



Six-Year Review 2 Health Effects Assessment: Summary Report

This document is intended to support EPA's second Six-Year Review of existing national primary drinking water regulations. The data presented in this document reflect literature searches through December 2007 and health risk assessments completed by March 1, 2009.

Acknowledgements

This document was prepared in part under EPA Contract EP-C-07-022, Work Assignments 0-04, 1-04, and 2-04.

The EPA Work Assignment Managers for this project were Dr. Amal Mahfouz and Dr. Nancy Chiu of the Office of Science and Technology in the Office of Water.

Technical input to this document was also provided by the following EPA staff:

Office of Science and Technology, Office of Water:

Ambika Bathija, Ph.D.
Octavia Conerly, M.S.P.H.
Nancy Chiu, Ph.D.
Joyce Donohue, Ph.D.
Elizabeth Doyle, Ph.D.
Steve Kueberuwa, M.S.
Amal Mahfouz, Ph.D.
Edward Ohanian, Ph.D.
Santhini Ramasamy, Ph.D., DABT, MPH

Office of Radiation and Indoor Air:

Neal Nelson, D.V.M., Ph.D.
Jerome Puskin, Ph.D.
Lowell Ralston, Ph.D.

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Six-Year Review 2 Health Effects Assessment: Summary Report

1. Introduction

The 1996 amendments to the Safe Drinking Water Act (SDWA), Section 1412(b)(9), require the United States Environmental Protection Agency (EPA) to review and, if appropriate, revise each existing National Primary Drinking Water Regulation (NPDWR) no less often than every six years. The SDWA Amendments also specify that any revision of a national primary drinking water regulation will maintain or provide for greater protection of public health. The goal of the cyclical review is to determine whether it is appropriate to consider changes (i.e., to “revise” or “take no action”) to existing NPDWRs based on changes in health effects or analytical or technological feasibility that have occurred since the regulations were promulgated. In response to this mandate, EPA developed a *Protocol for the Review of Existing National Primary Drinking Water Regulations* (USEPA, 2002a; USEPA, 2003a) based on recommendations of the National Drinking Water Advisory Council (NDWAC, 2000) and input from stakeholders representing a wide variety of interest groups. EPA has updated this protocol for the second review effort (USEPA, 2009a). The protocol outlines the approach to be used to review and identify NPDWRs that may warrant revision. The key elements that are considered in the review process are health effects, analytical methods, occurrence and exposure, treatment technology, and other regulatory provisions (e.g., monitoring and reporting requirements).

The Agency completed its first Six-Year Review (referred to here as “Six-Year Review 1”) in July 2003 (USEPA 2002b; USEPA, 2003b). In the Six-Year Review 1, EPA evaluated the information available at that time on the health effects, occurrence and exposure, treatment technologies, analytical methods, and other regulatory considerations for the Total Coliform Rule (TCR) and for 68 specific chemicals covered under various NPDWRs. The assessment of health effects for those 68 chemicals was presented in the *Six-Year Review, Chemical Contaminants – Health Effects Technical Support Document* (USEPA, 2003c). In completing Six-Year Review 1, the Agency determined that it was not appropriate to revise any of the 68 chemicals NPDWRs considered at that time and that it was appropriate to list TCR as a candidate for revision.

EPA has been performing its second Six-Year Review (referred to here as “Six-Year Review 2”) of the drinking water contaminants regulated under the SDWA. The Office of Science and Technology (OST) within the EPA’s Office of Water (OW) has the primary responsibility for performing the health effects assessments for the Six-Year Review 2. There are a total of 71¹ chemicals being reviewed under the Six-Year Review 2 effort. Sixty-six of the 68 chemicals that were considered in the Six-Year Review 1 in 2003 are also included in the Six-Year Review 2. Lead and copper are not included because of ongoing efforts initiated in 2006 to revise the Lead and Copper Rule. However, five chemicals not considered previously (arsenic; uranium; combined radiums (226 and 228); alpha particle emitters; and beta particle and photon

¹ Chromium is counted as a single chemical (total chromium), but separate assessments for Cr(VI) and Cr(III) are presented in this document.

emitters) for which new regulations have been promulgated more recently are included in this review. As of March 1, 2009, 30 of these 71 chemicals (listed below) had ongoing formal EPA health effects assessments.

Chemicals with ongoing health effects assessments (List A) are:

Acrylamide	Di(2-ethylhexyl)phthalate (DEHP)	Fluoride
Alpha Particle Emitters	1,2-Dichlorobenzene (o-Dichlorobenzene)	Pentachlorophenol
Antimony	1,4-Dichlorobenzene (p-Dichlorobenzene)	Polychlorinated Biphenyls (PCBs)
Arsenic	1,2-Dichloroethane (Ethylene Dichloride)	Combined Radiums (226 and 228)
Asbestos	<i>cis</i> -1,2-Dichloroethylene	Styrene
Benzo(a)pyrene	<i>trans</i> -1,2-Dichloroethylene	2,3,7,8-TCDD (Dioxin)
Beryllium	Dichloromethane (Methylene Chloride)	Tetrachloroethylene
Beta Particle and Photon Emitters	Ethylbenzene	Thallium ²
Cadmium		Trichloroethylene
Carbon Tetrachloride		Uranium
Cyanide		
Di(2-ethylhexyl)adipate (DEHA)		

The remaining 41 chemicals with no ongoing EPA health effects assessment (List B) are:

Alachlor	Endothall	Nitrite (as N)
Atrazine ³	Endrin	Oxamyl (Vydate)
Barium	Epichlorohydrin	Picloram
Benzene	Ethylene Dibromide (EDB; 1,2-Dibromoethane)	Selenium
Carbofuran	Glyphosate	Simazine ⁴
Chlordane	Heptachlor	Toluene
Chromium	Heptachlor Epoxide	Toxaphene
2,4-D (2,4-Dichlorophenoxy-acetic Acid)	Hexachlorobenzene	2,4,5-TP (Silvex; 2,4,5-Trichlorophenoxypropionic Acid)
Dalapon (2,2-Dichloropropionic Acid)	Hexachlorocyclopentadiene	1,2,4-Trichlorobenzene
1,2-Dibromo-3-chloropropane (DBCP)	Lindane (gamma-Hexachlorocyclohexane)	1,1,1-Trichloroethane
1,1-Dichloroethylene	Mercury (Inorganic)	1,1,2-Trichloroethane
1,2-Dichloropropane	Methoxychlor	Vinyl Chloride
Dinoseb	Monochlorobenzene (Chlorobenzene)	Xylenes (Total)
Diquat	Nitrate (as N)	

² EPA completed the risk reassessment for thallium in September of 2009 (USEPA, 2009b). Because the new assessment was not completed by March 1, 2009, the cutoff date for this review, the outcome of this assessment has not been included in the current review effort. EPA will consider the updated assessment in the next review cycle.

³ Although no risk assessment is ongoing, on October 7, 2009 (USEPA, 2009c), EPA announced its intent to launch a comprehensive reevaluation of its 2006 risk assessment for atrazine, as described later in this document.

⁴ Since the simazine risk assessment is based on atrazine data, any reassessment of simazine depends on the outcome of the reevaluation of the atrazine risk assessment.

For the 30 (List A) chemicals, EPA assessments (or National Academy of Sciences (NAS) assessments commissioned by EPA) are currently in progress or have recently been completed. Therefore, the review conducted for the Six-Year Review 2 process, as presented in this summary report for the List A chemicals, was limited to compiling existing and available external peer review draft EPA assessments, as well as NAS reports or Agency for Toxic Substances and Disease Registry (ATSDR) assessments completed since the last Six-Year Review. In collaboration with the OST, EPA's Office of Radiation and Indoor Air (ORIA) has begun the process of evaluation of new health data for the three radionuclides: alpha particle emitters, beta particle and photon emitters, and combined radiums (226 and 228).

For the other 41 chemicals, a more detailed review was undertaken by OST, including the evaluation of risk-based values from selected additional risk assessment sources, and the evaluation of selected primary literature sources.

The primary purpose of this document is to provide a screening-level review of the health effects component of the Six-Year Review 2 effort. The screening objective is to identify new quantitative and qualitative health information that could indicate a possible basis for revising the maximum contaminant level goal (MCLG) and, perhaps, revising the maximum contaminant level (MCL) for the chemicals being considered, taking occurrence and technological factors into consideration. The second objective of the health effects component was to identify chemicals that may warrant a new formal Agency health effects assessment or further follow-up and evaluation based on significant new health information identified during the literature search (performed by OST).

MCLGs are based on either the cancer classification (known or likely carcinogens typically have an MCLG of 0) or the oral reference dose (RfD). Therefore, the health effects technical review focused on whether there has been any change to the cancer classification and/or RfD values; suggesting a possible need for revision to the MCLG. A broad review of the health assessment literature was conducted to determine whether data are available that could result in revision to the MCLG. This review included review of recent EPA assessments, assessments by other organizations, and publications in the open literature.

Section 2 provides an overview of EPA health effects assessment methods, for both carcinogens and noncarcinogens, that are relevant to the health effects assessments conducted under this Six-Year Review.

Section 3 describes the overall process implemented to evaluate any new health effects of chemicals.

Section 4 presents the results of the health effects review, including the identification of those chemicals for which OST identifies a possible change, or consideration of a change, to the current MCLG.

Section 5 provides an overall summary of this document.

2. Overview of EPA Health Effects Assessment Methods

2.1 Noncarcinogens

For chemicals exhibiting a threshold for toxic effects, EPA establishes the MCLG based on an oral reference dose (RfD), and the MCL is often the same as the MCLG. A change in the RfD could lead to a change in the MCLG and thus possibly also in the MCL. The RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious noncancer effects during a lifetime. The RfD is derived as follows:

$$\text{RfD (mg/kg-day)} = \frac{\text{NOAEL or LOAEL or BMDL}}{\text{UF}}$$

where:

NOAEL	=	no-observed-adverse-effect level (mg/kg-day)
LOAEL	=	lowest-observed-adverse-effect level (mg/kg-day)
BMDL	=	lower confidence limit on the benchmark dose (mg/kg-day)
UF	=	uncertainty factor

No-Observed-Adverse-Effect Level (NOAEL): The highest exposure level at which there are no biologically significant increases in the frequency or severity of adverse effect between the exposed population and its appropriate control; some effects may be produced at this level, but they are not considered adverse or precursors of adverse effects.

Lowest-Observed-Adverse-Effect Level (LOAEL): The lowest exposure level at which there are biologically significant increases in frequency or severity of adverse effects between the exposed population and its appropriate control group.

Benchmark Dose (BMD): BMD modeling can be performed to identify potential critical effect levels for derivation of an RfD. The BMD is an alternative approach to deriving RfDs instead of using a NOAEL or LOAEL. The BMD is a dose that produces a predetermined change in response rate of an adverse effect (called the benchmark response or BMR) compared to background, and is determined by fitting a flexible mathematical model to the data. The BMD is the central estimate of that dose, and the BMDL is the corresponding lower limit of a one-sided 95% confidence interval on the BMD. In practice, the BMDL is often used as an alternative to the NOAEL as a point of departure in recent noncancer risk assessments.

Since the determination of the BMD and BMDL is dependent on the BMR, it is critical to select an appropriate BMR in the BMD modeling process. For quantal data, an excess risk of 10% generally has been the default BMR because the 10% response is at or near the limit of sensitivity in most cancer and noncancer bioassays. If a study has greater-than-usual sensitivity, then a lower BMR can be used, although the benchmark dose at a 10% response (BMD₁₀) and the lower 95% confidence limit on the BMD₁₀ (BMDL₁₀) are usually presented for comparison purposes. For continuous data, if there is a minimal level of change in the endpoint that is generally considered to be biologically significant, then that amount of change can be used to

define the BMR. In the absence of any other data on the adverse response level, a change in the mean equal to one control standard deviation from the control mean is generally used (USEPA, 2000a).

Uncertainty Factors (UF): The NOAELs, LOAELs or BMDLs selected for deriving the RfD may be determined from animal or human data. In calculating an RfD, the NOAEL, LOAEL or BMDL is divided by a composite uncertainty factor (UF). An UF is a product of several uncertainty factors accounting for variation in sensitivity among members of the human population, extrapolation from animal data to humans, extrapolation from a LOAEL to a NOAEL, extrapolation of subchronic data to lifetime, and database deficiencies. Each individual UF presented below may range between 1 and 10 to account for the uncertainty introduced either by variability or the absence of information. The specific magnitude of the value is based upon a combination of scientific evidence and professional judgment.

Some older RfD assessments also used a modifying factor (MF) in the calculation of the overall UF. Discontinuation of the MF was recommended in 2002 (USEPA, 2002c), and the IRIS glossary states that the MF was discontinued in 2004. The magnitude of the MF reflected the scientific uncertainties of the study and database not explicitly treated with standard uncertainty factors (e.g., the completeness of the overall database). Current practice is to address those uncertainties in the database uncertainty factor. A MF was greater than zero and less than or equal to 10, and the default value for the MF was 1.

The following paragraphs describe the component uncertainty factors, based on current EPA guidance for use of uncertainty factors for IRIS and similar programs. In addition to the considerations suggested below, others may be appropriate depending upon data availability, applicability, and quality. In particular, additional considerations are used in deriving an RfD for essential elements, taking into account recommended intake.

UF_H (human to sensitive human): A factor of 10 is used as the default when data from human populations are lacking or deficient, as well as when the data are from studies on average healthy humans. A factor of 3 can be used when the sensitivity of the human population used in the study is judged to be between that for sensitive and average healthy humans, such as when some, but not all, significant contributors to sensitivity are addressed, or when the study population is large enough to capture significant population variability. Chemical-specific data can also be used to adjust this factor, when adequate data are available. A factor of 1 is used when the data are from a good-quality epidemiology study evaluating effects in a sensitive population.

UF_A (animal to human): A factor of 10 is used as the default when extrapolating valid results from experimental animal studies, when results of studies of human exposure are not available or are inadequate. A factor of 3 can be used when results are obtained from an animal species that is physiologically similar to humans, such as nonhuman primates, or when pharmacokinetic modeling approaches are used in extrapolating from the animal data (USEPA, 1994a). Chemical-specific data can also be used to adjust this factor, when adequate data

are available. A factor of 1 can be used when valid results are obtained from an animal species that is known to be more sensitive than humans to the chemical of interest, or when comparative metabolic and/or toxicity data show that the experimental animal responds to the chemical or agent in a manner that is the same or very similar to the way that a human responds.

UF_L (LOAEL to NOAEL): A factor of 10 is used as the default when deriving an RfD from a LOAEL instead of a NOAEL. A factor of less than 10 (typically 3) can be used when there is sufficient evidence to suggest that the LOAEL used is based on an effect of minimal adversity. A factor of 1 is used when the critical effect level is a study NOAEL or when benchmark dose modeling (i.e., a BMDL) was used to identify the point of departure. The BMDL has been used as an alternative to the NOAEL as a point of departure in noncancer risk assessment. Although it has been proposed that an additional UF (for effect level extrapolation) be used when deriving a chronic risk value from a BMDL, current EPA guidance is not to use any such additional UF.

UF_S (subchronic to chronic): A factor of 10 is used as the default when less-than-chronic results (NOAEL or LOAEL) in humans or experimental animals are used in the absence of useful long-term human or animal data. A factor of 3 may be used for intermediate data, such as when some data on chronic exposures are available but the study did not evaluate some of the parameters shown to be affected in studies of shorter duration. A factor of 1 is used when the RfD is derived from a chronic study. A factor of 1 also can be used when less-than-chronic results are used, if it is known that the subchronic study is more sensitive than any chronic studies, or that the critical study evaluated the full duration of relevance for the critical effect (e.g., for certain reproductive or developmental effects or relevant acute effects such as cholinesterase inhibition).

UF_D (completeness of database): This UF is used when deriving a risk value from an “incomplete” database. The intermediate factor of 3 is often used when there is a single data gap (e.g., missing a multigenerational reproduction study, or missing a systemic toxicity study in one species).

The minimum database for a high confidence RfD includes two systemic toxicity studies of chronic or subchronic duration in different species, a two-generation reproductive study, and two developmental toxicity studies in different species. For the systemic toxicity studies, the key consideration is whether a range of endpoints was evaluated; duration extrapolation, if relevant, is addressed by UF_S. The minimum animal database for an RfD is a well-conducted subchronic study that evaluated a comprehensive array of endpoints, and established an unequivocal NOAEL and LOAEL. Note that EPA did not generally use the UF_D prior to approximately 1987. (The exception was the Office of Pesticide Programs, where database deficiencies were addressed with the use of a modifying factor, as discussed above.) After 1987, the UF_D was adopted by the IRIS program, but the UF_D was not used for regulations by OW until 1991, when a few, but not many, chemicals were assigned database factors. Therefore, some older RfDs that

were developed by EPA based on incomplete databases might be 3- to 10-fold lower if current uncertainty factor guidelines were followed.

2.2 Carcinogens

EPA's health effects assessment for carcinogens involves assessing both the weight of evidence for carcinogenicity and the potency. This section presents EPA's guidance for assessing carcinogens as it has evolved from the 1986 guidelines (USEPA, 1986a) through the final 2005 guidelines (USEPA, 2005a, 2005b).

2.2.1 Classification. Under the 1986 guidelines, the qualitative assessment began with a separate evaluation of the animal and human data, identifying the data as sufficient, limited, inadequate, "no data," or "no evidence of carcinogenicity." The animal and human data were combined with other available data for an overall weight-of-evidence evaluation, using the following groups:

Group A – Human carcinogen

Group B – Probable human carcinogen. This group is divided into B1 (agents for which there is "limited" evidence of carcinogenicity based on epidemiology data), and B2 (agents for which there is "sufficient" evidence of carcinogenicity from animal data, but "inadequate" or "no data" in humans).

Group C – Possible human carcinogen

Group D – Not classifiable as to human carcinogenicity

Group E – Evidence of non-carcinogenicity for humans

Proposed revisions to the 1986 cancer guidelines were released in 1996, and additional draft guidelines were released in 1999. (Although there were additional interim versions of the cancer guidelines, they were not applied in official final assessments.) These revised versions of the guidelines, like the current guidelines (finalized in 2005) described below, emphasized the use of descriptors coupled with a narrative based on the entire weight of evidence (rather than a cancer classification), and emphasized mode of action (MOA). However, the 1996 and 1999 versions used somewhat different sets of descriptors and different definitions of the data supporting each descriptor than the 2005 guidelines did. Under the proposed 1996 guidelines, there were just three broad categories of descriptors: known/likely, cannot be determined, not likely. Under the draft 1999 guidelines there were five categories of descriptors: carcinogenic to humans; likely to be carcinogenic to humans; suggestive evidence of carcinogenicity, but not sufficient to assess human carcinogenic potential; data are inadequate for an assessment of human carcinogenic potential; not likely to be carcinogenic to humans. The 1996 proposed and 1999 draft guidelines were also generally consistent with the 2005 approach to quantitation (see Section 2.2.2), although they differed in some minor details with respect to the modeling.

Under the 2005 guidelines, a descriptive weight of evidence judgment is made, based on all available animal, human, and mechanistic data, as to the likelihood that an agent is a human carcinogen and the conditions under which the carcinogenic effects may be expressed. Under the 2005 guidelines, descriptive terms for carcinogenicity replaced the terms used in the 1999 draft guidelines, which themselves replaced the 1986 alphanumeric cancer group designations noted

above. A cancer narrative is also included under the 2005 guidelines to provide a more complete description of the weight of evidence and conditions of carcinogenicity. The suggested descriptive terms under the 2005 guidelines are as follows:

- Carcinogenic to humans
- Likely to be carcinogenic to humans
- Suggestive evidence of carcinogenic potential
- Inadequate information to assess carcinogenic potential
- Not likely to be carcinogenic to humans

Compound descriptors are possible if a chemical has different carcinogenic responses with different routes of exposure, dose, or mode of action (MOA)⁵. MOA information enters into both the qualitative and quantitative portions of the assessment. The MOA determines such issues as the human relevance of the observed tumors and any route-specific differences (e.g., carcinogenic in the respiratory tract via the inhalation route, but not carcinogenic via the oral route). MOA must be considered separately for every target organ. Because of these considerations, one cannot directly translate the cancer classifications and risk values under the 1986 guidelines to narrative statements and risks under the 2005 guidelines. A full consideration of the weight of evidence, including consideration of any available MOA data, would be needed for an assessment under the 2005 guidelines.

The cancer classifications in this screening-level health review for Six-Year Review 2 chemicals are based only on the Agency's most recent available formal risk assessments. Note that EPA cancer assessments conducted between 1996 (following publication of the proposed guidelines) and 2001, when the Agency published a Federal Register notice (60 *FR* 59594) authorizing use of the 1999 draft guidelines on an interim basis, often presented two sets of cancer classifications – one following the 1986 guidelines, and one following the classification system of the then-most current official version of the guidelines. (Some assessments conducted during that time period, such as some from the Office of Pesticide Programs (OPP), presented the assessment under only the 1986 guidelines.)

2.2.2 Quantification. The quantitative aspect of cancer assessment also changed between the 1986 and 2005 guidelines. Under the 1986 guidelines, the cancer risk was calculated by fitting a model to the tumor data, and then calculating a 95% upper confidence limit on one of the coefficients in the model. The resulting number was the q1* (also known as the slope factor), producing an upper bound on the risk. In addition, in the 1986 guidelines, human equivalent doses were estimated from animal data using a scaling factor of body weight to the 2/3 power. Because the extrapolation approach was not sufficiently transparent, a modified approach is used under the 2005 guidelines. A two-step process is used for the quantitation step. First, a model is used to fit a dose-response curve in the range of the available tumor data. The model is used to calculate the point of departure (POD), the dose that is used for extrapolation to the low-dose region. According to the 2005 guidelines, the POD is the lowest dose that is adequately supported by the data. The ED10 (the dose corresponding to a 10% increase in tumors), and the

⁵ Mode of action is defined as a sequence of key events and processes, starting with interaction of an agent with a cell, proceeding through operational and anatomical changes, and resulting in cancer formation. It is contrasted with "mechanism of action," which implies a more detailed understanding and description of events.

LED10 (the 95% lower confidence limit on that dose) are also reported, and are often used as the POD. In the 1996 guidelines and in all later versions, the default for calculating human equivalent dose for oral exposure uses a scaling factor of body weight to the 3/4 power.

In the second step of the low-dose extrapolation, one extrapolates from the POD to the low-dose region of interest for environmental exposures. The approach for extrapolation depends on the MOA for carcinogenesis. If the chemical causes cancer through a mutagenic change to DNA, or if the MOA for causing cancer is not known, this extrapolation is conducted by drawing a line from the POD to the origin (zero dose, zero tumors, corrected for the background response). The slope of the line gives the unit risk (risk per unit dose, or risk per [mg/kg-day]). If there was a positive tumor response at all bioassay doses, the calculated slope is often very similar to that calculated using the q1* approach. In addition, under the supplemental guidance (USEPA, 2005b), affirmative determination of a mutagenic MOA (as opposed to defaulting to a mutagenic MOA based on insufficient data or limited data indicating potential mutagenicity) determines whether an age-dependent adjustment factor (ADAF) is used as part of the quantitative assessment, to account for additional sensitivity of children.

If the chemical is shown to cause cancer via a MOA that is not linear at low doses, *and* the agent does not demonstrate mutagenic or other activity consistent with linearity at low doses, a nonlinear extrapolation is conducted. In earlier versions of the cancer guidelines (USEPA, 1996a, 1999a) the point of departure was compared to the exposure of interest, resulting in a margin of exposure (MOE). However, these earlier guidelines did not define the acceptable MOE value. The 2005 guidelines state that “where tumors arise through a nonlinear MOA, an oral reference dose or inhalation reference concentration, or both, should be developed in accordance with EPA’s established practice of developing such values, taking into consideration the factors summarized in the characterization of the POD.” In these cases, an RfD-like value is calculated based on the key event⁶ for carcinogenesis or the tumor response.

2.3 How EPA Sets the MCLG and MCL

Because the identification of contaminants for possible revision based on health effects is dependent on whether or not the MCLG could change, a brief explanation of the derivation of the MCLG is warranted. The MCLG is the maximum level of a contaminant in drinking water at which no known or anticipated adverse health effects occur, allowing for an adequate margin of safety. As the name implies, an MCLG is a health goal; it is not an enforceable standard. EPA establishes the MCL based on the MCLG. The MCL is the maximum permissible level of a contaminant in water that is delivered to any user of a public water system, and it is an enforceable standard. The MCL is set as close as feasible to the MCLG.

As discussed in the next two sections, there are different approaches used to establish MCLGs for carcinogens and for noncarcinogens.

2.3.1 Carcinogens. For drinking water contaminants regulated prior to the 1996 SDWA, OW followed a three-category regulatory cancer classification system (Categories I, II,

⁶ The key event is defined as an empirically observed precursor step that is itself a necessary element of the mode of action or is a biologically based marker for such an element.

or III). These categories specify decisions as to degree of concern for an agent's carcinogenic potential as a contaminant of drinking water, and define to some extent the approach to risk management that is taken for establishing MCLGs.

EPA also used the six alphanumeric categories (A, B1, B2, C, D, and E) of the 1986 cancer guidelines (USEPA, 1986a) in establishing MCLGs. The six-group classification system is often equated to the three-category system in the NPDWR Federal Register announcements. Table 1 describes the three categories and, with few exceptions (e.g., beryllium), their usual equivalent alphanumeric classification. If a chemical is a known or probable human carcinogen by the oral route (Category I, generally Group A or B), the MCLG is generally set at zero because it is assumed, in the absence of other data, that there is no known threshold for carcinogenicity. If a chemical falls in Group C (Category II), the MCLG is derived using the RfD approach, as described in the next section, along with an additional risk management safety factor of 1 to 10. If a chemical falls into Group D or E (Category III), the MCLG is derived using the RfD approach as described in the next section. The methodology used under this approach for establishing MCLGs for chemicals with varying degrees of evidence of carcinogenicity is summarized in Table 1.

A generally similar approach applies to chemicals with cancer assessments developed under more recent EPA guidelines. The MCLG is generally set at zero for chemicals with a descriptor of *carcinogenic to humans* or *likely to be carcinogenic to humans*, and an additional risk management safety factor of 1 to 10 may be applied on a case-by-case basis, if needed for chemicals with a descriptor of *suggestive evidence of carcinogenic potential*.

2.3.2 Noncarcinogens. For noncarcinogens, the MCLG is derived from the RfD, which was discussed in Section 2.1. From the RfD, a Drinking Water Equivalent Level (DWEL) can be determined. A DWEL is a drinking water lifetime exposure level, assuming 100% exposure from that medium, at which adverse, noncarcinogenic health effects would not be expected to occur. The DWEL is derived as follows:

$$\text{DWEL (mg/L)} = \frac{\text{RfD} \times \text{BW}}{\text{I}}$$

where:

BW = Body Weight (70 kg for adults, 10 kg for children)

I = Intake from drinking water (2 L/day for adults, 1 L/day for children).

The MCLG is then derived by considering other known or potential sources of exposure, using the relative source contribution (RSC) factor.

$$\text{MCLG (mg/L)} = \text{DWEL} \times \text{RSC}$$

The RSC from drinking water is based on actual exposure data, or, if data are not available, a value of 20% is assumed for effects based on lifetime exposure. This allows 80% of the total

exposure to come from sources other than drinking water, such as exposure from food, inhalation, or dermal contact. For the few MCLGs based on adverse effects related to exposure in children, an RSC of 100% was usually applied because the source of exposure for the critical study was drinking water. However, in more recent assessments, even when actual data from other sources are available, EPA uses a maximum RSC value of 80% to allow for potential unidentified sources.

Table 1. EPA 1986 Cancer Classification System and Corresponding Three-Category Approach

Three-category approach for establishing MCLGs	Corresponding five-group classification system of 1986 cancer guidelines
MCLG generally set at zero	
<p>Category I:</p> <p>Known or probable human carcinogens: Strong evidence of carcinogenicity</p> <p>Sufficient human or animal evidence of carcinogenicity.</p>	<p>Generally Group A or B:</p> <p>A: Human carcinogen Sufficient evidence from epidemiological studies to support a causal association.</p> <p>B: Probable human carcinogen B1: Limited evidence of carcinogenicity from epidemiological studies. B2: Inadequate evidence or no data from epidemiological studies; sufficient evidence from animal studies.</p>
MCLG based on the RfD with an additional safety factor of up to 10 to account for possible carcinogenicity, or is based on excess cancer risk range of 10⁻⁵ to 10⁻⁶	
<p>Category II:</p> <p>Limited evidence of carcinogenicity</p> <p>Some limited but insufficient evidence of carcinogenicity from animal data.</p>	<p>Generally Group C:</p> <p>Possible human carcinogen</p> <p>Limited evidence of carcinogenicity in animals in the absence of human data.</p>
MCLG established using the RfD approach	
<p>Category III:</p> <p>Inadequate or no evidence of carcinogenicity in animals</p>	<p>Group D or Group E:</p> <p>D: Not classifiable as to human carcinogenicity Inadequate human and animal evidence of carcinogenicity, or no data available.</p> <p>E: Evidence of non-carcinogenicity for humans No evidence of carcinogenicity in two different animal species, or in both epidemiological and animal studies.</p>

2.4 Key Differences in Human Health Assessment Methods Between EPA and Other Organizations Discussed in this Document

As part of the evaluation of the List B chemicals, assessments by several other regulatory bodies or authoritative organizations were reviewed. Notable among these are the Agency for Toxic Substances and Disease Registry (ATSDR), California EPA (CalEPA), the World Health Organization (WHO), Health Canada, and the National Academy of Sciences (NAS). To provide

context to that review, key differences between the human health assessment methods of these other organizations and those of EPA are summarized here.

ATSDR establishes oral minimal risk levels (MRLs) for non-neoplastic endpoints for acute (14 days or less), intermediate (15 – 364 days), and chronic (365 days or more) exposure durations. MRLs for oral chronic exposure are similar to EPA's RfDs. However, ATSDR and EPA use different approaches when the database is limited to subchronic studies and no adequate chronic study is available. In such cases, EPA derives a chronic RfD from a subchronic study, incorporating an additional uncertainty factor to account for use of a subchronic study. ATSDR derives an intermediate duration MRL that protects against exposures up to 10% of a lifetime, and it does not incorporate an uncertainty factor to account for using a less-than-lifetime study. ATSDR does not perform quantitative cancer assessments or assign formal cancer classifications or descriptors, although an overall summary of the data pertaining to carcinogenic potential is provided.

CalEPA establishes a public health goal (PHG), which is a water concentration that is the State's equivalent to the MCLG. However, the PHG can be based on either cancer or noncancer endpoints. When the PHG is based on cancer endpoints, CalEPA estimates a cancer potency factor and then uses the potency factor to estimate the daily water intake that is equivalent to a 10^{-6} cancer risk, assuming adult body weight and drinking water intake. When the PHG is based on noncancer endpoints, CalEPA uses a procedure that is similar to EPA's approach for deriving an MCLG. CalEPA generally has used standard default adult parameters of 70 kg body weight and 2 L/day water consumption. However, for volatile organic compounds that have a potential to result in inhalation exposure from water (e.g. showering), CalEPA uses a higher daily water intake to account for the additional potential for exposure. This intake is often 4 L/day, but may be modified based on chemical-specific information. In addition, CalEPA uses a default RSC of 20%, similar to the approach of USEPA. However, CalEPA also appears to choose a non-default value for the RSC more frequently than does USEPA, although the rationale for moving from the default is not always clearly documented.

WHO establishes a "guideline value," a drinking water concentration that is developed in a process analogous to that for the MCLG. However, WHO uses different default assumptions for estimating water concentration from doses, including a 60 kg adult body weight, daily water consumption of 2 L/day, and an RSC of 10%. WHO develops one guideline value that is based either on cancer or noncancer. For genotoxic carcinogens a value may be based on a concentration calculated to correspond to a specified cancer risk. For example, for vinyl chloride, the drinking water concentration was based on a cancer risk of 1 in 10^5 .

For substances considered by Health Canada to have no threshold (i.e., mutagens and genotoxic carcinogens), it is assumed that there is some probability of harm to human health at any level of exposure. Health-based values for carcinogens are generally established on the basis of an estimation of lifetime cancer risk that would be considered "essentially negligible," which Health Canada has defined in the context of drinking water guidelines as a range from one new cancer above background per 100,000 people to one new cancer above background per 1,000,000 people (i.e., 10^{-5} to 10^{-6}) over a lifetime of 70 years. For noncarcinogens an approach similar to EPA's RfD methodology is used. For calculating water concentrations default values

of 70 kg body weight, 1.5 L water intake per day, and a RSC of either 20% or a value based on actual exposure data.

3. Process for Evaluating Chemicals for the Six-Year Review 2

The list of 71 chemicals was divided into two groups. For the 30 List A chemicals, either EPA assessments are currently in progress or recently completed, or NAS assessments commissioned by EPA are currently in progress or recently completed. Therefore, the review was limited to compiling existing final EPA assessments, as well as noting recent NAS and ATSDR assessments. Three radionuclides (alpha particle emitters, beta particle and photon emitters, and combined radiums (226 and 228)) were evaluated by ORIA separately with health evaluation and literature review in the areas specific to radiation. In the case of the remaining 41 chemicals, a more comprehensive evaluation was performed by OST, including evaluation of risk-based values from preferred and additional risk assessment sources, and evaluation of the selected primary literature sources.

3.1 Literature Search Process for the 41 List B Chemicals

Evaluation of each chemical began with a consideration of authoritative reviews/assessments by IRIS, OPP, the National Academy of Sciences (NAS), the Agency for Toxic Substances and Disease Registry (ATSDR), the National Toxicology Program (NTP); National Institute of Environmental Health Sciences (NIEHS), California EPA (CalEPA), World Health Organization (WHO), European Commission Concise International Chemical Assessment Documents (CICADS), International Programme on Chemical Safety/Environmental Health Criteria (IPCS/EHC), International Agency for Research on Cancer (IARC), Health Canada, Joint Expert Committee on Food Additives (JECFA), and Joint FAO/WHO Meeting on Pesticide Residues (JMPR). Each organization's most recent assessment was obtained for review when available. Additional checks were conducted to ensure that EPA, NAS, and ATSDR assessments released through March 1, 2009 were captured.

Literature searches were conducted to identify primary literature to supplement the information in the authoritative reviews. The following databases were searched: TOXLINE, MEDLINE®, Developmental and Reproductive Toxicology (DART®), Chemical Carcinogenesis Research Information System (CCRIS), and Hazardous Substances Data Bank (HSDB). The dates covered by the literature search were determined on an individual chemical basis, to ensure that the literature was adequately captured, but to avoid unnecessary duplication of work done in the authoritative reviews. In general, searches covered posting dates from 2003 (the year that the Six-Year Review 1 was finalized) through December 2007. However, if there was a recent IRIS, OPP, OW, or ATSDR document, the searches began 2 years before publication date of the latest toxicity assessment from IRIS/OPP/OW and 3 years before the publication date of any ATSDR toxicological profile. In addition, supplemental searching was done to cover earlier dates, going back to the late 1980s in many cases.

The searches and screening of the literature searches were intended to capture the health effects data; separate searches were conducted for (1) systemic toxicity and carcinogenicity and

for (2) reproductive and developmental toxicity. However, most of the studies on reproductive and developmental toxicity were captured by the general literature search, except that the reproductive/developmental search also included the developmental-specific database DART. The search terms were very broad, based on the chemical name, synonyms, and CAS number. A literature search review report was prepared for each chemical, describing the findings of any significant new studies published for general toxicity, carcinogenicity (including mode of action (MOA) and genotoxicity studies), and reproductive or developmental effects. Studies with a possible impact on the assessment were retrieved and reviewed; other studies of interest were noted based on the information presented in the abstract.

3.2 Screening Process for List A Chemicals

List A chemicals have an ongoing EPA assessment, or an ongoing or recently completed NAS assessment. Accordingly, no additional literature search was conducted for these chemicals. Instead, the review of the List A chemicals was limited to reviewing the available noncancer and cancer assessments from the following sources: OW, IRIS, OPP Reregistration Eligibility Decisions (RED), NAS, and ATSDR to determine if there were any compelling new data that should be considered during the Six-Year Review 2. In addition, qualitative and quantitative descriptions of the toxic and cancer effects from EPA documents for which external review versions are available were also reviewed, with the understanding that these external-peer-review-ready assessments are subject to further changes.

3.3 Screening Process for List B Chemicals

For the List B chemicals that are not the subject of an ongoing assessment by EPA or NAS, a more comprehensive evaluation was done, including evaluation of risk-based values from preferred and additional risk assessment sources, and evaluation of the selected primary literature sources. Literature searches on these chemicals were conducted as discussed above in Section 3.1. Newly identified studies that appeared relevant to the assessment of noncancer, cancer, or reproductive/developmental effects were obtained and screened for the possible impact of new data on current assessments.

