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# TEMPORARY EXPOSURE LIMITS FOR CHEMICALS

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# CHE-129 EXAM PREVIEW

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## Exam Preview:

1. Chemicals and exposures that might have chronic effects may require more sustained monitoring, follow-up, and counseling of exposed persons. For ERPG values, the duration of exposure is assumed to be up to 30 minutes.
  - a. True
  - b. False
2. As of December 2013, there were only \_\_\_\_ chemicals with final or interim AEGL values and only 148 chemicals with ERPG values. Yet thousands of chemicals are used every day at DOE facilities and throughout the United States.
  - a. 229
  - b. 243
  - c. 255
  - d. 261
3. Using Table 3.3 Route Adjustment Factors used for Different Routes of Administration, what is the route adjustment factor associated with an oral exposure?
  - a. 0.05
  - b. 0.1
  - c. 0.5
  - d. 1.0
4. Simple asphyxiants are biologically inert gases which can cause injury by displacing oxygen rather than by any inherent toxicity of their own. Simple asphyxiants include the noble gases as well as nitrogen and hydrogen.
  - a. True
  - b. False

5. According to the reference material, the TEEL values for simple asphyxiants are based on the level to which the simple asphyxiants reduce the oxygen concentration. The normal concentration of oxygen in air is 20.9% by volume. The minimum oxygen concentration that OSHA permits for Confined Space Entry (CSE) is \_\_\_\_%.
- 19.0
  - 19.5
  - 20.0
  - 20.5
6. Biological toxins (biotoxins) are proteins or other macromolecules of microbial, plant, or animal origin. Pound-for-pound, biological toxins are among the most deadly substances known to exist.
- True
  - False
7. Using Table 2.1 Comparison of AEGL, ERPG, and TEEL Values, which of the following classifications matches the description: 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.
- ERPG-3
  - TEEL-1
  - AEGL-1
  - AEGL-2
8. According to the reference material, A TEEL-1 is sometimes less than three times the published chemical-specific TWA.
- True
  - False
9. The chemical definition for “diesel fuel” is found online through ChemIDPlus®, an online database maintained by the National Library of Medicine. ChemIDPlus® defines diesel fuel as a “complex combination of hydrocarbons produced by the distillation of crude oil. It consists of hydrocarbons having carbon numbers predominantly in the range of C9 through \_\_\_\_.”
- C15
  - C18
  - C20
  - C22
10. According to the reference material, the TEEL values for simple asphyxiants are based on the level to which the simple asphyxiants reduce the oxygen concentration. What is the concentration level for TEEL-1, which can lead to impaired attention, thinking, and coordination?
- 45,000 ppm
  - 65,000 ppm
  - 120,000 ppm
  - 230,000 ppm

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## ACRONYMS

<b>ACGIH</b>	American Conference of Governmental Industrial Hygienists
<b>AEGL</b>	Acute Exposure Guideline Level
<b>AIHA</b>	American Industrial Hygiene Association
<b>C</b>	Ceiling Limit
<b>CAF</b>	Compound Adjustment Factor
<b>CAS</b>	Chemical Abstracts Service
<b>CASRN</b>	Chemical Abstracts Service Registry Number
<b>CDC</b>	Centers for Disease Control and Prevention
<b>CSE</b>	Confined Space Entry
<b>DHS</b>	U.S. Department of Homeland Security
<b>DOE</b>	U.S. Department of Energy
<b>DOT</b>	U.S. Department of Transportation
<b>EEGL</b>	Emergency Exposure Guidance Level
<b>EPA</b>	U.S. Environmental Protection Agency
<b>EPHA</b>	Emergency Planning Hazards Assessment
<b>ERPG</b>	Emergency Response Planning Guideline
<b>FEMA</b>	U.S. Federal Emergency Management Agency
<b>GGV</b>	Group Guidance Value
<b>HHR</b>	Health Hazard Rating
<b>HSDB</b>	Hazardous Substances Data Bank
<b>IDLH</b>	Immediately Dangerous to Life or Health
<b>LC<sub>50</sub></b>	Lethal Concentration that kills 50% of the test population
<b>LC<sub>eq</sub></b>	Lethal Concentration Equivalent
<b>LC<sub>Lo</sub></b>	Lowest reported Lethal Concentration
<b>LD<sub>50</sub></b>	Lethal Dose that kills 50% of the test species
<b>LD<sub>Lo</sub></b>	Lowest reported Lethal Dose
<b>LEL</b>	Lower Explosive Limit
<b>LOC</b>	Level of Concern
<b>MAK</b>	Maximale Arbeitsplatz-Konzentration (maximum workplace concentration) from the German Research Foundation
<b>NAC</b>	National Advisory Committee
<b>NARAC</b>	National Atmospheric Release Advisory Capability
<b>NAS</b>	National Academy of Sciences
<b>NA-41</b>	Office of Emergency Management
<b>NFPA</b>	National Fire Protection Association

<b>NIOSH</b>	National Institute for Occupational Safety and Health
<b>NNSA</b>	National Nuclear Security Administration
<b>NRC</b>	National Research Council
<b>OSHA</b>	Occupational Safety and Health Administration
<b>PAC</b>	Protective Action Criterion
<b>PEL</b>	Permissible Exposure Limit
<b>PNOS</b>	Particulates Not Otherwise Specified
<b>ppm</b>	parts per million
<b>RAF</b>	Route Adjustment Factor
<b>REL</b>	Recommended Exposure Limit
<b>RTECS</b>	Registry of Toxic Effects of Chemical Substances
<b>SAR</b>	Structure Activity Relationship
<b>Sax</b>	<i>Dangerous Properties of Industrial Materials</i>
<b>SCAPA</b>	Subcommittee on Consequence Assessment and Protective Actions
<b>STEL</b>	Short-Term Exposure Limit
<b>TAG</b>	TEEL Advisory Group
<b>TC<sub>Lo</sub></b>	Toxic Concentration Lowest
<b>TD<sub>Lo</sub></b>	Toxic Dose Lowest
<b>TEEL</b>	Temporary Emergency Exposure Limit
<b>TERA</b>	Toxicology Excellence for Risk Assessment
<b>TLV</b>	Threshold Limit Value
<b>TWA</b>	Time-Weighted Average
<b>WEEL</b>	Workplace Environmental Exposure Level



## 1 INTRODUCTION

Emergency exposure limits are essential components of planning for the uncontrolled release of hazardous chemicals. These limits, combined with estimates of exposure, provide the information necessary to identify and evaluate accidents for the purpose of taking appropriate protective actions. During an emergency response to an uncontrolled release, these limits may be used to evaluate the severity of the event, to identify potential outcomes, and to decide what protective actions should be taken. In anticipation of an uncontrolled release, these limits may also be used to estimate consequences and plan a response.

In 2005, the U.S. Department of Energy (DOE) issued its latest Emergency Management Order DOE O 151.1C (Order), which addresses managing chemical emergencies along with other Operational Emergencies. DOE uses Acute Exposure Guideline Levels (AEGLs), Emergency Response Planning Guidelines (ERPGs), and Temporary Emergency Exposure Limits (TEELs), in that priority, as the emergency exposure limits. DOE O 151.1D, issued in August 2016, continues the use of AEGLs, ERPGs, and TEELs.

DOE recognized that AEGL and ERPG values exist for a limited number of individual chemicals. DOE commissioned the development of TEEL values in 1992, so that DOE facilities can conduct Emergency Planning Hazard Assessments (EPHAs) and consequence assessments prior to and during emergency response for chemicals lacking AEGL or ERPG values. As the “T” in TEEL indicates, TEEL values are *temporary* limits for chemicals until AEGL values or ERPG values are developed, at which time the TEEL values should no longer be used.

Protective Action Criteria (PACs) are levels of radioactive or chemical materials that threaten or endanger the health and safety of workers or the public. As used in this document, PACs are a collective term for chemical limits that include AEGL, ERPG, and TEEL values. The PAC dataset is the list of chemicals with 60-minute AEGL, ERPG, and/or TEEL values.<sup>1</sup>

The objective of this document is to present the following information associated with TEEL values:

- The need for emergency exposure limits in general and for TEEL values in particular is described in Section 2.3.
- The methods used by a team of chemists/toxicologists established by DOE Headquarters to derive TEEL values for hazardous chemicals are listed in Section 3.

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<sup>1</sup>AEGL and ERPG values are developed in units of either ppm or mg/m<sup>3</sup>. In the PAC dataset, the AEGL and ERPG values are listed in both units for the convenience of the users. When converted to the other units, they are rounded to two significant digits (see DOE, 1992).

- Details regarding TEEL development administration are provided in Section 4.
- Quality assurance and control measures to ensure TEEL values are appropriately derived are described in Section 5.

## **2 FRAMEWORK FOR DEVELOPMENT AND APPLICATION OF TEEL VALUES**

### **2.1 Planning for Chemical Emergencies**

Chemical emergencies can occur as a result of either an accidental or intentional release. Fires, explosions, equipment malfunctions or failures, vehicle crashes, and similar incidents are possible accidental events. Persons immediately affected by these incidents could include those at the scene (e.g., at a workplace or involved in a vehicular crash), first responders (e.g., fire departments, law enforcement, emergency medical services, incident command) and other emergency personnel, and nearby workers, as well as members of the general public downwind of the incident. Intentional releases such as terrorist attacks or chemical warfare create similar problems but have some important differences. Chemicals in an intentional release are usually designed and selected with the intent of inflicting injury and can be released in a way designed to increase the extent and severity of injury (e.g., inflicted on a large population, in a confined space). For either an accidental or intentional release scenario, however, it is important to prepare for such emergencies to allow for the selection of protective actions that are the most effective for minimizing injury and illness.

Response planning actions include evaluating exposure, acquiring equipment, training first responders, developing methods to determine the potential area affected by the release of hazardous material, identifying populations at risk, and planning and selecting appropriate protective actions. This document is concerned with evaluating exposure; other aspects are beyond the scope of this document.

To aid in evaluating risks associated with chemical exposures, the U.S. Environmental Protection Agency (EPA), with the assistance of the National Academy of Sciences (NAS), develops AEGL values as exposure limits designed to aid planning for chemical emergencies (NAS, 2001). The American Industrial Hygiene Association (AIHA) develops ERPG values for similar purposes (AIHA, 2014). Although the specific processes for developing AEGL and ERPG values differ significantly, both processes result in values with a cogent scientific foundation.

Planning for emergencies at DOE facilities includes selecting or developing these criteria for protective action decision-making. DOE, including the National Nuclear Security Administration (NNSA), use AEGL, ERPG, and TEEL values in this order of preference, as PAC values. PAC values are the concentrations of airborne hazardous materials at which protective actions are needed. Emergency procedures for classifying Operational Emergencies and for implementing or recommending protective actions may also incorporate these criteria.

The planning process identifies hazards and the potential consequences from unplanned releases of (or loss of control over) hazardous chemicals using accepted assessment techniques based on PAC values assigned to the hazardous chemicals identified. The planning process may

identify the consequences of projected accidents so that additional inventory or process controls may be implemented to reduce the risk. Field measurements based on these exposure guidelines may be used to refine the area affected by a hazardous material release and to adjust protective actions as appropriate.

There are other organizations, inside and outside DOE, that use PACs for other purposes. For example, PAC values are used by DOE in the development of Documented Safety Analyses. However, the TEEL development program was created for DOE emergency management purposes. The Office of Emergency Management is not responsible for the use of TEELs for other purposes.

## **2.2 Exposure Assessment and Risk Assessment**

An essential aspect of protective action is the evaluation of real or potential exposures to chemicals. To do this, it is important to acquire, to the extent feasible, the following information:

- the identities of the chemicals;
- the amount released;
- their concentration in air;
- the potential duration of exposure (e.g., continuous or puff);
- characteristics of the population exposed; and
- the determinants of exposure (i.e., any circumstances that could alter exposure, such as the weather – wind speed, temperature – or the physical environment).

This information constitutes the raw material for assessing and managing the consequences in a specific incident. Translating this information into an estimate of injury also requires knowledge of the safe levels of exposure. Emergency exposure limits, such as AEGL, ERPG, and TEEL values, are the key additional ingredients for assessing the consequences of injury.

## **2.3 Need for TEEL Values**

As of December 2013, there were only 261 chemicals with final or interim AEGL values (EPA, 2014) and only 148 chemicals with ERPG values (AIHA, 2014). Yet thousands of chemicals are used every day at DOE facilities and throughout the United States. The risk of accidental release of chemicals without AEGL or ERPG values remains, as does the need for DOE to set emergency exposure limits. TEEL values serve this need. The first list of chemicals with TEEL values was

released in 1991 and included values for fewer than 100 chemicals.<sup>2</sup> As of 2013, the PAC dataset includes values for over 3,000 chemicals.<sup>3</sup>

## **2.4 Protective Action Criteria and Risk Management**

Risk management occurs in anticipation of and during chemical emergencies. PAC values provide the basis for consequence assessment for chemical emergencies and are used by DOE in emergency preparedness procedures and for Operational Emergencies.

Risk management can consist of actions taken during emergency planning, in anticipation of an accidental release, or actions taken during or after a release to mitigate the release or to reduce the magnitude of injury. Preventive measures may include reducing the quantity of chemicals in storage, removing chemicals (or reducing their quantities) stored in proximity to sensitive populations, providing for emergency response services, and using less toxic chemicals. Actions during a release can include containing the release; protecting persons at risk; providing first aid, triage, and other medical treatment; and initiating follow-up actions to mitigate injury and illness. In all such procedures, PAC values are essential to risk management and to planning.

## **2.5 Populations at Risk**

Virtually any member of any population can be exposed to toxic chemicals as a result of an accidental release, including persons who are members of susceptible subpopulations, such as infants, children, the elderly, and persons with asthma or other illnesses. PAC values should protect most members of the general population. However, some members of the exposed population may be affected when exposed to levels equal to the PAC values.

## **2.6 Nature and Severity of Toxic Effects**

The nature and severity of toxic effects from a specific chemical depend on its concentration, the duration of exposure, and the route of exposure. All emergency exposure limits to which this document refers assume exposure by inhalation because it is anticipated that inhalation will be the primary route of exposure in an emergency situation. However, some airborne chemicals can have additional, secondary effects through absorption through the skin, eyes, and mucus membranes. Organizations developing inhalation exposure limits specifically select toxicity studies that limit exposures through these secondary routes or account for additional exposure through application uncertainty factors.

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<sup>2</sup> This number is based on Revision 1.

<sup>3</sup> This number is based on Revision 27.

