Maine Bureau of Health

Ambient Air Guidelines

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CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ACRONYMS

AAG	Ambient Air Guideline
ACGIH	American Conference of Governmental Industrial Hygienists
ATSDR	Agency for Toxic Substance and Disease Registry
BEI	Biological Exposure Index
BMD	Benchmark Dose
BOH	Maine Bureau of Health
CA-OEHHA	California Environmental Protection Agency's Office of Environmental Health Hazard Assessment
HEAST	Health Effects Assessment Summary Tables
ILCR	Incremental Lifetime Cancer Risk
IRIS	Integrated Risk Information System
LOAEL	Lowest-Observed-Adverse-Effect-Level
MRL	Minimal Risk Level
NIOSH	National Institute for Occupational Safety and Health
NOAEL	No-Observed-Adverse-Effect-Level
OSHA	Occupational Safety and Health Administration
PPM	Parts per million
REL	Reference Exposure Level
RfC	Reference Concentration
RfD	Reference Dose
TLV	Threshold Limit Value
TWA	Time-Weighted Average
UCL	Upper Confidence Limit
USEPA	United States Environmental Protection Agency

1.0 INTRODUCTION

The Maine Bureau of Health's (BOH) Environmental Health Unit develops Ambient Air Guidelines (AAGs) to assist risk managers and the public in making decisions regarding the potential human health hazards associated with chemicals in air. AAGs are not promulgated by rule making and therefore are not issued as legally enforceable ambient air "standards." Rather, AAGs represent the Bureau's most recent recommendations for chemical concentrations in ambient air, below which there is minimal risk of a deleterious health effect resulting from long-term inhalation exposure.

The AAGs are intended to be solely health-based guidelines, and do not take into account analytical methods, treatment technology, or economic impacts. BOH last updated the AAGs in 1993 (BOH, 1993). At that time, the Department of Environmental Protection's Bureau of Air Quality assembled a list of chemicals for which AAGs were requested. For this revision, BOH derived AAGs for the same list of chemicals but used new toxicological data to update the AAGs. In addition, BOH has updated the protocol for developing AAGs. A table listing the AAGs derived as of April 2004 appears at the end of this document (Table 4). AAGs will also be posted on the website for the BOH's Environmental Health Unit (http://www.maine.gov/ehu). The April 2004 AAG list is intended to replace all previously released AAG lists.

This revision focuses exclusively on AAGs for effects due to chronic exposure ("chronic" refers to long-term exposure). Chronic AAGs represent long-term average air concentrations. Thus, chronic AAGs are most appropriately compared with long-term average air measurements (*e.g.*, yearly averages). As a screening measure, it is conservative (*i.e.*, health-protective) to compare chronic AAGs with short-term measurements[1]; however, if monitoring data suggest concentrations that substantially exceed chronic AAGs, it is important that the potential for acute toxicity be assessed. Acute toxicity occurs with brief exposure to high concentrations. Air concentrations that substantially exceed chronic AAGs should be compared with ambient air guidelines or standards based on acute toxicity values. Readers may wish to consult USEPA's Air Toxics Website (at www.epa.gov/ttn/atw/toxsource/summary.html) for guidance on air concentrations that are protective for acute toxicity.

Section 2.0 of this document provides an overview of chronic inhalation toxicity values. Section 3.0 discusses the process used to select toxicity values for use in developing AAGs. Section 4.0 describes how the toxicity values were used to develop AAGs. Section 5.0 details a few changes from the list of chemicals for which AAGs were developed. Section 6.0 describes how AAGs should be used, and Section 7.0 explains the AAG status designations given by BOH. Section 8.0 gives references. Finally, Appendix A details the BOH's analysis of alternative noncancer toxicity value sources.

[1] Chronic exposure to a chemical tends to cause toxicological effects at lower levels than acute exposure. Thus, chronic AAGs are lower than acute AAGs for the same chemical.

2.0 OVERVIEW OF INHALATION TOXICITY VALUES

The development of AAGs requires an initial step of identifying inhalation toxicity values upon which the AAGs will be based. Toxicity values represent quantitative estimates of the relationship between the dose to which a person is exposed and the expected toxicological response. Toxicity values are route-specific; *i.e.*, they are different for exposure via inhalation, ingestion, and dermal contact. With air exposures the concern is primarily intake via inhalation. The model used by risk assessors to assess the toxicity of chemicals is different for chemicals with carcinogenic effects than for chemicals with noncarcinogenic effects. This section briefly describes the inhalation toxicity values for noncarcinogenic and carcinogenic effects. As noted earlier, this revision of the AAGs focuses exclusively on chronic effects, and thus only chronic toxicity values are considered.

2.1 Inhalation Toxicity Values for Noncarcinogenic Effects

AAGs based on noncarcinogenic toxicological effects are set at a level believed to represent a minimal risk of a deleterious effect from lifetime exposure even for sensitive subpopulations. It is assumed that noncarcinogenic effects have a threshold response (*i.e.*, there is a dose below which toxic effects will not occur). An attempt is made to set AAGs such that exposure at the AAG will result in a daily dose below the threshold. This is believed to be accomplished through use of a *reference concentration*.

The *reference concentration* (RfC, given in units of mg/m3) is defined by the USEPA as an estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure for the human population, including sensitive subpopulations, that is likely to be without an appreciable risk of deleterious effects during a lifetime of exposure. The value of the RfC is chemical-specific. A lower value of the RfC implies greater toxicity of the substance.

The RfC is most often derived from studies of laboratory animals (bioassays), although human data are preferred. USEPA strives to use a bioassay that identifies a no-observed-adverse-effect-level (NOAEL), which is a dose level that did not result in adverse effects in the animals so exposed. When none of the available studies identifies a NOAEL, USEPA may choose a study that identifies a lowest-observable-adverse-effect level (LOAEL), the lowest level associated with an adverse effect, as the basis for a RfC.

In recent years, USEPA has begun to use a “benchmark dose” (BMD) in place of a NOAEL or LOAEL. A benchmark dose is a dose producing a predetermined level of change in adverse response compared to untreated animals. A BMD is estimated by fitting a mathematical dose-response model to data from a toxicological study. BMDs are preferred over NOAELs and LOAELs, in part because they take into account sample size and dose-response characteristics. In addition, the BMD approach places less reliance on the assumption of a threshold for noncancer effects, and makes use of available information on mechanism of action.

In order to predict the level of response in humans based on animal data, USEPA applies one or more uncertainty factors to the NOAEL, LOAEL, or BMD. First, if animal data are used, USEPA uses an uncertainty factor to extrapolate from responses in laboratory animals to

responses expected for the average human. Second, if the animal study does not include a NOAEL but rather a LOAEL, then USEPA applies an uncertainty factor to extrapolate from a LOAEL to NOAEL. Third, if the exposure duration in the study is less than chronic[2], USEPA uses an uncertainty factor to predict responses from chronic exposure. Fourth, USEPA may use an uncertainty factor to extrapolate from responses for the average human to possible sensitive sub-populations. Finally, if the toxicological database for a given chemical is missing information (such as data on developmental or reproductive effects), USEPA applies an uncertainty factor for limitations in the database. These uncertainty factors typically range from 3 to 10 and are combined multiplicatively. As a result, it is not unusual for RfCs to be 100 to 1000-times lower than the concentration that is reported to be without any observable adverse effect in an animal bioassay.

2.2 Inhalation Toxicity Values for Carcinogenic Effects

For chemicals classified by USEPA as *known* or *probable* human carcinogens[3], AAGs are derived using a quantitative estimate of the chemical's inhalation carcinogenic potency (called the *Unit Risk*, this is the toxicity value for carcinogenic effects). The value of the Unit Risk is chemical-specific, and the greater the value of the Unit Risk, the greater the carcinogenic potency of the substance.

The inhalation Unit Risk is defined by the USEPA as the upper bound excess lifetime cancer risk estimated to result from continuous exposure to an agent at a concentration of 1 ug/m^3 in air. The units are given as $(ug/m^3)^{-1}$. The Unit Risk is most often derived from studies of laboratory animals, traditionally by application of dose-response models that assume no threshold for carcinogenic effects (*i.e.*, any dose, no matter how small, will result in some risk) and that allow for linearity in response at low dose (*i.e.*, risk increases proportionally with dose at low doses). In deriving a cancer Unit Risk, USEPA usually selects the 95% upper confidence limit (UCL) on the Unit Risk. The use of the UCL means that 95% of toxicological experiments like the one forming the basis for the Unit Risk would result in cancer Unit Risk estimates at or below the UCL. Thus, the Unit Risk used by USEPA is a conservative (or "upper bound") estimate of the carcinogenic potency.

3.0 SELECTION OF TOXICITY VALUES

Inhalation toxicity values (RfCs and Unit Risks) are available from a number of sources, and any given chemical may have values available from more than one source. To choose among differing values for individual chemicals, BOH employed a two-step process. The first step was to establish a hierarchy of toxicity value sources from among the various sources available. The second step was to evaluate whether there was chemical-by-chemical agreement between toxicity values from different sources in the hierarchy. When there was significant difference between toxicity values for a given chemical (BOH defined a "significant" difference as at least a factor of three), BOH reviewed the documentation for the toxicity values in order to determine

[2] USEPA defines a chronic exposure as exposure that endures for more than 10% of the animal's lifespan.
[3] USEPA is moving away from the alphanumeric classification of carcinogens (groups A, B, C, D, and E) and toward descriptive classifications (e.g., "known human carcinogen, probable human carcinogen", etc.).

whether there was a readily apparent reason to depart from the hierarchy. These steps are discussed in Sections 3.1 and 3.2 below.

