

IDLH

IMMEDIATELY
DANGEROUS to
LIFE or HEALTH

VALUE PROFILE

1,3-Butadiene
CAS[®] No. 106-99-0

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

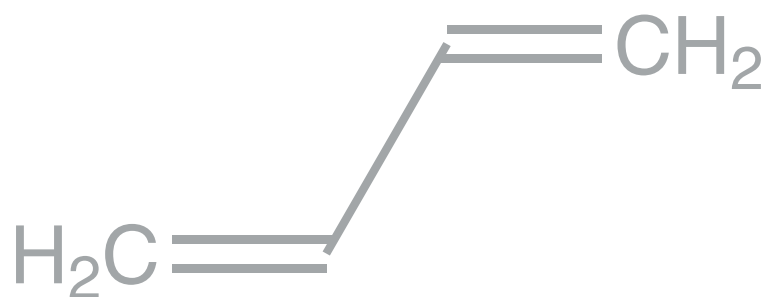


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Immediately Dangerous to Life or Health (IDLH) Value Profile

1,3-Butadiene

[CAS® No. 106-99-0]



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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) airborne 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 1,3-butadiene (CAS® # 106-99-0). The scientific basis, toxicologic data, and risk assessment approach used to derive the IDLH value are summarized to ensure transparency and scientific credibility.

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Abbreviations

ACGIH®	American Conference of Governmental Industrial Hygienists
AEGLs	Acute Exposure Guideline Levels
AIHA®	American Industrial Hygiene Association
BMC	benchmark concentration
BMD/BMC	benchmark dose/concentration
BMCL	benchmark concentration lower confidence limit
C	ceiling value
°C	degrees Celsius
CAS®	Chemical Abstracts Service, a division of the American Chemical Society
EC	European Commission
ERPGs™	Emergency Response Planning Guidelines
°F	degrees Fahrenheit
IDLH	immediately dangerous to life or health
LC₅₀	median lethal concentration
LC_{L0}	lowest concentration that caused death in humans or animals
LEL	lower explosive limit
LOAEL	lowest observed adverse effect level
mg/m³	milligram(s) per cubic meter
min	minutes
mmHg	millimeter(s) of mercury
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
NTP	National Toxicology Program
OSHA	Occupational Safety and Health Administration
PEL	permissible exposure limit
ppm	parts per million
RD₅₀	concentration of a chemical in the air that is estimated to cause a 50% decrease in the respiratory rate
REL	recommended exposure limit
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].

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

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

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

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

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

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

Immediately dangerous to life or health (IDLH) condition: A 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.

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

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

LC₁₀: The lowest lethal concentration of a substance in the air reported to cause death, usually for a small percentage of the test animals.

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

LD₁₀: 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 or MSHA for allowable occupational airborne exposure concentrations. PELs are legally enforceable and may be designated as ceiling limits, STELs, or TWA limits.

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

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

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

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

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

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

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

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

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

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

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1 Introduction

1.1 Overview of the IDLH Value for 1,3-Butadiene

IDLH value: 2,000 ppm (10% LEL)

Basis for IDLH value: Despite the availability of toxicity data capable of being used to calculate health-based estimates for 1,3-butadiene (see Tables 4 and 5), the majority of these estimates are greater than 10% of the lower explosive limit (>10% LEL). NIOSH has adopted a threshold of 10% LEL as a default basis for the IDLH values based on explosivity concerns [NIOSH 2013]. Since safety considerations related to the potential hazard of explosion must be taken into account, the IDLH value is set at the 10% LEL for 1,3-butadiene of **2,000 ppm**.

1.2 Purpose

This *IDLH Value Profile* presents (1) a brief summary of technical data associated with acute inhalation exposures to 1,3-butadiene

and (2) the rationale behind the immediately dangerous to life or health (IDLH) value for 1,3-butadiene. IDLH values are developed based on the scientific rationale and logic outlined in the *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 1,3-butadiene, the in-depth literature search was conducted through May 2016.

1.3 General Substance Information

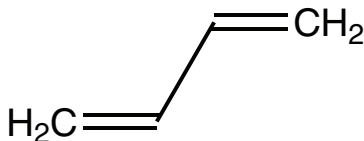
Chemical: 1,3-Butadiene

CAS No: 106-99-0

Synonyms: Butadiene; Divinyl; Biethylene; Erythrene*

Chemical category: Unsaturated, aliphatic hydrocarbons; Organic gases†

Structural formula:



References: *NLM [2016]; †IFA [2016]

