U.S. Army Public Health Center

TG No. 373, Supplement B

One-Hour Acute Reference Concentrations for Intermittent Environmental Exposures in the General Population

December 2020

APHC

Environmental Health Sciences and Engineering Directorate
Toxicology Directorate

Technical Guide 373 Support Webpages:

Publicly accessible site:

https://phc.amedd.army.mil/topics/envirohealth/hrasm/Pages/TG373.aspx

Department of Defense collaboration site:

https://www.milsuite.mil/book/groups/tg373/

Forward questions and comments to—

U.S. Army Public Health Center
Risk Assessment Capabilities Branch
Environmental Health Risk Assessment Division
Aberdeen Proving Ground, Maryland
usarmy.apg.medcom-aphc.list.racb@mail.mil

Contents

Appendices

Figures

Tables

Technical Guide 373, Supplement B
One-Hour Acute Reference Concentrations for Intermittent Environmental Exposures in the General Population
December 2020

1. PURPOSE

This document describes a method for selecting and developing chemical-specific exposure guidelines for the evaluation of intermittent (e.g., twice per year), 1-hour (hr) acute inhalation exposures in human health risk assessments. This method is designed for use in the evaluation of exposures to the general population.

2. REFERENCES AND TERMS

Appendix A provides the references cited, and the **Glossary** provides a list of acronyms.

3. BACKGROUND

Selection of an appropriate acute inhalation exposure guideline depends on the expected exposure characteristics, the time frame of interest, and the purpose of the assessment. Acute human exposure is defined by the U.S. Environmental Protection Agency (EPA) as an exposure of less than 2 weeks' duration (EPA 1989). In this application, however, the definition is restricted to exposure durations of approximately 1-hr but are potentially intermittent in their occurrence (e.g., twice per year), rather than 1-hr exposures that rarely occur at all. This specific definition is appropriate for risk assessments focusing on the non-emergency, routine operations of hazardous waste combustion facilities and munitions open burning, open detonation, and training and testing grounds operated by the military. However, this definition is not necessarily equivalent to all of the acute exposure definitions used by other agencies to establish some of the available acute guidelines.

3.1 Acute Reference Concentrations

Acute exposure guidelines are named differently depending upon the source of the values. Regardless of their source, the exposure guidelines generated using this document are referred to as acute reference concentrations (ARCs). They apply to the inhalation exposure pathway, representing "safe" 1-hr average concentrations that the public may experience infrequently (e.g., twice per year). Note that ARCs are intended specifically for preparing risk assessments of 1-hr acute exposures from non-emergency routine releases (less-than-lifetime exposure), not to be confused with chronic toxicity values (lifetime exposures). ARC values are expressed in units of milligrams per cubic meter (mg/m^3).

The ARCs may not necessarily apply to emergency (or rare) exposures or to specific populations (e.g., military populations). The degree to which these values are appropriate for any particular assessment should be determined on a case-by-case basis. Additionally, values generated using these methods are not designed to be extrapolated to other routes of exposure.

The process used to generate the ARCs presumes that the health impacts of concern for acute exposures include both local irritation and systemic, non-cancer effects associated with short duration (1-hr) exposures that may be intermittent over time. One-hour ARCs are designed to protect the health of the general population, which may be exposed on an intermittent basis throughout any given year. While the approach for generating ARCs described in this document is largely based on the hierarchy provided in EPA combustion guidance (EPA 2005), it does include a few deviations from that protocol (see **Section 5**).

3.2 Exposure Characteristics and Available Guidelines

Several organizations within the U.S. develop guidelines for short-term exposures to chemical substances. These exposure guidelines serve to protect a variety of groups, exposed for various lengths of time, and are derived from a vast array of toxicity endpoints ranging from discomfort or mild adverse health effects to serious, debilitating, and potentially life-threatening effects, up to and including death (EPA 2005). No single agency currently provides exposure guidelines for all potential chemicals of risk assessment concern. Consideration and occasional adjustment of the available exposure guidelines are necessary before their application to the general public because of the heterogeneity of the groups, toxic effects, and durations for which the alternative values are developed. For this reason, all values adopted will be referred to as ARCs, emphasizing that they have been either adjusted to fit the ARC definition or determined to fit the definition as developed.

3.2.1 Typical Exposure Characteristics for Combustion Facilities

Risk assessments of acute exposure to combustion facility emissions are based on air concentrations estimated from routine facility process upsets, referring to operating conditions where emissions are intermittently higher than normal (EPA 2005). Emissions from these process upsets are considered sufficiently higher so as to be independent of the longer-term chronic emissions (CalEPA 2008) but which are not expected to significantly increase emissions over the lifetime of the facility (EPA 2005). These upset conditions differ from accidental releases, which are associated with non-routine emissions that could result in complete equipment failure (e.g., fire). Because facility upsets are of short duration (about 1 hr or less) and “routine,” a facility’s emissions could exceed those of normal operating conditions more than once a year. Thus, the ARCs generated using these methods are designed to address these intermittent exposures.

In the absence of empirical data, regulatory agencies generally assume that emissions during upset conditions are 10 times higher than those during normal operating conditions (EPA 2005). Actual emissions during upsets may likely be lower and will depend upon the design, construction, and operation of the facility. The reporting of emissions during upsets will depend on the ability of the facility’s monitoring systems to characterize emissions during these events. It is important to also understand that the actual number of upset events that may occur each year will vary across facilities and may also vary year to year for any given facility.

3.2.2 Typical Exposure Characteristics for Military Open Burning, Open Detonation, and Munitions Training or Testing Operations

Risk assessments of acute/intermittent exposure to emissions from open burning and open detonation (OB/OD) grounds are based on modeled air concentrations that attempt to represent downwind dispersion of emissions associated with the short time frames of munitions detonation and burning events. The available risk management controls on OB/OD emissions include (1) strict permit conditions that typically limit the quantity of material that may be burned or detonated on an hourly and yearly basis, (2) restrictions that allow operations only under certain meteorological conditions, and (3) restrictions on the time of day that operations can occur. Unlike incinerator sources, routine "upset" conditions are not expected events associated with site operations or maintenance. Therefore, OB/OD risk assessments generally evaluate acute exposures by modeling the dispersion of emissions from a maximum hourly burn or detonation rate that is associated with the site.

As part of the military mission, munitions training and testing sites also present a situation where risk assessments may be performed to estimate the potential for public health concerns related to downwind exposure to munitions emissions. Like OB/OD evaluations, these assessments also evaluate acute exposures by modeling the downwind dispersion of emissions. In these analyses, however, the focus has typically been on one munitions item at a time, and different data are often available for estimating their emissions. The dispersion models used may also differ based on the type of munitions item being evaluated. Different dispersion models provide differing capabilities in terms of the averaging times for predicted concentrations (e.g., hourly average vs. 15-minute (min) average or instantaneous concentrations).

3.2.3 Project Considerations

For each project, particularly military-unique situations, the risk assessment team should assess the degree to which the ARCs developed using this method correspond to the expected exposure characteristics associated with the specific project. Following are three considerations; additional considerations appear in **Section 5.3**.

- Determine whether the project's dispersion model estimates 1-hr or 15-min predicted concentrations. Reference concentrations generated by this algorithm for 1-hr exposure times may need to be readjusted (or not adjusted) to integrate properly with output from models that are limited to 15-min predictions.

- Some of the available sources of acute inhalation exposure guidelines are intended for catastrophic exposures. These sources assume once-in-a-lifetime or emergency exposures and may not necessarily be designed to protect sensitive sub-populations.

- The wait period between exposures (the periodicity) is generally unknown or quite uncertain. This should be considered by risk managers when risk target levels are potentially exceeded for chemicals that are based on these surrogate guidelines. In order for the risk assessment team to properly characterize the uncertainties associated

with the use of heterogeneous sources of exposure guidelines, both the objective of the assessment and the local regulatory requirements should be considered. On a project-specific basis, deviation from any particular ARC generated by the use of this method may be warranted.

