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Derivation of Immediately Dangerous to Life or Health (IDLH) Values

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

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Foreword

Since the establishment of the original Immediately Dangerous to Life or Health (IDLH) values in 1974, the National Institute for Occupational Safety and Health (NIOSH) has continued to review available scientific data to improve the methodology used to derive acute exposure guidelines, in addition to the chemical-specific IDLH values. The primary objective of this Current Intelligence Bulletin (CIB) is to present a methodology, based on the modern principles of risk assessment and toxicology, for the derivation of IDLH values, which characterize the health risks of occupational exposures to high concentrations of airborne contaminants. The methodology for deriving IDLH values presented in the CIB incorporates the approach established by the National Advisory Committee on Acute Exposure Guideline Levels (AEGLs) for Hazardous Substances—consisting of members from the U.S. Environmental Protection Agency, U.S. Department of Defense, U.S. Department of Energy, U.S. Department of Transportation, other federal and state government agencies, the chemical industry, academia, labor, and other organizations from the private sector—during the derivation of community-based acute exposure limits. The inclusion of the AEGL methodology has helped ensure that the IDLH values derived with use of the guidance provided in this document are based on validated scientific rationale.

The intent of this document is not only to update the IDLH methodology used by NIOSH to develop IDLH values based on contemporary risk assessment practices, but also to increase the transparency behind their derivation. The increased transparency will provide occupational health professionals, risk managers, and emergency response personnel additional information that can be applied to improve characterization of the hazards of high concentrations of airborne contaminants. This will also facilitate a more informed decision-making process for the selection of respirators and establishment of risk management plans for non-routine work practices and emergency preparedness plans capable of better protecting workers.

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Executive Summary

Chemicals are a ubiquitous component of the modern workplace. Occupational exposures to chemicals have long been recognized as having the potential to adversely affect the lives and health 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 outcomes that may include irritation of the eyes and respiratory tract, severe irreversible health effects, impairment of the ability to escape from the exposure environment, and, in extreme cases, death. Airborne concentrations of chemicals capable of causing such adverse health effects or of impeding escape from high-risk conditions may arise from a variety of non-routine workplace situations affecting workers, 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).

Since the 1970s, the National Institute for Occupational Safety and Health (NIOSH) has been responsible for the development of acute exposure guidelines called Immediately Dangerous to Life or Health (IDLH) values, which are intended to characterize these high-risk conditions. Used initially as key components of the *NIOSH Respirator Selection Logic* [NIOSH 2004], IDLH values are established (1) to ensure that the worker can escape from a given contaminated environment in the event of failure of the respiratory protection equipment and (2) to indicate a maximum level above which only a highly reliable breathing apparatus, providing maximum worker protection, is permitted. In addition, occupational health professionals have employed these acute exposure guidelines beyond their initial purpose as a component of the *NIOSH Respirator Selection Logic*. Examples of such applications of the IDLH values include the development of Risk Management Plans (RMPs) for non-routine work practices governing operations in high-risk environments (e.g., confined spaces) and the development of Emergency Preparedness Plans (EPPs), which provide guidance for emergency response personnel and workers during unplanned exposure events.

Since the establishment of the IDLH values in the 1970s, NIOSH has continued to review available scientific data to improve the protocol used to derive acute exposure guidelines, in addition to the chemical-specific IDLH values. The information presented in this Current Intelligence Bulletin (CIB) represents the most recent update of the scientific rationale and the methodology (hereby referred to as the IDLH methodology) used to derive IDLH values. The primary objectives of this document are to

- Provide a brief history of the development of IDLH values
- Update the scientific bases and risk assessment methodology used to derive IDLH values from quality data
- Provide transparency behind the rationale and derivation process for IDLH values
- Demonstrate how scientifically credible IDLH values can be derived from available data resources.

The IDLH methodology outlined in this CIB reflects the modern principles and understanding in the fields of risk assessment, toxicology, and occupational health and provides the scientific rationale for the derivation of IDLH values based on contemporary risk assessment practices. According to this protocol, IDLH values are based on health effects considerations determined through a critical assessment of the toxicology and human health effects data. This approach ensures that the IDLH values reflect an airborne concentration of a substance that represents a high-risk situation that may endanger workers' lives or health. Relevant airborne concentrations are typically addressed through the characterization of inhalation exposures; however, airborne chemicals can also contribute to toxicity through other exposure routes, such as the skin and eyes. In this document, airborne concentrations are referred to as *acute inhalation limits or guidelines* to adhere to commonly used nomenclature.