Health effects assessments completed by the following EPA offices or other organizations were examined:

- EPA Office of Water Drinking Water Criteria Documents
- EPA Integrated Risk Information System (IRIS)
- EPA Office of Pesticide Programs (OPP)
- EPA Office of Radiation and Indoor Air (ORIA)
- National Academy of Sciences (NAS)
- Agency for Toxic Substances and Disease Registry (ATSDR)
- California EPA Public Health Goals (CalEPA)
- WHO Drinking Water Guidelines (WHO)
- Health Canada
- WHO's Concise International Assessment Documents (CICADs)
- Joint Expert Committee on Food Additives (JECFA)

- International Programme on Chemical Safety – Environmental Health Criteria Documents (IPCS, EHC)
- FAO/WHO Meeting on Pesticide Residues (JMPR)
- National Institute of Environmental Health Sciences (NIEHS) Report on Carcinogens
- International Agency for Research on Cancer (IARC)
- National Toxicology Program (NTP)

Based on the availability of new data identified in the literature and information from existing assessments from other organizations, conclusions were made regarding the need for EPA OW to update its MCLG based on the health effects data alone. In addition, the data on reproductive and developmental toxicity were evaluated to ensure that the MCLG takes these endpoints into account and to determine whether risk values based on these endpoints would be in the range of the RfD.

4. Results - Identifying Candidates for Possible MCLG Changes

Based on the approach described in Section 3.2, EPA identified those regulated chemical contaminants from the 71 considered for which there have been official Agency changes in the RfD and/or in the cancer risk assessment from oral exposure. Such changes could result in a change in the MCLG and, possibly, in the MCL. Therefore, these chemicals were further considered for Six Year Review 2 to evaluate whether they are candidates for regulatory revision.

Tables 2 through 5, presented together at the end of this document, provide key information on the chemicals evaluated in this assessment.

Table 2 lists the 71 chemicals included in the Six-Year Review 2 process, the basis for current OW rules⁷ (including RfDs and cancer groups on which the MCLGs are based), assessments by OPP and IRIS, and assessment dates. Although the date of “verification” is well-documented, numerous additional revisions to the IRIS summary may be documented in the “Revision History” for each chemical, and the “last revised” date may be several years after the verification date, particularly for chemicals verified prior to 1996. Therefore, the dates presented in Table 2 for IRIS assessments are approximate and refer to the most recent year in which a change was made to the IRIS file. Risk assessments conducted by IRIS and OPP can be found at www.epa.gov/iris/index.html and www.epa.gov/pesticides/reregistration/status.htm, respectively. The basis for the RfDs, including the critical effect, citation for the principal study, point of departure (value and whether it is a NOAEL, LOAEL, or BMDL), and breakdown of uncertainty factors, are also presented. For OPP assessments, the Food Quality Protection Act (FQPA)⁸ factor is provided, when relevant. In addition, for cancer assessments, the year of the guidelines followed is presented, since the approach varied with the year of the guidelines. For a number of the chemicals evaluated between 1996 and 2001, the assessment document provided the assessments under both the 1986 and 1996 guidelines. In such cases, Table 2 presents only the

⁷ The 2000 radionuclides rule was a collaboration between OW and ORIA. ORIA is the principal health assessor for radionuclides.

⁸ The FQPA mandated consideration of an additional uncertainty factor to ensure protection of children for pesticide safety evaluations.

assessment under the 1996 guidelines. All supporting EPA documents are listed in the reference section.

Additional information on the quantitative portion of the cancer assessments is presented in Table 3 for the List A and List B chemicals for which quantitative assessments are available. The table shows both the quantitative assessment and the methods used for modeling the data and for extrapolation from the animal data.

Assessments by other organizations reviewed for List A and List B chemicals are presented in Table 4. Where possible, noncancer limits initially expressed as water concentrations were converted to the reference value in dose as mg/kg-day, so that all values could be directly comparable at a glance. For List A chemicals only the latest final EPA assessment is included, as well as the most recent ATSDR or NAS assessment.

Table 5 summarizes the existing EPA assessments for all List B chemicals. In addition, Table 5 presents the results of this review for the List B chemicals based on the health effects evaluation. The column headed "New Data/Possible Impact on MCLG" addresses new data obtained since the latest OW assessment that could affect the MCLG. This column presents the response to two separate considerations. The first half addresses whether new data are available that could be used, or have been used, to develop an updated RfD. If the new data have already been used to develop a formal EPA assessment (as shown in other columns in Table 5), there is no additional notation. If the new data were identified in the literature search, it is indicated as "lit search." The second half of the column headed "New Data/Possible Impact on MCLG" addresses whether there is a potential for the new data to have an impact on the MCLG. New data that could be used to develop an RfD would not have an impact on the MCLG if the MCLG is zero. New cancer data would generally not affect the MCLG, unless the data changed the cancer descriptor. If the first half of the column is "no" for new data, the second half of the column is blank.

Potential concern for reproductive and developmental toxicity was based on consideration of the reproductive and developmental toxicity data summarized in the assessments by the organizations listed in Section 3.3, as well as review of studies identified in the literature search. The outcome of this review is described in Section 4.3 below.

The column in Table 5 headed "Possible New MCLG" notes whether there are data from formal EPA assessments indicating a possible need to update the MCLG. If "yes," the possible MCLG based on the new IRIS or OPP assessment is provided. This column reflects only possible changes based on the health evaluation, and does not include consideration of occurrence data or other risk management considerations. Footnotes provide additional details. For 7 chemicals (1,2,4-trichlorobenzene, atrazine, chromium, nitrate, nitrite, selenium, and simazine) new data were identified suggesting the need to consider whether a possible change to the MCLG might be likely, but the value of the MCLG change could not be determined without further critical review. These chemicals are noted as "to be determined" (TBD) in this column of the table. For 1,2,4-trichlorobenzene, chromium, nitrate, nitrite, and selenium, the following column indicates "yes" indicating that EPA is considering whether to nominate the chemical for a new assessment. For atrazine, on October 7, 2009 (74 FR 51593, USEPA, 2009c), the Agency

announced its intent to launch a comprehensive reevaluation of the 2006 OPP risk assessment for atrazine (USEPA, 2006a). Since simazine is based on atrazine data, any reassessment of simazine relies on the outcome of the reevaluation of the atrazine risk assessment.

4.1 Findings for List A Chemicals

As of March 1, 2009, 30 List A chemicals were the subjects of ongoing EPA assessments and therefore, the Agency is not recommending any changes to the MCLGs for them at this time. Most of these assessments are being conducted as part of the IRIS program, and information on the status of these assessments can be found on the IRIS Substance Assessment Tracking System website at <http://cfpub.epa.gov/ncea/iristrac/index.cfm>. Note that EPA completed the risk reassessment for thallium in September of 2009 (USEPA, 2009b). Because the new assessment was not completed by March 1, 2009, the cutoff date for this review, the outcome of this assessment has not been included in the current review effort. EPA will consider the updated assessment in the next review cycle.

Regarding the radionuclides on List A, since the promulgation of the final radionuclides rule (USEPA, 2000b), additional information has become available on the adverse health effects of ionizing radiation (including alpha particle emitters; beta particle and photon emitters; and combined radiums (226 and 228)), and on cellular and molecular mechanisms of damage. In particular, updated and new epidemiologic data on occupational, medical, and environmental exposures offer an improved basis for quantitative estimates of radiation-induced health effects in human populations at low doses and low dose rates. Novel cellular and molecular studies have begun to shed light on the complex mechanisms involved in radiation carcinogenesis, and this mechanistic understanding may help refine risk modeling and reduce uncertainties in risk estimates. Still other research studies have reported on radiation-associated non-cancer endpoints, heritable diseases, and risks to the developing fetus during in utero exposures. Much of this information has been reviewed and evaluated comprehensively in several recent reports published by national and international radiation protection advisory bodies, as discussed by USEPA (2007a, 2007b, 2007c).

In light of this new information, and as part of the six year review process, EPA's current radiation risk assessment methodology (which is described in detail in USEPA, 1994b; USEPA, 1999b, 1999c; and Eckerman et al., 2006) needs to be updated. In particular, the current methods and risk models do not incorporate the recent finding and recommendations in the BEIR VII Report (NRC, 2006a), UNSCEAR (2000), NCRP Report 139 (NCRP, 2001), IARC Volume 78 (WHO, 2001), ICRP Report 99 (2006), and several other newly-available, peer-reviewed publications on radiation-induced health effects, metabolism, and MOA. Therefore, ORIA has begun the process of revising its radiation risk methodology to incorporate this new cancer data, and possibly non-cancer data (USEPA, 2007a, 2007b, 2007c), and will determine, in collaboration with the Office of Water, whether or not the new data will have any impact on current radionuclide MCLGs or MCLs. ORIA has also prepared a draft white paper (USEPA, 2006b) that outlines proposed changes in its current methodology for estimating radiogenic cancers based on the contents of the BEIR VII Report (NRC, 2006a).

4.2 Findings for List B Chemicals

For the 41 List B chemicals, the Agency found new information suggesting the need to consider potential changes to the MCLGs for 14 chemicals. For the remaining 27 List B chemicals, the Agency did not find a reason to consider a change to the MCLG at this time. For 20 of those 27 chemicals, current information indicates there is no health effects basis for an MCLG change. However, as mentioned in the beginning of section 4, 7 chemicals were identified for new assessments or other follow-up based on the availability of new data. The decisions for these 7 chemicals are described in detail in section 4.2.2.

4.2.1 Findings for Consideration of a Change to the MCLG

New EPA assessments were available for 18 chemicals for which the MCLG is not zero, or for which the MCLG would change from zero as the result of a new cancer classification. For reasons discussed in the next section, EPA found that it was not appropriate to consider changes to the MCLG for four of these 18 chemicals: carbofuran, chromium, atrazine, and simazine. However, the Agency found new information suggesting the need to consider potential changes to the MCLG, based on the health evaluation for the following 14 chemicals.

- Alachlor
- Barium
- 2,4-D (2,4-Dichlorophenoxyacetic Acid)
- 1,1-Dichloroethylene
- Diquat
- Endothall
- Glyphosate
- Hexachlorocyclopentadiene
- Lindane
- Oxamyl (Vydate)
- Picloram
- Toluene
- 1,1,1-Trichloroethane
- Xylenes (Total)

As described in the following paragraphs, 12 of the 18 chemicals with updated Agency assessments had a new RfD developed by IRIS or OPP that could result in a change to the MCLG, one chemical (alachlor) had a change in the cancer assessment, and one chemical (1,1-dichloroethylene) had changes in both the noncancer and cancer assessments that led to a possible change in the MCLG. Based on health effects data only for these 14 chemicals, it is possible to consider a revision to their current MCLG values.

The chemicals for which the possible changes in the MCLGs would be based on the new IRIS or OPP RfDs are discussed in the next paragraph. Chemicals for which the cancer assessment could affect the MCLGs are described in the paragraph after that.

For barium, an RfD of 0.07 mg/kg-day was used in developing the MCLG (USEPA, 1991a, 1990a), while the current IRIS RfD (USEPA, 2005c) is 0.2 mg/kg-day. In addition, a preliminary estimation of the RSC by OST has been updated from 100% to 80%. For 2,4-D, an RfD of 0.01 mg/kg-day was used in developing the MCLG (USEPA, 1991b), while OPP (USEPA, 2005d) derived an RfD of 0.005 mg/kg-day. For diquat, an RfD of 0.0022 mg/kg-day was used in developing the MCLG (USEPA, 1992a), while OPP (USEPA, 1995a; 2001a) derived an RfD of 0.005 mg/kg-day. For endothall, an RfD of 0.02 mg/kg-day was used in developing the MCLG (USEPA, 1992b, 1992c), while OPP (USEPA, 2005e) derived an RfD of 0.007 mg/kg-day. For glyphosate, an RfD of 0.1 mg/kg-day was used in developing the MCLG (USEPA, 1992b, 1992d), and OPP (USEPA, 2002d, 2007d) developed an RfD of 2 mg/kg-day. For hexachlorocyclopentadiene, an RfD of 0.007 was used in developing the MCLG (USEPA, 1992a), while IRIS (USEPA, 2001b) developed an RfD of 0.006 mg/kg-day. For lindane, an RfD of 0.0003 mg/kg-day was used in developing the MCLG (USEPA, 1991b), while OPP (EPA, 2002g) developed an RfD of 0.0047 mg/kg/day.⁹ For oxamyl, an RfD of 0.025 mg/kg-day was used in developing the MCLG (USEPA, 1992e), while OPP (USEPA, 2000c) developed an RfD of 0.001 mg/kg-day. The OPP assessment for oxamyl supports the use of child body weight and water intake values in calculating the MCLG, since the critical study evaluated effects in young animals and human dietary data support the use of an RSC of 20% for children aged 1 to 6. For picloram, an RfD of 0.07 mg/kg-day was used in developing the MCLG (USEPA, 1992a, 1992f), while OPP (USEPA, 1995b) developed an RfD of 0.2 mg/kg-day. For toluene, an RfD of 0.2 mg/kg-day was used in developing the MCLG (USEPA, 1991b, 1990b), while the updated IRIS RfD is 0.08 mg/kg-day (USEPA, 2005f). For 1,1,1-trichloroethane, an RfD of 0.035 mg/kg-day was used in developing the MCLG (USEPA, 1987a), while IRIS (USEPA, 2007e) derived an RfD of 2 mg/kg-day. For xylenes, an RfD of 1.79 mg/kg-day was used in developing the MCLG (USEPA, 1991b, 1987b), and the updated IRIS RfD is 0.2 mg/kg-day (USEPA, 2003d).

Two chemicals had changes in their cancer assessments that suggested the need to consider a possible change in the MCLG. New cancer assessments that affected the possible value of the MCLG are available for 1,1-dichloroethylene (USEPA, 2002e) and alachlor (USEPA, 2006c). 1,1-Dichloroethylene was considered a category C carcinogen at the time that it was regulated, so a safety factor of 10 was applied for the MCLG (USEPA, 1987a, 1990c). The IRIS assessment (USEPA, 2002e) concluded that the data on 1,1-dichloroethylene are considered “inadequate for an assessment of human carcinogenic potential via the oral route,” and no additional factor would be applied in developing an updated MCLG. The RfD used in developing the 1,1-dichloroethylene MCLG (USEPA, 1987a, 1990c) was 0.01 mg/kg-day, and the new IRIS RfD is 0.05 mg/kg-day (USEPA, 2002e). Alachlor had an MCLG of zero (USEPA, 1991b) based on its cancer classification of B2, probable human carcinogen. A recent OPP assessment (USEPA, 2006c) updated the cancer assessment and recommended a cancer descriptor of “likely to be a human carcinogen at high doses, not likely to be a human carcinogen at low doses.” Based on the MOA assessment a nonlinear cancer dose-response assessment was

⁹ Note that lindane use has been canceled (USEPA, 2006d); the likely reduction in exposure could affect the RSC used to calculate the MCLG.

conducted using a point of departure of 0.5 mg/kg-day and a composite UF of 100, resulting in a health reference value of 0.005 mg/kg-day.

For the other four of the 18 chemicals for which new assessments containing updated RfDs were available – carbofuran, chromium, atrazine and simazine – EPA is not recommending a change in the MCLG at this time, for reasons discussed in the next section.

4.2.2 Findings for No Consideration of a Change to the MCLG

As noted above, there are 27 List B chemicals for which EPA is not recommending any change to the current MCLG.

For 15 chemicals, there were no new assessments indicating a need to update the MCLGs, and the literature search did not find any evidence of new data that would likely affect the MCLGs. These 15 chemicals are:

- Dalapon (2,2-Dichloropropionic Acid)
- 1,2-Dibromo-3-chloropropane (DBCP)
- 1,2-Dichloropropane
- Dinoseb
- Endrin
- Epichlorohydrin
- Heptachlor
- Heptachlor Epoxide
- Hexachlorobenzene
- Mercury (Inorganic)
- Methoxychlor
- Monochlorobenzene (Chlorobenzene)
- Toxaphene
- 2,4,5-TP (Silvex; 2,4,5-Trichlorophenoxypropionic Acid)
- 1,1,2-Trichloroethane

New assessments, including new RfDs, were available for four carcinogens. Because the MCLG is zero for carcinogens (categories A, B1, or B2 under the 1986 guidelines; “carcinogenic to humans” or “likely to be carcinogenic to humans” under the 2005 guidelines), changes to the RfDs for these chemicals will not affect their MCLGs. Therefore, no change to the MCLGs is needed for these four chemicals:

- Benzene
- Chlordane
- Ethylene Dibromide (EDB, 1,2-Dibromoethane)
- Vinyl Chloride

For another chemical, carbofuran, an RfD of 0.005 mg/kg-day was used in developing the MCLG (USEPA, 1991b, 1990d), while OPP (USEPA, 2006e) recently derived an RfD of 0.00006 mg/kg-day. OPP also derived an acute population-adjusted dose (aPAD) of 0.00006 mg/kg-day based on this RfD. In 2009, EPA revoked all tolerances (maximum residue limits) for carbofuran, which could prohibit all carbofuran residues on food (74 FR 23046, May 15, 2009 (USEPA, 2009d)). Following completion of the ongoing administrative process for resolving the safety of the tolerances, EPA plans to cancel the remaining uses of carbofuran.

This decision is expected to reduce exposure to carbofuran and its metabolite (3-hydroxycarbofuran) in food products, which would affect the RSC used to derive a possible MCLG. Therefore, EPA believes that it should factor in the effect of these actions, once completed, before it determines the potential for an MCLG revision. Consequently, EPA believes it is not appropriate to consider any revisions to the MCLG for carbofuran at this time.

Based on a review of the assessments presented in Tables 2 through 4, as well as the consideration of the recent literature, the available information suggests that new assessments may be needed for the following five chemicals. Therefore, no revision to the current MCLG is recommended at this time.

- Chromium
- Nitrate (as N)
- Nitrite (as N)
- Selenium
- 1,2,4-Trichlorobenzene

The reasons for recommending new assessments for these chemicals are as follows:

For chromium, a change in the MCLG based on the most recent IRIS assessments (USEPA, 1998a, 1998b) was not recommended, in light of the availability of new chronic oral bioassays, as described here. NTP has published recent studies (13-week and 2-year studies in rats and mice) by the oral route of exposure for both Cr(III) picolinate in feed and Cr(VI) as sodium dichromate dehydrate in drinking water. The Cr(VI) study is available as a final, peer-reviewed document (NTP, 2008), but the Cr(III) study is only available as a pre-peer review draft (NTP, 2007). The Cr (VI) study found *clear* evidence of carcinogenic activity of sodium dichromate dihydrate in male and female F344 rats based on increased incidences of squamous cell neoplasms of the oral cavity, specifically the squamous epithelium that lines the oral mucosa and tongue (NTP, 2008). NTP (2008) also concluded that there was *clear* evidence of carcinogenic activity of sodium dichromate dihydrate in male and female B6C3F1 mice based on increased incidences of neoplasms in the small intestine (adenomas and/or carcinomas of the duodenum, jejunum, or ileum). The NTP (2008) study also observed noncancer effects. Recent human studies (e.g., Sedman et al., 2006) also suggest a potential for carcinogenicity of Cr(VI) in drinking water.

A peer-reviewed report for the study of chromium picolinate [Cr(III)] is not yet available, but the draft report concluded that there was *equivocal evidence of carcinogenic activity* in male rats based on preputial gland adenoma, and *no evidence of carcinogenic activity* in female rats and in male and female mice (NTP, 2007). No adverse noncancer effects were reported.

The health effects data for chromium, particularly the Cr(VI) data on cancer, could have an effect on the MCLG. Although this document lists chromium as one of the five chemicals that may need a new assessment based on new data, it should be noted that EPA has already included Cr(VI) on the 2008 IRIS agenda (USEPA, 2007h) and is planning to develop a new health assessment.

The literature search for nitrate identified studies suggesting the potential for thyroid effects following drinking water exposure (Mukhopadhyay et al., 2005; Tajtakova et al., 2006; Zaki et al., 2004), consistent with a known MOA for nitrate. Nitrite is a competitive inhibitor of iodide uptake in the thyroid (Wolff and Maurey, 1963). Neurodevelopmental effects have been reported in a study of nitrite by Vorhees et al. (1984). In addition, Grosse et al. (2006) reported the results of a recent IARC working group review of nitrate and nitrite. This group concluded that ingested nitrate or nitrite, under conditions that result in endogenous nitrosation, is probably carcinogenic to humans (group 2A). Therefore, new noncancer and cancer assessments for nitrate are recommended to assess whether thyroid effects are the critical effect for a nitrate noncancer assessment, to assess the potential for human carcinogenicity, and to evaluate the dose response for both noncancer and cancer effects. Since nitrite is formed from nitrate and also shares the thyroid MOA with nitrate, the role of this action in nitrite toxicity is an issue that needs further evaluation, based on the current assessment. Based on this information, the Agency is considering whether to nominate nitrate and nitrite for an updated health effects assessment(s).

The literature search for selenium identified several new studies for selenium that may affect the RfD. Hawkes and Keim (2003) reported thyroid hormone and related metabolism changes in subjects treated with deficient, sufficient and excess dietary selenium. The excess selenium dose was associated with a slight decrease in T3 levels, a thyrotropin increase, and an increase in body weight compared to the selenium-sufficient subjects. The opposite responses occurred in the selenium-deficient subjects. Several other recent studies identified changes in sperm parameters and fertility in mice fed either selenium-deficient or excess selenium diets compared to adequate selenium diets (Shalini and Bansal, 2006; Kaur and Bansal, 2005). New data relevant to the cancer assessment are also available (e.g., Duffield-Lillico et al., 2003; Su et al., 2005). However, selenium is not a candidate for an MCLG of zero because of its status as a micronutrient. In addition, much has been learned about the metabolism of selenium since the IRIS (USEPA, 1991a) review and it may be appropriate to differentiate between inorganic selenium and organic selenium in the form of selenoproteins, selenomethionine, and selenocysteine for an assessment that applies to drinking water. The new health effects information and our improved understanding of selenium biology suggest a need to update the health effects assessment for selenium. On that basis the Agency is considering whether to nominate selenium for an updated health effects assessment.

Final reports of 2-year feeding studies of 1,2,4-trichlorobenzene in both mice and rats (Moore, 1994a, 1994b) have been submitted to EPA's Office of Pollution Prevention and Toxics

(OPPT), but have not been evaluated from a health effects assessment perspective. A preliminary review of the 2-year study indicates that there is clear evidence of carcinogenicity in mice, but not in rats. This study could affect both the cancer descriptor and quantitation for 1,2,4-trichlorobenzene, as well as the noncancer assessment, and therefore the MCLG. Therefore, the Agency is considering whether to nominate this chemical for a full assessment.

The following two chemicals are not being recommended for new assessments; however, EPA is recommending that they undergo further evaluation. No change in the MCLG is recommended for these chemicals at this time:

- Atrazine
- Simazine

A change in the MCLGs for atrazine and simazine based on the OPP (USEPA, 2006a, 2006f) assessment is not recommended at this time due to the availability of new substantive data regarding potential reproductive effects. During the first Six-Year Review, EPA decided that no revisions to the MCLG for atrazine were appropriate because of the then-pending completion of the risk assessment by OPP. That risk assessment has been completed (USEPA, 2006a), and an RfD was derived based upon the delay of luteinizing hormone surge in pregnant rats, (this delay resulted in developmental effects in offspring). In addition, the OPP assessment also concluded that the appropriate weight of evidence descriptor for carcinogenic potential is *not likely to be a human carcinogen*. This updated weight of evidence descriptor would affect the MCLG in that an additional factor of 10 to account for carcinogenicity would no longer be needed. OPP's 2006 reassessment warrants evaluation in the context of its impact on the MCLG. However, several additional studies relevant to reproductive or developmental effects, atrazine's critical effect, were located. In particular, one published study (Enoch et al., 2007) and one other study (Stanko et al., 2008) suggest that atrazine and its chlorometabolites may affect prenatal and postnatal development in both males and females. On October 7, 2009, the Agency announced its intent to launch a comprehensive new evaluation of atrazine to determine its effects on humans (74 FR 51593, USEPA, 2009c). At the end of this process, the Agency will decide whether to revise the 2006 risk assessment for atrazine and whether new restrictions are necessary to better protect public health. EPA will evaluate the pesticide's potential cancer and non-cancer effects on humans. Included in this new evaluation, to be conducted in 2010, will be the most recent studies on atrazine and its potential association with birth defects, low birth weight, and premature births. The Agency's examination of atrazine will be based on transparency and sound science, including independent scientific peer review, and will help determine whether a change in EPA's regulatory position on this pesticide is appropriate. Additional information is available at www.epa.gov/pesticides/reregistration/atrazine/atrazine_update.htm. Since the simazine assessment is based on studies using atrazine, any reevaluation of simazine relies on the impending reevaluation of the Agency's risk assessment for atrazine reassessment.

4.3 Consideration of Reproductive and Developmental Toxicity

The data on reproductive and developmental toxicity were evaluated to ensure that the MCLG for each of the 41 List B chemicals takes these endpoints into account. A screening level evaluation was conducted for each List B chemical, based on the available current Agency assessment(s), the results from the authoritative reviews/assessments, and the literature search results, to identify (1) whether reproductive and/or developmental effects have been associated with exposure to the chemical; and (2) if so, at what doses such effects occur, and whether these effects occur at lower doses than systemic toxicity. The available dose-response data were then used to evaluate the concern for reproductive and developmental toxicity (as indicated in Table 5 and described in more detail below). For chemicals where there is no potential for a new MCLG, this consideration addressed concern at the current MCL. For chemicals for which a revised MCLG is possible, this consideration reflects evaluation of whether there is a concern at the possible new MCLG and at the current MCL.

In considering whether the current Agency assessment is adequately protective for reproductive/developmental effects, the use of the database uncertainty factor (UF_D) in the current EPA assessment for a chemical was considered. EPA did not generally use this uncertainty factor prior to approximately 1987. After about 1987, the absence of information on reproductive and/or developmental toxicity was increasingly addressed with the database uncertainty factor, particularly for pesticides assessments in drinking water. The Safe Drinking Water Act Amendment of 1996 required health protection of sensitive populations, especially infants and children. Therefore, issues associated with fetuses, infants, and children are most often addressed by applying an UF_D . An RfD developed fully taking into account UF_D is expected to be protective of all effects, including reproductive and developmental toxicity, although this expectation should be confirmed when new research reduces the identified data gaps.

The 41 List B chemicals were broken out into groups based on whether there is a potential concern for reproductive or developmental effects at the potential MCLG, and the rationale for that decision. The six groups are discussed in the sections that follow.

4.3.1 Group 1: Chemicals with No Reproductive/Developmental Concern Based on Most Recent Agency Assessments Published After 1997

For the following 21 chemicals included in List B (Group 1) with an IRIS or OPP RfD developed after 1997, literature search updates were conducted as noted above to identify new studies that could impact the assigned UF_D . None were identified, except for atrazine and simazine. As described above in Section 4.2.2, the Agency recently announced its intent to launch a comprehensive reevaluation of the risk assessment for atrazine. Included in this new evaluation will be the most recent studies on atrazine and its potential association with birth defects, low birth weight, and premature births. Since the simazine assessment is based on studies of atrazine, any reevaluation of simazine relies on the impending reevaluation of the Agency's risk assessment on atrazine.

- Alachlor (USEPA, 2006g)

- Atrazine (USEPA, 2006a)
- Barium (USEPA, 2003e)
- Benzene (USEPA, 2003f)
- Carbofuran (USEPA, 2006e)
- Chlordane (USEPA, 1998c)
- Chromium (USEPA, 1998b, 1998a)
- 2,4-D (2,4-Dichlorophenoxyacetic Acid) (USEPA, 2005d)
- 1,1-Dichloroethylene (USEPA, 2002f)
- Diquat (USEPA, 2001a)
- Endothall (USEPA, 2005g)
- Ethylene Dibromide (EDB; 1,2-Dibromoethane) (USEPA, 2004a)
- Glyphosate (USEPA, 2007d)
- Hexachlorocyclopentadiene (USEPA, 2001b)
- Lindane (gamma-Hexachlorocyclohexane) (USEPA, 2006h)
- Oxamyl (Vydate) (USEPA, 2000c)
- Simazine (USEPA, 2006f)
- Toluene (USEPA, 2005f)
- 1,1,1-Trichloroethane (USEPA 2007e)
- Vinyl chloride (USEPA, 2000d)
- Xylenes (Total) (USEPA, 2003d)

4.3.2 Group 2: Chemicals with No Concern Based on Agency Assessment Published Prior to 1997 that Adequately Addressed Reproductive/Developmental Toxicity

For the following 6 chemicals in List B (Group 2), the RfD was developed before 1997, and the RfD documentation does address reproductive and developmental toxicity, either in the context of the database uncertainty factor, or in the context of a modifying factor (which predated the database uncertainty factor). Literature search updates were conducted for these chemicals, as noted above, to screen for new data. No new information was found that would result in a change to the database or modifying factor, with the exception of 1,2,4-trichlorobenzene, for which a new assessment is recommended. Based on the existing documentation and the results of the literature searches, there was no concern at the MCLG for reproductive or developmental effects for these chemicals.

- Dalapon (2,2-Dichloropropionic Acid) (USEPA, 1989a)
- Dinoseb (USEPA, 1989b)
- Methoxychlor (USEPA, 1991c)
- Picloram (USEPA, 1995b)
- Toxaphene (USEPA, 1991d)
- 1,2,4-Trichlorobenzene (USEPA, 1996b)

4.3.3 Group 3: Chemicals with No Concern Because Reproductive/Developmental Effects Seen Only at Doses at or Above the Effect Level for RfD

For the following four chemicals (Group 3) for which the RfD was developed before 1997, and for which there is no explicit documentation that the database uncertainty factor was considered as part of the assessment, literature searches were conducted, as described above. No studies were identified that would affect the RfD, although key new studies of reproductive toxicity of mercury were identified (Kahn et al, 2004; Atkinson et al., 2001). For the chemicals, other than mercury, there was no concern for reproductive or developmental effects at the MCL because such effects were seen only at doses comparable to or higher than the effect levels for the critical effect(s) used as the basis for the RfD and MCLG, taking into account other available information about the chemical and its effects, as well as data limitations.

The LOAEL from the Kahn et al. (2004) one-generation study of mercury is slightly below the LOAEL that served as the point of departure for the IRIS RfD (0.18 mg/kg-day vs 0.29 mg/kg-day). Decreased fertility was the critical effect, but the fertility index for all 3 dose groups (Table 3) was the same, 16% as compared to 44% for the controls. The poor fertility prevented the planned second generation component of this study. A comparable study by the same research group (Atkinson et al., 2001) using Sprague-Dawley rats also identified effects on fertility in the F₀ generation, with a LOAEL of 0.37 mg/kg-day for the males and 0.56 mg/kg-day for the paired females. Both the fertility index and live birth index were co-critical for the first generation. In the second generation there were no significant effects on fertility for any dose group. Clinical signs of toxicity (dermatologic effects) observed in the F₀ animals were not seen in the F₁ and F₂ animals, and the LOAEL for the live birth index in the F₂ generation increased to 0.74 mg/kg-day for the males and 1.1 mg/kg-day for the paired females. Although fertility was decreased in F₀ adults exposed to mercury, the offspring of those that conceived were resistant to the effects of mercury on fertility at the doses tested and more resistant than their parents' generation to the effects on live births. Under these circumstances, the 0.29 mg/kg-day LOAEL for autoimmune glomerulonephritis that is the basis for the RfD with a 1000-fold uncertainty factor appears to be adequately protective as the basis for the MCLG for mercury; therefore, a new assessment was not recommended. Additional research on the reproductive-developmental effects of mercury, building upon the studies of Kahn et al. (2004) and Atkinson et al. (2001), and including determination of whether one sex is more sensitive than the other, is justified.

- Endrin (USEPA, 1991e)
- Epichlorohydrin (USEPA, 1991b)
- Heptachlor Epoxide (USEPA, 1992g)
- Mercury (Inorganic) (USEPA, 1997a)

4.3.4 Group 4: Chemicals with No Concern Because Reproductive/Developmental Effects Occur at Doses Significantly Higher than the Intake at the MCL

Group 4 contains two carcinogens (with MCLGs of zero) for which there is no RfD ((1,2-dibromo-3-chloropropane (DBCP), and 1,2-dichloropropane), and two for which there is significant new noncancer data (heptachlor and hexachlorobenzene)). Literature search updates

were conducted for these chemicals, as described above. Based on this information, and the existing assessments, there was no concern for reproductive or developmental effects at the MCL for DBCP and 1,2-dichloropropane. DBCP and 1,2-dichloropropane are B2 carcinogens, for which the MCL is based on the practical quantitation limit (PQL; MCLG = 0). For these two chemicals, the reproductive/developmental effects were observed at doses significantly higher than the intake from drinking water (in mg/kg-day) at the MCL (assuming 2 L/day and 70 kg body weight). Therefore, the existing MCL is protective of reproductive and developmental effects. No new MCL is being proposed for these chemicals.

Heptachlor and hexachlorobenzene are carcinogens that are borderline for their developmental and reproductive effects. For both chemicals, the MCL is based on the PQL, but the intake from drinking water (in mg/kg-day) at the MCL (assuming 2 L/day and 70 kg body weight) is relatively close (less than a factor of 1000 lower) to the effect level for reproductive/developmental effects. However, these two chemicals (heptachlor and hexachlorobenzene) are not of concern because they are cancelled pesticides and occurrence is low.

- 1,2-Dibromo-3-chloropropane (DBCP)
- 1,2-Dichloropropane
- Heptachlor
- Hexachlorobenzene

4.3.5 Group 5: Chemicals with Significant Data Limitations Affecting Evaluation of Reproductive/Developmental Toxicity at the MCL

For three chemicals from List B (Group 5) (1,1,2-trichloroethane, 2,4,5-TP, and monochlorobenzene), limitations to the data precluded assessment of sensitive effect levels for reproductive and developmental toxicity, even after considering data identified in the updated literature search described above. These limitations either reflected the complete absence of adequate studies evaluating a sufficient range of endpoints, or the observation of reproductive or developmental toxicity via one route of exposure (e.g., via inhalation) in the absence of adequate oral studies evaluating those endpoints, or other significant issues affecting the assessment. For these three chemicals, additional research to improve the data quality could be useful, depending on whether occurrence data indicate that exposure is sufficient to warrant the research.

- Monochlorobenzene (Chlorobenzene)
- 2,4,5-TP (Silvex; 2,4,5-Trichlorophenoxypropionic Acid)
- 1,1,2-Trichloroethane

4.3.6 Group 6: Chemicals for which Reproductive/Developmental Effects Are a Potential Concern at the Current or Possible New MCLG

There are three chemicals from List B for which reproductive or developmental toxicity is a potential concern at the current or possible new MCLG (Group 6): nitrate, nitrite, and selenium, all three of which are also recommended for consideration for a new assessment.

- Nitrate (as N)
- Nitrite (as N)
- Selenium

As noted above in Section 4.2, new animal studies (Mukhopadhyay et al., 2005; Zaki et al., 2004) and epidemiology data (Tajtakova et al., 2006) suggest that nitrate in drinking water can have adverse effects on the thyroid, consistent with a known MOA for nitrate as a competitive inhibitor of iodide uptake in the thyroid (Wolff and Maurey, 1963); nitrite also acts as a competitive inhibitor of iodide uptake (Wolff and Maurey, 1963). The activity at the thyroid raises the concern about potential neurodevelopmental effects, but a number of issues relating to the MOA, including the unique sensitivity of rodents, thyroid homeostasis, and determination of the critical effect, need to be evaluated. Neurodevelopmental effects of nitrate (Markel et al., 1989) and nitrite (Vorhees et al., 1984) have been observed, but NAS (1995) considered the effects secondary to effects on learning behavior, rather than a direct effect of nitrate.

Several new relevant studies may affect the selenium RfD. The Hawkes and Keim (2003) study of selenium reported thyroid hormone and related metabolism changes in subjects treated with deficient, sufficient, and excess dietary selenium. The excess selenium dose was associated with a slight decrease in T3 levels, a thyrotropin increase, and an increase in body weight compared to the selenium-sufficient subjects. The opposite responses occurred in the selenium-deficient subjects. In addition, studies have reported changes in sperm parameters and fertility in mice fed either selenium-deficient or excess selenium diets containing sodium selenite, compared to adequate selenium diets (Shalini and Bansal, 2006; Kaur and Bansal, 2005). Changes in sperm parameters were also observed in F334 rats given sodium selenite in drinking water (NTP, 1994), but this study did not find these effects in mice given sodium selenite or in rats or mice given sodium selenate. The original RfD for selenium was based on blood levels of selenium in the human population studied, and did not differentiate between the essential selenoproteins and selenoamino acids (selenomethionine and selenocysteine) and inorganic selenium. Current knowledge about the biological role of selenoproteins, selenium essentiality, and various dietary sources of selenium, suggest a need to possibly differentiate between inorganic and organic selenium as part of the updated health effects assessment.