4. SOURCES OF ACUTE EXPOSURE GUIDELINES

The ARC values are generated using the exposure guidelines that are available from the following authorities using the hierarchy and decision logic presented in **Section 5**.

The following is an alphabetical list of exposure guideline sources:

- Agency for Toxic Substances and Disease Registry (ATSDR)
- American Conference of Governmental Industrial Hygienists (ACGIH®)
- American Industrial Hygiene Association (AIHA)
- California Environmental Protection Agency (CalEPA)
- Centers for Disease Control and Prevention (CDC)
- Department of Energy (DOE)
- National Advisory Committee on Acute Exposure Guidelines Levels (NAC/AEGL)
- National Institute of Occupational Safety and Health (NIOSH)
- Occupational Safety and Health Administration (OSHA)

4.1 Agency for Toxic Substances and Disease Registry

The ATSDR, a part of the CDC, develops toxicological profiles and collects and provides human health effects information for a list of hazardous substances commonly found at facilities on the National Priorities List (NPL).

The ATSDR develops exposure guidelines referred to as Minimal Risk Levels (MRLs). An MRL is defined “as an estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk of adverse noncancer health effects over a specified duration of exposure” (ATSDR 2016). The MRLs include both draft and final values for acute (1–14 days), intermediate (>14–364 days), and chronic (>365 days) exposure periods for both oral and inhalation exposures. Inhalation MRLs are expressed in units of parts per million (ppm) for gases and volatiles, and milligrams per cubic meter (mg/m^3) for particles. The MRLs are generally based on the most sensitive end point and do not consider serious health effects such as irreparable kidney or liver damage.

The MRLs are intended to protect public health, including that of infants and the elderly. The ATSDR states that “[exposure] to a level above the MRL does not mean that adverse health effects will occur” (ATSDR 2016). This is the case because MRLs are not intended to be action levels but are screening levels to assist the ATSDR and other agencies to identify hazardous substances that may warrant a closer evaluation.

The method adopted by the ATSDR for development of MRLs follows the practices used by the EPA to develop reference doses and reference concentrations (ATSDR 2016), and MRLs are included in each of the ATSDR's chemical-specific toxicological profile documents. Proposed MRLs undergo vigorous review, including a public comment period, before they are finalized. MRLs are intermittently updated at the ATSDR's discretion as new data become available.

4.2 American Conference of Governmental Industrial Hygienists

The ACGIH is a private, non-profit corporation whose members consist of industrial hygienists or other occupational health and safety professionals. The ACGIH publishes Threshold Limit Values® (TLVs®), which are air concentrations to which nearly all workers may be exposed safely over their occupational lifetime. TLVs are intended to serve as guidelines to assist trained industrial hygienists in making decisions related to workplace exposure to hazardous substances.

A committee within the ACGIH uses information from industrial experience and published, peer-reviewed literature to develop TLVs. Resulting TLVs are health-based, as no consideration is given to either economic or technical feasibility in the development process. However, the specific basis for each TLV may differ because the committee has not adopted a unified approach to develop the TLVs.

The ACGIH publishes three categories of TLVs: time-weighted averages (TWAs), short-term exposure levels (STELs), and a ceiling limit (C). The TLVs are updated annually and are commercially available from the ACGIH. The currently available update is 2017. The ACGIH also publishes separate documentation that describes how the TLVs are determined. The ACGIH's definitions for each TLV category are summarized below (ACGIH 2017):

- TLV-TWA: The TWA concentration for a conventional 8-hr workday and a 40-hr workweek to which it is believed that nearly all workers may be repeatedly exposed, day after day, without adverse effect.

- TLV-STEL: A 15-min TWA exposure that should not be exceeded at any time during a workday, even if the 8-hr TWA is within the TLV-TWA. The TLV-STEL is the concentration to which it is believed that workers can be exposed continuously for a short period of time without suffering from (1) irritation, (2) chronic or irreversible tissue damage, (3) dose-rate-dependent toxic effects, or (4) narcosis of sufficient degree to increase the likelihood of accidental injury, impaired self-rescue, or materially reduced work efficiency. The TWA-STEL will not necessarily protect against these effects if the daily TLV-TWA is exceeded.

- TLV-C: The concentration that should not be exceeded during any part of the working exposure.

4.3 American Industrial Hygiene Association

The AIHA, founded in 1939, is a nonprofit organization serving the needs of occupational and environmental health professionals who practice industrial hygiene in industry, government, labor, academic institutions, and independent organizations. The AIHA develops and publishes Emergency Response Planning Guidelines (ERPGs), which are designed as 1-hr planning guidelines to protect workers and the general public from the consequences of accidental chemical releases (AIHA 2016).

The ERPGs are threshold effect levels and are distinguished by varying degrees of severity of toxic effects. Three types of ERPG values are provided in the AIHA guides (AIHA 2016):

- ERPG-1: The maximum airborne concentration below which it is believed nearly all individuals could be exposed for up to 1 hour without experiencing other than mild, transient adverse health effects or without perceiving a clearly defined objectionable odor.

- ERPG-2: The maximum airborne concentration below which it is believed nearly all individuals could be exposed for up to 1 hour without experiencing or developing irreversible or other serious health effects or symptoms that could impair an individual's ability to take protective action.

- ERPG-3: The maximum airborne concentration below which it is believed nearly all individuals could be exposed for up to 1 hour without experiencing or developing life-threatening health effects.

The AIHA summary of the ERPG publication states that “[b]ecause human responses do not occur at precise exposure levels—they can extend over a wide range of concentrations—the values derived for ERPGs should not be expected to protect everyone, but should be applicable to most individuals in the general population” (AIHA 2016, p. 9).

4.4 California Environmental Protection Agency

The CalEPA Acute Reference Exposure Levels (AcRELs) are developed by the Office of Environmental Health Hazard Assessment (OEHHA) Air Toxicology and Epidemiology Section as part of its requirement to prepare risk assessment guidelines for facilities under the California Air Toxics Hot Spots Act (CalEPA 2008). The CalEPA acute recommended exposure limits (RELs) are available on-line (CalEPA 2016).

AcREL values are defined as exposures that are “not likely to cause adverse effects in a human population, including sensitive subgroups, exposed to that concentration for one hour on an intermittent basis” (CalEPA 2008, p. 70).

The AcRELs are based on the most sensitive, relevant, adverse health effect reported in the medical and toxicological literature. They are designed to protect the most sensitive individuals

in the population by inclusion of margins of safety. Since margins of safety are incorporated to address data gaps and uncertainties, exceeding the AcREL does not automatically indicate an adverse health impact (CalEPA 2008).

AcRELs are provided in $\mu g/m^3$ along with averaging times, the species used in the key study, toxicological endpoints, and effect severity levels. The AcRELs may potentially be developed for three endpoint severity levels (mild, severe, and life-threatening). These categories are based on the following toxicological findings in the database (CalEPA 2008):

- Mild adverse effect: Statistically significant findings of pre-clinical significance.
- Severe adverse effect: Clinically significant findings.
- Life-threatening: Potentially lethal effects.

In reviewing the available database for any given chemical, the CalEPA selects some of the AcRELs based on a severe effect category, while most are based on the mild effect category. The CalEPA recommends the use of AcRELs developed from data associated with severe adverse effects when an AcREL derived from mild adverse effects data is unavailable. The CalEPA suggests that such AcRELs may be replaced if more data, from toxicological literature or guideline committees, become available.

4.5 Centers for Disease Control and Prevention

The CDC's National Center for Environmental Health has published recommendations for airborne exposure limits (AELs) for several chemical warfare agents: GA, GB, VX, and Sulfur Mustard (CDC 2003, 2004). These AELs are designed to protect human health from potential adverse effects of exposure to chemical warfare agents. The AELs include four exposure criteria, which vary in their averaging time (from ≤ 30 min to 24 hrs): a General Population Limit (GPL), a Worker Population Limit (WPL), a Short-Term Exposure Limit (STEL), and an Immediately Dangerous to Life and Health (IDLH) criterion. The WPL, STEL, and IDLH criteria are designed to serve comparable purposes as other occupational criteria such as those published by the ACGIH, NIOSH, and OSHA (see **Sections 4.2 and 4.8**).

