IDLH

IMMEDIATELY DANGEROUS to LIFE or HEALTH

VALUE PROFILE

Hexafluoroacetone
CAS® No. 684-16-2

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Center for Disease Control and Prevention
National Institute of Occupational Safety and Health

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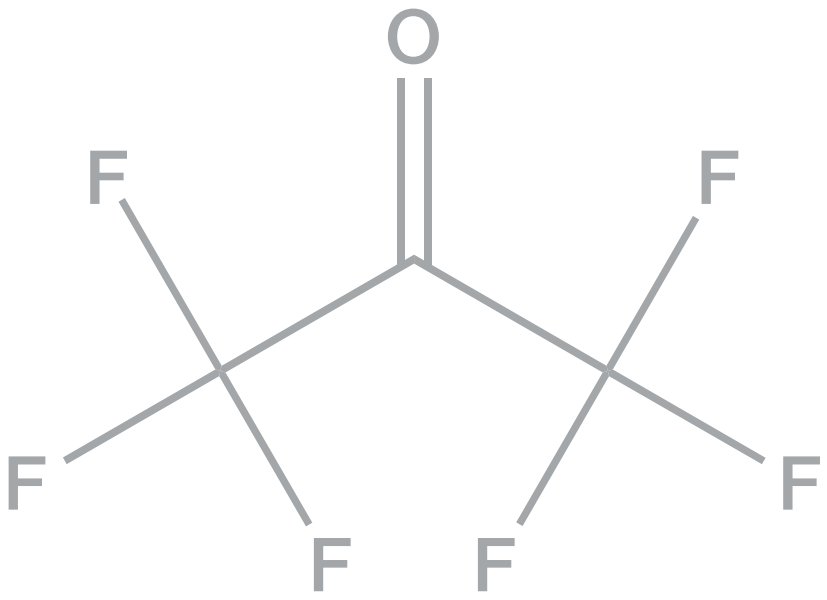
Immediately Dangerous to Life or Health (IDLH) Value Profile

Hexafluoroactone

[CAS® No. 684-16-2]



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Foreword

Chemicals are a ubiquitous component of the modern workplace. Occupational exposures to chemicals have the potential to adversely affect the health and lives of workers. Acute or short-term exposures to high concentrations of some airborne chemicals 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 nonroutine 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 nonroutine 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 hexafluoroacetone (CAS® #684-16-2). 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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Contents

Abbreviations

ACGIH®	American Conference of Governmental Industrial Hygienists
AEGLs	Acute Exposure Guideline Levels
AIHA®	American Industrial Hygiene Association
BMC	benchmark concentration
BMD	benchmark dose
BMCL	benchmark concentration lower confidence limit
C	ceiling value
°C	degrees Celsius
CAS®	Chemical Abstracts Service, a division of the American Chemical Society
ERPGs™	Emergency Response Planning Guidelines
°F	degrees Fahrenheit
GD	gestation day
IDLH	immediately dangerous to life or health
LC_{50}	median lethal concentration
LC_{LO}	lowest concentration that caused death in humans or animals
LEL	lower explosive limit
LOAEL	lowest observed adverse effect level
mg/m^3	milligram(s) per cubic meter
min	minutes
mmHg	millimeter(s) of mercury
NAC	National Advisory Committee
NAS	National Academy of Sciences
NIOSH	National Institute for Occupational Safety and Health
NOAEL	no observed adverse effect level
NOEL	no observed effect level
NR	not recommended
OSHA	Occupational Safety and Health Administration
PEL	permissible exposure limit
ppm	parts per million
RD_{50}	concentration of a chemical in the air that is estimated to cause a 50% decrease in the respiratory rate
REL	recommended exposure limit
SCP	Standards Completion Program (joint effort of NIOSH and OSHA)
STEL	short-term exposure limit
TLV®	Threshold Limit Value
TWA	time-weighted average
UEL	upper explosive limit
WEELs®	Workplace Environmental Exposure Levels
µg/kg	microgram(s) per kilogram of body weight

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, 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 predetermined change in response rate of an effect (called the benchmark response, or BMR) compared to background [U.S. EPA 2016] (additional information available at 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].