5. Summary

The 1996 amendments to the Safe Drinking Water Act (SDWA) require the United States Environmental Protection Agency (EPA) to review and, if appropriate, revise each existing NPDWR no less often than every six years. The Office of Water of EPA is conducting the Six-Year Review 2 of 71 water contaminants currently regulated under the SDWA. These include 66 chemicals that were considered in the Six-Year Review 1 in 2003 plus 5 others (arsenic, uranium, combined radiums (226 and 228), alpha particle emitters, and beta particle and photon emitters) for which new regulations have been promulgated more recently.

Because the 30 List A chemicals are the subject of ongoing EPA assessments, the Agency is not making any recommendations regarding changes to the MCLG for these chemicals at this time.

This assessment focused therefore on the evaluation of the 41 List B chemicals to determine whether new information is available that could affect the MCLGs and perhaps the MCLs. Assessments prepared by a wide range of authoritative bodies were reviewed, and the published literature was searched for new data on general toxicity, reproductive/ developmental toxicity, and carcinogenicity.

Based on this assessment, EPA identified 14 List B chemicals that had changes to their OPP or IRIS health assessments; these revisions suggest the need to consider potential changes to the MCLGs. These 14 chemicals are:

- Alachlor
- Barium
- 2,4-D (2,4-Dichlorophenoxyacetic Acid)
- 1,1-Dichloroethylene
- Diquat
- Endothall
- Glyphosate
- Hexachlorocyclopentadiene
- Lindane
- Oxamyl (Vydate)
- Picloram
- Toluene
- 1,1,1-Trichloroethane
- Xylenes (Total)

Note that the identification of chemicals qualifying for revision was conducted based on health effects and is independent of other considerations (e.g., analytical and treatment technology, occurrence data) that may influence the final selection of contaminants to be revised.

For the remaining 27 List B chemicals, the Agency did not find a reason to consider a change to the MCLG at this time. In most cases, current information indicates there is no health effects basis for an MCLG change. However, five chemicals were identified for which new assessments may be needed, based on the availability of new data. These chemicals are (with the two forms of chromium counting as one chemical together):

- Chromium
- Nitrate (as N)
- Nitrite (as N)
- Selenium
- 1,2,4-Trichlorobenzene

Two additional chemicals are not being recommended for new assessments, but they may require further evaluation, based on the availability of new data:

- Atrazine
- Simazine

For one additional chemical, carbofuran, EPA is awaiting further information on revocation of tolerances before taking any action.

In addition to these MCLG and new assessment recommendations, it is also important to note that there are four chemicals for which reproductive or developmental toxicity is a potential concern at the current or possible new MCLG. These are mercury, nitrate, nitrite, and selenium. Nitrite, nitrate, and selenium are recommended for new assessments. Research on gender sensitivity that builds on the studies of Kahn et al. (2004) and Atkinson et al. (2001) is recommended for mercury. Atrazine and simazine have an updated Agency assessment that evaluated reproductive and developmental effects. However, on October 7, 2009, the Agency announced its intent to launch a comprehensive reevaluation of the risk assessment for atrazine. Included in this new evaluation will be the most recent studies on atrazine and its potential association with birth defects, low birth weight, and premature births. Since the simazine assessment is based on studies using atrazine, any reevaluation of simazine relies on the reevaluation of atrazine. Three other chemicals (1,1,2-trichloroethane, 2,4,5-TP, monochlorobenzene) were also found to have substantive data gaps related to developmental and/or reproductive effects that make it difficult to determine if the MCLG is adequately protective. Additional research on these endpoints may be warranted for these chemicals, depending on the occurrence data.

Table 2. Summary of U.S. EPA Assessments for Six-Year Review 2 Chemicals^{10*}

Chemical (Date of regulation) (List A or B)	EPA/OW National Primary Drinking Water Regulation (NPDWR)					IRIS		OPP	
	MCLG mg/L	MCL mg/L (basis if MCL≠ MCLG)	RfD (mg/kg-day)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (Year of guidelines used)	DWEL (mg/L) & RSC	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/Citation	Cancer classification (year of guidelines used; year of assessment)	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (year of guidelines used; year of assessment)
Acrylamide (1991) (A)	0	Treatment technology ¹¹	0.0002/ 0.2 (NOAEL)/ 1000 (10H, 10A, 10S) neuropathic lesions/ Burek et al. 1980	B2, Probable human carcinogen (1986 guidelines)	0.007	0.0002 (1991)/ 0.2 (NOAEL)/ 1000 (10H, 10A, 10S) neuropathic lesions/ Burek et al. 1980 ¹²	B2, Probable human carcinogen (1986 guidelines, 1993) ¹³	--	--

¹⁰ For some chemicals, particularly pesticides, different offices cited the same study in different ways. To aid in clarity, when it could be confirmed that different references referred to the same study, a single consistent citation was used. When draft versions of updates to IRIS or OW documents are publicly available, the results of these assessments are also presented. However, it should be noted that these values are preliminary and subject to change.

¹¹ The NPDWR did not establish a MCL but did impose a treatment technology (TT) requirement that limits the allowable monomer levels in products used during drinking water treatment, storage, and distribution to 0.05 % acrylamide in polyacrylamide coagulant aids dosed at 1 part per million (ppm).

¹² An EPA risk assessment for acrylamide is currently in process. The IRIS Substance Assessment Tracking system website (<http://cfpub.epa.gov/ncea/iristrac/index.cfm>) should be consulted for the most current information on the status of this assessment. Based on the External Review Draft, acrylamide is classified as likely to be carcinogenic to humans. The updated IRIS RfD is 0.003 mg/kg-day based on a HEC of 0.076 mg/kg-day derived from a PBTK model for increased incidence of degenerative lesions of peripheral nerves in oral rat chronic studies (Johnson et al., 1986; Freidman et al., 1995) and an UF of 30 (10H, 3A).

¹³ An EPA health effects assessment for acrylamide is currently in process. Based on the IRIS External Review Draft acrylamide is classified as likely to be carcinogenic to humans.

Table 2. Summary of U.S. EPA Assessments for Six-Year Review 2 Chemicals^{10*}

Chemical (Date of regulation) (List A or B)	EPA/OW National Primary Drinking Water Regulation (NPDWR)					IRIS		OPP	
	MCLG mg/L	MCL mg/L (basis if MCL≠MCLG)	RfD (mg/kg-day)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (Year of guidelines used)	DWEL (mg/L) & RSC	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/Citation	Cancer classification (year of guidelines used; year of assessment)	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (year of guidelines used; year of assessment)
Alachlor (1991) (B)	0	0.002 (PQL)	0.01/ 1 mg/kg-day (NOAEL)/ 100 (10H, 10A)/ Hemosiderosis, hemolytic anemia/ Naylor et al. 1984	B2, Probable human carcinogen (1986 guidelines)	0.350 ug/L --	0.01 (1993)/ 1 mg/kg-day (NOAEL)/ 100 (10H, 10A)/ Hemosiderosis, hemolytic anemia/ Naylor et al. 1984	--	0.01 (1998)/ 1 mg/kg-day (NOAEL)/ 100 (10H, 10A)/ Hemosiderosis, hemolytic anemia/ Naylor et al. 1984 0.005 (1998d) ¹⁴ / 0.5 mg/kg-day (NOAEL) / 100 (10H, 10A)/ /nasal tumors/ Stout et al. 1984	“likely” to be a human carcinogen at high doses, but “not likely” at low doses, by all routes of exposure (1996 guidelines; 1998)
Alpha Particle Emitters (2000) (A)	0	15 pCi/L ¹⁵	--	A, Known human carcinogen (1986 guidelines)	--		-	--	--

¹⁴ The data indicate that alachlor’s tumorigenicity is operating by a nonlinear mode of action. OPP (USEPA, 1998d, 2001e, 2006g) concluded that alachlor causes nasal turbinate tumors via the generation of a reactive metabolite that leads to cytotoxicity and regenerative proliferation in the nasal epithelium; sustained cytotoxicity and proliferation is needed to lead to neoplasia. Based on this MOA assessment a non-linear dose response assessment is appropriate and the MCLG of 0 is no longer appropriate. Therefore, using the POD of 0.5 mg/kg-day identified by OPP for this endpoint and the UF of 100 (10H, 10A) would result in a health reference value of 0.005 mg/kg-day. Assuming 70 kg body weight, 2 L/day water consumption, and a 20% RSC, a water concentration derived from this value is 0.035 mg/L (rounded to 0.04 mg/L). The new MCLG would be based on the nonlinear cancer assessment.

¹⁵ ORIA is the principal health assessor for radionuclides. The 2000 radionuclides rule was a collaboration between OW and ORIA. See 40 CFR 141. The alpha particle emitters MCL excludes radon and uranium, but includes radium-226. A health assessment for alpha particle emitters is currently in progress. Because ORIA is conducting the assessment, alpha particle emitters are not addressed on the IRIS Substance Assessment Tracking system website, so the expected completion date is not publicly available.

Table 2. Summary of U.S. EPA Assessments for Six-Year Review 2 Chemicals^{10*}

Chemical (Date of regulation) (List A or B)	EPA/OW National Primary Drinking Water Regulation (NPDWR)					IRIS		OPP	
	MCLG mg/L	MCL mg/L (basis if MCL≠MCLG)	RfD (mg/kg-day)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (Year of guidelines used)	DWEL (mg/L) & RSC	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/Citation	Cancer classification (year of guidelines used; year of assessment)	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (year of guidelines used; year of assessment)
Antimony (1992) (A)	0.006	0.006	0.0004/0.43 (LOAEL)/1000 (10H, 10A, 10L)/ Decreased longevity, altered blood glucose and cholesterol/ Schroeder et al. 1970	D, not classifiable as to human carcinogenicity (1986 guidelines)	0.014 40%	0.0004 (1991) ¹⁶ /0.35 (LOAEL)/1000 (10H, 10A, 10L)/ Longevity, blood glucose, and cholesterol/ Schroeder et al. 1970	--	--	--
Arsenic (2001) (A)	0	0.01 ¹⁷	-- ¹⁸	A, Known human carcinogen (1986 guidelines)	--	0.0003 (1993) ¹⁹ /0.0008 (NOAEL)/3 (lack of reproductive and sensitivity data)/ Hyper-pigmentation, keratosis and possible vascular/ Tseng 1977 Tseng et al. 1968	A, Known human carcinogen (1986 guidelines, 1994) ²⁰	--	--

¹⁶ The IRIS reassessment of the health risks resulting from exposure to antimony identified during the first six-year review (USEPA, 2002h) is still in progress. The IRIS Substance Assessment Tracking system website (<http://cfpub.epa.gov/ncea/iristrac/index.cfm>) should be consulted for the most current information on the status of this assessment. Also, although the RfDs calculated for the NPDWR and for IRIS are based on the same study, their LOAELs differ; this may be due to different assumptions used in converting the LOAEL dose of 5 parts per million to mg/kg/day.

¹⁷ The MCL was set as close to the MCLG as feasible, taking into account costs and benefit, including the new discretionary authority for the Administrator to set an MCL less stringent than the feasible level if the benefits of an MCL set at the feasible level would not justify the costs.

¹⁸ Neither the arsenic rule nor the NRC reports conducted a dose response assessment for noncancer effects to develop an RfD.

¹⁹ EPA's draft Toxicological Review for arsenic (USEPA, 2005h) does not present an updated noncancer dose response assessment; therefore, the RfD currently on IRIS is the most appropriate. An IRIS assessment is currently in process. The IRIS Substance Assessment Tracking system website (<http://cfpub.epa.gov/ncea/iristrac/index.cfm>) should be consulted for the most current information on the status of this assessment.

Table 2. Summary of U.S. EPA Assessments for Six-Year Review 2 Chemicals^{10*}

Chemical (Date of regulation) (List A or B)	EPA/OW National Primary Drinking Water Regulation (NPDWR)					IRIS		OPP	
	MCLG mg/L	MCL mg/L (basis if MCL≠MCLG)	RfD (mg/kg-day)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (Year of guidelines used)	DWEL (mg/L) & RSC	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/Citation	Cancer classification (year of guidelines used; year of assessment)	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (year of guidelines used; year of assessment)
Asbestos (1991) (A)	7 million fibers/L	7 million fibers/L	--	Not available via ingestion; A, known human carcinogen (1986 guidelines) via inhalation	--	--	Not available via ingestion ²¹ ; A, known human carcinogen (1986 guidelines) via inhalation	--	--
Atrazine (1991) (B)	0.003	0.003	0.005/ 0.5 (NOAEL)/ 100 (10H, 10A)/ Decreased body weight gain in F2 pups; maternal toxicity/ Ciba-Geigy 1987	C, possible human carcinogen (1986 guidelines)	0.175 20% Also factor of 10 for class C	0.035 (1993)/ 3.5 (NOAEL)/ 100 (10H, 10A)/ Decreased body weight gain/ Ciba-Geigy 1986	--	0.018 (2006)/ 1.8 (NOAEL)/ 100 (10H, 10A)/ FQPA: 10 attenuation of the luteinizing hormone surge in females in a 6-month rat feeding study / Morseth et al. 1996	Not likely to be carcinogenic to humans (2006, 1999 guidelines) (Note that, although document was finalized in 2006, assessment was done in 2002, so used 1999 guidelines)

²⁰ EPA's draft Toxicological Review for arsenic (USEPA, 2005h) characterized arsenic as "carcinogenic to humans" (2005 guidelines (USEPA, 2005a)). An IRIS assessment is currently in process. The IRIS Substance Assessment Tracking system website (<http://cfpub.epa.gov/ncea/iristrac/index.cfm>) should be consulted for the most current information on the status of this assessment.

²¹ The IRIS reassessment of the noncancer health risks resulting from exposure to asbestos identified during the first six-year review (USEPA, 2002h) is still in progress.

Table 2. Summary of U.S. EPA Assessments for Six-Year Review 2 Chemicals^{10*}

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	MCLG mg/L	MCL mg/L (basis if MCL≠MCLG)	RfD (mg/kg-day)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (Year of guidelines used)	DWEL (mg/L) & RSC	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/Citation	Cancer classification (year of guidelines used; year of assessment)	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (year of guidelines used; year of assessment)
Barium (1991) (B)	2	2	0.07/ 0.21 (adjusted NOAEL)/ 3 H/ No changes in blood pressure, or serum chemistry / Wones et al. 1990	D, not classifiable as to human carcinogenicity (1986 guidelines)	2 100%	0.2 (2005)/ 63 (BMDL05); 84 (BMD05)/ 300 (10H, 10A, 3D)/ Nephropathy/ NTP 1994	Not likely to be carcinogenic to humans following oral exposure (1996 guidelines; 1998)	--	--
Benzene (1987) (B)	0	0.005 (PQL)	0.0007 – 0.002 (implied from the AADI)/ 1 (NOAEL)/ 1000 (10H, 10A, 10S)/ Slight leukopenia and erythrocytopenia/ Wolf et al. 1956	Group A, known human carcinogen (1984 proposed guidelines)	--	0.004 (2003)/ 1.2 (BMDL)/ 300 (10H, 3L, 3S, 3D)/ Decreased lymphocyte count/ Rothman et al. 1996	Known human carcinogen for all routes of exposure (1996 guidelines; 2000)	--	--
Benzo(a)pyrene (1992) (A)	0	0.0002 (PQL; analytical feasibility)	-- ²²	B2, Probable human carcinogen (1986 guidelines)	--	-- ²³	B2, Probable human carcinogen (1986 guidelines; 1994) ²⁴	--	--

²² The Office of Water Criteria Document (USEPA,1991cc) has not derived a Reference Dose (RfD) or a Drinking Water Exposure Level (DWEL) based on non-carcinogenic effects due to evidence of carcinogenicity at lower doses than those associated with systemic toxicity.

²³ An EPA risk assessment for BaP is currently in process. The IRIS Substance Assessment Tracking system website (<http://cfpub.epa.gov/ncea/irisstrac/index.cfm>) should be consulted for the most current information on the status of this assessment.

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Chemical (Date of regulation) (List A or B)	EPA/OW National Primary Drinking Water Regulation (NPDWR)					IRIS		OPP	
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Beryllium (1992) (A)	0.004	0.004	0.005/ 0.538 (NOAEL)/ 100 (10H, 10A)/ No effect/ Schroeder and Mitchener 1975	B2, probable human carcinogen (1986 guidelines)	0.2 20% Also factor of 10 for category II	0.002 (1998)/ 0.46 (BMDL10)/ 300 (10H, 10A, 3D)/ Ulcerative inflammatory lesions of small intestine/ Morgareidge et al. 1976 ²⁵	Carcinogenic potential of ingested beryllium cannot be determined (1996 guidelines; 1998) ²⁶	--	--
Beta Particle and Photon Emitters (2000) (A)	0	4 mrem/year ²⁷	--	A, Known human carcinogen (1986 guidelines)	--	--	--	--	--

²⁴ An EPA health effects assessment for BaP is currently in process. The IRIS Substance Assessment Tracking system website (<http://cfpub.epa.gov/ncea/iristrac/index.cfm>) should be consulted for the most current information on the status of this assessment.

²⁵ An EPA health effects assessment for beryllium is currently in progress. The IRIS Substance Assessment Tracking system website (<http://cfpub.epa.gov/ncea/iristrac/index.cfm>) should be consulted for the most current information on the status of this assessment.

²⁶ An EPA health effects assessment for beryllium is currently in progress. The IRIS Substance Assessment Tracking system website (<http://cfpub.epa.gov/ncea/iristrac/index.cfm>) should be consulted for the most current information on the status of this assessment.

²⁷ ORIA is the principal health assessor for radionuclides. A health assessment for beta particle and photon emitters is currently in progress. Because ORIA is conducting the assessment, beta particle and photon emitters are not addressed on the IRIS Substance Assessment Tracking system website, so the expected completion date is not publicly available. The 2000 radionuclides rule was a collaboration between OW and ORIA. See 40 CFR 141. The MCL is set as follows: “(a) The average annual concentration of beta particle and photon radioactivity from man-made radionuclides in drinking water shall not produce an annual dose equivalent to the total body or any internal organ greater than 4 millirem/year. (b) Except for the radionuclides listed in Table A [i.e., tritium and strontium-90], the concentration of manmade radionuclides causing 4 mrem total body or organ dose equivalents shall be calculated on the basis of a 2 liter per day drinking water intake using the 168 hour data listed in “Maximum Permissible Body Burdens and Maximum Permissible Concentrations of Radionuclides in Air or Water

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	MCLG mg/L	MCL mg/L (basis if MCL≠MCLG)	RfD (mg/kg-day)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (Year of guidelines used)	DWEL (mg/L) & RSC	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/Citation	Cancer classification (year of guidelines used; year of assessment)	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (year of guidelines used; year of assessment)
Cadmium (1991) (A)	0.005	0.005	0.0005/0.005 (LOAEL)/ 10 (1H, 10L) estimated LOAEL in human study/ Renal dysfunction/ Friberg et al. 1974	Group D carcinogen, not classifiable as to human carcinogenicity by the oral route of exposure (1986 guidelines) ²⁸	0.18 25% ²⁹	Water ³⁰ : 0.0005 (1994) ³¹ / 0.005 (NOAEL)/ 10 (10H)/ Significant proteinuria/ USEPA 1985a Food: 0.001 (1994)/ 0.01 (NOAEL)/ 10 (10H)/ Significant proteinuria USEPA 1985a	B1, Probable human carcinogen (1986 guidelines, 1992; no quantitative assessment for the oral route) ³²	--	--

for Occupational Exposure,” NBS Handbook 69 as amended August 1963, U.S. Department of Commerce. If two or more radionuclides are present, the sum of their annual equivalent to the total body or to any organ shall not exceed 4 millirem/year”

²⁸ Because of inadequate dose-response data to characterize the presence or lack of a carcinogenic hazard from oral exposure, the Agency regulated cadmium as a Group D carcinogen, not classifiable as to human carcinogenicity by the oral route of exposure.

²⁹ This departure from the default RSC of 20% was based on evidence of greater bioavailability from water in comparison with food (54 FR 22062).

³⁰ Since the fraction of ingested Cd that is absorbed appears to vary with the source (e.g., food vs. drinking water), different % absorption was used for food and water in the toxicokinetic model used to extrapolate from concentration in the kidney to intake in food or water; i.e. 2.5% absorption of cadmium from food and 5% absorption of the total cadmium dose from water. The model also assumes that 0.01% of the total body burden of cadmium is excreted per day.

³¹ An EPA health effects assessment for cadmium is currently in process. The IRIS Substance Assessment Tracking system website (<http://cfpub.epa.gov/ncea/irisstrac/index.cfm>) should be consulted for the most current information on the status of this assessment.

³² An EPA health effects assessment for cadmium is currently in process. The IRIS Substance Assessment Tracking system website (<http://cfpub.epa.gov/ncea/irisstrac/index.cfm>) should be consulted for the most current information on the status of this assessment.

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Carbofuran (1991) (B)	0.04	0.04	0.005/0.5 (NOAEL)/100 (10H, 10A)/ Acetylcholinesterase inhibition and testicular degeneration/ FMC Corp. 1983	E, evidence of noncarcinogenicity (1986 guidelines)	0.175 20%	0.005 (1987)/0.5 (NOAEL)/100 (10H, 10A)/ RBC and plasma cholinesterase inhibition, and testicular and uterine effects/ FMC Corp. 1983	--	0.00006 (2006) ³³ 0.03 (BMDL10)/100 (10H, 10A, 5D) Brain acetylcholinesterase inhibition/ FMC Corp. 2005	Not likely to be a human carcinogen (2005 guidelines)
Carbon tetrachloride (1987) (A)	0	0.005 (PQL; analytical feasibility)	0.0007/0.71 mg/kg (adjusted NOAEL)/1000 (10H, 10A, 10S)/ Liver lesions/ Bruckner et al. 1986	B2, probable human carcinogen (1986 guidelines)	--	0.0007 (1991) ³⁴ /0.71 mg/kg (adjusted NOAEL)/1000 (10H, 10A, 10S)/ Liver lesions/ Bruckner et al. 1986	B2, probable human carcinogen (1986 guidelines, 1991) ³⁵	--	--

³³ OPP's value for carbofuran is an acute RfD for cholinesterase inhibition, which OPP has determined is protective of chronic exposures; this RfD is 0.00006 mg/kg-day. OPP has also derived an aPAD of 0.00006 mg/kg-day based on this RfD.

³⁴ The IRIS draft assessment (USEPA, 2008b) for carbon tetrachloride lists an RfD of 0.004 mg/kg-day based on an adjusted BMDL10 of 3.9 mg/kg-day for elevated serum sorbitol dehydrogenase (SDH) was identified as a specific and sensitive biomarker of liver toxicity with an UF of 1000 (10H, 10A, 3S, 3D). The IRIS Substance Assessment Tracking system website (<http://cfpub.epa.gov/ncea/iristrac/index.cfm>) should be consulted for the most current information on the status of this assessment.

³⁵ The IRIS draft assessment (USEPA, 2008b) for carbon tetrachloride lists a cancer classification of "likely to be carcinogenic to humans by all routes of exposure" under 2005 guidelines. The IRIS Substance Assessment Tracking system website (<http://cfpub.epa.gov/ncea/iristrac/index.cfm>) should be consulted for the most current information on the status of this assessment.

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Chlordane (1991) (B)	0	0.002 (PQL)	0.00005/ 0.045 (LOAEL)/ 1000 (10H, 10A, 10L)/ Liver necrosis in male rats/ Yonemura et al. 1983	B2, probable human carcinogen (1986 guidelines)	--	0.0005 (1998)/ 0.15 (NOAEL)/ 300 (10H, 10A, 3D)/ Liver necrosis in mice/ Khasawinah and Grutsch 1989	Likely to be a carcinogen by all routes of exposure (1996 guidelines; 1998)	--	--
Chromium (VI) (1991 – regulation applies to total chromium) (B)	0.1	0.1	0.0048/ 2.41 (NOAEL)/ 100 (10H, 10A); MF=5/ None/ MacKenzie et al. 1958	D, not classifiable as to human carcinogenicity (1986 guidelines)	0.17 70%	0.003 (1998)/ 2.5 (NOAEL)/ 300 (10H, 10A, 3S); MF=3/ None/ MacKenzie et al. 1958	By the oral route: D, not classifiable as to human carcinogenicity (1986 guidelines; 1998)	--	--

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Chromium (III) (1991 – regulation applies to total chromium) (B)	0.1	0.1	0.0048/ 2.41 (NOAEL)/ 100 (10H, 10A) ; MF=5/ None/ MacKenzie et al. 1958	D, not classifiable as to human carcinogenicity (1986 guidelines)	0.17 70%	1.5 (1998)/ 1468 (NOAEL)/ 100 (10H, 10A); MF=10/ None/ Ivankovic and Preussmann 1975	Inadequate data to determine the potential carcinogenicity (1996 guidelines; 1998)	--	--
Cyanide (1992) (A)	0.2	0.2	0.02 ³⁶ / 10.8 (NOAEL)/ 100 (10H, 10A) (MF=5 for apparent tolerance via food compared to water)/ Absence of clinical and histological effects/ Howard and Hanzal 1955	D ³⁷ , not classifiable as to human carcinogenicity (1986 guidelines)	0.7 20%	0.02 (1993)/ 10.8 (NOAEL)/ 100 (10H, 10A) (MF=5 for apparent tolerance via food compared to water)/ Absence of clinical and histological effects/ Howard and Hanzal 1955 Philbrick et al. 1979 ³⁸	D, not classifiable as to human carcinogenicity (1986 guidelines, 1991) ³⁹	-- ⁴⁰	-- ⁴¹

³⁶ A 2006 Drinking Water Criteria Document External Review Draft is available for cyanide and ready for peer review (USEPA, 2006i). An RfD of 0.004 mg/kg-day was proposed, based on a BMDL of 1.3 mg/kg-day for decreased spermatid heads/testis and spermatid count (NTP, 1993) and an uncertainty factor of 300 (10H, 10A, 3D).

³⁷ A 2006 Drinking Water Criteria Document External Review Draft is available for cyanide and ready for peer review (USEPA, 2006i). The assessment proposed that, under the USEPA (2005a) guidelines for carcinogen risk assessment, the data are inadequate for an assessment of the human carcinogenic potential of cyanide.

³⁸ An IRIS assessment of cyanide is currently in progress. The IRIS Substance Assessment Tracking system website (<http://cfpub.epa.gov/ncea/iristrac/index.cfm>) should be consulted for the most current information on the status of this assessment.

³⁹ An IRIS assessment of cyanide is currently in progress. The IRIS Substance Assessment Tracking system website (<http://cfpub.epa.gov/ncea/iristrac/index.cfm>) should be consulted for the most current information on the status of this assessment.

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2,4-D (2,4-Dichloro-phenoxyacetic Acid) (1991) (B)	0.07	0.07	0.01/ 1 (NOAEL)/ 100 (10H, 10A)/ Hematologic, hepatic and renal toxicity/ Serota et al. 1983	D, not classifiable as to human carcinogenicity (1986 guidelines)	0.35 20%	0.01 (1988)/ 1 (NOAEL)/ 100 (10H, 10A)/ Hematologic, hepatic and renal toxicity/ Serota et al.1983	--	0.005 (2005)/ 5 (NOAEL) 1000 (10H, 10A, 10D)/ Decreased body weight gain (in females) and alterations in hematology and blood chemistry (in both sexes)/ Jeffries et al. 1995	D, not classifiable as to human carcinogenicity (1986 guidelines)

⁴⁰ OPP (USEPA, 2006j) lists an RfD for cyanide of 0.004 mg/kg-day based on a LOAEL of 0.4 mg/kg-day (and lack of a NOAEL) and an UF of 100 (10H, 10X, for lack of a LOAEL, steep dose-response curve, and severity of toxic effect) for clinical signs including nausea, vomiting, headaches, dizziness (Moertel et al., 1981, 1982).

⁴¹ OPP (USEPA, 2006j) states (for cyanide) that “the classification of the carcinogenic potential could not be determined due to the absence of acceptable cancer studies in rats and mice.”

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Dalapon (2,2-Dichloropropionic Acid) (1992) (B)	0.2	0.2	0.03/8 (NOAEL)/300 (10H, 10A, 3D)/ Increased kidney weight/ Paynter et al. 1960	D, not classifiable as to human carcinogenicity (1986 guidelines)	0.9 20%	0.03 (1989)/8.45 (NOAEL)/300 (10H, 10A, 3D)/ Increased kidney weight/ Paynter et al. 1960	--	--	--
Di(2-ethylhexyl) adipate (DEHA) (1992) (A)	0.4	0.4	0.6/170 (NOAEL)/300 (10H, 10A, 3 S and D combined)/ Body and liver weight changes in parents, reduced ossification and slightly dilated ureters in fetuses; reduced offspring weight gain, total litter weight, and litter size/ ICI 1988a,b	C, Possible human carcinogen (1986 guidelines)	20 20%	0.6 (1992) ⁴² /170 (NOAEL)/300 (10H, 10A, 3 S and D combined)/ Body and liver weight changes in parents, reduced ossification and slightly dilated ureters in fetuses; reduced offspring weight gain, total litter weight, and litter size/ ICI 1988a,b	C, Possible human carcinogen (1986 guidelines; 1994) ⁴³	--	--

⁴² An EPA health effects assessment for di(2 ethylhexyl) adipate is currently in process. The IRIS Substance Assessment Tracking system website (<http://cfpub.epa.gov/ncea/iristrac/index.cfm>) should be consulted for the most current information on the status of this assessment.

⁴³ An EPA health effects assessment for di(2 ethylhexyl) adipate is currently in process. The IRIS Substance Assessment Tracking system website (<http://cfpub.epa.gov/ncea/iristrac/index.cfm>) should be consulted for the most current information on the status of this assessment.

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Di(2-ethylhexyl) phthalate (DEHP) (1991) (A)	0	0.006 (PQL; analytical feasibility)	0.02/ 19 (LOAEL)/ 1000 (10H,10A, 10L/S for less than chronic study and LOAEL)/ Increase in relative liver weights/ Carpenter et al. 1953	B2, probable human carcinogen (1986 guidelines)	0.7 --	0.02 (1991) ⁴⁴ / 19 (LOAEL)/ 1000 (10H,10A, 10L/S for less than chronic study and LOAEL)/ Increase in relative liver weights/ Carpenter et al. 1953	B2, probable human carcinogen (1986 guidelines; 1993) ⁴⁵	--	--
1,2-Dibromo-3-chloropropane (DBCP) (1991) (B)	0	0.0002 (PQL)	--	B2, probable human carcinogen (1986 guidelines)	--	--	--	--	--

⁴⁴ A health effects assessment for DEHP is currently in process. The IRIS Substance Assessment Tracking system website (<http://cfpub.epa.gov/ncea/irisrac/index.cfm>) should be consulted for the most current information on the status of this assessment.

⁴⁵ A health effects assessment for DEHP is currently in process The IRIS Substance Assessment Tracking system website (<http://cfpub.epa.gov/ncea/irisrac/index.cfm>) should be consulted for the most current information on the status of this assessment.

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1,2-Dichlorobenzene (o-Dichlorobenzene) (1991) (A)	0.6	0.6	0.09/85.7 (NOAEL)/1000 (10H, 10A, 10D)/ No treatment-related adverse effects noted; renal tubular regeneration noted but not interpreted as dose-related/ NTP 1985	D, not classifiable as to human carcinogenicity (1986 guidelines)	3 20%	0.09 (1991) ⁴⁶ 85.7 (NOAEL)/1000 (10H, 10A, 10D), No treatment-related adverse effects noted; renal tubular regeneration noted but not interpreted as dose-related/ NTP 1985	D ⁴⁷ , not classifiable as to human carcinogenicity (1986 guidelines, 1991)	--	--

⁴⁶An IRIS External Review Draft for the dichlorobenzenes is available. It proposes a draft RfD of 0.03 mg/kg-day for 1,2-dichlorobenzene, based on a BMDL10 of 29.8 mg/kg-day for renal tubular degeneration (NTP, 1985), incorporating an uncertainty factor of 1000 (10A, 10H, 10D). The IRIS Substance Assessment Tracking system website (<http://cfpub.epa.gov/ncea/iristrac/index.cfm>) should be consulted for the most current information on the status of this assessment.

⁴⁷In the IRIS External Review Draft for the dichlorobenzenes, the draft cancer assessment is “inadequate information to assess carcinogenic potential” under the 2005 cancer guidelines. The IRIS Substance Assessment Tracking system website (<http://cfpub.epa.gov/ncea/iristrac/index.cfm>) should be consulted for the most current information on the status of this assessment.

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Chemical (Date of regulation) (List A or B)	EPA/OW National Primary Drinking Water Regulation (NPDWR)					IRIS		OPP	
	MCLG mg/L	MCL mg/L (basis if MCL≠MCLG)	RfD (mg/kg-day)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (Year of guidelines used)	DWEL (mg/L) & RSC	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/Citation	Cancer classification (year of guidelines used; year of assessment)	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (year of guidelines used; year of assessment)
1,4-Dichlorobenzene (p-Dichlorobenzene) (1987) (A)	0.075	0.075	0.1/150 (adjusted: 107 mg/kg-day) (NOAEL)/1000 (10H, 10A, 10S)/ Renal cortical degeneration in male rats/ Battelle 1980 NTP 1987	C, Possible human carcinogen (1986 guidelines)	3.75 20% (and a factor of 10 for class C, possible carcinogenicity)	-- ⁴⁸	-- ⁴⁹	--	--
1,2-Dichloroethane (Ethylene Dichloride) (1987) (A)	0	0.005 (PQL)	--	B2, probable human carcinogen (1986 guidelines)	--	-- ⁵⁰	B2 (1986 guidelines; 1991)	--	--

⁴⁸ An IRIS External Review Draft for the dichlorobenzenes is available. The IRIS Substance Assessment Tracking system website (<http://cfpub.epa.gov/ncea/irisrac/index.cfm>) should be consulted for the most current information on the status of this assessment. An RfD of 0.03 mg/kg-day was derived for 1,4-dichlorobenzene, based on a BMDL₁₀ of 9.06 mg/kg-day for hepatocellular hypertrophy (Naylor and Stout, 1996, cited as Monsanto, 1996) and an uncertainty factor of 10 (10H, 10A, 3D).

⁴⁹ In the IRIS External Review Draft for the dichlorobenzenes, the draft cancer assessment is “likely to be carcinogenic to humans by both the oral and inhalation routes” under the 2005 cancer guidelines. The IRIS Substance Assessment Tracking system website (<http://cfpub.epa.gov/ncea/irisrac/index.cfm>) should be consulted for the most current information on the status of this assessment.

⁵⁰ The IRIS reassessment of the health effects resulting from exposure to 1,2-dichloroethane identified during the first six-year review (USEPA, 2002f) is still in progress. The IRIS Substance Assessment Tracking system website (<http://cfpub.epa.gov/ncea/irisrac/index.cfm>) should be consulted for the most current information on the status of this assessment.

Table 2. Summary of U.S. EPA Assessments for Six-Year Review 2 Chemicals^{10*}

Chemical (Date of regulation) (List A or B)	EPA/OW National Primary Drinking Water Regulation (NPDWR)					IRIS		OPP	
	MCLG mg/L	MCL mg/L (basis if MCL≠MCLG)	RfD (mg/kg-day)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (Year of guidelines used)	DWEL (mg/L) & RSC	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/Citation	Cancer classification (year of guidelines used; year of assessment)	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (year of guidelines used; year of assessment)
1,1-Dichloroethylene (1987) (B)	0.007	0.007	0.01/ 10 (LOAEL)/ 1000 (10H, 10A, 10L)/ Liver toxicity (fatty change)/ Quast et al. 1983	C, possible human carcinogen (1986 guidelines)	0.35 20% Also factor of 10 for class C	0.05 (2002)/ 4.6 (BMDL10)/ 100 (10H, 10A)/ Liver toxicity (fatty change)/ Quast et al. 1983	Inadequate for an assessment of human carcinogenic potential by the oral route (1999 guidelines; 2002)	--	--
<i>cis</i> -1,2-Dichloroethylene (1991) (A)	0.07	0.07	0.01/ 32 (NOAEL)/ 3000 (10H, 10A, 10L, 3D)/ Decreases in hematocrit/ McCauley et al. 1990	--	0.35 20%	-- ⁵¹	D, not classifiable as to human carcinogenicity (1986 guidelines, 1995) ⁵²	--	--

⁵¹ An IRIS assessment (USEPA, 2007f) for *cis*-1,2-dichloroethylene lists an RfD of 0.01 mg/kg-day based on a BMDL10 of 30.4 mg/kg-day and an UF of 3000 (10A, 10H, 10S, 3D) for increased relative liver weight in male and female rats (McCauley et al., 1990, 1995). The IRIS Substance Assessment Tracking system website (<http://cfpub.epa.gov/ncea/iristrac/index.cfm>) should be consulted for the most current information on the status of this assessment.