The nature and severity of health effects are relevant to the planning process. Chemical exposures with acute effects require prompt action for primary prevention measures. If the effects are expected to be localized, short-lived, and self-limiting, then preventive actions can be appropriately limited. Chemicals and exposures that might have chronic effects may require more sustained monitoring, follow-up, and counseling of exposed persons. For ERPG values, the duration of exposure is assumed to be up to 60 minutes (AIHA, 2014). AEGL values are developed for five exposure times, including 60 minutes (NAS, 2001). Within DOE, the 60-minute AEGL value is used (DOE, 2007). TEEL values are developed by comparison with 60-minute AEGLs (DOE, 2012).

## **2.7 Comparison of AEGL, ERPG, and TEEL Values**

There are three PAC levels for each chemical in the PAC dataset. Each level represents an increase in the severity of biological effects. Definitions for the three PAC levels are found in Table 2.1.

**Table 2.1 Comparison of AEGL, ERPG, and TEEL Values**

<b>AEGL</b>	<b>ERPG</b>	<b>TEEL</b>
<b>AEGL-1</b> is 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 on cessation of exposure.	<b>ERPG-1</b> is the maximum airborne concentration below which it is believed that nearly all individuals could be exposed for up to 60 minutes without experiencing other than mild transient adverse health effects or perceiving a clearly defined, objectionable odor.	<b>TEEL-1</b> is the airborne concentration (expressed as ppm [parts per million] or mg/m <sup>3</sup> [milligrams per cubic meter]) of a substance above which it is predicted that the general population, including susceptible individuals, when exposed for more than one hour, could experience notable discomfort, irritation, or certain asymptomatic, non-sensory effects. However, these effects are not disabling and are transient and reversible upon cessation of exposure.
<b>AEGL-2</b> is 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.	<b>ERPG-2</b> is the maximum airborne concentration below which it is believed that nearly all individuals could be exposed for up to 60 minutes without experiencing or developing irreversible or other serious health effects or symptoms which could impair an individual's ability to take protective action.	<b>TEEL-2</b> is the airborne concentration (expressed as ppm or mg/m <sup>3</sup> ) of a substance above which it is predicted that the general population, including susceptible individuals, when exposed for more than one hour, could experience irreversible or other serious, long-lasting, adverse health effects or an impaired ability to escape.
<b>AEGL-3</b> is 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.	<b>ERPG-3</b> is the maximum airborne concentration below which it is believed that nearly all individuals could be exposed for up to 60 minutes without experiencing or developing life-threatening health effects.	<b>TEEL-3</b> is the airborne concentration (expressed as ppm or mg/m <sup>3</sup> ) of a substance above which it is predicted that the general population, including susceptible individuals, when exposed for more than one hour, could experience life-threatening adverse health effects or death.

### 3 TEEL DEVELOPMENT METHODOLOGY

#### 3.1 General Considerations

TEEL values are developed by a team of chemists/toxicologists established by DOE Headquarters for chemicals that do not have AEGL or ERPG values. TEEL values are also developed for chemicals that have missing AEGL or ERPG values. For example, jet fuels (Chemical Abstract Service Registry Number (CASRN) 70892-10-3) has AEGL-1 and AEGL-2 values but no AEGL-3 value; thus the PAC-3 for jet fuels is a TEEL-3. Chemicals are selected for deriving TEEL values if an Operational Emergency, as defined in DOE O 151.1C, could result from an uncontrolled release of the material or if they are otherwise deemed to pose a serious health threat to workers or the public in an emergency.

TEEL values differ from AEGL and ERPG values by the methods and the sources of data used to develop them. The processes used to develop AEGL and ERPG values are both painstaking and time-consuming. To produce exposure limits in a more timely fashion while maintaining high quality, TEEL values are developed using a methodology that incorporates existing published exposure limits and toxicity data.

A hierarchy of sources is used for developing TEEL values. This hierarchy is presented in Table 3.1. Existing published exposure limits are the preferred source of information. However, there are many chemicals for which there are no published exposure limits. For these chemicals, toxicity data from lethal dose/lethal concentration (Lethal Concentration, 50% ( $LC_{50}$ ), Lethal Dose, 50% ( $LD_{50}$ ), Lethal Concentration, Lowest ( $LC_{Lo}$ ), Lethal Dose, Lowest ( $LD_{Lo}$ ), Toxic Concentration, Lowest ( $TC_{Lo}$ ), and Toxic Dose, Lowest ( $TD_{Lo}$ )) experiments are used to develop TEEL values.

Unfortunately, there still remain a large number of chemicals for which there are no exposure limits and limited or no useful toxicity data. The TEEL development methodology incorporates calculations and default assumptions to fill gaps resulting from a lack of data. Structure Activity Relationships (SARs) and Health Hazard Ratings (HHRs) have been used to develop a full set of TEEL values when no other data are available. (See Section 3.4.4.)



**Table 3.1 TEEL Data Selection Hierarchy**

TEEL Data	Data Source
<b>TEEL-3</b>	
EEGL (30-minute)	NRC, 1985; 2007, 2008, 2009
IDLH (1990 values)	NIOSH, 1995
Other	Various
LC <sub>50</sub>	HSDB <sup>1</sup> /SAX <sup>2</sup> /RTECS <sup>3</sup>
LC <sub>Lo</sub>	HSDB/SAX/RTECS
LD <sub>50</sub>	HSDB/SAX/RTECS
LD <sub>Lo</sub>	HSDB/SAX/RTECS
<b>TEEL-2</b>	
EEGL (60-minute)	NRC, 1985, 2007, 2008, 2009
LOC	EPA, 1987
TLV-C	ACGIH, 2014
WEEL-C	AIHA, 2014 <sup>4</sup>
PEL-C	OSHA, 2015a
REL-C	CDC, 2007
MAK-C	German Research Foundation
Other	Various
TC <sub>Lo</sub>	HSDB <sup>1</sup> /SAX <sup>2</sup> /RTECS <sup>3</sup>
TD <sub>Lo</sub>	HSDB <sup>1</sup> /SAX <sup>2</sup> /RTECS <sup>3</sup>
<b>TEEL-1</b>	
TLV-STEL	ACGIH, 2014
WEEL-STEL	AIHA, 2014 <sup>4</sup>
PEL-STEL	OSHA, 2015a
REL-STEL	CDC, 2007
MAK-STEL	German Research Foundation
Other	Various
1. Hazardous Substances Data Bank (NLM, 2015) 2. Sax's Dangerous Properties of Industrial Materials (SAX, 2012) 3. Registry of the Toxic Effects of Chemical Substances (RTECS, 2015) 4. WEEL development moved to TERA January 1, 2012	

### 3.2 Exposure Limit-Based TEEL Values

The use of an Immediately Dangerous to Life and Health (IDLH) value as analogous to a level 3 emergency exposure limit and a Level of Concern (LOC) as analogous to a level 2 emergency exposure limit is based on “Technical Guidance for Hazardous Analysis,” a joint publication of

EPA, the Federal Emergency Management Agency (FEMA) and the U.S. Department of Transportation (DOT) (EPA, 1987). Craig, et. al., (1995) performed an analysis comparing the other available published exposure limits with ERPG values. Based on the results of the analysis, the exposure limits presented in Table 3.1 were found to be analogous to emergency exposures limits and were assigned to specific TEEL levels. For example, a ceiling limit is used as a TEEL-2 and a short-term exposure limit is used as a TEEL-1.

IDLH values published in 1990 are used due to a recommendation of the independent review committee that these values were based on species and routes of exposure that represented a good correlation to human inhalation exposure. If later IDLH values are used, they are first considered by the Review Panel (see Section 4.2).

### **3.2.1 Sources of Data**

The most frequently used exposure limits in TEEL development are:

- Threshold Limit Values (TLVs), adopted by the American Conference of Governmental Industrial Hygienists (ACGIH);
- Workplace Environmental Exposure Levels (WEELs), adopted by AIHA until 2011;
- Permissible Exposure Limits (PELs), promulgated by the Occupational Safety and Health Administration (OSHA);
- Recommended Exposure Limits (RELs) and IDLH values, recommended by the National Institute for Occupational Safety and Health (NIOSH);
- Maximale Arbeitsplatz-Konzentration (MAK), from the German Research Foundation; and
- Level of Concern (LOC) values, developed by the EPA.

These exposure limits are set according to different statutory or other criteria and, consequently for some chemicals, the various exposure limits differ. The hierarchy for the exposure limits reflects, in part, DOE management judgment based on the development procedures used by the agencies/organizations, as well as Federal agency guidance. EEGLs are given preference within both TEEL-3 and TEEL-2 because the National Research Council (NRC, now the National Academy of Sciences) has an in-depth peer-review process for EEGL values. As noted above, the precedence for IDLH and LOC within TEEL-3 and TEEL-2, respectively reflects published Federal guidance, i.e., EPA, 1987. Within TEEL-2 and TEEL-1, the precedence of TLVs and WEELs is a result of the independent review committee recommendations. TLVs and WEELs are updated and reviewed regularly, while OSHA PELs, in some cases, have not been updated since 1968.

### 3.2.2 Compound Adjustment Factors

Many exposure limits are listed as the element and the elemental part of a compound (e.g., “manganese and inorganic compounds, as Mn”). Many compounds, such as metal compounds, do not have compound-specific exposure limits. For these kinds of compounds, a Compound Adjustment Factor (CAF) for a compound-to-element molecular weight ratio is calculated.

The CAF is used when an exposure limit addresses both the element and its compounds and is solely concerned with the amount of material in the atmosphere. The exposure limit is based on the element itself. By using the CAF, we adjust the TEEL value for the compound so that we account for the same amount of the element in the air.

Using manganese oxide ( $\text{Mn}_3\text{O}_4$ ) as an example, manganese has an atomic weight of 54.94 and oxygen has an atomic weight of 16.0. Thus, manganese oxide has a molecular weight of 228.82  $[(54.94 \times 3) + (16 \times 4)]$ . The ratio of the molecular weight of manganese oxide to the atomic weight of manganese (multiplied times 3 because there are 3 atoms of manganese) is 1.39. Continuing with this example, the PEL-ceiling for manganese is  $5 \text{ mg/m}^3$ . The PEL-ceiling is multiplied by 1.39 (the CAF), resulting in a TEEL-2 of  $6.95 \text{ mg/m}^3$ .

Similar ratio adjustments are calculated for other compounds by taking the ratio of the molecular weight of the compound to the atomic weight of the most toxic element.

Solubility and insolubility are taken into account by the organization that derives the exposure limit. For some elements, two exposure limits are reported: one for soluble forms or compounds and the other for insoluble. In these cases, the TEEL value is derived by choosing the appropriate (soluble or insoluble) exposure limit for the specific compound of interest and then applying the CAF.

When appropriate, the compound adjustment factors are applied to all exposure limits except AEGL, ERPG, and LOC values.

### 3.3 Toxicity-Based TEEL Values

Published toxicity data are used to derive TEEL-2 and TEEL-3 values only. In order of preference, existing  $\text{TC}_{\text{Lo}}$  and  $\text{TD}_{\text{Lo}}$  data are used to estimate TEEL-2 values and  $\text{LC}_{50}$ ,  $\text{LC}_{\text{Lo}}$ ,  $\text{LD}_{50}$ , and  $\text{LD}_{\text{Lo}}$  data are used to estimate TEEL-3 values. The  $\text{LC}_{50}$  and  $\text{LC}_{\text{Lo}}$  are given priority because they are based on inhalation data – which is highest in the route of exposure hierarchy. The  $\text{LC}_{50}$  is preferred over the  $\text{LC}_{\text{Lo}}$ , and the  $\text{LD}_{50}$  is preferred over the  $\text{LD}_{\text{Lo}}$  because there are multiple data points used to derive the 50% value. The “Lo” data are usually a single data point. Thus there is more reliability in the  $\text{LC}_{50}$  and  $\text{LD}_{50}$  values. Table 3.1 shows the order of preference that exists to derive TEEL-2 and TEEL-3 values from toxicity data.

### 3.3.1 Sources and Types of Data

Toxicity data can be obtained from many sources. The three principal sources used for developing TEEL values are the Hazardous Substances Data Bank (NLM, 2105), Sax's Dangerous Properties of Industrial Materials (SAX, 2012), and the Registry of the Toxic Effects of Chemical Substances (RTECS, 2015). In selecting data from these sources, the following guidelines are followed:

- Only credible studies are used;
- If the studies are within 5 years of each other, the study with the lowest exposure concentration or dose is selected, yielding the more conservative TEEL value;
- If there is more than one set of data for a particular toxic parameter from studies conducted more than 5 years apart:
  - The study of greater reliability is selected first (e.g., using a Klimisch<sup>4</sup> score or Good Laboratory Practice status);
  - If that cannot be determined, the most recent study is selected;
  - If the most recent study cannot be determined, the study with the lowest exposure concentration or dose is selected, yielding the more conservative TEEL value; and
- If there are questions about which study should be selected as the starting point for TEEL derivation, the review panel, as described in Section 4.2, evaluates the data and makes a recommendation to DOE Office of Emergency Management.

### 3.3.2 Toxicity Data Selection

Similar to TEEL values based on published exposure limits, there is a priority order of data used to derive TEEL values from published toxicity data. Parameters are selected for deriving TEEL values by species, route of administration, toxicity endpoint, and exposure time.

Data from human exposures are given primary consideration over data from other species. However, caution should be employed when using human data, as human data may be from an accidental exposure or a therapeutic dose. Data from monkey exposures are preferred over other non-human species, followed by dog, rat, mouse, rabbit, guinea pig, cat, and pig. Toxicity data are limited to only these nine species in TEEL development.

During an Operational Emergency, the primary concern is exposures to airborne concentrations of the chemicals. Therefore, data from inhalation exposures are preferred to data from other routes of administration. Following inhalation, the order of preference is oral, dermal,

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<sup>4</sup>Klimisch, et al. (1997). A systematic approach for evaluating the quality of experimental toxicological and ecotoxicological data. *Regulatory Toxicology and Pharmacology*, 25,1-5.

intraperitoneal, and intravenous routes administration. Toxicity data are limited to these five routes of administration in TEEL development.

Toxicity data, specifically  $TC_{Lo}$  and  $TD_{Lo}$  data, should report acutely toxic endpoints such as ataxia, narcosis, skin burns, or ulcers. Toxic endpoints, such as changes in enzyme levels or olfaction, are not acutely toxic endpoints and are not applicable to TEEL development. In addition, tumorigenic and reproductive effects data are not appropriate for TEEL development as they result from chronic (long-term) and/or repeated exposures.

Data are selected from experiments with exposure times closest to 60 minutes. If the only data available are from repeated exposure studies, then data for the least number of days of exposure are selected. If the number of hours is also provided, then data that has the least total hours of exposure are selected. When exposure times have not been specified in the data sources and there are no other toxicity data available, the following default times are used:

- 15 minutes for humans;
- 240 minutes for rat and 120 minutes for mouse acute exposures;
- 360 minutes for repeated or intermittent exposures; and
- 1,440 minutes for continuous exposures.

