IDLH

IMMEDIATELY DANGEROUS to LIFE or HEALTH

VALUE PROFILE

Iron Pentacarbonyl
CAS® No. 13463-40-6

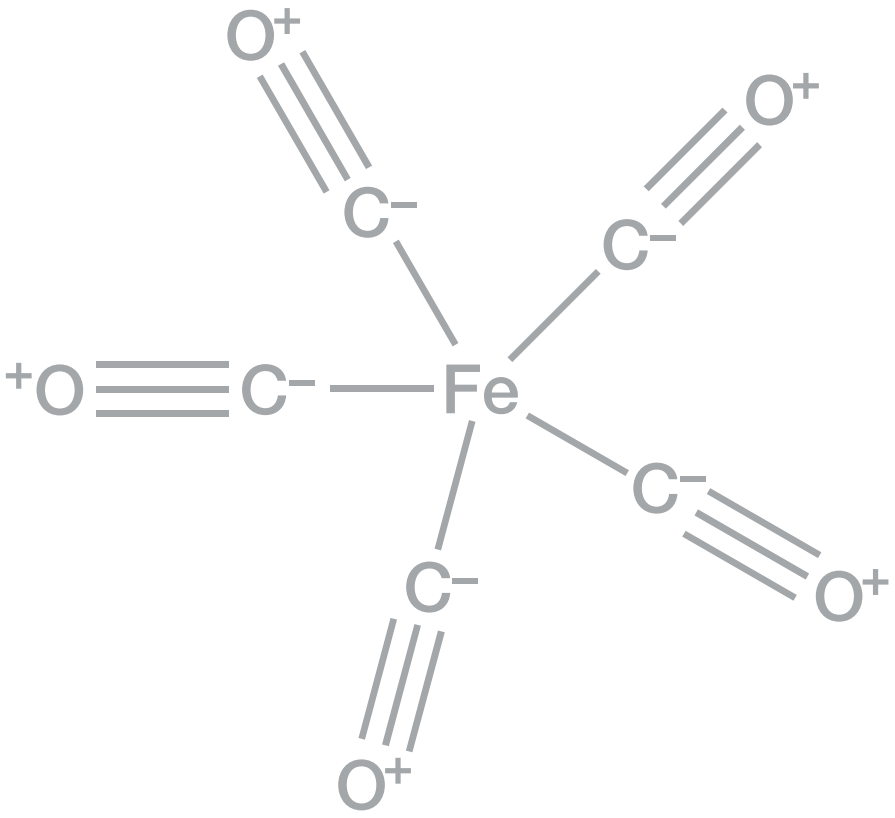
DEPARTMENT OF HEALTH AND HUMAN SERVICES
Center for Disease Control and Prevention
National Institute of Occupational Safety and Health

This page intentionally left blank.

Immediately Dangerous to Life or Health (IDLH) Value Profile

Iron Pentacarbonyl

[CAS® No. 13463-40-6]



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

Disclaimer

Mention of any company or product does not constitute endorsement by the National Institute for Occupational Safety and Health (NIOSH). In addition, citations to websites external to NIOSH do not constitute NIOSH endorsement of the sponsoring organizations or their programs or products. Furthermore, NIOSH is not responsible for the content of these websites.

Ordering Information

To receive this document or information about other occupational safety and health topics, contact NIOSH:

Telephone: 1-800-CDC-INFO (1-800-232-4636)
TTY: 1-888-232-6348
E-mail: cdcinfo@cdc.gov

or visit the NIOSH website: www.cdc.gov/niosh

For a monthly update on news at NIOSH, subscribe to *NIOSH eNews* by visiting www.cdc.gov/niosh/eNews.

Suggested Citation

NIOSH [2016]. Immediately dangerous to life or health (IDLH) value profile: iron pentacarbonyl. By Dotson GS, Maier A, Parker A, Haber L. Cincinnati, OH: US Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication 2016-166.

