IMMEDIATELY DANGEROUS TO LIFE OR HEALTH (IDLH) VALUE PROFILE

FOR

HEXAFLUOROACETONE (HFA)

[CAS NO. 684-16-2]

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 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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## Abbreviations

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

**Benchmarch 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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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.

\( LC_{01} \): 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. Mode of action is distinguished from the more detailed mechanism of action, which 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 non-governmental 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 (STELs), or time-weighted average (TWA) limits.

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

Permissible Exposure Limit (PEL): 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, STEL, 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, STEL, 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, short-term (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 a TWA or ceiling limit.
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1.0 Introduction

1.1 Overview of the IDLH Value for Hexafluoroacetone

<table>
<thead>
<tr>
<th>IDLH Value: 9 ppm (61 mg/m³)</th>
</tr>
</thead>
</table>

| Basis for IDLH Value:  | A rat LC₅₀ value of 900 ppm for a 30-minute exposure period is the basis of the IDLH value for hexafluoroacetone [Borzelleca and Lester 1965], 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 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 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 hexafluoroacetone, the in-depth literature search was conducted through February 2014.

1.3 General Substance Information

Chemical: Hexafluoroacetone

CAS No: 684-16-2

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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:

![Structural formula of hexafluoroacetone](image)

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>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight</td>
<td>166.03†</td>
</tr>
<tr>
<td>Chemical formula</td>
<td>C₃F₆O</td>
</tr>
<tr>
<td>Description</td>
<td>Colorless gas</td>
</tr>
<tr>
<td>Odor</td>
<td>Disagreeable, musty</td>
</tr>
<tr>
<td>Odor Threshold</td>
<td>Not available</td>
</tr>
<tr>
<td>UEL</td>
<td>Not applicable*</td>
</tr>
<tr>
<td>LEL</td>
<td>Not applicable*</td>
</tr>
<tr>
<td>Vapor pressure</td>
<td>5.0 mmHg at 25°C (77°F)†</td>
</tr>
<tr>
<td>Flash point</td>
<td>Noncombustible†</td>
</tr>
<tr>
<td>Ignition temperature</td>
<td>Noncombustible†</td>
</tr>
<tr>
<td>Solubility</td>
<td>Soluble in water; hydrolyses†</td>
</tr>
</tbody>
</table>

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

† OSHA [2014]
‡ IFA [2014]
‡ HSDB [2014]
## Table 2: Alternative Exposure Guidelines for Hexafluoroacetone

<table>
<thead>
<tr>
<th>Organization</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Original (SCP) IDLH value</td>
<td>None</td>
</tr>
<tr>
<td>NIOSH REL</td>
<td>Not available</td>
</tr>
<tr>
<td>OSHA PEL [2014]</td>
<td>0.1 ppm TWA [skin]</td>
</tr>
<tr>
<td>ACGIH TLV [2014]</td>
<td>Not available</td>
</tr>
<tr>
<td>AIHA ERPG [2010]</td>
<td>ERPG-1: not derived; ERPG-2: 1 ppm; ERPG-3: 50 ppm</td>
</tr>
<tr>
<td>AIHA WEEL [2010]</td>
<td>Not available</td>
</tr>
</tbody>
</table>

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; WEEL – workplace environmental exposure level

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### Table 3: AEGL Values for Hexafluoroacetone

<table>
<thead>
<tr>
<th>Classification</th>
<th>10-min</th>
<th>30-min</th>
<th>1-hour</th>
<th>4-hour</th>
<th>8-hour</th>
<th>Endpoint [reference]</th>
</tr>
</thead>
<tbody>
<tr>
<td>AEGL-1</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>Insufficient data</td>
</tr>
<tr>
<td>AEGL-2</td>
<td>0.40 ppm</td>
<td>0.40 ppm</td>
<td>0.20 ppm</td>
<td>0.050 ppm</td>
<td>0.025 ppm</td>
<td>NOAEL for developmental effects in rat [E. I. du Pont de Nemours and Co. 1989]</td>
</tr>
<tr>
<td></td>
<td>2.7 mg/m³</td>
<td>2.7 mg/m³</td>
<td>1.4 mg/m³</td>
<td>0.34 mg/m³</td>
<td>0.17 mg/m³</td>
<td></td>
</tr>
<tr>
<td>AEGL-3</td>
<td>160.0 ppm</td>
<td>160.0 ppm</td>
<td>80.0 ppm</td>
<td>20.0 ppm</td>
<td>10.0 ppm</td>
<td>Lethality threshold estimated from rat LC₅₀ data [E. I. du Pont de Nemours and Co. 1962a,b]</td>
</tr>
<tr>
<td></td>
<td>1,100.0 mg/m³</td>
<td>1,100.0 mg/m³</td>
<td>540.0 mg/m³</td>
<td>140.0 mg/m³</td>
<td>68.0 mg/m³</td>
<td></td>
</tr>
</tbody>
</table>

**Abbreviation:** AEGL – acute exposure guideline levels; mg/m³ – milligrams per cubic meter; min – minute; NR – not recommended due to insufficient data; ppm – parts per million

**References:** NAS [2012]
2.0 Animal Toxicity Data

Several acute inhalation studies were identified for hexafluoroacetone. Borzelleca and Lester [1965] exposed rats to a series of concentrations (range not reported) for 0.5, 3 or 6 hours. LC$_{50}$ values of 900 ppm and 275 ppm were reported for 30-minute and 3-hour exposures, respectively; 6-hour values were not reported. Minor to no lung effects were reported for all the concentrations. The author also reported that postmortem exam 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 (0/4 died), but 3/4 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 sacrificed the rats at 7-57 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.

