs included dyspnea, tachypnea, gasping, tremors, and convulsions. For acetonitrile, the concentration ranged from 500–5000 ppm. Willhite [1981] reported a 60-minute LC₅₀ value of 2,693 ppm (95% CI 1,955–4,272) for acetonitrile.

Saillenfait et al. [1993] investigated the effects of acetonitrile in pregnant Sprague-Dawley rats. Treatment groups (n=20) were exposed for 6 hours a day during gestation days 6–20 to the following nominal concentrations: 0, 900, 1,200, 1,500, or 1,800 ppm. Eight of the twenty dams (40%) treated at 1,800 ppm died. Maternal body weight gain during the gestation days 6–21 was significantly reduced in comparison to controls. In the 1,500 and 1,800 ppm treatment groups, maternal absolute weight gain was approximately 60% of controls. Incidence of pregnancy was not significantly affected. The authors reported an increase in the significant mean percentage of non-surviving implants per litter and mean percentage resorption site per litter in the 1,800 ppm treatment group. No significant effects on the mean number for implantation sites, fetal sex ratio, or fetal pup weights occurred in the 900 to 1,500 ppm treatment groups. No observed significant changes in the incidents of skeletal or soft tissue anomalies were observed in any treatment group. Saillenfait et al. [1993] concluded that exposures to 1,800 ppm cause embryo lethality.

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

Table 4: Lethal concentration data for acetonitrile

Reference	Species	LC ₅₀ (ppm)	LC _{Lo} (ppm)	Time (min)	Adjusted 30-min concentration* (ppm)	Composite uncertainty factor	30-min equivalent derived value (ppm) [†]	Final value [‡] (ppm)
Pozzani et al. [1959]	Guinea Pig	5,655	—	240	20,743	30 [§]	691.4	691
Pozzani et al. [1959]	Monkey	2,510	—	420	13,062	30 [§]	435.4	435
Pozzani et al. [1959]	Rats	7,551	—	480	42,715	30 [§]	1,424	1,424
Pozzani et al. [1959]	Rabbit	2,828	—	240	10,373	30 [§]	345.8	346
Willhite [1981]	Mouse	2,693	—	60	4,120	30 [§]	137.3	137

*For exposures other than 30 minutes the ten Berge et al. [1986] relationship is used for duration adjustment (C_n x t = k); NAS [2014] provided an empirically estimated n of 1.6 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 adjustment of LC₅₀ values to LC₀₁ values, use of lethal concentration threshold in animals, interspecies differences and human variability.

Table 5: Non-lethal concentration data for acetonitrile

Reference	Species (reference)	Critical nonlethal effect	NOAEL (ppm)	Time (min)	Adjusted 30-min concentration* (ppm)	Composite uncertainty factor	30-min equivalent derived value (ppm) [†]	Final value [‡] (ppm)
Saillenfait et al. [1993]	Rats	No-effect level for maternal and fetal lethality	1,500	360	7,089	30 [§]	236.3	236

*For exposures other than 30 minutes the ten Berge et al. [1986] relationship is used for duration adjustment (C_n x t = k); NAS [2014] provided an empirically estimated n of 1.6 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 to an escape-impairing effect.

3 Human Data

Three male volunteers inhaled 40-160 ppm acetonitrile for 4 hours in an exposure chamber [Pozzani et al. 1959]. One study participant reported slight chest tightness and cooling sensation in the lung following the 40 ppm exposure, other participants did

not report symptoms at this concentration. At the 160 ppm exposure, one of the previously unaffected subjects reported slight transitory flushing of face after 2 hours and slight bronchial tightness 5 hours later that resolved overnight.

4 Summary

Limited human data on acetonitrile were identified. Pozzani et al. [1959] reported that effects of acetonitrile in human volunteers exposed for 4 hours to airborne concentrations ranging from 40–160 ppm. Although this data provided some insight into the effects of acetonitrile on humans, it is insufficient to serve as the basis of an IDLH value.

Animal data from studies that investigated the effects of acute exposures to acetonitrile in rats, rabbits, guinea pigs, dogs, and monkeys [Monsanto 1986; Pozzani et al. 1959; Willhite 1981] were evaluated. Among these species, mice appear to be the most sensitive species [Willhite 1981]. The mouse LC_{50} value of 2,693 ppm for a 60 minute exposure to acetonitrile was selected as the basis for the IDLH value. Duration adjustment resulted in the calculation of a 30-minute equivalent LC_{50} value of 4,120 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 potential IDLH value of 137 ppm.

Saillenfait et al. [1993] provided an alternative point of departure for the IDLH value. This study investigated the reproductive effects of repeated exposures to acetonitrile on female rats. Inhalation exposures to 1,800 ppm for 6 hours a day during gestation days 6–20 resulted in the death of 40% of exposed rats, decreased

maternal body weight gain, mean percentage of non-surviving implants per litter, and mean percentage resorption site per litter. These effects were not reported at the next treatment level of 1,500 ppm. A potential IDLH value was calculated using 1,500 ppm as a NOAEL. Duration adjustment of this value from 6 hours resulted in a 30-minute equivalent NOAEL value of 7,089 ppm. An uncertainty factor of 30 was applied to account for interspecies differences, human variability, and extrapolation to an escape-impairing effect resulting in a potential IDLH value of 236 ppm.