3.1 Establishing a Hierarchy of Toxicity Value Sources

It is common practice in risk assessment to rely on existing toxicity values, and to establish a hierarchy of preference among toxicity value sources (*e.g.*, USEPA Air Toxics Website, USEPA OSWER Directive 9285.7). The hierarchy of sources is usually prioritized according to appropriateness and scientific rigor.

In 1993, BOH used the following hierarchy of toxicity values to develop AAGs:

1. Bureau of Health risk assessments[4]
2. USEPA IRIS values
3. USEPA Health Effects Assessment Summary Tables HEAST values
4. Risk assessments from other agencies, primarily Rhode Island Ambient Air Guidelines.
5. ACGIH Threshold Limit Values (TLVs), Ceiling Limits, and Short-Term Exposure Limits.

At the top of many agencies' hierarchies is the USEPA's Integrated Risk Information System (IRIS). Among USEPA sources of chronic toxicity values, IRIS contains values considered "gold standards". IRIS values have undergone both internal and external peer review and enjoy agency-wide acceptance. It should be noted that values on IRIS might be overdue for reevaluation (for example, the inhalation carcinogenicity assessment for chloroform is dated 1987). However, because of the rigorous review process, IRIS values are viewed as USEPA's preferred source of toxicity values, and it is likewise BOH's preference to look first to IRIS as a source for toxicity values. However, among the 77 chemicals with existing Maine AAGs, only 20 have USEPA IRIS noncancer inhalation toxicity values and only 16 have IRIS cancer inhalation toxicity values (as of January 2004). IRIS has neither cancer nor noncancer inhalation toxicity values for 44 of the 77 chemicals. As a result, it was necessary to consider other sources of toxicity values. As some sources provide only noncancer or only cancer toxicity values, these endpoints were considered separately, as detailed below.

3.1.1 Hierarchy for Noncancer Endpoints

For noncarcinogenic endpoints, there are a number of other sources of inhalation toxicity values, including:

- Agency for Toxic Substances and Disease Registry (ATSDR) Minimal Risk Levels or MRLs,
- USEPA's Health Effects Assessment Summary Tables (HEAST) Reference Concentrations (RfCs),

[4] When the 1993 AAGs were developed, the Bureau of Health had recently conducted in-depth reviews of the toxicological data for a handful of chemicals. These reviews have not been updated since 1993.

- California EPA's Office of Environmental Health Hazard Assessment (CA-OEHHA) Reference Exposure Levels or RELs,
- Occupational health values such as the American Conference of Governmental Industrial Hygienists (ACGIH) Threshold Limit Values (TLVs) and National Institute of Occupational Safety and Health (NIOSH) Relative Exposure Limits (RELs), and
- Cross-route extrapolation of toxicity values (*e.g.*, estimating an inhalation value from an oral value).

These sources each have different features. Several provide values that are intended to be protective of the general public including sensitive subgroups (*e.g.*, CA-OEHHA, ATSDR, and HEAST), while others are intended to protect the average worker population (*e.g.*, ACGIH and NIOSH occupational values). Some provide dose-response information for a small number of chemicals (ATSDR) while others include information for many more chemicals (ACGIH). Finally, some sources are updated regularly while others (HEAST) are not. Table 1 summarizes the major features of the available sources.

Table 1. Features of Noncancer Toxicity Value Sources

Source	Peer-Reviewed	Updated Regularly	Health-Based	Targets General Population	Includes Large Number of Chemicals
IRIS RfC	√	√	√	√	√
ATSDR MRL	√	√	√	√	
HEAST RfC			√	√	√
CA-OEHHA REL	√	√	√	√	√
ACGIH TLV	√	√	√		√
NIOSH REL	√	√	√		

BOH narrowed the list to four sources of noncancer inhalation toxicity values. BOH first selected those sources that incorporated peer review into the development process, excluding HEAST. Second, BOH chose ACGIH occupational toxicity values over NIOSH toxicity values. Both sources target occupationally exposed populations, and the two often (but not always) have identical toxicity values for the same chemicals. However, ACGIH includes toxicity values for a larger selection of chemicals than NIOSH does. For this reason, BOH included ACGIH toxicity values but not NIOSH values. The final sources used for noncancer AAG development are IRIS RfCs, ATSDR MRLs, California OEHHA RELs, and ACGIH TLVs. In addition, BOH considered cross-route extrapolation using oral toxicity values on IRIS.

In order to develop an objective basis for prioritizing these sources, BOH began with the premise that IRIS values represent the standard against which all other sources are measured. As a means of evaluating the appropriateness of other sources, BOH quantified the level of agreement between the alternative toxicity values and those on IRIS for the same chemicals. Specifically, for each source, a linear regression analysis (in log space) was conducted to assess the agreement

between the IRIS values and alternative values for the same chemicals. The hierarchy of noncancer toxicity value sources was established based on the results of the regression analysis, with preference given to those sources with values most highly correlated with IRIS values. The regression analyses used to develop the hierarchy are detailed in Appendix A.

Based on this analysis, BOH established the following hierarchy of noncancer toxicity values:

1. IRIS Reference Concentration (RfC)
2. California Office of Environmental Health Hazard Assessment (CA-OEHHA) Reference Exposure Levels (RELs),
3. Agency for Toxic Substance and Disease Registry (ATSDR) Chronic Inhalation Minimal Risk Levels (MRLs),
4. American Conference of Governmental Industrial Hygienists (ACGIH) Threshold Limit Values-Time Weighted Average (TLV-TWAs),

3.1.2 Hierarchy for Cancer Endpoints

For carcinogenic endpoints, BOH identified only one alternative source of inhalation toxicity values: California EPA's Office of Environmental Health Hazard Assessment (CA-OEHHA). Unit Risks from this source are peer reviewed and have the features shown in Table 1 for CA-OEHHA RELs. For carcinogenic endpoints, IRIS was given top preference and the selection process moved directly to the second step, where toxicity values that differed by three-fold or more were compared.

3.2 Choosing Between Toxicity Values that Differ by 3-Fold or More

Updates to the IRIS database can be slow, and as a result, some toxicity values on the IRIS database may be outdated. In order to ensure that AAGs were not derived from outdated IRIS values (or outdated values from other sources), BOH compared the toxicity values from the top sources (IRIS, CA-OEHHA, and ATSDR for noncancer, IRIS and CA-OEHHA for cancer endpoints) to determine whether the toxicity values for each chemical differed by three-fold or more[5]. The goal was to highlight toxicity values that might be outdated, especially outdated IRIS values, to ensure that the highest quality toxicity value was used to derive the AAG for a given chemical. BOH identified twelve chemicals with noncancer toxicity values that differed by 3-fold or more and six chemicals with IRIS and CA-OEHHA cancer Unit Risks that differed by 3-fold or more.

For these 18 chemicals, BOH reviewed the background documentation for the differing values. Specifically, for each source, BOH determined the date that each toxicity value was derived and the critical study upon which the toxicity value was based. Tables 2 and 3 show the toxicity values, dates of derivation, and critical studies for these chemicals for noncancer and cancer endpoints, respectively. For each chemical, BOH determined whether the primary source had reviewed the critical study used by the secondary source. If so, BOH deferred to the hierarchy.

[5] Because of the additional uncertainty associated with the use of ACGIH toxicity values (see Appendix A for further information), BOH did not include these in the comparison.

Maine Bureau of Health Ambient Air Guidelines
April 2004

Table 2. Comparisons between Noncancer Toxicity Values that Vary by 3-Fold or More

Chemical	Primary Toxicity Value (mg/m^3)	Source	Date of Derivation	Critical Study(s)	Secondary Toxicity Value (mg/m^3)	Source	Date of Derivation	Critical Study(s)	Did primary source review critical study used by secondary source?	Chosen basis for AAG[a]
1,3-Butadiene	2.E-03	IRIS RfC	Nov-02	NTP, 1993	2.E-02	CA-OEHHA REL	Dec-00	NTP, 1993	Yes	IRIS RfC
Chloroform	3.E-01	CA-OEHHA REL	Apr-00	Torkelson et al., 1976	1.E-01	ATSDR MRL	Mar-97	Bomski et al., 1967	Yes	CA REL
1,2-Dichloroethane	4.E-01	CA-OEHHA REL	Dec-00	Spreafico et al., 1980	2.E+00	ATSDR MRL	May-01	Cheever et al., 1990	Yes	CA REL
Epichlorhydrin	1.E-03	IRIS RfC	Apr-92	Quast et al., 1979	3.E-03	CA-OEHHA REL	Dec-00	Quast et al., 1979	Yes	IRIS RfC
Formaldehyde	3.E-03	CA-OEHHA REL	Feb-00	Wilhelmsson and Holmstrom, 1992	1.E-02	ATSDR MRL	Apr-99	Holmstrom et al., 1989	Yes	CA REL
Hydrogen Sulfide	2.E-03	IRIS RfC	Jul-03	Brenneman et al., 2000	1.E-02	CA-OEHHA REL	Apr-00	CIIT, 1983	Yes	IRIS RfC
Manganese	5.E-05	IRIS RfC	Dec-93	Roels et al., 1992	2.E-04	CA-OEHHA REL	Apr-00	Roels et al., 1992	Yes	IRIS RfC
Mercury	3.E-04	IRIS RfC	Jun-95	Fawer et al., 1983; Piikivi and Tolonen, 1989; Piikivi and Hanninen, 1989; Piikivi, 1989; Ngim et al., 1992; Liang et al., 1993	9.E-05	CA-OEHHA REL	Feb-00	Fawer et al., 1983; Piikivi and Tolonen, 1989; Piikivi and Hanninen, 1989; Piikivi, 1989; Ngim et al., 1992; Liang et al., 1993	Yes	IRIS RfC
Naphthalene	3.E-03	IRIS RfC	Sep-98	NTP, 1992	9.E-03	CA-OEHHA REL	Apr-00	NTP, 1992	Yes	IRIS RfC
Styrene	1.E+00	IRIS RfC	Jul-93	Mutti et al., 1984	3.E-01	ATSDR MRL	Sep-92	Mutti et al., 1984	Yes	IRIS RfC
Tetrachloroethylene	4.E-02	CA-OEHHA REL	Oct-93	Buben and O'Flaherty, 1985	2.E-01	ATSDR MRL	Oct-96	Ferroni et al., 1992	No[b]	CA REL[c]
Xylenes	1.E-01	IRIS RfC	Feb-03	Korsak et al., 1994	7.E-01	CA-OEHHA REL	Apr-00	Uchida et al., 1993	Yes	IRIS RfC