Effects of hexafluoroacetone appear to be systemically mediated, 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 also be related to the developmental toxicity of hexafluoroacetone. Exposure of pregnant rats to 6.9 ppm for 6 hours/day on gestation days (GD) 7-16 resulted in increased resorptions, malformations, and variations [E.I. du Pont de Nemours & Co. 1969]. Exposure to 1 ppm in the same study resulted in increased variations (no statistical test information available) and decreased body weight, while the only effect in the mothers was increased liver weight. The study authors considered the fetal
effects to be more severe than the concurrent maternal effects. This repeated exposure study is not appropriate as the basis for the IDLH value, but it does raise the question of whether acute hexafluoroacetone exposure during a key developmental window could 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 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., 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

<table>
<thead>
<tr>
<th>Reference</th>
<th>Species (reference)</th>
<th>LC50 (ppm)</th>
<th>LCLo (ppm)</th>
<th>Time (min)</th>
<th>Adjusted 30-min Concentration* (ppm)</th>
<th>Composite Uncertainty Factor</th>
<th>Derived Value (ppm)†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Borzelleca and Lester [1965]</td>
<td>Dog</td>
<td>5,000‡</td>
<td>--</td>
<td>45</td>
<td>5,724</td>
<td>100‡</td>
<td>57</td>
</tr>
<tr>
<td>E.I. du Pont de Nemours &amp; Co. [1962]</td>
<td>Rat</td>
<td>300§</td>
<td>--</td>
<td>240</td>
<td>2,400</td>
<td>100§</td>
<td>24</td>
</tr>
<tr>
<td>E.I. du Pont de Nemours &amp; Co. [1965]</td>
<td>Rat</td>
<td>--</td>
<td>3,600†</td>
<td>30</td>
<td>3,600</td>
<td>30†</td>
<td>120</td>
</tr>
<tr>
<td>Borzelleca and Lester [1965]+</td>
<td>Rat</td>
<td>900</td>
<td>--</td>
<td>30</td>
<td>900</td>
<td>100‡</td>
<td>9</td>
</tr>
<tr>
<td>Borzelleca and Lester [1965]§</td>
<td>Rat</td>
<td>275</td>
<td>--</td>
<td>180</td>
<td>1,650</td>
<td>100±</td>
<td>17</td>
</tr>
</tbody>
</table>

**Abbreviation:**  
LC – lethal concentration; LC50 – median lethal concentration; LCLo – lowest concentration of a chemical that caused death in humans or animals; min – minute; ppm – parts per million

*For exposures other than 30 minutes the ten Berge et al. [1986] relationship is used for duration adjustment (Cn x 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.

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

‡ 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

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

§ No lethality

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

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Table 5: Non-lethal Concentration Data for Hexafluoroacetone

<table>
<thead>
<tr>
<th>Reference</th>
<th>Species</th>
<th>NOAEL (ppm)</th>
<th>LOAEL (ppm)</th>
<th>Time (min)</th>
<th>Adjusted 30-min Concentration*</th>
<th>Composite Uncertainty Factor</th>
<th>Derived Value (ppm)†</th>
</tr>
</thead>
<tbody>
<tr>
<td>E.I. du Pont de Nemours &amp; Co. [1962a] rat</td>
<td>200</td>
<td>240</td>
<td>1,600</td>
<td>30</td>
<td></td>
<td>53</td>
<td></td>
</tr>
<tr>
<td>E.I. du Pont de Nemours &amp; Co. [1962b] rat</td>
<td>100</td>
<td>240</td>
<td>800</td>
<td>30</td>
<td></td>
<td>2727</td>
<td></td>
</tr>
<tr>
<td>E.I. du Pont de Nemours &amp; Co. [1989] rat</td>
<td>6.9</td>
<td>360</td>
<td>82.8</td>
<td>10 ± 8</td>
<td></td>
<td>10†</td>
<td>8</td>
</tr>
</tbody>
</table>

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

* For exposures other than 30 minutes the ten Berge et al. [1986] relationship is used for duration adjustment (Cn x 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.
† 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 based on the nature and severity of the endpoint observed.
‡ The cardiac sensitization response is a concentration-dependent threshold effect; dogs exposed to similar chemicals for longer durations responded in a similar manner, so no time adjustment was applied.
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.
Comprehensive uncertainty factor assigned to account for adjusting from a LOAEL to NOAEL, interspecies differences and human variability.
3.0 Human Data

There are no acute lethality data available for humans. 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.

4.0 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 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 different between the AEGL-2 and IDLH value.
5.0 References

ACGIH (American Conference of Governmental Industrial Hygienists) [2014]. Annual TLVs® (Threshold Limit Values) and BEIs® (Biological Exposure Indices) booklet. Cincinnati, OH: ACGIH Signature Publications.


AIHA (American Industrial Hygiene Association) [2010]. Emergency response planning guidelines (ERPG) and workplace environmental exposure levels (WEEL) handbook. Fairfax, VA: American Industrial Hygiene Association Press.


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