The emphasis on health effects is consistent with both the traditional use of IDLH values as a component of the respirator selection logic and the growing applications of IDLH values in RMPs for non-routine work practices governing operations in high-risk environments (e.g., confined spaces) and the development of EPPs. Incorporated in the IDLH methodology are the standing guidelines and procedures [NAS 2001] used for the development of community-based acute exposure limits called Acute Exposure Guideline Levels (AEGLs). The inclusion of the AEGL methodology has helped ensure that the health-based IDLH values derived with use of the guidance provided in this document are based on validated scientific rationale.

The IDLH methodology is based on a weight-of-evidence approach that applies scientific judgment for critical evaluation of the quality and consistency of scientific data and in extrapolation from the available data to the IDLH value. The weight-of-evidence approach refers to critical examination of all available data from diverse lines of evidence and the derivation of a scientific interpretation on the basis of the collective body of data, including its relevance, quality, and reported results. This is in contrast to a purely hierarchical or strength-of-evidence approach, which relies on rigid decision criteria for selecting a critical adverse effect, a point of departure (POD), or the point on the dose–response curve from which dose extrapolation is initiated and for applying default uncertainty factors (UFs) to derive the IDLH value. Conceptually, the derivation process for IDLH values is similar to that used in other risk-assessment applications, including these steps:

- Hazard characterization
- Identification of critical adverse effects
- Identification of a POD
- Application of appropriate UFs, based on the study and POD
- Determination of the final risk value.

However, the use of a weight-of-evidence approach allows for integration of all available data that may originate from different lines of evidence into the analysis and the subsequent derivation of an IDLH value. Ideally, this ensures that the analysis is not restricted to a limited dataset or a single study for a specific chemical. In particular, application of the appropriate UFs to each potential POD allows for consideration of the impact of the overall dataset as well as the uncertainties associated with each potential key study in determining the final IDLH value.

The primary steps (*see Figure 3–1*) applied in the establishment of an IDLH value include the following:

- Critical review of human and animal toxicity data to identify potential relevant studies and characterize the various lines of evidence that can support the derivation of the IDLH value
- Determination of a chemical's mode of action (MOA) or description of how a chemical exerts its toxic effects
- Application of duration adjustments (time scaling) to determine 30-minute-equivalent exposure concentrations and the conduct of other dosimetry adjustments, as needed
- Selection and application of a UF for POD or critical adverse effect concentration, identified from the available studies to account for issues associated with interspecies and intraspecies differences, severity of the observed effects, data quality, or data insufficiencies
- Development of the final recommendation for the IDLH value from the various alternative lines of evidence, with use of a weight-of-evidence approach to all of the data.

NIOSH recognizes that in some cases a health-based IDLH value might not account for all workplace hazards, such as safety concerns or considerations. Here are some examples of situations and conditions that might preclude the use of a health-based IDLH value:

- The airborne concentration of a substance is sufficient to cause oxygen deprivation (oxygen concentration <19.5%), a life-threatening condition
- The concentration of particulate matter generated during a process significantly reduces visibility, preventing escape from the hazardous environment
- The airborne concentration of a gas or vapor is greater than 10% of the lower explosive limit (LEL) and represents an explosive hazard.