### **3.3.3 Calculating Concentration Equivalent Values using Route Adjustment Factors**

Deriving TEEL values from other than inhalation routes of exposure requires converting the lethal or toxic dose into an “equivalent air concentration,” using default body weights and breathing rates. This is the “concentration equivalent value,” abbreviated as  $LC_{eq}$ . Default values for mean body weight (kilograms - kg) and breathing rate (cubic meters per day -  $m^3/day$ ) used in TEEL value development are shown in Table 3.2 and are drawn from Sax (2012).

**Table 3.2 Default Mean Body Weight and Breathing Rate Values for Different Species\***

Species	Mean Body Weight (bw) (kg)	Mean Breathing Rate (br) (m <sup>3</sup> /day)
Human (Male)	70	20
Human (Female)	50	16
Cat	2	1.25
Dog	10	3.66
Guinea pig	0.5	0.283
Monkey	5	3.94
Mouse	0.025	0.035
Pig	60	20
Rabbit	2	1.3
Rat	0.2	0.153
*SAX, 2012		

The amount of a chemical absorbed varies with the route of administration. For example, intravenous is one of the most efficient routes of administration because a large percentage of the chemical administered is absorbed. Consequently, it is important to adjust the routes of administration based on predicted absorption and distribution efficiency. The Route Adjustment Factors (RAFs) used in TEEL development are shown in Table 3.3. In practice, these values would vary from chemical to chemical, depending on solubility in body fluids, metabolic changes, and other factors.

**Table 3.3 Route Adjustment Factors used for Different Routes of Administration**

Route of Administration	RAF
Inhalation	1.0
Intraperitoneal	1.0
Intravenous	1.0
Oral	0.5
Skin	0.05
Skin-insoluble	0.05
Skin-soluble	0.1

The following equations show how the mean body weight (bw), breathing rate (br), and RAF are used to develop TEEL values from dose-based toxicity data.

Given:

$LD_{50} = 75 \text{ mg/kg}$ , oral route, and the animal is a dog

$LC_{eq} = LD_{50} \times (bw \div br) \times RAF$

$LC_{eq} = 75 \text{ mg/kg/day} \times (10 \text{ kg} \div 3.66 \text{ m}^3/\text{day}) \times 0.5$

Result:

$LC_{eq} = 102 \text{ mg/m}^3$

### 3.3.4 Adjustment Factors used to Convert Concentration-Based and Concentration-Equivalent Values to TEEL Values

For each toxicity parameter, specific adjustment factors have been calculated to develop TEEL values from concentration equivalent values. Recall that concentration equivalent values are calculated from various toxicity data points such as  $LC_{50}$  or  $LD_{50}$ . To convert concentration equivalent values into TEEL values, toxicity parameter-specific adjustment factors have been developed. These adjustment factors were calculated by analyzing the relationship between AEGL values and toxicity data. It is assumed that any model based on AEGL values will also be valid for TEEL values. The results of this analysis are shown in Table 3.4. The white paper describing the analyses and results used to derive these adjustment factors is presented in Appendix A.

**Table 3.4 Adjustment Factors to Derive Toxicity-Based TEEL Values**

Adjustment Factors	TEEL-3				TEEL-2	
	$LC_{50}$	$LC_{Lo}$	$LD_{50}$	$LD_{Lo}$	$TC_{Lo}$	$TD_{Lo}$
	36	37	3.3	2.5	13	2.9

Continuing from the example in Section 3.3.3, the following equations show how to use the adjustments factors for converting a concentration-equivalent value in to a TEEL value.

Given:

$TEEL-3 = LC_{eq} \text{ (Line 4, Section 3.3.3, above)} \div LD_{50} \text{ adjustment factor}$

$TEEL-3 = 102 \text{ mg/m}^3 \div 3.3$

Result:

$TEEL-3 = 30.9 \text{ mg/m}^3$

After rounding:  $TEEL-3 = 31 \text{ mg/m}^3$

### 3.3.5 Time Scaling

When extrapolating concentration-based toxicity data (i.e., LC<sub>50</sub>, LC<sub>Lo</sub>, and TC<sub>Lo</sub>) from exposures that are different from 60 minutes, time scaling will be done using the ten Berge equation (ten Berge et al., 1986):

$$C^n \times t = k$$

In this equation, “C” is the exposure concentration, “n” represents a chemical-specific or even a toxic endpoint-specific exponent, “t” is the exposure time, and “k” is a constant. For TEEL value development, the NAS/AEGL default value of n=1 is used to extrapolate from shorter exposure times up to 60 minutes, and a value of n=3 is used to extrapolate from longer exposure times down to 60 minutes. For a detailed description of these default values, see the AEGL Standing Operating Procedures (NAS, 2001).

Given a 15-minute LC<sub>50</sub> of 12 ppm:

$$C^1 \times t = k$$

$$(12 \text{ ppm})^1 \times 15 \text{ min} = 180 \text{ ppm} \cdot \text{min}$$

Then for a 1-hour TEEL-3

$$C^1 \times 60 \text{ min} = 180 \text{ ppm} \cdot \text{min}$$

$$C = 3 \text{ ppm}$$

Result – TEEL-3 = 3 ppm.

## 3.4 Developing TEEL Values when Exposure Limits and Toxicity Data are Missing

The methods described below are used to derive TEEL values when there are gaps in or missing toxicity data. These methods provide the emergency planner with a full range of consequence values with which to assess the potential impacts of a chemical.

### 3.4.1 TEEL Values Derived from PAC Values at Other Levels

If there are not sufficient data to derive all three levels of TEEL values (i.e., TEEL-1, -2, or -3), then the missing TEEL value(s) can be derived from existing values using the multiplying factors presented in Table 3.5. These multiplying factors were derived from the means of the ratios of AEGL-3 to AEGL -2 values and AEGL-2 to AEGL-1 values. The white paper describing the analyses and results that were used to derive these multiplying factors are presented in Appendix B.



The calculations in Table 3.5 are presented in order of preference:

To calculate a TEEL-2:

- If there is a PAC-3, calculate the TEEL-2 as the  $\text{PAC-3} \div 6$ .
- If there is not a PAC-3, calculate the TEEL-2 as the  $\text{PAC-1} \times 11$ .

To calculate a TEEL-1:

- If there is a PAC-2 based on a published exposure limit such as an AEGL-2, LOC, or TLV-ceiling, calculate the TEEL-1 as the  $\text{PAC-2} \div 11$ .
- If the TEEL-2 is calculated from  $\text{TC}_{\text{Lo}}$  or  $\text{TD}_{\text{Lo}}$  data and if there is a published Time-Weighted Average (TWA), such as a TLV, WEEL, PEL, REL, or MAK, calculate the TEEL-1 as the  $\text{TWA} \times 3$ .
- If the TEEL-2 was calculated from the PAC-3 and if there is a published TWA value, such as a TLV, WEEL, PEL, or REL, calculate the TEEL-1 as the  $\text{TWA} \times 3$ .
- If there is no published TWA, calculate the TEEL-1 as the  $\text{PAC-2} \div 11$ .

A TEEL-1 is never less than three times the published chemical-specific TWA (e.g., TLV or PEL). All calculations are performed prior to rounding the values.

**Table 3.5 Multiplying Factors used to Fill Gaps in TEEL Value Sets**

TEEL Values	Calculations
TEEL-3	$\text{PAC-2 or TEEL-2} \times 6$
TEEL-2	$\text{PAC-3 or TEEL-3} \div 6$ $\text{PAC-1 or TEEL-1} \times 11$
TEEL-1	$\text{PAC-2 or TEEL-2} \div 11$ $\text{TWA} \times 3^*$
* This calculation is used by ACGIH for excursions above the TWA when there is no other published STEL. ACGIH, 2014	

### 3.4.2 TEEL Values Derived for Isomers and Compounds in Multiple Forms

#### 3.4.2.1 Chemicals with Multiple Isomers

For any chemical with multiple isomers listed in the PAC dataset, the available data for all of the isomers will be reviewed at the same time. If the reviews of the data indicate that the toxicities of all isomers are similar, then the entries may be combined into a single entry in the PAC dataset. There are chemicals for which data are not available for all of the isomers. PAC values for one isomer may be used for the isomer lacking any data. Combining chemicals into a single entry in the PAC dataset will require approval from DOE Office of Emergency Management.

### 3.4.2.2 Metal Compounds and Salts

Metal compounds that exist in multiple forms will be reviewed at the same time. An example of a metal compound with multiple forms that is in the PAC dataset is calcium chloride. Calcium chloride has entries for an anhydrous form and three distinct hydrated forms. There are some hydrated forms for which no data exist. In these instances, TEEL values will be based on the PAC values of another form, such as the anhydrous form, if it has data from which to derive TEEL values. A molecular weight adjustment that takes into consideration the molecular weight differences between the two forms will be performed.

### 3.4.3 TEEL Values Developed for Petroleum Products

Many petroleum products have no specific molecular formulae. They are either listed as a carbon number range or are described as “of generic composition.” In addition, there are limited chemical-specific exposure limits and toxicity data are of varying quality. Thus, TEEL values for many petroleum products are developed using a different methodology than is used for other chemicals.

Developing TEEL values for the petroleum products utilizes chemical-specific data when available but allows for the use of surrogate values based on established product types—the surrogate chemicals. In TEEL development, a surrogate value is the value that is used as a substitute value when there are no other useable data available. Surrogate values are used as the points of departure from which the TEEL values for other petroleum products will be developed.

To aid in assigning the appropriate surrogate value, published chemical definitions of the surrogate chemicals are used to compare to the definition of the substance in question. For example, the chemical definition for “diesel fuel” is found online through ChemIDPlus®, an online database maintained by the National Library of Medicine (NLM, 2015). ChemIDPlus® defines diesel fuel as a “complex combination of hydrocarbons produced by the distillation of crude oil. It consists of hydrocarbons having carbon numbers predominantly in the range of C9 through C20.”

When there is a definition or a chemical description, or if the carbon number, vapor pressure, boiling point, or viscosity can be determined, more precision is added to assigning the surrogate values.

#### 3.4.4 Points of Departure for Developing TEEL Values

1. If there are published chemical-specific exposure limits or toxicity data, the basic TEEL development methodology is followed.
2. For diesel fuel in any form, the TLV-TWA for diesel fuel is multiplied by 3 to give the TEEL-1. The TLV-TWA is used until AEGLs or ERPGs are developed for diesel fuel.
3. For gasoline in any form, the ERPG values for gasoline (CASRN 86290-81-5) are used, until AEGLs are developed.
4. AEGLs for jet fuels (CASRNs 8008-20-6 and 70892-10-3) are used as the TEEL values for jet fuels and kerosene in any form.
5. For hydrocarbon solvents, the IDLH for Stoddard solvent (CASRN 8052-41-3) is used as the TEEL-3.
6. For petroleum distillates and naphtha, in any form, the IDLH for naphtha (coal tar) (CASRN 8030-30-6) or petroleum distillates (CASRN 8002-05-9) is used as the TEEL-3.
7. If there are no data available and the carbon number or a range of carbon numbers of the petroleum product can be determined or estimated, the ACGIH Group Guidance Values (GGVs) are used as the point of departure for the TEEL values. ACGIH published the GGVs to be used with a reciprocal calculation procedure (ACGIH, 2014). When more than one value is listed for a group, the most conservative value is used. For additional information, see Table 1 in Appendix H of the ACGIH TLV Booklet (ACGIH, 2014). The GGV is multiplied by 3 to give the TEEL-1.

PAC values for all petroleum products in the PAC dataset are expressed in  $\text{mg}/\text{m}^3$ .

#### 3.4.5 TEEL Values Derived from Health Hazard Ratings

SAX, the National Fire Protection Association (NFPA), safety data sheets, and other sources publish Health Hazard Ratings (HHRs) for some chemicals. If there are no suitable toxicity data in HSDB, SAX, or RTECS, then toxicity can be estimated from a HHR. The following are the definitions and estimated toxicity values used to develop TEEL values from HHRs.

Sax defines an HHR=3 as an LD<sub>50</sub> less than 400mg/kg. Because any values less than 400mg/kg would be an arbitrary selection and because the different TEEL levels may not be equal, the upper end of the HHR ranges in SAX must be used:

HHR = 1	LD <sub>50</sub> rat oral = 40,000 mg/kg
HHR = 2	LD <sub>50</sub> rat oral = 4,000 mg/kg
HHR = 3	LD <sub>50</sub> rat oral = 400 mg/kg

The LD<sub>50</sub> data are used to calculate TEEL values in the same way as if the LD<sub>50</sub> data were extracted from HSDB or another data source.

### **3.4.6 TEEL Values Derived from Structure-Activity Relationships**

If there are no exposure limits or suitable toxicity data, or if a particular chemical is not listed in any database, the toxicity of a chemical can be estimated from structurally similar chemicals for which there are data.

### **3.4.7 Adjustments to Final TEEL Values**

#### **3.4.7.1 Ratios of Toxicity-Based to Exposure Limit-Based TEEL-2 Values**

In calculating TEEL values from exposure limits, it is possible to develop overly conservative values due to the uncertainty factors used to develop occupational exposure limits for the chemical. The TEEL development process may apply these factors twice. For a chemical, this can be evaluated by calculating the ratio of the toxicity-based TEEL-2 to the exposure limit-based TEEL-2. The resulting ratio is the basis of a correction factor that is used to adjust the exposure limit-based TEEL-2 value.

If the ratio is between 10 and 100, then the exposure limit-based TEEL-2 is multiplied by 10. If the ratio is greater than 100, then the exposure limit-based TEEL-2 is multiplied by 100. This adjustment allows the TEEL-2 value to be less restrictive (Craig, et. al., 2000). AEGL, ERPG, and LOC values are excluded from this adjustment. The TEEL review panel (see Section 4.2) will examine the applicable data in all instances when the ratio adjustment factor is proposed.

#### **3.4.7.2 Significant Figures and Rounding Guidelines for Final TEEL Values**

TEEL values derived from existing published exposure limits are not rounded; they are maintained the same as they appear in the original source document. All calculated TEEL values are rounded to two significant figures. Where applicable, the conversion from ppm to mg/m<sup>3</sup> is made before rounding. The resulting TEEL value in mg/m<sup>3</sup> is then rounded to two significant figures.

The significant figures of a number are the digits that contribute to the precision of that number. The left-most, non-zero number is the most significant figure; the right-most, non-zero number is the least significant. The number of significant figures is determined by counting the numbers from the least significant number to the most significant number. For example, the number 678 has three significant figures and the number 120 has two significant figures. If there is a decimal in the number, then the right-most number is the least significant figure, even if it is zero.