4.6 Emergency Management Issues Special Interest Group

The DOE's Emergency Management Issues Special Interest Group (EMI SIG) supports the DOE emergency management community by providing technical information transfer and training services.

In 2004, the DOE Subcommittee on Consequence Assessment and Protective Actions (SCAPA) joined the EMI SIG (EMI SIG 2011). The SCAPA committee publishes the Protective Action Criteria (PAC) dataset which is comprised of AEGLs, ERPGs, Temporary Emergency Exposure Limits (TEELs), and values from other sources. All of these values are found in existing sources except the TEELs, which are designed to serve as surrogate emergency exposure guidelines until peer-reviewed guidelines are available from other agencies.

TEELs are derived for use in emergency planning. The TEEL derivation methodology has been published in the *Journal of Applied Toxicology* (Craig et al. 2000) and in a DOE-commissioned report (Craig and Lux 1998). The TEELs are 1-hour threshold concentrations in air that are given according to three levels of severity (EMI SIG 2016). These levels of severity align to fill the data needs of the dataset, when the chemical has not been evaluated by either the AEGL or ERPG committees. The levels of the PACs are defined as follows:

- PAC-1: The airborne concentration of a substance above which it is predicted that the general population, including susceptible individuals, when exposed for more than 1 hour, could experience notable discomfort, irritation, or certain asymptomatic, non-sensory effects. These effects are not disabling and are transient and reversible upon cessation of exposure.

- PAC-2: The airborne concentration of a substance above which it is predicted that the general population, including susceptible individuals, when exposed for more than 1 hour, could experience irreversible or other serious, long-lasting, adverse health effects or an impaired ability to escape.

- PAC-3: The airborne concentration of a substance above which it is predicted that the general population, including susceptible individuals, when exposed for more than 1 hour, could experience life-threatening adverse health effects or death.

Generally, the PAC dataset compilation involves the use of previously published occupational concentration limits and selected data from the toxicological literature (Craig et al. 2000). The use of TEELs carries a level of uncertainty greater than that of other guidelines because TEELs are designed to fill data gaps and are considered temporary values. This temporary status generally means each value has not undergone a formal peer-review process.

Furthermore, the method used to compile the PAC dataset may vary based on the source of the data. A majority of the PAC values are based on a hierarchy that includes guidelines published by agencies whose primary goal is to protect worker health in an occupational environment. Some occupational guidelines are adopted outright. Other occupational guidelines, such as the TLV-TWA published by the ACGIH, are multiplied by a factor of 3 if used for TEEL-1, and a factor of 5 if used for TEEL-2 (Craig et al. 2000). Although some TEELs are based on toxicity data, the use of toxicity data is considered only when occupational guidelines are not available. Since the underlying sources for the derivation of TEELs are largely based on guidelines intended for workplace exposure, and no added margins of safety (such as those employed by the CalEPA, see **Section 3.4**) are used, TEELs do not carry the same margin of safety that other values do.

4.7 National Advisory Committee for Acute Exposure Guidelines Levels

The EPA's NAC/AEGL develops AEGL values for chemicals that could potentially cause dangerous inhalation exposures to persons through accidental releases to air or by means of a terrorist action. The AEGLs are intended to address the risk to humans resulting from once-in-a-lifetime, or rare, exposure to airborne chemicals (NAC/AEGL 2016). In this context, the NAC/AEGL defines acute exposure to be single, non-repetitive exposures lasting not more than 8 hours.

AEGLs are threshold exposure limits; that is, they are exposure levels below which specified adverse health effects are not likely to occur. The levels are applicable for emergency exposures from 10 min to 8 hrs. Three levels are developed for each of five exposure periods (10 min, 30 min, 1 hr, 4 hrs, and 8 hrs) and are expressed as ppm or mg/m^3 of air. The levels are intended for the general public, including susceptible individuals. Each of the three AEGLs is distinguished by varying degrees of severity of toxic effects, as summarized below (NAC/AEGL 2016).

- AEGL-1: The airborne concentration of a substance above which it is predicted that the general population, including susceptible individuals, could experience notable discomfort, irritation, or certain asymptomatic non-sensory effects. However, the effects are not disabling and are transient and reversible upon cessation of exposure. Airborne concentrations below the AEGL-1 represent exposure levels that can produce mild and progressively increasing but transient and non-disabling odor, taste, and sensory irritation or certain asymptomatic, non-sensory effects.

- AEGL-2: The 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.

- AEGL-3: The 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.

Regarding the comparison of the AEGLs to environmental data, the NAC/AEGL committee states that "[w]ith increasing airborne concentrations above each AEGL, there is a progressive increase in the likelihood of occurrence and the severity of effects described for each corresponding AEGL. Although the AEGL values represent threshold levels for the general public, including susceptible subpopulations, such as infants, children, the elderly, persons with asthma, and those with other illnesses, it is recognized that individuals, subject to unique or idiosyncratic responses, could experience the effects described at concentrations below the corresponding AEGL" (NRC 2001, p. 3).

The NAC/AEGL developed AEGLs through the Federal Advisory Committee and stakeholder concept, where the process for development of values was "the most comprehensive ever used for the determination of short-term exposure limits for acutely toxic chemicals" (NRC 2001, p.

26). The committee consisted of members of the EPA, the Department of Defense, and other state and federal agencies; industry, academe, and other organizations. The development process included the following stages:

1. Draft AEGLs: Draft values represent preliminary and internal committee proposals within the AEGL development process. Draft values are not used in the hierarchy of data collection presented in this document.

2. Proposed AEGLs: These values represent an initial consensus or majority agreement of the NAC/AEGL members. These values are published in the Federal Register for a 30-day review and comment period.

3. Interim AEGLs: These values represent the consensus of the NAC/AEGL committee after resolution of issues raised during public review and comment. These are presented to the National Research Council Subcommittee on Acute Exposure Guidelines Levels (NRC/AEGL 2016) for review and concurrence.

4. Final AEGLs: Final values are published by the National Research Council of the National Academy of Sciences, when the NAC/AEGL and NRC/AEGL committees resolve issues raised during the review process. Although labeled as “final,” these AEGLs may be subject to revision when new data become available.

Current AEGLs (proposed, interim, and final) are accessible from the NAC/AEGL website (NAC/AEGL 2016), where chemicals can be searched for by name or Chemical Abstract Services Registry Number (CASRN).

4.8 National Institute for Occupational Safety and Health and the Occupational Safety and Health Administration

The *NIOSH Pocket Guide to Chemical Hazards* (NIOSH 2007) provides general industrial hygiene information applicable to occupational populations. While NIOSH is not a regulatory authority, its Pocket Guide includes all the substances for which NIOSH has RELs and those with legally-enforceable permissible exposure limits (PELs), as found in the Occupational Safety and Health Standards (Code of Federal Regulations (CFR) 1993).

The three types of NIOSH RELs are TWA, STEL, and ceiling limit. Each of these is defined below (NIOSH 2007).

- REL-TWA: A time-weighted average concentration for up to a 10-hour workday during a 40-hour workweek.

- REL-STEL: A 15-min TWA exposure that should not be exceeded at any time during a workday, unless otherwise noted in the Pocket Guide. Note: These values are used as a point of comparison later within this document.

- REL-C: A ceiling limit that should not be exceeded at any time, unless otherwise noted in the Pocket Guide. Note: These values are used as a point of comparison later within this document.

The TWA and ceiling limit OSHA PELs are defined differently than the RELs (CFR 1993):

- PEL-TWA: A time-weighted average concentration that must not be exceeded during any 8-hour workshift of a 40-hour workweek.

- PEL-STEL: A 15-min TWA exposure that should not be exceeded at any time during a workday, unless noted. Note: These values are used as a point of comparison later within this document.