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

Table 1: Physiochemical properties of 1,3-butadiene

Property	Value
Molecular weight	54.09*
Chemical formula	C ₄ H ₆
Description	Colorless gas
Odor	Mild aromatic or gasoline-like
Odor threshold	0.45 ppm [†]
UEL	16.3% [‡]
LEL	2.0%*
Vapor pressure	2110 mmHg at 25°C (77°F) [§]
Flash point	-76.11°C (-105°F) [§]
Ignition temperature	414.44°C (788°F) [§]
Solubility	Slightly soluble in water [‡]

References: *NIOSH [2016]; [†]AIHA [1989]; [‡]IFA [2016]; [§]HSDB [2016]

Table 2: Alternative exposure guidelines for 1,3-butadiene

Organization	Value
Revised (1994) IDLH value*	2000 ppm [LEL]
NIOSH REL [†]	None
OSHA PEL [‡]	1 ppm TWA; 5 ppm STEL
ACGIH TLV [§]	2 ppm, TWA
AIHA ERPG [¶]	ERPG-1: 10 ppm; ERPG-2: 200 ppm; ERPG-3: 5,000
AIHA WEEL [¶]	None

References: *NIOSH [1994]; [†]NIOSH [2016]; [‡]OSHA [1996]; [§]ACGIH [2015]; [¶]AIHA [2014]

Table 3: Interim AEGL values for 1,3-butadiene

Classification	10-min	30-min	1-hour	4-hour	8-hour	Endpoint [reference]
AEGL-1*	670 ppm	670 ppm	670 ppm	670 ppm	670 ppm	Difficulty in focusing in humans [Carpenter et al. 1944]
	1,500 mg/m ³	1,500 mg/m ³	1,500 mg/m ³	1,500 mg/m ³	1,500 mg/m ³	
AEGL-2	6,700 ppm†	6,700 ppm†	5,300 ppm†	3,400 ppm†	2,700 ppm†	No effects in humans [Carpenter et al. 1944]
	15,000 mg/m ³	15,000 mg/m ³	12,000 mg/m ³	7,500 mg/m ³	6,000 mg/m ³	
AEGL-3	27,000 ppm§	27,000 ppm§	22,000 ppm§	14,000 ppm‡	6,800 ppm†	Lethality in rats [Shugaev 1969]
	60,000 mg/m ³	60,000 mg/m ³	49,000 mg/m ³	31,000 mg/m ³	15,000 mg/m ³	

Reference: NAS [2008]

*It is noted that the derivation of the respective AEGL-values excludes potential mutagenic or carcinogenic effects after single exposure, which may occur at lower concentrations.

†>10% LEL

‡>50% LEL

§> 100% LEL

2 Animal Toxicity Data

Several lethality studies in animals were available. The lowest LC₅₀ value of 122,000 ppm was reported by Shugaev [1969]. In this study, mice were exposed to varying concentrations of 1,3-butadiene for 2 hours. Prior to death, deep narcosis was seen. The authors also reported a LC₁₆ value of 91,000 ppm and a LC₈₄ value of 169,000 ppm.

In a carcinogenicity study, Bucher et al. [1993] exposed mice to 0, 1,000, 5,000, or 10,000 ppm of 1,3-butadiene for a single 2-hour period and held the animals for 2 years prior to microscopic examination of tissues. Even at the highest concentration, there was no mortality. No effects were reported.

Although metabolism is qualitatively similar across species, there are substantial quantitative differences, with the toxic epoxide metabolite formed at much higher levels in mice than in rats. The higher susceptibility of mice compared to rats is attributed to this difference, together with the higher ventilation rate in mice. Based on the lower ventilation rate in humans and the limited in vitro metabolism data, humans are considered to be more similar to rats than mice.

EC [2002] and USEPA [2002] concluded that 1,3-butadiene is carcinogenic to humans. NTP [2014] identified 1,3-butadiene as, “Known to be a human carcinogen.” IARC

[2008] classified 1,3-butadiene as, “Carcinogenic to humans (Group 1).” 1,3-butadiene is carcinogenic to rats and mice, with mice being more susceptible than rats [EC 2002; USEPA 2002]. Bucher et al. [1993] did not observe an increased tumor incidence in mice exposed concentrations up to 10,000 ppm for a single 2-hour period and held for 2 years prior to microscopic examination of tissues. Based on this acute study, no additional factor was added to account for 1,3-butadiene carcinogenicity. Extrapolation from the chronic data indicates a risk greater than 1×10^{-3} for a 30-minute exposure at concentrations equal to IDLH value. Grosse et al. [2007] summarizes the carcinogenicity for 1,3-butadiene. Sielken and Valdez-Flores [2015] provides an in-depth overview of the occupational and general population cancer risk for 1,3-butadiene.

Table 4 summarizes the LC data identified in animal studies and provides 30-minute equivalent derived values for 1,3-butadiene. 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, BMCL, NOAEL, LOAEL), adjusted 30-minute concentration, and the justification for the composite uncertainty factors applied to calculate the derived values.