⁵² An IRIS assessment for *cis*-1,2-dichloroethylene lists the cancer classification as “inadequate information to assess carcinogenic potential” under 2005 guidelines. The IRIS Substance Assessment Tracking system website (<http://cfpub.epa.gov/ncea/iristrac/index.cfm>) should be consulted for the most current information on the status of this assessment.

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Chemical (Date of regulation) (List A or B)	EPA/OW National Primary Drinking Water Regulation (NPDWR)					IRIS		OPP	
	MCLG mg/L	MCL mg/L (basis if MCL≠MCLG)	RfD (mg/kg-day)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (Year of guidelines used)	DWEL (mg/L) & RSC	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/Citation	Cancer classification (year of guidelines used; year of assessment)	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (year of guidelines used; year of assessment)
<i>trans</i> -1,2-Dichloroethylene (1991) (A)	0.1	0.1	0.02/17 (NOAEL)/1000 (10H, 10A, 10S)/ Males: increases in serum alkaline phosphatase; females: decrease in relative thymus weight/ Barnes et al. 1985	D, not classifiable as to human carcinogenicity (1986 guidelines)	0.6 20%	0.02 ⁵³ (1989)/17 (NOAEL)/1000 (10H, 10A, 10S)/ Males: increases in serum alkaline phosphatase/ Barnes et al. 1985	-- ⁵⁴	--	--
Dichloromethane (Methylene Chloride) (1992) (A)	0	0.005 (PQL; analytical feasibility)	0.06/5.85 (NOAEL)/100 (10H, 10A)/ Liver toxicity/ Serota et al. 1986	--	2 --	0.06 (1988) ⁵⁵ /5.85 (NOAEL)/100 (10H, 10A)/ Liver toxicity/ NCA 1983	B2, probable human carcinogen (1986 guidelines; 1995)	--	--

⁵³ An updated EPA assessment for *trans*-1,2-dichloroethylene is currently undergoing inter-Agency review. The IRIS Substance Assessment Tracking system website (<http://cfpub.epa.gov/ncea/iristrac/index.cfm>) should be consulted for the most current information on the status of this assessment. The IRIS draft proposed a RfD of 0.30 mg/kg-day based on a BMDL₁₀ of 867.3 mg/kg-day for increased relative liver weight in male mice (NTP, 2002) divided by a composite uncertainty factor of 3000 (10A, 10H, 10S, 3D).

⁵⁴ The draft assessment for *trans*-1,2-dichloroethylene characterizes the data as “inadequate information to assess carcinogenic potential” under the EPA 2005 guidelines.

⁵⁵ IRIS is currently reassessing dichloromethane. The IRIS Substance Assessment Tracking system website (<http://cfpub.epa.gov/ncea/iristrac/index.cfm>) should be consulted for the most current information on the status of this assessment.

Table 2. Summary of U.S. EPA Assessments for Six-Year Review 2 Chemicals ^{10*}

Chemical (Date of regulation) (List A or B)	EPA/OW National Primary Drinking Water Regulation (NPDWR)					IRIS		OPP	
	MCLG mg/L	MCL mg/L (basis if MCL≠MCLG)	RfD (mg/kg-day)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (Year of guidelines used)	DWEL (mg/L) & RSC	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/Citation	Cancer classification (year of guidelines used; year of assessment)	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (year of guidelines used; year of assessment)
1,2-Dichloropropane (1991) (B)	0	0.005 (PQL)	--	B2, probable human carcinogen (1986 guidelines)	--	--	--	--	--
Dinoseb (1992) (B)	0.007	0.007	0.001/ 1 (LOAEL)/ 1000 (10H, 10A, 10L)/ Reduction in thyroid weight; endometrial hyperplasia and hypospermatogenesis; testicular degeneration/ Hazleton 1977 Brown 1981	D, not classifiable as to human carcinogenicity (1986 guidelines)	0.04 20%	0.001 (1989)/ 1 (LOAEL)/ 1000 (10H, 10A, 10L)/ Decreased pup weight during lactation period. Decreased parental weight gain/ Dow Chemical Company 1981	D, not classifiable as to human carcinogenicity (1986 guidelines; 1993)	--	--
Diquat (1992) (B)	0.02	0.02	0.002/ 0.22 (NOAEL)/ 100 (10H, 10A)/ Cataracts/ Colley 1985	D, not classifiable as to human carcinogenicity (1986 guidelines)	0.077 20%	0.0022 (1995)/ 0.22 (NOAEL)/ 100 (10H, 10A)/ Minimal lens opacity and cataracts/ Colley 1985	--	0.005 (1995,2001)/ 0.5 (NOAEL)/ 100 (10H, 10A)/ (Hopkins 1990)	E, evidence of noncarcinogenicity (1986 guidelines; 2001)

Table 2. Summary of U.S. EPA Assessments for Six-Year Review 2 Chemicals^{10*}

Chemical (Date of regulation) (List A or B)	EPA/OW National Primary Drinking Water Regulation (NPDWR)					IRIS		OPP	
	MCLG mg/L	MCL mg/L (basis if MCL≠MCLG)	RfD (mg/kg-day)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (Year of guidelines used)	DWEL (mg/L) & RSC	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/Citation	Cancer classification (year of guidelines used; year of assessment)	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (year of guidelines used; year of assessment)
Endothall (1992) (B)	0.1	0.1	0.02/ 2 (NOAEL)/ 100 (10H, 10A)/ Increased organ weight and organ-to-body weights for stomach and small intestine/ Keller 1965	D, not classifiable as to human carcinogenicity (1986 guidelines)	0.7 20%	0.02 (1991)/ 100 ppm, equivalent to 2 mg/kg-day (NOEL)/ 100 (10H, 10A)/ Increased absolute and relative weights of stomach and small intestine/ Keller 1965	--	0.007 (2005)/ 2 (LOAEL)/ 300 (10H, 10A, 3L)/ Proliferative lesions of the gastric epithelium/ Trutter 1995	Unlikely to be carcinogenic to humans (1999 guidelines)
Endrin (1992) (B)	0.002	0.002	0.0003/ 0.025 (NOAEL)/ 100 (10H, 10A)/ Mild histopathologic changes in liver, occasional convulsions/ Velsicol Chemical Corporation. 1969	D, not classifiable as to human carcinogenicity (1986 guidelines)	0.009 20%	0.0003 (1991)/ 0.025 (NOAEL)/ 100 (10H, 10A)/ Mild histopathologic changes in liver, occasional convulsions/ Velsicol Chemical Corporation. 1969	D, not classifiable as to human carcinogenicity (1986 guidelines; 1993; verified 1988)	--	--
Epichlorohydrin (1991) (B)	0	NA ⁵⁶	0.002/ 2.16 (LOAEL)/ 1000 (10H, 10A, 10L)/ Renal tubular degeneration/ Laskin et al. 1980	B2, probable human carcinogen (1986 guidelines)	--	--	B2, probable human carcinogen (1986 guidelines)	--	--

⁵⁶ Instead of an MCL, EPA specifies a treatment technique that limits the allowable level of epichlorohydrin monomer in the polymer that is added to drinking water as a flocculent to remove particulates.

Table 2. Summary of U.S. EPA Assessments for Six-Year Review 2 Chemicals^{10*}

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	MCLG mg/L	MCL mg/L (basis if MCL≠MCLG)	RfD (mg/kg-day)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (Year of guidelines used)	DWEL (mg/L) & RSC	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/Citation	Cancer classification (year of guidelines used; year of assessment)	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (year of guidelines used; year of assessment)
Ethylbenzene (1991) (A)	0.7	0.7	0.097/136 mg/kg-day (adjusted: 97.1 mg/kg-day) (NOEL)/1000 (10H, 10A, 10S)/ Liver and kidney weight increase, and slight liver and kidney histopathology/ Wolf et al. 1956	D, Not classifiable as to human carcinogenicity (1986 guidelines)	3.4 20%	0.1 (1991) ⁵⁷ /136 mg/kg-day (adjusted: 97.1 mg/kg-day) (NOEL)/1000 (10H, 10A, 10S)/ Liver and kidney toxicity/ Wolf et al. 1956	D, Not classifiable as to human carcinogenicity (1986 guidelines; 1991) ⁵⁸	--	--

⁵⁷ In the first six year review final notice (68 FR 42908; USEPA 2003b), EPA noted that an EPA health effects assessment for ethylbenzene is currently in process.

⁵⁸ An EPA health effects assessment for ethylbenzene is currently in process. The IRIS Substance Assessment Tracking system website (<http://cfpub.epa.gov/ncea/iristrac/index.cfm>) should be consulted for the most current information on the status of this assessment.

Table 2. Summary of U.S. EPA Assessments for Six-Year Review 2 Chemicals^{10*}

Chemical (Date of regulation) (List A or B)	EPA/OW National Primary Drinking Water Regulation (NPDWR)					IRIS		OPP	
	MCLG mg/L	MCL mg/L (basis if MCL≠MCLG)	RfD (mg/kg-day)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (Year of guidelines used)	DWEL (mg/L) & RSC	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/Citation	Cancer classification (year of guidelines used; year of assessment)	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (year of guidelines used; year of assessment)
Ethylene Dibromide (EDB; 1,2-Dibromoethane) (1991) (B)	0	0.00005 (PQL)	--	B2, probable human carcinogen (1986 guidelines)	--	0.009 (2004)/ 27 (LOAEL)/ 3000 (10H, 10A, 10L, 10D)/ Testicular atrophy, liver peliosis, and adrenal cortical degeneration/ NCI 1978	Likely to be carcinogenic to humans (1999 guidelines; 2004)	--	--
Fluoride (1986) (A)	4.0	4.0	No RfD ⁵⁹ / 20 mg/day (LOAEL)/ (2.5H)/ crippling skeletal fluorosis/ Shapiro 1983 Koop 1984 WHO 1984	--	-- 100%	0.06 ⁶⁰ / 1989/ 0.06 (NOAEL)/ 1(1H)/ objectionable dental fluorosis/ Hodge 1950	--	--	--

⁵⁹ EPA published a secondary maximum contaminant level (SMCL) for fluoride of 2.0 mg/L to protect against dental fluorosis (an adverse cosmetic effect) (NPDWR for fluoride, April 2, 1986 (51FR: 11397)).

⁶⁰ The IRIS Substance Assessment Tracking system website (<http://cfpub.epa.gov/ncea/iristrac/index.cfm>) should be consulted for the most current information on the status of this assessment.

Table 2. Summary of U.S. EPA Assessments for Six-Year Review 2 Chemicals ^{10*}

Chemical (Date of regulation) (List A or B)	EPA/OW National Primary Drinking Water Regulation (NPDWR)					IRIS		OPP	
	MCLG mg/L	MCL mg/L (basis if MCL≠MCLG)	RfD (mg/kg-day)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (Year of guidelines used)	DWEL (mg/L) & RSC	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/Citation	Cancer classification (year of guidelines used; year of assessment)	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (year of guidelines used; year of assessment)
Glyphosate (1992) (B)	0.7	0.7	0.1/ 10 (NOAEL)/ 100 (10H, 10A)/ Increased incidence of renal tubular dilation in F3b offspring/ Monsanto Company 1981	E, evidence of noncarcinogenicity (1986 guidelines)	4 20%	0.1 (1990)/ 10 (NOAEL)/ 100 (10H, 10A)/ Increased incidence of renal tubular dilation in F3b offspring/ Monsanto Company 1981	D, not classifiable (1986 guidelines; 1990)	2 (2007)/ 175 (NOAEL)/ 100 (10H, 10A)/ Diarrhea, nasal discharge, and death/ Monsanto Company 1980b	E, evidence of noncarcinogenicity (1986 guidelines)
Heptachlor (1991) (B)	0	0.0004 (PQL)	0.0005/ 0.15 (NOAEL)/ 300 (10H, 10A, 3D)/ Increased liver to body weight ratio in males/ Witherup et al. 1955	B2, probable human carcinogen (1986 guidelines)	--	0.0005 (1991)/ 0.15 (NOAEL)/ 300 (10H, 10A, 3D)/ Increased liver to body weight ratio in males/ Witherup et al. 1955	B2, probable human carcinogen (1986 guidelines; 1991)	0.0005 (1992)/ 0.15 (NOAEL)/ 300 (10H, 10A, 3D)/ Liver lesions and increased relative liver weight/ Witherup et al. 1955	B2, probable human carcinogen (1986 guidelines; 1992)
Heptachlor Epoxide (1991) (B)	0	0.0002 (PQL)	0.000013/ 0.0125 (LOAEL)/ 1000 (10H, 10A, 10L)/ Increase in liver-to-body weight ratio/ Dow Chemical Company 1958	B2, probable human carcinogen (1986 guidelines)	--	0.000013 (1991)/ 0.0125 (LEL)/ 1000 (10H, 10A, 10L)/ Increase in liver-to-body weight ratio/ Dow Chemical Company 1958	B2, probable human carcinogen (1986 guidelines; 1993)	0.000013 (1992)/ 0.0125 (LEL)/ 1000 (10H, 10A, 10L)/ Increase in liver-to-body weight ratio/ Dow Chemical Company 1958	B2, probable human carcinogen (1986 guidelines)

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	MCLG mg/L	MCL mg/L (basis if MCL≠MCLG)	RfD (mg/kg-day)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (Year of guidelines used)	DWEL (mg/L) & RSC	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/Citation	Cancer classification (year of guidelines used; year of assessment)	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (year of guidelines used; year of assessment)
Hexachlorobenzene (1992) (B)	0	0.001 (PQL)	0.0008/ 0.08 (NOAEL)/ 100 (10H, 10A)/ Hepatic centrilobular basophilic chromogenesis/ Arnold et al. 1985	B2, probable human carcinogen (1986 guidelines)	--	0.0008 (1991)/ 0.08 (NOAEL)/ 100 (10H, 10A)/ Hepatic centrilobular basophilic chromogenesis/ Arnold et al. 1985	B2, probable human carcinogen (1986 guidelines; 1996)	--	--
Hexachlorocyclopentadiene (1992) (B)	0.05	0.05	0.007/ 7.14 (adj. NOAEL)/ 1000 (10H, 10A, 10S)/ Focal inflammation of the forestomach and stomach lesions/ SRI 1981	D, not classifiable as to human carcinogenicity (1986 guidelines)	0.3 20%	0.006 (2001)/ 6 (BMDL10)/ 1000 (10H, 10A, 10 ^{1/2} S, 10 ^{1/2} D)/ Chronic irritation of forestomach (forestomach lesions)/ Abdo et al. 1984	Unknown risk as to oral exposure (1996 guidelines; 2001)	--	--

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	MCLG mg/L	MCL mg/L (basis if MCL≠MCLG)	RfD (mg/kg-day)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (Year of guidelines used)	DWEL (mg/L) & RSC	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/Citation	Cancer classification (year of guidelines used; year of assessment)	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (year of guidelines used; year of assessment)
Lindane (gamma-Hexachloro-cyclohexane) (1991) (B)	0.0002	0.0002	0.0003/0.33 (NOAEL)/1000 (10H, 10A, 10S)/ Liver and kidney toxicity/ RCC 1983	C, possible human carcinogen (1986 guidelines)	0.01 20% Also factor of 10 for class C	0.0003 (1988)/0.33 (NOAEL)/1000 (10H, 10A, 10S)/ Liver and kidney toxicity/ RCC 1983	--	0.0047 (2002)/0.47 (NOAEL)/100 (10H, 10A)/ FQPA: 3 Hepatocyte hypertrophy, increased liver weight, increased platelets/ Amyes 1989a,b,1993	Suggestive evidence of carcinogenicity, but not sufficient to assess human carcinogenic potential (1999 guidelines; 2002)
Mercury (Inorganic) (1991) (B)	0.002	0.002	0.0003 ⁶¹ / / 1000 (Not specified)/ Mercuric chloride-induced autoimmune glomerulonephritis/ USEPA 1987c Druet et al. 1978 Bernaudin et al. 1981 Andres 1984	--	0.01 20%	0.0003 (1995)/0.317 (LOAEL)/1000 (10A,H, 10L, 10S)/ Autoimmune glomerulonephritis/ USEPA 1987c Druet et al. 1978 Bernaudin et al. 1981 Andres 1984	C, possible human carcinogen (1986 guidelines; 1995)	--	--

⁶¹ The RfD for mercury was back-calculated from the DWEL using 2 L water consumption and 70 kg body weight in the following equation (0.01 mg/L x 2 L) / 70 kg = 0.00029 mg/kg-day, rounded to 0.0003 mg/kg-day.

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Methoxychlor (1991) (B)	0.04	0.04	0.005/ 5.01 (NOAEL)/ 1000 (10H, 10A, 10D)/ Excessive loss of litters; decreased body weight/ Trutter 1986	D, not classifiable as to human carcinogenicity (1986 guidelines)	0.175 20%	0.005 (1991)/ 5.01 (NOAEL)/ 1000 (10H, 10A, 10D)/ Excessive loss of litters/ Trutter 1986	D, not classifiable as to human carcinogenicity (1986 guidelines; 1990)	--	--
Monochlorobenzene (Chlorobenzene) (1991) (B)	0.1	0.1	0.02/ 19 (NOAEL)/ 1000 (10H, 10A, 10S)/ Histopathologic changes in the liver/ Monsanto Company 1967 Knapp et al. 1971	D, not classifiable as to human carcinogenicity (1986 guidelines)	0.7 20%	0.02 (1993)/ 19 (adjusted dose) (NOAEL)/ 1000 (10H, 10A, 10S)/ Histopathologic changes in the liver/ Monsanto Company 1967	D, not classifiable as to human carcinogenicity (1986 guidelines; 1991)	--	--
Nitrate (as N) (1991) (B)	10	10	1.6 nitrate-nitrogen/ 1.6 (10 mg/L) (NOAEL)/ 1/ Methemoglobinemia in infants/ Bosch et al. 1950 Walton 1951	--	10 ⁶² --	1.6 nitrate-nitrogen/ (1991)/ 1.6 (10 mg/L) (NOAEL)/ 1/ Methemoglobinemia in infants/ Bosch et al. 1950 Walton 1951	--	--	--

⁶² Nitrate assessment is based on the concentration in the drinking water for an exposed human population

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	MCLG mg/L	MCL mg/L (basis if MCL≠ MCLG)	RfD (mg/kg-day)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (Year of guidelines used)	DWEL (mg/L) & RSC	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/Citation	Cancer classification (year of guidelines used; year of assessment)	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (year of guidelines used; year of assessment)
Nitrite (as N) (1991) (B)	1	1	0.16 nitrite - nitrogen/ Nitrate RfD of 1.6 nitrate-nitrogen ⁶³ / 1 (MF = 10)/ Methemoglobinemia in infants/ Bosch et al. 1950 Walton 1951	--	1 --	0.1 nitrite-nitrogen (1991)/ 1 ⁶⁴ (10 mg/L nitrate-nitrogen) (NOAEL)/ 1 (MF = 10)/ Methemoglobinemia in infants/ Walton 1951	--	--	--

⁶³ Extrapolated from nitrate RfD of 1.6 mg/kg-day, assuming 10% of nitrate converted to nitrite. Assumes a 4 kg child ingesting 0.64 L/day.

⁶⁴ 10 mg/L converted to 1.0 mg/kg-day assuming 10 kg child ingesting 1 L/day.

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	MCLG mg/L	MCL mg/L (basis if MCL≠MCLG)	RfD (mg/kg-day)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (Year of guidelines used)	DWEL (mg/L) & RSC	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/Citation	Cancer classification (year of guidelines used; year of assessment)	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (year of guidelines used; year of assessment)
Oxamyl (Vydate) (1992) (B)	0.2	0.2	0.025/ 2.5 (NOAEL)/ 100 (10H, 10A)/ Decreased body weight gain/ Kennedy 1986	E, evidence of noncarcinogenicity (1986 guidelines)	0.9 20%	0.025 (1991)/ 2.5 (NOEL)/ 100 (10H, 10A)/ Decreased body weight gain and food consumption/ E.I. du Pont de Nemours and Company 1972	--	0.001 (2000)/ 0.1 (NOAEL)/ 100 (10H, 10A)/ Clinical signs and decreased plasma RBC and brain cholinesterase inhibition in females/ Malley 1997a,b	E, evidence of noncarcinogenicity (1986 guidelines)
Pentachlorophenol (1991) (A)	0	0.001 (PQL; analytical feasibility)	0.03/ 3 (NOAEL)/ 100 (10H, 10A)/ pigmentation of kidneys/ Schwetz et al. 1978	B2, probable human carcinogen (1986 guidelines)	1.1	0.03 (1993) ⁶⁵ / 3 (NOAEL)/ 100 (10H, 10A)/ pigmentation of kidneys/ Schwetz et al. 1978	B2, probable human carcinogen (1986 guidelines; 1993) ⁶⁶	-- ^{67, 68}	B2, probable human carcinogen (1986 guidelines; 1994)

⁶⁵ An updated draft IRIS assessment (USEPA, 2007g) chose a chronic feeding study in dogs by Mecler (1996) as the principal study for PCP based on hepatotoxicity. IRIS derived an RfD of 0.005 mg/kg-day based on a LOAEL of 1.5 mg/kg-day as the point of departure and an uncertainty factor of 300 (10H, 10A, 3L). A draft IRIS assessment for pentachlorophenol is currently in progress. The IRIS Substance Assessment Tracking system website (<http://cfpub.epa.gov/ncea/iristrac/index.cfm>) should be consulted for the most current information on the status of this assessment.

⁶⁶ A draft IRIS assessment (USEPA, 2007g) for pentachlorophenol is currently in progress and states that under the 2005 Guidelines PCP is “likely to be carcinogenic to humans.” The IRIS Substance Assessment Tracking system website (<http://cfpub.epa.gov/ncea/iristrac/index.cfm>) should be consulted for the most current information on the status of this assessment.

⁶⁷ OPP (USEPA, 2004b) prepared a draft risk assessment for pentachlorophenol for systemic toxicity based on the LOAEL of 1.5 mg/kg-day for hepatotoxicity in dogs as discussed above for the draft IRIS assessment and a recommended margin of exposure of 300.

⁶⁸ OPP is developing a RED for release in September 2008.

Table 2. Summary of U.S. EPA Assessments for Six-Year Review 2 Chemicals ^{10*}

Chemical (Date of regulation) (List A or B)	EPA/OW National Primary Drinking Water Regulation (NPDWR)					IRIS		OPP	
	MCLG mg/L	MCL mg/L (basis if MCL≠MCLG)	RfD (mg/kg-day)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (Year of guidelines used)	DWEL (mg/L) & RSC	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/Citation	Cancer classification (year of guidelines used; year of assessment)	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (year of guidelines used; year of assessment)
Picloram (1992) (B)	0.5	0.5	0.07/ 7 (NOAEL)/ 100 (10H, 10A)/ Increased relative and absolute liver weights/ Dow Chemical Company 1982	D, not classifiable as to human carcinogenicity (1986 guidelines)	2.45 20%	0.07 (1992)/ 7 (NOEL)/ 100 (10H, 10A)/ Increased relative and absolute liver weights/ Dow Chemical Company 1982	--	0.2 (1995)/ 20 (NOAEL)/ 100 (10H, 10A)/ FQPA: NA Changes in centrilobular hepatocytes/ Landry et al. 1986	E, evidence of noncarcinogenicity (1986 guidelines)

Table 2. Summary of U.S. EPA Assessments for Six-Year Review 2 Chemicals^{10*}

Chemical (Date of regulation) (List A or B)	EPA/OW National Primary Drinking Water Regulation (NPDWR)					IRIS		OPP	
	MCLG mg/L	MCL mg/L (basis if MCL≠ MCLG)	RfD (mg/kg-day)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (Year of guidelines used)	DWEL (mg/L) & RSC	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/Citation	Cancer classification (year of guidelines used; year of assessment)	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (year of guidelines used; year of assessment)
Polychlorinated biphenyls (PCBs) (1991) (A)	0	0.0005 (PQL)	0.0001/ 0.01 (LOAEL)/ 100 (10H, 10A)/ Reduction in body weight of offspring/ Barsotti and van Miller 1984	B2, probable human carcinogen (1986 guidelines)	--	⁶⁹ Aroclor 1016: 7E-5 (1993)/ 0.007 (NOAEL)/ 100 (3H, 3A, 3S, 3D)/ Reduced birth weights/ Barsotti and van Miller 1984 Levin et al. 1988 Schantz et al. 1989, 1991 Aroclor 1254: 2E-5 (1994)/ 0.005 (LOAEL)/ 300 (10H, 3A, 3S 3L)/ Ocular exudate, inflamed and prominent Meibomian glands, distorted growth of finger and toe nails; decreased antibody (IgG and IgM) response to sheep erythrocytes/ Arnold et al. 1993a,b Tryphonas et al. 1989, 1991a,b	B2, probable human carcinogen (1986 guidelines) ⁷⁰	--	--

⁶⁹ IRIS does not present an RfD for polychlorinated biphenyls. Rather, IRIS directs readers to the RfD files for the individual Aroclor mixtures. EPA stated that an IRIS risk assessment for polychlorinated biphenyls is currently in progress. The IRIS Substance Assessment Tracking system website (<http://cfpub.epa.gov/ncea/iristrac/index.cfm>) should be consulted for the most current information on the status of this assessment.

⁷⁰EPA stated that an IRIS risk assessment for polychlorinated biphenyls is currently in progress. However, IRIS Track does not list PCBs currently.

Table 2. Summary of U.S. EPA Assessments for Six-Year Review 2 Chemicals ^{10*}

Chemical (Date of regulation) (List A or B)	EPA/OW National Primary Drinking Water Regulation (NPDWR)					IRIS		OPP	
	MCLG mg/L	MCL mg/L (basis if MCL≠ MCLG)	RfD (mg/kg-day)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (Year of guidelines used)	DWEL (mg/L) & RSC	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/Citation	Cancer classification (year of guidelines used; year of assessment)	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (year of guidelines used; year of assessment)
Combined Radiums (226 and 228) (2000) (A)	0	5 pCi/L ⁷¹	--	A, Known human carcinogen (1986 guidelines)	--	--	--	--	--
Selenium (1991) (B)	0.05	0.05	None/ 3.2/ 15 (H, L, accounting for special status as essential element)/ Minimum dietary intake of selenium in area with chronic selenosis of 3.2 mg/day, for a 70 kg adult/ Yang et al. 1983	--	-- 50%	0.005 (1991)/ 0.015 (NOAEL)/ 3 (3H)/ Clinical selenosis/ Yang et al. 1989	D, not classifiable (1986 guidelines; 1991)	--	--

⁷¹ ORIA is the principal health assessor for radionuclides. A health assessment for combined radiums (226 and 228) is currently in progress. Because ORIA is conducting the assessment, combined radiums (226 and 228) is not addressed on the IRIS Substance Assessment Tracking system website, so the expected completion date is not publicly available. The 2000 radionuclides rule was a collaboration between OW and ORIA. See 40 CFR 141. The MCL is based on combined radium-226 and radium-228.

Table 2. Summary of U.S. EPA Assessments for Six-Year Review 2 Chemicals^{10*}

Chemical (Date of regulation) (List A or B)	EPA/OW National Primary Drinking Water Regulation (NPDWR)					IRIS		OPP	
	MCLG mg/L	MCL mg/L (basis if MCL≠MCLG)	RfD (mg/kg-day)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (Year of guidelines used)	DWEL (mg/L) & RSC	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/Citation	Cancer classification (year of guidelines used; year of assessment)	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (year of guidelines used; year of assessment)
Simazine (1992) (B)	0.004	0.004	0.005/ 0.52 (NOAEL)/ 100 (10H, 10A)/ Reduction in weight gains; hematological changes in females/ McCormick et al. 1988	C, possible human carcinogen (1986 guidelines)	0.175 20% Also factor of 10 for class C	0.005 (1994)/ 0.52 (NOAEL)/ 100 (10H, 10A)/ Reduction in weight gains; hematological changes in females/ McCormick et al. 1988	--	0.018 (2006)/ 1.8 (NOAEL)/ 100 (10H, 10A)/ FQPA: 10 estrous cycle alterations and LH surge/ Morseth et al. 1996	Not likely to be carcinogenic to humans” The guidelines applied were not identified, but the most recent assessment of carcinogenic potential occurred in 2005.
Styrene (1991) (A)	0.1	0.1	0.2/ 200 (NOAEL)/ 1000 (10H, 10A, 10S)/ Reduced red blood cells, iron deposits in liver/ Quast et al. 1979	C, possible human carcinogen (1986 guidelines)	7 20%	0.2 (1990) ⁷² / 200 (NOAEL)/ 1000 (10H, 10A, 10S)/ Reduced red blood cells, iron deposits in liver/ Quast et al. 1979	--	--	--

⁷² The IRIS Substance Assessment Tracking system website (<http://cfpub.epa.gov/ncea/iristrac/index.cfm>) should be consulted for the most current information on the status of this assessment.

Table 2. Summary of U.S. EPA Assessments for Six-Year Review 2 Chemicals^{10*}

Chemical (Date of regulation) (List A or B)	EPA/OW National Primary Drinking Water Regulation (NPDWR)					IRIS		OPP	
	MCLG mg/L	MCL mg/L (basis if MCL≠ MCLG)	RfD (mg/kg-day)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (Year of guidelines used)	DWEL (mg/L) & RSC	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/Citation	Cancer classification (year of guidelines used; year of assessment)	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (year of guidelines used; year of assessment)
2,3,7,8-TCDD (Dioxin) (1988) (A)	0	3 x 10 ⁻⁸ / (PQL)	1 x 10 ⁻⁹ / 1 x 10 ⁻⁶ (LOAEL)/ 1000 (10H, 10A, 10L)/ Reduced gestation index, decreased fetal weight, increased liver-to-body weight ratio, dilated renal pelvis/ Murray et al. 1979	B2, probable human carcinogen (1986 guidelines)	3.5 x 10 ⁻⁸ --	-- ⁷³	-- ⁷⁴	--	--
Tetrachloro-ethylene (1991) (A)	0	0.005/ (PQL; analytical feasibility)	0.0143/ 14.3 (adjusted NOAEL)/ 1000 (10H, 10A, 10S)/ Increased liver weight and hepatic triglycerides levels/ Buben and O'Flaherty 1985	B2, probable human carcinogen (1986 guidelines)	0.5	0.01 (1988) ⁷⁵ / 14 (adjusted NOAEL)/ 1000 (10H, 10A, 10S)/ Increased liver weight and hepatic triglycerides levels/ Buben and O'Flaherty 1985	--	--	--

⁷³ An IRIS 2003 External Review Draft is available. The IRIS Substance Assessment Tracking system website (<http://cfpub.epa.gov/ncea/iristrac/index.cfm>) should be consulted for the most current information on the status of the assessment of 2,3,7,8-TCDD (Dioxin).

EPA proposed using an MOE approach (MOE = POD/exposure), rather than an RfD approach, due to the inability to determine levels that are likely to be without appreciable effects of lifetime exposure.

⁷⁴ An IRIS 2003 External Review Draft is available. IRIS Track lists the assessment as initiated with a final. The IRIS Substance Assessment Tracking system website (<http://cfpub.epa.gov/ncea/iristrac/index.cfm>) should be consulted for the most current information on the status of this assessment.

EPA proposed that dioxin is a "human carcinogen."

⁷⁵ An IRIS 2006 External Review Draft is available. The IRIS Substance Assessment Tracking system website (<http://cfpub.epa.gov/ncea/iristrac/index.cfm>) should be consulted for the most current information on the status of this assessment.

Table 2. Summary of U.S. EPA Assessments for Six-Year Review 2 Chemicals^{10*}

Chemical (Date of regulation) (List A or B)	EPA/OW National Primary Drinking Water Regulation (NPDWR)					IRIS		OPP	
	MCLG mg/L	MCL mg/L (basis if MCL≠MCLG)	RfD (mg/kg-day)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (Year of guidelines used)	DWEL (mg/L) & RSC	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/Citation	Cancer classification (year of guidelines used; year of assessment)	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (year of guidelines used; year of assessment)
Thallium (1992) (A)	0.0005	0.002 (PQL; analytical feasibility)	0.00007/ 0.25 (NOAEL)/ 3000 (10H, 10A, 10S, 3D)/ No treatment related effects/ Stolz et al. 1986	D, not classifiable as to human carcinogenicity (1986 guidelines)	0.002 20%	0.00007 ⁷⁶ (1990)/ 0.25 (converted to 0.2 NOAEL as thallium)/ 3000 (10H, 10A, 10S, 3D)/ Some increase in serum enzymes (SGOT and LDH), hypoglycemia, alopecia/ USEPA 1986b	D, not classifiable as to human carcinogenicity (1986 guidelines) ⁷⁷	--	--

⁷⁶ Previously, the IRIS database contained separate IRIS summaries for each of the five soluble thallium salts. The previous RfD values for these salts (soluble and insoluble) were based on the same principal study (MRI, 1988; previously cited as USEPA, 1986b) as the current assessment presented in the Agency Review draft of the Toxicological Review for Thallium and Compounds (USEPA, 2008a). The current assessment, however, provides a value for the thallium (I) ion only that is applicable to soluble thallium (I) salts. The difference between the previous and current RfD values for the soluble thallium salts is largely attributable to a different interpretation of the study results and different assignment of uncertainty factors. In the previous assessment, the high-dose group in the principal study was identified as the no-observed-adverse-effect level (NOAEL), whereas in the current assessment, the mid-dose group is considered to be the NOAEL. Although the previous and current assessments both use a composite UF of 3000, the value of specific UFs differ between the assessments. It was determined (based on physical-chemical property differences and the lack of water solubility information) that thallium (I) sulfate is not an appropriate surrogate for the derivation of RfD values for the insoluble thallium salts (e.g., thallium oxide), for other trivalent thallium salts, or for thallium (I) selenite. USEPA (2008a) identified a NOAEL of 0.04 mg thallium ion/kg-day for alopecia and applied a UF of 3000 (10A, 10H, 3S, 10D), resulting in an RfD of 1 x 10⁻⁵ mg thallium ion/kg-day. USEPA (2008a) presents an RfD of 2 x 10⁻⁵ mg/kg-day for each of the soluble thallium (I) salts that is estimated by adjusting for the molecular weight of the salt compared with the ion. A water concentration based on the new IRIS RfD and incorporating a 20% relative source concentration, is 0.00007 mg thallium ion/L. EPA completed the risk reassessment for thallium in September of 2009 (USEPA, 2009b). Because the new assessment was not completed by March 1, 2009, the cutoff date for this review, the outcome of this assessment has not been included in the current review effort. EPA will consider the updated assessment in the next review cycle.

⁷⁷ The 2008 IRIS draft concluded that there is inadequate information to assess carcinogenic potential for thallium.