DHHS (NIOSH) Publication No. 2016-166

September 2016

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 iron pentacarbonyl (CAS #13463-40-6). The scientific basis, toxicologic data, and risk assessment approach used to derive the IDLH value are summarized to ensure transparency and scientific credibility.

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

This page intentionally left blank.

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
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
MLE	maximum likelihood estimate
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_{L0}: 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 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.

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.

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:

Education and Information Division

Devin Baker, M.Ed.

Charles L. Geraci, Ph.D.

Thomas J. Lentz, Ph.D.

Richard W. Niemeier, Ph.D. (retired)

Chris Whittaker, Ph.D.

NIOSH Office of the Director

John Decker, M.S., R.Ph.

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

Jeremy Brower, Ph.D., Associate Research Scientist, Lovelace Respiratory Research Institute, Albuquerque, NM

Mary A. Fox, Ph.D., Assistant Professor, Co-Director, Risk Sciences and Public Policy Institute, Department of Health Policy and Management, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD

Randal J. Keller, Ph.D., C.I.H, D.A.B.T., Professor, Department of Occupational Safety and Health, Jesse D. Jones College of Science, Engineering and Technology, Murray State University, Murray, KY

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

Leslie Stayner, M.Sc., Ph.D., Professor of Epidemiology and Biostatistics, School of Public Health, and Director of Occupational and Environmental Epidemiology, Occupational and Environmental Health and Safety Education and Research Center, University of Illinois at Chicago, Chicago, IL; Adjunct Research Professor, Center for Research on Environmental Epidemiology (CREAL), Barcelona, Spain

This page intentionally left blank.

1 Introduction

1.1 Overview of the IDLH Value for Iron Pentacarbonyl

IDLH value: 0.4 ppm

Basis for IDLH value: The IDLH value is based on a rat nonlethal concentration of 5.2 ppm in the 4-hour Biodynamics [1988] study, which corresponds to a concentration of 10.4 ppm after a 30-minute duration adjustment. Reported effects at this concentration included lacrimation and nasal discharge, which are classified as potentially escape-impairing. Applying a composite uncertainty factor of 30 to account for adjusting from a LOAEL to NOAEL, steep exposure-response relationship, interspecies differences, and human variability yields an IDLH value of 0.4 ppm.

1.2 Purpose

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

1.3 General Substance Information

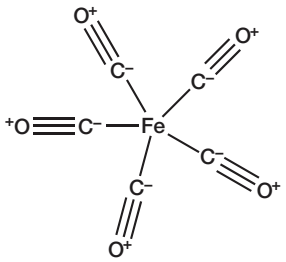
Chemical: Iron pentacarbonyl

CAS No: 13463-40-6

Synonyms: Iron carbonyl; Pentacarbonyliron*

Chemical category: Iron compounds; metal carbonyls†

Structural formula:



References: *NLM [2016]; †IFA [2016]

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

Table 1: Physiochemical Properties of Iron Pentacarbonyl

Property	Value
Molecular weight	195.90*
Chemical formula	C_5FeO_5
Description	Colorless to yellow to dark red, oily liquid
Odor	Moldy, musty
Odor threshold	Not available
UEL	12.5†
LEL	3.7†
Vapor pressure	35 torr at 25°C (77°F)*
Flash point	-15°C (5°F); closed cup*
Ignition temperature	320°C (608°F)‡
Solubility	Insoluble in water and dilute acids; readily soluble in most organic solvents*

References: *ACGIH [2015]; †IFA [2016]; ‡HSDB [2016]

Table 2: Alternative Exposure Guidelines for Iron Pentacarbonyl

Organization	Value
Revised (1994) IDLH value*	None
NIOSH REL‡	0.1 ppm TWA; 0.2 ppm STEL
OSHA PEL†	0.1 ppm TWA; 0.2 ppm STEL
ACGIH TLV®§	0.1 ppm TWA; 0.2 ppm STEL
AIHA ERPGs™¶	None
AIHA WEELs®¶	None

