

Proposed Acute Exposure Concentration Limits for COPCs with Regulatory Guidelines

July 2018

X-Y Yu T Brouns J Yao



Prepared for the U.S. Department of Energy under Contract DE-AC05-76RL01830

DISCLAIMER

This report was prepared as an account of work sponsored by an agency of the United States Government. Neither the United States Government nor any agency thereof, nor Battelle Memorial Institute, nor any of their employees, makes any warranty, express or implied, or assumes any legal liability or responsibility for the accuracy, completeness, or usefulness of any information, apparatus, product, or process disclosed, or represents that its use would not infringe privately owned rights. Reference herein to any specific commercial product, process, or service by trade name, trademark, manufacturer, or otherwise does not necessarily constitute or imply its endorsement, recommendation, or favoring by the United States Government or any agency thereof, or Battelle Memorial Institute. The views and opinions of authors expressed herein do not necessarily state or reflect those of the United States Government or any agency thereof.

PACIFIC NORTHWEST NATIONAL LABORATORY operated by BATTELLE for the UNITED STATES DEPARTMENT OF ENERGY under Contract DE-AC05-76RL01830

Printed in the United States of America

Available to DOE and DOE contractors from the Office of Scientific and Technical Information, P.O. Box 62, Oak Ridge, TN 37831-0062; ph: (865) 576-8401 fax: (865) 576-5728 email: reports@adonis.osti.gov

Available to the public from the National Technical Information Service 5301 Shawnee Rd., Alexandria, VA 22312 ph: (800) 553-NTIS (6847) email: orders@ntis.gov <http://www.ntis.gov/about/form.aspx> Online ordering: http://www.ntis.gov



This document was printed on recycled paper. (8/2010)

Proposed Acute Exposure Concentration Limits for COPCs with Regulatory Guidelines

X-Y Yu T Brouns J Yao

July 2018

Prepared for the U.S. Department of Energy under Contract DE-AC05-76RL01830

Pacific Northwest National Laboratory Richland, Washington 99352

Executive Summary

Acute exposure concentration limits based on available regulatory guidelines are recommended for Chemicals of Potential Concern identified for Hanford Tank Farm operations. Acute regulatory guidelines for 12 of the 61 current Chemicals of Potential Concern were identified in databases developed by authoritative government agencies or private entities.

Acronyms and Abbreviations

ACGIH	American Conference of Governmental Industrial Hygienists				
AEGL	Acute Exposure Guideline Level				
AIHA	American Industrial Hygiene Association				
CAS Number	Chemical Abstracts Service Registry Number				
CNS	central nervous system				
COPC	Chemicals of Potential Concern				
DOE	U.S. Department of Energy				
EEGL	Emergency Exposure Guidance Level				
EPA	U.S. Environmental Protection Agency				
ERPG	Emergency Response Planning Guideline				
HTF	Hanford Tank Farm				
HTFOEL	Hanford Tank Farm Occupational Exposure Limit				
HTFTEC	Hanford Tank Farm Transient Exposure Concentration				
LOAEL	Lowest-observed-adverse-effect Level				
MAK	Maximale Arbeitsplatz-Konzentration (Maximum Workplace Concentration) from the German Research Foundation				
NAC	National Advisory Committee				
NIOSH	National Institute for Occupational Safety and Health				
NOAEL	No-Observed-Adverse-Effect Level				
NRC	National Research Council				
OSHA	Occupational Safety and Health Administration				
OEL	Occupational Exposure Limit				
PAC	Protective Action Criterion (a generic term for any of the several emergency exposure limit values)				
PEL	Permissible Exposure Limit				
PEL-C	Permissible Exposure Limit Ceiling				
PEL-TWA	Permissible Exposure Limit Time-Weighted Average				
PNNL	Pacific Northwest National Laboratory				
ppb	parts per billion				
ppm	parts per million				
RD ₅₀	The concentration that elicits a respiratory rate decrease of 50%				
REL	Recommended Exposure Limit				
SMAC	Spacecraft Maximum Allowable Concentration				

STEL	Short-Term Exposure Limit
TEC	transient-effect concentration
TEEL	Temporary Emergency Exposure Limit
TLV	Threshold Limit Value
TWA	Time-Weighted Average
WEEL	Workplace Environmental Exposure Level

Contents

Exec	cutive	Summa	ry	iii		
Acro	onyms	s and Ab	breviations	v		
1.0	1.0 Introduction/Project Description					
	1.1	Summary of Acute Regulatory Guidelines and Transient-Effect Concentration				
		Develo	pment	1.1		
	1.2	Definition of Key Threshold Values Used in Acute Regulatory Guidelines or Transient				
		Effect Concentration Evaluations				
		1.2.1	Definition of Threshold Limit Values	1.3		
		1.2.2	Threshold Limit Value-Time-Weighted Average	1.4		
		1.2.3	Acute Exposure Guideline Levels	1.4		
		1.2.4	Emergency Response Planning Guideline	1.4		
		1.2.5	Protective Action Criterion/Temporary Emergency Exposure Limit	1.5		
		1.2.6	Short-Term Exposure Limit	1.5		
		1.2.7	Permissible Exposure Limit	1.5		
		1.2.8	Threshold Limit Value-Ceiling	1.5		
		1.2.9	Recommended Exposure Limit	1.6		
		1.2.10	Time-Weighted Average	1.6		
		1.2.11	Workplace Environmental Exposure Levels	1.6		
		1.2.12	Immediately Dangerous to Life or Health	1.6		
		1.2.13	Emergency Exposure Guidance Level	1.6		
		1.2.14	No-Observed-Adverse-Effect Level	1.6		
		1.2.15	Lowest-Observed-Adverse-Effect Level	1.6		
		1.2.16	Maximal Arbeitsplatz-Konzentration (Maximum Workplace Concentration)	1.7		
		1.2.17	Occupational Exposure Limit	1.7		
		1.2.18	Spacecraft Maximum Allowable Concentration	1.7		
		1.2.19	RD ₅₀	1.7		
		1.2.20	Peak Exposures	1.7		
2.0	Reco	ommende	ed Acute Regulatory Values	2.1		
	2.1 Acute Regulatory Values					
	2.2	Summa	ary of Available Acute Regulatory Values from Government and Private Agencies.	2.2		
		2.2.1	Inorganic Compounds	2.2		
		2.2.2	Hydrocarbons	2.3		
		2.2.3	Alcohols	2.5		
		2.2.4	Ketones	2.6		
		2.2.5	Aldehydes	2.7		
		2.2.6	2-Propenal	2.9		
		2.2.7	Amines	2.10		
		2.2.8	Isocyanates	2.10		
3.0	Summary					
4.0) References					

Figure

1	Process Used to Establish Acute Regulatory Values and TECs
	Table
1	Acute Regulatory Values

1.0 Introduction/Project Description

In 2016, Chemicals of Potential Concern (COPC) related to Hanford Tank Farm (HTF) operations were evaluated for new regulatory information that would warrant updating chronic Occupational Exposure Limits (OEL). OELs used to guide safe HTF operations are termed _{HTF}OELs and were originally defined in an earlier Pacific Northwest National Laboratory (PNNL) technical report (PNNL-15736, Poet and Timchalk 2006). This report complements the chronic OEL update (Weber et al. 2018) and focuses on identifying acute regulatory guidelines for COPCs, reported by authoritative government or private agencies, which can assist operational risk management and workforce communications at the Hanford site. Regulatory values published up through 2016 were surveyed and used in this report.

COPCs may have both chronic and acute exposure impacts. The exposure limits defined for HTF operations are based principally on COPC concentrations that may cause adverse, chronic effects over a normal work day or work week and lifetime of occupational exposure. Concentrations of COPCs that may cause acute effects over short-term exposure are typically much higher than the chronic effect concentrations that are the basis for current HTFOELs. Symptoms of irritation and discomfort have been reported by workers within or near tank farms on the Hanford site. Because these symptoms are suspected to be related to chemical vapor exposure, recommendations were made to evaluate acute odor and toxicity effect levels and to identify ceiling exposure limit values for headspace chemicals (Wilmarth et al. 2014). To address these recommendations and provide additional understanding of the potential health effects of short-term COPC exposures, an effort was initiated to identify and document acute, transient-effect concentrations (TECs). TECs represent the potential exposure concentration where short-term discomfort, irritation, or other temporary effect may be experienced by the exposed individual, but without long-term, irreversible impacts. The potential use of TECs for HTF operations supports the Industrial Hygiene Technical Basis and communications to help inform the workforce and differentiate between observed area tank vapor concentrations, source concentrations, vapor action levels (e.g., 50% of chronic OEL), and typically higher TECs that could result in reversible, short-term irritation or other effects.