Table 2. Summary of U.S. EPA Assessments for Six-Year Review 2 Chemicals ^{10*}

Chemical (Date of regulation) (List A or B)	EPA/OW National Primary Drinking Water Regulation (NPDWR)					IRIS		OPP	
	MCLG mg/L	MCL mg/L (basis if MCL≠MCLG)	RfD (mg/kg-day)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (Year of guidelines used)	DWEL (mg/L) & RSC	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/Citation	Cancer classification (year of guidelines used; year of assessment)	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (year of guidelines used; year of assessment)
Toluene (1991) (B)	1	1	0.2/ 223 (NOAEL)/ 1000 (10H, 10A, 10S)/ Increased kidney weight/ NTP 1990	D, not classifiable as to human carcinogenicity (1986 guidelines)	7 20%	0.08 (2005)/ 238 (BMDL)/ 3000 (10H, 10A, 10S, 3D)/ Increased kidney weights/ NTP 1990	Data are inadequate to assess carcinogenic potential (2005 guidelines; 2005)	--	--
Toxaphene (1991) (B)	0	0.003 (PQL)	0.0004/ 0.36 (NOAEL)/ 100 (10H, 10A)/ Histological changes in liver, kidney, and thyroid/ Chu et al. 1986,1988	B2, probable human carcinogen (1986 guidelines)	--	--	B2, probable human carcinogen (1986 guidelines; 1991)	--	--
2,4,5-TP (Silvex; 2,4,5-Trichlorophenoxypropionic Acid) (1991) (B)	0.05	0.05	0.008 0.75 (NOAEL)/ 100 (10H, 10A)/ Histopathological changes in the liver/ Mullison 1966	D, not classifiable as to human carcinogenicity (1986 guidelines)	0.3 20%	0.008 (1988)/ 0.75 (NOAEL)/ 100 (10H, 10A)/ Histopathological changes in the liver/ Mullison 1966	D, not classifiable (1986 guidelines; 1988)	--	--

Table 2. Summary of U.S. EPA Assessments for Six-Year Review 2 Chemicals ^{10*}

Chemical (Date of regulation) (List A or B)	EPA/OW National Primary Drinking Water Regulation (NPDWR)					IRIS		OPP	
	MCLG mg/L	MCL mg/L (basis if MCL≠MCLG)	RfD (mg/kg-day)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (Year of guidelines used)	DWEL (mg/L) & RSC	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/Citation	Cancer classification (year of guidelines used; year of assessment)	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (year of guidelines used; year of assessment)
1,2,4-Tri-chlorobenzene (1992) (B)	0.07	0.07	0.01/ 14.8 (NOAEL)/ 1000 (10H, 10A, 10S)/ Increased adrenal weights; vacuolization of zona fasciculata in the cortex/ Robinson et al. 1981	D, not classifiable as to human carcinogenicity (1986 guidelines)	0.35 20%	0.01 (1996)/ 14.8 (NOAEL)/ 1000 (10H, 10A, 10S/D)/ Increased adrenal weights; vacuolization of zona fasciculata in the cortex/ Robinson et al. 1981	D, not classifiable (1986 guidelines; 1996)	--	--
1,1,1-Tri-chloroethane (1985) (B)	0.2	0.2	0.035/ 35.1 (LOAEL) 1000 (10H, 10A, 10L)/ Histological changes in liver/ McNutt et al. 1975	D, not classifiable as to human carcinogenicity (1986 guidelines)	1 20%	2.0 (2007)/ 2155 (BMDL ₁₀)/ 1000 (10H, 10A, 3S, 3D)/ Reduced body weight/ NTP 2000	Inadequate information to assess carcinogenic potential (2005 guidelines, 2007)	--	--

Table 2. Summary of U.S. EPA Assessments for Six-Year Review 2 Chemicals^{10*}

Chemical (Date of regulation) (List A or B)	EPA/OW National Primary Drinking Water Regulation (NPDWR)					IRIS		OPP	
	MCLG mg/L	MCL mg/L (basis if MCL≠MCLG)	RfD (mg/kg-day)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (Year of guidelines used)	DWEL (mg/L) & RSC	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/Citation	Cancer classification (year of guidelines used; year of assessment)	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (year of guidelines used; year of assessment)
1,1,2-Trichloroethane (1992) (B)	0.003	0.005 (PQL)	0.004/4 (NOAEL) 1000 (10H, 10A, 10S)/ Adverse effects on liver, depressed humoral immune status/ Sanders et al. 1985 White et al. 1985	C, possible human carcinogen (1986 guidelines)	0.137 20% Also factor of 10 for class C	0.004 (1995)/ 3.9 (NOAEL)/ 1000 (10H, 10A, 10S)/ Clinical serum chemistry/ Sanders et al. 1985 White et al. 1985	C, possible human carcinogen (1986 guidelines; 1994)	--	--
Trichloroethylene (1985) (A)	0	0.005 (PQL; analytical feasibility)	0.007/7.34 (LOAEL)/ 1000 (unspecified)/ Increased liver weight/ Kimmerle and Eben 1973	B2, probable human carcinogen (1986 guidelines) ⁷⁸	--	-- ⁷⁹	-- ⁸⁰	--	--

⁷⁸ NCEA (USEPA, 2001d) characterized trichloroethylene as highly likely to produce cancer in humans (1996, 1999 Guidelines).

⁷⁹ A 2001 EPA NCEA Draft Health Risk Assessment proposed an RfD of 3×10^{-4} , based on liver weight to bodyweight ratio changes, incorporating an uncertainty factor of 3000 (50H, 100A, S, L) (Tucker et al., 1982). The IRIS Substance Assessment Tracking system website (<http://cfpub.epa.gov/ncea/irisrac/index.cfm>) should be consulted for the most current information on the status of this assessment.

⁸⁰ A 2001 EPA NCEA Draft Health Risk Assessment (USEPA, 2001d) described trichloroethylene as “Highly likely to produce cancer in humans” (1996, 1999 guidelines).

Table 2. Summary of U.S. EPA Assessments for Six-Year Review 2 Chemicals^{10*}

Chemical (Date of regulation) (List A or B)	EPA/OW National Primary Drinking Water Regulation (NPDWR)					IRIS		OPP	
	MCLG mg/L	MCL mg/L (basis if MCL≠MCLG)	RfD (mg/kg-day)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (Year of guidelines used)	DWEL (mg/L) & RSC	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/Citation	Cancer classification (year of guidelines used; year of assessment)	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (year of guidelines used; year of assessment)
Uranium (2000) (A)	0	0.03 ⁸¹ (feasibility and cost-benefit analysis)	0.0006 ug/kg/day/ 0.06 (LOAEL)/ 100 (10H, 3A, 3L) (minimum LOAEL)/ Renal toxicity/ Gilman et al. 1998	A, known human carcinogen (1986 guidelines) (No quantitative assessment) ⁸²	20 ug/L 80%	0.003 (1989) ⁸³ / 2.8 (LOAEL)/ 1000 (10H, 10A, 10S) Initial body weight loss; moderate nephrotoxicity/ Maynard and Hodge 1949 (No quantitative assessment via oral route)	--	--	--
Vinyl chloride (1987) (B)	0	0.002 (PQL)	Adjusted acceptable daily intake: 0.046 mg/L/ 0.13 (NOAEL)/ 100 (10H, 10A)/ None/ Til et al. 1983	A, known human carcinogen (1986 guidelines)	--	0.003 (2000)/ 0.13 (0.09 HED) (NOAEL)/ 30 (10H, 3A)/ Liver cell polymorphism/ Til et al. 1983, 1991	Known carcinogen by the oral route (1996 guidelines; 2000)	--	--

⁸¹ ORIA is the principal health assessor for radionuclides. The 2000 radionuclides rule was a collaboration between OW and ORIA. See 40 CFR 141.

⁸² The Office of Water Criteria Document (USEPA,1991b) has derived risk specific concentration for a cancer risk of 1E-4 for lifetime consumption of various isotopes of uranium using the RADRISK program. For example, for combined U234 and U238 a concentration of 120 pCi/L is associated with a 1E-4 cancer risk.

⁸³ The IRIS RfD for natural uranium has been withdrawn. The IRIS Substance Assessment Tracking system website (<http://cfpub.epa.gov/ncea/iristrac/index.cfm>) should be consulted for the most current information on the status of this assessment.

Table 2. Summary of U.S. EPA Assessments for Six-Year Review 2 Chemicals ^{10*}

Chemical (Date of regulation) (List A or B)	EPA/OW National Primary Drinking Water Regulation (NPDWR)					IRIS		OPP	
	MCLG mg/L	MCL mg/L (basis if MCL≠MCLG)	RfD (mg/kg-day)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (Year of guidelines used)	DWEL (mg/L) & RSC	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/Citation	Cancer classification (year of guidelines used; year of assessment)	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (year of guidelines used; year of assessment)
Xylenes (Total) (1991) (B)	10	10	1.79/ 179 (adj. NOAEL)/ 100 (10H, 10A)/ decreased body weight gains/ NTP 1986	D, not classifiable as to human carcinogenicity (1986 guidelines)	63 20%	0.2 (2003), 179 (adj. NOAEL)/ 1000 (10H, 10A, 10D)/ decreased body weight gains/ NTP 1986	Data are inadequate to assess carcinogenic potential (1999 guidelines; 2003)	--	--

Abbreviations: AADI = - Adjusted acceptable daily intake or adjusted average daily intake; ADI = average daily intake; Adj. = adjusted for intermittent exposure; BMDL = lower 95% confidence limit on the benchmark dose; DWEL = drinking water equivalent level; FQPA = Food Quality Protection Act; HED = Human equivalent dose; IRIS = Integrated Risk Information System; MCL = maximum contaminant level; MCLG = maximum contaminant level goal; MEL = minimum effect level; NOAEL = no observed adverse effect level; LEL = lowest effect level; LOAEL = lowest observed adverse effect level; NA = not applicable; OPP = Office of Pesticide Programs; ORIA = Office of Radiation and Indoor Air; OW = Office of Water; PQL = practical quantitation limit, also termed “analytical feasibility”; RfD = Reference dose; RSC = relative source contribution; UF = uncertainty factor (with H = intraspecies UF; A = interspecies UF; L = UF for LOAEL to NOAEL; S = UF for subchronic to chronic extrapolation; D = database UF)

Table 3. Summary of EPA Quantitative Cancer Assessments for List A and B Chemicals

Chemical (List A or B)	OW			IRIS			OPP		
	Quantitative Estimate	Adjustment factor ⁸⁴	Extrapolation Method ⁸⁵	Quantitative Estimate	Adjustment factor	Extrapolation Method	Quantitative Estimate	Adjustment factor	Extrapolation Method
Acrylamide (A)	Potency : 3.7 per mg/kg-day; Drinking water concentration at 10-5 risk level: 1E-4 mg/L,	(BW)2/3	Linearized multistage model	Potency: 4.5 per mg/kg-day; Drinking water concentration at 10-5 risk level: 8E-5 mg/L ⁸⁶	(BW)2/3	Linearized multistage model	--	--	--
Alachlor (B)	--	--	--	--	--	--	0.005 mg/kg-day ⁸⁷	--	Nonlinear MOA
Alpha Particle Emitters (A)	-- ⁸⁸	--	FGR-13; linear no threshold model	--	--	--	--	--	--

⁸⁴ The adjustment factor was often not presented in summary documents reviewed. Unless specified otherwise the approach shown was based on typical methods at the time the assessment was completed.

⁸⁵ The extrapolation method was often not presented in summary documents reviewed. Unless specified otherwise the approach shown was based on typical methods at the time the assessment was completed.

⁸⁶ An EPA risk assessment for acrylamide is currently in process. Based on the IRIS External Review Draft EPA derived a human oral slope factor of 0.5 per mg/kg-day is based on human equivalent BMDL₁₀ derived from a PBTK model. The HEC BMDL₁₀ was based on the male rat BMD₁₀ of 0.7 mg/kg-day and BMDL₁₀ of 0.3 mg/kg-day for the combined risk of male rats bearing TVM or thyroid tumors. The human slope factor for acrylamide should not be used with exposures exceeding the POD (LED₁₀), because above this level the fitted dose-response model better characterizes what is known about the carcinogenicity of acrylamide.

⁸⁷ The data indicate that alachlor's tumorigenicity is operating by a nonlinear mode of action. OPP (USEPA, 1998d, 2001e, 2006c) concluded that alachlor causes nasal turbinate tumors via the generation of a reactive metabolite that leads to cytotoxicity and regenerative proliferation in the nasal epithelium; sustained cytotoxicity and proliferation is needed to lead to neoplasia. Based on this MOA assessment a non-linear dose response assessment is appropriate. Therefore, using the POD of 0.5 mg/kg-day identified by OPP for this endpoint and the UF of 100 (10H, 10A) would result in a health reference value of 0.005 mg/kg-day.

⁸⁸ ORIA is the principal health assessor for radionuclides. The 2000 radionuclides rule was a collaboration between OW and ORIA. The 2000 rulemaking (USEPA, 2000b) and supporting document (USEPA, 2000g) presented the concentration (in pCi/L) corresponding to 1E-4 lifetime total cancer risk and to 5E-5 lifetime fatal cancer risk; the individual cancer risk per unit intake factors for the individual radionuclides are provided in FGR-13 (USEPA, 1999c).

Table 3. Summary of EPA Quantitative Cancer Assessments for List A and B Chemicals

Chemical (List A or B)	OW			IRIS			OPP		
	Quantitative Estimate	Adjustment factor ⁸⁴	Extrapolation Method ⁸⁵	Quantitative Estimate	Adjustment factor	Extrapolation Method	Quantitative Estimate	Adjustment factor	Extrapolation Method
Arsenic (A)	⁸⁹ Risk at a MCL of 10 ug/L provided ranges from 1E-4 to 6E-4 depending on adjustment factors used for arsenic in food and cooking water	--	--	Potency: 1.5 per mg/kg-day; Drinking water concentration at 10-5 risk level: 2E-4 mg/L	Based on human study	Time- and dose-related formulation of the multistage model (USEPA 1988a)	--	--	--
Asbestos (A)	Potency: 1.4E-13 per fiber/L; Drinking water concentration at 10-5 risk level: 7.1E7 fiber/L	(BW)2/3	Linearized multistage model	--	--	--	--	--	--
Benzene (B)	Potency ⁹⁰ : Drinking water concentration at 10-5 risk level: 6.8E-3 mg/L	Based on human studies	Linearized multistage model	Potency: 1.5E-2 to 5.5E-2 per mg/kg-day; Drinking water concentration at 10-5 risk level: 0.01 – 0.1 mg/L	Based on human studies	Linear extrapolation from occupational	--	--	--

⁸⁹ A cancer slope factor was not identified in EPA DWCD. However, the NPDWR (USEPA, 2001c) provides risk estimates at various potential alternative MCLs.

⁹⁰ The DWCD did not provide a cancer slope factor; rather, the risk specific dose was extrapolated from the inhalation unit risk of 0.02407 per ppm derived from epidemiology studies of leukemia following benzene inhalation.

Table 3. Summary of EPA Quantitative Cancer Assessments for List A and B Chemicals

Chemical (List A or B)	OW			IRIS			OPP		
	Quantitative Estimate	Adjustment factor ⁸⁴	Extrapolation Method ⁸⁵	Quantitative Estimate	Adjustment factor	Extrapolation Method	Quantitative Estimate	Adjustment factor	Extrapolation Method
Benzo(a)pyrene (A)	Potency: 5.79 per mg/kg-day; Drinking water concentration at 10-5 risk level: 6E-5 mg/L	(BW)2/3	Linearized multi-stage model; Two-stage conditional upper bound (5.9 per mg/kg-day); two-stage 10% response (9.0 per mg/kg-day); Weibull-type (4.5 per mg/kg-day)	Potency: 7.3 per mg/kg-day; Drinking water concentration at 10-5 risk level: 5E-5 mg/L	NS	Linearized Multistage Model	--	--	--
Beryllium (A)	Potency : 4.3 per mg/kg-day Drinking water concentration at 10-5 risk level: 8E-5 mg/L	(BW)2/3	Linearized multistage model	--	--	--	--	--	--
Beta Particle and Photon Emitters(A)	-- ⁹¹	--	FGR-13; linear no threshold model	--	--	--	--	--	--
Carbon tetrachloride (A)	Potency: 0.13 per mg/kg-day; Drinking water concentration at 10-5 risk level: 2.7E-3 mg/L	(BW)2/3	improved multistage model	Potency ⁹² : 0.13 per mg/kg-day; Drinking water concentration at 10-5 risk level: 3E-3 mg/L	(BW)2/3	Linearized Multistage Model	--	--	--

⁹¹ ORIA is the principal health assessor for radionuclides. The 2000 radionuclides rule was a collaboration between OW and ORIA. The 2000 rulemaking (USEPA, 2000b) and supporting document (USEPA, 2000g) presented the concentration (in pCi/L) corresponding to the 4 mrem/year standard, and the associated risk; the individual cancer risk per unit intake factors for the individual radionuclides are provided in FGR-13 (USEPA, 1999c).

⁹² The IRIS draft assessment (2008b) for carbon tetrachloride states that the studies of carbon tetrachloride carcinogenicity by the oral exposure route are not sufficient to derive a quantitative estimate of cancer risk using low-dose linear approaches, it lists a cancer classification of “likely to be carcinogenic to humans by all routes of exposure” under 2005 guidelines.

Table 3. Summary of EPA Quantitative Cancer Assessments for List A and B Chemicals

Chemical (List A or B)	OW			IRIS			OPP		
	Quantitative Estimate	Adjustment factor ⁸⁴	Extrapolation Method ⁸⁵	Quantitative Estimate	Adjustment factor	Extrapolation Method	Quantitative Estimate	Adjustment factor	Extrapolation Method
Chlordane (B)	Potency: 1.3 per mg/kg-day; Drinking water concentration at 10-5 risk level: 2.7E-4 mg/L	(BW)2/3	Linearized multistage model	Potency: 0.35 per mg/kg-day; Drinking water concentration at 10-5 risk level: 1E-3 mg/L	(BW)3/4	Linearized multistage model	--	--	--
Di(2-ethylhexyl)adipate (DEHA) (A)	Potency: 1.2E-3 per mg/kg-day; Drinking water concentration at 10-5 risk level: 3E-1 mg/L	(BW)2/3	Linearized multistage procedure;	Potency: 1.2E-3 per mg/kg-day; Drinking water concentration at 10-5 risk level: 3E-1 mg/L	(BW)2/3	Linearized multistage model	--	--	--
Di(2-ethylhexyl)phthalate (DEHP) (A)	Potency: 0.014 per mg/kg-day; Drinking water concentration at 10-5 risk level: 3E-2 mg/L	(BW)2/3	Linearized multistage model	Potency: 0.014 per mg/kg-day; Drinking water concentration at 10-5 risk level: 3E-2 mg/L	(BW)2/3	Linearized multistage procedure	--	--	--
1,2-Dibromo-3-chloropropane (DBCP) (B)	Potency: 1.4 per mg/kg-day; Drinking water concentration at 10-5 risk level: 0.00025 mg/L	(BW)2/3	Linearized multistage model	--	--	--	--	--	--

Table 3. Summary of EPA Quantitative Cancer Assessments for List A and B Chemicals

Chemical (List A or B)	OW			IRIS			OPP		
	Quantitative Estimate	Adjustment factor ⁸⁴	Extrapolation Method ⁸⁵	Quantitative Estimate	Adjustment factor	Extrapolation Method	Quantitative Estimate	Adjustment factor	Extrapolation Method
1,4-Dichlorobenzene (p-Dichlorobenzene) (A)	From Rat Study: Potency: 2E-2 per mg/kg-day; Drinking water concentration at 10-5 risk level: 1.8E-2 mg/L	(BW)2/3	Linearized multistage model	--	--	--	⁹³	--	--
	From Mouse Study: Potency: 6E-3 per mg/kg-day; Drinking water concentration at 10-5 risk level: 5.8E-2 mg/L	(BW)2/3	Linearized multistage model						
1,2-Dichloroethane (Ethylene Dichloride) (A)	Potency ⁹⁴ : Drinking water concentration at 10-5 risk level: 6 E-3 mg/L	(BW)2/3	Linearized multistage model	Potency: 0.091 per mg/kg-day; Drinking water concentration at 10-5 risk level: 4 E-3 mg/L	(BW)2/3	Linearized multistage model with time to death analysis	--	--	--
Dichloromethane (Methylene Chloride) (A)	Potency: 7.5E-3; Drinking water concentration at 10-5 risk level: 5E-2 mg/L	(BW)2/3	Linearized multistage model	Potency: 7.5E-3 per mg/kg-day; Drinking water concentration at 10-5 risk level: 5E-2 mg/L	(BW)2/3	Linearized multistage procedure	--	--	--
1,2-Dichloropropane (B)	Potency: 6.7E-2 per mg/kg-day; Drinking water concentration at 10-5 risk level: 5.2E-3 mg/L	(BW)2/3	Linearized multistage model	--	--	--	--	--	--

⁹³ OPP is developing a RED for release in March 2008

⁹⁴ Potency not available, and cannot be calculate from the drinking water concentration using standard methods, because the calculation of the drinking water concentration included consumption from fish.

Table 3. Summary of EPA Quantitative Cancer Assessments for List A and B Chemicals

Chemical (List A or B)	OW			IRIS			OPP		
	Quantitative Estimate	Adjustment factor ⁸⁴	Extrapolation Method ⁸⁵	Quantitative Estimate	Adjustment factor	Extrapolation Method	Quantitative Estimate	Adjustment factor	Extrapolation Method
Epichlorohydrin (B)	Potency: 9.9 x 10 ⁻³ per mg/kg-day; Drinking water concentration at 10 ⁻⁵ risk level: 4E-2 mg/L	(BW)2/3	Linearized multistage model	Potency: 9.9 x 10 ⁻³ per mg/kg-day; Drinking water concentration at 10 ⁻⁵ risk level: 4E-2 mg/L	(BW)2/3	Linearized multistage model	--	--	--
Ethylene Dibromide (EDB; 1,2-Dibromoethane) (B)	Potency: 85 per mg/kg-day; Drinking water concentration at 10 ⁻⁵ risk level: 4E-6 mg/L	(BW)2/3	The model was derived from Thorslund, 1982; the equation derived in Thorslund (1982) assumed an equivalency mg/surface area and had an error in the derivation of a term.	Potency: 2 per mg/kg-day; Drinking water concentration at 10 ⁻⁵ risk level: 2E-4	(BW)3/4	LED10 with linear extrapolation; slope factors calculated from multiple tumor sites and summed using statistically appropriate model.	--	--	--
Heptachlor (B)	Potency: 4.5 per mg/kg-day; Drinking water concentration at 10 ⁻⁵ risk level: 8E-5 mg/L	(BW)2/3	Linearized multistage model	Potency: 4.5 per mg/kg-day; Drinking water concentration at 10 ⁻⁵ risk level: 8E-5 mg/L	(BW)2/3	Linearized multistage model	--	--	--
Heptachlor Epoxide (B)	Potency: 9.1 per mg/kg-day; Drinking water concentration at 10 ⁻⁵ risk level: 4E-5 mg/L	(BW)2/3	Linearized multistage model	Potency: 9.1 per mg/kg-day; Drinking water concentration at 10 ⁻⁵ risk level: 4E-5 mg/L	(BW)2/3	Linearized multistage model	--	--	--
Hexachlorobenzene (B)	Slope factor: 1.6 per mg/kg-day; Drinking water concentration at 10 ⁻⁵ risk level: 2E-4 mg/L	(BW)2/3	Linearized multistage model	Slope factor: 1.6 per mg/kg-day; Drinking water concentration at 10 ⁻⁵ risk level: 2E-4 mg/L	(BW)2/3	Linearized multistage model	--	--	--

Table 3. Summary of EPA Quantitative Cancer Assessments for List A and B Chemicals

Chemical (List A or B)	OW			IRIS			OPP		
	Quantitative Estimate	Adjustment factor ⁸⁴	Extrapolation Method ⁸⁵	Quantitative Estimate	Adjustment factor	Extrapolation Method	Quantitative Estimate	Adjustment factor	Extrapolation Method
Lindane (gamma-Hexachlorocyclohexane) (B)	Potency: 1.3 per mg/kg-day Drinking water concentration at 10-5 risk level: 3E-4 mg/L	(BW)2/3	Linearized multistage model	--	--	--	--	--	--
Pentachlorophenol (A)	Potency: 0.12 per mg/kg-day; Drinking water concentration at 10-5 risk level: 3E-3 mg/L	(BW)2/3	Linearized multistage model	Potency ⁹⁵ : 0.12 per mg/kg-day; Drinking water concentration at 10-5 risk level: 3E-3 mg/L	(BW)2/3	Linearized multistage model	Potency ⁹⁶ : 0.07 per mg/kg-day; Drinking water concentration at 10-5 risk level: 5E-3 mg/L	(BW)3/4	Linearized multistage model
Polychlorinated biphenyls (PCBs) (A)	Potency: 7.7 per mg/kg-day; Drinking water concentration at 10-5 risk level: 5E-5 mg/L	(BW)2/3	Linearized multistage model	Potency ⁹⁷ Range 0.07 to 2.0 per mg/kg-day Drinking water concentration at 10-5 risk level range: 2E-4 to 5E-3 mg/L	(BW)3/4	Linear extrapolation below LED10s	--	--	--

⁹⁵ A draft IRIS assessment (USEPA,2007g) for pentachlorophenol is currently in progress and states that under the 2005 Guidelines PCP is “likely to be carcinogenic to humans.” A multistage model using linear extrapolation from the point of departure (based on increased incidence of hepatocellular and adrenal gland tumors in male mice) was performed to derive an oral slope factor of $4 \times 10^{-1} \text{ (mg/kg-day)}^{-1}$ for PCP. The recommended slope factor should not be used with exposures greater than 0.3 mg/kg-day (the point of departure for the site with the greatest response for tPCP-exposed male mice), because above this point the slope factor may not approximate the observed dose-response relationship adequately.

⁹⁶ OPP is developing a RED for release in September 2008

⁹⁷ The cancer potency of PCB mixtures is determined using a tiered approach that depends on the information available. They are organized into tier descriptions. The "High risk and persistence" tier includes PCBs with an upper-bound slope factor of 2.0 per mg/kg-day and a Central-estimate slope factor of 1.0 per mg/kg-day. Criteria for use include food chain exposure, sediment or soil ingestion, dust or aerosol inhalation, dermal exposure, if an absorption factor has been applied, presence of dioxin-like, tumor-promoting, or persistent congeners, and early-life exposure (all pathways and mixtures). The "low risk and persistence" tier includes PCBs with an upper-bound slope factor of 0.4 per mg/kg-day, and with a central-estimate slope factor of 0.3 per mg/kg-day. Criteria for use include ingestion of water-soluble congeners, inhalation of evaporated congeners, dermal exposure, or if no absorption factor has been applied. The "lowest risk and persistence" tier includes PCBs with an upper-bound slope factor of 0.07 per mg/kg-day and a central-estimate slope factor of 0.04 per mg/kg-day. Criteria for use include congener or isomer analyses verify that congeners with more than 4 chlorines comprise less than 1/2% of total PCBs.

Table 3. Summary of EPA Quantitative Cancer Assessments for List A and B Chemicals

Chemical (List A or B)	OW			IRIS			OPP		
	Quantitative Estimate	Adjustment factor ⁸⁴	Extrapolation Method ⁸⁵	Quantitative Estimate	Adjustment factor	Extrapolation Method	Quantitative Estimate	Adjustment factor	Extrapolation Method
Combined Radiums (226 and 228) (A)	⁹⁸ --	--	FGR-13; linear no threshold model	--	--	--	--	--	--
Simazine (B)	Potency: 0.12 per mg/kg-day; Drinking water concentration at 10-5 risk level: 3E-3 mg/L	(BW)2/3	Weibull 83	--	--	--	--	--	--
Styrene (A)	Potency: 3E-2 per mg/kg-day; Drinking water concentration at 10-5 risk level: 1E-2 mg/L	(BW)2/3	Linearized multistage model	--	--	--	--	--	--
2,3,7,8-TCDD (Dioxin) (A)	Cancer potency: 156,000 per mg/kg-day; Drinking water concentration at 10-5 risk level: 2E-6mg/L	(BW)2/3	Linearized multistage model	-- ⁹⁹	--	--	--	--	--
Tetrachloroethylene (A)	Potency: 5E-2 per mg/kg-day; Drinking water concentration at 10-5 risk level: 7E-3 mg/L	(BW)2/3	Linearized multistage model	-- ¹⁰⁰	--	--	--	--	--

⁹⁸ ORIA is the principal health assessor for radionuclides. The 2000 radionuclides rule was a collaboration between OW and ORIA. The 2000 rulemaking (USEPA, 2000b) and supporting document (USEPA, 2000g) presented the concentration (in pCi/L) corresponding to 1E-4 lifetime total cancer risk and to 5E-5 lifetime fatal cancer risk; the individual cancer risk per unit intake factors for the individual radionuclides are provided in FGR-13 (USEPA, 1999c).

⁹⁹ An IRIS 2003 External Review Draft is available. A cancer potency factor of 0.001 per mg TEQ/kg BW/day (slope factor is 10-3 risk level) was proposed.

¹⁰⁰ An IRIS 2006 External Review Draft is available.

Table 3. Summary of EPA Quantitative Cancer Assessments for List A and B Chemicals

Chemical (List A or B)	OW			IRIS			OPP		
	Quantitative Estimate	Adjustment factor ⁸⁴	Extrapolation Method ⁸⁵	Quantitative Estimate	Adjustment factor	Extrapolation Method	Quantitative Estimate	Adjustment factor	Extrapolation Method
Toxaphene (B)	Potency: 1.1 per mg/kg-day; Drinking water concentration at 10-5 risk level: 3E-4 mg/L	(BW)2/3	Linearized multistage model	Potency: 1.1 per mg/kg-day; Drinking water concentration at 10-5 risk level: 3E-4 mg/L	(BW)2/3	Linearized multistage model	--	--	--
1,1,2-Trichloroethane (B)	Potency ¹⁰¹ : 0.091 per mg/kg-day; Drinking water concentration at 10-5 risk level: 0.004 mg/L	(BW)2/3	Linearized multistage model	Potency: 0.057 per mg/kg-day, ; Drinking water concentration at 10-5 risk level: 0.006 mg/L	(BW)2/3	Linearized multistage model	--	--	--
Trichloroethylene (A)	Cancer slope factor: 1.1E-2 per mg/kg-day; Drinking water concentration at 10-5 risk level: 3E-2 mg/L	(BW)2/3	Improved multistage linearized model	-- ¹⁰²	--	--	--	--	--

¹⁰¹ The term “potency” refers to either the q1* or slope factor depending on the modeling approach that was used. In some cases the summary document did not report the potency estimate. In such cases, the potency was back-calculated from reported unit risks or risk specific concentrations to facilitate data comparisons.

¹⁰² An EPA 2001 NCEA Draft Health Risk Assessment for trichloroethylene is available. The document derived a cancer slope factor range of 2 x 10⁻² to 4 x 10⁻¹ mg/kg-day. trichloroethylene was described as “Highly likely to produce cancer in humans” (1996, 1999 guidelines).

Table 3. Summary of EPA Quantitative Cancer Assessments for List A and B Chemicals

Chemical (List A or B)	OW			IRIS			OPP		
	Quantitative Estimate	Adjustment factor ⁸⁴	Extrapolation Method ⁸⁵	Quantitative Estimate	Adjustment factor	Extrapolation Method	Quantitative Estimate	Adjustment factor	Extrapolation Method
Vinyl chloride (B)	Potency: 2.3 per mg/kg-day; Drinking water concentration at 10-5 risk level: 1.5E-4 mg/L	(BW) ^{2/3}	Linearized multistage model	Potency: adult exposure: 0.72 (LMS); 0.75 (LED) per mg/kg-day. For continuous exposure from childhood on: 1.4 (LMS); 1.5 (LED) per mg/kg-day; Drinking water concentration at 10-5 risk level adult exposure 5E-4 mg/L:	PBPK model	Linearized multistage model, LED10/linear extrapolation	--	--	--

Table 4. Summary of Assessments by Other Organizations For List A¹⁰³ and B Chemicals

Chemical (List A or B)	Most Recent EPA		ATSDR (year)	CalEPA (year)		WHO ¹⁰⁴ (year) Includes JECFA, JMPR, CICAD, EHC		Health Canada (year)		NAS (year)	IARC (year)	NIEHS (year)
	RfD mg/kg- day (year, office)	Cancer classification (year, office)		MRL mg/kg- day	RfD mg/kg-day	Cancer classificatio n ¹⁰⁵	Tolerable Daily Intake (TDI) mg/kg-day	Cancer classifi- cation ¹⁰⁶	Tolerable Daily Intake (TDI) mg/kg-day			
Acryla- mide (A)	0.0002 (USEPA, 1991b)	B2, Probable human carcinogen (USEPA, 1993a)	--							--		
Alachlor (B)	0.01 (USEPA, 1998d) 0.005 (USEPA, 1998d)	Likely to be a human carcinogen at high doses; not likely to be a human carcinogen at low doses (USEPA, 2006c) ¹⁰⁷	--	--	Likely to be a human carcinogen at high doses; not likely to be a human carcinogen at low doses (1997a)	--	--	--	--	--	--	--

¹⁰³ Only the latest EPA assessment, ATSDR assessments published since 2002, or recent NAS assessments were reviewed for List A chemicals.

¹⁰⁴ WHO refers to Drinking Water Guidelines, unless otherwise specified. If another organization within WHO (JECFA, JMPR, CICAD, EHC) has a different value than WHO, it is included as a separate line. If another organization reports the same value as WHO, it is indicated by footnote.

¹⁰⁵ CalEPA and WHO assessments often do not provide an explicit overall qualitative cancer assessment. In that case, a phrase was inserted to capture the essence of the bottom line for these organizations.

¹⁰⁶ CalEPA and WHO assessments often do not provide an explicit overall qualitative cancer assessment. In that case, a phrase was inserted to capture the essence of the bottom line for these organizations.

¹⁰⁷ The data indicate that alachlor's tumorigenicity is operating by a nonlinear mode of action. OPP (USEPA, 1998d, 2001e, 2006c) concluded that alachlor causes nasal turbinate tumors via the generation of a reactive metabolite that leads to cytotoxicity and regenerative proliferation in the nasal epithelium; sustained cytotoxicity and proliferation is needed to lead to neoplasia. Based on this MOA assessment a non-linear dose response assessment is appropriate and the MCLG of 0 is no longer appropriate. Therefore, using the POD of 0.5 mg/kg-day identified by OPP for this endpoint and the UF of 100 (10H, 10A) would result in a health reference value of 0.005 mg/kg-day. Assuming 70 kg body weight, 2 L/day water consumption, and a 20% RSC, a water concentration derived from this value is 0.035 mg/L (rounded to 0.04 mg/L). The new MCLG would be based on the nonlinear cancer assessment.

Table 4. Summary of Assessments by Other Organizations For List A¹⁰³ and B Chemicals

Chemical (List A or B)	Most Recent EPA		ATSDR (year)	CalEPA (year)		WHO ¹⁰⁴ (year) Includes JECFA, JMPR, CICAD, EHC		Health Canada (year)		NAS (year)	IARC (year)	NIEHS (year)
	RfD mg/kg- day (year, office)	Cancer classification (year, office)		MRL mg/kg- day	RfD mg/kg-day	Cancer classificatio n ¹⁰⁵	Tolerable Daily Intake (TDI) mg/kg-day	Cancer classifi- cation ¹⁰⁶	Tolerable Daily Intake (TDI) mg/kg-day			
Alpha Particles Emitters (A)	--	A, Known human carcinogen (USEPA, 2000b)	--	--	-- (2003h) ¹⁰⁸	--	--	-- (2006) ¹⁰⁹	-- (1995) ¹¹⁰	-- (1988a) ¹¹¹	“Internalize d radionuclide s that emit α-particles are <i>carcinogeni c to humans (Group 1)</i> ” (2001a) ¹¹²	--

¹⁰⁸ The CalEPA assessment did not present a qualitative cancer classification, but did address cancer risk.

¹⁰⁹ Guidelines for Canadian Drinking Water Quality Summary Table, Health Canada, March 2006.

¹¹⁰ The Health Canada assessment did not present a qualitative cancer classification, but did address cancer risk.

¹¹¹ NAS (1988a). Health Risks of Radon and Other Internally Deposited Alpha-Emitters. BEIR IV. National Academy of Sciences, National Research Council. National Academy Press, Washington, DC.

¹¹² IARC (2001a). IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Volume 78, Ionizing Radiation, Part 2: Some Internally Deposited Radionuclides. World Health Organization, International Agency for Research on Cancer. IARC Press. Lyon, France.

Table 4. Summary of Assessments by Other Organizations For List A¹⁰³ and B Chemicals

Chemical (List A or B)	Most Recent EPA		ATSDR (year)	CalEPA (year)		WHO ¹⁰⁴ (year) Includes JECFA, JMPR, CICAD, EHC		Health Canada (year)		NAS (year)	IARC (year)	NIEHS (year)
	RfD mg/kg- day (year, office)	Cancer classification (year, office)	MRL mg/kg- day	RfD mg/kg-day	Cancer classification ¹⁰⁵	Tolerable Daily Intake (TDI) mg/kg-day	Cancer classifi- cation ¹⁰⁶	Tolerable Daily Intake (TDI) mg/kg-day	Cancer classifi- cation			
Antimony (A)	0.0004 (USEPA, 1992h)	D, not classifiable as to human carcinogenic ity (1986 guidelines) (USEPA,199 2h)	No int. or chronic oral MRL (1992)	0.0014 (1997b) ¹¹³	Negative oral dosing animal carcinogenic ity and limited evidence following inhalation insufficient to serve as basis for PHG (1997b)	0.006 (2003a, WHO)	--	0.0002 (1999)	Group V, inadequat e data for evaluation of carcinoge nicity (1999)	--	Antimony trioxide: Group 2B, possibly carcinogenic in humans Antimony trisulfide: Group 3, not classifiable as to human carcinogenic ity (1989)	--

¹¹³ The public health goal derived by CalEPA is based on noncancer effects. The RfD-equivalent shown was calculated based on the NOAEL and UF provided by CalEPA for noncancer effects.