a. Defer to hierarchy if primary source reviewed critical study used by secondary source. See Section 3.2 of text for additional explanation.
b. The critical study for the MRL is from 1992, and may or may not have been published when the toxicological review for the REL was completed.
c. USEPA is currently developing a RfC for tetrachloroethylene. Pending the release of the RfC, BOH has used the REL to calculate the noncancer AAG; however the final AAG is not based on noncancer effects, but rather on cancer effects.

Table 3. Comparisons Between Cancer Toxicity Values that Vary by 3-Fold or More

Chemical	IRIS Unit Risk (per ug/m^3)	Date of Derivation	Critical Study(s)	CA-OEHHA Unit Risk (per ug/m^3)	Date of Derivation	Critical Study(s)	Did IRIS review study used by CA-OEHHA?	Chosen basis for AAG[a]
Benzene	2.2E-6 to 7.8E-6	2000	Rinsky et al., 1981, 1987; Paustenbach et al., 1993; Crump and Allen, 1984; Crump, 1992, 1994; USEPA, 1998.	2.90E-05	1984	Rinsky et al., 1981	Yes	IRIS
1,3-Butadiene	3.00E-05	2002	Delzell et al., 1995	1.70E-04	1992	Melnick et al., 1990	Yes	IRIS
Chloroform	2.30E-05	1987	NCI, 1976	5.30E-06	1990	CDHS, 1990, Bogen et al., 1989, Jorgensen et al., 1985; NCI, 1976.	No	CA-OEHHA[b]
Chromium (VI)	1.20E-02	1998	Mancuso, 1975	1.50E-01	1985	Mancuso, 1975	Yes	IRIS
Epichlorhydrin	1.20E-06	1994	Laskin et al., 1980	2.30E-05	1988	Konishi et al., 1980	Yes	IRIS
Vinyl Chloride	4.4E-6 to 8.8E-6	2000	Maltoni et al., 1981, 1984	7.80E-05	1990	Drew et al., 1983	Yes	IRIS

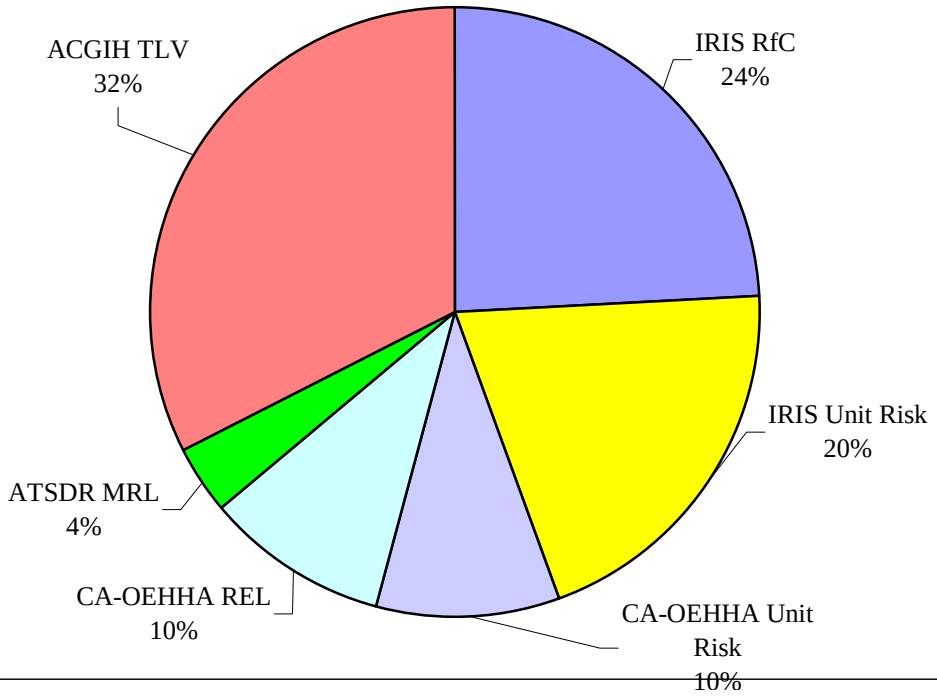
a. Defer to IRIS if IRIS reviewed critical study used by CA-OEHHA. See Section 3.2 of text for additional explanation.

b. The USEPA IRIS record indicates that the unit risk for chloform is under review. BOH review indicated that CA-OEHHA unit risk was based on more current data and modeling. Thus, the CA-OEHHA unit risk was used to derive an interim AAG pending USEPA's revision to the IRIS unit risk.

For many of the noncancer toxicity values, the difference between two sources was the result of different uncertainty factors rather than different critical studies. If the documentation suggested that the primary source might not have reviewed the critical study used by the secondary source, BOH conducted additional research into both values before selecting a toxicity value for use in AAG development. Tables 2 and 3 document the toxicity values used in deriving AAGs for each of the 18 chemicals.

Figure 1 shows a breakdown of the toxicity values used to derive the 2004 AAGs.

Figure 1. Sources of Toxicity Values Used in Derivation of 2004 AAGs



4.0 DERIVATION OF AMBIENT AIR GUIDELINES

The Bureau of Health uses a risk-based approach for developing AAGs. AAGs are set to be protective of both carcinogenic effects and noncarcinogenic effects, to the extent that data are available. Separate AAGs are derived for both noncarcinogenic and carcinogenic effects when toxicity values for both endpoints are available from the above sources. The calculation of AAGs for noncarcinogenic and carcinogenic effects is intended to provide the Bureau with the necessary information to recommend an AAG for a given chemical that is protective of both cancer and noncancer effects. When two AAGs are calculated for a given chemical using the methods described in Section 4.1 for noncarcinogenic effects and Section 4.2 for carcinogenic

effects, the lower of the two values is selected as the AAG and is thus considered protective of both cancer and noncancer effects.

4.1 Derivation of Ambient Air Guidelines for Noncarcinogenic Effects

Chronic AAGs for noncarcinogenic effects are set equal to the corresponding RfCs or to equivalent values intended to approximate the RfC. CA-OEHHA RELs and ATSDR MRLs are used without alteration in place of IRIS RfCs. The analysis conducted by the Bureau of Health (Appendix A) indicates that both MRLs and RELs provide good approximation of RfCs. In addition, the protocols used to derive both RELs and MRLs are intended to result in exposure limits that are comparable to RfCs (*i.e.*, they are protective for continuous exposure even for sensitive members of the human population).

By contrast, occupational values (ACGIH TLVs) must be modified before use. First, the original value based on occupational exposure parameters (these assume exposure for 8 hours per day, 5 days per week) is divided by a factor of 4.2 to convert to an equivalent value for continuous exposure (exposure for 24 hours per day, 7 days per week). This adjustment is performed using the following equation (1):

$$TLVadj = TLVx\ (5/7)x(8/24)$$

Second, the adjusted value is divided by an uncertainty factor of 100. This uncertainty factor is consistent with the application of a 10-fold uncertainty factor for interindividual variation (to account for segments of the population that are more sensitive than the average healthy worker) and a 10-fold uncertainty factor for extrapolation from an observed effect level to a no-observed effect level (many, but not all TLVs are set at a level that may cause mild effects). Based on the analysis conducted by the Bureau of Health, the application of this uncertainty factor will result in modified TLVs that reasonably approximate corresponding RfCs. More information on the rationale for this uncertainty factor is available in Appendix A. Each AAG is calculated from the adjusted TLV as follows (Equation 2):

$$AAG = TLVadj \div 100$$

In deriving the April 2004 AAGs, BOH has relied upon the January 2004 online versions of IRIS, ATSDR MRLs, and CA-OEHHA chronic RELs, as well as the ACGIH 2003 TLVs document.