For a subset of COPCs, established acute regulatory guidelines exist. These guidelines are defined by government or private agencies engaged in exposure concentration limit development for occupational, general-public, or emergency-response applications. These regulatory guidelines are generally rooted in peer-reviewed toxicological research. Such research results and guidelines are used to guide development of acute TECs that have not previously been established for HTF operations (i.e., HTFTECs).

1.1 Summary of Acute Regulatory Guidelines and Transient-Effect Concentration Development

Available acute regulatory guidelines were investigated for the 61 chemicals on the current Hanford COPC list published by Washington River Protection Solutions.¹ This report provides a summary of the recommended acute regulatory values for 12 chemicals in the current COPC list. In the future, more toxicological information, if available, will be evaluated to assess and recommend TECs for additional chemicals in the Hanford COPC list that do not currently have acute regulatory values. Although furan, biphenyl, and two nitrile compounds also were surveyed, acute TECs for those compounds are not recommended in this report. It is deemed that these compounds need more thorough review. Figure 1 describes the process used to establish acute regulatory values and TECs.

¹ https://hanfordvapors.com/wp-content/uploads/2017/11/WRPS-1604188.1-COPC-List.pdf



^a POD: point of departure; ^b UF: uncertainty factor

Figure 1. Process Used to Establish Acute Regulatory Values and TECs

Several key resources were used to identify existing acute exposure guidelines, including Short-Term Exposure Limit (STEL), Acute Exposure Guideline Level (AEGL), and Emergency Response Planning Guideline (ERPG) values. Priority in identifying acute exposure sources was given to values reported by the American Conference of Governmental Industrial Hygienists (ACGIH) and the Occupational Safety and Health Administration (OSHA) due to contractual obligations of Hanford cleanup contractors to adhere to specific ACGIH exposure limits and OSHA as a legal authority. This follows the same principle used in the chronic _{HTF}OEL development for COPCs.

Of importance are STEL values that are 15-minute Time-Weighted Average (TWA) limits that should not be exceeded at any time during a work day (ACGIH 2016). The sources of STEL values are the National Institute of Occupational Safety and Health (NIOSH), OSHA, and ACGIH. Because STEL and Threshold Limit Value-Ceiling (TLV-C) values are most relevant to acute occupational scenarios, they are recommended and adopted as the acute regulatory guideline when available. Equally important are Permissible Exposure Limit (PEL) values that are regulatory in nature. PELs are limits on the amount or concentration of a substance in the air, and they also may contain a skin designation. PELs are measured either as PEL-Ceiling (PEL-C) or PEL-TWA. A PEL-C is a 15-minute TWA exposure that shall not be exceeded at any time during the working day. A PEL-TWA is an 8-hour TWA value. PEL-Cs shall not exceed PEL-TWAs. A PEL-TWA shall not be exceeded in any 8-hour work shift of a 40-hour work week. When TLV-C values have not been established, PEL values—particularly PEL-C values—may be adopted as acute regulatory guidelines.

If STEL, TLV-C, or PEL values are not available as acute regulatory guidelines, AEGL and ERPG values or the underlying data that supported their development is considered as a basis for _{HTF}TECs. These values have a rank order that is based on severity of the adverse health effect. AEGL-1 values are

concentration limits at which a person would "... experience notable discomfort, irritation, or certain asymptomatic, non-sensory effects." These effects, however, are transient, reversible, and not disabling when the exposure stops. ERPG-1 values are threshold limits at which individuals could be "... exposed for up to 1 hour without experiencing more than mild, transient adverse health effects or without perceiving a clearly defined objectionable odor." AEGL-1 and ERPG-1 values and the research data that supported their development can be used as bases for acute TECs in the absence of STEL values, as they are most similar to the possible sporadic, transient exposure that may be experienced onsite. However, care must be taken to account for an occupational application versus general public. When AEGL-1 values do not exist, ERPG-1 values are considered.

Use of the ACGIH excursion rule (ACGIH 2016) was recommended to arrive at an OEL-Ceiling (OEL-C), similar to TLV-C, as an exposure control (Wilmarth et al. 2014). This approach may permit rapid selection of limit values for chemicals that do not have STEL values. Acute TECs for peak events are the product of multiplying the OEL – TWA \times 5. The Hanford Tank Vapor Assessment Team stated that they believe, "... it would be prudent to establish the 3-times-the OEL (OEL – TWA \times 3 or OEL – STEL \times 3) as a conservative default acute TEC-C. Washington River Protection Solutions would use 10% of the OEL-C in the same manner that it uses 10% of the OEL for an 8-hour TWA" (Wilmarth et al. 2014). While this approach provides an empirical estimate of the potential risk, it is not based on toxicity studies. Therefore, values derived from the excursion rule are only used as references in this work but not adopted as _{HTF}TEC in our recommendation. Recommendations on acute regulatory values for several chemicals with existing acute exposure guidelines are discussed and summarized in Chapter 2.

1.2 Definition of Key Threshold Values Used in Acute Regulatory Guidelines or Transient-Effect Concentration Evaluations

1.2.1 Threshold Limit Values (TLV)

Technical information on TLVs was taken from the ACGIH TLV and Biological Exposure Indices Handbook (ACGIH 2016). TLVs refer to airborne concentrations of chemical substances and represent conditions under which it is believed nearly all workers may be repeatedly exposed, day-after-day, over a working lifetime, without adverse health effects. Because the information that is available for a specified chemical substance varies over time, TLVs should be regularly updated. Chemical substances with equivalent TLVs (i.e., the same numerical values) cannot be assumed to have similar toxicological effects or similar biologic potency. TLVs do not represent a fine line between a healthy versus an unhealthy work environment or the point at which material impairment of health will occur. TLVs will not adequately protect all workers. Some individuals may experience discomfort or even more serious adverse health effects when exposed to a chemical substance at the TLV or even at concentrations below the TLV. There are many possible reasons for increased susceptibility to a chemical substance, including age, gender, ethnicity, genetic factors (i.e., predisposition), lifestyle choices (e.g., diet, smoking, abuse of alcohol and other drugs, etc.), medications, and pre-existing medical conditions (e.g., aggravation of asthma or cardiovascular disease). Some individuals may become more responsive to one or more chemical substances following previous exposures (e.g., sensitized workers). Susceptibility to the effects of chemical substances may be altered during different periods of fetal development and throughout an individual's reproductive lifetime. Some changes in susceptibility may also occur at different work levels (e.g., light versus heavy work) or when exercising-situations in which cardiopulmonary demand is higher. In addition, variations in temperature (e.g., extreme heat or cold) and relative humidity may alter an individual's response to a toxicant. The documentation for any given TLV should be periodically reviewed and updated, keeping in mind that other factors may modify biological responses.

1.2.2 Threshold Limit Value-Time-Weighted Average (TLV-TWA)

TLV-TWA typically represents the TWA concentration for a conventional 8-hour work day and a 40-hour work week, to which it is believed nearly all workers may be repeatedly exposed, day-after-day, for a working lifetime without adverse effect. However, as discussed above, different regulatory agencies may report TLV-TWA based on different work shift schedules. There are established guidelines that can be applied to calculate adjustments that account for differences in exposure due to changes in work shift times. In cases where NIOSH RELs were identified as a regulatory guideline, the documented 10-hour TLV-TWA is applied directly to the 8-hour time period reported for implementation as a chronic HTFOEL. It is noted that the typical "in farm" time for HTF workers is less than 8 hours per day. Therefore, the TLV values listed for chronic exposures are conservative. It is possible that future efforts could examine the merit of exposure standard adjustments proposed by the Australian Institute of Occupational Hygienists (AIOH 2016). These suggested standard adjustments consider differences between ceiling standards, mild irritants, standards set by technological feasibility or good hygiene practices, acute toxicants, cumulative toxicants, and both acute and cumulative toxicants.

1.2.3 Acute Exposure Guideline Levels (AEGL)

AEGLs represent threshold exposure limits for the general public and are applicable to emergency exposure periods ranging from 10 minutes to 8 hours. Three levels—AEGL-1, AEGL-2, and AEGL-3— have been developed for each of five exposure periods (10 and 30 minutes, and 1, 4, and 8 hours) and are distinguished by varying degrees of severity of toxic effects. The three AEGLs are defined as follows:

- AEGL-1 is the airborne concentration (expressed as parts per million [ppm] or milligrams per cubic meter [mg/m³]) 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.
- AEGL-2 is the airborne concentration (expressed as ppm or mg/m³) 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 is the airborne concentration (expressed as ppm or mg/m³) of a substance above which it is predicted that the general population, including susceptible individuals, could experience life-threatening health effects or death.

