Recent Developments of an Updated Methodology for Deriving Immediately Dangerous to Life or Health (IDLH) Values: Science Methods and Comparison to Other Acute Limit Values

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Abstract

Objective: NIOSH is updating the methods used in deriving Immediately Dangerous to Life or Health (IDLH) values. This presentation provides an analysis of proposed IDLH values resulting from the application of the methodology update. Challenging issues in health effects data interpretation are highlighted using a case study approach.

Methods: The analyses presented were performed through systematic data evaluation using revised weight of evidence procedures that are incorporated into the proposed changes to the IDLH methods. Key aspects of the method include more rigorous documentation of the evaluation of key studies to identify a point of departure, application of duration adjustment procedures, and updated considerations for uncertainty factor application.

Results: We applied the proposed methodology to data sets for over 40 chemicals of diverse nature. Thus, a rigorous testing of the range of issues likely to be encountered in data evaluation was conducted. We found that the methods provide for concise presentation of conclusions, while allowing for a transparent approach to address diverse data sets. For example, the methods ably address a wide range of endpoints ranging in severity from lethality to escape-impairing irritation. The methods provide clarity in interpreting the relevance of different toxicological effects. Data sets from human experience or animal toxicology by different routes of exposure are well accommodated. An updated and transparent approach is included in the method to describe the impacts of uncertainties in extrapolation from different data sets.

What is an IDLH value?

IDLH values derived by the National Institute of Occupational Safety and Health (NIOSH):

- Have an important history in defining work practice requirements with potential entry into high exposure environments, and
- Are derived as 30-min maximum airborne concentrations above which only a highly reliable breathing apparatus providing maximum worker protection is permitted.

Evolution of the IDLH and Current Update Project

- NIOSH has been investigating methods to improve the derivation of Immediately Dangerous to Life or Health (IDLH) values.
- NIOSH research has been conducted to evaluate key science considerations in IDLH development.
- The result of these efforts was the development of an updated methodology, that is undergoing peer review.
- This poster highlights some of the key changes in the methodology and the relationship between the IDLH values and other acute exposure limits.

Acute Exposure Guidelines

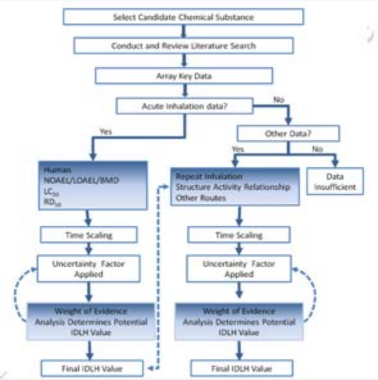
Application	Organization	Exposure Guideline Name
Occupational		
Routine	ACGIH	Threshold Limit Value, Short Term Exposure Limit (TLV-STEL®; TLV-Ceiling)
	AIHA	Workplace Environmental Exposure Levels, Short Term Exposure Limit (WEEL-STEL™)
	NIOSH	Recommended Exposure Limit (REL)
	OSHA	Permissible Exposure Level (PEL)
	U.S. EPA	Pesticide application and new chemical registration limits
Non-routine	NIOSH	Immediately Dangerous to Life and Health (IDLH)
	U.S. DoD	War fighter or submarine air quality limits
General Public		
Routine	Cal EPA	Acute reference exposure limits (REL)
	TCEQ	Effects screening levels (ESL)
	U.S. EPA	Acute Reference Concentrations (aRfC)
Non-Routine	AIHA	Emergency Response Planning Guidelines (ERPG™)
	NAS/NRC	Acute Emergency Guideline Levels (AEGL)
	U.S. DOE	Temporary Emergency Exposure Levels (TEEL)

Proposed IDLH derivation method

- IDLH values are based on health effects considerations determined through a critical assessment of the toxicology and human health effects data conceptually similar to that used in other risk assessment applications.
- The updated protocol is based on a weight-of-evidence (WOE) approach that applies scientific judgment for the critical evaluation of the quality and consistency of the scientific data, and includes:
  - 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 conduct of other dosimetry adjustments as needed;
  - Selection and application of an UF to the POD or critical adverse effect concentration identified from the available studies; and
  - Development of the final recommendation for the IDLH value from the various alternative lines of evidence using a weight of evidence approach with all of the data.

WOE defined

- The weight of evidence approach refers to the critical examination of all the available data from diverse lines of evidence and the derivation of a scientific interpretation based on the collective body of data including its relevance, quality and reported results.
- WOE approach is more an integrative, and is used to develop the IDLH value based on consideration of alternatives and different lines of evidence, instead of using a strict data hierarchy.



