IDLH

IMMEDIATELY DANGEROUS to LIFE or HEALTH VALUE PROFILE

Butane

CAS® No. 106-97-8

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

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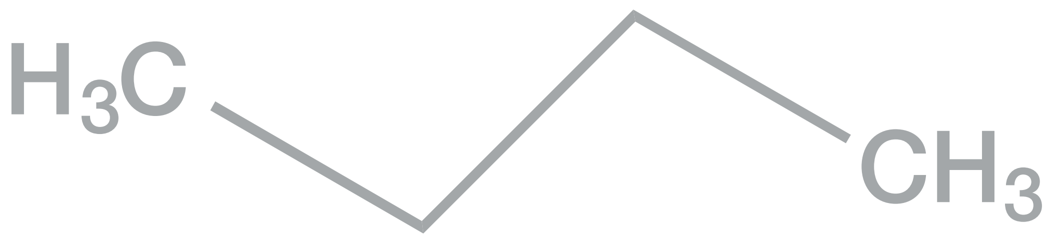

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Foreword

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

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

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

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

The purpose of this technical report is to present the IDLH value for butane (CAS® #106-97-8). The scientific basis, toxicologic data, and risk assessment approach used to derive the IDLH value are summarized to ensure transparency and scientific credibility.

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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
mg/m^3	milligram(s) per cubic meter
min	minutes
mmHg	millimeter(s) of mercury
NAC	National Advisory Committee
NAS	National Academy of Sciences
NIOSH	National Institute for Occupational Safety and Health
NOAEL	no observed adverse effect level
NOEL	no observed effect level
NR	not recommended
OSHA	Occupational Safety and Health Administration
PEL	permissible exposure limit
ppm	parts per million
RD_{50}	concentration of a chemical in the air that is estimated to cause a 50% decrease in the respiratory rate
REL	recommended exposure limit
SCP	Standards Completion Program (joint effort of NIOSH and OSHA)
STEL	short-term exposure limit
TLV®	Threshold Limit Value
TWA	time-weighted average
UEL	upper explosive limit
WEELs®	Workplace Environmental Exposure Levels
µg/kg	microgram(s) per kilogram of body weight

Glossary

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

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

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

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

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

Benchmark dose/concentration (BMD/BMC): A dose or concentration that produces a predetermined change in response rate of an effect (called the benchmark response, or BMR) compared to background [U.S. EPA 2016] (additional information available at http://www.epa.gov/ncea/bmds/).

Benchmark response (BMR): A predetermined change in response rate of an effect. Common defaults for the BMR are 10% or 5%, reflecting study design, data variability, and sensitivity limits used.

BMCL: A statistical lower confidence limit on the concentration at the BMC [U.S. EPA 2016].

Bolus exposure: A single, relatively large dose.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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1 Introduction

1.1 Overview of the IDLH Value for Butane

IDLH value: 1,600 ppm (>10% LEL)

Basis for IDLH value: Despite the availability of toxicity data capable of being used to calculate health-based estimates for butane (see Table 4), these estimates are all 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 value, based on explosivity concerns [NIOSH 2013]. The LEL for butane is 1.6%, or 16,000 ppm [NIOSH 2016]. The IDLH value for butane is set at 1,600 ppm (10% LEL).

1.2 Purpose

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

1.3 General Substance Information

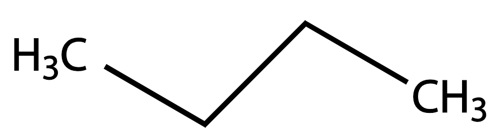
Chemical: Butane

CAS No: 106-97-8

Synonyms: Butyl hydride; Diethyl; Methylethyl methane*

Chemical category: Aliphatic, saturated hydrocarbons; Organic gases†

Structural formula:



References: *NLM [2016]; †IFA [2016]

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

Table 1: Physiochemical properties of butane

Property	Value
Molecular weight	58.1[§]
Chemical formula	C_4H_{10}
Description	Colorless gas
Odor	Gasoline-like; Natural gas
Odor threshold	none
UEL	8.4%[§]
LEL	1.6%[§]
Vapor pressure	760 torr at 25°C (77°F)[*]
Flash point	-60°C (-76°F)[‡]
Ignition temperature	287.78°C (550°F)[‡]
Solubility	Insoluble to slightly soluble in water; very soluble in ethanol, ether, and chloroform[*]

References: [*]ACGIH [2015]; [‡]HSDB [2016]; [§]NIOSH [2016]

Table 2: Alternative exposure guidelines for butane

Guideline	Value
Original (SCP) IDLH value[*]	None
NIOSH REL[‡]	800 ppm (1,900 mg/m³), TWA
OSHA PEL[†]	None
ACGIH TLV®[§]	1,000 ppm (2,370 mg/m³), STEL
AIHA ERPGs™[¶]	None
AIHA WEELs®[¶]	None

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

Table 3: AEGL values for butane

Classification	10-min	30-min	1-hour	4-hour	8-hour	Endpoint [reference]
AEGL-1	**	6,900 ppm* 16,000 mg/m³	5,500 ppm* 13,000 mg/m³	5,500 ppm* 13,000 mg/m³	5,500 ppm* 13,000 mg/m³	Drowsiness in humans [Patty and Yant 1929]
AEGL-2	***	**	**	**	**	Dazed appearance in guinea pigs [Nuckolls 1933]
AEGL-3	***	***	***	***	***	LC_{01} in mice [Shugaev 1969]