Although basing the IDLH value for acetonitrile on Saillenfait et al. [1993] study is a viable option, NIOSH has selected the Willhite [1981] study as the basis of the IDLH value for acetonitrile. This study provided a point of departure (i.e., LC_{50} value of 2,693 ppm) based on single exposure to acetonitrile for 60 minute, which aligns more closely with the exposure scenarios associated with an IDLH condition (i.e., acute, short-term exposures for 30 minutes or less). In comparison, Saillenfait et al. [1993] relies on a repeat exposure study design (i.e., total of 14 exposures) and uses a 6-hour exposure duration. Both of these factors introduce additional uncertainty into the analysis. The IDLH value of 138 ppm for acetonitrile based on the Willhite [1981] study resulted in the most health protective IDLH value.

5 References

- ACGIH [2016]. Annual TLVs® (Threshold Limit Values) and BEIs® (Biological Exposure Indices) booklet. Cincinnati, OH: ACGIH Signature Publications.
- AIHA [2006]. AIHA Emergency Response Planning (ERP) Committee procedures and responsibilities. Fairfax, VA: American Industrial Hygiene Association, <https://www.aiha.org/get-involved/AIHAGuidelineFoundation/EmergencyResponsePlanningGuidelines/Documents/ERP-SOPs2006.pdf>.
- AIHA [2014]. Emergency response planning guidelines (ERPG) and workplace environmental exposure levels (WEEL) handbook. Fairfax, VA: American Industrial Hygiene Association Press, <https://www.aiha.org/get-involved/AIHAGuidelineFoundation/EmergencyResponsePlanningGuidelines/Documents/2014%20ERPG%20Values.pdf>.
- HSDB [2017]. Hazardous Substances Data Bank. Bethesda, MD: National Library of Medicine, <http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB>.
- IFA (Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung) [2017]. GESTIS: database on hazardous substances, <http://www.dguv.de/ifa/gestis/gestis-stoffdatenbank/index-2.jsp>.
- Monsanto [1986]. A study of the acute inhalation toxicity (4-hour LC₅₀) of acetonitrile in rats. EPA OTS0510333.
- NAS [2001]. Standing operating procedures for developing Acute Exposure Guideline Levels for hazardous chemicals. National Academy of Sciences, National Research Council (NRC), Committee on Toxicology, Subcommittee on Acute Exposure Guideline Levels. Washington, DC: National Academy Press, ISBN: 0-309-07553-X, http://www.epa.gov/sites/production/files/2015-09/documents/sop_final_standing_operating_procedures_2001.pdf.
- NAS [2014]. Acute Exposure Guideline Levels (AEGs) for selected airborne chemicals. Vol. 16. Acetonitrile (CAS Reg. No. 107-14-2). National Academy of Sciences, National Research Council, Committee on Toxicology, Subcommittee on Acute Exposure Guideline Levels. Washington, DC: National Academy Press, https://www.epa.gov/sites/production/files/2014-10/documents/aliphatic_nitriles_final_volume_16_2014_3.pdf.
- NIOSH [1994]. Documentation for immediately dangerous to life or health concentrations (IDLHs): acrylonitrile. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, <http://www.cdc.gov/niosh/idlh/intridl4.html>.
- NIOSH [2004]. NIOSH respirator selection logic. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2005-100, <http://www.cdc.gov/niosh/docs/2005-100/pdfs/2005-100.pdf>.
- NIOSH [2013]. NIOSH Current Intelligence Bulletin 66: derivation of immediately dangerous to life or health (IDLH) values. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2014-100, <http://www.cdc.gov/niosh/docs/2014-100/pdfs/2014-100.pdf>.
- NIOSH [2017]. NIOSH pocket guide to chemical hazards. Cincinnati, OH: U.S.

- Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2005-149, <http://www.cdc.gov/niosh/npg/>.
- NLM [2017]. ChemIDplus lite. Washington, DC: National Library of Medicine, <http://chem.sis.nlm.nih.gov/chemidplus/>.
- OSHA [2017]. Chemical sampling information, https://www.osha.gov/dts/chemicalsampling/toc/toc_chemsamp.html.
- Pozzani UC, Carpenter CP, Palm PC, Weil CS, Nair JH [1959]. An investigation of the mammalian toxicity of acetonitrile. *J Occup Med* 1:634–642.
- Saillefait AM, Bonnet P, Guenier JP, de Ceaurriz J [1993]. Relative developmental toxicities of inhaled aliphatic mononitriles in rats. *Fundam Appl Toxicol* 20(3):365–375.
- ten Berge WF, Zwart A, Appelman LM [1986]. Concentration-time mortality response relationship of irritant and systematically acting vapors and gases. *J Haz Mat* 13:301–309.
- U.S. EPA [2016]. Integrated Risk Information System (IRIS). Washington, DC: U.S. Environmental Protection Agency, <http://www.epa.gov/iris/>.
- Willhite CC [1981]. Inhalation toxicity of acute exposure to aliphatic nitriles. *Clin Toxicol* 18:991–1003.

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