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

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

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

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

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

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

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

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

LC_{01}: The statistically determined concentration of a substance in the air that is estimated to cause death in 1% of the test animals.

LC_{50}: 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_{LO}: The lowest lethal concentration of a substance in the air reported to cause death, usually for a small percentage of the test animals.

LD_{50}: 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_{LO}: 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, short-term exposure (STELs), or time-weighted average (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.

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

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

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

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

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

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

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

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

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

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1 Introduction

1.1 Overview of the IDLH Value for Hexafluoroacetone

IDLH value: 9 ppm (61 mg/m^3)

Basis for IDLH Value: A rat LC_{50} value of 900 ppm for a 30-minute exposure period is the basis of the IDLH value for hexafluoroacetone [Borzelleca and Lester 1965], because it was the lowest value among studies with the most appropriate exposure duration. A composite uncertainty factor of 100 was applied to account for extrapolation from a lethal concentration in animals, animal to human differences, human variability, and uncertainties in the database, including uncertainties about the potential for developmental toxicity from acute exposure, as well as the lack of data on female reproductive toxicity and functional measures of reproductive toxicity, resulting in a recommended IDLH value of 9 ppm.

1.2 Purpose

This *IDLH Value Profile* presents (1) a brief summary of technical data associated with acute inhalation exposures to hexafluoroacetone and (2) the rationale behind the immediately dangerous to life or health (IDLH) value for hexafluoroacetone. 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 LC_{50} values). For hexafluoroacetone, the in-depth literature search was conducted through May 2016.

1.3 General Substance Information

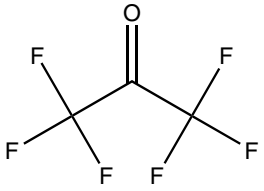
Chemical: Hexafluoroacetone

CAS No: 684-16-2

Synonyms: HFA; 1,1,1,3,3,3-Hexafluoro-2-propanone; Hexafluoro-2-propanone; Perfluoroacetone*

Chemical category: Substituted ketones oxo compounds; Organic fluorine compounds; Organic gases†

Structural formula:



References: *NLM [2016]; †IFA [2016]

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

Table 1: Physiochemical properties of hexafluoroacetone

Property	Value
Molecular weight	166.02
Chemical formula	C_3F_6O
Description	Colorless gas
Odor	Disagreeable, musty
Odor threshold	Not available
UEL	Not applicable*
LEL	Not applicable*
Vapor pressure	5.0 torr at 25°C (77°F)
Flash point	Noncombustible†
Ignition temperature	Noncombustible†
Solubility	Soluble in water; hydrolyses†

References: *OSHA [2016], †IFA [2016], ‡ACGIH [2015]

Table 2: Alternative exposure guidelines for hexafluoroacetone

Organization	Value
Original (SCP) IDLH value*	None
NIOSH REL‡	TWA 0.1 ppm (0.7 mg/m^3) [skin]
OSHA PEL†	None
ACGIH TLV®§	0.1 ppm TWA
AIHA ERPGs™¶	ERPG-1: not derived; ERPG-2: 1 ppm; ERPG-3: 50 ppm
AIHA WEELs®¶	None

References: *NIOSH [1994]; †OSHA [2016]; ‡NIOSH [2016]; §ACGIH [2015]; ¶AIHA [2014]

Table 3: AEGL values for hexafluoroacetone

Classification	10-min	30-min	1-hour	4-hour	8-hour	Endpoint [reference]
AEGL-1	NR	NR	NR	NR	NR	Insufficient data
AEGL-2	0.40 ppm 2.7 mg/m^3	0.40 ppm 2.7 mg/m^3	0.20 ppm 1.4 mg/m^3	0.050 ppm 0.34 mg/m^3	0.025 ppm 0.17 mg/m^3	NOAEL for developmental effects in rat [E. I. du Pont de Nemours and Co. 1989]
AEGL-3	160.0 ppm 1,100.0 mg/m^3	160.0 ppm 1,100.0 mg/m^3	80.0 ppm 540.0 mg/m^3	20.0 ppm 140.0 mg/m^3	10.0 ppm 68.0 mg/m^3	Lethality threshold estimated from rat LC_{50} data [E. I. du Pont de Nemours and Co. 1962a,b]

Abbreviation: NR – not recommended, because of insufficient data.