1.2.4 Emergency Response Planning Guideline (ERPG)

ERPGs estimate the concentrations at which most people will begin to experience health effects if they are exposed to a hazardous airborne chemical for 1 hour. Sensitive members of the public—such as old, sick, or very young people—are not covered by these guidelines, and they may experience adverse effects at concentrations below the ERPG values. The three ERPG tiers are defined as follows:

- ERPG-1 is the maximum airborne concentration below which nearly all individuals could be exposed for up to 1 hour without experiencing more than mild, transient adverse health effects or without perceiving a clearly defined objectionable odor.
- ERPG-2 is the maximum airborne concentration below which 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 is the maximum airborne concentration below which nearly all individuals could be exposed for up to 1 hour without experiencing or developing life-threatening health effects.

1.2.5 Protective Action Criterion (PAC)/Temporary Emergency Exposure Limit (TEEL)

PACs are essential components for planning and response to uncontrolled releases of hazardous chemicals. These criteria, combined with estimates of exposure, provide the information needed to evaluate chemical release events for the purpose of taking appropriate protective actions. During an emergency response, these criteria may be used to evaluate the severity of the event, identify potential outcomes, and decide what protective actions should be taken. These criteria may also be used to estimate the severity of consequences of an uncontrolled release and to plan for an effective emergency response. PAC values are based on AEGLs, ERPGs, and TEELs. The three benchmarks present threshold levels for:

- PAC-1 Mild, transient health effects
- PAC-2 Irreversible or other serious health effects that could impair the ability to take protective action
- PAC-3 Life-threatening health effects.

1.2.6 Short-Term Exposure Limit (STEL)

A STEL is a 15-minute TWA exposure that should not be exceeded at any time during a work day. The ACGIH suggests that STELs should not be exceeded even if the 8-hour TWA is within the TLV-TWA. Multiple exposures up to the STEL should be less than 15 minutes, should occur no more than 4 times per day, and there should be at least 60 minutes between successive exposures in this range. OSHA does not commonly use the term STEL, but instead has established PEL ceiling limits and peak limits in which a worker's exposure to any substance should at no time exceed the ceiling exposure limit given for that substance. If instantaneous monitoring is not feasible, then the ceiling should be assessed as a 15-minute TWA.

1.2.7 Permissible Exposure Limit (PEL)

A PEL is a legally enforceable OEL promulgated by OSHA. PELs are measured in one of two ways: PEL-C or 8-hour PEL-TWA. If instantaneous monitoring is not feasible, the ceiling shall be assessed as a 15-minute TWA exposure which shall not be exceeded at any time during the working day. The PEL-C value shall not exceed the 8-hour PEL-TWA value for a compound. The PEL-TWA is a time-averaged value given for a substance in any 8-hour work shift of a 40-hour work week. For a select subset of chemicals, OSHA has set "acceptable maximum peak" concentrations that may not be exceeded for short time periods (from 4 to 30 minutes). PEL values are regulatory in nature; as such, they are enforceable and must be followed.

1.2.8 Threshold Limit Value-Ceiling (TLV-C)

TLV-C represents the concentration of a chemical substance that should not be exceeded during any part of the working exposure under any circumstance. If instantaneous measurements are not available, sampling should be conducted for the minimum period of time sufficient to detect exposures at or above the ceiling value. Regulatory agencies such as ACGIH believe that TLVs based on physical irritation should be considered no less binding than those based on physical impairment. There is increasing evidence that physical irritation may initiate, promote, or accelerate adverse health effects through interaction with other chemical or biologic agents or through other mechanisms.

1.2.9 Recommended Exposure Limit (REL)

RELs are OELs published by NIOSH.

1.2.10 Time-Weighted Average (TWA)

The TWA is the average concentration limit of a chemical in air for a specified time period, typically 8 hours per day for 40 hours per week. This value is weighted throughout the working period.

1.2.11 Workplace Environmental Exposure Levels (WEEL)

WEELs are health-based OELs for chemicals that do not have PELs, TLVs, or RELs developed and published by American Industrial Hygiene Association (AIHA) until 2011.

1.2.12 Immediately Dangerous to Life or Health

Immediately Dangerous to Life or Health is the concentration of a chemical in air that is likely to cause death or immediate or delayed permanent adverse health effects or prevent escape from such an environment.

1.2.13 Emergency Exposure Guidance Level (EEGL)

An EEGL is one of the guidance levels for specific contaminants (reviewed and developed by a subcommittee of the National Research Council [NRC]) derived for U.S. Navy personnel operating under emergency conditions for which regulatory agencies have not set standards.

1.2.14 No-Observed-Adverse-Effect Level (NOAEL)

The NOAEL is the largest concentration or amount of a substance found by experiment or observation that causes no detectable adverse alteration of morphology, functional capacity, growth, development, or life span of the target organism under defined exposure conditions.

1.2.15 Lowest-Observed-Adverse-Effect Level (LOAEL)

The LOAEL is the lowest concentration or amount of a substance (dose), found by experiment or observation, that causes an adverse effect on morphology, functional capacity, growth, development, or life span of a target organism distinguishable from normal (control) organisms of the same species and strain under defined exposure conditions.

1.2.16 Maximal Arbeitsplatz-Konzentration (Maximum Workplace Concentration) (MAK)

The MAK is the maximum permissible concentration of a substance as a gas, vapor, or aerosol in the air at the workplace that, according to current knowledge, does not normally affect worker health or cause unreasonable nuisance even with repeated and long-term exposure, usually 8 hours a day, but assuming an average weekly working time of 40 hours. MAKs are developed by the German Research Foundation.

1.2.17 Occupational Exposure Limit (OEL)

An OEL is an upper limit on the acceptable concentration of airborne hazardous substances in the workplace for a particular material or class of materials. OELs are generally set by competent national authorities and enforced by legislation to protect occupational safety and health.

1.2.18 Spacecraft Maximum Allowable Concentration (SMAC)

SMACs are established by the NRC's Committee on Toxicology at the request of the National Aeronautics and Space Administration. SMACs are intended to provide guidance on chemical exposures during normal operations of spacecraft as well as in emergency situations. Short-term SMACs refer to concentrations of airborne substances (such as a gas, vapor, or aerosol) that will not compromise the performance of specific tasks by astronauts during emergency conditions or cause serious or permanent toxic effects. Such exposures might cause reversible effects, such as mild skin or eye irritation, but they are not expected to impair judgment or interfere with proper responses to emergencies. Long-term SMACs are intended to avoid adverse health effects (either immediate or delayed) and to prevent detrimental change in crew performance under continuous exposure to chemicals in the closed environment of the space station for as long as 180 days.

1.2.19 RD₅₀

 RD_{50} is defined as the 10-minute exposure concentration producing a 50% respiratory rate decrease in mice or rats and can be used to estimate severe respiratory irritation. Prolonged exposure to an RD_{50} concentration has been shown to produce respiratory tract lesions consistent with irritation.

1.2.20 Peak Exposures

The ACGIH TLV Committee provided guidance on limiting peak exposures for the substances that have TLV-TWA values established but without TLV-STEL limits. It is recommended that transient increases in worker exposure levels may exceed three times the value of the TLV-TWA level for no more than 15 minutes at a time, on no more than four occasions spaced 1 hour apart during a work day, and under no circumstances should they exceed five times the value of the TLV-TWA level. In addition, the 8-hour TWA is not to be exceeded for an 8-hour work period (ACGIH 2016).

2.0 Recommended Acute Regulatory Values

COPCs fall into two general categories, 1) COPCs with available regulatory guidelines and 2) COPCs without available regulatory guidelines. Existing acute regulatory values can be directly applied to the industrial hygiene program and this document identifies the subset of COPCs within this category. The development of acute exposure guidelines for COPCs without available regulatory values (i.e., TECs) is the subject of a separate and subsequent effort being pursued.

Table 1 lists the recommended acute regulatory values for several chemicals with existing acute exposure guidelines. Discussions of the bases for these recommendations are provided in the following sections.

Chemical		CAS Number ^a	Chronic _{HTF} OEL	Recommended Acute Regulatory Value	Source ^b
Inorganic	Compounds				
1	Ammonia	7664-41-7	25 ppm ^c	35 ppm	STEL ^d
2	Mercury	7439-97-6	0.025 mg/m ³	0.1 mg/m ³	PEL-C ^e
Hydrocar	bons				
3	1,3-Butadiene	106-99-0	1 ppm	5 ppm	STEL
4	Benzene	71-43-2	0.5 ppm	2.5 ppm	STEL
Alcohols					
5	Methanol	67-56-1	200 ppm	250 ppm	STEL
Ketones					
6	2-Hexanone	591-78-6	5 ppm	10 ppm	STEL
7	3-Buten-2-one	78-94-4	0.2 ppm	0.2 ppm	TLV-C ^f
Aldehydes					
8	Formaldehyde	50-00-0	0.3 ppm	0.3 ppm	TLV-C
9	Acetaldehyde	75-07-0	25 ppm	25 ppm	TLV-C
10 (P1) ^g	2-Propenal	107-02-8	0.1 ppm	0.1 ppm	TLV-C
Amines					
11	Ethylamine	75-04-7	5 ppm	15 ppm	STEL
Isocyanate					
12	Methyl Isocyanate	624-83-9	20 ppb ^h	60 ppb	STEL

 Table 1. Acute Regulatory Values

^a Chemical Abstracts Service (CAS) Registry Number

^b Key sources for the recommended actual regulatory values.