Rounding TEEL values is done according to the conventions found in DOE-HDBK-1014/1-92, *DOE Fundamentals Handbook, Mathematics* (DOE, 1992). When rounding to two significant figures, look at the number immediately to the right of the second significant figure. If the number to the right is 5 or higher, round up. If the number to the right is less than 5, round down. For example, the number 423 rounded to two significant figures is 420 and the number 425 rounded to two significant figures is 430.

### **3.5 Special Considerations**

#### **3.5.1 Particulates Not Otherwise Specified**

Particulates Not Otherwise Specified (PNOS) have been assigned a TLV-TWA of 10 mg/m<sup>3</sup>. This TLV-TWA applies only to solids and non-volatile liquids for which dispersion would be as an aerosol cloud. [See Appendix B of the ACGIH 2014 TLVs and BEIs booklet (ACGIH, 2014)].

#### **3.5.2 Simple Asphyxiants**

Simple asphyxiants are biologically inert gases which can cause injury by displacing oxygen rather than by any inherent toxicity of their own. Simple asphyxiants include the noble gases as well as nitrogen and hydrogen. Because the risk of harm is associated with displacement of oxygen, all simple asphyxiants have the same TEEL values. The TEEL values for simple asphyxiants are based on the level to which the simple asphyxiants reduce the oxygen concentration. The normal concentration of oxygen in air is 20.9% by volume. The minimum oxygen concentration that OSHA permits for Confined Space Entry (CSE) is 19.5%. If the concentration of a simple asphyxiant reaches approximately 65,000 ppm by volume, it would displace enough air to reduce the oxygen concentration to the OSHA CSE limit (OSHA, 2015b). This is the TEEL-1 value. As the concentration of oxygen drops to lower levels (e.g., 12-16%), thresholds will be reached that lead to impaired attention, thinking, and coordination (NIOSH, 2004). Very low oxygen concentrations (6-10%) result in nausea and lethargic movements and may result in unconsciousness (NIOSH, 2004; OSHA, 2015b). The TEEL-2 is set at 230,000 ppm. At this concentration, the simple asphyxiant would cause the oxygen concentration to drop to 16%. The TEEL-3 is set at 400,000 ppm. At this concentration, the simple asphyxiant would cause the oxygen concentration to drop to 12.5%.

Nitrogen is different from the other simple asphyxiants because nitrogen constitutes 78% of a normal atmosphere. The TEEL values for nitrogen are given as total nitrogen. This is the sum of the atmospheric nitrogen plus the amount of additional nitrogen that is needed to reduce the oxygen concentrations to the same levels as the TEEL values for the other simple asphyxiants. The TEEL-1 for nitrogen is 796,000 ppm, which equates to an oxygen concentration of 19.5%. The TEEL-1 for the other simple asphyxiants is 65,000 ppm, which also equates to an atmospheric oxygen concentration of 19.5%. Similarly, the TEEL-2 for nitrogen is 832,000 ppm and the TEEL-3 is 869,000. These values equate to oxygen concentrations of 16% and 12.5%, respectively.

TEEL values for gases or vapors, with original units in ppm, have upper limit maximums. The restrictions are the same values as those for the simple asphyxiants. The hypothesis is that any gas that reaches the above-listed concentrations would behave as an asphyxiant by reducing the oxygen concentration in the atmosphere.

### **3.5.3 Radioactive Compounds**

Ionizing radiation is the hazard of concern for most radioactive isotopes. However, certain low-specific-activity radionuclides or mixtures are also known to be chemically toxic. For practical purposes, this concern is limited to uranium of low enrichment in the form of compounds that are relatively soluble in body fluids (e.g., carbonates, nitrates, fluorides, and sulfates). Depending on the exact proportions of the different uranium isotopes, the chemical toxicity becomes the dominant concern as the nominal enrichment (U-235 weight percent) decreases through the range from about 16% to 5%. In addition, TEEL values have also been derived for thorium and some of its compounds.

## **3.6 TEEL Values for Biological Toxins**

### **3.6.1 Biological Toxins**

Biological toxins (biotoxins) are proteins or other macromolecules of microbial, plant, or animal origin. Pound-for-pound, biological toxins are among the most deadly substances known to exist. TEEL values have been or will be developed for proteins or other macromolecules of microbial, plant, or animal origin. TEEL values will not be developed for viruses or live bacteria.

The data sources, data hierarchies, species and routes of exposure hierarchies, calculations, and assumptions currently used to develop TEEL values will be followed initially when developing TEEL values for biotoxins. Deviations from these procedures may be required due to the unique nature and rarity of some biotoxins. In these cases, primary data sources such as specific journal articles will be examined to find the appropriate data needed to develop TEEL values.

### **3.6.2 Exposure Limits used for TEEL Development for Biotoxins**

The procedure for TEEL development for biological toxins begins with the same hierarchy of data used to develop TEEL values for other chemicals. Published exposure limits exist for only a small number of biological toxins.

The following sources will be contacted or consulted to see if they have developed any exposure limits:

- U.S. Environmental Protection Agency (EPA);
- National Institute for Occupational Safety and Health (NIOSH);
- Centers for Disease Control and Prevention (CDC);
- American Conference of Governmental Industrial Hygienists (ACGIH);
- Occupational Safety and Health Administration (OSHA);
- U.S. Department of Agriculture (USDA); and
- U.S. Department of Homeland Security (DHS) – Division of Chemical and Biological Threats.

If exposure limits have been developed by other organizations such as the European Commission - European Chemicals Bureau or other public or private entities, they are considered next. It is prudent to obtain the technical support documents for these exposure limits.

### **3.6.3 Toxicity-Based Data for Developing TEEL Values for Biotoxins**

HSDB, SAX, and RTECS are searched for relevant data. Once specific toxicity data are found in a secondary data source, the citation or journal article is retrieved, if possible. If after these data sources are searched and little or no data are found, a literature search using Google Scholar or other similar search engines is performed to find journal and other appropriate publications. Preference is given to articles that report data as toxicity endpoints such as an LC<sub>50</sub> or LD<sub>50</sub>.

If these sources are searched and little or no data are found, the following data are considered valid publications:

- Abstracts from scientific conferences can be used if actual data are presented rather than a summary;
- Data from clinical and/or therapeutic uses may be used after careful scrutiny of the original paper;

- Articles reporting accidental exposures can be useful for identifying possible health effects. However, reported values which may be estimated doses are not valid for TEEL development;
- Articles, text chapters, and fact sheets can be used to obtain information; and
- Case studies can be used if there is nothing else.

Human data are preferred over data from other species. However, human data reported for therapeutic uses may not be applicable to TEEL development. For example, secondary data sources may report results of case studies describing the effectiveness of BOTOX<sup>®</sup> (Botulinum toxin A) as a specific medical treatment. The dose given to elicit a specific cosmetic or therapeutic response in humans is not useful for TEEL development.

After human data, preference is given to monkeys, dogs, rats, mice, rabbits, guinea pigs, cats, and pigs—in that order of hierarchy. The exception to this hierarchy is the existence of farm animal data. Farm animal data may be more relevant than data from a laboratory experiment due to the worldwide contamination of animal feed by some biological toxins (e.g., mycotoxins). The TEEL review panel should develop a recommendation on use of farm animal data or any other deviation from the process (see Section 4.2).

If a species is used other than those listed in the aforementioned hierarchy, species-specific data (e.g., average breathing rate) should be obtained to complete TEEL development. With respect to route of exposure, preference is given to inhalation exposures followed by oral, dermal, intraperitoneal, and intravenous—in that order. The TEEL review panel can supplant this hierarchy if the data show that toxicity is dependent on the route of exposure.



## **4 TEEL VALUE DEVELOPMENT ADMINISTRATION**

### **4.1 Request for TEEL Value**

A DOE field location that needs TEEL values for a chemical can submit a request to DOE Office of Emergency Management using a form found on the Subcommittee on Consequence Assessment and Protective Actions (SCAPA) website

(<https://sp.eota.energy.gov/EM/SCAPA%20Shared%20Documents/NewTEELRequestForm.pdf>).

The request is evaluated based on chemical toxicity, potential for its release, quantity stored, and physical or chemical properties. If warranted, TEEL values are developed according to the methodology described in Section 3. These are reported to the requestor and added to the PAC dataset at the next update.

### **4.2 Review Panel Assignment**

While TEEL development has been a default methodology, there have been situations in the past and there will continue to be circumstances that require the application of professional judgment. A small technical review panel has been established by DOE Office of Emergency Management to provide such judgment. All members of the review panel consider the situation. If the review panel is not unanimous, the majority and minority opinions are reported to DOE Office of Emergency Management. The review panel:

- resolves conflicts in TEEL values resulting from application of the default process by evaluating all available factors and data;
- considers whether any of the data available for use in the default process should be excluded; and
- recommends appropriate exceptions to the default process to produce a high-quality TEEL value.

### **4.3 Specific Instructions for the Review Panel**

The following are the technical instructions provided to the review panel to guide their assessment of TEEL values:

- If the ratio adjustment factor (Section 3.4.6.1) is used, consider the factors and data available to determine appropriate TEEL values that reflect the definitions for each level;
- In instances where the TEEL values conflict with their definitions, such as TEEL-2 greater than the TEEL-3, review all factors and data used to derive the values;
- Apply professional judgment when selecting data that are the most reasonable and defensible. Document any deviations from the default procedure;

- Review data from a source that cannot be confirmed, and determine if the data should be used;
- Review data sources that are of undetermined reliability, and determine if the source should be used;
- Resolve cases where data may result in any of the following: TEEL-1=TEEL-2=TEEL-3; and
- Perform a “test of reasonableness” on TEEL values before publication, and make appropriate exceptions to the default process to produce a high-quality value.

#### **4.4 The TEEL Advisory Group**

TEEL value development<sup>5</sup> is supported directly through the DOE Office of Emergency Management, which is responsible for developing, maintaining, and testing the Emergency Management System at DOE sites and facilities.

The TEEL Advisory Group (TAG) provides technical support on TEEL values and related issues to the DOE Office of Emergency Management. The seven TAG members are appointed by the DOE Office of Emergency Management. The Chair of SCAPA also serves as an ex officio member of the TAG. As stated in its charter (DOE, 2015a), the objectives of the TAG are to:

- promote consistency in calculations and application of TEEL values;
- provide quality control for the development of the TEEL values;
- keep abreast of evolving science and techniques in the field of toxicology;
- provide technical support on TEEL-related issues to DOE Office of Emergency Management; and
- promote the understanding and use of PAC values within DOE, other government agencies, and private interests.

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<sup>5</sup> TEEL development started as a project under the auspices of SCAPA, which provides technical information and recommendations for emergency preparedness to assist in safeguarding the workers and the public (DOE, 2015b). TEEL development shifted directly to the Office of Emergency Management prior to the publication of DOE-HDBK-1046-2008.

## **5 REVIEW PROCESS AND PUBLICATIONS**

### **5.1 Quality Assurance and Quality Control**

Although the development of TEEL values uses an automated methodology, it is essential that the sources, data, and methodology be subject to review on an ongoing and regular basis. This provides the assurance that the outcomes are valid and that the procedures are repeatable and empirical. Oversight for quality assurance and quality control activities is provided by the TAG. The quality control process for the development of TEEL values is performed by the review panel discussed in Section 4.2.

Prior to publication of a new revision, a “beta” version is made available to members of the TAG, to personnel at the National Atmospheric Release Advisory Capability (NARAC), and select other parties. After completion of the “beta” review and any necessary changes, the revision is published.

### **5.2 Documentation**

Changes, updates, and revisions to the PAC dataset are documented. Changes include changes to data, updating exposure limits when they change, and simple formatting edits. When a change is made, a new master file of the PAC dataset is created, with the date of the change and the revision number being part of the new file name. This ensures version control of the master file.

### **5.3 Publication of Protective Action Criteria**

As a rule of thumb, DOE has sought to publish a new revision on an annual basis. This schedule is subject to change due to a variety of factors that are considered by DOE management.

Current PAC values, including AEGL, ERPG, and TEEL values, are published on the Internet at: <https://sp.eota.energy.gov/pac> (DOE, 2016).

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The most recent versions of the listed references are used in TEEL value development, e.g., the 2014 handbooks and guides to occupational exposures. The existing TEEL values are updated as new AEGLs, ERPGs, TLVs, WEELs, etc. are published.

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## GLOSSARY

**American Conference of Governmental Industrial Hygienists (ACGIH)**

Professional association of industrial hygienists.

**American Industrial Hygiene Association (AIHA)**

Professional association of industrial hygienists.

**Ceiling limit**

The upper limit of chemicals in workplace air not to be exceeded at any time.

**Chemical Abstracts Service (CAS)**

The organization that assigns registry numbers (CASRNs) to chemicals.

**Emergency Exposure Guidance Level (EEGL)**

One of the guidance levels for specific contaminants (reviewed and developed by a subcommittee of the U.S. Nuclear Regulatory Commission) derived for U.S. Navy personnel operating under emergency conditions for which regulatory agencies have not set standards.

**Emergency planning hazards assessment**

The application of rigorous hazard analysis techniques that provide sufficient detail to assess a broad spectrum of postulated events or conditions involving the potential onsite release of hazardous materials and to analyze the resulting consequences.

**Good Laboratory Practice**

A quality system of management controls for research laboratories and organizations to try to ensure the uniformity, consistency, reliability, reproducibility, quality, and integrity of chemical (including pharmaceuticals) non-clinical safety tests—from physio-chemical properties through acute to chronic toxicity tests.

**Hazardous Substances Data Bank (HSDB)**

A peer-reviewed database on toxic effects of chemicals, managed by the National Library of Medicine.

**Immediately Dangerous to Life or Health (IDLH)**

The concentration of a chemical in air which, if exposed, a person should leave immediately.

**Lethal Concentration, 50% (LC<sub>50</sub>)**

The concentration of a substance in air that kills 50% of the test population.

**Lethal Concentration, Lowest (LC<sub>Lo</sub>)**

Lowest concentration of a substance in air that has been shown to cause death in a test population.

**Lethal Dose, 50% (LD<sub>50</sub>)**

The dose of a substance administered by any route (other than inhalation) that causes death to 50% of the test population.

**Lethal Dose, Lowest (LD<sub>Lo</sub>)**

The lowest dose of a substance administered by any route (other than inhalation) that has been shown to cause death in a test population.

**National Fire Protection Association (NFPA)**

An international nonprofit organization that develops, publishes, and disseminates more than 300 consensus codes and standards intended to minimize the possibility and effects of fire and other risks.