4.2 Derivation of Ambient Air Guidelines for Carcinogenic Effects

Ambient air guidelines for carcinogenic effects are calculated using the Unit Risk (described above in Section 2.2) and the target incremental lifetime cancer risk (ILCR). The target ILCR is the allowable level of increased lifetime cancer risk over background rates of cancer risk. Under the assumption of a non-threshold mode of action for carcinogens, there is some increased cancer

risk with any amount of exposure. Historically, federal and state standards and guidelines to limit exposure to chemical carcinogens present in environmental media and food have been set at target ILCR levels ranging from one in ten thousand (1×10^{-4}) to one in one million (1×10^{-6}). As a general policy, BOH has used a target ILCR of one in a hundred thousand (1×10^{-5}) as a reference in the derivation of action levels (BOH, 2000, 2001). Accordingly, AAGs derived by the Bureau based on carcinogenic effects are established at a target ILCR level of one in a hundred thousand (1×10^{-5}).

The equation for deriving AAGs based on carcinogenic effects is as follows (Equation 3):

$$AAG = ILCR / UnitRisk$$

For chemicals classified as *possible* (group "C" under the 1986 Guidelines for Carcinogen Risk Assessment) human carcinogens, the BOH uses a different approach. If a Unit Risk value is available either from IRIS or from California's OEHHA for a chemical classified as a *possible* (Group C) human carcinogen, the Bureau will use it in equation (3) to derive an AAG for carcinogenic effects. This AAG based on carcinogenic effects will then be compared to the AAG for noncarcinogenic effects. The lower of the two values will be used as the basis for the listed AAG. In the absence of a Unit Risk from IRIS or CA-OEHHA, BOH applied an Uncertainty Factor of 10 to the AAG calculated based on noncarcinogenic effects to account for potential carcinogenicity. The use of an uncertainty factor to address potential carcinogenicity is consistent with the Bureau's method for deriving Maximum Exposure Guidelines for chemicals in water (BOH, 2000), as well as with USEPA guidance on developing drinking water regulations and health advisories (USEPA, 1990). This method was used to calculate the AAG for naphthalene.

In deriving the April 2004 AAGs, the Bureau of Health has relied upon the January 2004 online version of IRIS and the CA-OEHHA Unit Risk tables.

5.0 CHANGES FROM THE 1993 CHEMICAL LIST

In this revision to the AAGs, wherever possible, BOH has provided AAGs for more species of the metals included in the 1993 revision. For example, whereas the 1993 revision provided an AAG for insoluble nickel refinery dust, this revision includes AAGs for that species as well as nickel oxide, nickel subsulfide, and a general category for nickel and compounds. These additions reflect the availability of toxicity values from reliable sources (IRIS, CA-OEHHA, ATSDR) for these species. To the extent that analytical data include the identification of individual metal species, the availability of species-specific AAGs will improve the understanding of health hazards associated with airborne metals. In the absence of species-specific analytical data, BOH recommends the use of the most conservative (*i.e.*, lowest) AAG among the metal species that could plausibly exist in the air sample.

This revision provides an AAG for hydrogen cyanide rather than for free cyanide (as provided in the 1993 revision). ATSDR (1997) notes that most of the cyanide in air will be present as hydrogen cyanide. In addition, IRIS reports an RfC for hydrogen cyanide, but no inhalation

toxicity values for free cyanide. Thus, BOH believes it is preferable to report the AAG for hydrogen cyanide.

6.0 DESIGNATION OF AMBIENT AIR GUIDELINE STATUS

AAGs are designated either *Final* or *Interim*. The purpose of these designations is to communicate the Bureau's confidence in the toxicity data used in deriving the AAG. An AAG is designated as *Final* if inhalation toxicity data for that chemical are obtained from IRIS, CA-OEHHA, or ATSDR. AAGs based on ACGIGH TLVs are designated as *Interim* to convey the additional uncertainty in these AAGs.

The 2004 Ambient Air Guidelines are shown in Table 4. A comparison between the 1993 and 2004 AAGs is given in Table 5.

Table 4. Chronic Ambient Air Guidelines, April, 2004

Chemical	CASRN	AAG Status	Chronic AAG (ppm)	Conversion Factor (from ppm to mg/m^3)	Chronic AAG (mg/m^3)	Chronic AAG (ug/m^3)	Toxicity Endpoint	Basis for AAG
Acetic anhydride	108-24-7	Interim	1.E-02	4.2	5.E-02	5.E+01	NC	ACGIH TLV
Acetone	67-64-1	Final	1.E+01	2.4	3.E+01	3.E+04	NC	ATSDR MRL
Ammonia	7664-41-7	Final	1.E-01	0.70	1.E-01	1.E+02	NC	IRIS RfC
Antimony (and compounds, as Sb)	7440-36-0	Interim	NA	NA	1.E-03	1.E+00	NC	ACGIH TLV
Antimony hydride	7803-52-3	Interim	NA	NA	1.E-03	1.E+00	NC	ACGIH TLV
Antimony trioxide	1309-64-4	Final	NA	NA	2.E-04	2.E-01	NC	IRIS RfC
Arsenic (inorganic)	7440-38-2	Final	NA	NA	2.E-06	2.E-03	C	IRIS Unit Risk
Barium (and soluble compounds, as Ba)	7440-39-3	Interim	NA	NA	1.E-03	1.E+00	NC	ACGIH TLV
Barium sulfate	7727-43-7	Interim	NA	NA	2.E-02	2.E+01	NC	ACGIH TLV
Benzene	71-43-2	Final	4.E-04	3.2	1.E-03	1.E+00	C	IRIS Unit Risk
Benzo(a)pyrene	50-32-8	Final	9.E-07	10.3	9.E-06	9.E-03	C	CA-OEHHA Unit Risk
Beryllium	7440-41-7	Final	NA	NA	4.E-06	4.E-03	C	IRIS Unit Risk
Biphenyl	92-52-4	Interim	5.E-04	6.3	3.E-03	3.E+00	NC	ACGIH TLV
Bis(2-ethylhexyl)phthalate	117-81-7	Final	3.E-04	16	4.E-03	4.E+00	C	CA-OEHHA Unit Risk
Butadiene, 1,3-	106-99-0	Final	2.E-04	2.2	3.E-04	3.E-01	C	IRIS Unit Risk
Butanol, 1-	71-36-3	Interim	5.E-02	3.0	1.E-01	1.E+02	NC	ACGIH TLV
Butyl Acetate, n-	123-86-4	Interim	4.E-01	4.8	2.E+00	2.E+03	NC	ACGIH TLV
Cadmium (compounds)	7440-43-9	Final	NA	NA	6.E-06	6.E-03	C	IRIS Unit Risk
Carbon tetrachloride	56-23-5	Final	1.E-04	6.3	7.E-04	7.E-01	C	IRIS Unit Risk
Chlorine	7782-50-5	Final	7.E-05	2.9	2.E-04	2.E-01	NC	CA-OEHHA REL
Chlorine dioxide	10049-04-4	Final	7.E-05	2.8	2.E-04	2.E-01	NC	IRIS RfC
Chloroform	67-66-3	Final	4.E-04	4.9	2.E-03	2.E+00	C	CA-OEHHA Unit Risk
Chromium (as CrIII)	7440-47-3	Interim	NA	NA	1.E-03	1.E+00	NC	ACGIH TLV
Chromium (VI), mist &aerosol	18540-29-9	Final	NA	NA	8.E-07	8.E-04	C	IRIS Unit Risk
Chromium (VI), particulate	18540-29-10	Final	NA	NA	8.E-07	8.E-04	C	IRIS Unit Risk
Cobalt	7440-48-4	Final	NA	NA	1.E-04	1.E-01	NC	ATSDR MRL
Copper (fume, as Cu)	7440-50-8	Interim	NA	NA	5.E-04	5.E-01	NC	ACGIH TLV
Copper (dust and mists, as Cu)	7440-50-8	Interim	NA	NA	2.E-03	2.E+00	NC	ACGIH TLV
Dichlorobenzene, 1,2-	95-50-1	Interim	6.E-02	6.0	4.E-01	4.E+02	NC	ACGIH TLV
Dichloroethane, 1,2-	107-06-2	Final	1.E-04	4.0	4.E-04	4.E-01	C	IRIS Unit Risk
Dioxane, 1,4-	123-91-1	Final	4.E-04	3.6	1.E-03	1.E+00	C	CA-OEHHA Unit Risk
Diphenylmethane diisocyanate (monomer & polymer)	101-68-8 and 9016-87-9	Final	6.E-05	10.2	6.E-04	6.E-01	NC	IRIS RfC
Dioxins & Furans (as 2,3,7,8-TCDD)	NA	Final	NA	NA	3.E-10	3.E-07	C	CA-OEHHA Unit Risk
Epichlorohydrin	106-89-8	Final	3.E-04	3.8	1.E-03	1.E+00	NC	IRIS RfC
Epoxypropane, 1,2-	75-56-9	Final	1.E-03	2.4	3.E-03	3.E+00	C	IRIS Unit Risk
Ethanolamine	141-43-5	Interim	7.E-03	2.5	2.E-02	2.E+01	NC	ACGIH TLV
Ethoxyethanol, 2-	110-80-5	Final	5.E-02	3.7	2.E-01	2.E+02	NC	IRIS RfC
Ethyl acetate	141-78-6	Interim	1.E+00	3.6	3.E+00	3.E+03	NC	ACGIH TLV
Ethyl benzene	100-41-4	Final	2.E-01	4.3	1.E+00	1.E+03	NC	IRIS RfC
Ethylene oxide	75-21-8	Final	6.E-05	1.8	1.E-04	1.E-01	C	CA-OEHHA Unit Risk
Fluorides (as F)	NA	Interim	NA	NA	6.E-03	6.E+00	NC	ACGIH TLV
Formaldehyde	50-00-0	Final	7.E-04	1.2	8.E-04	8.E-01	C	IRIS Unit Risk
Formic acid	64-18-6	Interim	1.E-02	1.9	2.E-02	2.E+01	NC	ACGIH TLV
Fufural	98-01-1	Interim	5.E-03	3.9	2.E-02	2.E+01	NC	ACGIH TLV
Hydrazine	302-01-2	Final	2.E-06	1.3	2.E-06	2.E-03	C	IRIS Unit Risk
Hydrogen chloride	7647-01-0	Final	1.E-02	1.5	2.E-02	2.E+01	NC	IRIS RfC
Hydrogen cyanide	74-90-8	Final	NA	NA	3.E-03	3.E+00	NC	IRIS RfC
Hydrogen sulfide	7783-06-4	Final	1.E-03	1.4	2.E-03	2.E+00	NC	IRIS RfC
Isopropanol	67-63-0	Final	3.E+00	2.5	7.E+00	7.E+03	NC	CA-OEHHA REL
Manganese	7439-96-5	Final	NA	NA	5.E-05	5.E-02	NC	IRIS RfC
Mercury (elemental)	7439-97-6	Final	4.E-05	8.2	3.E-04	3.E-01	NC	IRIS RfC
Methanol	67-56-1	Final	3.E+00	1.3	4.E+00	4.E+03	NC	CA-OEHHA REL
Methoxyethanol	109-86-4	Final	6.E-03	3.1	2.E-02	2.E+01	NC	IRIS RfC
Methyl chloride	74-87-3	Final	4.E-02	2.1	9.E-02	9.E+01	NC	IRIS RfC