^c ppm = parts per million

^d STEL values are 15 min short-term exposure levels

^e PEL values are recommended by OSHA and are regulatory in nature (OSHA 2016).

^f TLV-C represents the concentration of a chemical substance that should not be exceeded during any part of the working exposure (ACGIH 2015).

^g 2-Propenal is a new addition to the COPC list as of September 2017. The designation P1 is used to identify this new COPC, as it was a proposed addition when this study began.

^h ppb = parts per billion

2.1 Acute Regulatory Values

Table 1 lists acute regulatory values for COPCs that are based on STEL, TLV, and PEL values. These acute values are based on a nominal 15-minute exposure time, or as short a duration as necessary to quantify the COPC concentration. Inhalation toxicological data were a higher priority consideration during evaluation of available data and guidelines. Because these short-term exposure values reflect existing regulatory guidelines, they are proposed for adoption at the Hanford site to assist operational risk management, and workforce communications.

2.2 Summary of Available Acute Regulatory Values from Government and Private Agencies

Chemicals are presented in the same order as listed in Table 1.

2.2.1 Inorganic Compounds

2.2.1.1 Ammonia (7664-41-7)

Ammonia Recommendation: 35 ppm STEL

Justification: NIOSH and ACGIH both recommend STEL values for ammonia. The ACGIH is a prioritized source for regulatory information due to contractual obligations with the U.S. Department of Energy (DOE). The ACGIH handbook (ACGIH, 2015) lists a 35 ppm STEL for ammonia, which is recommended to assist operational risk management and workforce communications at the Hanford site.

Available Guidelines

ACGIH STEL = 35 ppm

NIOSH STEL = 35 ppm.

OSHA STEL = 35 ppm. The NRC recommends that the EEGL for 1 hour be 100 ppm.

The National Aeronautics and Space Administration recommended the SMAC for 1 hour to be 30 ppm.

Ammonia is irritating upon immediate contact with mucous membranes of the eyes, mouth, and respiratory tract. Humans experience either faint or no irritation after exposure to ammonia at 30 ppm for 10 minutes. Therefore, 30 ppm was used to derive the AEGL-1 value. No interspecies factor is applied because the AEGL value is based on human data. An intraspecies uncertainty factor of 1 was selected because ammonia is efficiently scrubbed in the upper respiratory tract and confined to the nasal cavity and possibly eyes if irritation occurs. The AEGL-1 value of 30 ppm for all time points is supported by observations that humans reported similar intensities of response after exposure to 50 ppm for 10 minutes to 2 hours.

The AEGL-2 values were based on "offensive" irritation to the eyes and respiratory tract experienced by human subjects exposed to 110 ppm of ammonia for 2 hours (Verberk 1977). The 1-hour AEGL-2 values for ammonia by the National Advisory Committee (NAC) are 220 ppm, 220 ppm, and 160 ppm for 10 minute, 30 minute, and 1 hour, respectively. An interspecies uncertainty factor is not applied because the AEGL values are based on human data. An intraspecies uncertainty factor of 1 is selected because

ammonia is a contact irritant. Time scaling across the pertinent timeframes was based on the ten Berge et al. (1986) dose-response regression equation $Cn \times t = k$ where C is concentration and k is a constant. The value of n is 2, which was derived from mouse and rat lethality data. The 2-hour exposure value of 110 ppm was adopted as the 4-hour and 8-hour values, because the maximum severity rating for irritation changed little between 30 minutes and 2 hours. Therefore, it is not expected to change for exposures up to 8 hours. The 30-minute value also was adopted as the 10-minute AEGL-2 value, because time scaling would yield a 10-minute value of 380 ppm, which might impair escape.

AIHA recommends an ERPG-2 level of 150 ppm. This value was recommended largely based on an exposure study involving human subjects exposed to 140 ppm for 2 hours (MacEwen and Vernot 1972, Verberk 1977). Unconditioned subjects did not experience lacrimation at this level as only one of five subjects could smell ammonia at 140 ppm. The ERPG-2 value is lower than the AEGL-2 1-hour value. Both AEGL-2 and ERPG-2 values were derived based on the same human exposure study.

The ERPG-1 level is 25 ppm. Nothing more than mild eye, nose, throat, or respiratory tract irritation was noted in exposures ranging from 25 to 50 ppm for at least 10 minutes. The odor of ammonia is detectable at 25 ppm but no adverse effects are anticipated. The ACGIH STEL value is 35 ppm (ACGIH, 2015), which is higher than the AEGL-1 15-minute value.

2.2.1.2 Mercury (7439-97-6)

Mercury Recommendation: 0.1 mg/m³ Ceiling

Justification: OSHA is a prioritized source for regulatory information due to legal authority. The OSHA PEL-C of 0.1 mg/m³ for mercury is recommended to assist operational risk management and workforce communications at the Hanford site.

Available Guidelines

OSHA enforces a PEL-C of 0.1 mg/m³ (OSHA, 2016).

The AIHA recommended an ERPG-2 of 2.0 mg/m³ based on animal studies. Mercury vapor is odorless and produces no irritation or other early warning signs. In known human and animal studies, any adverse effects from exposure to mercury vapor have been delayed for more than 1 hour; therefore, AIHA did not recommend an ERPG-1 value. For the same reason, AEGL-1 values were not recommended. ACGIH stated that there were insufficient data to recommend a TLV-STEL (ACGIH, 2015).

The point of departure for the AEGL-2 was a single 2-hour exposure of pregnant rats to 4 mg/m³ of mercury vapor (Morgan et al. 2002). This exposure was a NOAEL for developmental effects in rats. An interspecies uncertainty factor of 1 and an intraspecies uncertainty factor of 3 were used to adjust the value. For time scaling, the resulting 2-hour value of 1.33 mg/m^3 was time-scaled using n = 3 and n = 1 for longer and shorter exposure durations, respectively.

2.2.2 Hydrocarbons

2.2.2.1 1,3-Butadiene (106-99-0)

1,3-Butadiene Recommendation: 5 ppm STEL

Justification: OSHA is a prioritized source for regulatory information due to legal authority. The OSHA STEL of 5 ppm for 1,3-butadiene is recommended to assist operational risk management and workforce communications at the Hanford site.

Available Guidelines

The OSHA STEL is 5 ppm.

The AIHA recommended ERPG-2 is 200 ppm. This value is based on fetotoxicity data and comparative metabolism between species. Fetal toxicity in mice was observed at 200 ppm (Irvine 1981; Hackett et al. 1987a, 1987b). The ERPG-1 level is 10 ppm. At this level, the odor is detectable (>1.6 ppm odor threshold), but it is considered aromatic and not objectionable at this level. However, at higher concentrations, the odor becomes objectionable.

The study by Carpenter et al. (1944) is considered most relevant as the point of departure for interim AEGL-2 development. In this study, two human volunteers showed no AEGL-2 effects during an 8-hour exposure of 8000 ppm. Although a rat study also was considered, it was determined that these data did not provide an appropriate point of departure for AEGL-2 determination as the maternal growth inhibition probably is caused by repeated exposure and is unlikely to occur from a single exposure at the same dose (Van Raaij et al. 2003). The 8000 ppm exposure concentration is a NOAEL in semichronic exposure and is considered to be very conservative as a point of departure for AEGL-2. An intraspecies factor of 3 is considered sufficient. The value of $8000 \div 3 = 2700$ ppm for 8 hours was extrapolated across the time periods using the dose-response regression equation $Cn \times t = k$. The value of 3 is selected for n as a reasonable upper bound. Because the point of departure is longer than 4 hours, the AEGL-2 10-minute value is the same as the AEGL-2 30-minute value. The point of departure for AEGL-1 derivation is exposure to 2000 ppm for 7 hours (Carpenter et al. 1944). Because there were only two human subjects, an intraspecies factor of 3 is considered. Therefore, AEGL-1 is calculated as 2000 ppm ÷ 3 resulting in approximately 670 ppm. Because the type of effect (i.e., local eye effects) is considered to be related to the concentration rather than the exposure time, AEGL-1 values are set equal for all exposure periods. The AEGL-1 value is significantly higher than the OSHA STEL. Because AEGL-1 is based on limited human data and on eye effects, it is possible that AEGL-1 may not be exactly suitable as acute regulatory value. The latter is more concerned with respiratory tract, respiratory irritant, and carcinogenic effects.