Table 4. Summary of Assessments by Other Organizations For List A¹⁰³ and B Chemicals

Chemical (List A or B)	Most Recent EPA		ATSDR (year)	CalEPA (year)		WHO ¹⁰⁴ (year) Includes JECFA, JMPR, CICAD, EHC		Health Canada (year)		NAS (year)	IARC (year)	NIEHS (year)
	RfD mg/kg- day (year, office)	Cancer classification (year, office)	MRL mg/kg- day	RfD mg/kg-day	Cancer classificatio n ¹⁰⁵	Tolerable Daily Intake (TDI) mg/kg-day	Cancer classifi- cation ¹⁰⁶	Tolerable Daily Intake (TDI) mg/kg-day	Cancer classifi- cation			
Arsenic (A)	0.0003 (USEPA, 1993b)	A, Human carcinogen (USEPA, 1996a, 2001c)	0.0003 (chronic MRL 2007a)							--		
Asbestos (A)	--	Not available via ingestion; A, known human carcinogen via inhalation route (USEPA, 1986a) (USEPA, 1993c)	No int. or chronic oral MRL (2001)	0.04 (2003a) ¹¹⁴	--	--	--	--	--	--	Group 1, carcinogenic to humans (1987a)	Known to be a human carcinoge n (2005a)
Atrazine (B)	0.018 (USEPA, 2006a)	Not likely to be carcinogenic to humans (USEPA, 1999a) (USEPA, 2006a)	0.003 (intermediate MRL, (ATSDR, 2003a))	0.005 (1999a) ¹¹⁵	--	0.0005 (WHO, 2003b)	Evidence suggests nongenot oxic mode of action (WHO, 2003b)	0.0005 (1993)	Group III, possibly carcinoge nic to humans (1993)	--	Group 3, not classifiable as to human carcinogenic ity (1999a)	--

¹¹⁴ The public health goal derived by CalEPA is based on noncancer effects. The RfD-equivalent shown was calculated based on the NOAEL and UF provided by CalEPA for noncancer effects.

¹¹⁵ The public health goal derived by CalEPA is based on noncancer effects. The RfD-equivalent shown was calculated based on the NOAEL and UF provided by CalEPA for noncancer effects.

Table 4. Summary of Assessments by Other Organizations For List A¹⁰³ and B Chemicals

Chemical (List A or B)	Most Recent EPA		ATSDR (year)	CalEPA (year)		WHO ¹⁰⁴ (year) Includes JECFA, JMPR, CICAD, EHC		Health Canada (year)		NAS (year)	IARC (year)	NIEHS (year)
	RfD mg/kg- day (year, office)	Cancer classification (year, office)	MRL mg/kg- day	RfD mg/kg-day	Cancer classificatio n ¹⁰⁵	Tolerable Daily Intake (TDI) mg/kg-day	Cancer classifi- cation ¹⁰⁶	Tolerable Daily Intake (TDI) mg/kg-day	Cancer classifi- cation			
Barium (B)	0.2 (USEPA, 2005c)	Not likely to be carcinogenic to humans via oral route; carcinogenic potential cannot be determined via inhalation route (USEPA, 1996a,) 1998e)	0.2 (chronic MRL, 2007b)	0.07 (2003b) ¹¹⁶	--	0.7 mg/L (guideline value, 2004a) ¹²	--	0.73 mg/L (maximum allowable concentratio n (MAC), 1990) ¹²	Group VA, inadequat e data for evaluation (1990)	--	--	--
Benzene (B)	0.004 (USEPA, 2003f)	Known human carcinogen for all routes of exposure (USEPA, 1996a) (USEPA, 2000e)	0.0005 (chronic MRL, 2007c)	0.009 (2001a) ¹¹⁷	PHG based on cancer risk from leukemias (2001a)	-- ¹¹⁸	--	-- ¹¹⁹	Group I, document ed human carcinoge n (1986c)	--	Group 1, carcinogenic to humans (1987b)	Known to be a human carcinoge n (2005)

¹¹⁶ The public health goal derived by CalEPA is based on noncancer effects. The RfD-equivalent shown was calculated based on the NOAEL and UF provided by CalEPA for noncancer effects.

¹¹⁷ The public health goal derived by CalEPA is based on cancer potency. The RfD-equivalent shown was calculated based on the NOAEL and UF provided by CalEPA for noncancer effects.

¹¹⁸ A guideline value was provided in mg/L based on 10⁻⁵ cancer risk; noncancer values were not available.

Table 4. Summary of Assessments by Other Organizations For List A¹⁰³ and B Chemicals

Chemical (List A or B)	Most Recent EPA		ATSDR (year)	CalEPA (year)		WHO ¹⁰⁴ (year) Includes JECFA, JMPR, CICAD, EHC		Health Canada (year)		NAS (year)	IARC (year)	NIEHS (year)
	RfD mg/kg- day (year, office)	Cancer classification (year, office)		MRL mg/kg- day	RfD mg/kg-day	Cancer classificatio n ¹⁰⁵	Tolerable Daily Intake (TDI) mg/kg-day	Cancer classifi- cation ¹⁰⁶	Tolerable Daily Intake (TDI) mg/kg-day			
Benzo(a) pyrene (A)	--	Probable human carcinogen (Group B2, 1986a) (USEPA, 1994c)	No int. or chronic oral MRL (1995)							--		
Beryllium (A)	0.002 (USEPA, 1998f)	Carcinogeni c potential of ingested beryllium cannot be determined (1999a guidelines) (USEPA, 1998f)	0.002 (chronic MRL, 2002a)	0.0002 (2003c) ¹²⁰	--	0.002 (IPCS, 2001)	--	--	--	-- (2007) ¹²¹	Group 1, known human carcinogen (1993a)	--

¹¹⁹ A MAC value was provided in mg/L based on cancer risk; noncancer values were not available

¹²⁰ The public health goal derived by CalEPA is based on noncancer effects. The RfD-equivalent shown was calculated based on the NOAEL and UF provided by CalEPA for noncancer effects.

¹²¹ NAS (2007) Health Effects of Beryllium Exposure: A Literature Review. Committee on Beryllium Alloy Exposures, Committee on Toxicology, National Research Council, National Academy Press, Washington, DC.

Table 4. Summary of Assessments by Other Organizations For List A¹⁰³ and B Chemicals

Chemical (List A or B)	Most Recent EPA		ATSDR (year)	CalEPA (year)		WHO ¹⁰⁴ (year) Includes JECFA, JMPR, CICAD, EHC		Health Canada (year)		NAS (year)	IARC (year)	NIEHS (year)
	RfD mg/kg- day (year, office)	Cancer classification (year, office)		RfD mg/kg-day	Cancer classificatio n ¹⁰⁵	Tolerable Daily Intake (TDI) mg/kg-day	Cancer classifi- cation ¹⁰⁶	Tolerable Daily Intake (TDI) mg/kg-day	Cancer classifi- cation			
Beta Particle and Photon Emitters (A)	--	A, Known human carcinogen (USEPA, 2000b)	--	--	-- (2003i) ¹²²	--	--	-- (2006) ¹²³	-- (1995) ¹²⁴	-- (1990) ¹²⁵ (2006a) ¹²⁶	“Internalize d radionuclide s that emit β-partic les are carcinogeni c to humans (Group 1).” (2001a) ¹²⁷	--
Cadmium (A)	0.005 (USEPA, 1994d)	D, Not classifiable as to human carcino- genicity by the oral route of exposure (USEPA, 1991b)	0.0002 (MRL 1999a)							0.005 (SNARL 1983)		

¹²² The CalEPA assessment did not present a qualitative cancer classification, but did address cancer risk.

¹²³ Guidelines for Canadian Drinking Water Quality Summary Table, Health Canada, March 2006.

¹²⁴ The Health Canada assessment did not present a qualitative cancer classification, but did address cancer risk.

¹²⁵ NAS (1990). Health Effects of Exposure to Low Levels of Ionizing Radiation. BEIR V. National Academy of Sciences, National Research Council. National Academy Press, Washington, DC.

¹²⁶ NAS (2006a). Health Risks from Exposure to Low Levels of Ionizing Radiation. BEIR VII Phase 2. National Academy of Sciences, National Research Council. National Academy Press, Washington, DC

¹²⁷ IARC (2001). IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Volume 78, Ionizing Radiation, Part 2: Some Internally Deposited Radionuclides. World Health Organization, International Agency for Research on Cancer. IARC Press. Lyon, France.

Table 4. Summary of Assessments by Other Organizations For List A¹⁰³ and B Chemicals

Chemical (List A or B)	Most Recent EPA		ATSDR (year)	CalEPA (year)		WHO ¹⁰⁴ (year) Includes JECFA, JMPR, CICAD, EHC		Health Canada (year)		NAS (year)	IARC (year)	NIEHS (year)
	RfD mg/kg- day (year, office)	Cancer classification (year, office)	MRL mg/kg- day	RfD mg/kg-day	Cancer classificatio n ¹⁰⁵	Tolerable Daily Intake (TDI) mg/kg-day	Cancer classifi- cation ¹⁰⁶	Tolerable Daily Intake (TDI) mg/kg-day	Cancer classifi- cation			
Carbofuran (B)	0.005 (USEPA, 1987d)	--	--	0.003 (2000a) ¹²⁸	No evidence of carcinogenic ity (2000a)	0.002 (ADI, (JMPR, 1996))	--	0.01 (ADI, (Health Canada, 1991))	--	-- 1983 ¹²⁹	--	--
Carbon tetrachlo- ride (A)	0.0007 (USEPA, 1987a)	Probable human carcinogen (USEPA, 1986a) (USEPA, 1991f)	0.007 (Intermediate MRL 2005a)							--		
Chlordane (B)	0.0005 (USEPA, 1998c)	Likely carcinogen by all routes of exposure (USEPA, 1996a) (USEPA, 1998c)	0.0006 (chronic MRL, 1994a)	0.00001 (1997c) ¹³⁰	PHG based on animal carcinogenic ity (1997c)	0.0005 (ADI, (JMPR, 1986a))	--	--	--	--	Group 2B, possibly carcinogenic to humans (2001b)	--

¹²⁸ The public health goal derived by CalEPA is based on noncancer effects. The RfD-equivalent shown was calculated based on the NOAEL and UF provided by CalEPA for noncancer effects.

¹²⁹ NAS (1983) Drinking Water and Health, Vol. 5. Safe Drinking Water Committee, Board on Toxicology and Environmental Health Hazards, National Research Council, National Academy of Sciences, Washington, DC

¹³⁰ The public health goal derived by CalEPA is based on cancer potency. The RfD-equivalent shown was calculated based on the NOAEL and UF provided by CalEPA for noncancer effects.

Table 4. Summary of Assessments by Other Organizations For List A¹⁰³ and B Chemicals

Chemical (List A or B)	Most Recent EPA		ATSDR (year)	CalEPA (year)		WHO ¹⁰⁴ (year) Includes JECFA, JMPR, CICAD, EHC		Health Canada (year)		NAS (year)	IARC (year)	NIEHS (year)
	RfD mg/kg- day (year, office)	Cancer classification (year, office)	MRL mg/kg- day	RfD mg/kg-day	Cancer classificatio n ¹⁰⁵	Tolerable Daily Intake (TDI) mg/kg-day	Cancer classifi- cation ¹⁰⁶	Tolerable Daily Intake (TDI) mg/kg-day	Cancer classifi- cation			
Chromium (VI) (Regula- tion applies to total chromium) (B)	0.003 (USEPA, 1998a)	Via oral: D, not classifiable as to human carcinogenic ity (USEPA, 1986a) No assessment for the oral route provided under the 1996 guidelines (USEPA, 1996a) (USEPA, 1998a)	No int. or chronic oral MRL (2000a)	--	--	-- ¹³¹	--	-- ¹³²	--	--	Group 1, carcinogenic to humans (1990)	Known to be a human carcinoge n (2005a)

¹³¹ A guideline value was provided in mg/L based on 10⁻⁵ cancer risk; noncancer values were not available.

¹³² A MAC value was provided in mg/L based on cancer risk; noncancer values were not available

Table 4. Summary of Assessments by Other Organizations For List A¹⁰³ and B Chemicals

Chemical (List A or B)	Most Recent EPA		ATSDR (year)	CalEPA (year)		WHO ¹⁰⁴ (year) Includes JECFA, JMPR, CICAD, EHC		Health Canada (year)		NAS (year)	IARC (year)	NIEHS (year)
	RfD mg/kg- day (year, office)	Cancer classification (year, office)	MRL mg/kg- day	RfD mg/kg-day	Cancer classificatio n ¹⁰⁵	Tolerable Daily Intake (TDI) mg/kg-day	Cancer classifi- cation ¹⁰⁶	Tolerable Daily Intake (TDI) mg/kg-day	Cancer classifi- cation			
Chromium (III) (Regula- tion applies to total chromium) (B)	1.5 (USEPA, 1998b)	Via oral: There are inadequate data to determine the potential carcinogenic ity of trivalent chromium ¹³³ (USEPA, 1998b)	No int. or chronic oral MRL (2000a)	--	--	-- ¹³⁴	--	-- ¹³⁵	--	--	Group 3, not classifiable as to carcinogenic ity to humans (1990)	--

¹³³ The assessment also noted that “the classification of hexavalent chromium as a known human carcinogen raises a concern for the carcinogenic potential of trivalent chromium.”

¹³⁴ A guideline value was provided in mg/L based on 10⁻⁵ cancer risk; noncancer values were not available.

¹³⁵ A MAC value was provided in mg/L based on cancer risk; noncancer values were not available

Table 4. Summary of Assessments by Other Organizations For List A¹⁰³ and B Chemicals

Chemical (List A or B)	Most Recent EPA		ATSDR (year)	CalEPA (year)		WHO ¹⁰⁴ (year) Includes JECFA, JMPR, CICAD, EHC		Health Canada (year)		NAS (year)	IARC (year)	NIEHS (year)
	RfD mg/kg- day (year, office)	Cancer classification (year, office)	MRL mg/kg- day	RfD mg/kg-day	Cancer classificatio n ¹⁰⁵	Tolerable Daily Intake (TDI) mg/kg-day	Cancer classifi- cation ¹⁰⁶	Tolerable Daily Intake (TDI) mg/kg-day	Cancer classifi- cation			
Cyanide (A)	0.02 (USEPA, 1992i)	D, Not classifiable as to human carcino- genicity (USEPA, 1986a) (USEPA, 1992i)	0.05 (intermediate oral MRL 2006a)							--		
2,4-D (2,4- Di-chloro- phenoxy- acetic Acid) (B)	0.005 (USEPA, 2005d)	D, not classifiable as to human carcinogeni city (USEPA, 1986a) (USEPA, 2005d)	--	0.005 (2007a) ¹³⁶	Negative animal carcinogeni city, and mixed limited epidemiolog y insufficient basis to serve as basis for PHG	--	--	0.01 (ADI, 1991c)	--	--	2B, possibly carcinogenic to humans (1987d)	--
Dalapon (2,2- Dichloropr opionic Acid) (B)	0.03 (USEPA, 1992j)	--	--	0.028 (1997d) ¹³⁷	--	--	--	--	--	--	--	--

¹³⁶ The public health goal derived by CalEPA is based on noncancer effects. The RfD-equivalent shown was calculated based on the NOAEL and UF provided by CalEPA for noncancer effects.

Table 4. Summary of Assessments by Other Organizations For List A¹⁰³ and B Chemicals

Chemical (List A or B)	Most Recent EPA		ATSDR (year)	CalEPA (year)		WHO ¹⁰⁴ (year) Includes JECFA, JMPR, CICAD, EHC		Health Canada (year)		NAS (year)	IARC (year)	NIEHS (year)
	RfD mg/kg- day (year, office)	Cancer classification (year, office)	MRL mg/kg- day	RfD mg/kg-day	Cancer classificatio n ¹⁰⁵	Tolerable Daily Intake (TDI) mg/kg-day	Cancer classifi- cation ¹⁰⁶	Tolerable Daily Intake (TDI) mg/kg-day	Cancer classifi- cation			
Di(2-ethylhexyl) adipate (DEHA) (A)	0.6 (USEPA, 1992a)	C, Possible human carcinogen (USEPA, 1986a) (USEPA, 1994e)	--							--		
Di(2-ethylhexyl) phthalate (DEHP) (A)	0.02 (USEPA, 1991g)	B2, Probable human carcinogen (USEPA, 1986a) (USEPA, 1993d)	0.06 (chronic MRL 2002b)									
1,2-Dibromo-3-chloropropane (DBCP) (B)	--	B2, probable human carcinogen (USEPA, 1986a) (USEPA, 1988b)	0.002 (intermediate MRL, 1992)	0.00003 (1999k) ¹³⁸	PHG based on animal carcinogenicity (1999k)	-- ¹³⁹	guideline values based on animal carcinogenicity (2003f)	--	--	--	Group 2B, possibly carcinogenic to humans (1999h)	Reasonably anticipated to be a human carcinogen (2005a)

¹³⁷ The public health goal derived by CalEPA is based on noncancer effects. The RfD-equivalent shown was calculated based on the NOAEL and UF provided by CalEPA for noncancer effects.

¹³⁸ The public health goal derived by CalEPA is based on cancer potency. The RfD-equivalent shown was calculated based on the NOAEL and UF provided by CalEPA for noncancer effects.

¹³⁹ A guideline value was provided in mg/L based on 10⁻⁵ cancer risk; noncancer values were not available.

Table 4. Summary of Assessments by Other Organizations For List A¹⁰³ and B Chemicals

Chemical (List A or B)	Most Recent EPA		ATSDR (year)	CalEPA (year)		WHO ¹⁰⁴ (year) Includes JECFA, JMPR, CICAD, EHC		Health Canada (year)		NAS (year)	IARC (year)	NIEHS (year)
	RfD mg/kg- day (year, office)	Cancer classification (year, office)	MRL mg/kg- day	RfD mg/kg-day	Cancer classification n ¹⁰⁵	Tolerable Daily Intake (TDI) mg/kg-day	Cancer classification ¹⁰⁶	Tolerable Daily Intake (TDI) mg/kg-day	Cancer classifi- cation			
1,2- Dichloro- benzene (o- Dichloro- benzene) (A)	0.09 (USEPA, 1991b)	D, Not classifiable as to human carcinogenic ity (USEPA198 6a) (USEPA, 1991h)	0.3 (chronic MRL, 2006b)							0.3 mg/L (NTP, 1982)		
1,4- Dichloro- benzene (p- Dichloro- benzene) (A)	0.1 (USEPA, 1987a)	C, Possible human carcinogen	0.07 (chronic MRL 2006)							0.0134 (NAS, 1977, 1983) ADI)		

Table 4. Summary of Assessments by Other Organizations For List A¹⁰³ and B Chemicals

Chemical (List A or B)	Most Recent EPA		ATSDR (year)	CalEPA (year)		WHO ¹⁰⁴ (year) Includes JECFA, JMPR, CICAD, EHC		Health Canada (year)		NAS (year)	IARC (year)	NIEHS (year)
	RfD mg/kg-day (year, office)	Cancer classification (year, office)		RfD mg/kg-day	Cancer classification ¹⁰⁵	Tolerable Daily Intake (TDI) mg/kg-day	Cancer classification ¹⁰⁶	Tolerable Daily Intake (TDI) mg/kg-day	Cancer classification			
1,2-Di-chloro-ethane (Ethylene Dichloride) (A)	--	B2 (USEPA, 1986a) (USEPA, 1991i)										
1,1-Di-chloro-ethylene (B)	0.05 (USEPA, 2002f)	Inadequate for an assessment of human carcinogenic potential (USEPA 1999a, 2002f)	0.009 (chronic MRL, 1994b)	0.003 (1999i) ¹⁴⁰	Primarily negative evidence in animal carcinogenicity insufficient to serve as basis of PHG (1999i)	0.046 (WHO, 2004k) ¹⁴¹	--	0.003 (ADI, 1994)	Class IIIIB, Possibly carcinogenic to humans (1994)	0.02 (NRC, 1983) ¹⁴²	Group 3, not classifiable as to carcinogenicity to humans (1999d)	--
<i>cis</i> -1,2-Dichloro-ethylene (A)	0.01 (USEPA, 1990c)	D, Not classifiable as to human carcinogenicity (USEPA, 1991b)	0.3 (intermediate oral MRL 1996a)							--		

¹⁴⁰ The public health goal derived by CalEPA is based on noncancer effects. The RfD-equivalent shown was calculated based on the NOAEL and UF provided by CalEPA for noncancer effects.

¹⁴¹ CICAD (IPCS, 2003) reports the same TDI

¹⁴² NAS developed a suggested no-adverse-response level (SNARL); the RfD-equivalent shown was calculated based on the NOAEL and UF provided by NAS for noncancer effects.

Table 4. Summary of Assessments by Other Organizations For List A¹⁰³ and B Chemicals

Chemical (List A or B)	Most Recent EPA		ATSDR (year)	CalEPA (year)		WHO ¹⁰⁴ (year) Includes JECFA, JMPR, CICAD, EHC		Health Canada (year)		NAS (year)	IARC (year)	NIEHS (year)
	RfD mg/kg- day (year, office)	Cancer classification (year, office)	MRL mg/kg- day	RfD mg/kg-day	Cancer classificatio n ¹⁰⁵	Tolerable Daily Intake (TDI) mg/kg-day	Cancer classificati on ¹⁰⁶	Tolerable Daily Intake (TDI) mg/kg-day	Cancer classificati on			
<i>trans</i> -1,2-Dichloroethylene (A)	0.02 (USEPA, 1990e)	D, Not classifiable as to human carcinogenicity (USEPA, 1990e)	0.2 (intermediate MRL 1996b)							--		
Dichloromethane (Methylene Chloride) (A)	0.06 (USEPA, 1993e)	B2, Probable human carcinogen (USEPA, 1986a, 1995c)	0.06 (chronic MRL 2000b)							--		
1,2-Dichloropropane (B)	--	B2, probable human carcinogen (USEPA, 1986a, 1990h)	0.09 (chronic MRL, 1989)	0.13 (1999b) ¹⁴³	PHG based on animal carcinogenicity (1999b)	0.014 (WHO, 2003c)	Evidence for carcinogenicity limited, threshold approach appropriate (WHO, 2003c)	--	--	--	Group 3, not classifiable (1999b)	--

¹⁴³ The public health goal derived by CalEPA is based on cancer potency. The RfD-equivalent shown was calculated based on the NOAEL and UF provided by CalEPA for noncancer effects.

Table 4. Summary of Assessments by Other Organizations For List A¹⁰³ and B Chemicals

Chemical (List A or B)	Most Recent EPA		ATSDR (year)	CalEPA (year)		WHO ¹⁰⁴ (year) Includes JECFA, JMPR, CICAD, EHC		Health Canada (year)		NAS (year)	IARC (year)	NIEHS (year)
	RfD mg/kg- day (year, office)	Cancer classification (year, office)		MRL mg/kg- day	RfD mg/kg-day	Cancer classificatio n ¹⁰⁵	Tolerable Daily Intake (TDI) mg/kg-day	Cancer classifi- cation ¹⁰⁶	Tolerable Daily Intake (TDI) mg/kg-day			
Dinoseb (B)	0.001 (USEPA, 1992k)	D, not classifiable as to human carcinogenic ity (USEPA, 1986a, 1992k)	--	0.001 (1997e) ¹⁴⁴	--	--	--	0.001 (ADI, 1992c)	No strong evidence of carcinoge nic potential (1992c)	0.006 (NRC,1983) ¹⁴⁵	--	--
Diquat (B)	0.0022 (USEPA, 1995d)/ 0.005 (USEPA, 1995a)	E, evidence of non- carcinogenic ity (USEPA, 1986a, 2001a)	--	0.0022 (2000b) ¹⁴⁶	--	0.002 (ADI, (WHO, 2004b) ¹⁴⁷	--	0.008 (ADI, (Health Canada, 1986a)	--	--	--	--
Endothall (B)	0.007 (USEPA, 2005e)	Not likely to be carcinogenic to humans (USEPA, 1999a,2005e)	--	0.08 (1997f) ¹⁴⁸	Evidence of carcinogenic ity is equivocal (1997f)	--	--	--	--	--	--	--

¹⁴⁴ The public health goal derived by CalEPA is based on noncancer effects. The RfD-equivalent shown was calculated based on the NOAEL and UF provided by CalEPA for noncancer effects.

¹⁴⁵ NAS developed a suggested no-adverse-response level (SNARL); the RfD-equivalent shown was calculated based on the NOAEL and UF provided by NAS for noncancer effects.

¹⁴⁶ The public health goal derived by CalEPA is based on noncancer effects. The RfD-equivalent shown was calculated based on the NOAEL and UF provided by CalEPA for noncancer effects.

¹⁴⁷ JMPR (1993) reports the same ADI.

¹⁴⁸ The public health goal derived by CalEPA is based on noncancer effects. The RfD-equivalent shown was calculated based on the NOAEL and UF provided by CalEPA for noncancer effects.

Table 4. Summary of Assessments by Other Organizations For List A¹⁰³ and B Chemicals

Chemical (List A or B)	Most Recent EPA		ATSDR (year)	CalEPA (year)		WHO ¹⁰⁴ (year) Includes JECFA, JMPR, CICAD, EHC		Health Canada (year)		NAS (year)	IARC (year)	NIEHS (year)
	RfD mg/kg- day (year, office)	Cancer classification (year, office)	MRL mg/kg- day	RfD mg/kg-day	Cancer classification n ¹⁰⁵	Tolerable Daily Intake (TDI) mg/kg-day	Cancer classification ¹⁰⁶	Tolerable Daily Intake (TDI) mg/kg-day	Cancer classification			
Endrin (B)	0.0003 (USEPA, 1992l)	D, not classifiable as to human carcinogenic ity (USEPA, 1986a, 1992l)	0.0003 (chronic MRL, 1996c)	0.00025 (1999c) ¹⁴⁹	No evidence of carcinogenic ity (1999c)	0.0002 (provisional TDI, (WHO, 2004c))	Insufficie nt evidence to indicate carcinoge nic hazard to humans (IPCS, 1992), EHC)	--	--	--	Group 3, not classifiable as to human carcinogenic ity (1987c)	--
Epichloro- hydrin (B)	0.002 (USEPA, 1987e)	B2, probable human carcinogen (USEPA, 1986a, 1994f)	--	--	--	0.00014 (WHO, 2004d)	--	--	--	--	Group 2A, probably carcinogenic to humans (1999c)	Reasonabl y anticipate d to be a human carcinoge n (2005a)

¹⁴⁹ The public health goal derived by CalEPA is based on noncancer effects. The RfD-equivalent shown was calculated based on the NOAEL and UF provided by CalEPA for noncancer effects.

Table 4. Summary of Assessments by Other Organizations For List A¹⁰³ and B Chemicals

Chemical (List A or B)	Most Recent EPA		ATSDR (year)	CalEPA (year)		WHO ¹⁰⁴ (year) Includes JECFA, JMPR, CICAD, EHC		Health Canada (year)		NAS (year)	IARC (year)	NIEHS (year)
	RfD mg/kg- day (year, office)	Cancer classification (year, office)	MRL mg/kg- day	RfD mg/kg-day	Cancer classificatio n ¹⁰⁵	Tolerable Daily Intake (TDI) mg/kg-day	Cancer classifi- cation ¹⁰⁶	Tolerable Daily Intake (TDI) mg/kg-day	Cancer classifi- cation			
Ethyl- benzene (A)	0.097 (USEPA, 1987f)	D, Not classifiable as to human carcinogenic ity (USEPA, 1986a, 1991j)	0.5 (intermediate MRL (ATSDR, 2007d))							--		
Ethylene Dibromide (EDB; 1,2- Dibromoet hane) (B)	0.009 (USEPA, 2004a)	Likely to be carcinogenic to humans (USEPA, 1999a, 2004a)	No int. or chronic oral MRL (1992b)	0.0025 (2003d) ¹⁵⁰	Known to cause cancer (2003d)	-- ¹⁵¹	Probably carcinoge nic to humans (WHO, 2004e)	--	--	--	Group 2A, probably carcinogenic to humans (1999d)	Reasonabl y anticipate d to be a human carcinoge n (2005a)
Fluoride (A)	-- ¹⁵²	--	0.05 (chronic MRL (ATSDR, 2003b))							(NRC, 2006c)		

¹⁵⁰ The public health goal derived by CalEPA is based on cancer potency. The RfD-equivalent shown was calculated based on the NOAEL and UF provided by CalEPA for noncancer effects.

¹⁵¹ A guideline value was provided in mg/L based on 10⁻⁵ cancer risk; noncancer values were not available.

¹⁵² No RfD has been determined for fluoride. The MCLG was based directly on a LOAEL of 20 mg/day, divided by an uncertainty factor of 2.5 and a drinking water intake of 2 L/day.

Table 4. Summary of Assessments by Other Organizations For List A¹⁰³ and B Chemicals

Chemical (List A or B)	Most Recent EPA		ATSDR (year)	CalEPA (year)		WHO ¹⁰⁴ (year) Includes JECFA, JMPR, CICAD, EHC		Health Canada (year)		NAS (year)	IARC (year)	NIEHS (year)
	RfD mg/kg- day (year, office)	Cancer classification (year, office)	MRL mg/kg- day	RfD mg/kg-day	Cancer classificatio n ¹⁰⁵	Tolerable Daily Intake (TDI) mg/kg-day	Cancer classifi- cation ¹⁰⁶	Tolerable Daily Intake (TDI) mg/kg-day	Cancer classifi- cation			
Glyphosate (B)	1.75 (USEPA, 2002d)	E, evidence of non- carcinogeni- city in humans (USEPA, 1986a, 2002d)	--	0.175 (2007b) ¹⁵³	--	0-0.3 (ADI, (JMPR, 1986b))	--	0.3 (negligible daily intake (NDI), 1987)	--	--	--	--
Heptachlor (B)	0.0005 (USEPA, 1992g)	B2, probable human carcinogen (USEPA, 1986a, 1992g)	0.0001 (intermediate MRL, 2007e)	0.0015 (1999d) ¹⁵¹	PHG based on animal carcinogeni- city (1999d)	0.0001 (ADI, (WHO, 2004f)) ¹⁵⁵	--	--	--	--	Group 2B, possibly carcinogenic to humans (2001b)	--
Heptachlor Epoxide (B)	0.000013 (USEPA, 1992g)	B2, probable human carcinogen (USEPA, 1986a, 1992g)	0.0001 (intermediate MRL, 2007e)	0.0000125 (1999e) ¹⁵³	PHG based on animal carcinogeni- city (1999e)	0.0001 (ADI, (WHO, 2004f))	--	--	--	--	Group 2B, possibly carcinogenic to humans (2001b)	--

¹⁵³ The public health goal derived by CalEPA is based on noncancer effects. The RfD-equivalent shown was calculated based on the NOAEL and UF provided by CalEPA for noncancer effects.

¹⁵⁴ The public health goal derived by CalEPA is based on cancer potency. The RfD-equivalent shown was calculated based on the NOAEL and UF provided by CalEPA for noncancer effects.

¹⁵⁵ JMPR (1991) reports the same ADI.

¹⁵⁶ The public health goal derived by CalEPA is based on cancer potency. The RfD-equivalent shown was calculated based on the NOAEL and UF provided by CalEPA for noncancer effects.

Table 4. Summary of Assessments by Other Organizations For List A¹⁰³ and B Chemicals

Chemical (List A or B)	Most Recent EPA		ATSDR (year)	CalEPA (year)		WHO ¹⁰⁴ (year) Includes JECFA, JMPR, CICAD, EHC		Health Canada (year)		NAS (year)	IARC (year)	NIEHS (year)
	RfD mg/kg- day (year, office)	Cancer classification (year, office)	MRL mg/kg- day	RfD mg/kg-day	Cancer classification n ¹⁰⁵	Tolerable Daily Intake (TDI) mg/kg-day	Cancer classifi- cation ¹⁰⁶	Tolerable Daily Intake (TDI) mg/kg-day	Cancer classifi- cation			
Hexa- chloro- benzene (B)	0.0008 (USEPA, 1991k)	B2, probable human carcinogen (USEPA, 1986a, 1991k)	0.00005 (chronic MRL, 2002c)	0.00003 (2003g) ¹⁵⁴	PHG based on animal carcinogenic ity (2003g)	0.0006 (tentative NDI, 1986c, JMPR)	--	--	--	--	Group 2B, possibly carcinogenic to humans (2001e)	Reasonabl y anticipat ed to be a human carcinoge n (2005a)
Hexa- chloro- cyclo- pentadiene (B)	0.006 (USEPA, 2001b)	Not likely to be a human carcinogen via inhalation route; Potential by the oral route is indeterminat e based on a lack of data (USEPA, 1999a, 2001b)	0.1 (intermediate MRL, 1999b)	0.01 (1999f) ¹⁵⁸	--	--	--	--	--	--	--	--

¹⁵⁷ The public health goal derived by CalEPA is based on cancer potency. The RfD-equivalent shown was calculated based on the NOAEL and UF provided by CalEPA for noncancer effects.

¹⁵⁸ The public health goal derived by CalEPA is based on noncancer effects. The RfD-equivalent shown was calculated based on the NOAEL and UF provided by CalEPA for noncancer effects.

Table 4. Summary of Assessments by Other Organizations For List A¹⁰³ and B Chemicals

Chemical (List A or B)	Most Recent EPA		ATSDR (year)	CalEPA (year)		WHO ¹⁰⁴ (year) Includes JECFA, JMPR, CICAD, EHC		Health Canada (year)		NAS (year)	IARC (year)	NIEHS (year)
	RfD mg/kg- day (year, office)	Cancer classification (year, office)	MRL mg/kg- day	RfD mg/kg-day	Cancer classificatio n ¹⁰⁵	Tolerable Daily Intake (TDI) mg/kg-day	Cancer classifi- cation ¹⁰⁶	Tolerable Daily Intake (TDI) mg/kg-day	Cancer classifi- cation			
Lindane (gamma- Hexachloro cyclo- hexane) (B)	0.0047 (USEPA, 2002g)	Suggestive evidence of carcinogenic ity, but not sufficient to assess human carcinogenic potential (USEPA, 1999a, 2002g)	0.00001 (intermediate MRL, 2005b)	0.000012 (1999g) ¹⁵⁹	PHG based on animal carcinogenic ity (1999g)	0.005 (ADI, (WHO, 2004g)) ¹⁶⁰ / 0.06 (acute RfD, (JMPR, 2002a))	Unlikely to pose carcinoge nic risk to humans (JMPR, 2002a)	--	--	--	<i>inadequate</i> evidence for hexachloroc yclohexanes in humans; <i>sufficient</i> <i>evidence</i> that alpha-HCH, lindane and technical HCH are carcinogenic in mice; there is <i>limited</i> <i>evidence</i> that beta-HCH is carcinogenic in mice. (1987b)	Reasonabl y anticipat ed to be a human carcinoge n (2005a)

¹⁵⁹ The public health goal derived by CalEPA is based on cancer potency. The RfD-equivalent shown was calculated based on the NOAEL and UF provided by CalEPA for noncancer effects.

¹⁶⁰ JMPR (2002a) reports the same ADI.

Table 4. Summary of Assessments by Other Organizations For List A¹⁰³ and B Chemicals

Chemical (List A or B)	Most Recent EPA		ATSDR (year)	CalEPA (year)		WHO ¹⁰⁴ (year) Includes JECFA, JMPR, CICAD, EHC		Health Canada (year)		NAS (year)	IARC (year)	NIEHS (year)
	RfD mg/kg- day (year, office)	Cancer classification (year, office)	MRL mg/kg- day	RfD mg/kg-day	Cancer classificatio n ¹⁰⁵	Tolerable Daily Intake (TDI) mg/kg-day	Cancer classifi- cation ¹⁰⁶	Tolerable Daily Intake (TDI) mg/kg-day	Cancer classifi- cation			
Mercury (Inorganic) (B)	0.0003 (USEPA, 1995e)	C, possible human carcinogen for Methylmerc ury; D, not classifiable as to human carcinogeni city for elemental mercury (USEPA, 1986a, 1995f)	0.002 (intermediate MRL, 1999c)	0.00023 (1999h) ¹⁶¹	--	0.002 (TDI,(CICA D, 2003))/ 0.0016 (provisional tolerable weekly intake, (JECFA, 2004b)) ; all based on methylmerc ury	--	0.03 (1986b); based on methylmerc ury	--	--	Group 3, not classifiable as to human carcinogeni city (1993b)	--
Methoxy- chlor (B)	0.005 (USEPA, 1991c)	D, not classifiable as to human carcinogeni city (USEPA, 1986a, 1990p)	0.005 (intermediate MRL, 2002d)	0.005 (1999i) ¹⁶²	--	0.005 (TDI, (WHO, 2004h))/ 0.1 (ADI, (JMPR, 1977))	--	0.1 (ADI, 1991b)	--	--	Group 3, not classifiable as to its carcinogeni city to humans (1987b)	--

¹⁶¹ The public health goal derived by CalEPA is based on noncancer effects. The RfD-equivalent shown was calculated based on the NOAEL and UF provided by CalEPA for noncancer effects.