- PEL-C: Unless otherwise stated, a ceiling limit that must not be exceeded during any part of the workday. If instantaneous monitoring is unavailable, then the ceiling is to be assessed against a 15-min TWA exposure. Note: These values are used as a point of comparison later within this document.

In both sources, concentrations are given in ppm, mg/m^3, mpp/cf (millions of particles per cubic foot of air as determined from counting an impinger sample), or $fibers/cm^3$ (fibers per cubic centimeter). The "(total)" designation indicates that the REL or PEL listed is for "total particulate" versus the "(resp)" designation, which refers to the "respirable fraction" of the airborne particulate.

5. METHOD FOR GENERATING ACUTE REFERENCE CONCENTRATIONS

Acute reference concentrations (ARCs) are generated using the hierarchy and decision logic presented in this section (see **Figure 1**). The hierarchy is arranged in order of preference based on (1) the guidance provided in the Human Health Risk Assessment Protocol (HHRAP) for Hazardous Waste Combustion Facilities (EPA 2005), (2) the applicability to protection of the general public for 1-hour exposure durations that occur on an intermittent basis, and (3) the degree of peer review. Deviations from the HHRAP are discussed in **Section 5.5**.

5.1 Measurement Units

Caution must be exercised with respect to specifying the correct measurement units for developing project datasets. This is especially the case here, with the use of multiple sources of guidelines which themselves use a mix of measurement units.

To standardize risk assessment calculations, the ARCs are generated for units of mg/m^3. The following equations can be used to convert values to the proper measurement scale. These equations provide accurate conversion at 25°C and 760 torr (ACGIH 2016). Additionally, the conversion to mg/m^3 units is required by this method prior to any time-adjustment of MRL values (see **Section 5.2**).

$$\text{Concentration in } \text{mg/m}^3 = \frac{(\text{Concentration in ppm})(\text{gram molecular weight})}{24.45} \quad \text{(Equation 1)}$$

$$\text{Concentration in ppm} = \frac{(\text{Concentration in mg/m}^3)(24.45)}{(\text{gram molecular weight})} \quad \text{(Equation 2)}$$

Where:
24.45 = Molecular Weight adjustment constant in liters/mole
(equals the molar volume of air at 25°C and 760 torr)

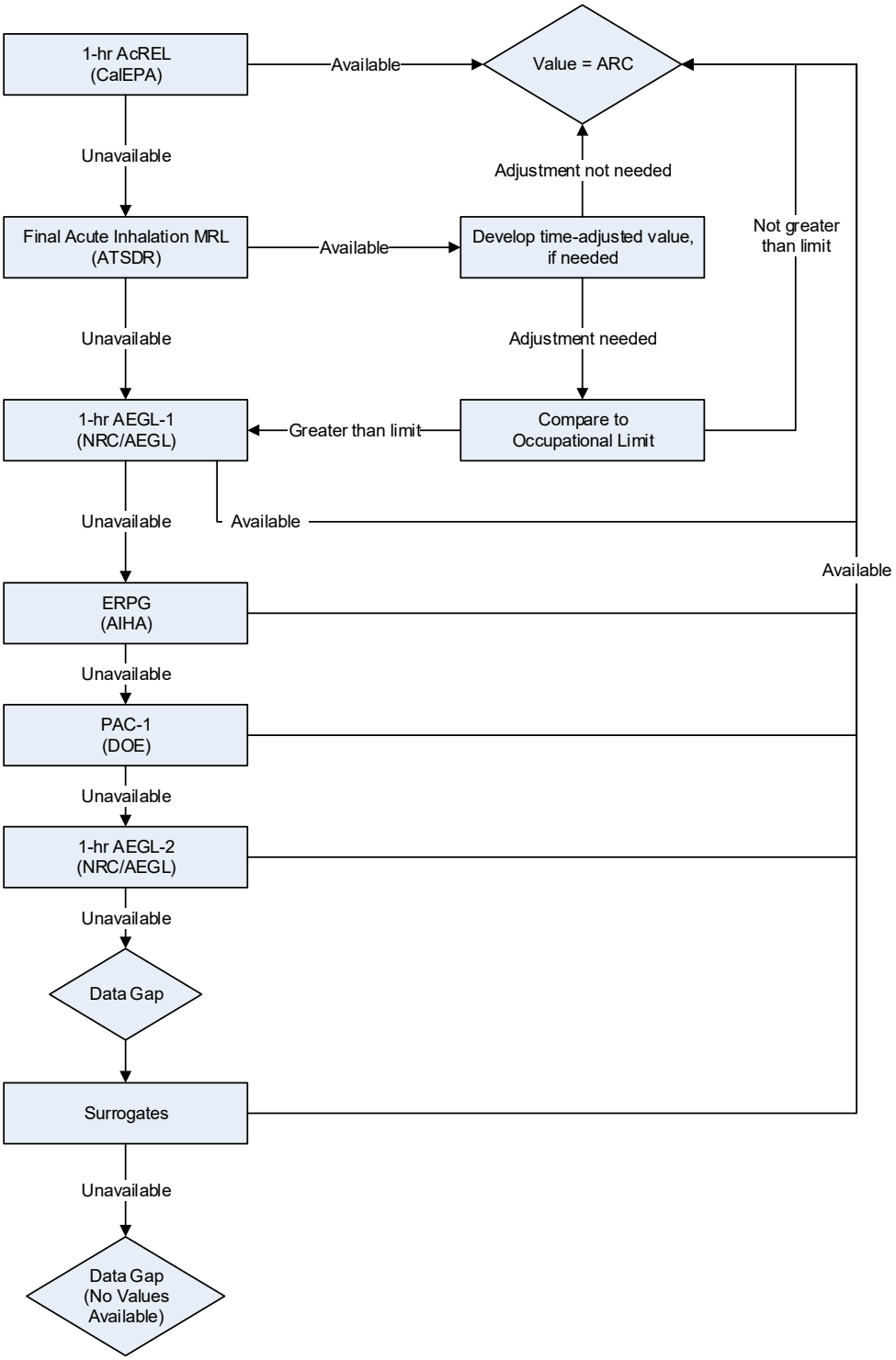

Figure 1. Hierarchy of Acute Reference Concentration Selection

5.2 Adjustment of Guidelines not Originally Developed for 1-hour Exposures

This method includes the adjustment of certain exposure guidelines that were originally developed for use with exposure times of less than or greater than 1 hour. As described in the following sections, concentration-time adjustments are made to such guidelines. Because this adjustment introduces an added layer of uncertainty, such derived concentrations are not accepted as ARCs unless they are no greater than occupational STEL/ceiling limits that are used by industrial hygienists as "not-to-exceed" guidelines. The ACGIH TLVs, CDC AELs, NIOSH RELs, and OSHA PELs are used for this purpose (these sources are reviewed in **Section 4**). For a hierarchy of the use of these datasets, see **Section 5.2.3**.

If a time-adjusted, derived concentration is found to be greater than the STEL/ceiling limit, then either the next exposure guideline hierarchy sources are consulted for a value, or the limit is selected as a tentative 1-hr ARC (refer to Figure 1). Even though such tentative 1-hr ARCs are based on 15-min averaging times, they will not be adjusted because they represent "not-to-exceed" guidelines in their original intention.

In summary, all adjusted ARCs are either—

- A time-adjusted value derived from an original acute guideline source, or
- An occupational limit-based concentration.

The amount of uncertainty introduced by both of these methods is large, and the highest is for limit-based ARCs. The risk assessment report must therefore highlight these uncertainties (when applicable) when characterizing risk.