2.2.2.2 Benzene (71-43-2)

Benzene Recommendation: 2.5 ppm STEL

Justification: The ACGIH is a prioritized source for regulatory information due to contractual obligations with DOE. The ACGIH STEL of 2.5 ppm for benzene is recommended to assist operational risk management and workforce communications at the Hanford site.

Available Guidelines

The ACGIH STEL is 2.5 ppm (Paxton et al. 1994, Crump 1994, Schnatter et al. 1996). There is a Notice of Intended Change to reduce the TLV-TWA to 0.1 ppm. Occupational exposure to benzene causes human leukemogen; therefore, it is categorized as a Confirmed Human Carcinogen, assigned as A1. A skin notation also has been proposed.

The OSHA STEL is 5 ppm.

The NIOSH STEL is 1 ppm.

The NRC recommended a 1-hour EEGL of 50 ppm. It estimated that exposures below 900 ppm would not pose a significant (1/10,000) cancer risk for a 1-hour emergency exposure (NRC 1986).

The AIHA recommended an ERPG-2 value of 150 ppm. Also, 150 ppm is below the concentration at which some evidence of developmental toxicity was observed in experimental animals (Kuna and Kapp 1981, Reinhardt et al. 1971). The ERPG-1 level is 50 ppm. The average odor threshold is 61 ppm. Some light transient neurotoxic effects are expected at a level of 50 ppm.

The interim AEGL-1 values are derived based on a human inhalation study. The point of departure is 110 ppm for 2 hours (Srbova et al. 1950). Because central nervous system (CNS) effects are the consequence of systemic benzene exposure, time extrapolation is applied. The value of n = 2 is used for shorter exposure times and n = 1 for longer exposure times. The interspecies uncertainty factor is 1, and the intraspecies uncertainty factor is 3. Following this methodology, the 15-min AEGL-1 is 104 ppm.

The interim AEGL-2 values are 800, 1100, and 800 ppm for 10-minute, 30-minute, and 1-hour values, respectively. The prominent effect of acute benzene exposure is CNS depression. This is a continuum from very slight dizziness to narcosis, the level that impairs escape should be identified for AEGL-2 derivation. No adequate dose-response studies are available for humans. Animal data are used as the point of departure. Molnar et al. (1986) showed increased locomotor activity in rats exposed for 4 hours at 4000 ppm and decreased activity at 5940 ppm. The highest level showing no AEGL-2 effect is 4000 ppm for 4 hours in rats compared with another studies. For scaling, n = 2 is chosen for short time extrapolation, because n = 3 is too conservative. For extrapolation to longer durations, n = 1 is used based on data presented in Von Oettingen (1940) on light and deep narcosis in cats. The interspecies factor of 3 is chosen because CNS-dependent effects of benzene do not vary among species. An intraspecies factor of 3 was used because the variability between groups in the population does not vary more than a factor of 2 to 3. The total uncertainty factor is 10.

With respect to CNS depression in animals, benzene is less or equipotent to other alkylbenzenes and toluene (Molnar et al. 1986, Tegeris and Balster 1994, Frantik et al. 1994), which means the AEGL-2 values for benzene should be within the same order of magnitude as the CNS-based AELG-2 values for toluene, for example. The interim AEGL-2 values for toluene are 990, 570, and 510 ppm for the 10 minute, 30 minute, and 1 hour periods, respectively. The proposed AEGL-2 levels for xylenes are 990, 480, 430 ppm for the 10 minute, 30 minute, and 1 hour, periods, respectively. Both toluene and xylene reach steady status in the blood within 2 to 4 hours. Benzene does not reach a steady state in blood tissue before 4 hours. Therefore, the benzene time extrapolation should continue over the whole AEGL time frame. Following this method, the 15-minute AEGL-2 value is determined to be 1600 ppm.

2.2.3 Alcohols

2.2.3.1 Methanol (67-56-1)

Methanol Recommendation: 250 ppm STEL

Justification: The ACGIH is a prioritized source for regulatory information due to contractual obligations with DOE. The ACGIH STEL of 250 ppm for methanol is recommended to assist operational risk management and workforce communications at the Hanford site.

The ACGIH recommends a STEL of 250 ppm with a skin notation (NIOSH 1997, Gosselin et al. 1984, McNally 1937, Browning 1965, Henson 1960, Rowe and McCollister 1982).

The OSHA STEL is 250 ppm (skin notation).

The NIOSH REL STEL is 250 ppm (skin notation). The effects considered were blindness and metabolic acidosis.

National Academy of Sciences EEGLs are 800 ppm (10 minutes), 400 ppm (30 minutes), 200 ppm (1 hour.), and 10 ppm (24 hours), based on monkey fatality studies.

AIHA recommended the ERPG-2 value to be 1000 ppm largely based on workers exposed to between 1000 and 2000 ppm methanol for 30 minutes or less. The ERPG-1 value is recommended to be 200 ppm based on a study of workers exposed repeatedly to methanol. The threshold for producing headaches and dizziness was reported to be approximately 200 ppm.

The interim AEGL-1 values were calculated based on the exposure of 800 ppm for 8 hours. A factor of 3 was applied for intraspecies variability because inter-individual variability with regard to slight CNS effects (e.g., headache) is likely to exist. The value was scaled to appropriate exposure periods according to the dose-response regression equation $Cn \times t = k$, using n = 3 for shorter exposure periods because of the lack of suitable experimental data for deriving the concentration exponent. The 30-minute AEGL-1 value was adopted as the 10-minute value because no studies were available to demonstrate the absence of notable discomfort.

The interim U.S. Environmental Protection Agency (EPA) AEGL-2 values were based on developmental toxic effects. At a NOAEL of 2000 ppm for 7 hours, the corresponding end-of-exposure blood methanol concentration was measured as 487 mg/L (Rogers et al. 1993). A total uncertainty factor of 10 was used. An uncertainty factor of 1 was applied for interspecies variability because a pharmacokinetic model was used to account for the toxic kinetic differences between species. An uncertainty factor of 10 was used for intraspecies variability because no information on developmental toxic effects of methanol on humans is available. Using the pharmacokinetic model for blood methanol concentrations after inhalation exposure (Perkins et al. 1995), the exposure concentrations were calculated to result in a blood methanol concentration of 48.7 mg/L in humans. These calculated exposure concentrations at different time integrals were rounded and presented as the AEGL-2 values.

2.2.4 Ketones

2.2.4.1 2-Hexanone (591-78-6)

2-Hexanone Recommendation: 10 ppm STEL

Justification: The ACGIH is a prioritized source for regulatory information due to contractual obligations with DOE. The ACGIH TLV STEL value of 10 ppm for 2-Hexanone (also commonly known as methyl-n-butyl ketone) is recommended to assist operational risk management and workforce communications at the Hanford site.

The ACGIH TLV STEL of 10 ppm is based on skin notation (DiVincenzo et al. 1978). This chemical is known to have the potential to induce testicular toxicity.

2.2.4.2 **3-Buten-2-one** (78-94-4)

3-Buten-2-one Recommendation: 0.2 ppm Ceiling

Justification: The ACGIH is a prioritized source for regulatory information due to contractual obligations with DOE. The ACGIH TLV-C value of 0.2 ppm for 3-buten-3-one (also commonly known as methyl vinyl ketone) is recommended to assist operational risk management and workforce communications at the Hanford site.

Available Guidelines

The ACGIH TLV-C is 0.2 ppm based on the relative irritancy derived from the mouse RD₅₀ (Schaper 1993) and investigation by Muller and Greff (1984).

The AEGL-1 values are based on a rat inhalation study. A NOAEL of 0.5 ppm was demonstrated for nasal lesions in both rats and mice. The point of departure for deriving the AEGL-1 values is irritation with a NOAEL of 0.5 ppm after multiple exposures to 1 ppm (Morgan et al. 2000). No interspecies uncertainty factor was used because similar NOAELs were obtained in multiple species. An uncertainty factor of 3 was used for sensitive population or intraspecies variation. A factor of 10 was considered unnecessary because methyl vinyl ketone causes contact irritation. The associated response is not expected to vary among individuals or vary with duration of exposure; therefore, 0.5 ppm \div 3 = 0.17 ppm, which we rounded to 0.2 ppm for simplicity in reporting. The 15-minute AEGL-1 value is proposed to be the same as the interim 30-minute AEGL-1 value. This value is rounded to be 0.2 ppm as the acute exposure concentration limit. This value is the same as the ACGIH TLV-C value.