**Operational Emergency**

An event or condition that involves the uncontrolled release of a hazardous material and either immediately threatens or endangers personnel who are in close proximity of the event; has the potential for dispersal beyond the immediate vicinity of the release in quantities that threaten the health and safety of onsite personnel or the public in collocated facilities, activities, and/or offsite; and has a potential rate of dispersal sufficient to require a time-urgent response to implement protective actions for workers and the public.

**Permissible Exposure Limits (PELs)**

A legally enforceable occupational exposure limit promulgated by the Occupational Safety and Health Administration.

**Particulates Not Otherwise Specified (PNOS)**

Term applied to substances not characterized in some other way.

**parts per million (ppm)**

A conventional measure of concentration of a chemical gas or vapor in air, by volume.

**Route Adjustment Factor (RAF)**

A unitless parameter to adjust exposure for different absorption efficiencies by different routes (e.g., oral, dermal, etc.).

**Recommended Exposure Limits (RELs)**

Occupational exposure limits published by NIOSH.

**Registry of Toxic Effects of Chemical Substances (RTECS)**

A proprietary database that is a compendium of the results of toxicological experiments.

**Structure Activity Relationship (SAR)**

A procedure for predicting a chemical's effects from its chemical structure.



**N. Irving Sax (SAX)**

The original editor of *Dangerous Properties of Industrial Materials*.

**Short-Term Exposure Limit (STEL)**

A 15-minute TWA exposure limit that should not be exceeded at any time during a work day.

**Subcommittee on Consequence Assessment and Protective Actions (SCAPA)**

Provides the U.S. Department of Energy/National Nuclear Security Administration and its contractors with technical information and recommendations for emergency preparedness to assist in safeguarding the health and safety of workers and the public.

**TEEL Advisory Group (TAG)**

An advisory group to DOE that provides advice and oversight on TEELs.

**Toxicology Excellence for Risk Assessment (TERA)**

A 501(c)3 not-for-profit organization based in Cincinnati, Ohio – became home of the WEEL Committee on January 1, 2012.

**Toxic concentration, lowest (TC<sub>Lo</sub>)**

Lowest reported concentration causing toxic effects in a test population.

**Toxic dose, lowest (TD<sub>Lo</sub>)**

Lowest reported dose causing toxic effects in a test population.

**Threshold Limit Values (TLVs)**

An occupational exposure limit developed and published by ACGIH.

**Time-Weighted Average (TWA)**

The average concentration of a chemical in air for a specified time period, commonly 8 hours.

**Workplace Environmental Exposure Levels (WEELs)**

Health-based occupational exposure limits for chemicals that lack PELs, TLVs, or RELs, developed and published by AIHA until 2011. TERA became home of the WEEL Committee January 1, 2012..

## APPENDIX A

### DERIVATION OF THE TOXICITY DATA ADJUSTMENT FACTORS USED IN TEEL VALUE DEVELOPMENT

September 2013

#### SUMMARY

The purpose is to update the adjustment factors used to develop TEEL values from toxicity data listed in Craig, et. al., (2000), Table 5, and in DOE-HDBK-1046-2008, *Temporary Emergency Exposure Limits for Chemicals: Methods and Practice*, Table 3.2 (DOE, 2008).

The adjustment factors originally used in the TEEL development methodology were developed from an analysis of ratios of toxicity data to Emergency Response Planning Guidelines (ERPGs). When Craig, et. al., (2000) performed these calculations, ERPGs were used because they were the primary Protective Action Criteria (PACs) used at U.S. Department of Energy (DOE) facilities. At present the primary PACs used at DOE facilities are Acute Exposure Guideline Levels (AEGLs). Thus, the analysis used to develop six new adjustment factors following the basic approach used by Craig, et. al., (2000), but using ratios of toxicity data to AEGL values is described.

The ratios of toxicity data to corresponding AEGL-2 or AEGL-3 values were calculated. Then the means of those ratios were calculated and the six means were rounded to two significant digits. Those six means are the proposed adjustment factors. The recommendation that these adjustment factors be used in future TEEL development was submitted to the DOE Office of Emergency Management. DOE accepted the recommendation. Table 1 shows each adjustment factor with its corresponding toxicity parameter to which it will be applied when deriving future TEEL values.

**Table 1.** Adjustment Factors

	TEEL-3				TEEL-2	
Toxicity Parameter	LC <sub>50</sub>	LD <sub>50</sub>	LC <sub>Lo</sub>	LD <sub>Lo</sub>	TC <sub>Lo</sub>	TD <sub>Lo</sub>
Proposed Adjustment Factor	36	3.3	37	2.5	13	2.9

## BACKGROUND

The U.S. Department of Energy (DOE) requires all DOE facilities with significant chemical inventories to prepare for chemical emergencies. Evaluating and preparing for chemical emergencies, however, is not unique to DOE. The Environmental Protection Agency (EPA) with the assistance of the National Academy of Sciences (NAS) develops Acute Exposure Guideline Levels (AEGLs) to help in planning for chemical emergencies (EPA, 2010). The American Industrial Hygiene Association (AIHA) develops Emergency Response Planning Guidelines (ERPGs) as planning tools for emergency response to chemical releases (AIHA, 2013). However, AEGL and ERPG values together exist for roughly 400 chemicals. Recognizing that there are many chemicals at DOE facilities that present emergency planning concerns, and for which there are no AEGL or ERPG values, the DOE supports the development of Temporary Emergency Exposure Limits (TEELs) until ERPG or AEGL values are derived (DOE, 2012). As used here, PACs is a collective term that includes AEGL, ERPG, and TEEL values.

In 2000, Craig, et. al., described the default methodology that was originally used for developing TEEL values. The default methodology was also documented in DOE-HDBK-1046-2008, *Temporary Emergency Exposure Limits for Chemicals: Methods and Practice*, “the Handbook,” (DOE, 2008). In 2009, DOE commissioned an independent review of the default methodology by a group of subject matter experts. The independent reviewers recommended several changes to the default TEEL development methodology. DOE will document the changes to the default methodology in an updated version of the DOE Handbook. However, the methods and procedures found in Craig, et. al., (2000) continue to provide the basic framework for developing TEEL values.

TEEL values are developed for three levels: TEEL-1, TEEL-2, and TEEL-3. Each level represents an increase in the severity of the potential effects from exposure to a chemical in an emergency situation. Definitions for the TEEL levels can be found in Table 2.1 in The Handbook (DOE, 2008).

The TEEL development methodology is based on a hierarchy of data types. First in this hierarchy are published exposure limits such as Threshold Limits Values (TLVs) published by the American Conference of Governmental Industrial Hygienists (ACGIH). Because published exposure limits exist for a limited number of chemicals, TEEL values are also developed from published toxicity data found in secondary data sources, such as the Hazardous Substances Data Bank (HSDB).

The original data extraction procedures and the calculations used to develop TEEL values from toxicity data were described in Craig, et. al., (2000). The independent reviewers made several recommendations to DOE regarding the selection of toxicity data used in TEEL value development. The data extraction procedures used in this analysis incorporate the recommendations of the independent review committee.

Toxicity data are only used for developing TEEL values in the absence of published exposure limits. More specifically, toxicity data are used to develop TEEL-2 and TEEL-3 values. When available, Toxic Concentration, Lowest ( $TC_{Lo}$ ) or Toxic Dose ( $TD_{Lo}$ ) data (in this priority order) are used to develop TEEL-2 values. Lethal Concentration, 50% ( $LC_{50}$ ), Lethal Concentration, Lowest ( $LC_{Lo}$ ), Lethal Dose, 50% ( $LD_{50}$ ), and Lethal Dose, Lowest ( $LD_{Lo}$ ) (in this priority order) are used to develop TEEL-3 values.

The  $LC_{50}$  and  $LC_{Lo}$  are given priority because they are based on inhalation data – which is highest in the route of exposure hierarchy. The  $LC_{50}$  is preferred over the  $LC_{Lo}$ , and the  $LD_{50}$  is preferred over the  $LD_{Lo}$  because there are multiple data points used to derive the 50% value. The “Lo” data are usually a single data point. Thus there is more reliability in the  $LC_{50}$  and  $LD_{50}$  values.

Craig, et. al., (2000) described the procedures used to derive the first adjustment factors that were used to develop TEEL values from toxicity data. When they performed their analysis, ERPG values were the only emergency planning guidelines used at DOE facilities. Consequently, the methodology for developing TEEL values from toxicity data began with analyzing the relationships between ERPG values and the toxicity parameters listed above. They extracted toxicity data for all 77 chemicals with ERPG values at the time, and calculated ratios of  $LC_{50}$ ,  $LD_{50}$ ,  $LC_{Lo}$ , and  $LD_{Lo}$  data to ERPG-3 values, and ratios of  $TC_{Lo}$  and  $TD_{Lo}$  data to ERPG-2 values. The means of these ratios were rounded and became the adjustment factors used to calculate TEEL values from toxicity data (Craig, et. al., 2000; DOE, 2008). Since the time of their analysis, AEGL values have been developed by EPA and the National Research Council (EPA, 2010) for 258 chemicals. In addition, AEGL values are now the primary PAC values used in DOE emergency planning (DOE, 2005).

For the analysis described here, AEGL values were selected as the basis for deriving the new adjustment factors for three reasons:

- The DOE Office of Emergency Management has defined TEEL values based on the definitions of 60-minute AEGL values;
- Sixty-minute AEGL values are the primary PAC values used at DOE facilities; and
- The current AEGL dataset provides a larger number of chemicals upon which to base the derivation of the adjustment factors.

## METHODS

For this analysis, ratios of AEGL values were calculated to corresponding toxicity data. Toxicity data was extracted from secondary data sources for all chemicals with AEGL-2 &/or -3 values. All of the chemicals with AEGL-2, and/or -3 values were entered into an Excel® workbook with

their corresponding AEGL values. There are 258 chemicals with Final or Interim AEGL-2 and/or AEGL-3 values.

**Toxicity Data.** For each of the 258 chemicals, LC<sub>50</sub>, LD<sub>50</sub>, LC<sub>Lo</sub>, LD<sub>Lo</sub>, TC<sub>Lo</sub>, and TD<sub>Lo</sub> data, if available, was extracted. The HSDB was the first source used for obtaining the toxicity data. *Sax's Dangerous Properties of Industrial Materials*, 11<sup>th</sup> & 12<sup>th</sup> eds. (Lewis, 2005; Lewis, 2012) and the Registry of Toxic Effects of Chemical Substances (RTECS) were used second and third, respectively, to fill in data gaps. Data gaps were defined as any toxicity parameter data point that was not found in HSDB. For each toxicity parameter, the following data, if available, were extracted:

- Species
  - Human
  - Monkey
  - Dog
  - Rat
  - Mouse
  - Rabbit
  - Guinea pig
  - Cat
  - Pig
- Dose (in mg/kg) or exposure concentration (in ppm or mg/m<sup>3</sup>),
- Routes of exposure
  - Inhalation (for LC<sub>50</sub>, LC<sub>Lo</sub>, and TC<sub>Lo</sub>)
  - Oral
  - Dermal
  - Intravenous
  - Intraperitoneal
- Exposure time (in minutes – closest to 60 minutes)

The toxicity data extraction procedures used in this analysis incorporate the recommendations of the independent review committee<sup>6</sup>. The new procedures require more scrutiny of the toxicity data, than was performed historically in TEEL development.

### ***Calculation of the Concentration Equivalent Values and the Ratios***

When deriving TEEL values from toxicity data, concentration equivalent values in mg/m<sup>3</sup> are calculated from the published toxicity data using species-specific breathing rates and body

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<sup>6</sup> Email from David Freshwater: "Implementation of Outside Review Recommendations;" 12/21/2010

weights. The methodology described in Section 3.4 of the Handbook (DOE, 2008) was used as a point of departure, but the calculations were modified in the following ways:

- New route adjustment factors were used (see Table 2).
- Exposure times were adjusted to 60 minutes
- The ten Berge equation was used to adjust exposure times to 60-minutes
- “Human equivalent toxicity” values were not used in this analysis.<sup>7</sup>

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<sup>7</sup> When toxicity data from species other than humans were used to develop TEEL values, this value was calculated using the species body weight and average breathing rate and human body weight and average breathing rate (Craig et. al., 2000).

**Table 2.** Route Adjustment Factors<sup>8</sup>

Inhalation	Oral	Dermal	Intraperitoneal	Intravenous
1	0.5	0.05/0.1*	1	1
*0.05 is used for insoluble compounds, and 0.1 is used for soluble compounds				

The exposure times of the LC<sub>50</sub>, LC<sub>Lo</sub>, and TC<sub>Lo</sub> data were adjusted to 60 minutes using the ten Berge equation:  $C^n \times t = k$  (ten Berge et al., 1986). When extrapolating from longer exposure times to 60 minutes, the exponent  $n = 3$  is used; when extrapolating from shorter exposure times to 60 minutes, the exponent  $n = 1$  is used. These are default values for  $n$  recommended by the NAC/AEGL Committee when there are not enough data to derive a chemical-specific value for  $n$  (NAS, 2001).

The ratios of the concentration equivalent values to corresponding AEGL values were used in the statistical analyses.

## STATISTICAL ANALYSIS AND FINDINGS

The means, medians, modes, sample variance, standard deviations (SD), confidence intervals (using an  $\alpha$  of 0.05), and the skewness and kurtosis statistics of the ratios of the concentration equivalent values to AEGL values were calculated. Skewness is a measure of the symmetry of a data set where a zero skewness statistic represents absolute symmetry. Kurtosis is a parameter that describes the shape (peakedness) of a variable's probability distribution. Normal distributions produce a kurtosis statistic of approximately zero. The descriptive statistics for these datasets showed that none of the data are normally distributed. The means, medians, and modes differ from each other, and the standard deviations are significantly greater than the means. The data are also kurtotic, and in most cases, the skewness statistic is large. It is possible to meet the assumptions of normality by log-transforming the data using the natural log of the number (Munro, 1997). Log-transformation puts all of the variables onto a common scale of variation. The ratios were transformed, using the natural log of the number. The means, medians, modes, sample variance, SDs, confidence intervals, and the skewness and kurtosis statistics of the log-transformed ratios were re-calculated. The log-transformed ratios were used for subsequent analyses and derivation of the adjustment factors.

## RESULTS

The ratios of toxicity data to AEGL values are not normally distributed; therefore, those data were not used in this analysis and are not shown.

<sup>8</sup> Email from David Freshwater: "Implementation of Outside Review Recommendations;" 12/21/2010

The descriptive statistics of the log-transformed ratios are presented in Tables 3 and 4. As can be seen, the datasets meet the assumptions of normality. In each case, the means, medians, and modes are similar, the standard deviations are no longer significantly greater than the means, and the skewness and kurtosis statistics are near zero.