5.2.1 General Time-Adjustment

Exposure guidelines published for exposure periods other than 1-hr are adjusted using the ten Berge relationship based on guidance provided by the EPA and CalEPA. For risk assessment uses, the toxic load modification to Haber's Law developed by ten Berge (ten Berge et al. 1986) is discussed in the HHRAP and in the CalEPA Hot Spots program guidance (EPA 2005, CalEPA 2008). The HHRAP presents the ten Berge toxic load model shown in **Equation 3**.

$$C^n \times T = K \qquad \text{(Equation 3)}$$

Where:
C= Concentration (mg/m^3)
n= Dimensionless Haber's Law exponent greater than 0
K= Constant (i.e., based on a known concentration and exposure time)
T= Time of exposure (hr)

Solving equation 3 for the desired 1-hr concentration results in **Equation 4**:

Step 1: $Ks = Kt$

Step 2: $Cs^n \times Ts = Ct^n \times Tt$

Step 3: $$Ct = Cs \times \left(\frac{Ts}{Tt}\right)^{\frac{1}{n}}$$ (Equation 4)

Where:
Ks = Exposure constant based on study values protective of minimal risks
Kt = Toxic load model desired exposure constant
Cs = Study dose - protective against minimal risks (ppm or mg/m³)
Ct = Toxic load model derived 1-hr concentration (mg/m³)
n = Dimensionless Haber's Law exponent greater than 0
Ts = Total time of the study dose concentration Cs exposure resulting in the anticipated toxicological effect (hr) - typically continuity (hrs/day) x duration (days)
Tt = Toxic load model desired exposure time associated with the derived concentration (1 hr)
Note: For this application, we assume ***n*** = 1 when ***Ts*** < ***Tt*** and ***n*** = 3 when ***Ts*** > ***Tt*** (see text below).

Selecting chemical-specific values for the exponent *n* in **Equation 4** for chemicals reaching this stage of the method is problematic because values are not likely to exist in the literature or in guidance sources. Therefore, as a screening approach, we assume that n = 1 when extrapolating up from a shorter exposure duration to 1 hour, as recommended by the HHRAP and the CalEPA Hot Spots program (EPA 2005, CalEPA 2008). We also assume that n = 3 when extrapolating down from a longer exposure duration to 1 hour, as recommended by CalEPA (2008). Using these defaults addresses potential issues associated with chemicals that are concentration-dependent, that is, when the concentration of the chemical plays more of a role in toxicity that the duration of exposure. The National Research Council (NRC) has concluded that n = 3 is more appropriate due to approximations using the 95th percentile of the range of values from toxic load model (NRC 2001). The NRC has determined use of this exponent makes concentration more important than time. Thus, the resultant ARCs are health-protective when extrapolating from greater than 1-hour exposures.

5.2.2 Adjustment of Acute Inhalation MRLs

When considering to adjust an acute inhalation MRL, it is first necessary to determine the exposure time used in the underlying study. The relevant study used to support the MRL is published in the respective ATSDR toxicological profile. It may also be necessary to determine whether a conversion factor was used to adjust an intermittent exposure to a continuous exposure. To be consistent with CalEPA's rationale for substances based on reproductive/developmental endpoints and considered sensory irritants, an acute MRL for those substances should not be adjusted and thus should not be placed within datasets compiled using this method.

ATSDR acute inhalation MRL values are representative of 1–14 day exposure periods intended to protect public health. Since these MRL values are not published as 1-hour exposure periods, they are evaluated and adjusted using the MRL-to-ARC decision process shown in **Figure 2**.

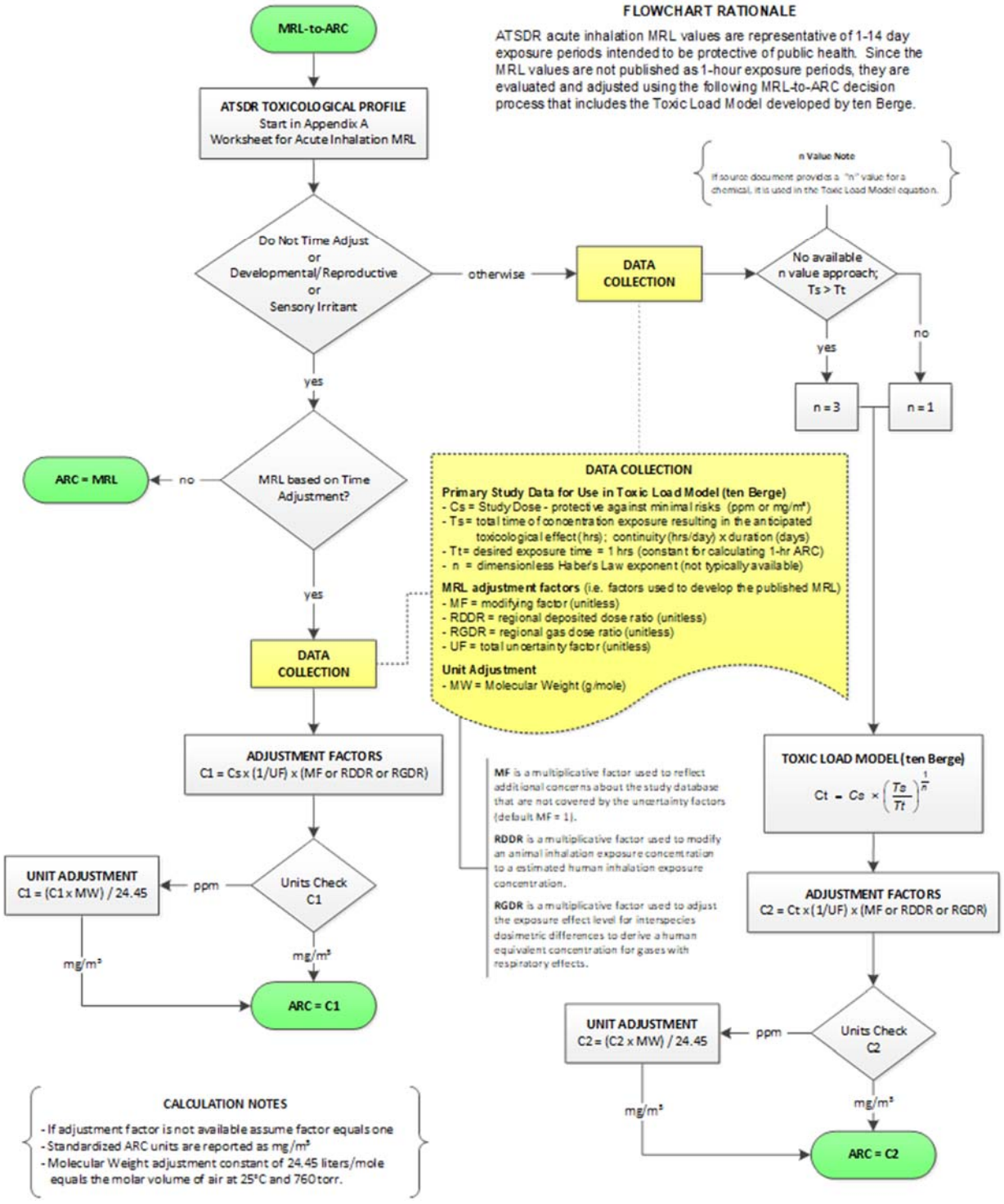

Figure 2. MRL-to-ARC Decision Process, including the ten Berge Toxic Load Model

Following are examples of the three possible extrapolation methods shown in **Figure 2**.

Example 1: ARC = MRL, Ethylene glycol (107-21-1)

The ATSDR Toxicological Profile for Ethylene glycol (107-21-1) publishes an acute inhalation MRL of 2 mg/m^3. The value key study is Wills JH, Coulston F, Harris ES, et al. 1974. A no-observable-adverse-effect level (NOAEL) study dose (Cs) of 23 mg/m^3 and critical effect endpoint of respiratory irritation were determined to be the foundation for the derived MRL protective of public health. Humans, near continuous exposure to ethylene glycol aerosol for 20–22 hrs/day for 14 days, were tolerant of infrequent respiratory irritation without developing other observed toxicological effects. The final published MRL was not time adjusted because the critical effect was concentration-dependent, not duration-dependent. An uncertainty factor of 10 for human variability was applied to the NOAEL.