The AEGL-2 values are based on a study by Morgan et al. (2000). The lowest concentration causing nasal cavity necrosis was 2 ppm in rats and mice, and this exposure concentration was a NOAEL for lung lesions in rats. The AEGL-2 values are based on respiratory tract irritation at 2 ppm that could impair escape for some individuals. The concentration-exposure time relationship for many irritant and systemically acting vapors and gases may be described by the dose-response regression equation $Cn \times t = k$, with n ranging from 0.8 to 3.5 (ten Berge et al. 1986). Temporal scaling was performed using n = 3 for time points ≤ 6 hours, and n = 1 for longer times (NRC 2001). An uncertainty factor of 3 was used for intraspecies extrapolation. The 10-minute AEGL-2 value was set equivalent to the 30-minute value due to uncertainties in extrapolating from the experimental exposure durations of ≥ 4 hours to 10 minutes.

2.2.5 Aldehydes

2.2.5.1 Formaldehyde (50-00-0)

Formaldehyde Recommendation: 0.3 ppm Ceiling

Justification: The ACGIH is a prioritized source for regulatory information due to contractual obligations with DOE (ACGIH 2015). The ACGIH TLV-C value of 0.3 ppm for formaldehyde is recommended to assist operational risk management and workforce communications at the Hanford site.

The ACGIH recommends a TLV-C value of 0.3 ppm with an A2 carcinogen designation through 2016. In 2017, the ACGIH recommends a STEL value of 0.3 ppm largely based on the threshold for sensory irritation consistent with recommendations from other agencies including the Agency for Toxic Substances and Disease Registry, National Academy of Sciences, World Health Organization, MAK, Scientific Committee on Occupational Exposure Limit Values, etc. The 2017 ACGIH classification also reports information on skin and respiratory sensitization in addition to carcinogenic classification (ACGIH 2017).

OSHA recommends a PEL of 0.75 ppm as an 8-hour TWA or 2 ppm as a 15-min STEL.

The AIHA recommends an ERPG-2 level of 10 ppm.

The AIHA ERPG-2 value is based on human exposure data. Exposure to concentrations >10 ppm formaldehyde for 1 hour could produce severe eye, nasal, and throat irritation that impair protective actions. The ERPG-1 value of 1 ppm is based on human exposure data. Formaldehyde concentrations of greater than 1 ppm would be detected and perceived as objectionable by a large percentage of the population.

The NRC 1-hour AEGLs (interim values) are 0.90 ppm for AEGL-1 and 14 ppm for AEGL-2 for exposures 1 hour in duration. The endpoint is eye and nose irritation to which adaptation occurs. A 14 ppm value is proposed for both the AEGL-2 10-minute and 30-minute exposures. Because the key toxic effect is irritation, the threshold value at 15 minutes should not differ from that at 10 minutes. As to the derivation of AEGL-1, 0.9 ppm was selected as the basis. This value came from human subjects who reported eye irritation responses ranging from none to slight irritation with air concentrations ranging from 0.35 to 0.9 ppm. The 0.9 ppm concentration was applied across all exposure durations because several studies show there is adaptation or irritation at this low concentration.

2.2.5.2 Acetaldehyde (75-07-0)

Acetaldehyde Recommendation: 25 ppm Ceiling

Justification: The ACGIH is a prioritized source for regulatory information due to contractual obligations with DOE. The ACGIH TLV-C value of 25 ppm for acetaldehyde is recommended to assist operational risk management and workforce communications at the Hanford site.

Available Guidelines

The ACGIH recommends a TLV-C value of 25 ppm with an A3 carcinogen designation (i.e., confirmed animal carcinogen with unknown relevance to humans) as a 15-minute ceiling to reduce the potential for ocular and upper respiratory tract irritation.

AIHA recommends an ERPG-2 level of 200 ppm. Human volunteers who reported no eye irritation at 200 ppm did exhibit red eyes and transient conjunctivitis after 15-minute exposures. Subjects exposed to 134 ppm for 30 minutes experienced mild upper respiratory tract irritation. The ERPG-1 value is 10 ppm. Concentrations above 10 ppm might be perceived as a clearly defined objectionable odor.

NAC has proposed an interim AEGL-1 value of 45 ppm for the 10-minute, 30-minute, and 1-hour exposure durations, respectively. The interim AEGL-2 values for 10-minute, 30-minute, and 1-hour exposure durations proposed by NAC are 340 ppm, 340 ppm, and 270 ppm, respectively. The AEGL-1

was derived from an exposure study in which mild respiratory irritation was observed at a measured concentration of 134 ppm for 30 minutes. This concentration was chosen as the point of departure for AEGL-1 derivation. An uncertainty factor of 3 is applied to account for intraspecies variability. Because little variation is expected for direct eye irritation effects, no time scaling is applied. The 45-ppm value is used across the AEGL time points.

Inhalation of acetaldehyde by humans may lead to coughing; irritation of the nose, throat and eyes; persistent lacrimation; corneal epithelial damage; photophobia; foreign body sensation; pulmonary edema; and anesthesia. The dose-response of these effects is unknown. AEGL-2 values were derived based on limited animal data. The default time scaling method is applied using the dose-response regression equation $Cn \times t = k$, with n = 1 for longer duration exposures and n = 3 for shorter duration exposures. Because the starting point for time extrapolation is 4 hours or longer, the same AEGL-2 value is used for both the 10-minute and 30-minute exposure durations.

2.2.6 2-Propenal (107-02-8)

2.2.6.1 2-Propenal

2-Propenal Recommendation: 0.1 ppm Ceiling

Justification: The ACGIH is a prioritized source for regulatory information due to contractual obligations with DOE. The ACGIH TLV-C value of 0.1 ppm for 2-propenal (also commonly known as acrolein) is recommended to assist operational risk management and workforce communications at the Hanford site.

Available Guidelines

The ACGIH TLV-C value is 0.1 ppm with a skin notation.

The OSHA PEL-C is 0.1 ppm.

Data from human studies were used to derive AEGL-1 values. Very slight eye irritation and annoyance of discomfort were observed in human subjects at 0.9 ppm. An intraspecies uncertainty factor of 3 was applied resulting in 0.3 ppm, because minor ocular contact irritation is unlikely to vary among humans. The 0.3 ppm value is held constant across exposure durations because minor irritancy is generally a threshold effect, and prolonged exposure is unlikely to result in a greatly enhanced effect (NRC 2001). The AEGL-1 value is considered protective because earlier data suggested no irritation in humans exposed to acrolein at 0.06 ppm for 5 minutes.

The AEGL-2 10-minute, 30-minute, and 1-hour exposures recommended by the NAC are 0.44, 0.18, and 0.10 ppm, respectively. The 1-hour human exposure of 0.3 ppm was adjusted by temporal scaling to obtain the 10- and 30-minute values. The dose-response regression equation $Cn \times t = k$ was used for scaling, where n = 1.2 was derived from lethality data in rats exposed to acrolein from 1 to 4 hours. An interspecies factor of 1 and an intraspecies factor of 3 were applied in the derivation of AEGL values for 10-minute and 30-minute exposures.

AIHA recommends an ERPG-1 level of 0.05 ppm and an ERPG-2 level of 0.15 ppm. Acrolein at this level may be mildly irritating to both the eyes and the respiratory tract. Mild eye irritation has been reported at a concentration as low as 0.09 ppm as described in the AEGL-1 derivations. Odor threshold concentrations have ranged from 0.03 to 0.16 ppm. The ERPG-1 level of 0.05 ppm is believed to cause no more than odor detection or mild irritation for nearly all individuals.

2.2.7 Amines

2.2.7.1 Ethylamine (75-04-7)

Ethylamine Recommendation: 15 ppm STEL

Justification: The ACGIH is a prioritized source for regulatory information due to contractual obligations with DOE. The ACGIH STEL value of 15 ppm for ethylamine is recommended to assist operational risk management, and workforce communications at the Hanford site.

Available Guidelines

ACGIH STEL value of 15 ppm for ethylamine.

Data from other alkylamines were used in AEGL-1 derivations. Specifically, methylamine was used for ethylamine. Two studies were used to determine the point of departure, one from a single 6-hour exposure of male rats to 75 ppm (Kinney et al. 2008) and another 30-minute exposure of Wistar rats to 465 ppm (Jeevaratnam and Sriramachari 1994). A total uncertainty factor of 10 (3 for interspecies, 3 for intraspecies, and 2 as a modifying factor) was used in the Kinney et al. (2008) value. The 10-minute to 8-hour AEGL-1 was derived as 75 ppm \div 10 \times 2 = 15 ppm for methylamine. Using the Sriramachari and Jeevaratnam (1994) study as the base, a total uncertainty factor of 10 is used. In addition, a modifying factor of 3 is used, because only one exposure duration was used in that study. Therefore, (465 ppm \div 10) \div 3 = 15 ppm. To adjust the difference between ethylamine and methylamine, a factor of 2 is used, 15 ppm \div 2 = 7.5 ppm. AEGL-1 value is not used as the acute regulatory value.