Science Issue: Point of Departure (POD)

Selection of the critical study to serve as the basis for the IDLH designed to prevent:

- Lethality
- Serious or irreversible effects
- Effects that might impair escape from exposure

Critical effect determination takes into consideration:

- Study quality (toxic endpoint, species used and number of subjects)
- Study relevance (exposure and duration are relevant)
- Severity of effects (e.g., none, mild, severe, % lethality, escape impairing)

Science Issue: Uncertainty Factor (UF)

- Application of the appropriate UF 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.
- A range of preferred UFs is shown for each of the typical types of effect levels that are available as a POD. The final UF reflects chemical specific data.

Typical Composite UFs

Point of Departure	Typical UF Range
LC_{50} (in an animal study)	10 to 100
LC_{01}, LC_{Lo}, or $BMCL_{10}$ for lethality in animals	3 to 30
LC_{Lo} in humans	1 to 10
LOAEL for an escape impairing or irreversible effect in animals	3 to 30
NOAEL for an escape impairing or irreversible effect in animals, or animal RD_{50}	1 to 10
LOAEL for an escape impairing or irreversible effect in humans	1 to 10
NOAEL for an escape impairing or irreversible effect in humans	1 to 3

Science Issues: Duration Adjustment

The following approach is used in extrapolating across durations for development of IDLH values:

- No extrapolation is needed if the study exposure is 30 minutes,
- For acute studies of other durations – ten Berge (1986) equation is used for extrapolation (see below),
- Chemical specific "n" value is derived for ten Berge equation if study data is available (species and MOA are relevant),
- Default "n" values are used if chemicals specific data is not available.
  - n = 3 when extrapolating from exposures greater than 30 minutes
  - n = 1 when extrapolating from exposures less than 30 minutes.

$$\text{30-min adjusted value} = C_1 \times \left(T_1 \div 30\right)^{1/n}$$

Science Issue: Safety Hazards

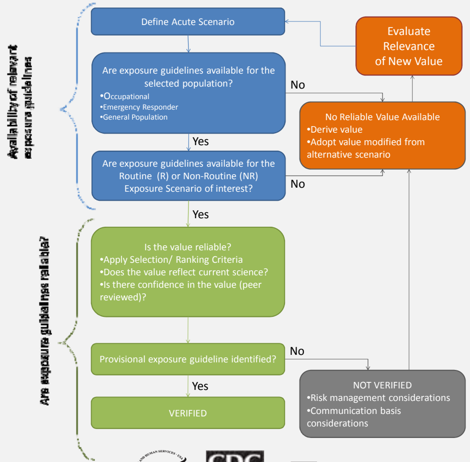
NIOSH recognizes that in some cases a health-based IDLH value might not account for all workplace hazards, (i.e., safety concerns), these situations include but are not limited to:

- Airborne concentration causes oxygen deprivation (oxygen concentration <19.5%), which represents a life-threatening condition (e.g. argon gas, carbon dioxide, and nitrogen),
- Particulate matter concentration significantly reduces visibility preventing escape from the hazardous environment,
- Airborne concentration represents an explosive hazard (greater than 10% of the lower explosive limit (LEL), e.g. acetone, ethyl acetate, and n-pentane); or
- Health based IDLH value is greater than the time-weighted average (TWA) occupational exposure limit (OEL) multiplied by the assigned protection factor (APF) for the most protective respirator (e.g., chromic acid, chromates, and lead compounds).

Selection of Acute Limits

How to decide which value among many?

- Mandated regulatory hierarchy,
- Other considerations to weigh in decision
  - Relevance of the guide value to the scenario of interest,
  - The degree to which the exposure guidance includes current literature and methods (development and *full* review date), and
  - Confidence in the value.
- IDLH values considered in process of acute value selection for occupational, non-routine exposures.



Example of Acute Exposure Limits for Vinyl Acetate

Limit	Value
TLV®	10 ppm, TWA; 15 ppm, STEL
WEEL™	Not established
NIOSH REL	4 ppm (15 mg/m³), 15-minute
PEL	Not established
IDLH (proposed)	100 ppm (352 mg/m³)
ERPG	ERPG-1: 5 ppm; ERPG-2: 75 ppm; ERPG-3: 500 ppm
AEGL	30-min AEGL 1: 6.7 ppm (24 mg/m³) 30-min AEGL 2: 230 ppm (810 mg/m³) 30-min AEGL 3: 760 ppm (2700 mg/m³)
Cal EPA REL	200 µg/m³ (50 ppb)
TCEQ ESL	150 µg/m³

Conclusions

- The revised methodology is likely to generate significant improvements in the interpretation and robust application of the IDLH values.
- IDLH values play an important role as credible peer-reviewed values as part of the IH tool box of acute exposure limits.
- These science enhancements and communication of the role of the IDLH values relative to other values is important due to the increasing role of the IH in addressing diverse occupational, emergency, and environmental exposure scenarios.

Acknowledgment and Disclaimer

- The findings and conclusions in this presentation have not been formally disseminated by NIOSH and should not be construed to represent any agency determination or policy.