References: NAS [2012].

2 Animal Toxicity Data

Several acute inhalation studies were identified for hexafluoroacetone. Borzelleca and Lester [1965] exposed groups of 10 albino rats (5 males, 5 females) to varying concentrations of hexafluoroacetone for 0.5, 3, or 6 hours. Despite the failure to report the specific concentrations used during each experiment, Borzelleca and Lester [1965] provided a 30-minute LC_{50} value of 900 ppm and a 3-hour LC_{50} value of 275 ppm. Minor or no lung effects were reported for all the concentrations, and the majority of the fatalities occurred 2 to 6 days after exposure. In the same study, Borzelleca and Lester [1965] exposed anesthetized dogs to hexafluroacetone under various exposure conditions. Lethality did not occur in dogs (n = 3) exposed for 30 minutes to 5,000 ppm; in comparison, one dog died following exposure for 45 minutes to 5,000 ppm. Exposure to 10,000 ppm for 30 or 45 minutes resulted in the death of 2 of 3 dogs in each treatment group. The author also reported that postmortem examination revealed pulmonary hemorrhage and edema in dogs exposed to 5,000 and 10,000 ppm for either 30 or 45 minutes. E.I. du Pont de Nemours & Co. [1965] found that exposure to 3,600 ppm for 30 minutes was not lethal to rats (0 of 4 died), but 3 of 4 rats died after exposure to 4,800 ppm for 30 minutes. Rats in all groups, down to the lowest concentration of 2,400 ppm, exhibited signs of irritation, including lacrimation, salivation, nasal discharge, and intermittent gasping.

Acute exposure to hexafluoroacetone also causes testicular damage. Rats exposed to 100 ppm for 4 hours exhibited slight to moderate testicular damage [E.I. du Pont de Nemours & Co. 1962]. More severe damage, including aspermatogenesis and interstitial damage, were observed at 200 ppm and higher. E.I. du Pont de Nemours & Co. [1965] exposed rats to 200 ppm hexafluoroacetone for 4 hours and killed the rats at 7 to 57 days post-exposure. The observed testicular degeneration and decreased testicular weight were only slowly (or partially) reversible. At 57 days, there was some recovery, but some spermatogenic tubules still contained no germinal cells.

Inhalation exposure to hexafluoroacetone results in systemic effects, with pulmonary damage in rats occurring only at air concentrations exceeding minimal lethality levels. Contact irritation also occurs. Gillies and Lee [1983] suggested that the testicular effects of hexafluoroacetone are due to its alterations of lipid metabolism and the resulting inhibition of sterol synthesis. This hypothesized pathway for male reproductive effects suggests that hexafluoroacetone may also affect female reproductive hormones and thus female reproductive function, but no data investigating this hypothesis were located.

These possibly hormonally mediated effects may be related to the developmental toxicity of hexafluoroacetone. E.I. du Pont de Nemours & Co. [1989] exposed (nose only) pregnant rats to 0.11, 1.0, or 6.9 ppm hexafluroacetone for 6 hours/day on gestation days (GD) 7 to 16. The results indicated that exposure at 6.9 ppm of hexafluoroacetone resulted in significant increases in resorptions, malformations, developmental

variations, and variations due to retarded development; the 1 ppm exposure group exhibited increased incidences of skeletal developmental variations and decreased fetal weights [E.I. du Pont de Nemours & Co. 1989]. The authors considered the fetal effects to be more severe than the concurrent maternal effects. The results of this repeated exposure study raise the question of whether acute hexafluoroacetone exposure during a key developmental stage could potentially cause developmental effects. For a single 6-hour exposure period at the LOAEL for severe effects of 6.9 ppm from this study, the

equivalent 30-minute duration-adjusted concentration is 83 ppm.