Table 4: Lethal concentration data for 1,3-butadiene

Reference	Species	LC ₅₀ (ppm)	Other lethality (ppm)	Time (min)	Adjusted 30-min concentration* (ppm)	Composite uncertainty factor	30-min equivalent derived value (ppm) [†]	Final value [‡] (ppm)
Shugaev [1969]	Mouse	122,000	—	120	193,663	30 [§]	6,455	6,500
Shugaev [1969]	Mouse	—	91,000 ^{††}	120	144,454	30 ^{**}	4,815	4,800
Shugaev [1969]	Rat	128,000	—	240	256,000	30 [§]	8,533	8,500
Shugaev [1969]	Rat	—	79,000 ^{††}	240	158,000	30 ^{**}	5,267	5,300

*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 concentration divided by the composite uncertainty factor.

[‡]Values rounded to the appropriate significant figure.

[§]Composite uncertainty factor to account for adjustment of LC₅₀ values to LC₀₁ values, use of lethal concentration threshold in animals, interspecies differences and human variability.

[†]Reported as LC₁₆ value

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

^{††}Reported as LC₀₄ value

Table 5: Non-lethal concentration data for 1,3-butadiene

Reference	Species (reference)	Critical nonlethal effect	NOAEL (ppm)	LOAEL (ppm)	Time (min)	Adjusted 30-min concentration* (ppm)	Composite uncertainty factor	30-min equivalent derived value (ppm) [†]	Final value [‡] (ppm)
Bucher et al. [1993]	Mouse	No observed effects	10,000	—	120	15,874	3 [§]	5,291	5,300
Carpenter et al. [1944]	Human	Discomfort of the eyes, difficulty focusing	—	4,000	360	9,160	3 [¶]	3,053	3,000
Carpenter et al. [1944]	Human	Discomfort of the eyes, difficulty focusing	—	2,000	420	4,820	3 [¶]	1,607	1,600
Carpenter et al. [1944]	Human	Discomfort of the eyes, difficulty focusing	—	8,000	480	20,159	3 [¶]	6,720	6,700

*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 concentration divided by the composite uncertainty factor.

[‡]Values rounded to the appropriate significant figure.

[§]Composite uncertainty factor to account for interspecies differences and human variability.

[¶]Composite uncertainty factor to account for human variability.

3 Human Data

No information was located on concentrations lethal to humans. Information regarding human exposure to 1,3-butadiene is available from several clinical and epidemiological studies. Larionov et al. [1934] exposed volunteers to 10,000 ppm of 1,3-butadiene for 5 minutes. Blood pressure and respiration were monitored, but only nose and throat irritation were reported. Exposure to 10,000 ppm for 5 minutes resulted in slight irritation and dryness of the nose and mouth with some

increase in pulse rate but no effect on blood pressure or respiration [Shugaev 1968].

Carpenter et al. [1944] exposed two males to 2,000 ppm 1,3-butadiene for 7 hours, 4,000 ppm for 6 hours, or 8,000 ppm for 8 hours, with a 1-hour lunch break in the middle of the exposure period; exposure concentrations were monitored regularly. Effects reported included slight discomfort of the eyes and difficulty in focusing. There was no effect on a tapping test or steadiness test.

4 Summary

Despite the availability of toxicity data capable of being used to calculate health-based estimates for 1,3-butadiene (see Tables 4 and 5), the majority of these estimates are greater than 10% of the lower explosive limit (>10% LEL). NIOSH has adopted a threshold of 10% LEL as a default basis for the IDLH values based on explosivity concerns [NIOSH 2013]. Since safety considerations related to the potential hazard of explosion must be taken into account, the IDLH value is set at the 10% LEL for 1,3-butadiene of 2,000 ppm.

If the explosive hazards of 1,3-butadiene are controlled or toxicity issues are the primary concern, a health-based IDLH value could be derived from numerous datasets. Based on effects seen in humans, a LOAEL for potentially escape-impairing effects was identified at 8,000 ppm for a 6-hour exposure

[Carpenter et al. 1944]. The exposure concentration adjusted for a 30-minute exposure is 20,159 ppm. A composite uncertainty factor of 3 was applied to account for extrapolation from a human variability. This results in an IDLH value of 6,700 ppm. This value is supported by lethality studies. Shugaev [1969] reported a rat 4-hour LC_{50} value of 128,000 ppm and a mouse 2-hour LC_{50} value of 122,000 ppm. Extrapolating to a 30-minute duration and applying a composite uncertainty factor of 30 to account for extrapolation from a concentration that is lethal to animals, animal to human differences and human variability results in potential IDLH values of 8,500 ppm and 6,500 ppm, respectively. Based on the overall data, and taking into account that the rat is a better model for humans than the mouse, this would result in a health-based IDLH value of 6,700 ppm.