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

Table 3: AEGL Values for Iron Pentacarbonyl

Classification	10-min	30-min	1-hour	4-hour	8-hour	Endpoint [reference]
AEGL-1	NR	NR	NR	NR	NR	Not applicable
AEGL-2	0.077 ppm 0.61 mg/m^3	0.077 ppm 0.61 mg/m^3	0.060 ppm 0.48 mg/m^3	0.037 ppm 0.30 mg/m^3	0.025 ppm 0.20 mg/m^3	Based on a 3-fold reduction in the AEGL-3 values
AEGL-3	0.23 ppm 1.8 mg/m^3	0.23 ppm 1.8 mg/m^3	0.18 ppm 1.4 mg/m^3	0.11 ppm 0.88 mg/m^3	0.075 ppm 0.60 mg/m^3	Estimated lethality threshold in rats (1.0 ppm determined by BMD analysis [BASF 1995]); n = 1 or 3; uncertainty factor = 10 (3 for both interspecies variability and individual variability)

Reference: NAS [2010]

2 Animal Toxicity Data

The majority of acute studies for iron pentacarbonyl provided data on lethality, with little additional information to assess potential escape-impairing effects. Using a dynamic exposure chamber without analytical monitoring, Gage [1970] reported that no effects were seen in rats exposed for eighteen 5.5-hour periods at 7 ppm, but a single 5.5-hour exposure to 33 ppm was lethal to 3 of 8 rats. Postmortem examination showed pulmonary edema, indicating that lung effects are a critical target for this chemical. Sunderman et al. [1959] conducted lethality studies with mice and rats. Groups of 20 Swiss albino mice were exposed to concentrations equivalent to 204, 270, 387, or 470 ppm of iron pentacarbonyl for 30 minutes. The authors reported a 30-minute LC_{50} value of 273 ppm for mice. Wistar rats were treated at concentrations equivalent to 69, 114, 159, 187, and 193 ppm. Sunderman et al. [1959] reported a 30-minute LC_{50} value of 118 ppm in rats. These results indicate that rats are more susceptible than mice to iron pentacarbonyl. Biodynamics [1988] reported that rats exposed to 5.2 ppm of iron pentacarbonyl for 4 hours showed effects 1 to 2 hours post exposure but essentially no toxicity during exposure. The observed effects included lacrimation and nasal discharge at a slightly higher incidence than in controls. Necropsy of these rats revealed red lungs in some, but the actual number was not reported, and the observation was considered of equivocal significance on the basis of gross pathology only. Together, the studies of Gage [1970] and Biodynamics [1988] show minimal irritant effects in the range of 5 to 7 ppm of iron pentacarbonyl, even for single acute exposure periods significantly longer than 30 minutes. BASF [1995] reported 1 of 10 rats died following a single 6-hour exposure to 2.91 ppm of iron pentacarbonyl; 5 of 10 died within 4 days after receiving two 6-hour exposures. Because of the delayed mortality seen in this and other studies, it is not known whether additional rats would have died following the single exposure if there had been additional post-exposure monitoring. NAS [2010] calculated maximum likelihood estimate (MLE) LC_{01} and BMCL LC_{05} values based on the data reported in the BASF [1995] study via log-probit benchmark dose analysis of a BASF [1995] study. The results of this yielded an MLE LC_{01} for lethality of 1.9 ppm and a $BMCL_{05}$ for lethality of 0.8 ppm. These estimates assume that a single exposure would have killed 5/10 animals, as a worst-case scenario, in light of the delayed deaths. However, rats exposed to 1.0 ppm for 28 days did not exhibit any clinical signs, suggesting a steep exposure-response curve, and that 1.0 ppm is a very conservative estimate of the lethality threshold from a single exposure.