**Table 3.** Descriptive Statistics: Log-transformed Ratios – Lethality Data to AEGL-3 Values

Statistic	LC <sub>50</sub>	LD <sub>50</sub>	LC <sub>Lo</sub>	LD <sub>Lo</sub>
Count	395	837	252	159
Mean	2.86	0.03	2.65	-0.58
Median	2.70	-0.14	2.63	-0.87
Mode	7.36	-2.5	2.45	N/A
SD	1.67	2.00	1.78	2.24
Variance	2.80	4.01	3.18	5.02
Kurtosis	1.46	0.53	0.68	0.36
Skewness	0.36	0.55	-0.10	0.38
Confidence Interval ( $\alpha = 0.05$ )	$\pm 0.17$	$\pm 0.14$	$\pm 0.22$	$\pm 0.35$

**Table 4.** Descriptive Statistics: Log-transformed Ratios – Toxicity Data to AEGL-2 Values

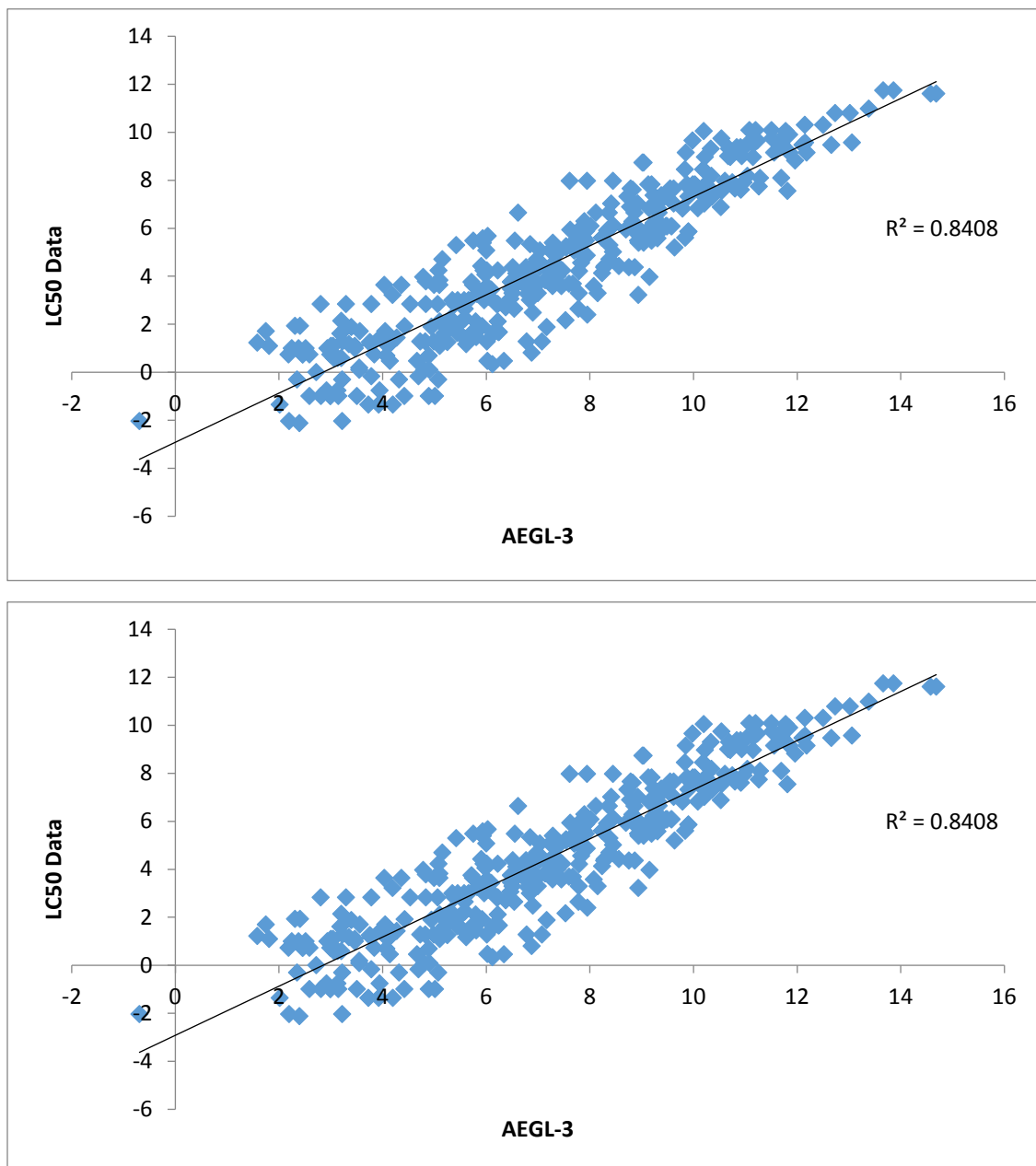
Statistic	TC <sub>Lo</sub>	TD <sub>Lo</sub>
Count	122	92
Mean	1.20	-0.39
Median	1.43	-0.41
Mode	0.74	N/A
SD	1.98	2.10
Variance	3.94	4.40
Kurtosis	-0.61	0.79
Skewness	-0.14	-0.48
Confidence Interval ( $\alpha = 0.05$ )	$\pm 0.36$	$\pm 0.43$

Outliers from the log-transformed datasets were removed. For these analyses, outliers were defined as any ratio that was greater than or equal to the mean of the ratios plus two times the standard deviation, and any ratio that was less than or equal to the mean minus two times the

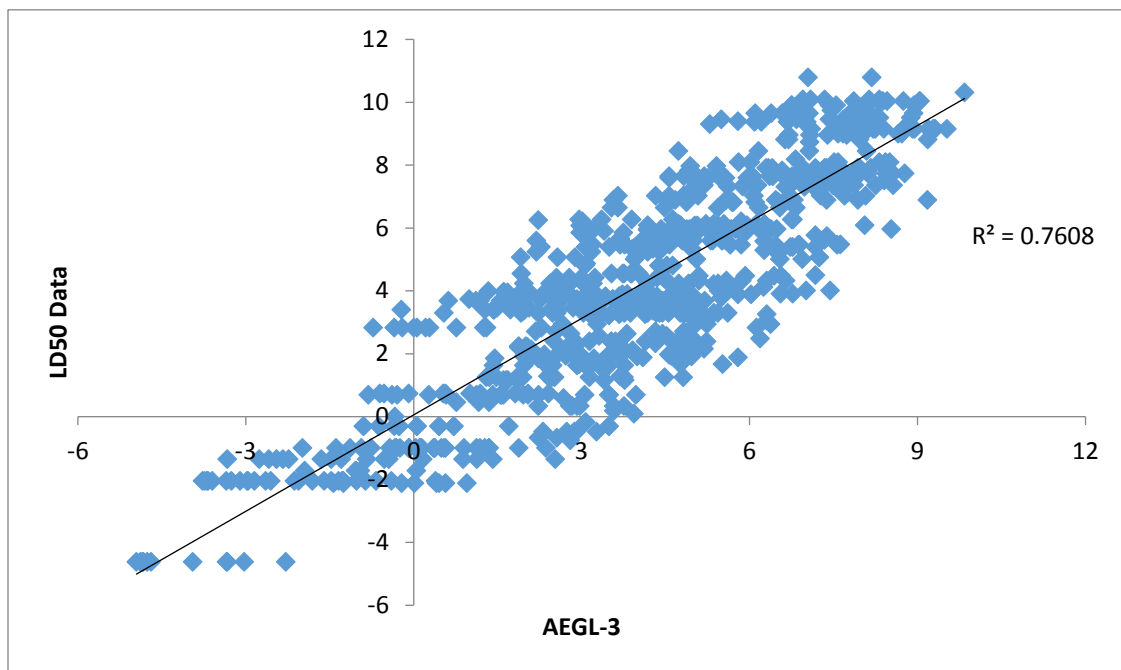
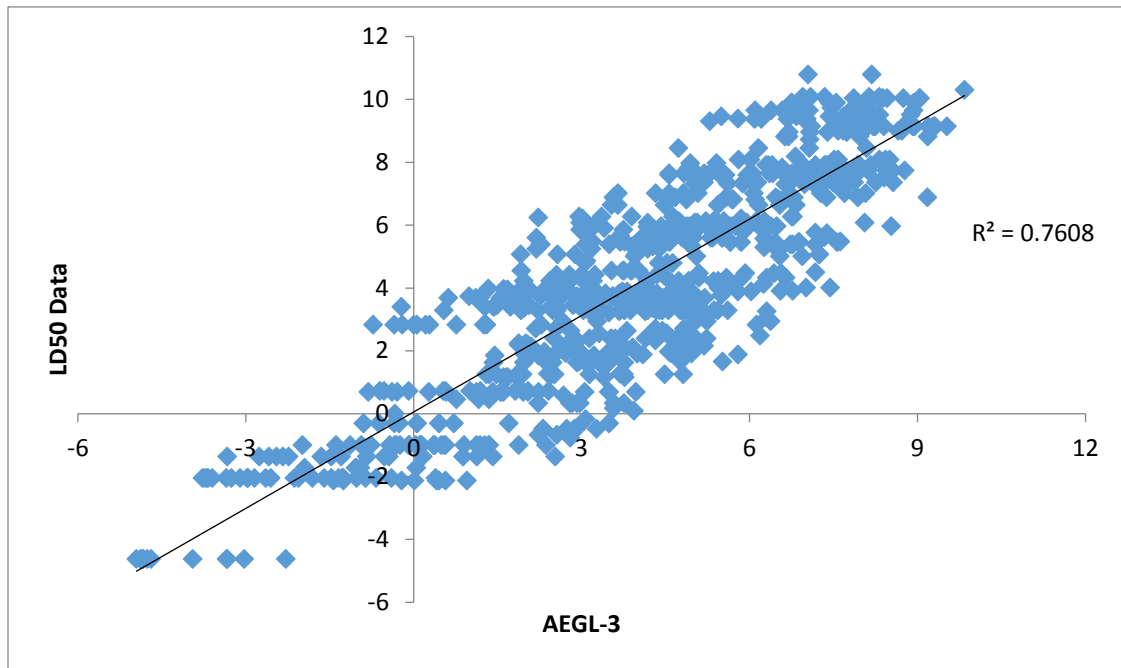


standard deviation. New means and confidence intervals were calculated on the adjusted, log-transformed datasets.

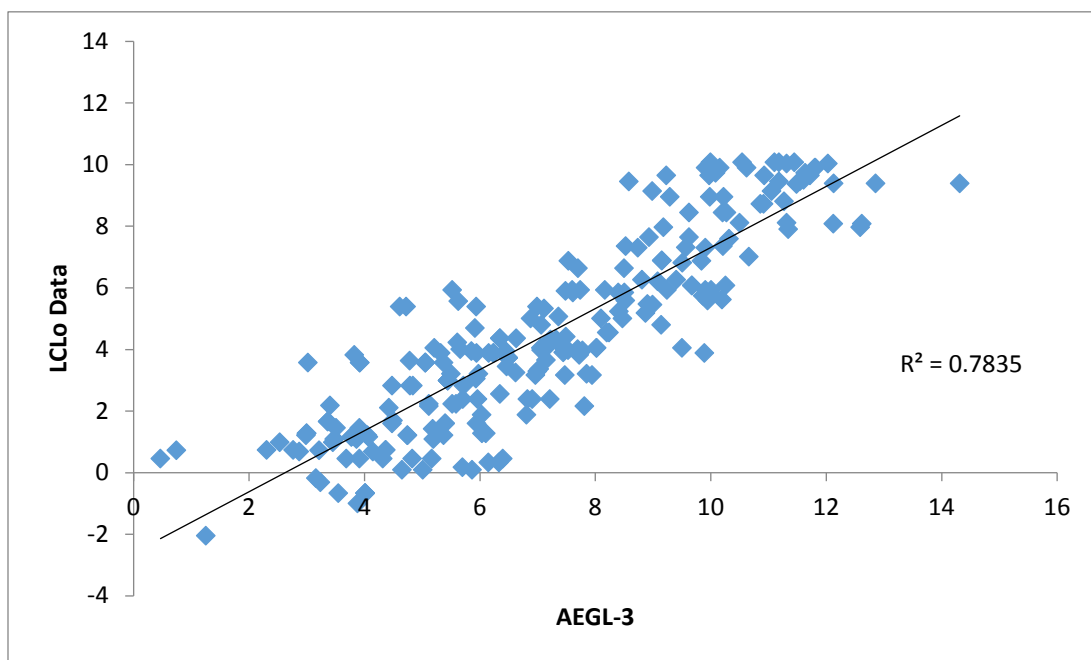
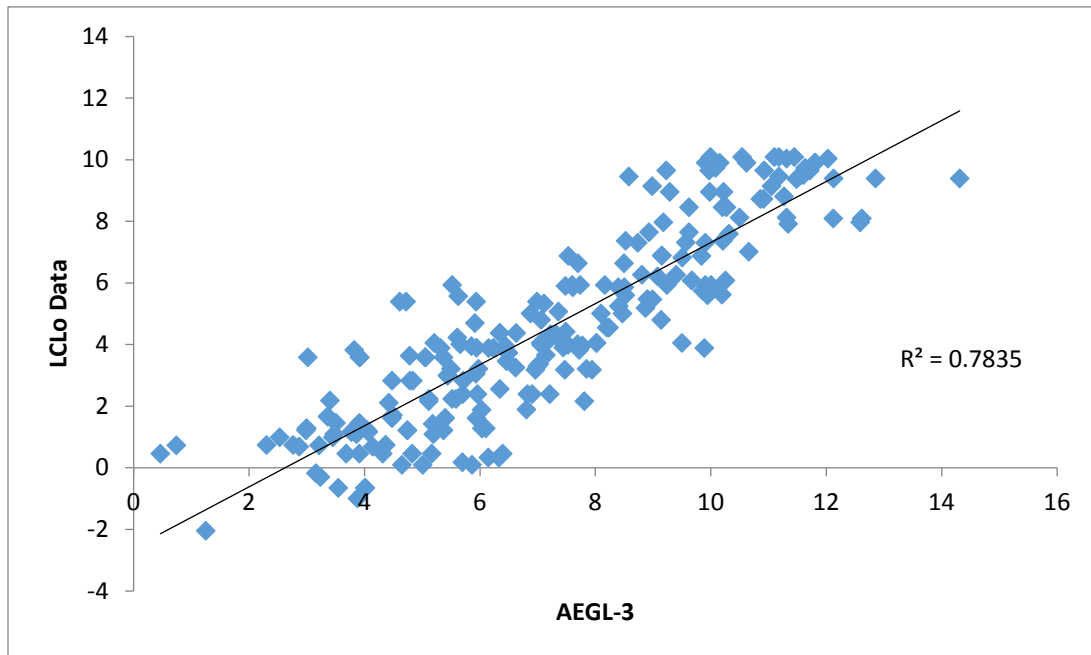
The results of the regression analyses performed on the six toxicity parameters and the corresponding AEGL values are shown in Figures 1 through 6. The data shown in these figures have the outliers removed.