Table 4. Chronic Ambient Air Guidelines, April, 2004

Chemical	CASRN	AAG Status	Chronic AAG (ppm)	Conversion Factor (from ppm to mg/m^3)	Chronic AAG (mg/m^3)	Chronic AAG (ug/m^3)	Toxicity Endpoint	Basis for AAG
Methyl ethyl ketone	78-93-3	Final	2.E+00	2.9	5.E+00	5.E+03	NC	IRIS RfC
Methyl isobutyl ketone	108-10-1	Interim	1.E-01	4.1	5.E-01	5.E+02	NC	ACGIH TLV
Methyl mercaptan	74-93-1	Interim	1.E-03	2.0	2.E-03	2.E+00	NC	ACGIH TLV
Methyl methacrylate	80-62-6	Final	2.E-01	4.1	7.E-01	7.E+02	NC	IRIS RfC
Methylene chloride	75-09-2	Final	6.E-03	3.5	2.E-02	2.E+01	C	IRIS Unit Risk
Naphthalene	91-20-3	Final	6.E-05	5.2	3.E-04	3.E-01	NC	IRIS RfC/10
Nickel and compounds (as Ni)	7440-02-0	Final	NA	NA	4.E-05	4.E-02	C	CA-OEHHA Unit Risk
Nickel (insoluble refinery dust)	NA	Final	NA	NA	4.E-05	4.E-02	C	IRIS Unit Risk
Nickel oxide	1313-99-1	Final	NA	NA	1.E-04	1.E-01	NC	CA-OEHHA REL
Nickel subsulfide	12035-72-2	Final	NA	NA	2.E-05	2.E-02	C	IRIS Unit Risk
Nitric acid	7697-37-2	Interim	5.E-03	2.6	1.E-02	1.E+01	NC	ACGIH TLV
Oxalic Acid	144-62-7	Interim	6.E-04	3.7	2.E-03	2.E+00	NC	ACGIH TLV
Phenol	108-95-2	Final	5.E-02	3.8	2.E-01	2.E+02	NC	CA-OEHHA REL
Selenium (and compounds other than hydrogen selenide)	7782-49-2	Final	NA	NA	2.E-02	2.E+01	NC	CA-OEHHA REL
Styrene	100-42-5	Final	2.E-01	4.3	1.E+00	1.E+03	NC	IRIS RfC
Sulfuric Acid	7664-93-9	Final	2.E-04	4.0	1.E-03	1.E+00	NC	CA-OEHHA REL
Tetrachloroethylene	127-18-4	Final	2.E-04	6.8	2.E-03	2.E+00	C	CA-OEHHA Unit Risk
Tetrahydrofuran	109-99-9	Interim	5.E-01	2.9	1.E+00	1.E+03	NC	ACGIH TLV
Titanium dioxide	13463-67-1	Interim	NA	NA	2.E-02	2.E+01	NC	ACGIH TLV
Titanium tetrachloride	7550-45-0	Final	NA	NA	1.E-04	1.E-01	NC	ATSDR MRL
Toluene	108-88-3	Final	1.E-01	3.8	4.E-01	4.E+02	NC	IRIS RfC
Trichloroethane, 1,1,1-	71-55-6	Final	2.E-01	5.5	1.E+00	1.E+03	NC	CA-OEHHA REL
Trichloroethylene	79-01-6	Final	9.E-04	5.4	5.E-03	5.E+00	C	CA-OEHHA Unit Risk
Trichlorotrifluoroethane	76-13-1	Interim	2.E+00	7.7	2.E+01	2.E+04	NC	ACGIH TLV
Turpentine	8006-64-2	Interim	5.E-02	5.6	3.E-01	3.E+02	NC	ACGIH TLV
Vinyl chloride	75-01-4	Final	4.E-04	2.6	1.E-03	1.E+00	C	IRIS Unit Risk
Xylenes	1330-20-7	Final	2.E-02	4.3	1.E-01	1.E+02	NC	IRIS RfC
Zinc chloride fume	7646-85-7	Interim	NA	NA	2.E-03	2.E+00	NC	ACGIH TLV
Zinc oxide dust	1314-13-2	Interim	NA	NA	5.E-03	5.E+00	NC	ACGIH TLV

Key to Abbreviations:
AAG = Ambient Air Guideline
ACGIH TLV = American Conference of Governmental Industrial Hygienists Threshold Limit Value - Time Weighted Average
ATSDR MRL = Agency for Toxic Substance and Disease Registry Minimal Risk Level
C = Carcinogenic Efffects
CA-OEHHA REL = California Office of Environmental Health Hazard Assessment Reference Exposure Level
CA-OEHHA Unit Risk = California Office of Environmental Health Hazard Assessment Unit Risk
CASRN = Chemical Abstracts System Registration Number
IRIS RfC = USEPA Integrated Risk Information System Reference Concentration
IRIS Unit Risk = USEPA Integrated Risk Information System Unit Risk
NA = Not available
NC = Noncarcinogenic Effects

