

7. Toxicity Assessment

7.1 Introduction

The toxicity assessment presents information on the nature of adverse health effects associated with air toxics considered in PATA, and provides an estimate of the dose-response relationship for each air toxic. Dose-response is the relationship between the extent of exposure and increased likelihood and/or severity of adverse effects.

Understanding this relationship provides the basis for the development of the risk concentration levels values used in the PATA, which are summarized in Table 7.1.

Carcinogens are considered to be any chemical for which there is sufficient evidence that exposure may result in continuing uncontrolled cell division (i.e., cancer) in humans or animals. The likelihood that an air toxic is a human carcinogen is evaluated using the EPA (2003b) weight-of-evidence classification approach. Data derived from human and animal studies are reviewed, and the carcinogenicity of a chemical is characterized as: (1) carcinogenic to humans, (2) likely to be carcinogenic to humans, (3) suggestive evidence of carcinogenic potential, (4) inadequate information to assess carcinogenic potential, or (5) not likely to be carcinogenic to humans (EPA 2003b). Non-carcinogens are thus any chemical for which there is no current evidence of carcinogenicity. However, some chemicals may exert both carcinogenic and non-carcinogenic health effects, so both endpoints are evaluated quantitatively provided that sufficient toxicity data are available. The endpoints for these two types of effects are assessed differently because the mechanisms by which chemicals cause cancer are assumed to be fundamentally different from the processes that cause non-carcinogenic effects. The principal difference reflects the assumption that non-carcinogenic effects exhibit a threshold dose below which no observable adverse effects occur, whereas no such threshold is typically assumed for carcinogenic effects.

Cancer and non-cancer health effects are evaluated quantitatively in the PATA using two different numeric values. A reference concentration (RfC) is typically used to protect against effects other than cancer; and a unit risk estimate (URE) is used to estimate the probability of contracting cancer as a result of exposure to an air toxic. The RfC is an estimate of a concentration in air to which a human population might be exposed (including sensitive subgroups) that is likely to be without appreciable risks of deleterious effects during a lifetime. The uncertainty in this concentration spans perhaps an order of magnitude. The URE is an upper-bound estimate of the excess cancer risk resulting from a lifetime of continuous exposure to an agent at a concentration of 1 $\mu\text{g}/\text{m}^3$ in air. It should be noted that unit risk estimates (UREs) are derived using the assumption that the average adult inhalation rate is 20 cubic meters per day (m^3/day) and the average adult body weight is 70 kilograms; an approach which may lead to an underestimate of risk in non-adult populations.

7.2 Sources and Prioritization of Toxicity Information

Dose-response assessment information for toxic air pollutants considered by the PATA was obtained from various sources. Some pollutants have been subjected to dose-response assessments by different state and federal regulatory agencies. Because different scientists developed these assessments at different times for purposes that

were similar but not identical, the results are not totally consistent. In some cases interagency differences are substantial, especially between assessments done many years apart. To resolve these differences, DEQ applied a consistent priority scheme to the available dose-response information. Information was assigned greater weight if (1) it was conceptually consistent with the EPA risk assessment guidelines and (2) it received a high level of review. This process of prioritizing information was aimed at ensuring the assessment was based on the best available science.

7.2.1 U.S. EPA Integrated Risk Information System (IRIS)

The EPA publishes dose-response assessments that have achieved full intra-agency consensus on its Integrated Risk Information System (IRIS), which is regularly updated. All IRIS assessments since 1996 have also undergone external scientific peer review. Externally peer-reviewed draft RfCs and UREs under development for the IRIS process were given first priority. These assessments reflect the most recent available toxicity information and data analysis and were used in some cases to replace existing values on IRIS. This was only done for assessments that had already undergone peer review and subsequent revision to reflect peer comments. PATA specifically did not use draft assessments that have not yet undergone such review because the EPA judged that the soundness of assessments should receive a higher priority than the date on which they were performed. In other words, an older assessment that had received strong scientific review was preferred to a more recent un-reviewed assessment. This decision is fully consistent with the restructuring of the IRIS review process in 1996 to require such external peer review. The DEQ believes that using un-reviewed information for the PATA would undermine its quality. Where externally peer reviewed IRIS draft assessments were not available, the PATA relied on information currently in the EPA's IRIS database. For substances lacking IRIS assessments, ATSDR (Agency for Toxic Substances and Disease Registry) MRLs (Minimum Risk Levels for non-cancer effects) received next preference, followed by CalEPA RELs (Reference Exposure Levels) and UREs.

7.2.3 Agency for Toxic Substances and Disease Registry (ATSDR)

The ATSDR, which is part of the U.S. Department of Health and Human Services, develops and publishes Minimal Risk Levels for many toxic substances. The MRL is defined as an estimate of the daily human exposure to a substance that is likely to be without an appreciable risk of adverse effects (other than cancer) over a specified duration of exposure. MRLs can be derived for acute, intermediate, and chronic duration exposures following inhalation and ingestion. The ATSDR describes MRLs as concentrations to be used by health assessors in selecting environmental contaminants for further evaluation. MRLs are presented with only one significant figure and are considered concentrations below which contaminants are unlikely to pose a health threat. Concentrations above an MRL do not necessarily represent a threat, and MRLs are therefore not intended for use as predictors of adverse health effects or for setting cleanup levels. Inhalation MRLs were used in the non-cancer portion of this assessment when IRIS RfCs were not available because the concept, definition, and derivation of MRLs and RfCs are philosophically consistent (though not identical). The ATSDR publishes MRLs as part of pollutant-specific toxicological profile documents, and also in a table of "comparison values" that the ATSDR regularly updates and distributes. No ATSDR MRL values were required by PATA.