The acute toxicity studies show a significant difference in lethal concentrations in rats across the available studies. It is convenient that the study by Sunderman et al. [1959] was for the duration of interest and included sufficient information to calculate an LC_{50} value, but a static exposure scenario was used, leading to significant uncertainty in the actual exposure levels. The Biodynamics [1988] and BASF [1995] studies were conducted with modern exposure methods and identified much lower effect levels but involved greater time extrapolation, and the BASF [1995] study includes the additional uncertainties due to the multiple exposures and inadequate information on post-exposure deaths following a single exposure. Thus, the appropriate IDLH value derivation would yield a value generally near this exposure range.

Table 4 summarizes the LC data identified in animal studies and provides 30-minute-

equivalent derived values for iron pentacarbonyl. 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, and 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 Iron Pentacarbonyl

Reference	Species	LC_{50} (ppm)	LC_{Lo} (ppm)	Time (min)	Adjusted 30-minute Concentration* (ppm)	Composite Uncertainty Factor	30-min Equivalent Derived Value (ppm)†	Final Value (ppm)‡
Sunderman et al. [1959]	Mouse	273	—	30	273	30§	9.1	9.1
Armit [1980]	Rabbit	250	—	45	286	30§	9.53	9.5
Sunderman et al. [1959]	Rat	118	—	30	118	30§	3.93	3.9
Biodynamics [1988]	Rat	10	—	240	20	30§	0.67	0.7
BASF [1995]	Rat	3¶	—	720	9	30§	0.3	0.3
BASF [1995]	Rat	—	3**	360	7	10††	0.7	0.7
BASF [1995]	Rat	—	1‡‡	360	2.3	10††	0.23	0.2

*For exposures greater than 30 minutes, the ten Berge et al. [1986] relationship is used for adjustment ($C^n \times t = k$). Empirically estimated n values were not 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 concentration divided by the composite uncertainty factor.

‡Values rounded to the appropriate significant figure.

§Composite uncertainty factor to account for adjustment of LC_{50} values to LC_{01} values, use of lethal concentration threshold in animals, interspecies differences, and human variability.

¶5/10 rats died within 4 days after two 6-hour exposures.

**1/10 rats died after a single 6-hour exposure.

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

‡‡Modified $BMCL_{05}$ for lethality after a single 6-hour exposure.

Table 5: Nonlethal Concentration Data for Iron Pentacarbonyl

Reference	Species	Critical nonlethal effect	NOAEL (ppm)	LOAEL (ppm)	Time (min)	Adjusted 30-minute Concentration* (ppm)	Composite Uncertainty Factor	30-min Equivalent Derived Value (ppm)†	Final Value (ppm)‡
Biodynamics [1988]§	Rat	Lacrimation and nasal discharge	—	5.2	240	10.4	30¶	0.35	0.4

*For exposures greater than 30 minutes, the ten Berge et al. [1986] relationship is used for adjustment (Cn x t = k). Empirically estimated n values were not 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 concentration divided by the composite uncertainty factor.

‡Value rounded to the appropriate significant figure.

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

¶Composite uncertainty factor assigned to account for adjusting from a LOAEL to NOAEL, steep exposure-response relationship, interspecies differences, and human variability.

3 Human Data

No information was identified that provided adequate estimates of observed effects following exposure in humans. Stokinger [1981] reported that the effects of human exposure to iron pentacarbonyl are similar to those of nickel carbonyl exposure. Such effects are giddiness and headache, dyspnea, and vomiting, which were alleviated after removal from exposure. Symptoms such as fever, cyanosis, and coughing lasting up to 36 hours after exposure have also been reported. Death may occur several days after exposure.

4 Summary

The assembled data on iron pentacarbonyl reveal a steep exposure-response relationship and a small gap between concentrations associated with severe nonlethal effects and death in test animals. Reported effects of concern include delayed onset of death following acute exposure. The IDLH value for iron pentacarbonyl is based on a rat nonlethal concentration of 5.2 ppm in the 4-hour Biodynamics [1988] study, which corresponds to a concentration of 10.4 ppm after a 30-minute duration adjustment. Reported effects at this concentration included lacrimation and nasal discharge, which are classified as potentially escape impairing. Applying a composite uncertainty factor of 30 to account for extrapolation from a LOAEL to a NOAEL, severe effects in animals (i.e., steep exposure-response relationship), interspecies differences, and human variability results in an IDLH value of 0.4 ppm.