No data from human studies were available for the development of AEGL-2 values. In the absence of empirical data for AEGL-2, the values for ethylamine were based on its analogue methylamine. Both compounds are primary amines with similar toxicities. The AEGL-3 and AEGL-2 values for methylamine were based on the threshold for lethality and severe irritation, respectively, which are suitable endpoints for the respective levels. The ratio between the AEGL-3 and AEGL-2 values for methylamine at 60 minutes was used to modify the AEGL-3 values for ethylamine to derived AEGL-2 values. The ratio between the 1-hour AEGL-3 and AEGL-2 values for methylamine is 5.5. This number was applied to the AEGL-3 values to derive the AEGL-2 values.

2.2.8 Isocyanates

2.2.8.1 Methyl Isocyanate (624-83-9)

Methyl Isocyanate Recommendation: 60 ppb STEL

Justification: The ACGIH is a prioritized source for regulatory information due to contractual obligations with DOE. The ACGIH STEL value of 60 ppb for methyl isocyanate is recommended to assist operational risk management and workforce communications at the Hanford site.

The ACGIH TLV-STEL is 0.06 ppm or 60 ppb updated in 2014 (ACGIH 2014) with skin notation and as a dermal sensitizer. The TLV base cited upper respiratory track and eye irritation.

The AIHA ERPG-2 is 0.25 ppm. This value is based on the RD_{50} value of 1.3 ppm and the fact that 1 ppm was a NOAEL in mice exposed 6 hours/day for 4 or 8 days. The ERPG-1 level is 25 ppb. This level is slightly higher than the ACGIH TLV and OSHA PEL 8-hour TWAs, which are based on the irritation properties of this chemical. Exposure to 0.05 ppm resulted in mild, transient eye irritation. Methyl isocyanate can be identified by its odor at this level.

The EPA did not recommend any AEGL-1 values due to lack of data. However, it is noted that both the duration of exposure and the concentration contribute to the severity of methyl isocyanate induced irritation. The EPA AEGL-2 values for methyl isocyanate are 0.40, 0.13, and 0.067 ppm for 10 minute, 30 minute, and 1 hour exposure durations, respectively. The AEGL values are substantially less than the ERPG-2 values because of the different end points. The AEGL-2 value was based on reduced fetal body weight. Systemic toxicity data from rats and mice were used to derive AEGL-2 values. The single exposure concentration of 2 ppm for 3 hours was an experimentally derived LOAEL for reduced fetal body weights in the absence of maternal toxicity (Varma 1987). An increase in cardiac arrhythmias occurred in rats 4 month after a 2-hour exposure to 3 ppm (Tepper et al. 1987). Identical AEGL-2 values are derived based on the exposure of 3 ppm for 2 hours and 2 ppm for 3 hours. Values are scaled for the derivation of 10- and 30-minute time points using the dose-response regression equation Cn × t = k, where n = 1.

The n value was empirically derived from regression analysis of lethality data for rats. The experimental concentration was reduced by a factor 3 to estimate a threshold for effects on cardiac arrhythmias or fetal body weights. A total uncertainty factor of 30 was applied including 3 for interspecies variation due to the similarity between rats and mice and 10 for intraspecies variation because of the unknown mechanism for developmental toxicity.

3.0 Summary

We identified available regulatory guidelines for COPCs to assist operational risk management, and workforce communications at the Hanford site based on technical references published up to 2016. Of the 61 COPCs, acute regulatory guidelines were identified for 12 chemicals listed in Table 1. COPCs not listed in Table 1 are undergoing additional review to determine whether acute exposure guidelines, termed TECs, can be developed. Recommendations for TECs will be provided in subsequent reports, as appropriate. Recommended acute regulatory values reported in Table 1 are complementary to chronic HTTFOEL values, and thus provide additional information to support HTF operations. These values have been developed by authoritative government agencies and private entities (e.g., ACGIH, NIOSH, OSHA, etc.). Their guideline documents are the scientific bases for the recommendations. If the chemicals have been investigated by ACGIH, OSHA, or NIOSH, the available STEL or ceiling values are recommended as the acute regulatory values.

4.0 References

American Conference of Governmental Industrial Hygienists (ACGIH). 2014. "Threshold Limit Values for Chemical Substances and Physical Agents & Biological Exposure Indices." Available at www.acgih.org.

American Conference of Governmental Industrial Hygienists (ACGIH). 2016. "Threshold Limit Values for Chemical Substances and Physical Agents & Biological Exposure Indices." Available at www.acgih.org.

American Conference of Governmental Industrial Hygienists (ACGIH). 2017. "Threshold Limit Values for Chemical Substances and Physical Agents & Biological Exposure Indices." Available at www.acgih.org.

Australian Institute of Occupational Hygienists (AIOH). 2016. *Adjustment of Workplace Exposure Standards for Extended Work Shifts: Position Paper*. 2nd Edition, prepared by the AIOH Exposure Standards Committee, Tullamarine, Victoria, Australia. Available at https://www.aioh.org.au/documents/item/14.

Browning E. 1965. "Methanol." *Toxicity and Metabolism of Organic Solvents*. Chapter 37, pp 311–323, Elsevier Publishing Company, Amsterdam/London/New York. http://www.thetruthaboutstuff.com/pdf/(144)%20Browning,%201965%20Toxicity%20and%20Metabolis m%200f%20Industrial%20Solvents.pdf.

Carpenter CP, CB Shaffer, CS Weir, and HF Smyth. 1944. "Studies on the Inhalation of 1,3-Butadiene." *Journal of Industrial Hygiene and Toxicology* 26(3):69–78. Abstract at https://www.cabdirect.org/cabdirect/abstract/19442701466.

Crump K. 1994. "Risk of Benzene-Induced Leukemia: A Sensitivity Analysis of the Pliofilm Cohort with Additional Follow-Up and New Exposure Estimates." *Journal of Toxicology and Environmental. Health* 42(2):219–242. DOI: 10.1080/15287399409531875.

DiVincenzo GD, ML Hamilton, CJ Kaplan, WJ Krasavage, and JL O'Donoghue. 1978. "Studies on the Respiratory Uptake and Excretion and the Skin Absorption of Methyl n-Butyl Ketone in Humans and Dogs." *Toxicology and Applied Pharmacology* 44:593–604. DOI: <u>10.1016/0041-008X(78)90267-3</u>.

Frantik E, M Hornychova, and M Horvath. 1994. "Relative Acute Neurotoxicity of Solvents: Isoeffective Air Concentrations of 48 Compounds Evaluated in Rats and Mice." *Environmental Research* 66:173–185. DOI: 10.1006/enrs.1994.1053.

Gosselin RE, RP Smith, and HC Hodge. 1984. *Clinical Toxicology of Commercial Products*. Section III, Therapeutics Index, pp 275-279, Williams & Wilkins, Baltimore, Maryland.

Hackett PL, MR Sikov, TJ Mast, MG Brown, RL Buschbom, ML Clark, JR Decker, JJ Evanoff, RL Rommerreim, SE Rowe, and RB Westerberg. 1987a. *Inhalation Developmental Toxicology Studies of 1, 3-Butadiene in the Rat.* PNL-6414, Pacific Northwest Laboratory, Richland, Washington. https://www.osti.gov/scitech/servlets/purl/5664174.

Hackett PL, MR Sikov, TJ Mast, MG Brown, RL Buschbom, ML Clark, JR Decker, JJ Evanoff, RL Rommerreim, SE Rowe, and RB Westerberg. 1987b. *Inhalation Developmental Toxicology Studies: Teratology Study of 1, 3-Butadiene in Mice*. PNL-6414, Pacific Northwest Laboratory, Richland, Washington. https://www.osti.gov/scitech/servlets/purl/5555439.

Henson EV. 1960. "The Toxicology of Some Aliphatic Alcohols – Part II." *Journal of Occupational Medicine* 2(10):497–502.

Irvine LFH. 1981. *1, 3-Butadiene: Inhalation Teratogenicity Study in the Rat.* Report No. 2788-522/, prepared by Harrogate Hazleton Laboratories Europe Ltd., the International Institute of Synthetic Rubber Producers, Houston, Texas.

Jeevaratnam K and S Sriramachari. 1994. "Comparative Toxicity of Methyl Isocyanate and Its Hydrolytic Derivatives in Rats. I. Pulmonary Histopathology in the Acute Phase." *Archives of Toxicology* 69: 39–44.

http://download.springer.com/static/pdf/468/art% 253A10.1007% 252Fs002040050136.pdf?originUrl=http %3A%2F%2Flink.springer.com%2Farticle%2F10.1007%2Fs002040050136&token2=exp=1495816973~acl=%2Fstatic%2Fpdf%2F468%2Fart%25253A10.1007%25252Fs002040050136.pdf%3ForiginUrl%3D http%253A%252F%252Flink.springer.com%252Farticle%252F10.1007%252Fs002040050136*~hmac=7 64f86aca76df4b986926d23d8c3d77710bdae35d04e29f3781696ba5fcf122a

Kinney LA, R Valentine, HC Chen, and GL Kennedy. 2008. "Inhalation Toxicology of Methylamine." *Inhalation Toxicology* 2: 29–39. DOI: 10.3109/08958379009145243.