Table 5. Comparison Between 1993 and 2004 Chronic AAGs

Chemical	CASRN	1993 Chronic AAG (mg/m^3)	Basis for 1993 AAG	2004 Chronic AAG (mg/m^3)	Basis for 2004 AAG
Acetic anhydride	108-24-7	NA	NA	5.E-02	ACGIH TLV
Acetone	67-64-1	4.E-01	IRIS RfD	3.E+01	ATSDR MRL
Ammonia	7664-41-7	1.E-01	IRIS RfC	1.E-01	IRIS RfC
Antimony (and compounds, as Sb)	7440-36-0	4.E-02	RI	1.E-03	ACGIH TLV
Antimony hydride	7803-52-3	NA		1.E-03	ACGIH TLV
Antimony trioxide	1309-64-4	NA		2.E-04	IRIS RfC
Arsenic (inorganic)	7440-38-2	2.E-06	IRIS Unit Risk	2.E-06	IRIS Unit Risk
Barium (and soluble compounds, as Ba)	7440-39-3	5.E-04	HEAST RfC	1.E-03	ACGIH TLV
Barium sulfate	7727-43-7	NA		2.E-02	ACGIH TLV
Benzene	71-43-2	1.E-03	IRIS Unit Risk	1.E-03	IRIS Unit Risk
Benzo(a)pyrene	50-32-8	6.E-06	HEAST Unit Risk	9.E-06	CA-OEHHA Unit Risk
Beryllium	7440-41-7	4.E-06	IRIS Unit Risk	4.E-06	IRIS Unit Risk
Biphenyl	92-52-4	4.E-04	RI	3.E-03	ACGIH TLV
Bis(2-ethylhexyl)phthalate	117-81-7	3.E-03	IRIS-ORAL	4.E-03	CA-OEHHA Unit Risk
Butadiene, 1,3-	106-99-0	6.E-06	IRIS Unit Risk	3.E-04	IRIS Unit Risk
Butanol, 1-	71-36-3	4.E-01	IRIS RfD	1.E-01	ACGIH TLV
Butyl Acetate, n-	123-86-4	NA	NA	2.E+00	ACGIH TLV
Cadmium (compounds)	7440-43-9	6.E-06	IRIS Unit Risk	6.E-06	IRIS Unit Risk
Carbon tetrachloride	56-23-5	7.E-04	IRIS Unit Risk	7.E-04	IRIS Unit Risk
Chlorine	7782-50-5	6.E-03	Maine RfC	2.E-04	CA-OEHHA REL
Chlorine dioxide	10049-04-4	2.E-04	IRIS RfC	2.E-04	IRIS RfC
Chloroform	67-66-3	4.E-04	IRIS Unit Risk	2.E-03	CA-OEHHA Unit Risk
Chromium (as CrIII)	7440-47-3	2.E-06	HEAST RfC	1.E-03	ACGIH TLV
Chromium (VI), mist &aerosol	18540-29-9	9.E-07	IRIS Unit Risk	8.E-07	IRIS Unit Risk
Chromium (VI), particulate	18540-29-10	9.E-07	IRIS Unit Risk	8.E-07	IRIS Unit Risk
Cobalt	7440-48-4	NA	NA	1.E-04	ATSDR MRL
Copper (fume, as Cu)	7440-50-8	NA	NA	5.E-04	ACGIH TLV
Copper (dust and mists, as Cu)	7440-50-8	NA	NA	2.E-03	ACGIH TLV
Dichlorobenzene, 1,2-	95-50-1	1.E-01	HEAST RfC	4.E-01	ACGIH TLV
Dichloroethane, 1,2-	107-06-2	4.E-04	IRIS Unit Risk	4.E-04	IRIS Unit Risk
Dioxane, 1,4-	123-91-1	3.E-03	IRIS-ORAL	1.E-03	CA-OEHHA Unit Risk
Diphenylmethane diisocyanate (monomer & polymer)	101-68-8 and 9016-87-9	2.E-05	HEAST RfC	6.E-04	IRIS RfC
Dioxins & Furans (as 2,3,7,8-TCDD)	NA	3.E-09	Maine Unit Risk	3.E-10	CA-OEHHA Unit Risk
Epichlorohydrin	106-89-8	1.E-03	IRIS RfC	1.E-03	IRIS RfC
Epoxypropane, 1,2-	75-56-9	3.E-03	IRIS Unit Risk	3.E-03	IRIS Unit Risk
Ethanolamine	141-43-5	NA	NA	2.E-02	ACGIH TLV
Ethoxyethanol, 2-	110-80-5	2.E-01	IRIS RfC	2.E-01	IRIS RfC
Ethyl acetate	141-78-6	3.E+00	IRIS RfD	3.E+00	ACGIH TLV
Ethyl benzene	100-41-4	1.E+00	IRIS RfC	1.E+00	IRIS RfC
Ethylene oxide	75-21-8	1.E-04	IRIS Unit Risk	1.E-04	CA-OEHHA Unit Risk
Fluorides (as F)	NA	1.E-01	RI	6.E-03	ACGIH TLV
Formaldehyde	50-00-0	4.E-04	Maine Unit Risk	8.E-04	IRIS Unit Risk
Formic acid	64-18-6	NA	NA	2.E-02	ACGIH TLV
Fufural	98-01-1	5.E-02	HEAST RfC	2.E-02	ACGIH TLV
Hydrazine	302-01-2	2.E-06	IRIS Unit Risk	2.E-06	IRIS Unit Risk
Hydrogen chloride	7647-01-0	7.E-03	IRIS RfC	2.E-02	IRIS RfC
Hydrogen cyanide	74-90-8	NA	NA	3.E-03	IRIS RfC
Hydrogen sulfide	7783-06-4	9.E-04	HEAST RfC	2.E-03	IRIS RfC
Isopropanol	67-63-0	NA	NA	7.E+00	CA-OEHHA REL
Manganese	7439-96-5	4.E-04	IRIS RfC	5.E-05	IRIS RfC
Mercury (elemental)	7439-97-6	3.E-04	HEAST RfC	3.E-04	IRIS RfC
Methanol	67-56-1	2.E+00	IRIS RfD	4.E+00	CA-OEHHA REL
Methoxyethanol	109-86-4	2.E-02	IRIS RfC	2.E-02	IRIS RfC
Methyl chloride	74-87-3	NA	NA	9.E-02	IRIS RfC
Methyl ethyl ketone	78-93-3	3.E-01	HEAST RfC	5.E+00	IRIS RfC

DRAFT - 4/26/04
Maine Bureau of Health Ambient Air Guidelines
January 2004

Table 5. Comparison Between 1993 and 2004 Chronic AAGs

Chemical	CASRN	1993 Chronic AAG (mg/m^3)	Basis for 1993 AAG	2004 Chronic AAG (mg/m^3)	Basis for 2004 AAG
Methyl isobutyl ketone	108-10-1	8.E-02	HEAST RfC	5.E-01	ACGIH TLV
Methyl mercaptan	74-93-1	NA	NA	2.E-03	ACGIH TLV
Methyl methacrylate	80-62-6	NA	NA	7.E-01	IRIS RfC
Methylene chloride	75-09-2	2.E-02	IRIS Unit Risk	2.E-02	IRIS Unit Risk
Naphthalene	91-20-3	1.E-01	HEAST RfD	3.E-04	IRIS RfC/10
Nickel and compounds (as Ni)	7440-02-0	NA	NA	4.E-05	CA-OEHHA Unit Risk
Nickel (insoluble refinery dust)	NA	4.E-05	IRIS Unit Risk	4.E-05	IRIS Unit Risk
Nickel oxide	1313-99-1	NA	NA	1.E-04	CA-OEHHA REL
Nickel subsulfide	12035-72-2	NA	NA	2.E-05	IRIS Unit Risk
Nitric acid	7697-37-2	NA	NA	1.E-02	ACGIH TLV
Oxalic Acid	144-62-7	NA	NA	2.E-03	ACGIH TLV
Phenol	108-95-2	NA	NA	2.E-01	CA-OEHHA REL
Selenium (and compounds other than hydrogen selenide)	7782-49-2	NA	NA	2.E-02	CA-OEHHA REL
Styrene	100-42-5	1.E+00	IRIS RfC	1.E+00	IRIS RfC
Sulfuric Acid	7664-93-9	NA	NA	1.E-03	CA-OEHHA REL
Tetrachloroethylene	127-18-4	1.E-04	Maine Unit Risk	2.E-03	CA-OEHHA Unit Risk
Tetrahydrofuran	109-99-9	NA	NA	1.E+00	ACGIH TLV
Titanium dioxide	13463-67-1	NA	NA	2.E-02	ACGIH TLV
Titanium tetrachloride	7550-45-0	NA	NA	1.E-04	ATSDR MRL
Toluene	108-88-3	NA	NA	4.E-01	IRIS RfC
Trichloroethane, 1,1,1-	71-55-6	1.E+00	HEAST RfC	1.E+00	CA-OEHHA REL
Trichloroethylene	79-01-6	2.E-03	HEAST Unit Risk	5.E-03	CA-OEHHA Unit Risk
Trichlorotrifluoroethane	76-13-1	3.E+01	HEAST RfC	2.E+01	ACGIH TLV
Turpentine	8006-64-2	NA	NA	3.E-01	ACGIH TLV
Vinyl chloride	75-01-4	1.E-04	HEAST Unit Risk	1.E-03	IRIS Unit Risk
Xylenes	1330-20-7	3.E-01	HEAST RfC	1.E-01	IRIS RfC
Zinc chloride fume	7646-85-7	NA	NA	2.E-03	ACGIH TLV
Zinc oxide dust	1314-13-2	NA	NA	5.E-03	ACGIH TLV

Key to Abbreviations:

AAG = Ambient Air Guideline
ACGIH TLV = American Conference of Governmental Industrial Hygienists Threshold Limit Value - Time Weighted Average
ATSDR MRL = Agency for Toxic Substance and Disease Registry Minimal Risk Level
CA-OEHHA REL = California Office of Environmental Health Hazard Assessment Reference Exposure Level
CA-OEHHA Unit Risk = California Office of Environmental Health Hazard Assessment Unit Risk
HEAST RfC = USEPA Health Effects Assessment Summary Tables Reference Concentration
HEAST Unit Risk = USEPA Health Effects Assessment Summary Tables Unit Risk
IRIS RfC = USEPA Integrated Risk Information System Reference Concentration
IRIS RfD = Reference Concentration extrapolated from USEPA Integrated Risk Information System Oral Reference Dose
IRIS Unit Risk = USEPA Integrated Risk Information System Unit Risk
IRIS-ORAL = Unit Risk extrapolated from USEPA Integrated Risk Information System Oral Cancer Slope Factor
Maine Unit Risk = Maine Bureau of Health Unit Risk
NA = Not available
RI = Rhode Island Ambient Air Guidelines

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Appendix A

Development of Hierarchy of Chronic Noncancer Toxicity Values for AAG Derivation.

A. Development of Hierarchy of Chronic Noncancer Toxicity Values for AAG Derivation.

This appendix discusses the analyses that were conducted to prioritize sources of noncancer toxicity values. Results of the analyses are presented herein, along with the ensuing hierarchy for noncancer toxicity values.

A.1 Overview

Noncancer inhalation toxicity values on IRIS are called "Reference Concentrations" or RfCs and are given in units of mg/m^3. An RfC is defined as "an estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure to human populations (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime" (USEPA, 2003). IRIS RfCs are derived using a thoroughly documented and peer-reviewed process and are BOH's preferred noncancer toxicity values.

As described in Section 2.0, BOH considered three sources of alternative inhalation toxicity values for noncancer endpoints when IRIS RfCs were not available: CA-OEHHA Reference Exposure Levels (RELs), ATSDR MRLs, and ACGIH TLVs. In addition, BOH considered the use of inhalation toxicity values extrapolated from oral toxicity values on IRIS (Reference Doses or RfDs).