ATSDR MRL calculation:

MRL = Cs x (1/UF) = 23 mg/m^3 x (1/10) = 2.3 mg/m^3
MRL = 2 mg/m^3 (rounded to one significant figure)

Where:
Cs = 23 mg/m^3
UF = 10 unitless

ARC selection:

Following the Figure 2 flowchart, the select ARC equals the existing MRL because critical effect is a sensory irritant, and the published MRL was not time adjusted. The published MRL is reported in mg/m^3; therefore, no MRL unit adjustment is warranted.

ARC = MRL = 2 mg/m^3

Example 2: ARC = C1, Sulfur mustard (505-60-2)

The ATSDR Toxicological Profile for Sulfur mustard (505-60-2) published an acute inhalation MRL of 0.0007 mg/m^3. The value key study is Guild WJF, Harrison KP, Fairley A, et al. 1941. A lowest-observed-adverse-effect level (LOAEL) study dose (Cs) of 0.06 mg/m^3 and critical effect endpoint of minimal ocular effects (generalized conjunctival reaction) were used as the basis for the derived MRL. Humans, exposed to sulfur mustard, 8 hrs/day for 3 days, scarcely displayed conjunctival reactions. The final published MRL was adjusted to a continuous 24-hr acute exposure. Uncertainty factors of 3 for use of minimal LOAEL and 10 for human variability were applied the time-adjusted LOAEL (total UF = 30).

ATSDR MRL calculation:

MRL = Cs x (T_{adj}) x (1/UF)
MRL = 0.06 mg/m^3 x (8/24) x (1/30) = 0.00067 mg/m^3
MRL = 0.0007 mg/m^3 (rounded to one significant figure)

Where:
Cs = 0.06 mg/m3
T_{adj} = 8 hrs/day x 1 day/24 hrs (time adjustment)
UF = 30 unitless

ARC calculation:

Following Figure 2 flowchart, the select ARC equals C1 because critical effect is a sensory irritant (ocular effects) and the published MRL was time adjusted. The study dose is reported in mg/m^3; therefore, no C1 unit adjustment is warranted. The only adjustment factor is for total uncertainty (UF).

Apply Adjustment Factor:

C1 = Cs x (1/UF) = 0.06 mg/m^3 x (1/30) = 0.002 mg/m^3

Where:
Cs = 0.06 mg/m^3
UF = 30 unitless

ARC = C1 = 0.002 mg/m^3

Example 3: ARC = C2, Vanadium, total (7440-62-2-T)

The ATSDR Toxicological Profile for Vanadium (7440-62-2) published an acute inhalation MRL of 0.0008 mg/m^3. The value key study comprises National Toxicology Program toxicology and carcinogenesis studies of vanadium pentoxide (CAS No. 1314-62-1) in F344/N rats and B6C3F1 mice (inhalation). As part of the study, groups of rats were exposed to vanadium pentoxide, 6 hrs/day 5 days/week for 16 days. A LOAEL study dose (Cs) of 0.56 mg/m^3 and critical effect endpoint of lung inflammation were used as the basis for the derived MRL. Rats, exposed to 0.56 mg/m^3 vanadium pentoxide 6 hrs/day for 13 days, showed an increase in incidence of lung inflammation. This outcome is the basis for the concentration exposure (0.56 mg/m^3) resulting in the anticipated toxicological effect. The final published MRL was adjusted to a continuous 7-day acute exposure. Uncertainty factors of 3 for use of minimal LOAEL, 3 for extrapolation and 10 for human variability were applied to the time-adjusted LOAEL (total UF = 90). In addition, a regional deposited dose ratio (RDDR), equal to 0.732, was used to adjust to an estimated human equivalent dose.

ATSDR MRL calculation:

MRL = Cs x T_{adj} x RDDR x (1/UF)
MRL = 0.56 mg/m^3 x ((6 hrs/24 hrs) x (5 days/7 days)) x 0.732 x (1/90) = 0.000813 mg/m^3
MRL = 0.0008 mg/m^3 (rounded to one significant figure)

Where:
Cs = 0.56 mg/m3
T_{adj} = (6 hrs/day x 1 day/24 hrs) x (5 days/week x 1 week/7days) (time adjustment)
RDDR = 0.732 unitless
UF = 90 unitless

ARC calculation:

Following the Figure 2 flowchart, the select ARC equals C2, applying the toxic load model. The study dose is reported in mg/m^3; therefore, no C2 unit adjustment is warranted. The adjustment factor for RDDR and total uncertainty (UF) are applied as in the MRL calculation.

Calculate Ct (toxic load model desired concentration):

$$Ct = Cs \times \left(\frac{Ts}{Tt}\right)^{\frac{1}{n}} = 0.56 \times \left(\frac{78}{1}\right)^{\frac{1}{3}} = 2.39 \text{ mg/m}^3$$

Apply Adjustment Factors:

C2 = Ct x RDDR x (1/UF) = 2.39 x 0.732 x (1/90) = 0.0194 mg/m^3
C2 = 0.02 mg/m^3 (rounded to one significant figure)

Where:
Cs = 0.56 mg/m^3
Continuity = 6 hrs/day
Duration = 13 days
Ts = Continuity x Duration = 6 hrs/day x 13 days = 78 hrs
Tt = 1 hrs
N = 3 (based on Ts > Tt)
RDDR = 0.732 unitless
UF = 90 unitless

Note: *Ts* is the total time of concentration exposure resulting in the anticipated toxicological effect (hrs).

ARC = C2 = 0.02 mg/m^3

5.2.3 Occupational Limits

As described in the ACGIH, CDC, and NIOSH/OSHA sections above (4.2, 4.5, and 4.7, respectively), occupational guidelines include STELs and ceiling limits. A STEL is a 15-min time-weighted exposure that generally must not be exceeded at any time during the workday. A ceiling limit is the maximum concentration that must not be exceeded at any time. Generally, if instantaneous monitoring is not available, a 15-min TWA should be compared to the ceiling limit.

The rationale for incorporating such limits in this method is as follows. Since STELs and ceiling limits should not be exceeded during the workday or at any time in order to protect workers, the final ARCs should probably not exceed these limits even though they are intended for workplace exposures and have a different exposure averaging time (i.e., ≤ 15 min versus 1 hr).

Since there are multiple occupational guidelines, the following hierarchy is used for the establishment of the occupational limit for use in this method. See Section 5.5 for the hierarchy rationale.

For chemical warfare agents only:

1. CDC AEL-STEL values

For all other substances:

2. NIOSH REL-STEL values
3. ACGIH TLV-STEL values
4. OSHA PEL-STEL values
5. NIOSH REL-ceiling limit values
6. ACGIH TLV-ceiling limit values
7. OSHA PEL-ceiling limit values

5.3 Filling Data Gaps

When a data gap exists for a substance after the process described above has been implemented, the following methods can be considered for deriving ARCs:

- Use of surrogate compounds.
- Use of subchronic toxicity values adjusted for exposure duration.
- Use of Quantitative Structure Activity Relationships (QSAR).
- Derivation of values from information in peer-reviewed, open literature.

These methods can require many hours of work for each compound and may not always be defensible. Therefore, the final decision as to which methods to use will be based on consultations between risk assessors, toxicologists, regulating authorities, and other subject matter experts (e.g., chemists). Preferably, a technical report documenting the methods used to develop an interim ARC will be generated. Such technical reports can be readily cited in risk assessment reports and included as standalone documents.

5.4 Surrogates

Often, data are unavailable for a chemical of interest found during risk assessment sampling. In these situations, subject matter experts may assign surrogate data on an ad hoc basis to continue the risk assessment process. The values assigned are generally taken from structurally similar chemicals, or chemicals that are recognized as representative of a group or class of chemicals. Over time, a list of default surrogates has been compiled for use when a data gap has been found. **Table 1** presents a list of regularly used surrogates; new surrogates may be assigned as needed.