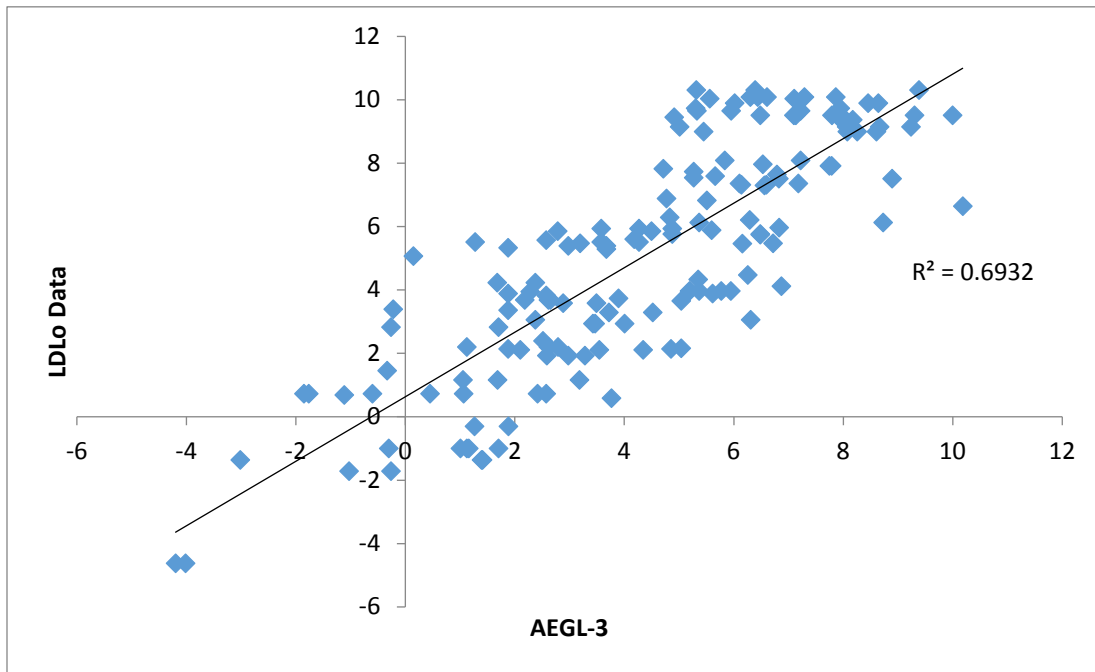
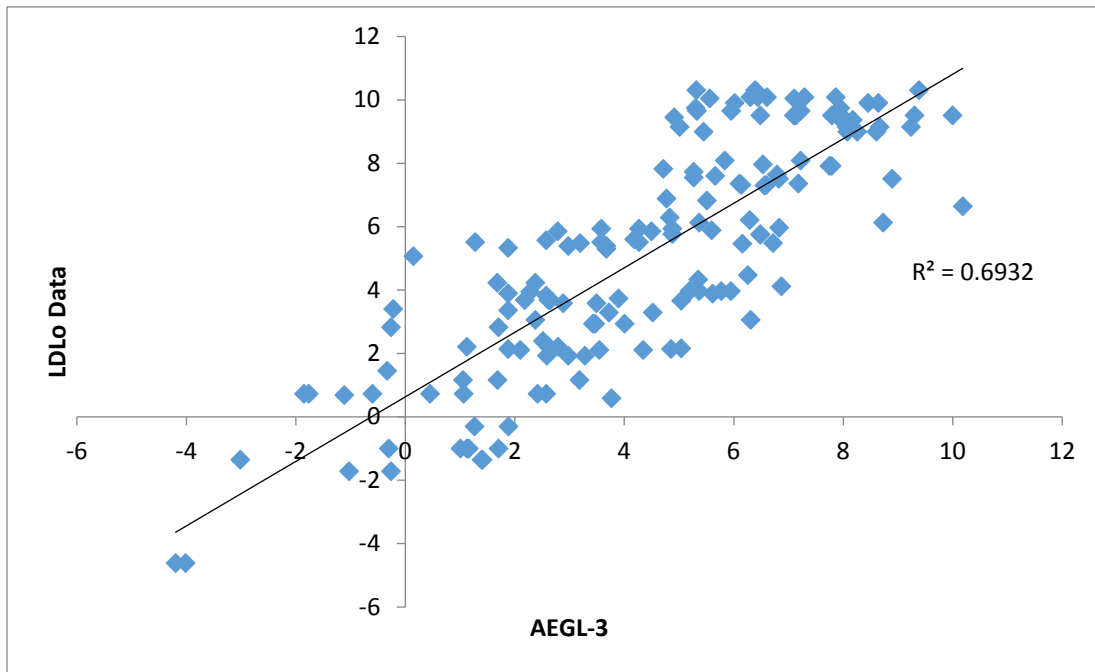
**Figure 1.** Regression analysis showing linear relationship between the log-transformed LC<sub>50</sub> data and AEGL-3 values.



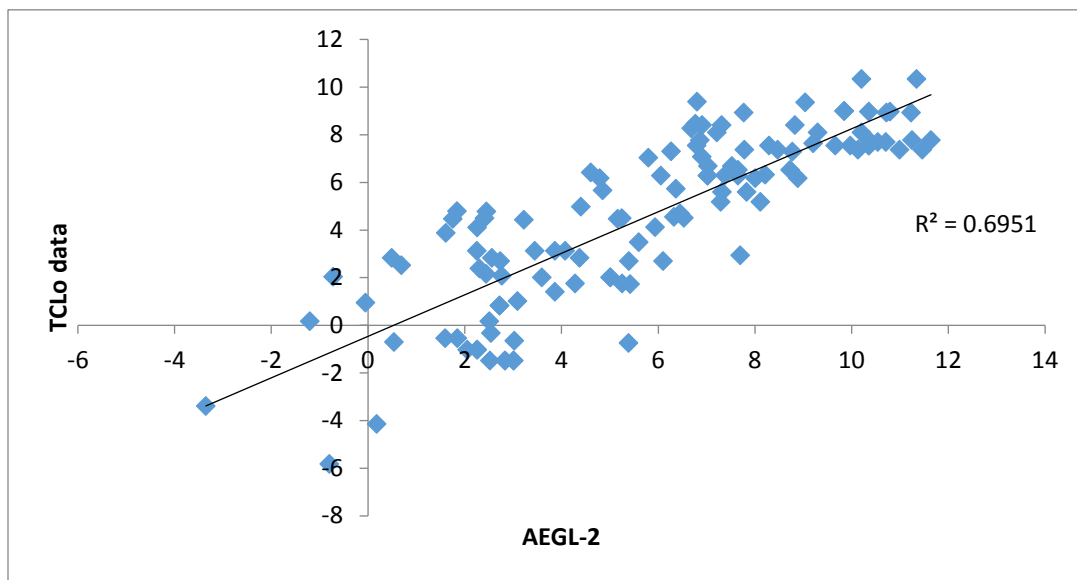
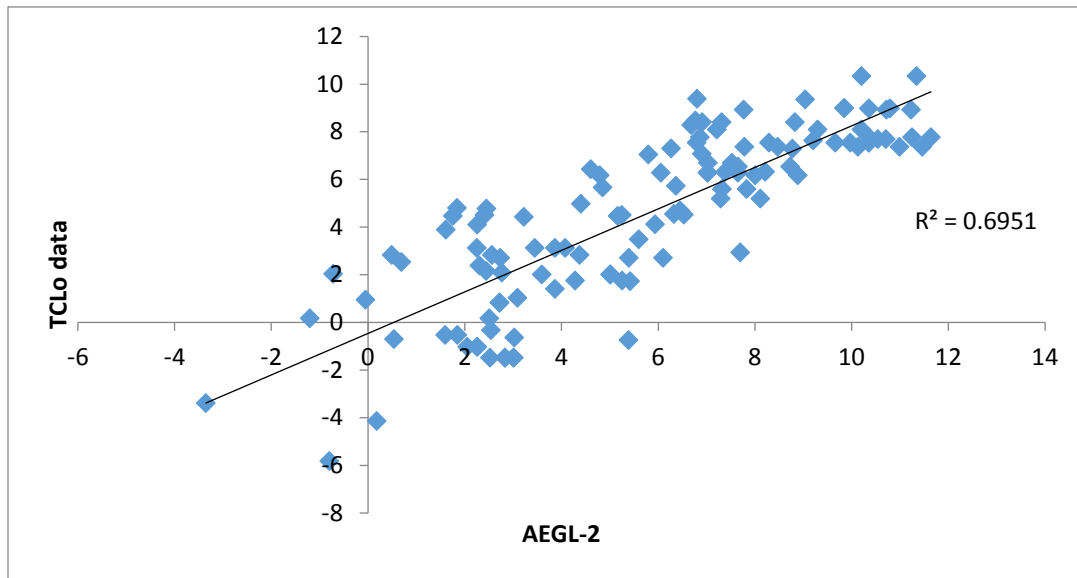
**Figure 2.** Regression analysis showing linear relationship between the log-transformed LD<sub>50</sub> data and AEGL-3 values



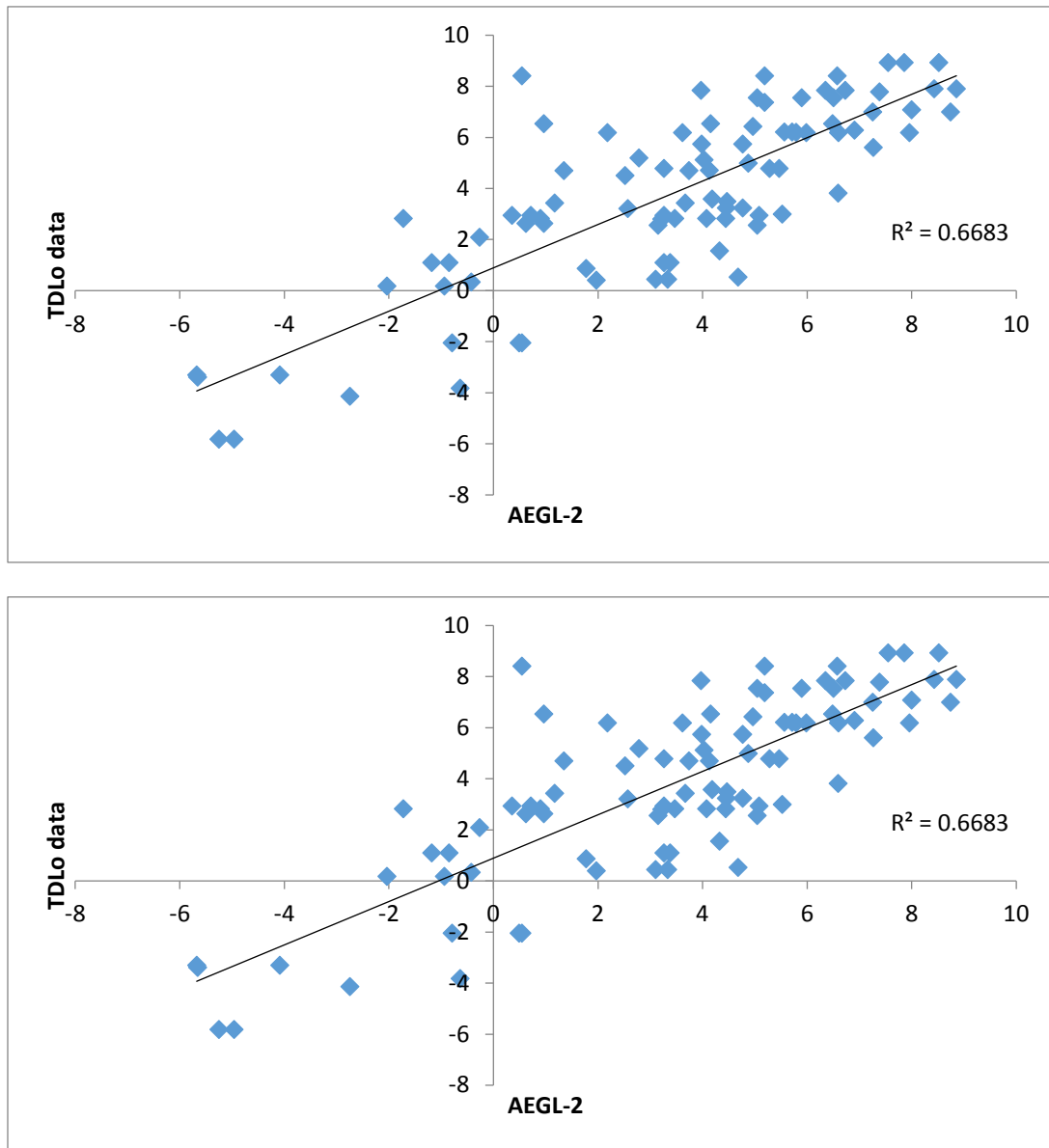
**Figure 3.** Regression analysis showing linear relationship between the log-transformed LC<sub>Lo</sub> data and AEGL-3 values.



**Figure 4.** Regression analysis showing linear relationship between the log-transformed LD<sub>Lo</sub> data and AEGL-3 values.



**Figure 5.** Regression analysis showing linear relationship between the log-transformed TC<sub>Lo</sub> data and AEGL-2 values.



**Figure 6.** Regression analysis showing linear relationship between the log-transformed  $TD_{Lo}$  data and AEGL-2 values.

Log-transformed values do not correspond to actual distributions, so they are not a direct representation of the real distribution. In addition, the back-transformed mean of log-transformed values is not the same as the mean of the original raw values. So neither the log-transformed means nor back-transformed means from the datasets were suitable; therefore, a different approach was used.

The raw datasets do not meet the assumptions of a normal distribution; for example, the standard deviations are very large. The objective is to comply with the definition of an outlier, as defined above, to reduce distortion of the means. However, the means minus two standard

deviations result in negative numbers; none of the ratios in the raw datasets are negative numbers. As a solution, the statistical analyses performed on the log-transformed datasets were used and ratios that met our definition of outliers were removed, that is the mean  $\pm 2 \times \text{SD}$ . These ratios and their corresponding chemicals in the raw datasets were then removed as outliers. The descriptive statistics for the adjusted raw datasets are presented in Table 5.