It should be noted that the IDLH value for iron pentacarbonyl differs substantially 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]. Data to calculate an AEGL-2 value for iron pentacarbonyl were deemed insufficient, resulting in the establishment of an AEGL-2 equal to 1/3 of the calculated AEGL-3 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 life-threatening health effects or death [NAS 2001, 2010]. The AEGL-3 value for 30 minutes was set at 0.23 ppm and was based on lethal threshold estimates in rats reported in BASF [1995]. NIOSH used nonlethality data reported in Biodynamics [1988] as the basis of the IDLH value of 0.4 ppm for iron pentacarbonyl. The small difference between the AEGL-3 value and IDLH value is due to alternative primary data, selection of the critical health endpoints, and duration adjustments.

5 References

ACGIH [2015]. 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.

Armit HW [1908]. The toxicology of nickel carbonyl. Part II. J Hygiene *8*:565–600.

BASF [1995]. Study on inhalation toxicity of eisenpentacarbonyl as a vapor in rats-28 day test. Ludwigshafen, Germany: BASF (Badische Anilin & Soda Fabrik), Department of Toxicology. Environmental Protection Agency, Office of Toxics Substances, Document #88-950000244.

Biodynamics [1988]. An acute inhalation toxicity study of iron pentacarbonyl in the rat. Final report. Environmental Protection Agency, Office of Toxic Substances, Document #88-920001300.

Gage JC [1970]. The subacute inhalation toxicity of 107 industrial chemicals. Br J Ind Med *27*:1–18.

HSDB [2016]. 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) [2016]. GESTIS: database on hazardous substances, http://gestis-en.itrust.de/nxt/gateway.dll?f=templates&fn=default.htm&vid=gestiseng:sdbeng.

NAS [2001]. Standing operating procedures for developing Acute Exposure Guidelines 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, IBSN: 0-309-07553-X, http://www.epa.gov/sites/production/files/2015-09/documents/sop_final_standing_operating_procedures_2001.pdf.

NAS [2010]. Acute Exposure Guideline Levels (AEGLs) for selected airborne chemicals. Vol. 6. Chapter 7: Iron pentacarbonyl. National Academy of Sciences, Committee on Toxicology and Committee on Acute Exposure Guideline Levels, Board on Environmental Studies and Toxicology, National Research Council. Washington, DC: National Academy Press, http://www.epa.gov/sites/production/files/2014-11/documents/iron_pentacarbonyl_final_volume6_2007.pdf.

NIOSH [1994]. Documentation for immediately dangerous to life or health concentrations (IDLHs). 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 [2016]. 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 [2016]. ChemIDplus lite. Washington, DC: National Library of Medicine, http://chemsis.nlm.nih.gov/chemidplus/. OSHA [2016]. Chemical sampling information, https://www.osha.gov/dts/chemicalsampling/toc/toc_chemsamp.html.

Stokinger HE [1981]. Metals. In: Clayton GD, Clayton FE, eds. Patty's industrial hygiene and toxicology. 4th ed. New York: John Wiley & Sons, pp. 1792–1807.

Sunderman F, West B, Kincaid J [1959]. A toxicity study of iron pentacarbonyl. Arch Ind Health *19*:11–13.

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/.

This page intentionally left blank.

Delivering on the Nation's promise:
safety and health at work for all people
through research and prevention

To receive NIOSH documents or more information about occupational safety and health topics, contact NIOSH at

1–800–CDC–INFO (1–800–232–4636)
TTY: 1–888–232–6348
E-mail: cdcinfo@cdc.gov

or visit the NIOSH Website at www.cdc.gov/niosh.

For a monthly update on news at NIOSH, subscribe to *NIOSH eNews* by visiting www.cdc.gov/niosh/eNews.

DHHS (NIOSH) Publication No. 2016–166