5.5 Deviations from the Human Health Risk Assessment Protocol

The approach for developing the hierarchy of ARCs described in this document deviates slightly from that of the HHRAP (EPA 2005). However, the overall approach follows the basic principles the EPA uses in developing its recommended hierarchy of values for assessing acute inhalation exposures. These principles are based on the rationale that the acute values should consider (1) intermittent exposures from occasional, non-emergency facility upsets, and (2) the preference for values intended for 1-hour exposures. The EPA (2005) has concluded that most of the existing sources are intended for one-time only exposures (e.g., AEGLs) and has revised its original hierarchical approach by placing CalEPA AcRELs at the top of the current recommended hierarchy. Previously, the AEGL-1 and ERPG-1 values were preferred over CalEPA values (EPA 1998).

Table 1. Default Assignments of Surrogate ARC Values to Chemicals without ARC Values

Chemicals Without Original ARC Values		Surrogate Chemicals with ARC Values (used to fill data gaps)	
Chemical	**CASRN**	**Surrogate Chemical**	**Surrogate CASRN**
Barium, total	7440-39-3-T	Barium, elemental	7440-39-3
Chromium, total	7440-47-3-T	Chromium, elemental	7440-47-3
Cobalt, total	7440-48-4-T	Cobalt, elemental	7440-48-4
Iron, total	7439-89-6-T	Iron, elemental	7439-89-6
Lead, total	7439-92-1-T	Lead, elemental	7439-92-1
Lithium, total	7439-93-2-T	Lithium, elemental	7439-93-2
Mercury, total	7439-97-6-T	Mercury, elemental	7439-97-6
Molybdenum, total	7439-98-7-T	Molybdenum, elemental	7439-98-7
Selenium, total	7782-49-2-T	Selenium, elemental	7782-49-2
Silver, total	7440-22-4-T	Silver, elemental	7440-22-4
Tin, total	7440-31-5-T	Tin, elemental	7440-31-5
Trimethylbenzenes	25551-13-7	1,3,5-Trimethylbenzene	108-67-8
Uranium, depleted	0-588*	Uranium, elemental	7440-61-1
Uranium, total	7440-61-1-T	Uranium, soluble salts	0-049*
Zinc, total	7440-66-6-T	Zinc, elemental	7440-66-6

Since the HHRAP is intended to serve only as guidance, this method adopts its principles and complements it with additional information to form the recommended hierarchy presented in section 3. This hierarchy "deviates" from the HHRAP in two ways.

1. ATSDR MRLs are included. Although the HHRAP mentions the ATSDR as an agency which publishes guidelines or criteria for acute inhalation exposures, the HHRAP does not include the MRLs in its recommended hierarchy. The MRLs are consistent with the HHRAP's intent to prefer guidelines that consider intermittent exposures. Compared to the AEGLs or the ERPGs, the MRLs are most similar to the CalEPA AcRELs. The only disadvantage of using MRLs is that they are not necessarily developed for 1-hour exposures but rather for exposures ranging from 1 hour to 2 weeks. This problem is circumvented by using the CalEPA method as discussed in **Section 5.2.2**.

2. Time-adjusted concentrations are capped, not allowing them to exceed occupational limits. This action is not actually a deviation from the HHRAP; rather, it is a method of ensuring the adjusted values are reasonable given the uncertainty of the approach. Since occupational limits are available for short-term exposures, any time-adjusted 1-hour value that exceeds the occupational limit is not useful, especially when the occupational limits are intended for 15-min exposures. Without more information about how the occupational limits are derived, they cannot be ignored. At the same time, it is not practical to evaluate the derivation of each occupational limit, at least at the screening level.

5.6 Fundamental Uncertainties

Uncertainty exists as to whether the acute reference concentrations developed by this methodology represent adequate safe concentrations for the general public. Due to differing underlying databases, objectives, and techniques, the uncertainty is neither uniform across chemicals nor across sources of information. Regardless, risk management decisions are needed in the face of this uncertainty.

The method defined in this document will result in project datasets of acute reference concentrations that can reasonably be used for screening-level risk assessments. The sources of uncertainty should be understood, and attempts should be made to reduce these uncertainties where possible. The following paragraphs (presented in no particular order) identify the most important sources of uncertainty within this methodology:

Extrapolations using the toxic load model equation. The most appropriate way to extrapolate to different exposures times would be to evaluate each chemical one-by-one. Because doing so would be labor-intensive, and much of the required data would be unavailable, the default approach used herein is reasonable. The effect of applying a default value for *n* in **Equation 4** is unknown, but the application is accepted by numerous government agencies.

- Use of occupational guidelines. It is not clear whether TEELs, the occupational STEL, or ceiling limits are sufficiently protective of sensitive sub-populations found within the general public. Sufficient data that would provide clarity are not generally available.

- Making proper comparisons. There is uncertainty in the degree to which the ARC values are sufficiently scaled in terms of exposure periodicity. That is, how rare or how frequent is the exposure that best suits the ARCs? Alternatively, are the ARCs sufficient as comparison guidelines for various sites with invariably different intermittent exposure profiles? These questions can only be answered on a site-by-site basis. For example, if reliable site-specific data suggest that there are few exposures per year, then using comparison values for intermittent exposures that assume possible exposures up to once every 2 weeks may not be justified. If the possible exposure is assumed to occur only once a year, then it may be more appropriate to alter the hierarchy (e.g., place the AEGLs as the primary source). The decision to do so should also be site-specific.

- Using different goals and derivation methods across guideline sources. This practice is unavoidable given the large number of potential chemicals of concern and the practical need for each guideline-development organization to focus on specific issues. The result is variation in what different organizations decide in terms of specific guideline concentrations. This inconsistency makes it difficult to truly “know” what the most appropriate guideline is in every case.

- Lag times exist between relevant new research findings, guideline source updates, and derivation methodologies. Uncertainty is introduced into any “static" hierarchy of guideline sources in terms of what may be “known” in the literature compared to what is translated into improved exposure guideline values for use in risk assessment. Additionally, the different sources of exposure guidelines are updated at different rates; some are not updated frequently. As time progresses, reevaluations of this methodology will likely need to replace "older" values. However, regular updates may be impractical due to the paucity of available toxicological data for intermittent acute exposures for most chemicals.

6. SUMMARY OF CHANGES

This is the first publication of this TG 373 Supplement. Over time, if it is determined to be inconsistent with evolving methodologies and/or regulations, it should be revised. Key changes made during such revisions should be highlighted in this section.

APPENDIX A

REFERENCES

Agency for Toxic Substances and Disease Registry (ATSDR). 2016. *Minimal Risk Levels (MRLs) for Hazardous Substances*. Available at: http://www.atsdr.cdc.gov/mrls/index.asp

ATSDR. 2006a. *Toxicological Profile for 1,1,1-Trichloroethane (CASRN 71-55-6).* Available at: http://www.atsdr.cdc.gov/toxprofiles/tp70.html

ATSDR. 2006b. *Toxicological Profile for Hydrogen Sulfide (CASRN 7783-06-4).* Available at: http://www.atsdr.cdc.gov/ToxProfiles/tp.asp?id=389&tid=67.

ATSDR. 2000. *Toxicological Profile for Toluene (CASRN 108-88-3).* Available at: http://www.atsdr.cdc.gov/toxprofiles/tp56.html

ATSDR. 1998. *Toxicological Profile for 2-Butoxyethanol (CASRN 111-76-2) and 2-Butoxyethanol Acetate (CASRN 112-07-2).* Available at: http://www.atsdr.cdc.gov/toxprofiles/tp118.html

American Conference of Governmental Industrial Hygienists (ACGIH). 2017. *2017 TLVs and BEIs Based on the Documentation of the Threshold Limit Values for Chemical Substances and Physical Agents & Biological Exposure Indices.* Cincinnati, Ohio: ACGIH.

American Industrial Hygiene Association (AIHA) Guideline Foundation. 2016. *The AIHA 2016 Emergency Response Planning Guidelines (ERPG) and Workplace Environmental Exposure Level (WEEL) Handbook.* Fairfax, Virginia: AIHA Guideline Foundation.