Toxicity values from ATSDR and CA-OEHHA are intended to afford a level of protection similar to that of IRIS values. CA-OEHHA defines its RELs as "concentrations or doses at or below which adverse effects are not likely to occur following specified exposure conditions". CA-OEHHA describes the process it uses to develop RELs as "fundamentally the same as that used by USEPA in developing inhalation RfCs and oral RfDs" (CA-OEHHA, 2002). ATSDR defines its MRL much the same, as "an estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk of adverse noncancer health effects over a specified duration of exposure" (ATSDR, 2003). MRLs are derived using virtually the same process as USEPA RfCs. Oral RfDs on IRIS are derived using the same process as RfCs and reflect the same level of protection.

ACGIH TLVs differ from the foregoing values both in their derivation and in their intent. TLVs are derived using consensus judgment by a committee, and the basis is highly variable (Calabrese and Kenyon, 1991). Further, TLVs are intended to protect a select segment of the human population, i.e., the healthy worker population. They are not intended to be protective for the general population, which may contain more sensitive individuals (e.g., infants or the elderly). These inherent differences make the use of TLVs to derive AAGs more complicated. However, as Calabrese and Kenyon (1991) point out, the large number of TLVs and the size of the peer-reviewed toxicity database behind them make TLVs a good starting point for setting AAGs for a large number of chemicals.

To determine which source(s) of inhalation toxicity values best approximates IRIS RfCs, BOH assembled a database comprising all chemicals with IRIS RfCs (as of December 2002). BOH then compiled CA-OEHHA chronic RELs, ATSDR chronic MRLs, ACGIH TLVs (where cancer

was not a stated critical effect), and oral RfDs for these same chemicals. Regression analyses were conducted to determine how well the toxicity values in each source predicted the corresponding RfCs.

Alternative toxicity values were included only when the chemical and form were identical to that specified in the IRIS database for the corresponding RfC. For example, although CA-OEHHA has a chronic REL for chromic trioxide as chromic acid mist, it was not clear that this was the same form as the IRIS RfC for chromium mist and aerosol, so this comparison pair was not included. However, in one case, the RfC was given for a pair of chemicals (2,4 and 2,6-toluene diisocyanate) while the TLV was given only for the 2,4 isomer. Similarly, the RfC for methylene diphenyl diisocyanate applied to both the monomeric and polymeric forms, while the CA-OEHHA REL and ACGIH TLV were given for the monomer only. In the latter two cases, the comparison pairs were included, since the RfC was assumed to apply to either the individual forms or the mixtures.

In addition, comparisons between IRIS RfCs and inhalation values extrapolated from oral RfDs were only included if the critical effect for the oral RfD did not reflect a portal-of-entry effect. A portal-of-entry effect occurs when the critical effect of the toxicity value occurs at the site of chemical administration. In other words, if stomach lesions are the critical effect for a chemical administered orally, it would not be appropriate to use these data to predict effects after inhalation exposure due to differences in the tissue types exposed after oral and inhalation exposure. Extrapolation from oral to inhalation effects is considered appropriate if the critical effect is *distal* (away from the site of entry) or *systemic* (throughout the body). Examples of the latter include effects on the liver or blood system.

A.2 Data Preparation

Some of the alternative toxicity values required modification in order to render them comparable to the corresponding IRIS RfCs. The modifications were required to convert occupational exposure limits to equivalent non-occupational values and to convert oral toxicity values to equivalent inhalation values. All comparisons were conducted in units of mg/m3.

Before regression analyses could be performed on ACGIH TLVs, these exposure limits had to be converted to equivalent non-occupational values. Occupational exposure limits are developed with the assumption that exposure occurs no more than 8 hours per day, 5 days per week over a lifetime. For non-occupational values, these exposure limits had to be revised to reflect the assumption that exposure could occur 24 hours per day, 7 days per week. The occupational values were adjusted by multiplying each value by the ratio of 8/24 hours and by the ratio of 5/7 days (thus, the non-occupational value is equal to the occupational value divided by 4.2).

The extrapolation of oral RfDs (in mg/kg-day) to equivalent RfCs (mg/m3) requires the calculation of the air concentration that would result in a daily intake equal to the RfD. Using standard USEPA exposure assumptions of 20 m^3/day inhalation rate and 70 kg body weight, the oral RfD (in mg/kg-day) is multiplied by 70/20 to estimate an equivalent RfC in mg/m^3. BOH recognizes that this calculation oversimplifies the extrapolation from oral intake to an equivalent inhalation value. Differences in chemical uptake, metabolism, and distribution between the

gastrointestinal tract and the lungs are complex and often chemical-specific. However, as a first approximation, this adjustment is appropriate.

A.3 Data Analysis and Results

For each source, the logarithm of the IRIS toxicity value was regressed against the logarithm of the value from the alternate source (e.g., MRL, CA-OEHHA REL, adjusted TLV, and adjusted oral RfD). Logarithmic transformations were necessary because inhalation toxicity values vary over many orders of magnitude. The statistical regression analyses were coupled with visual displays of the data to evaluate the strength of the correlations.

The regression analyses showed the CA-OEHHA Chronic REL to be the best predictor of RfC (R^2 of 0.91), and the ATSDR MRL a close second (R^2 of 0.86). The adjusted oral RfD provided the poorest prediction of RfC (R^2 of 0.33). Table A-1 provides a summary of the regression results. The ACGIH TLV showed good correlation with the RfC, however the intercept of the regression line (-2.15 in log space) indicates that, while the TLV increases proportionately with RfC, there is a substantial offset value. In other words, the TLV is consistently higher than the corresponding RfC. The logarithmically transformed data are plotted in Figures A-1 through A-4 (at the end of the document). These figures show plots of log RfC against log REL, log MRL, log TLV, and log converted RfD, respectively.

Table A-1. Summary of Regression Results for Alternative Chronic Noncancer Toxicity Values.

Alternative Chronic Noncancer Toxicity Value	No. of Observations (n)	Correlation Coefficient (R^2)	Significance of F	Intercept	Slope
CA-OEHHA Relative Exposure Level (REL)	37	0.91	1.21E-19	-0.39	0.92
ATSDR Minimal Risk Level (MRL)	18	0.86	3.37E-08	-0.08	0.97
ACGIH Threshold Limit Value (TLV, Adjusted*)	47	0.74	5.67E-15	-2.17	1.04
IRIS Oral RfD Converted to Equivalent RfC	18	0.33	1.26E-02	-0.82	0.86

* Adjusted for equivalent full-time exposure.

A.4 Noncancer Endpoint Hierarchy

BOH's hierarchy for selecting noncancer inhalation toxicity values follows the results of the regression analysis, in order[6]:

5. IRIS RfC
6. CA-OEHHA REL
7. ATSDR Chronic MRL
8. Adjusted ACGIH TLV
9. Extrapolation from oral RfD if the critical effect is not a portal-of-entry effect.

CA-OEHHA RELs and ATSDR MRLs are used without alteration in place of IRIS RfCs. The regression analysis and visual review of the data indicate that both MRLs and RELs provide good approximation of RfCs. In addition, the protocols used to derive both RELs and MRLs are intended to result in exposure limits that are protective for sensitive members of the human population.

By contrast, occupational values such as ACGIH TLVs must be modified before use. First, as was done for the regression analysis, the original value based on occupational exposure parameters is converted to an equivalent value for continuous exposure (divided by 4.2, as described above). However, as the plot of RfC vs. TLV (Figure B-3) shows, the adjustment for continuous exposure does not result in an exposure limit approximating the RfC, for several reasons. First, occupational exposure limits are intended to protect average members of the working population, who tend to be healthy. Second, TLVs are not derived with a fixed protocol, but rather by committee consensus. Thus, TLVs may be based on human or animal toxicity data, short- or long-term studies, and on observed effect levels with our without an additional safety factor.

The regression analysis indicates that, on average, TLVs are 147 times higher (this value is derived from the intercept of the regression, -2.17 in log space) than RfCs, even after the TLVs have been adjusted for continuous exposure. BOH believes that applying a 100-fold uncertainty factor to TLVs after adjustment for continuous exposure will result in ambient air guidelines that are reasonably protective for sensitive individuals. This uncertainty factor is consistent with the application of a 10-fold uncertainty factor for interindividual variation (to account for segments of the population that are more sensitive than the average healthy worker) and a 10-fold uncertainty factor for extrapolation from an observed effect level to a no-observed effect level.

Calabrese and Kenyon (1991) recommended the use of several individual uncertainty factors to adjust from TLVs to AAGs. The authors recommended that application of the uncertainty factors be evaluated on a chemical-by-chemical basis. Calabrese and Kenyon advocated the use

[6] USEPA's Air Toxics Website outlines a similar hierarchy with IRIS > ATSDR MRLs > CA-OEHHA RELs. The web site does not include ACGIH toxicity values. USEPA ranks ATSDR MRLs above CA-OEHHA RELs because the MRLs are "philosophically consistent" with USEPA's guidelines for RfD/RfC development. It is BOH's belief that CA-OEHHA RELs are also philosophically consistent with USEPA approaches to noncancer toxicity values, and that the regression results warrant ranking the California values higher than ATSDR values. Ultimately, a very small number of chemicals would be affected by this difference, as shown in the table in Section A.2.4.

of a factor of 4.2 to adjust for continuous exposure (as done by BOH) for chemicals with toxic endpoints other than sensory irritation. In addition, the authors proposed a 10-fold uncertainty factor for interindividual variation, a 5-fold uncertainty factor if the occupational level is associated with adverse effects (e.g., if equivalent to a LOAEL), and an uncertainty factor between 1 and 10 "as appropriate". In contrast, BOH intends to apply an uncertainty factor of 100 whenever TLVs are used to derive AAGs. As noted above, this appears to be sufficiently protective based on the regression analysis, and eliminates the requirement for a resource-intensive chemical-by-chemical analysis.