7.2.4 California Environmental Protection Agency (CalEPA)

The CalEPA Air Resources Board has developed dose-response assessments for many substances, based both on carcinogenicity and health effects other than cancer. The process for developing these assessments is similar to that used by the EPA to develop IRIS values and is based on significant external scientific peer review. The non-cancer information includes available inhalation health risk guidance values expressed as chronic inhalation reference exposure levels (RELs). The CalEPA defines the REL as a concentration level at (or below) which no health effects are anticipated, a concept that is substantially similar to the EPA's approach to non-cancer dose-response assessment. The CalEPA's quantitative dose-response information on carcinogenicity by inhalation exposure is expressed in terms of the URE, defined similarly to the EPA's URE. The PATA used chronic RELs and specific CalEPA UREs in the same way as RfCs and UREs when no IRIS or ATSDR values exist.

7.2.5 U.S. EPA Office of Air Quality & Planning Standards (OAQPS)

EPA's Office of Air Quality Planning and Standards (OAQPS) has tabulated dose-response assessments for use in risk assessments of hazardous air pollutants into a table with values for long-term (chronic) inhalation and oral exposures (there is also a table with values for short-term or acute inhalation exposures). The chronic table (dated 10/28/03) compiles assessments from various sources for many of the 188 substances listed as hazardous air pollutants ("air toxics") under the Clean Air Act Amendments of 1990. Sources of chronic dose-response assessments were arranged in priority order according to conceptual consistency with EPA risk assessment guidelines and level of peer review. The table shows only the assessment result from the highest-priority source. The table also reflects decisions made about several chemicals on the basis of chemical-specific information. For the oral exposure pathway, the only assessment results shown are those for persistent and bioaccumulative substances likely to pose important non-inhalation risks when emitted from air sources. Each value in the chronic table is best visualized as an estimate within a range of possible values, a range that may change as better data become available. Polycyclic organic matter (POM) was the only air toxic whose URE was drawn from the OAQPS table.

Table 7.1 Summary of benchmark values for air toxics considered by PATA

AIR TOXIC	Cancer URE (1/(ug/m ³))	URE Source	Cancer Benchmark (ug/m ³) ^(a)	Non-Cancer Benchmark (ug/m ³) ^(b)	Source
Acetaldehyde - Primary	2.2×10^{-6}	IRIS	0.45	9	IRIS
Acrolein - Primary ^(c, j)	n/a	n/a	n/a	0.02	IRIS
Arsenic Compounds ⁽ⁱ⁾	4.3×10^{-3}	IRIS	0.0002	0.03	CalEPA
Benzene ⁽ⁱ⁾	7.8×10^{-6}	IRIS	0.13	0.03	IRIS
1,3-Butadiene	3.0×10^{-5}	IRIS	0.03	0.002	IRIS
Chloroform ^(d)	2.3×10^{-5}	IRIS	0.043	0.098	ATSDR
Chromium Compounds ^(e)	1.2×10^{-2}	IRIS	0.00008	0.1	IRIS
Diesel PM	---	---	0.1 ^(f)	5 ^(c)	USEPA OAQPS Table 1
Formaldehyde - Primary ^(g, j)	1.9×10^{-5}	IRIS	0.077	9.8	ATSDR
Nickel Compounds ^(h)	4.8×10^{-4}	IRIS	0.002	0.2 ⁽ⁱ⁾	ATSDR
Perchloroethylene (Tetrachloroethene)	5.6×10^{-6}	CalEPA	0.18	0.27	ATSDR
Polycyclic Organic Matter (POM) ⁽ⁱ⁾	5.5×10^{-5}	OAQPS	0.018	---	---

(a) Benchmark = Acceptable Risk (1×10^{-6}) ÷ URE

(b) Same as the non-cancer reference concentration (RfC).

(c) For non-cancer health impacts only.

(d) The narrative WOE in new IRIS assessment states that chloroform is likely to be carcinogenic by all routes of exposure under conditions that lead to cytotoxicity and regenerative hyperplasia in susceptible tissues, via a nonlinear mode of action. For this reason, the newly revised IRIS oral assessment lacks a carcinogenic potency slope because EPA has judged that the RfD should protect against cytotoxicity and therefore against cancer. EPA is currently developing an inhalation assessment, but the IRIS file still contains the old inhalation URE, which is used in this assessment.

(e) Value based on Chromium (VI) compounds.

- (f) Interim value for diesel particulate matter from internal combustion engines only, recommended by the Air Toxics Science Advisory Committee (ATSAC), based on a review of the available scientific literature.
- (g) A new EPA IRIS assessment is underway in light of an analysis that supports a URE on the order of 5.5×10^{-9} per $\mu\text{g}/\text{m}^3$. This value is substantially lower than the current IRIS URE of 1.3×10^{-5} per $\mu\text{g}/\text{m}^3$. (Chemical Industry Institute of Toxicology, 1999. Formaldehyde: Hazard characterization and dose-response assessment for carcinogenicity by the route of inhalation. Revised edition. Research Triangle Park, North Carolina.)
- (h) Value based on nickel subsulfide.
- (i) Value based on nickel compounds.
- (j) Special subpopulations (e.g., the elderly, people with pre-existing illnesses, fetuses of pregnant women, and infants and children) may be more susceptible to the adverse effects of exposure to air toxics. CalEPA has identified this air toxic as possibly causing infants and children to be especially susceptible to illness.