California Environmental Protection Agency (CalEPA) Office of Environmental Health Hazard Assessment (OEHHA). 2016. *Air – Hot Spots – Acute RELs* [database]. Available at: http://oehha.ca.gov/air/general-info/oehha-acute-8-hour-and-chronic-reference-exposure-level-rel-summary

CalEPA OEHHA. 2009. *Toxicity Criteria Database.* Available at: http://oehha.ca.gov/risk/pdf/tcdb072109cas.pdf

CalEPA OEHHA. 2008. *Air Toxics Hot Spots Risk Assessment Guidelines. Technical Support Document for the Derivation of Noncancer Acute Reference Exposure Levels.* Available at: https://oehha.ca.gov/media/downloads/crnr/noncancertsdfinal.pdf

Centers for Disease Control and Prevention (CDC). 2004. *Interim Recommendations for Airborne Exposure Limits for Chemical Warfare Agents H and HD (Sulfur Mustard).* Federal Register 69:24164-24168. Atlanta, Georgia: CDC.

CDC. 2003. *Final Recommendations for Protecting Human Health from Potential Adverse Effects of Exposure to Agents GA (Tabun), GB (Sarin), and VX.* Federal Register 68:58348-58351. Atlanta, Georgia: CDC.

CDC. 1991. *Preventing Lead Poisoning in Young Children.* Atlanta, Georgia: CDC.

Code of Federal Regulations (CFR). Occupational Safety and Health Standards. 1993 (as amended, 2017). Air contaminants. 29 CFR 1910.1000. Available at: https://www.ecfr.gov

Craig DK, Davis JS, Hansen DJ, et al. 2000. Derivation of temporary emergency exposure limits (TEELs). *J Appl Toxicol* 20(1):11–20. doi: 10.1002/(sici)1099-1263(200001/02)20:1<11::aid-jat622>3.0.co;2-q

Craig DK and CR Lux. 1998. *Methodology for Deriving Temporary Emergency Exposure Limits (TEELs)(U).* Aiken, South Carolina: Westinghouse Safety Management Solutions, Westinghouse Savanna River Company.

Emergency Management Issues Special Interest Group (EMI SIG). 2016. *Protective Action Criteria (PAC): Chemicals with AEGLs, ERPGs, and TEELs.* Available at: https://sp.eota.energy.gov/pac/

Guild WJF, Harrison KP, Fairley A, et al. 1941. The effect of mustard gas vapor on the eyes. Chemical Board, Physiological Sub-Committee, and Panel of Ophthalmic Specialists. Porton Report 2297. Chemical Defense Experimental Station, Porton, United Kingdom.

National Advisory Committee on Acute Exposure Guideline Levels (NAC/AEGL). 2016. *AEGL Program: The Development of Acute Exposure Guideline Levels (AEGLs)*. Available at: https://www.epa.gov/aegl

National Institute for Occupational Safety and Health (NIOSH). 2007. *NIOSH Pocket Guide to Chemical Hazards.* Publication No. 2005-149. Available at: https://www.cdc.gov/niosh/npg/

National Research Council (NRC) Subcommittee on Acute Exposure Guideline Levels. 2001. *Standing Operating Procedures for Developing Acute Exposure Guideline Levels for Hazardous Chemicals.* Available at: https://www.epa.gov/aegl

ten Berge WF, A Zwart, and LM Appleman. 1986. Concentration—time mortality response relationship of irritant and systemically acting vapours and gases. *J Hazard Mater* 13(3):301–309. Available at: https://doi.org/10.1016/0304-3894(86)85003-8

U.S. Environmental Protection Agency (EPA). 2008. *Integrated Risk Information System (IRIS)* [database]. Available at: www.epa.gov/iris

EPA. 2005. *Human Health Risk Assessment Protocol for Hazardous Waste Combustion Facilities* (EPA530-R-05-006). Washington, D.C.: EPA Office of Solid Waste and Emergency Response (OSWER).

EPA.1998. *Human Health Risk Assessment Protocol for Hazardous Waste Combustion Facilities, Peer Review Draft, Volume 1* (EPA530-D-98-001A, B & C). Washington, D.C.: EPA OSWER.

EPA. 1994a. *Guidance Manual for the Integrated Exposure Uptake Biokinetic Model for Lead in Children* (EPA/540/R-93/081, PB93-963510). Washington, D.C.: EPA Office of Emergency and Remedial Response.

EPA. 1994b. *Revised Interim Soil Lead Guidance for CERCLA Sites and RCRA Corrective Action Facilities, OSWER Directive No. 9355.4-12* (EPA/540/F-94/043, PB94-963282). Washington, D.C.: EPA Office of Emergency and Remedial Response.

EPA. 1989. *Risk Assessment Guidance for Superfund Volume 1 Human Health Evaluation Manual (Part A), Interim Final* (EPA/540/1-89/002). Washington, D.C.: EPA Office of Emergency and Remedial Response.

Wills JH, Coulston F, Harris ES, et al. 1974. Inhalation of aerosolized ethylene glycol by man. *Clin Toxicol* 7(5):463–476. doi: 10.3109/15563657408988020

GLOSSARY

ACGIH
American Conference of Governmental Industrial Hygienists

ACGIH C
American Conference of Governmental Industrial Hygienists Ceiling Limit Value

ACGIH TLV
American Conference of Governmental Industrial Hygienists Threshold Limit Value

AcREL
Acute Reference Exposure Level

ADP
Chemical warfare agent degradation product

AEGL
Acute Exposure Guideline Level

AEL
Airborne Exposure Limit

AIHA
American Industrial Hygiene Association

ARC
acute reference concentration

ATSDR
Agency for Toxic Substances and Disease Registry

C
Ceiling Limit

CalEPA
California Environmental Protection Agency

CASRN
Chemical Abstract Services Registry Number

CDC
Centers for Disease Control and Prevention

CDC AEL
Centers for Disease Control and Prevention Airborne Exposure Limit

DOE
Department of Energy

EMI SIG
Emergency Management Issues Special Interest Group

EPA
Environmental Protection Agency

ERPG
Emergency Response Planning Guideline

fibers/cm^3
fibers per cubic centimeter

GA
Tabun

GB
Sarin

GPL
General Population Limit

HHRAP
Human Health Risk Assessment Protocol

hr
hour

IDLH
Immediately Dangerous to Life and Health

LOAEL
lowest-observed-adverse-effect level

MF
modifying factor (unitless)

mg/m^3
milligrams per cubic meter

mpp/cf
millions of particles per cubic foot

MRL
Minimal Risk Level

MW
molecular weight (g/mole)

NAC/AEGL
National Advisory Committee on Acute Exposure Guidelines Levels

NIOSH
National Institute of Occupational Safety and Health

NIOSH C
National Institute of Occupational Safety and Health Ceiling Limit Values

NIOSH REL
National Institute of Occupational Safety and Health Recommended Exposure Limits

NOAEL
no-observed-adverse-effect level

NPL
National Priorities List

NRC
National Research Council

NRC/AEGL
National Research Council Subcommittee on Acute Exposure Guidelines Levels

OB/OD
open burning/open detonation

OEHHA
Office of Environmental Health Hazard Assessment (CalEPA)

OSHA
Occupational Safety and Health Administration

OSHA-C
Occupational Safety and Health Administration Ceiling Limit Value

OSWER
Office of Solid Waste and Emergency Response (EPA)

PAC
Protective Action Criteria

PEL
Permissible Exposure Limit

ppm
parts per million

QSAR
Quantitative Structure Activity Relationships

RDDR
regional deposited dose ratio (unitless)

REL
Recommended Exposure Limit

resp
respirable fraction

RGDR
regional gas dose ratio (unitless)

SCAPA
Subcommittee on Consequence Assessment and Protective Actions

SOP
standard operating procedure

STEL
Short-Term Exposure Limit

TEEL
Temporary Emergency Exposure Limit

TLV
Threshold Limit Value

TWA
time-weighted average

UF
total uncertainty factor (unitless)

VX
O-ethyl *S*-[2-(diisopropylamino)ethyl] methylphosphonothioate

WPL
worker population limit