A.5 Evaluation of Likely Sources for Noncancer Toxicity Values

Having established a hierarchy of noncancer toxicity values based on best prediction of IRIS values, it is important to consider the size of each source's database and the likelihood that any given source will be used to define noncancer toxicity values for use in ambient air guideline development. Table A-2 shows a breakdown of toxicity values from IRIS, CA-OEHHA, ATSDR, and ACGIH. As the table shows, IRIS reports verified RfCs for 65 chemicals. CA-OEHHA reports chronic RELs for 93 chemicals, 37 of which also have IRIS RfCs. Thus, CA-OEHHA contains chronic RELs for 56 chemicals that have no IRIS RfCs (among these 56, 17 are individual chlorinated dioxins and furans). The remainder of the table shows ATSDR MRLs for a few chemicals that have no IRIS RfC (11 chemicals) and shows that ACGIH provides a rich source of noncancer toxicity values (581 chemicals and chemical processes in total).

Table A-2. Number of Chemicals Having Toxicity Values Available from Various Sources

	IRIS RfC	CA-OEHHA Chronic REL	ATSDR Chronic Inhalation MRL	ACGIH Noncancer-based TLV
IRIS RfC	65	37	18	47
CA-OEHHA REL		93*	18	52
ATSDR MRL			29	27
ACGIH-TLV				581**

* Includes individual RELs for 17 chlorinated dioxins and furans
** Includes some production processes, e.g., antimony trioxide production

Figure A-1.
IRIS RfC vs CA-OEHHA Chronic REL

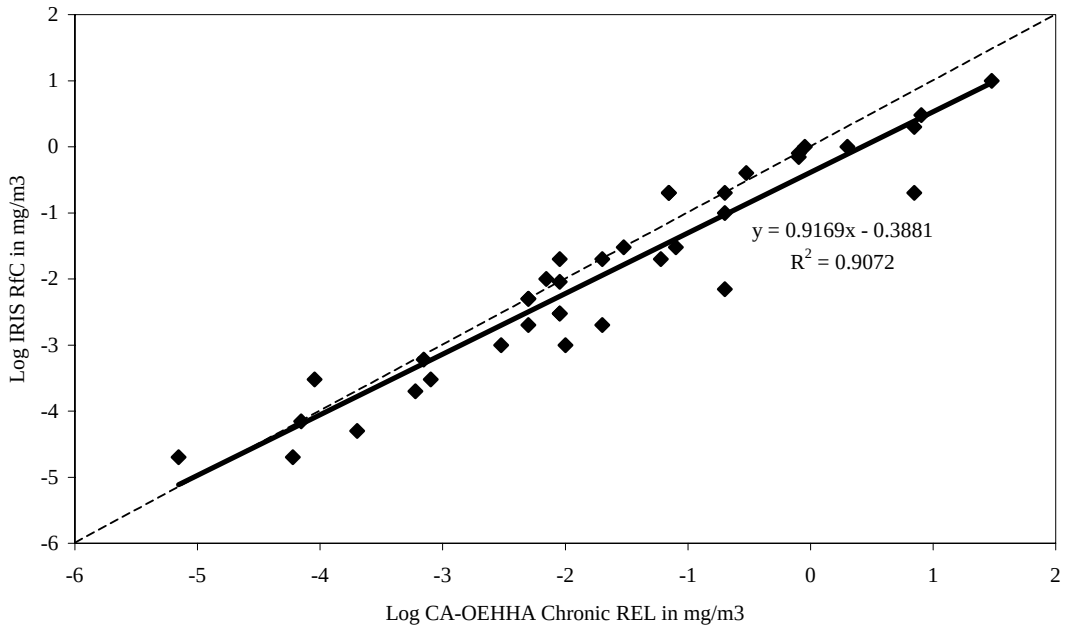

Figure A-2.
IRIS RfC vs ATSDR Chronic MRL

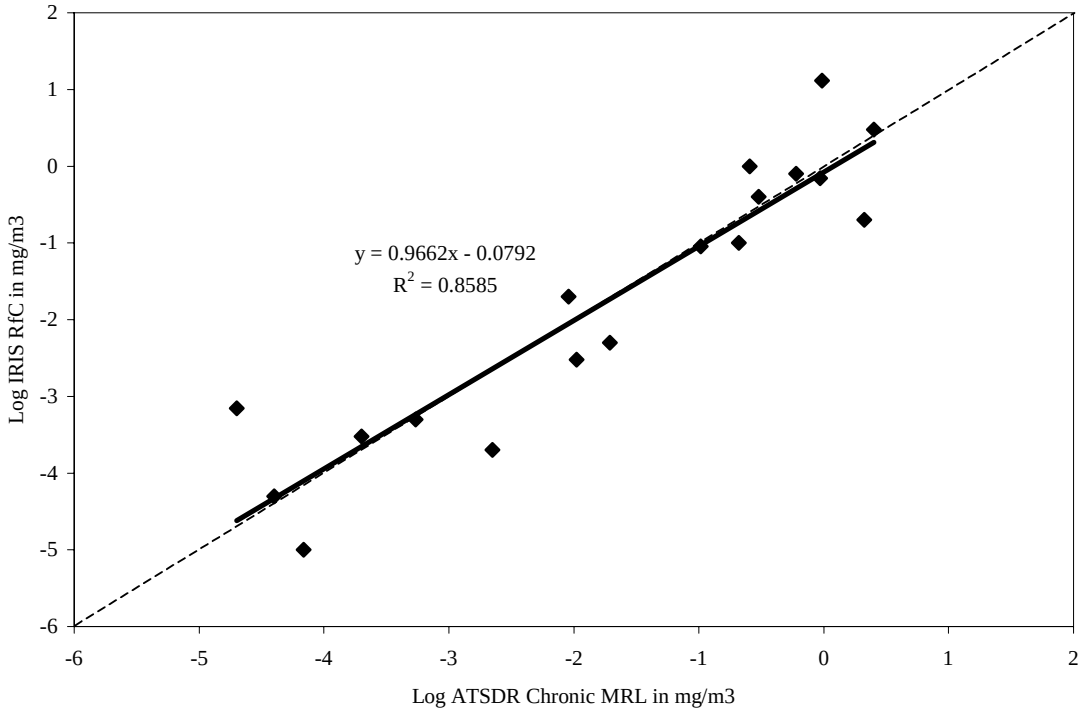

Figure A-3.
IRIS RfC vs Adjusted ACGIH TLV-TWA

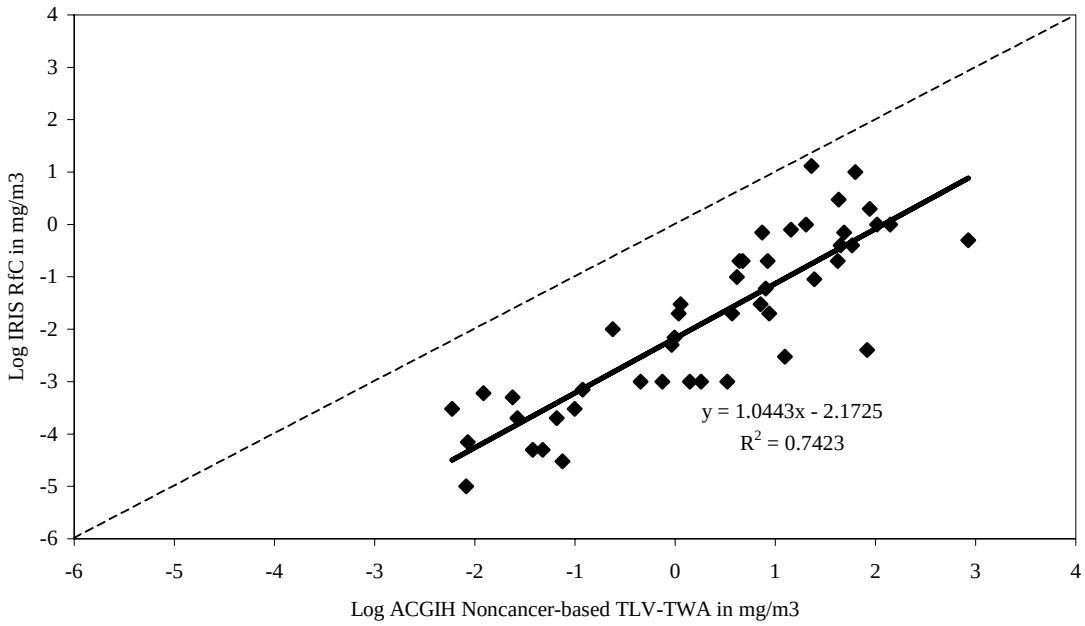

Figure A-4.
IRIS RfC vs Oral RfD Converted to Equivalent RfC