5 References

- ACGIH [2015]. Annual TLVs® (Threshold Limit Values) and BEIs® (Biological Exposure Indices) booklet. Cincinnati, OH: ACGIH Signature Publications.
- AIHA [1989]. Odor thresholds for chemicals with established occupational health standards. Fairfax, VA: American Industrial Hygiene Association Press.
- 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>.
- Bucher JR, Melnick RL, Hildebrandt PK [1993]. Lack of carcinogenicity in mice exposed once to high concentrations of 1,3-butadiene. *J Nat Cancer Inst* 85:1866–1867.
- Carpenter CP, Shaffer CB, Weil CS, Smyth HF Jr [1944]. Studies on the inhalation of 1,3-butadiene; with a comparison of its narcotic effect with benzol, toluol, and styrene, and a note on the elimination of styrene by the human. *J Ind Hyg Toxicol* 26(3):69–78.
- EC (European Commission) [2002]. European Union Risk Assessment Report: 1,3-butadiene. Volume 20. EUR 20420 EN. European Commission, European Chemical Bureau, Institute for Health and Consumer Products, <http://www.echa.europa.eu/documents/10162/1f512549-5bf8-49a8-ba51-1cf67dc07b72>.
- Grosse Y, Baan R, Straif K, Secretan B, El Ghissassi F, Bouvard V, Altieri A, Coglianò V [2007]. Carcinogenicity of 1,3-butadiene, ethylene oxide, vinyl chloride, vinyl fluoride, and vinyl bromide. *Lancet Oncol* 8(8):679–80.
- HSDB [2016]. Hazardous Substances Data Bank. Bethesda, MD: National Library of Medicine, <http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB>.
- IARC (International Agency for Research on Cancer) 2008. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Volume 97: 1,3-butadiene, ethylene oxide and vinyl halides. World Health Organization, IARC, <http://monographs.iarc.fr/ENG/Monographs/vol97/mono97.pdf>.
- 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>.
- Larionov LF, Shtessel' TA, Nusel'man EI [1934]. The physiological action of butadiene, butene-2 and isoprene. *Kazanskii Meditsinskii Zhurnal* 30:440–445 (HSE translation no. 10855).
- NAS [2001]. Standing operating procedures for developing acute exposure guideline levels for hazardous chemicals. National Academy of Sciences, National Research Council, Committee on Toxicology, Subcommittee on Acute Exposure Guideline Levels. Washington, DC: National Academy Press, ISBN: 0-309-07553-X, http://www.epa.gov/sites/production/files/2015-09/documents/sop_final_standing_operating_procedures_2001.pdf.
- NAS [2008]. Interim acute exposure guideline levels (AEGs) for 1,3-butadiene (CAS No. 106-99-0). National Academy of Sciences, National Research Council, Committee on Toxicology, Subcommittee on Acute Exposure Guideline Levels. Washington, DC: National Academy Press, <https://www.epa.gov/sites/>

- production/files/2014-08/documents/butadiene_interim_dec_2008.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, <http://chem.sis.nlm.nih.gov/chemidplus/>.
- NTP (National Toxicology Program) [2014]. Substance Profile: 1,3-Butadiene. Report on Carcinogens, Thirteenth Edition. Research Triangle Park, NC: U.S. Department of Health and Human Services, Public Health Service, <https://ntp.niehs.nih.gov/ntp/roc/content/profiles/butadiene.pdf>.
- OSHA [1996]. 29 CFR 1910.1051 1,3-Butadiene. Washington, DC: U.S. Department of Labor, Occupational Safety and Health Administration, https://www.osha.gov/pls/oshaweb/owadisp.show_document?p_table=STANDARDS&p_id=10087.
- Shugaev BB [1968]. Distribution in the organism and toxicity of aliphatic hydrocarbons. *Farmakol Toxikol* 31:162–165.
- Shugaev BB [1969]. Concentrations of hydrocarbons in tissues as a measure of toxicity. *Arch Environ Health* 18:878–882.
- Sielken RL, Valdez-Flores C [2015]. A comprehensive review of occupational and general population cancer risk: 1,3-Butadiene exposure–response modeling for all leukemia, acute myelogenous leukemia, chronic lymphocytic leukemia, chronic myelogenous leukemia, myeloid neoplasm and lymphoid neoplasm. *Chemico-Biological Interactions* 241:50–58.
- 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.
- USEPA (United States Environmental Protection Agency) [2002]. Health assessment of 1,3-butadiene. EPA/600/P-10 98/001F, <http://www.epa.gov/iris/supdocs/butasup.pdf>.
- USEPA [2016]. Integrated risk information system (IRIS), <http://www.epa.gov/iris/>.



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