¹⁶² The public health goal derived by CalEPA is based on noncancer effects. The RfD-equivalent shown was calculated based on the NOAEL and UF provided by CalEPA for noncancer effects.

Table 4. Summary of Assessments by Other Organizations For List A¹⁰³ and B Chemicals

Chemical (List A or B)	Most Recent EPA		ATSDR (year)	CalEPA (year)		WHO ¹⁰⁴ (year) Includes JECFA, JMPR, CICAD, EHC		Health Canada (year)		NAS (year)	IARC (year)	NIEHS (year)
	RfD mg/kg- day (year, office)	Cancer classification (year, office)	MRL mg/kg- day	RfD mg/kg-day	Cancer classificatio n ¹⁰⁵	Tolerable Daily Intake (TDI) mg/kg-day	Cancer classifi- cation ¹⁰⁶	Tolerable Daily Intake (TDI) mg/kg-day	Cancer classifi- cation			
Mono- chloro- benzene (Chloro- benzene) (B)	0.02 (USEPA, 1993f)	D, not classifiable as to human carcinogeni- city (USEPA, 1986a, 1991j)	0.4 (intermediate MRL, 1990a)	0.063 (2003e) ¹⁶³	--	0.086 (TDI, (WHO, 2004i)/ 0.1 (TDI, (EHC, 1991))	--	0.0089 (ADI, (Health Canada, 1988a))	Group IIIB, possibly carcinoge- nic to man (1988a)	--	--	--
Nitrate (as N) (B)	1.6 (USEPA, 1991)	--	--	45 mg/L (nitrate); equivalent to 10 mg/L nitrate- nitrogen (PHG, (CalEPA, 1997g)) ¹⁶⁴ , ¹⁶⁵	--	3.7 (nitrate ion, ADI, (WHO, 2004i)) ¹⁶⁶	--	45 mg/L (nitrate); equivalent to 10 mg/L nitrate- nitrogen (MAC, (Health Canada, 1992a)) ¹⁶⁷	Possibly carcinoge- nic to humans (1992a)	Unlikely to contribute to human cancer risk (1995)	--	--

¹⁶³ The public health goal derived by CalEPA is based on noncancer effects. The RfD-equivalent shown was calculated based on the NOAEL and UF provided by CalEPA for noncancer effects.

¹⁶⁴ The public health goal derived by CalEPA is based on noncancer effects. The RfD-equivalent shown was calculated based on the NOAEL and UF provided by CalEPA for noncancer effects.

¹⁶⁵ The noncancer value is presented as mg/L only. The value is derived by dividing the NOAEL which is a concentration in drinking water for humans by the uncertainty factor.

¹⁶⁶ JECFA (2003) reports the same ADI.

¹⁶⁷ The noncancer value is presented as mg/L only. The value is derived by dividing the NOAEL which is a concentration in drinking water for humans by the uncertainty factor.

Table 4. Summary of Assessments by Other Organizations For List A¹⁰³ and B Chemicals

Chemical (List A or B)	Most Recent EPA		ATSDR (year)	CalEPA (year)		WHO ¹⁰⁴ (year) Includes JECFA, JMPR, CICAD, EHC		Health Canada (year)		NAS (year)	IARC (year)	NIEHS (year)
	RfD mg/kg- day (year, office)	Cancer classification (year, office)		MRL mg/kg- day	RfD mg/kg-day	Cancer classificatio n ¹⁰⁵	Tolerable Daily Intake (TDI) mg/kg-day	Cancer classifi- cation ¹⁰⁶	Tolerable Daily Intake (TDI) mg/kg-day			
Nitrite (as N) (B)	0.16 (USEPA, 1990h)	--	--	45 mg/L (nitrate); equivalent to 10 mg/L nitrate- nitrogen (PHG, (CalEPA, 1997g)) ^{168,} ¹⁶⁹	--	0.07 (ADI, (WHO, 2007))/ 0.07 (ADI, (JECFA, 2003))	--	3.2 mg/L (as nitrite ion) (MAC, (Health Canada, 1992a)) ¹⁷⁰	Possibly carcinoge nic to humans (1992a)	Unlikely to contribute to human cancer risk (1995)	--	--
Oxamyl (Vydate) (B)	0.001 (USEPA, 2000c)	“Not likely” to be carcinogenic in humans (USEPA, 1999, 2000c)	--	0.025 (1997h) ¹⁷¹	Classificatio n not stated, but indicates oxamyl not a mutagen or carcinogen (1997h)	0.009 (ADI, (JMPR, 2002b))	Classifica tion not stated, but indicates oxamyl is “Not carcinoge nic (JMPR, 2002b)	--	--	--	--	--

¹⁶⁸ The public health goal derived by CalEPA is based on noncancer effects. The RfD-equivalent shown was calculated based on the NOAEL and UF provided by CalEPA for noncancer effects.

¹⁶⁹ The noncancer value is presented as mg/L only. The value is derived by dividing the NOAEL which is a concentration in drinking water for humans by the uncertainty factor.

¹⁷⁰ The noncancer value is presented as mg/L only. The value is derived by dividing the NOAEL which is a concentration in drinking water for humans by the uncertainty factor.

¹⁷¹ The public health goal derived by CalEPA is based on noncancer effects. The RfD-equivalent shown was calculated based on the NOAEL and UF provided by CalEPA for noncancer effects.

Table 4. Summary of Assessments by Other Organizations For List A¹⁰³ and B Chemicals

Chemical (List A or B)	Most Recent EPA		ATSDR (year)	CalEPA (year)		WHO ¹⁰⁴ (year) Includes JECFA, JMPR, CICAD, EHC		Health Canada (year)		NAS (year)	IARC (year)	NIEHS (year)
	RfD mg/kg-day (year, office)	Cancer classification (year, office)		MRL mg/kg- day	RfD mg/kg-day	Cancer classification n ¹⁰⁵	Tolerable Daily Intake (TDI) mg/kg-day	Cancer classification ¹⁰⁶	Tolerable Daily Intake (TDI) mg/kg-day			
Pentachlorophenol (A)	0.03 (USEPA, 1993g)	B2, Probable human carcinogen (USEPA, 1986a, 2004b)	0.001 (chronic MRL 2001a)							0.021 (1986 SNARL)		
Picloram (B)	0.2 (USEPA, 1995b)	E, evidence of non-carcinogenicity (USEPA, 1986a, 1995b)	--	0.07 (1997i) ¹⁷²	--	--	--	0.02 (NDI, (Health Canada, 1988b))	--	0.15 (1983)	Group 3, not classifiable as to human carcinogenicity (1991)	
Poly-chlorinated biphenyls (PCBs) (A)	0.00007 (USEPA, 1996c)	B2, Probable human carcinogen (USEPA, 1986a, 1997b)	0.00002 (chronic MRL 2000c)							--		
Combined Radiums (226 and 228) (A)	--	A, Known human carcinogen (USEPA, 2000f)	No int. or chronic oral MRL (1990a)	--	-- (2006) ¹⁷³	--	--	--	-- ¹⁷⁴	-- (1988) ¹⁷⁵	“Internalized radionuclides that emit α-particles are carcinogenic to humans (Group 1).” (2001c) ¹⁷⁶	--

¹⁷² The public health goal derived by CalEPA is based on noncancer effects. The RfD-equivalent shown was calculated based on the NOAEL and UF provided by CalEPA for noncancer effects.

Table 4. Summary of Assessments by Other Organizations For List A¹⁰³ and B Chemicals

Chemical (List A or B)	Most Recent EPA		ATSDR (year)	CalEPA (year)		WHO ¹⁰⁴ (year) Includes JECFA, JMPR, CICAD, EHC		Health Canada (year)		NAS (year)	IARC (year)	NIEHS (year)
	RfD mg/kg- day (year, office)	Cancer classification (year, office)	MRL mg/kg- day	RfD mg/kg-day	Cancer classificatio n ¹⁰⁵	Tolerable Daily Intake (TDI) mg/kg-day	Cancer classificati on ¹⁰⁶	Tolerable Daily Intake (TDI) mg/kg-day	Cancer classificati on			
Selenium (B)	0.005 (USEPA, 1991k)	D, not classifiable as to human carcinogenic ity (USEPA, 1986a,1991k)	0.005 (chronic MRL, 2003c)	--	--	0.004 (WHO, 2003d)	Does not appear to be carcinoge nic (WHO, 2003d)	0.5-0.7 minimum dose for toxic effects (1992)/ 0.02-0.12 minimum dietary requirement (1992d)	data are insufficie nt to allow an evaluation of the carcinoge nicity (1992d)	0.4 (tolerable upper intake level, (NAS, 2000))/ 0.055 mg/day (RDA, (NAS, 2000))	Group 3, Insufficient evidence (1975)	--
Simazine (B)	0.018 (USEPA, 2006f)	Considered not likely to be carcinogenic to humans (USEPA, 2005a, 2006f)	No int. or chronic oral MRL (2003a)	0.0005 (2001b) ¹⁷⁴	Uncertainty factor used to derive PHG to account for limited evidence of carcinogenic ity (2001b)	0.00052 (WHO, 2003e)	--	0.0013 (NDI, 1989)	--	--	Group 3, not classifiable as to its carcinogenic ity to humans (1999e)	--

¹⁷³ The CalEPA assessment did not present a qualitative cancer classification, but did address cancer risk.

¹⁷⁴ The Health Canada assessment did not present a qualitative cancer classification, but did address cancer risk.

¹⁷⁵ NAS (1988). Health Risks of Radon and Other Internally Deposited Alpha-Emitters. BEIR IV. National Academy of Sciences, National Research Council. National Academy Press, Washington, DC.

¹⁷⁶ IARC (2001c). IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Volume 78, Ionizing Radiation, Part 2: Some Internally Deposited Radionuclides. World Health Organization, International Agency for Research on Cancer. IARC Press. Lyon, France.

¹⁷⁷ The public health goal derived by CalEPA is based on cancer potency. The RfD-equivalent shown was calculated based on the NOAEL and UF provided by CalEPA for noncancer effects.

Table 4. Summary of Assessments by Other Organizations For List A¹⁰³ and B Chemicals

Chemical (List A or B)	Most Recent EPA		ATSDR (year)	CalEPA (year)		WHO ¹⁰⁴ (year) Includes JECFA, JMPR, CICAD, EHC		Health Canada (year)		NAS (year)	IARC (year)	NIEHS (year)
	RfD mg/kg- day (year, office)	Cancer classification (year, office)	MRL mg/kg- day	RfD mg/kg-day	Cancer classificatio n ¹⁰⁵	Tolerable Daily Intake (TDI) mg/kg-day	Cancer classifi- cation ¹⁰⁶	Tolerable Daily Intake (TDI) mg/kg-day	Cancer classifi- cation			
Styrene (A)	0.2 (USEPA, 1991m)	C, Possible human carcinogen (1986 guidelines) (USEPA, 1991b)	No int. or chronic oral MRL (2007f)							--		
2,3,7,8- TCDD (Dioxin) (A)	--	B2, Probable human carcinogen (USEPA, 1986a, 1988c)	1.0×10^{-9} (chronic MRL 1998)							1.0×10^{-7} (ADI (NRC, 1977)). Review of EPA draft assessmen t (NRC, 2006b)		

Table 4. Summary of Assessments by Other Organizations For List A¹⁰³ and B Chemicals

Chemical (List A or B)	Most Recent EPA		ATSDR (year)	CalEPA (year)		WHO ¹⁰⁴ (year) Includes JECFA, JMPR, CICAD, EHC		Health Canada (year)		NAS (year)	IARC (year)	NIEHS (year)
	RfD mg/kg- day (year, office)	Cancer classification (year, office)	MRL mg/kg- day	RfD mg/kg-day	Cancer classificatio n ¹⁰⁵	Tolerable Daily Intake (TDI) mg/kg-day	Cancer classifi- cation ¹⁰⁶	Tolerable Daily Intake (TDI) mg/kg-day	Cancer classifi- cation			
Tetrachloro ethylene (A)	0.0143 (USEPA 1990i)	B2, Probable human carcinogen (USEPA, 1986a, 1990i)	No int. or chronic MRL (1997)							--		
Thallium ¹⁷⁸ (A)	7.0 x 10 ⁻⁵ (USEPA, 1992m)	There is inadequate information to assess the carcinogenic potential (USEPA, 2005a, 2008a)	--							--		
Toluene (B)	0.08 (USEPA, 2005f)	There is inadequate information to assess the carcinogenic potential (USEPA, 2005a, 2005f)	0.02 (intermediate MRL, 2000d)	0.022 (1999j) ¹⁷⁵	--	0.22 (WHO, 2004j)	--	0.22 (1996)	--	--	Group 3, not classifiable as to carcinogenic ity to humans (1999f)	--

¹⁷⁸ EPA completed the risk reassessment for thallium in September of 2009 (USEPA 2009b). Because the new assessment was not completed by March 1, 2009, the cutoff date for this review, the outcome of this assessment has not been included in the current review effort. EPA will consider the updated assessment in the next review cycle.

¹⁷⁹ The public health goal derived by CalEPA is based on noncancer effects. The RfD-equivalent shown was calculated based on the NOAEL and UF provided by CalEPA for noncancer effects.

Table 4. Summary of Assessments by Other Organizations For List A¹⁰³ and B Chemicals

Chemical (List A or B)	Most Recent EPA		ATSDR (year)	CalEPA (year)		WHO ¹⁰⁴ (year) Includes JECFA, JMPR, CICAD, EHC		Health Canada (year)		NAS (year)	IARC (year)	NIEHS (year)
	RfD mg/kg- day (year, office)	Cancer classification (year, office)	MRL mg/kg- day	RfD mg/kg-day	Cancer classificatio n ¹⁰⁵	Tolerable Daily Intake (TDI) mg/kg-day	Cancer classifi- cation ¹⁰⁶	Tolerable Daily Intake (TDI) mg/kg-day	Cancer classifi- cation			
Toxaphene (B)	0.0004 (USEPA, 1996d)	B2, probable human carcinogen (USEPA, 1986a, 1991, IRIS)	0.001 (intermediate MRL, 1996d)	0.00035 (2003f) ¹⁸⁰	PHG based on animal carcinogenic ity (2003f)	--	--	--	--	--	Group 2B, possibly carcinogenic to humans (2001d)	Reasonabl y anticipate d to human carcinoge n (2005a)
2,4,5-TP (Silvex; 2,4,5- Trichloro- phenoxy- propionic Acid) (B)	0.008 (USEPA, 1988d)	D, not classifiable as to human carcinogenic ity (USEPA, 1986a, 1988d)	--	0.0009 (2003) ¹⁸¹	Primarily negative animal carcinogenic ity, and mixed epidemiolog y insufficient basis to serve as basis for PHG (1999)--	0.003 (TDI, 2004, WHO) ¹⁸² / 0-0.003 (ADI, 1979, JMPR)	--	--	--	0.00075 (ADI, (NRC, 1977))	2B, possibly carcinogenic to humans (1987d)	--

¹⁸⁰ The public health goal derived by CalEPA is based on cancer potency. The RfD-equivalent shown was calculated based on the NOAEL and UF provided by CalEPA for noncancer effects.

¹⁸¹ The public health goal derived by CalEPA is based on noncancer effects. The RfD-equivalent shown was calculated based on the NOAEL and UF provided by CalEPA for noncancer effects.

¹⁸² 2,4,5-TP is included in the plan of work of the rolling revision of the WHO Guidelines for Drinking-water Quality.

Table 4. Summary of Assessments by Other Organizations For List A¹⁰³ and B Chemicals

Chemical (List A or B)	Most Recent EPA		ATSDR (year)	CalEPA (year)		WHO ¹⁰⁴ (year) Includes JECFA, JMPR, CICAD, EHC		Health Canada (year)		NAS (year)	IARC (year)	NIEHS (year)
	RfD mg/kg- day (year, office)	Cancer classification (year, office)		MRL mg/kg- day	RfD mg/kg-day	Cancer classificatio n ¹⁰⁵	Tolerable Daily Intake (TDI) mg/kg-day	Cancer classifi- cation ¹⁰⁶	Tolerable Daily Intake (TDI) mg/kg-day			
1,2,4-Tri- chloro- benzene (B)	0.01 (USEPA, 1996b)	D, not classifiable as to human carcinogenic ity (USEPA, 1986a, 1996b)	--	0.0015 (1999) ¹⁸³	Positive indication of carcinogenic ity in animal data study too preliminary to serve as basis for PHG (1999)	0.0077 (2004, WHO)	--	--	--	--	--	--
1,1,1- Trichloro- ethane (B)	2 (USEPA, 2007e)	Inadequate information to assess carcinogenic potential (USEPA, 2005a, 2007e)	20 (intermediate MRL, 2006)	0.076 (2006) ¹⁸⁴	Not classifiable as to carcinogenic ity on the basis of inadequate human and animal data (2006)	0.6 (2003, WHO)	--	--	--	--	--	--
1,1,2- Trichloro- ethane (B)	0.004 (USEPA, 1995g)	C, possible human carcinogen (USEPA, 1986a, 1994c)	0.04 (intermediate MRL, 1989)	0.0004 (2006) ¹⁸⁵	PHG based on animal carcinogenic ity (2006)	--	--	--	--	--	Group 3, not classifiable as to human carcinogenic ity (1999)	--

¹⁸³ The public health goal derived by CalEPA is based on noncancer effects. The RfD-equivalent shown was calculated based on the NOAEL and UF provided by CalEPA for noncancer effects.

¹⁸⁴ The public health goal derived by CalEPA is based on noncancer effects. The RfD-equivalent shown was calculated based on the NOAEL and UF provided by CalEPA for noncancer effects.

Table 4. Summary of Assessments by Other Organizations For List A¹⁰³ and B Chemicals

Chemical (List A or B)	Most Recent EPA		ATSDR (year)	CalEPA (year)		WHO ¹⁰⁴ (year) Includes JECFA, JMPR, CICAD, EHC		Health Canada (year)		NAS (year)	IARC (year)	NIEHS (year)
	RfD mg/kg- day (year, office)	Cancer classification (year, office)	MRL mg/kg- day	RfD mg/kg-day	Cancer classificatio n ¹⁰⁵	Tolerable Daily Intake (TDI) mg/kg-day	Cancer classifi- cation ¹⁰⁶	Tolerable Daily Intake (TDI) mg/kg-day	Cancer classifi- cation			
Trichloro- ethylene (A)	0.007 (USEPA, 1985b)	Probable human carcinogen (USEPA, 1985b)	No int. or chronic oral MRL (1997)							2006b		
Uranium (A)	0.003 (USEPA, 1991b)	--	0.002 (intermediate MRL 1999d)							--		
Vinyl chloride (B)	0.003 (USEPA, 2000d)	Known human carcinogen by inhalation and oral routes of exposure; highly likely to be carcinogenic by dermal route (USEPA, 1999a, 2000d)	0.003 (chronic MRL, 2006c)	0.0013 (2000c) ¹⁸⁵	PHG based on animal carcinogenic ity (2000c)	-- ¹⁸⁷	Genotoxic carcinoge n (IPCS, 1999)/ Carcinoge nic in experime ntal animals and man (JECFA, 2004a)	-- ¹⁸⁸	Group 1: carcinoge nic to humans (1992b)	--	Group 1, carcinogenic to humans (1987e)	--

¹⁸⁵ The public health goal derived by CalEPA is based on cancer potency. The RfD-equivalent shown was calculated based on the NOAEL and UF provided by CalEPA for noncancer effects.

¹⁸⁶ The public health goal derived by CalEPA is based on cancer potency. The RfD-equivalent shown was calculated based on the NOAEL and UF provided by CalEPA for noncancer effects.

¹⁸⁷ A guideline value was provided in mg/L based on 10⁻⁵ cancer risk; noncancer values were not available.

Table 4. Summary of Assessments by Other Organizations For List A¹⁰³ and B Chemicals

Chemical (List A or B)	Most Recent EPA		ATSDR (year)	CalEPA (year)		WHO ¹⁰⁴ (year) Includes JECFA, JMPR, CICAD, EHC		Health Canada (year)		NAS (year)	IARC (year)	NIEHS (year)
	RfD mg/kg- day (year, office)	Cancer classification (year, office)	MRL mg/kg- day	RfD mg/kg-day	Cancer classificatio n ¹⁰⁵	Tolerable Daily Intake (TDI) mg/kg-day	Cancer classifi- cation ¹⁰⁶	Tolerable Daily Intake (TDI) mg/kg-day	Cancer classifi- cation			
Xylenes (Total) (B)	0.2 (USEPA, 2003d)	Data are inadequate for an assessment of the carcinogenic potential (USEPA, 1999a, 2003d)	0.2 (chronic MRL, 2007g)	0.25 (1997j) ¹⁸⁵	--	0.179 (WHO, 2003e)	--	--	--	--	Group 3, not classifiable as to their carcinogenic ity to humans (1999g)	--

¹⁸⁸ A MAC value was provided in mg/L based on cancer risk; noncancer values were not available

¹⁸⁹ The public health goal derived by CalEPA is based on noncancer effects. The RfD-equivalent shown was calculated based on the NOAEL and UF provided by CalEPA for noncancer effects.

Table 5. Summary for List B Chemicals

Chemical (Date of regulation)	Regulation					IRIS		OPP		New Data/Possible Impact on MCLG ¹⁹⁰		Potential Repro/Dev Concern at MCL ¹⁹¹	Possible New MCLG (mg/L) ¹⁹²	Nominate for New Assessment?
	MCLG mg/L	MCL mg/L (basis if MCL≠MCLG)	RfD (mg/kg-day)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (Year of guidelines used)	DWEL (mg/L) & RSC	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/Citation	Cancer classification (year of guidelines used; year of assessment)	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (year of guidelines used; year of assessment)	Non-cancer	Cancer			
Alachlor (1991)	0	0.002 mg/L (PQL)	0.01/1 (NOAEL)/100 (10H, 10A) Hemosiderosis and hemolytic anemia/ Naylor et al.1984 also cited as Monsanto 1984	B2, probable human carcinogen (1986 guidelines)	--	0.01/1 (NOAEL)/100 (10H, 10A) Hemosiderosis and hemolytic anemia/ Naylor et al.1984 also cited as Monsanto 1984	--	0.01 (2005)/1 (NOAEL)/100 (10H, 10A) Hemosiderosis and hemolytic anemia/ Naylor et al.1984 also cited as Monsanto 1984	Likely to be a human carcinogen at high doses; not likely to be a human carcinogen at low doses (2005 guidelines; 2006)	No/No	Yes/Yes	No	Yes 0.04 ¹⁹³	No

¹⁹⁰ Data in this column address two separate questions: (1) Are there new data since the latest Office of Water assessment that could be used, or have been used, to develop an updated RfD? If the new data have already been used to develop a formal EPA assessment (as shown in previous columns), there is no additional notation. If the new data were identified in the literature search, rather than from an updated Agency assessment, this consideration is indicated as “lit search.” (2) Might the new data have an impact on the MCLG? New data that could be used to develop an RfD would not have an impact on the MCLG if the MCLG is zero. New cancer data would generally not affect the MCLG, unless the data changed the cancer descriptor. If the first half of the column is “no” for new data, the second half of the column is blank.

¹⁹¹ If there is a potential new MCLG, this addresses concern at the potential new MCLG. If there no potential new MCLG, then this addresses concern at the current MCLG. If the MCLG is zero, such as for carcinogens, then this addresses concern at the current MCL.

¹⁹² The quantitative responses (i.e. “Yes” or “No”) and the potential new MCLG numeric values (in mg/L) are based strictly on the health evaluation (not occurrence data or other risk management considerations) using the RSC values currently applied to each NPDWRs except where specifically noted. Both qualitative and quantitative responses in this column are subject to changes based on additional consideration of the RSC (only for selected chemicals if deemed necessary), occurrence data, treatment technology, etc.

¹⁹³ The data indicate that alachlor’s tumorigenicity is operating by a nonlinear mode of action. OPP (USEPA, 1998d, 2001e, 2006c) concluded that alachlor causes nasal turbinate tumors via the generation of a reactive metabolite that leads to cytotoxicity and regenerative proliferation in the nasal epithelium; sustained cytotoxicity and proliferation is needed to lead to neoplasia. Based on this MOA assessment a non-linear dose response assessment is appropriate and the MCLG of 0 is no longer appropriate. Therefore, using the POD of 0.5 mg/kg-day identified by OPP for this endpoint and the UF of 100 (10H, 10A) would result in a health reference value of 0.005 mg/kg-day. Assuming 70 kg body weight, 2 L/day water consumption, and a 20% RSC, a water concentration derived from this value is 0.035 mg/L (rounded to 0.04 mg/L). The new MCLG would be based on the nonlinear cancer assessment.

Table 5. Summary for List B Chemicals

Chemical (Date of regulation)	Regulation					IRIS		OPP		New Data/Possible Impact on MCLG ¹⁹⁰		Potential Repro/Dev Concern at MCL ¹⁹¹	Possible New MCLG (mg/L) ¹⁹²	Nominate for New Assessment?
	MCLG mg/L	MCL mg/L (basis if MCL≠ MCLG)	RfD (mg/kg-day)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (Year of guidelines used)	DWEL (mg/L) & RSC	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/Citation	Cancer classification (year of guidelines used; year of assessment)	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (year of guidelines used; year of assessment)	Non-cancer	Cancer			
Atrazine (1991)	0.003	0.003	0.005/ 0.5 (NOAEL)/ 100 (10H, 10A)/ Decreased body weight gain in F2 pups; maternal toxicity/ Ciba-Geigy 1987	C, possible human carcinogen (1986 guidelines)	0.175 20% Also factor of 10 for class C	0.035 (1993)/ 3.5 (NOAEL)/ 100 (10H, 10A)/ Decreased body weight gain/ Ciba-Geigy 1986	--	0.018 (2006)/ 1.8 (NOAEL)/ 100 (10H, 10A)/ attenuation of the luteinizing hormone surge in females in a 6-month rat feeding study / Morseth et al. 1996	Not likely to be carcinogenic to humans (2006, 1999 guidelines) (Note that, although document was finalized in 2006, assessment was done in 2002, so used 1999 guidelines)	Yes/Yes	Yes/Yes	No ¹⁹⁴	TBD ¹⁹⁵	No ¹⁹⁶
Barium (1991)	2	2	0.07/ 0.21 (adjusted NOAEL)/ 3 H/ No changes in blood pressure, or serum chemistry / Wones et al. 1990	D, not classifiable as to human carcinogenicity (1986 guidelines)	2 100%	0.2 (2005)/ 63 (BMDL05)/ 300 (10H, 10A, 3D)/ Nephropathy/ NTP 1994	Not likely to be carcinogenic to humans following oral exposure (1996 guidelines; 1998)	--	--	Yes/Yes	No	No	Yes ¹⁹⁷ 6	No

¹⁹⁴ See next footnote for a description of issues on potential reproductive effects.

¹⁹⁵ Several new studies relevant to reproductive or developmental effects, atrazine's critical effect, were located. In particular, one published study (Enoch et al., 2007) and one other study (Stanko et al., 2008) suggest that atrazine and its chlorometabolites may affect prenatal and postnatal development in both males and females. Although the new OPP RfD based on Morseth et al. (1996) suggests a potential for a change in the MCLG value, further evaluation of the newly available data is needed to determine if a change is justified and, if so, the appropriate value of the revised MCLG. On October 7, 2009 (74 FR 51593, USEPA, 2009c), EPA announced its intent to reevaluate atrazine. At the end of this process, the Agency will decide whether to revise its current risk assessment (USEPA, 2006a); such a revision could lead to a revised MCLG.

¹⁹⁶ Atrazine is not being nominated for a new assessment; however, on October 7, 2009 (74 FR 51593, USEPA, 2009c), EPA announced its intention to launch a comprehensive reevaluation of its 2006 OPP atrazine risk assessment.

¹⁹⁷ Using the IRIS RfD of 0.2 mg/kg-day and assuming 70 kg body weight, 2 liters water intake per day, a DWEL of 7 mg/L can be derived. This would result in a new MCLG of 6 mg/L. This value is three times the current value. An RSC of 80% was determined using the *Exposure Decision Tree* approach described in the Methodology for Deriving Ambient Water Quality Criteria for the Protection of Human Health (USEPA, 2000h). The dietary component of the RSC estimate was based on data from the United Kingdom Total Diet Study and not on data from the United States. Dietary data for the United States are not available. The diet in the United Kingdom is relatively consistent with that in the United States and qualifies for use in the RSC analysis.

Table 5. Summary for List B Chemicals

Chemical (Date of regulation)	Regulation				IRIS		OPP		New Data/Possible Impact on MCLG ¹⁹⁰		Potential Repro/Dev Concern at MCL ¹⁹¹	Possible New MCLG (mg/L) ¹⁹²	Nominate for New Assessment?	
	MCLG mg/L	MCL mg/L (basis if MCL≠ MCLG)	RfD (mg/kg-day)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (Year of guidelines used)	DWEL (mg/L) & RSC	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/Citation	Cancer classification (year of guidelines used; year of assessment)	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (year of guidelines used; year of assessment)	Non-cancer				Cancer
Benzene (1987)	0	0.005 (PQL)	0.0007 – 0.002 / (ADI)/ 1 (NOAEL)/ 1000 (10H, 10A, 10S)/ Slight leukopenia and erythrocytopenia/ Wolf et al. 1956	--	--	0.004 (2003)/ 1.2 (BMDL)/ 300 (10H, 3L, 3S, 3D)/ Decreased lymphocyte count/ Rothman et al. 1996	Known human carcinogen for all routes of exposure (1996 guidelines;2000)	--	--	Yes/No	Yes/No	No	No	No
Carbofuran (1991)	0.04	0.04	0.005/ 0.5 (NOAEL)/ 100 (10H, 10A)/ Acetylcholinesterase inhibition and testicular degeneration/ FMC Corp. 1983	E, evidence of noncarcinogenicity (1986 guidelines)	0.18 20%	0.005 (1987)/ 0.5 (NOAEL)/ 100 (10H, 10A)/ RBC and plasma cholinesterase inhibition, and testicular and uterine effects/ FMC Corp. 1983	--	0.00006 (2006) ¹⁹⁸ 0.03 (BMDL10)/ 100 (10H, 10A, 5D)/ Brain acetylcholinesterase inhibition/ FMC Corp. et al. 2005	Not likely to be a human carcinogen (2005 guidelines)	Yes/Yes	No	No	No ¹⁹⁹	No
Chlordane (1991)	0	0.002 (PQL)	0.00005/ 0.045 (LOAEL)/ 1000 (10A, 10H, 10L)/ Liver necrosis in male rats/ Yonemura et al. 1983	B2, probable human carcinogen (1986 guidelines)	--	0.0005 (1998)/ 0.15 (NOAEL)/ 300 (10H, 10A, 3D)/ Liver necrosis in mice/ Khasawinah & Grutsch 1989	Likely to be a carcinogen by all routes of exposure (1996 guidelines; 1998)	--	--	Yes/No	No/No	No	No	No
Chromium (VI) (1991 – regulation applies to total chromium)	0.1	0.1	0.0048/ 2.41 (NOAEL)/ 100 (10H, 10A) ; MF=5/ None/ MacKenzie et al. 1958	D, not classifiable as to human carcinogenicity (1986 guidelines)	0.17 70%	0.003 (1998)/ 2.5 (NOAEL)/ 300 (10H, 10A, 3S); MF=3/ None/ MacKenzie et al. 1958	By the oral route: D, not classifiable as to human carcinogenicity (1986 guidelines; 1998)	--	--	Yes (lit search)/ Yes ²⁰⁰	Yes (lit search)/ Yes ²⁰¹	No	TBD (pending review of 2008 NTP report)	Yes

¹⁹⁸ OPP's value for carbofuran is an acute RfD for cholinesterase inhibition, which OPP has determined is protective of chronic exposures; this RfD is 0.00006 mg/kg-day. OPP has also derived an aPAD of 0.00006 mg/kg-day based on this RfD.

¹⁹⁹ A new MCLG can be derived based on the updated OPP RfD of 0.00006 mg/kg-day, using a 10 kg child, a 1 L/day water consumption, and a 20% RSC; the revised MCLG is 0.000012 mg/L. The RSC of 20% was selected based on the actual food dietary exposure (100%) from children aged 1 to 6 (USEPA, 2005a). However, this pesticide registration is in the process of being cancelled due to its acute toxicity and high dietary exposure for children, so EPA is not recommending a change to the MCLG at this time.

²⁰⁰ A final report for a 2-year NTP bioassay of sodium dichromate is available (NTP 2008). The study found histiocytic cellular infiltration in the liver, small intestine, and pancreatic and mesenteric lymph nodes of rats and mice, and diffuse epithelial hyperplasia in the small intestine of male and female mice. A screening-level RfD of 0.0008 mg/kg-day can be derived based on a minimal LOAEL of 0.25 mg Cr/kg-day for chronic inflammation in the liver of female rats in this study, and an uncertainty factor of 300 (10A, 10H, 3L).

Table 5. Summary for List B Chemicals

Chemical (Date of regulation)	Regulation					IRIS		OPP		New Data/Possible Impact on MCLG ¹⁹⁰		Potential Repro/Dev Concern at MCL ¹⁹¹	Possible New MCLG (mg/L) ¹⁹²	Nominate for New Assessment?
	MCLG mg/L	MCL mg/L (basis if MCL≠MCLG)	RfD (mg/kg-day)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (Year of guidelines used)	DWEL (mg/L) & RSC	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/Citation	Cancer classification (year of guidelines used; year of assessment)	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (year of guidelines used; year of assessment)	Non-cancer	Cancer			
Chromium (III) (1991 – regulation applies to total chromium)	0.1	0.1	0.0048/ 2.41 (NOAEL)/ 100 (10H, 10A); MF=5/ None/ MacKenzie et al. 1958	D, not classifiable as to human carcinogenicity (1986 guidelines)	0.17 70%	1.5 (1998)/ 1468 (NOAEL)/ 100 (10H, 10A); MF=10/ None/ Ivankovic and Preussmann, 1975 (insoluble salts)	Inadequate data to determine the potential carcinogenicity (1996 guidelines; 1998)	--	--	Yes (lit search)/ Yes ²⁰²	Yes (lit search)/ No ²⁰³	No	TBD (pending review of 07 NTP report); Cr III is a micronutrient	Yes
2,4-D (2,4-Di-chloro-phenoxy-acetic Acid) (1991)	0.07	0.07	0.01/ 1 (NOAEL)/ 100 (10H, 10A)/ Hematologic, hepatic and renal toxicity/ Serota et al. 1983	D, not classifiable as to human carcinogenicity (1986 guidelines)	0.35 20%	0.01 (1988)/ 1 (NOAEL)/ 100 (10H, 10A)/ Hematologic, hepatic and renal toxicity/ Serota et al. 1983	--	0.005 (2005)/ 5 (NOAEL) 1000 (10H, 10A, 10D)/ Decreased body weight gain (in females) and alterations in hematology and blood chemistry (in both sexes)/ Jeffries et al. 1995	D, not classifiable as to human carcinogenicity (1986 guidelines)	Yes/Yes	No	No	Yes ²⁰⁴ 0.04	No
Dalapon (2,2-Dichloroproprionic Acid) (1992)	0.2	0.2	0.03/ 8 (NOAEL)/ 300 (10A, 10H, 3D)/ Increased kidney weight/ Paynter et al. 1960	D, not classifiable as to human carcinogenicity (1986 guidelines)	0.9 20%	0.03 (1989)/ 8.45 (NOEL)/ 300 (10A, 10H, 3D)/ Increased kidney weight/ Paynter et al. 1960	--	--	--	No	No	No	No	No

²⁰¹ A final report for a 2-year NTP bioassay of sodium dichromate is available (NTP 2008). This study found clear evidence of carcinogenic activity of sodium dichromate dihydrate in male and female F344 rats based on increased incidences of squamous cell neoplasms of the oral cavity, and clear evidence of carcinogenic activity of sodium dichromate dihydrate in male and female B6C3F1 mice based on increased incidences of neoplasms in the small intestine.