In such cases, it is important that safety hazards or other considerations be taken into account. Information on the safety hazards will be incorporated in the support documentation (*see Appendix A*) for an IDLH value, to aid occupational health professionals in the development of RMPs for non-routine work practices governing operations in high-risk environments (e.g., confined spaces) and EPPs. In the event that the derived health-based IDLH value exceeds 10% of the LEL concentration for a flammable gas or vapor, the air concentration that is equal to 10% of the LEL will become the default IDLH value for the chemical. The following hazard statement will be included in the support documentation: "The health-based IDLH value is greater than 10% of the LEL (>10% LEL) of the chemical of interest in the air. Safety considerations related to the potential hazard of explosion must be taken into account." In addition, the notation ">10% LEL" will appear beside the IDLH value in the *NIOSH Pocket Guide to Chemical Hazards* [NIOSH 2005] and other NIOSH publications. The equivalent default approach for dust would be based on 10% of the minimum explosive concentration (MEC). However, determining the combustibility of dusts is complicated and dictated by the relationship between multiple dust-specific factors including, but not limited to, particle size distribution, minimum ignition energy, explosion intensity, and dispersal in the air [Cashdollar 2000]. The ability to quantify dust-specific concentrations that could represent explosive hazards for risk assessment purposes is limited and often not possible given the absence of critical data, such as chemical-specific MEC and other previously identified factors. Despite the absence of specific guidance, NIOSH will critically assess the explosive nature of a dust when sufficient technical data are available. If determined to be appropriate, the findings of this assessment will be incorporated into the derivation process to ensure that the IDLH value is protective against both health and safety hazards. When an explosive hazard is identified for an aerosol, NIOSH will include the following hazard statement: "Dust may represent an explosive hazard. Safety considerations related to hazard of explosion must be taken into account." In addition, the notation (Combustible Dust) will appear in other NIOSH publications.

Supplemental information is included in this CIB to provide insight into (1) the literature search strategy, (2) the scheme used to prioritize and select chemicals for which an IDLH value will be established, and (3) an overview of the analysis applied by NIOSH to develop a scientifically based approach for the selection of the UF during the derivation of IDLH values. In addition, Appendix A presents an example of the derivation of an IDLH value for chlorine (CAS# 7782-50-5), based on the scientific rationale and process outlined in this CIB. The example highlights the primary steps in establishment of an IDLH value, including a critical review of the identified human and animal data, discussion of the selection of the POD and UF, and extrapolation of the 30-minute-equivalent exposure concentration from animal toxicity data.

Contents

Abbreviations and Acronyms

ACGIH	American Conference of Governmental Industrial Hygienists
AIHA	American Industrial Hygiene Association
AEGL	Acute Exposure Guideline Level (published by NRC)
AUC	area under the curve
ATSDR	Agency for Toxic Substances and Disease Registry
BBDR	biologically based dose response
BMC	benchmark concentration
BMCL	benchmark concentration lower-bound confidence limit
BMD	benchmark dose
BMDS	Benchmark Dose Software (developed by USEPA)
"C"	ceiling value
CA	carcinogen
Cal/EPA	California Environmental Protection Agency
CAS#	Chemical Abstracts Service Registry Number
CDC	Centers for Disease Control and Prevention
CFATS	Chemical Facility Anti-Terrorism Standards (developed by DHS)
CFR	Code of Federal Regulations
CHEMID	online chemical identification database (developed by NLM)
CIB	Current Intelligence Bulletin (developed by NIOSH)
C_{max}	peak (maximum) concentration
CNS	central nervous system
COHb	carboxyhemoglobin
Conc	concentration
DHHS	U.S. Department of Health and Human Services
DHS	U.S. Department of Homeland Security
DOD	U.S. Department of Defense
DOE	U.S. Department of Energy
DOL	U.S. Department of Labor
DOT	U.S. Department of Transportation
DT	developmental toxicant
EC	effective concentration

EEGL	Emergency and Continuous Exposure Guidance Levels (published by NRC)
EINECS	European INventory of Existing Commercial chemical Substances
EMBASE	online biomedical journal abstract and indexing database (subscription based)
EPP	Emergency Preparedness Plan
ERPG	Emergency Response Planning Guidelines (developed by AIHA)
ERG	Emergency Response Guidebook (developed by DOT)
EU	European Union
FEL	frank effect level
FACA	Federal Advisory Committee Act
GI	gastrointestinal
GLP	Good Laboratory Practices
HAZARDTEXT®	online hazardous substance database (subscription based)
HazMap	online occupational exposure to hazardous agents database (developed by NLM)
HCN	hydrogen cyanide
hr	hour
HPV	high production volume
HSDB	Hazardous Substance Data Bank (developed by NLM)
HSEES	Hazardous Substance Emergency Events Surveillance (developed by ATSDR)
IARC	International Agency for Research on Cancer
ICSC	International Chemical Safety Cards (developed by IPCS)
IDLH	Immediately Dangerous to Life or Health (developed by NIOSH)
i.p.	intraperitoneal
IPCS	International Programme on Chemical Safety
IRIS	Integrated Risk Information System (developed by USEPA)
IRR	irritant
ITER	International Toxicity Estimates for Risk database (developed by TERA)
JSC	Johnson Space Center (division of NASA)
k	a constant reflected in equations expressing “conc × time” relationships
kg	kilogram
L	liter
LC	lethal concentration