Table 4 summarizes the LC data identified in animal studies and provides 30-minute-equivalent derived values for hexafluoroacetone. Table 5 provides nonlethal concentration data reported from animal studies with 30-minute-equivalent derived values. Information in these tables includes species of test animals, toxicological metrics (i.e., LC, 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 hexafluoroacetone

Reference	Species (reference)	LC_{50} (ppm)	LC_{Lo} (ppm)	Time (min)	Adjusted 30-min concentration* (ppm)	Composite uincertainty factor	30-min equivalent derived value (ppm)†	Final value (ppm)‡
Borzelleca and Lester [1965]	Dog	5,000§	—	45	5,724	100¶	57.24	57
E.I. du Pont de Nemours & Co. [1962]	Rat	300††	—	240	2,400	100¶	24.0	24
E.I. du Pont de Nemours & Co. [1965]	Rat	—	3,600‡‡	30	3,600	30**	120	120
Borzelleca and Lester [1965]§§	Rat	900	—	30	900	100¶	9.0	9.0
Borzelleca and Lester [1965]	Rat	275	—	180	1,650	100¶	16.5	17

*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 default values were used (n = 3 for exposures greater than 30 minutes and n = 1 for exposures less than 30 minutes). 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 LC value divided by the composite uncertainty factor.

‡Values rounded to the appropriate significant figure.

§1 of 2 dogs died.

¶Composite uncertainty factor to account for the use of lethal concentration threshold in animals, interspecies differences, human variability, and uncertainties in the database that focus on issues pertaining to developmental toxicity from acute exposure, absence of data on female reproductive toxicity, and functional measures of reproductive toxicity.

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

††2 of 4 rats died.

‡‡No lethality.

§§Identified study is the primary basis of the IDLH value for hexafluoroacetone.

Table 5: Nonlethal concentration data for hexafluoroacetone

Reference	Species	Critical nonlethal effect	NOAEL (ppm)	LOAEL (ppm)	Time (min)	Adjusted 30-min concentration*	Composite uncertainty factor	30-min equivalent derived value (ppm)†	Final Value (ppm) ‡
E.I. du Pont de Nemours & Co. [1962]	rat	Slight to moderate testicular damage	—	200	240	1,600	30§	53.33	53
E.I. du Pont de Nemours & Co. [1962]	rat	Moderate testicular damage	—	100	240	800	30§	26.67	27

*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 default values were used (n = 3 for exposures greater than 30 minutes and n = 1 for exposures less than 30 minutes). 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-min value divided by the composite uncertainty factor. The composite uncertainty factor used varies for each study on the basis of the nature and severity of the endpoint observed.

‡Values rounded to the appropriate significant figure.

§Composite uncertainty factor assigned to account for adjusting from a LOAEL to NOAEL, severe effects, interspecies differences, human variability, and uncertainty about the threshold for escape-impairing effects.

3 Human Data

No data are available to describe the non-lethal effects or lethal concentration in humans associated with the inhalation of hexafluoroacetone. Kutznetsova [1972] reported that exposure to hexafluoroacetone at 4 ppm is irritating to the respiratory tract, but specific descriptions were not provided on the exposure conditions that induce irritation or on the severity of the observed effects.

4 Summary

Among the acute lethality studies, the rat LC_{50} value of 900 ppm for a 30-minute exposure period [Borzelleca and Lester 1965] was chosen as the basis for the IDLH value for hexafluoroacetone since it was the lowest value among studies with the most appropriate exposure duration. A composite uncertainty factor of 100 was applied to account for extrapolation from a lethal concentration in animals, animal to human differences, human variability, and uncertainties in the database, including uncertainties about the potential for developmental toxicity from acute exposure, as well as the lack of data on female reproductive toxicity and functional measures of reproductive toxicity, resulting in an IDLH value for hexafluoroacetone of 9 ppm.

It should be noted that the IDLH value for hexafluoroacetone 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 hexafluoroacetone is based on a NOAEL for developmental effects in rats [NAS 2012]. NIOSH based the IDLH value for hexafluoroacetone on lethality data from a rat study [Borzelleca and Lester 1965]. More precisely, the point of departure was a LC_{50} value of 900 ppm for a 30-minute exposure period. The use of differing studies and endpoints results in the order of magnitude difference between the AEGL-2 and IDLH value.

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