**Table 5.** Descriptive Statistics of the Adjusted Datasets: Mean Values  $\pm (2 \times \text{SD})$

Statistic	LC <sub>50</sub>	LD <sub>50</sub>	LC <sub>Lo</sub>	LD <sub>Lo</sub>	TC <sub>Lo</sub>	TD <sub>Lo</sub>
Count	369	792	235	154	120	89
Mean	36	3.3	37	2.5	13	2.9
Median	14.3	0.84	14.1	0.41	4.2	0.67
Mode	1.7	0.08	11.5	N/A	2.1	N/A
SD	62	6.8	63	5.1	24.3	4.8
Variance	3912	46.6	4020	26.2	591.4	22.9
Kurtosis	15.18	17.1	16.2	14.1	11.5	5.4
Skewness	3.7	3.8	3.8	3.4	3.2	2.3
Confidence Interval ( $\alpha = 0.05$ )	$\pm 6.4$	$\pm 0.48$	$\pm 8.15$	$\pm 0.81$	$\pm 4.40$	$\pm 1.01$

## CONCLUSIONS AND RECOMMENDATIONS

Adjustment factors were derived using a process similar to that described by Craig, et. al., (2000), but the analysis used AEGL values instead of ERPG values. In this analysis, the means of the ratios of the toxicity parameters to their corresponding AEGL values were calculated. The means were rounded to two significant digits following accepted mathematical conventions. Those means are the adjustment factors. A comparison of these adjustment factors to the original adjustment factors described in Craig, et. al., (2000) is presented in Table 6.

**Table 6.** Proposed and Original Adjustment Factors Used to Derive TEEL Values from Toxicity Data

	TEEL-3				TEEL-2	
	LC <sub>50</sub>	LD <sub>50</sub>	LC <sub>Lo</sub>	LD <sub>Lo</sub>	TC <sub>Lo</sub>	TD <sub>Lo</sub>
Proposed Adjustment Factors	36	3.3	37	2.5	13	2.9
Craig, et. al., 2000; DOE, 2008	100	2	100	1	15	1.5

Using these adjustment factors will change numerous TEEL values. TEEL values derived from LC<sub>50</sub>, LC<sub>Lo</sub> and TC<sub>Lo</sub> data will increase. TEEL values derived LD<sub>50</sub>, LD<sub>Lo</sub>, and TD<sub>Lo</sub> data will decrease. The adjustment factors were submitted to the DOE Office of Emergency Management with the recommendation that they be used in future TEEL development. DOE accepted the recommendation.



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## APPENDIX B

### STATISTICS IN SUPPORT OF TEEL VALUE METHODOLOGY MULTIPLICATION FACTORS

*This whitepaper was released in June 2011. **NOTE:** Since this paper was written in 2011, website locations are listed as they were when the paper was written. TEEL website locations transitioned in 2016 from ATL websites to <https://sp.eota.energy.gov/pac/>.*

#### SUMMARY

Multiplying factors are used to develop Temporary Emergency Exposure Limits (TEEL) values from other Protective Action Criteria (PACs) when there are not enough suitable data to support derivation of TEEL values by other means. The multiplying factors in DOE-HDBK-1046-2008, *Temporary Emergency Exposure Limits for Chemicals: Methods and Practice* (DOE 2008) were developed before Acute Exposure Guideline Levels (AEGLs) existed. This appendix describes a process in which AEGLs were used to reexamine the basis of these multiplying factors. Ratios for all matched pairs of AEGL-3 to AEGL-2, and AEGL-2 to AEGL-1 values were calculated. The mean of the AEGL-2 to AEGL-1 ratios is 11.19. The mean of the AEGL-3 to AEGL-2 ratios is 5.67. Therefore, a value of six is used as the new multiplying factor for developing PAC-3 values from PAC-2 values and vice versa. A value of eleven is the multiplying factor used to calculate PAC-2 from PAC-1 values and vice versa.

#### BACKGROUND

The first list of TEEL values was released in 1992. In 1995, Craig, et. al., published the original methodology for developing TEEL values. This methodology was based on hierarchies of commonly available and published exposure limits, such as Permissible Exposure Limits (PELs) promulgated by the Occupational Safety and Health Administration (OSHA). In 2000, Craig, et. al., published an updated methodology for developing TEEL values. This default methodology is also documented in DOE-HDBK-1046-2008, *Temporary Emergency Exposure Limits for Chemicals: Methods and Practice* (DOE, 2008).

TEEL values are developed for three levels; TEEL-1, TEEL-2, and TEEL-3. Each level represents an increase in the severity of biological effects. Definitions for each of the Protective Action Criteria (PAC) levels can be found online at <http://www.atlintl.com/DOE/teels/teel/teeldef.html>. As used here, Protective Action Criteria (PACs) is a collective term that includes AEGL, ERPG, and TEEL values.

TEEL-1, -2, and -3 have the same definitions as the 60-minute AEGL-1, -2, and -3. A list of chemicals with AEGL, ERPG, and TEEL values can be found online at <http://www.atlintl.com/DOE/teels/teel.html> (DOE, 2010).

For some chemicals, there are no AEGL or ERPG values and there are not enough suitable data available to develop all four TEEL values. In these cases, the missing value(s) is derived from an existing value. Craig, et al., (2000) describes the original multiplying factors that are used to derive a missing TEEL value from an existing PAC value, either above or below the missing value.

This analysis addressed two multiplying factors: one used to derive a PAC-3 from a PAC-2, and vice versa; the other one used to derive a PAC-1 from a PAC-2. Until now, the first multiplying factor had been derived by estimating the means of ratios of ERPG-3 to ERPG-2 values (calculated to be ~5.0); the second one had been derived by estimating the mean of ratios of ERPG-2 to ERPG-1 values (calculated to be ~7.0) (Craig, et. al., 2000).

There are approximately 260 chemicals with AEGL values (EPA, 2010) compared to 142 chemicals with ERPG values (AIHA, 2010). Further, there were only 77 chemicals ERPG values when Craig, et. al., (2000) derived the first multiplying factors. Using a larger dataset usually improves the likelihood that the results accurately represent the population from which they are drawn.

## METHODS

AEGLs were selected as the basis for deriving new multiplying factors for three reasons: (a) The DOE Office of Emergency Management, has defined TEEL values based on the definitions of AEGLs; (b) AEGL values are now the primary PACs used at DOE facilities; and (c) The current AEGL dataset provides a large sample of chemicals upon which to base the derivation. ATL staff compiled a list of chemicals with AEGL-1 and AEGL-2 values, and another list of chemicals with AEGL-2 and AEGL-3 values (EPA, 2010). There are 162 chemicals with AEGL-1 and AEGL-2 values, and 250 chemicals with AEGL-2 and AEGL-3 values.

EPA describes the methods and data they use for developing AEGL values in chemical-specific Technical Support Documents (TSDs) on the EPA-AEGL website

(<http://www.epa.gov/opptintr/aegl/>). As documented in these chemical-specific TSDs, if the authors were not able to find appropriate chemical-specific data to develop an AEGL-2, then the AEGL-2 is derived by reducing AEGL-3 value by a factor of three (For an example, see the TSD for phenyl mercaptan,

[http://www.epa.gov/oppt/aegl/pubs/phenyl\\_mercaptan\\_interim\\_nov\\_2007\\_v1.pdf](http://www.epa.gov/oppt/aegl/pubs/phenyl_mercaptan_interim_nov_2007_v1.pdf)).

Chemicals were eliminated from the list containing AEGL-2 and AEGL-3 values if the AEGL-2 had been calculated from the AEGL-3 value. This reduced the number of chemicals for the AEGL-3 to AEGL-2 ratio analysis to 214. Similar calculations used to derive AEGL-1 values from AEGL-2 values were not found. Thus, no chemicals were removed from that list before the analyses were performed; the number of chemicals for the AEGL-2 to AEGL-1 ratio analysis was 162.

The counts, means, medians, modes, sample variance, standard deviations (SD), and the skewness and kurtosis statistics for the AEGL-3 to AEGL-2, and the AEGL-2 to AEGL-1 ratios were calculated. Outliers were removed from both data sets. In this analysis, outliers were defined as any ratio that was greater than or equal to the mean of the ratios plus two standard deviations, and any ratio that was less than or equal to the mean minus two standard deviations.

The adjusted data sets were used for subsequent bivariate statistical analyses. The ratios of the AEGL-1 to AEGL-2 and the AEGL-2 to AEGL-3 values were analyzed using Pearson's correlation and regression analyses.

## RESULTS

The results of the descriptive statistics for the two adjusted datasets show that both datasets meet the assumptions of normality. The means, medians, modes, and standard deviations are similar and the data are only slightly kurtotic and skewed. See Table 1. The mean ratio of AEGL-3 to AEGL-2 values is 5.67 and the mean ratio of AEGL-2 to AEGL-1 values is 11.19. Rounded to 6 and 11 respectively, these values are the bases for the new multiplying factors.

**Table 1.** Descriptive Statistics of the Adjusted Ratio Datasets

Statistic	AEGL-3/AEGL-2	AEGL-2/AEGL-1
Count	211	158
Mean	5.67	11.19
Median	3.75	7.73
Mode	4.52	12.17
SD	6.64	10.28
Variance	44.13	105.62
Kurtosis	16.83	3.65
Skewness	3.77	1.87
Confidence Interval ( $\alpha = 0.05$ )	$\pm 0.90$	$\pm 1.61$

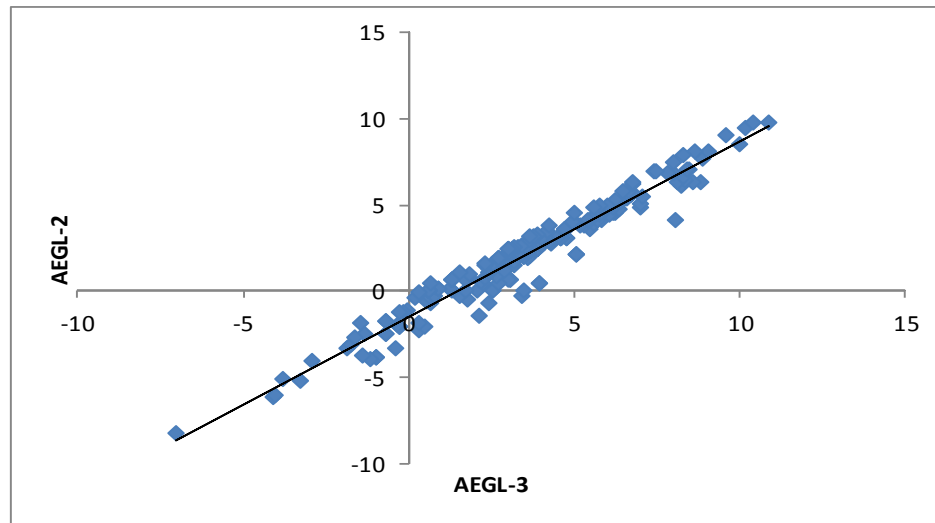
The results of the Pearson's correlation and regression analyses for both datasets are presented in Table 2. The Pearson's correlation coefficient ( $r$ ) indicates the extent to which the ratios lie on a straight line. A large correlation coefficient indicates that the correlation between the variables is strong. As can be seen in Table 2, both correlation coefficients are greater than 0.9. This indicates that there are strong correlations between the AEGL values.

The regression analyses show that the variability in the AEGL-3 values will predict the variability in the AEGL-2 values 92% of the time, and the variability of the AEGL-1 values will predict the variability in the AEGL-2 values 88% of the time. The results of these analyses show that there is a predictive relationship between the AEGL-1 and AEGL-2 values, and between the AEGL-2 and AEGL-3 values.

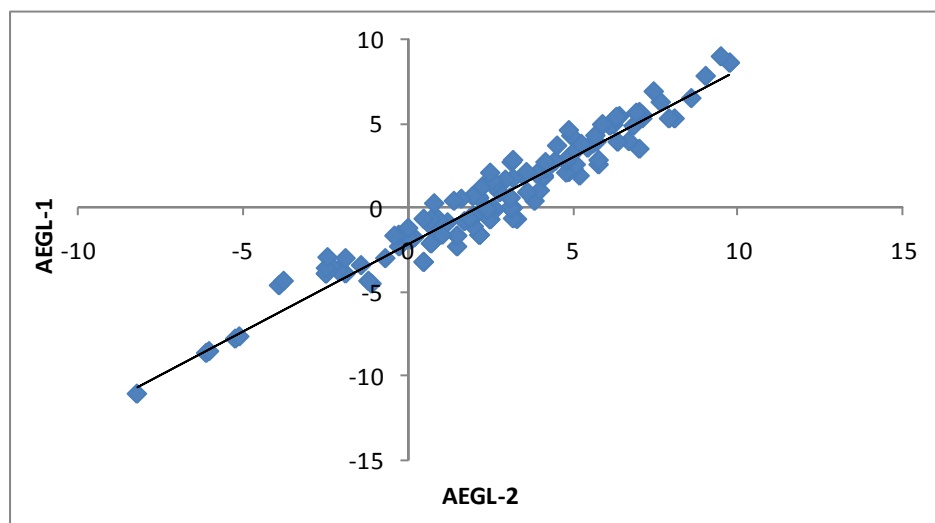
**Table 2.** Statistical Analyses – Correlations Performed on the Adjusted Datasets

Values	Pearson's $r$ (N)	$r^2$ (N)
AEGL-3 & AEGL-2	0.959	0.920
AEGL-2 & AEGL-1	0.937	0.879

Figures 1 and 2 show the strong linear relationship between the AEGL-3 & AEGL-2 values, and between the AEGL-2 & AEGL-1 values. The data are plotted on a logarithmic scale to show all data points.



**Figure 1.** Linear regression results showing the relationship between AEGL-2 & AEGL-3 values



**Figure 2.** Linear regression results showing the relationship between AEGL-1 & AEGL-2 values

## CONCLUSIONS AND RECOMMENDATIONS

The new multiplying factors were derived using a process similar to that described in Craig, et. al., (2000). The primary difference is that AEGL values were used instead of ERPG values. The means and the confidence intervals were calculated for the adjusted ratio datasets. The means were rounded to the nearest whole numbers. The rounded mean of the AEGL-3 to AEGL-2 ratios is six, and the rounded mean of the AEGL-2 to AEGL-1 ratios is eleven. The two corresponding multiplying factors originally used in TEEL development are presented in Table 4 with the new adjustment factors for comparison.

**Table 4.** Comparison of the Proposed Multiplying Factors to the Current Multiplying Factors

	TEEL-3:TEEL-2	TEEL-2:TEEL-1
<b>Proposed Factors</b>	6	11
<b>Current Factors (DOE, 2008)</b>	5	7



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