Reference: NAS [2012]

Lower Explosive Limit = 19,000 ppm
* = >10% LEL; ** = >50% LEL; *** = >100% LEL
AEGL 1 - 10 min = ** 10,000 ppm
AEGL 2 - 10 min = *** 24,000 ppm; 30 min/60 min/4 hr/8 hr = ** 17,000 ppm
AEGL 3 - 10 mins = *** 77,000 ppm; 30 min/60 min/4 hr/8 hr = *** 53,000 ppm
For values denoted as † safety considerations against the hazard(s) of explosion(s) must be taken into account.
For values denoted as ** and *** extreme safety considerations against the hazard(s) of explosion(s) must be taken into account.

2 Animal Toxicity Data

Lethal concentrations of butane were evaluated in rats and mice. Shugaev [1969] reported LC_{50} values of 278,000 ppm in rats exposed to butane for 4 hours, and 287,000 ppm in mice exposed for 2 hours. No other signs of toxicity were reported. Several studies evaluated acute toxicity under static conditions; these studies were not considered appropriate for derivation of an IDLH value.

Nonlethal animal-exposure data with classical endpoints were limited to a single study. In guinea pigs, Nuckolls [1933] observed irregular and rapid breathing in animals exposed to 21,000 ppm for 2 hours, which escalated to retching and a dazed appearance at 50,000 ppm for 2 hours. Although the animals were able to walk, this exposure was considered potentially escape-impairing. Furthermore, although this is an older study, exposure concentrations were monitored and adjusted to maintain the nominal exposure levels. Other studies found that butane is a cardiac sensitizer [Chenoweth 1946; Krantz et al. 1948] and can cause hemodynamic effects (decreased cardiac output, decreased ventricular or aortic pressure) [Zakhari 1977], but these studies were not considered appropriate for IDLH value derivation because of the limited details and exposure under anesthesia.

Table 4 provides nonlethal-exposure data on humans and animals from studies with 30-minute-equivalent derived values for butane. Information in these tables includes species of test animals, toxicological metrics (i.e., LC, BMCL, NOAEL, and LOAEL), adjusted 30-minute concentration, and the justification for the composite uncertainty factors applied to calculate the derived values.

Table 4: Nonlethal-concentration data for butane

Reference	Species	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)‡
Nuckolls [1933]	Guinea pig	Irregular and rapid breathing; retching	—	50,000	120	79,371	10§	7,937	7,937
Patty and Yant [1929]	Human	No effect	10,000	—	10	3,333	1¶	3,333	3,333

*For exposures other than 30 minutes, the ten Berge et al. [1986] relationship is used for duration adjustment (C^n 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. Additional information on the calculation of duration-adjusted concentrations can be located 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 adjustment from a severe effect threshold in humans and human variability.

3 Human Data

Numerous case reports involving acute inhalation of butane are available. Many of these reports document cases of the intentional inhalation, or "huffing," of butane-containing products as a means to become intoxicated [Doring et al. 2002; Kile et al. 2006; Sen and Erdivanli 2015]. The health effects documented in these studies include ventricular fibrillation, encephalopathy, pulmonary distress, and death. Although there are a number of case reports on lethality in humans from exposure to butane, none of the available studies provided information on exposure levels. In the only human study report on exposure concentrations, Patty and Yant [1929] described no symptoms except drowsiness in individuals that were exposed to up to 1% butane concentrations (10,000 ppm) for 10 minutes. Despite the absence of exposure data, available studies indicate that acute inhalation of butane may result in life-threatening health effects.

4 Summary

Despite the availability of toxicity data capable of being used to calculate health-based estimates for butane (see Table 4), these estimates are all 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 to account for safety considerations related to the potential hazard of explosion [NIOSH 2013]. The LEL for butane is 1.6%, or 16,000 ppm [NIOSH 2016]. The IDLH value is set at the 10% LEL for butane of 1,600 ppm.

If the explosive hazards of butane are controlled or toxicity issues are the primary concern, a health-based IDLH value could be derived from numerous datasets. The lowest LC_{50} value identified was 287,000 ppm for 2 hours in mice [Shugaev 1969]. The duration-adjusted LC_{50} value for a 30-minute exposure is 382,700 ppm. An uncertainty factor of 30 would be applied to account for extrapolation from a concentration that is lethal to animals, animal to human differences, and human variability, resulting in a potential IDLH value of 13,000 ppm. However, a more appropriate study from which to base the IDLH value is available. A LOAEL for signs of disorientation and toxicity was identified in guinea pigs exposed to 50,000 ppm for 2 hours [Nuckolls 1933]. The duration-adjusted LOAEL for a 30-minute exposure is 73,371 ppm. An uncertainty factor of 10 is applied to account for extrapolation from a concentration that causes escape-impairing effects in animals, animal to human differences, and human variability, resulting in an IDLH value of 7,937 ppm. This value is supported by the human data [Patty and Yant 1929], which indicated drowsiness following exposure to 10,000 ppm for 10 minutes, although there were uncertainties with the study. The IDLH value is a health-based value and may not protect from physical hazards associated with butane exposure. For example, safety concerns may result when butane exposures exceed 1,600 ppm, which is 10% of the LEL.

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