Kuna RA and RW Kapp, Jr. 1981. "The Embryotoxic/Teratogenic Potential of Benzene Vapor in Rats." *Toxicology and Applied Pharmacology* 57(1):1–7. DOI: 10.1016/0041-008X(81)90018-1.

MacEwen JD and EH Vernot. 1972. *Toxic Hazards Research Unit Annual Technical Report*. SysteMed Corporation Report W-72003, Aerospace Medical Research Laboratory Report TR-72-62, Wright-Patterson Air Force Base, Ohio. https://ntrs.nasa.gov/archive/nasa/casi.ntrs.nasa.gov/19730013316.pdf.

McNally WD. 1937. Toxicology. Industrial Medicine Publisher, p 615, Chicago, Illinois.

Molnar J, K Paksy, and M Naray. 1986. "Changes in the Rat's Motor Behaviour During 4-Hr Inhalation Exposure to Prenarcotic Concentrations of Benzene and its Derivatives." *Acta Physiologica Hungarica* 67(3):349–354.

https://www.researchgate.net/publication/19409540_Changes_in_the_rat%27s_motor_behaviour_during_ 4-hr_inhalation_exposure_to_prenarcotic_concentrations_of_benzene_and_its_derivatives.

Morgan DL, HC Price, RW O'Conner, and MC Cunningham. 2000. "Upper Respiratory Tract Toxicity of Inhaled Methylvinyl Ketone in F-344 rats and B6C3F1 Mice." *Toxicological Sciences* 58(1):182–194. https://www.researchgate.net/publication/12272265_Upper_respiratory_tract_toxicity_of_inhaled_methyl vinyl_ketone_in_F344_rats_and_B6C3F1_mice.

Morgan DL, SM Chanda, HC Price, R Fernando, J Liu, E Brambila, RW O'Connor, RP Beliles, and S Barone, Jr. 2002. "Disposition of Inhaled Mercury Vapor in Pregnant Rats: Maternal Toxicity and Effects on Developmental Outcome." *Toxicological Sciences* 66:261–273. http://www.deq.state.or.us/aq/toxics/docs/morgan.pdf. Muller J and G Greff. 1984. "Investigation into the Relationship between the Toxicity of Molecules of Industrial Interest and Physicochemical Properties: Upper Respiratory Tract Irritation Test Applied to Four Chemical Families." *Food and Chemical Toxicology* 22(8):661–664.

National Research Council (NRC). 1986. *Emergency and Continuous Exposure Guidance Levels for Selected Airborne Contaminants*. Vol. 6, "Benzene and Ethylene Oxide," Committee on Toxicology, National Research Council, National Academy Press, Washington D.C.

National Research Council (NRC). 2001. *Standard Operating Procedures for Developing Acute Exposure Guideline Levels for Hazardous Chemicals*. National Academy Press, Washington, D.C. https://www.nap.edu/read/10122/chapter/1#xiv.

Occupational Safety and Health Administration (OSHA). 2016. "Annotated OSHA Z-2 Table." <u>https://www.osha.gov/dsg/annotated-pels/tablez-2.html</u>. Last assessed on July 13, 2018.

Paxton MB, VM Chinchilli, SM Brett, and JV Rodricks. 1994. "Leukemia Risk Associated with Benzene Exposure in the Pliofilm Cohort II." *Risk Analysis* 14(2):155–161. DOI: 10.1016/0167-6687(96)82422-X.

Perkins RA, KW Ward, and GM Pollack. 1995. "A Pharmacokinetic Model of Inhaled Methanol in Humans and Comparison to Methanol Disposition in Mice and Rats." *Environmental. Health Perspectives* 103:726–733. DOI: 10.1289/ehp.95103726.

Poet TS and C Timchalk. 2006. *Proposed Occupational Exposure Limits for Non-Carcinogenic Hanford Waste Tank Vapor Chemicals*. PNNL-15736, Pacific Northwest National Laboratory, Richland, Washington. http://www.pnl.gov/main/publications/external/technical_reports/PNNL-15736.pdf.

Reinhardt CF, A Azar, ME Maxfield, PE Smith, Jr., and LS Mullin. 1971. "Cardiac Arrhythmias and Aerosol Sniffing." *Archives of Environmental Health* 22(2):265–279.

Rogers JM, ML Mole, N Chernoff, BD Barbee, CI Turner, TR Logsdon, and RJ Kavlock. 1993. "The Developmental Toxicity of Inhaled Methanol in the CD-1 Mouse, with Quantitative Dose-Response Modeling for Estimation of Benchmark Doses." *Teratology* 47(3):175–188. DOI: 10.1002/tera.1420470302.

Rowe VK and SB McCollister. 1982. "Alcohols." *Patty's Industrial Hygiene and Toxicology*, 3rd Rev., Vol 2C, Toxicology, pp 4528-4541, GD Clayton and FE Clayton, (Eds.), John Wiley & Sons, New York.

Schnatter AR, MJ Nicholich, and MG Bird. 1996. "Determination of Leukemogenic Benzene Exposure Concentrations: Refined Analyses of the Plioflim Cohort." *Risk Analysis* 16(6):833–840. https://www.researchgate.net/publication/14235982_Determination_of_Leukemogenic_Benzene_Exposur e_Concentrations_Refined_Analyses_of_the_Pliofilm_Cohort.

Srbova J, JTeisinger, and S Skramovsky. 1950. "Absorption and Elimination of Inhaled Benzene in Man." *Archives of Industrial Hygiene and Occupational Medicine* 2(1):1–8.

Tegeris JS and RL Balster. 1994. "A Comparison of the Acute Behavioral Effects of Alkylbenzenes Using a Functional Observation Battery in Mice." *Fundamental and Applied Toxicology* 22:240–250. DOI: 10.1093/toxsci/22.2.240.

ten Berge WF, A Zwart, and LM Appelman. 1986. "Concentration-Time Mortality Response Relationship of Irritant and Systemically Acting Vapors and Gases." *Journal of Hazardous Materials* 13(3):301–309. DOI: 10.1016/0304-3894(86)850038.

Tepper JS, MJ Wiester, DL Costa, WP Watkinson, and MF Weber. 1987. "Cardiopulmonary Effects in Awake Rats Four and Six Months after Exposure to Methyl Isocyanate." *Environmental Health Perspectives* 72:95–103.

U.S. National Institute for Occupational Safety and Health (NIOSH). 1997. "Criteria for a Recommended Standard—Occupational Exposure to Methanol." DHEW (NIOSH) Pub No 76-148 1976. In: NIOSH Criteria Documents Plus CD-ROM. DHHS (NIOSH) Pub No 97-106; NTIS Pub No pB-5022-18, U.S. National Technical Information Service, Springfield, Virginia.

Van Raaij MTM, PAH Janssen, and AH Piersma. 2003. *The relevance of Developmental Toxicity Endpoints for Acute Limit Setting*. RIVM Report 601900004/2003, Bilthoven, The Netherlands. http://www.rivm.nl/bibliotheek/rapporten/601900004.html

Varma DR. 1987. "Epidemiological and Experimental Studies on the Effects of Methyl Isocyanate on the Course of Pregnancy." *Environmental Health Perspectives* 72:153–157. DOI: <u>10.1289/ehp.8772153</u>.

Verberk MM. 1977. "Effects of Ammonia on Volunteers." *International Archives of Occupational. Environmental Health* 39(2):73–81. DOI: 10.1007/BF00380887.

Von Oettingen WF. 1940. Publ. Health Bulletin 255. U.S. Public Health Service, Washington D.C.

Weber T, JN Smith, and JG Teeguarden. 2018. *Proposed* _{HTF}OELs for Chronic Exposures – COPCs with Regulatory Guidelines. PNNL-26777 Rev. 0, Pacific Northwest National Laboratory, Richland, Washington.

Wilmarth WR, MA Maier, TW Armstrong, RL Ferry, JL Henshaw, RA Holland, MA Jayjock, MH Le, JC Rock, and C Timchalk. 2014. *Hanford Tank Vapor Assessment Report*. SRNL-RP-2014-00791, Savannah River National Laboratory, Aiken, South Carolina.



www.pnnl.gov

902 Battelle Boulevard P.O. Box 999 Richland, WA 99352 1-888-375-PNNL (7665)