LD	lethal dose
LEL	lower explosive limit
L/min	liters per minute
LOAEL	lowest observed adverse effect level
LOEL	lowest observed effect level
m^3	cubic meter
MEC	minimum explosive concentration
MEDITEXT®	online medical and toxicology database (subscription based)
mg/m^3	milligrams per cubic meter of air
mg/m^3-min	milligrams per cubic meter of air per minute
min	minute
MOA	mode of action
MSHA	Mine Safety and Health Administration
NAC/AEGL	National Advisory Committee for Acute Exposure Guideline Levels for Hazardous Substances
NASA	National Aeronautics and Space Administration
NAS/NRC	National Academy of Sciences/National Research Council
NIOSH	National Institute for Occupational Safety and Health
NIOSHTIC2	bibliographic database of NIOSH-supported occupational safety and health publications
NJ-HSFS	New Jersey Hazardous Substance Fact Sheets
NLM	National Library of Medicine
NOAEL	no observed adverse effect level
NOEL	no observed effect level
NRC	National Research Council
NTP	National Toxicology Program
OECD	Organisation for Economic Co-operation and Development
OEL	occupational exposure limit
OSHA	Occupational Safety and Health Administration
PAL	Provisional Advisory Levels (developed by DHS)
PBPK	physiologically based pharmacokinetic
PEL	Permissible Exposure Limit (developed by OSHA and MSHA)
ppm	parts per million
POD	point of departure
PUBMED	online biomedical literature citation database (developed by NLM)

RD	respiratory depression
REL	Recommended Exposure Limit (developed by NIOSH)
RfC	inhalation reference concentration
RIVM	Netherlands National Institute for Public Health and the Environment
RMP	Risk Management Plan
R-phrases	risk phrases (developed by EU)
RTECS	Registry of Toxic Effects of Chemical Substances
SCAPA	Subcommittee on Consequence Assessment and Protective Actions
SCBA	self-contained breathing apparatus
SCP	Standards Completion Program (developed by NIOSH and OSHA)
SMAC	Spacecraft Maximum Allowable Concentration (developed by NASA, published by NRC)
SOP	Standing Operating Procedures
SPEGL	Short-term Public Emergency Guidance Levels (developed by NRC)
STEG	short-term exposure guidelines
STEL	Short Term Exposure Limit
ST	short-term exposure limit
TEEL	Temporary Emergency Exposure Limit (developed by DOE)
TERA	Toxicology Excellence for Risk Assessment
TIH	toxic inhalation hazard (developed by DOT)
TLV®	Threshold Limit Value (developed by ACGIH)
TOXLINE	online toxicology literature database (developed by NLM)
TWA	time-weighted average
UF	uncertainty factor
USEPA	U.S. Environmental Protection Agency
WEEL	Workplace Environmental Exposure Limits (developed by AIHA)
WHO	World Health Organization

Glossary*

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

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

Acute Reference Concentration (RfC): An estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure for an acute duration (24 hours or less) of the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. It can be derived from a NOAEL, LOAEL, or benchmark concentration, with uncertainty factors (UFs) generally applied to reflect limitations of the data used. Generally used in USEPA noncancer health assessments [USEPA 2010].

Acute Toxicity: Any poisonous effect produced within a short period of time following an exposure, usually 24 to 96 hours.

Acute Toxicity Test: Experimental animal study to determine what adverse effects occur in a short time (usually up to 14 days) after a single dose of a chemical or after multiple doses given in up to 24 hours.

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

Analytical (Actual) Concentration: The test article concentration to which animals are exposed (i.e., the concentration in the animals' breathing zone), as measured by analytical (GC, HPLC, etc.) or gravimetric methods. The analytical or gravimetric concentration (not the nominal concentration) is usually used for concentration response assessment.

Assigned Protection Factor (APF): The minimum anticipated protection provided by a properly functioning respirator or class of respirators to a given percentage of properly

*Except where specific references are given, glossary definitions are from numerous sources such as AIHA [2008], Hayes [2008], IUPAC [2007], NAS [1986, 2001], NASA [1999], NIOSH [2005], OSHA [2003], US DHS [2007], US DOE [2008], and US DOT [2008].