²⁰² The current IRIS assessment for Chromium III is for insoluble salts. A draft report for a 2-year NTP bioassay of chromium picolinate (a soluble form of chromium III) is available (NTP 2007). No adverse noncancer effects were reported. This assessment recommends that no new RfD for Cr(III) be derived until the final NTP study report is available.

²⁰³ A draft of the 2-year NTP bioassay of chromium picolinate is available, but has not yet been peer-reviewed (NTP 2007). The draft report concluded that there was equivocal evidence of carcinogenicity in male rats and no evidence of carcinogenicity in female rats and male and female mice. This assessment recommends that when a final report from NTP is completed, the carcinogenic potential of ingested Cr(III) be reevaluated.

²⁰⁴ No new data are available that would support the development of an updated RfD. OPP's 2005 RfD (USEPA, 2005d) is considered to be the most appropriate RfD for 2,4-D. Using the recent OPP update of the RfD would reduce the MCLG to 0.04 mg/L based on the OPP (USEPA, 2005d) RfD of 0.005 mg/kg-day, 70 kg body weight, 2 L water consumption and 20% RSC.

Table 5. Summary for List B Chemicals

Chemical (Date of regulation)	Regulation					IRIS		OPP		New Data/Possible Impact on MCLG ¹⁹⁰		Potential Repro/Dev Concern at MCL ¹⁹¹	Possible New MCLG (mg/L) ¹⁹²	Nominate for New Assessment?
	MCLG mg/L	MCL mg/L (basis if MCL≠ MCLG)	RfD (mg/kg-day)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (Year of guidelines used)	DWEL (mg/L) & RSC	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/Citation	Cancer classification (year of guidelines used; year of assessment)	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (year of guidelines used; year of assessment)	Non-cancer	Cancer			
1,2-Dibromo-3-chloropropane (DBCP) (1991)	0	0.0002 (PQL)	--	B2, probable human carcinogen (1986 guidelines)	--	--	--	--	--	No	No	No	No	No
1,1-Dichloroethylene (1987)	0.007	0.007	0.01/ 10 (LOAEL)/ 1000 (10H, 10A, 10L)/ Liver toxicity (fatty change)/ Quast et al. 1983	C, possible human carcinogen (1986 guidelines)	0.35 20% Also factor of 10 for class C	0.05 (2002)/ 4.6 (BMDL10)/ 100 (10H, 10A)/ Liver toxicity (fatty change)/ Quast et al. 1983	Inadequate for an assessment of human carcinogenic potential by the oral route (1999 guidelines; 2002)	--	--	Yes/Yes	No	No	Yes ²⁰⁵ 0.35	No
1,2-Dichloropropane (1991)	0	0.005 (PQL)	--	B2, probable human carcinogen (1986 guidelines)	--	--	--	--	--	Yes (lit search)/ No	No	No	No	No
Dinoseb (1992)	0.007	0.007	0.001/ 1 (LOAEL)/ 1000 (10H, 10A, 10L)/ Reduction in thyroid weight; endometrial hyperplasia and hypospermatogenesis; testicular degeneration/ Hazleton 1977 and Brown 1981	D, not classifiable as to human carcinogenicity (1986 guidelines)	0.04 20%	0.001 (1989)/ 1 (LOAEL)/ 1000 (10H, 10A, 10L)/ Decreased pup weight during lactation period. Decreased parental weight gain/ Dow Chemical Company 1981	D, not classifiable as to human carcinogenicity (1986 guidelines; 1993)	--	--	No	No	No	No	No
Diquat (1992)	0.02	0.02	0.0022/ 0.22 (NOAEL)/ 100 (10H, 10A)/ Cataracts/ Colley et al. 1985	D, not classifiable as to human carcinogenicity (1986 guidelines)	0.077 20%	0.0022 (1995)/ 0.22 (NOEL)/ 100 (10H, 10A)/ Minimal lens opacity and cataracts/ Colley et al. 1985	--	0.005 (chronic) (1995, 2001)/ 0.5 (NOAEL)/ 100 (10H, 10A)/ Cataracts in females and decreased adrenal and epididymides weights in males/Hopkins 1990	E, evidence of noncarcinogenicity (1986 guidelines; 2001)	Yes/Yes	No	No	Yes ²⁰⁶ 0.035 (rounded to 0.04)	No

²⁰⁵ IRIS (2002) concluded that the data on 1,1-DCE are *inadequate* for an assessment of human carcinogenic potential by the oral route. Due to the change in cancer descriptor based on the IRIS assessment, the factor of 10 used in the derivation of the current MCLG for a C carcinogen is removed. Based on the updated IRIS (2002) RfD of 0.05 mg/kg-day, 70 kg body weight, 2 L water consumption and 20% RSC, the revised MCLG is 0.35 mg/L.

²⁰⁶ Using the updated OPP RfD of 0.005 mg/kg-day, assuming 70 kg body weight, 2 liters water intake per day and 20% RSC increases the MCLG to 0.035 mg/L (rounded to 0.04 mg/L).

Table 5. Summary for List B Chemicals

Chemical (Date of regulation)	Regulation					IRIS		OPP		New Data/Possible Impact on MCLG ¹⁹⁰		Potential Repro/Dev Concern at MCL ¹⁹¹	Possible New MCLG (mg/L) ¹⁹²	Nominate for New Assessment?
	MCLG mg/L	MCL mg/L (basis if MCL≠ MCLG)	RfD (mg/kg-day)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (Year of guidelines used)	DWEL (mg/L) & RSC	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/Citation	Cancer classification (year of guidelines used; year of assessment)	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (year of guidelines used; year of assessment)	Non-cancer	Cancer			
Endothall (1992)	0.1	0.1	0.02/2 (NOAEL)/ 100 (10H, 10A)/ Increased organ weight and organ-to-body weights for stomach and small intestine/ Keller 1965	D, not classifiable as to human carcinogenicity (1986 guidelines)	0.7 20%	0.02 (1991)/ 100 ppm (NOEL)/ 100 (10H, 10A)/ Increased absolute and relative weights of stomach and small intestine/ Keller 1965	--	0.007 (2005)/ 2 (LOAEL)/ 300 (10H, 10A, 3L)/ Proliferative lesions of the gastric epithelium/ Trutter 1995	Unlikely to be carcinogenic to humans (1999 guidelines)	Yes/Yes	No	No	Yes ²⁰⁷ 0.05	No
Endrin (1992)	0.002	0.002	0.0003/ 0.025 (NOAEL)/ 100 (10H, 10A)/ Mild histopathological lesions in liver, occasional convulsions/ Velsicol Chemical Corporation 1969	D, not classifiable as to human carcinogenicity (1986 guidelines)	0.009 20%	0.0003 (1991)/ 0.025 (NOAEL)/ 100 (10H, 10A)/ Mild histopathological lesions in liver, occasional convulsions/ Velsicol Chemical Corporation 1969	D, not classifiable as to human carcinogenicity (1986 guidelines; 1993; verified 1988)	--	--	No	No	No	No	No
Epichlorohydrin (1991)	0	NA ²⁰⁸	0.002/ 2.16 (LOAEL)/ 1000 (10H, 10A, 10L)/ Renal tubular degeneration/ Laskin et al. 1980	B2, probable human carcinogen (1986 guidelines)	--	--	B2, probable human carcinogen (1986 guidelines; 1986)	--	--	Yes (lit search)/ No	Yes (lit search)/ No	No	No	No
Ethylene Dibromide (EDB; 1,2-Dibromoethane) (1991)	0	0.00005 (PQL)	--	B2, probable human carcinogen (1986 guidelines)	--	0.009 (2004)/ 27 (LOAEL)/ 3000 (10H, 10A, 10L, 10D)/ Testicular atrophy, liver peliosis, and adrenal cortical degeneration/ NCI 1978	Likely to be carcinogenic to humans (1999 guidelines; 2004)	--	--	Yes/No	No	No	No	No

²⁰⁷ Using the updated OPP RfD of 0.007 mg/kg-day, assuming 70 kg body weight, 2 liters water intake per day and 20% RSC reduces the MCLG to 0.05 mg/L.

²⁰⁸ Instead of an MCL, the NPDWR is based on TT. The Treatment Technology limitation on epichlorohydrin is that the EPI/DMA polymeric coagulant aids can not contain more than 0.01% monomer and the maximum use level is 20 mg/L polymer. Thus, the level of epichlorohydrin in the water at-the-tap should not exceed 2 ppb (0.0001 x 20 mg/L = 0.002 mg/L). This value is associated with a theoretical cancer risk of 5.6 x 10⁻⁷ based on a DW unit risk of 2.8 x 10⁻⁷ per ug/L ((56 FR 3526 (USEPA, 1991b)).

Table 5. Summary for List B Chemicals

Chemical (Date of regulation)	Regulation					IRIS		OPP		New Data/Possible Impact on MCLG ¹⁹⁰		Potential Repro/Dev Concern at MCL ¹⁹¹	Possible New MCLG (mg/L) ¹⁹²	Nominate for New Assessment?
	MCLG mg/L	MCL mg/L (basis if MCL≠MCLG)	RfD (mg/kg-day)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (Year of guidelines used)	DWEL (mg/L) & RSC	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/Citation	Cancer classification (year of guidelines used; year of assessment)	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (year of guidelines used; year of assessment)	Non-cancer	Cancer			
Glyphosate (1992)	0.7	0.7	0.1/ 10 (NOAEL)/ 100 (10H, 10A)/ Increased incidence of renal tubular dilation in F3b offspring/ Monsanto Company 1981	D, not classifiable (1986 guidelines; 1990)	4 20%	0.1 (1990)/ 10 (NOAEL)/ 100 (10H, 10A)/ Increased incidence of renal tubular dilation in F3b offspring/ Monsanto Company 1981	D, not classifiable (1986 guidelines; 1990)	2 (2007)/ 175 (NOAEL)/ 100 (10H, 10A)/ Maternal toxicity (diarrhea, nasal discharge, and death) in a developmental toxicity rabbit study/ Monsanto Company 1981	E, evidence of noncarcinogenicity (1986 guidelines)	Yes/Yes	No	No	Yes ²⁰⁹ 14	No
Heptachlor (1991)	0	0.0004 (PQL)	0.0005/ 0.15 (NOAEL)/ 300 (10H, 10A, 3D)/ Increased liver to body weight ratio in males/ Witherup et al. 1955	B2, probable human carcinogen (1986 guidelines)	--	0.0005 (1991)/ 0.15 (NOAEL)/ 300 (10H, 10A, 3D)/ Increased liver to body weight ratio in males/ Witherup et al. 1955	B2, probable human carcinogen (1986 guidelines; 1991)	0.0005 (1992)/ 0.15 (NOAEL)/ 300 (10H, 10A, 3D)/ Liver lesions and increased relative liver weight/ Witherup et al. 1955	B2, probable human carcinogen (1986 guidelines; 1992)	Yes (lit search)/ No	No	No ²¹⁰	No	No
Heptachlor Epoxide (1991)	0	0.0002 (PQL)	0.000013/ 0.0125 (LOAEL)/ 1000 (10H, 10A, 10L)/ Increase in liver-to-body weight ratio/ Dow Chemical Company, 1958	B2, probable human carcinogen (1986 guidelines)	--	0.000013 (1991)/ 0.0125 (LEL)/ 1000 (10H, 10A, 10L)/ Increase in liver-to-body weight ratio/ Dow Chemical Company 1958	B2, probable human carcinogen (1986 guidelines; 1993)	0.000013 (1992)/ 0.0125 (LEL)/ 1000 (10H, 10A, 10L)/ Increase in liver-to-body weight ratio/ Dow Chemical Company 1958	B2, probable human carcinogen (1986 guidelines)	No	No	No	No	No
Hexachlorobenzene (1992)	0	0.001 (PQL)	0.0008/ 0.08 (NOAEL)/ 100 (10H, 10A)/ Hepatic centrilobular basophilic chromogenesis/ Arnold et al. 1985	B2, probable human carcinogen (1986 guidelines)	--	0.0008 (1991)/ 0.08 (NOAEL)/ 100 (10H, 10A)/ Hepatic centrilobular basophilic chromogenesis/ Arnold et al. 1985	B2, probable human carcinogen (1986 guidelines; 1996)	--	--	Yes (lit search)/ No	Yes (lit search)/ No	No ²¹¹	No	No

²⁰⁹ Using the updated OPP RfD of 2 mg/kg-day, assuming 70 kg body weight, 2 liters water intake per day and 20% RSC increases the MCLG to 14 mg/L. Note that OPP rounded from 1.75 mg/kg-day to 2 mg/kg-day for the revised RfD.

²¹⁰ A LOAEL of 0.03 mg/kg-day was identified for immunotoxicity and neurotoxicity in rats exposed in utero, during lactation, and postnatally until day 21 or 42 of age (Moser et al., 2001; Smialowicz et al., 2001). The MCL of 0.0004 mg/L is based on the PQL, but intake from drinking water (in mg/kg-day) at the MCL (assuming 2 L water intake per day and 70 kg body weight) is relatively close to the effect level for developmental effects. However, heptachlor is not of concern because of its status as a cancelled pesticide and because its occurrence is low.

Table 5. Summary for List B Chemicals

Chemical (Date of regulation)	Regulation				IRIS		OPP		New Data/Possible Impact on MCLG ¹⁹⁰		Potential Repro/Dev Concern at MCL ¹⁹¹	Possible New MCLG (mg/L) ¹⁹²	Nominate for New Assessment?	
	MCLG mg/L	MCL mg/L (basis if MCL≠MCLG)	RfD (mg/kg-day)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (Year of guidelines used)	DWEL (mg/L) & RSC	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/Citation	Cancer classification (year of guidelines used; year of assessment)	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (year of guidelines used; year of assessment)	Non-cancer				Cancer
Hexachlorocyclopentadiene (1992)	0.05	0.05	0.007/ 7.14 (adj. NOAEL)/ 1000 (10H, 10A, 10S)/ Focal inflammation of the forestomach and stomach lesions/ SRI 1981 (later published as Abdo et al. 1984)	D, not classifiable as to human carcinogenicity (1986 guidelines)	0.3 20%	0.006 (2001)/ 6 (BMDL10)/ 1000 (10H, 10A, 10 ^{1/2} S, 10 ^{1/2} D)/ Chronic irritation of forestomach (forestomach lesions)/ Abdo et al. 1984	Unknown risk as to oral exposure (1996 guidelines; 2001)	--	--	No	No	No	Yes ²¹² 0.04	No
Lindane (gamma-Hexachlorocyclohexane) (1991)	0.0002	0.0002	0.0003/ 0.33 (NOAEL)/ 1000 (10H, 10A, 10S)/ Liver and kidney toxicity/ RCC 1983	C, possible human carcinogen (1986 guidelines)	0.01 20% Also factor of 10 for class C	0.0003 (1988)/ 0.33 (NOAEL)/ 1000 (10H, 10A, 10S)/ Liver and kidney toxicity/ RCC 1983	--	0.0047 (2002)/ 0.47 (NOAEL)/ 100 (10H, 10A)/ Hepatocyte hypertrophy, increased liver weight, increased platelets/ Amyes 1989a,b,1993	Suggestive evidence of carcinogenicity, but not sufficient to assess human carcinogenic potential (1999 guidelines)	Yes/Yes	No	No	Yes 0.001-0.03 (value depends on UF chosen) ²¹³	No
Mercury (Inorganic) (1991)	0.002	0.002	0.0003 ²¹⁴ / 1000 (Not specified)/ Mercuric chloride-induced autoimmune glomerulonephritis /USEPA 1987c; Druet et al. 1978; Bernaudin et al. 1981; Andres 1984	--	0.01 20%	0.0003 (1995)/ 0.29 (LOAEL)/ 1000 (10A,H; 10L; 10S)/ Autoimmune glomerulonephritis/ USEPA 1987c; Druet et al. 1978; Bernaudin et al. 1981; Andres 1984	C, possible human carcinogen (1986 guidelines; 1995)	--	--	Yes/No	No	No	No	No

²¹¹ A NOAEL of 0.01 mg/kg-day was identified for histopathological changes in ovaries observed in 90-day monkey studies (Bourque et al., 1995; Babineau et al., 1991; Jarrell et al., 1993; Sims et al., 1991). The MCL of 0.001 mg/L is based on the PQL, but intake from drinking water (in mg/kg-day) at the MCL (assuming 2 L water intake per day and 70 kg body weight) is relatively close to the effect level for reproductive effects. However, hexachlorobenzene is not of concern because of its status as a cancelled pesticide and because its occurrence is low.

²¹² Using the updated IRIS (2001) RfD of 0.006 mg/kg-day, assuming 70 kg body weight, 2 liters water intake per day and 20% RSC decreases the MCLG to 0.04 mg/L.

²¹³ Using the updated OPP (USEPA, 2006h) RfD of 0.0047 mg/kg-day, assuming 70 kg body weight, 2 liters water intake per day and 20% RSC and a risk management factor of 10 based on the cancer classification results in a MCLG of 0.003 mg/L. The actual change will depend on the use of any additional uncertainty factors.

²¹⁴ The RfD for mercury was back-calculated from the DWEL using 2 L water consumption and 70 kg body weight in the following equation $(0.01 \text{ mg/L} \times 2 \text{ L}) / 70 \text{ kg} = 0.00029 \text{ mg/kg-day}$, rounded to 0.0003 mg/kg-day.

Table 5. Summary for List B Chemicals

Chemical (Date of regulation)	Regulation				IRIS		OPP		New Data/Possible Impact on MCLG ¹⁹⁰		Potential Repro/Dev Concern at MCL ¹⁹¹	Possible New MCLG (mg/L) ¹⁹²	Nominate for New Assessment?	
	MCLG mg/L	MCL mg/L (basis if MCL≠ MCLG)	RfD (mg/kg-day)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (Year of guidelines used)	DWEL (mg/L) & RSC	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/Citation	Cancer classification (year of guidelines used; year of assessment)	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (year of guidelines used; year of assessment)	Non-cancer				Cancer
Methoxy-chlor (1991)	0.04	0.04	0.005/ 5.01 (NOAEL)/ 1000 (10H, 10A, 10D)/ Excessive loss of litters; decreased body weight/ Trutter 1986	D, not classifiable as to human carcinogenicity (1986 guidelines)	0.175 20%	0.005 (1991)/ 5.01 (NOAEL)/ 1000 (10H, 10A, 10D)/ Excessive loss of litters/ Trutter 1986.	D, not classifiable as to human carcinogenicity (1986 guidelines; 1990)	--	--	Yes (lit search)/ No	Yes (lit search)/ No	No	No ²¹⁵	No
Mono-chloro-benzene (Chloro-benzene) (1991)	0.1	0.1	0.02/ 19 (NOAEL)/ 1000 (10H, 10A, 10S)/ Histopathologic changes in the liver/ Monsanto Company 1967; Knapp et al. 1971	D, not classifiable as to human carcinogenicity (1986 guidelines)	0.7 20%	0.02 (1993)/ 19 (adjusted dose) (NOAEL)/ 1000 (10H, 10A, 10S)/ Histopathologic changes in the liver/ Monsanto Company 1967	D, not classifiable as to human carcinogenicity (1986 guidelines; 1991)	--	--	No	No	No ²¹⁶	No	No
Nitrate (as N) (1991)	10	10	1.6 nitrate- nitrogen/ 1.6 (10 mg/L) (NOAEL)/ 1/ Methemoglobinemia in infants/ Bosch et al. 1950; Walton, 1951	--	10 ²¹⁷ --	1.6 nitrate- nitrogen/ (1991)/ 1.6 (10 mg/L) (NOAEL)/ 1/ Methemoglobinemia in infants/ Bosch et al., 1950; Walton, 1951	--	--	--	Yes (lit search)/ Yes	Yes (lit search)/ Yes	Yes ²¹⁸	TBD ²¹⁹	Yes

²¹⁵ The present EPA RfD used in support of the existing MCLG/MCL remains adequate to protect against reproductive and developmental effects. This is because a 1000 fold UF (including a factor of 10 for database uncertainties) was already applied to the NOAEL of 5 mg/kg-day in the rabbit developmental study to be protective from such potential effects or others yet unidentified at the time the RfD was calculated in support of the existing MCLG/MCL.

²¹⁶ Significant data limitations precluded the evaluation of potential concern for reproductive or developmental toxicity.

²¹⁷ Nitrate assessment is based on the concentration in water in a human population.

²¹⁸ See next footnote for a description of issues related to potential developmental effects for nitrate.

²¹⁹ Data suggest that nitrate in drinking water can have adverse effects on the thyroid by a mode of action that can be associated with neurodevelopmental effects. Several studies suggest nitrate in drinking water can have adverse effects on the thyroid (Mukhopadhyay et al. 2005; Tajtakova et al. 2006; Zaki et al., 2004). In addition, a neurodevelopmental study (Markel et al., 1989) identified a LOAEL for neurobehavioral effects that is at the same dose level as the current RfD. A number of issues related to the mode of action, including the unique sensitivity of rodents, thyroid homeostasis, and determination of the critical effect need to be evaluated further in a reassessment of this chemical. In addition, Grosse et al. (2006) reported the results of a recent IARC Working group review of nitrate and nitrite. This group concluded that ingested nitrate or nitrite under conditions that result in endogenous nitrosation is probably carcinogenic to humans (group 2A). A new assessment for nitrate is recommended for both the noncancer and cancer assessments.

Table 5. Summary for List B Chemicals

Chemical (Date of regulation)	Regulation				IRIS		OPP		New Data/Possible Impact on MCLG ¹⁹⁰		Potential Repro/Dev Concern at MCL ¹⁹¹	Possible New MCLG (mg/L) ¹⁹²	Nominate for New Assessment?	
	MCLG mg/L	MCL mg/L (basis if MCL≠ MCLG)	RfD (mg/kg-day)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (Year of guidelines used)	DWEL (mg/L) & RSC	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/Citation	Cancer classification (year of guidelines used; year of assessment)	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (year of guidelines used; year of assessment)	Non-cancer				Cancer
Nitrite (as N) (1991)	1	1	0.16 nitrite - nitrogen/ Nitrate RfD of 1.6 nitrate-nitrogen ²²⁰ / 1 (MF = 10)/ Methemoglobinemia in infants/ Bosch et al. 1950; Walton 1951	--	1 --	0.1 nitrite-nitrogen (1991)/ 1 ²²¹ (10 mg/L nitrate-nitrogen) (NOAEL)/ 1 (MF = 10)/ Methemoglobinemia in infants/ Walton 1951	--	--	--	Yes (lit search)/ Yes	Yes (lit search)/ Yes	Yes ²²²	TBD ²²³	Yes
Oxamyl (Vydate) (1992)	0.2	0.2	0.025/ 2.5 (NOAEL)/ 100 (10H, 10A)/ Decreased body weight gain/ Kennedy 1986; E.I. du Pont de Nemours and Company. 1972; Kennedy, 1986 is the published version.	E, evidence of noncarcinogenicity (1986 guidelines)	0.9 20%	0.025 (1991)/ 2.5 (NOEL)/ 100 (10H, 10A)/ Decreased body weight gain and food consumption/ E.I. du Pont de Nemours and Company 1972	--	0.001 (2000)/ 0.1 (NOAEL)/ 100 (10H, 10A)/ Clinical signs and decreased plasma RBC and brain cholinesterase inhibition in females/ Malley 1997a,b	E, evidence of noncarcinogenicity (1986 guidelines)	Yes/Yes	No	No	Yes 0.002 ²²⁴	No
Picloram (1992)	0.5	0.5	0.07/ 7 (NOAEL)/ 100 (10H, 10A)/ Increased relative and absolute liver weights/ Dow Chemical Company 1982	D, not classifiable as to human carcinogenicity (1986 guidelines)	2.45 20%	0.07 (1992)/ 7 (NOEL)/ 100 (10H, 10A)/ Increased relative and absolute liver weights/ Dow Chemical Company 1982	--	0.2 (1995)/ 20 (NOAEL)/ 100 (10H, 10A)/ Changes in centrilobular hepatocytes/ Landry et al. 1986	E, evidence of noncarcinogenicity (1986 guidelines)	Yes/Yes	No	No	Yes ²²⁵	No

²²⁰ Extrapolated from nitrate RfD of 1.6 mg/kg-day, assuming 10% of nitrate converted to nitrite. Assumes a 4 kg child ingesting 0.64 L/day.

²²¹ 10 mg/L converted to 1.0 mg/kg-day assuming 10 kg child ingesting 1 L/day.

²²² Several new studies have been identified that suggest nitrate in drinking water can have adverse effects on the thyroid as described above, and nitrite itself can act via the same mode of action. In addition, a developmental toxicity study of nitrite in rats (Vorhees et al., 1984) observed neurobehavioral effects. Since nitrite is formed from nitrate, and the current nitrite RfD is based on nitrate data, these data identify a potential concern for reproductive and developmental effects at the current MCLG that will need to be evaluated further in a reassessment of this chemical.

²²³ See same issue as for nitrate.

²²⁴ A potential new MCLG of 0.002 mg/L is based on the OPP acute RfD of 0.001 mg/kg-day. The resulting concentration of 0.002 mg/L is derived using child body weight of 10 kg, a water intake of 1 L/day, and a RSC of 20%. The RSC was selected based on the actual food dietary exposure (81%) for children aged from 1-6 years old as documented in the Oxamyl RED document (USEPA, 2000c). Since the most sensitive effects of oxamyl are acute effects on cholinesterase activity, the lifetime health advisory is based on this acute study, and is equal to the one day 10-kg child health advisory.

²²⁵ OPP has developed an oral RfD of 0.2 mg/kg-day based on a NOAEL of 20 mg/kg-day for liver effects observed in a 2-year feeding study in F344 rats (Landry et al., 1986). The resulting DWEL would be 7 mg/L assuming a 70 kg body weight and 2 L water consumption. The MCLG would be 1 mg/L assuming 20% RSC.

Table 5. Summary for List B Chemicals

Chemical (Date of regulation)	Regulation				IRIS			OPP		New Data/Possible Impact on MCLG ¹⁹⁰		Potential Repro/Dev Concern at MCL ¹⁹¹	Possible New MCLG (mg/L) ¹⁹²	Nominate for New Assessment?
	MCLG mg/L	MCL mg/L (basis if MCL≠ MCLG)	RfD (mg/kg-day)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (Year of guidelines used)	DWEL (mg/L) & RSC	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/Citation	Cancer classification (year of guidelines used; year of assessment)	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (year of guidelines used; year of assessment)	Non-cancer	Cancer			
Selenium (1991)	0.05	0.05	None ²²⁶	--	--	0.005 (1991)/ 0.015 (NOAEL)/ 3 (3H)/ Clinical selenosis/ Yang et al. 1989	D, not classifiable (1986 guidelines; 1991)	--	--	Yes (lit search)/ Yes	Yes ²²⁷ , Yes ²²⁸	Yes ²²⁸	TBD ²²⁹	Yes
Simazine (1992)	0.004	0.004	0.005/ 0.52 (NOAEL)/ 100 (10H, 10A)/ Reduction in weight gains; hematological changes in females/ McCormick et al. 1988	C, possible human carcinogen (1986 guidelines)	0.175 20% Also factor of 10 for class C	0.005 (1994)/ 0.52 (NOAEL)/ 100 (10H, 10A)/ Reduction in weight gains; hematological changes in females/ McCormick et al. 1988	--	0.018 (2006)/ 1.8 (NOAEL)/ 100 (10H, 10A)/ estrous cycle alterations and LH surge/ noted in Morseth et al. 1996	Not likely to be carcinogenic to humans using data on its atrazine analogue the most recent assessment of carcinogenic potential occurred in 2005.	Yes/Yes	Yes/Yes	No ²³⁰	TBD ²³¹	No
Toluene (1991)	1	1	0.2/ 223 (NOAEL)/ 1000 (10H, 10A, 10S)/ Increased kidney weight/ NTP 1990	D, not classifiable as to human carcinogenicity (1986 guidelines)	7 20%	0.08 (2005)/ 238 (BMDL)/ 3000 (10H, 10A, 10S, 3D)/ Increased kidney weights/ NTP 1990	Data are inadequate to assess carcinogenic potential (2005 guidelines; 2005)	--	--	Yes/Yes	No	No	Yes ²³² 0.6	No

²²⁶ EPA published the current NPDWR for selenium on January 30, 1991 (56FR 3526). The Agency based the MCLG on an a maximal safe intake of 0.4 mg/day from a study in China by Yang et al. (1989) and a cancer classification of D, not classifiable as to human carcinogenicity. The 0.4 mg/day safe level was based on data that extrapolated from blood selenium levels to estimated dietary intake in the studied population. As described in the Federal Register, the derivation of the MCLG does not follow routine policies for MCLG derivation in partial deference to selenium's status as a nutrient. There is no specific reference to an RfD in the Federal Register notice for the Selenium MCLG/MCL.

²²⁷ The data support evaluation under the 2005 Guidelines for Carcinogen Risk Assessment, but selenium as a micronutrient cannot be an MCLG 0 candidate.

²²⁸ Hawkes and Keim (2003) reported thyroid hormone and related metabolism changes in subjects treated with deficient, sufficient and excess dietary selenium. In addition, several studies have reported changes in sperm parameters and fertility in mice administered sodium selenite (e.g., Shalini and Bansal, 2006; Kaur and Bansal, 2005). Changes in sperm parameters were also observed in F334 rats given sodium selenite in drinking water (NTP, 1994), but this study did not find these effects in mice given sodium selenite or in rats or mice given sodium selenate. These data identify a potential concern for reproductive and developmental effects at the current MCLG that will need to be evaluated further in a reassessment of this chemical.

²²⁹ One new study that could lower the RfD, a human study by Hawkes and Keim (2003) with a LOAEL of about 0.004 mg/kg-day. In addition, much has been learned about the metabolism of selenium since the IRIS review and it may be appropriate to differentiate between inorganic selenium and organic selenium in the form of selenoproteins, selenomethionine and selenocysteine for an assessment that applies to drinking water.

²³⁰ See description for atrazine regarding potential for reproductive or developmental concern at the MCL.

²³¹ See description for atrazine regarding the October 2009 EPA announcement (USEPA, 2009c) of a comprehensive reevaluation of atrazine risk and its effect on potential changes to the simazine MCLG.

Table 5. Summary for List B Chemicals

Chemical (Date of regulation)	Regulation				IRIS		OPP		New Data/Possible Impact on MCLG ¹⁹⁰		Potential Repro/Dev Concern at MCL ¹⁹¹	Possible New MCLG (mg/L) ¹⁹²	Nominate for New Assessment?	
	MCLG mg/L	MCL mg/L (basis if MCL≠MCLG)	RfD (mg/kg-day)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (Year of guidelines used)	DWEL (mg/L) & RSC	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/Citation	Cancer classification (year of guidelines used; year of assessment)	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (year of guidelines used; year of assessment)	Non-cancer				Cancer
Toxaphene (1991)	0	0.003 (PQL)	0.0004 (short-term) ²³³ / 0.36 (NOAEL)/ 1000 (10H, 10A, 10 MF for data gaps for potential neurodevelopmental and immunological effects)/ Parental histological changes in liver, kidney, and thyroid/ Chu et al. 1986, 1988	B2, probable human carcinogen (1986 guidelines)	--	--	B2, probable human carcinogen (1986 guidelines; 1991)	--	--	No	No	No	No	No
2,4,5-TP (Silvex; 2,4,5-Trichlorophenoxypropionic Acid) (1991)	0.05	0.05	0.008 0.75 (NOAEL)/ 100 (10H, 10A)/ Histopathological changes in the liver/ Mullison 1966	D, not classifiable as to human carcinogenicity (1986 guidelines)	0.3 20%	0.008 (1988)/ 0.75 (NOAEL)/ 100 (10H, 10A)/ Histopathological changes in the liver/ Mullison 1966; Gehring and Besto 1978	D, not classifiable (1986 guidelines; 1988)	--	--	No	No	No ²³⁴	No	No
1,2,4-Trichlorobenzene (1992)	0.07	0.07	0.01/ 14.8 (NOAEL)/ 1000 (10H, 10A, 10S)/ Increased adrenal weights; vacuolization of zona fasciculata in the cortex/ Robinson et al. 1981	D, not classifiable as to human carcinogenicity (1986 guidelines)	0.35 20%	0.01 (1996)/ 14.8 (NOAEL)/ 1000 (10H, 10A, 10S/D)/ Increased adrenal weights; vacuolization of zona fasciculata in the cortex/ Robinson et al. 1981	D, not classifiable (1986 guidelines; 1996)	--	--	Yes (lit search)/ Yes	Yes (lit search)/ Yes	No	TBD ²³⁵	Yes

²³² Using the IRIS RfD of 0.08 mg/kg-day and assuming 70 kg body weight, 2 liters water intake per day, a DWEL of 2.8 mg/L can be derived. Assuming a RSC of 20% would result in a new MCLG of 0.6 mg/L. This value is 60% the current value.

²³³ Toxaphene is a carcinogen, thus, the RfD is a short-term RfD for screening only when spills occur.

²³⁴ Significant data limitations precluded the evaluation of potential concern for reproductive or developmental toxicity.

²³⁵ A 2-year carcinogenicity assay in mice and rats (Moore, 1994a,b) found no evidence of carcinogenicity in rats, but in mice a high incidence of hepatocellular carcinoma was observed in both sexes in the 2 higher dose groups (8/49, 5/50, 27/50*, and 50/50* for males; 1/50, 1/50, 28/50*, and 46/50* for females). This study report needs to be comprehensively reviewed since it is possible that this study could affect both the cancer classification and the MCLG for 1,2,4-TCB.

Table 5. Summary for List B Chemicals

Chemical (Date of regulation)	Regulation					IRIS		OPP		New Data/Possible Impact on MCLG ¹⁹⁰		Potential Repro/Dev Concern at MCL ¹⁹¹	Possible New MCLG (mg/L) ¹⁹²	Nominate for New Assessment?
	MCLG mg/L	MCL mg/L (basis if MCL≠ MCLG)	RfD (mg/kg-day)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (Year of guidelines used)	DWEL (mg/L) & RSC	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/Citation	Cancer classification (year of guidelines used; year of assessment)	RfD (mg/kg-day) (year)/ Point of Departure/ UF (breakdown of UFs)/Effect/ Citation	Cancer classification (year of guidelines used; year of assessment)	Non-cancer	Cancer			
1,1,1-Trichloroethane (1987)	0.2	0.2	0.035/35 (LOAEL) ²³⁶ / 1000 (10H, 10A, 10L)/ Histology changes in liver/ McNutt et al. 1975	D, not classifiable as to human carcinogenicity	1 20%	2 (2007)/ 2155 (BMDL10)/ 1000 (10H, 10A, 3S, 3D)/ Decreased body weight in females/ NTP 2002	Inadequate information to assess carcinogenic potential (2005 guidelines; 2007)	--	--	Yes/Yes	No	No	Yes ¹⁴ ²³⁷	No
1,1,2-Trichloroethane (1992)	0.003	0.005 (PQL)	0.004/3.9 (NOAEL)/ 1000 (10H, 10A, 10S)/ Adverse effects on liver, depressed humoral immune status/ Sanders et al. 1985 White et al. 1985	C, possible human carcinogen (1986 guidelines)	0.137 20% Also factor of 10 for class C	0.004 (1995)/ 3.9 (NOAEL)/ 1000 (10H, 10A, 10S)/ Clinical serum chemistry/ Sanders et al. 1985 White et al. 1985	C, possible human carcinogen (1986 guidelines; 1994)	--	--	No	No	No ²³⁸	No	No
Vinyl chloride (1987)	0	0.002 (PQL)	Adjusted acceptable daily intake: 0.046 mg/L/ 0.13 (NOAEL)/ 100 (10H, 10A)/ None/ Til et al. 1983	A, known human carcinogen (1986 guidelines)	--	0.003 (2000)/ 0.13 (0.09 HED) (NOAEL)/ 30 (10H, 3A)/ Liver cell polymorphism/ Til et al. 1983, 1991	Known carcinogen by the oral route (1996 guidelines; 2000)	--	--	Yes/No	Yes/No	No	No	No
Xylenes (Total) (1991)	10	10	1.79/179 (adj. NOAEL)/ 100 (10H, 10A)/ decreased body weight gains/ NTP 1986	D, not classifiable as to human carcinogenicity (1986 guidelines)	63 20%	0.2 (2003), 179 (adj. NOAEL)/ 1000 (10H, 10A, 10D)/ decreased body weight gains/ NTP 1986	Data are inadequate to assess carcinogenic potential (1999 guidelines; 2003)	--	--	Yes/Yes	No	No	Yes ²³⁹ 1	No

²³⁶ The point of departure of 35.1 mg/kg-day for the RfD was derived from an inhalation study. The LOAEL of 1365 mg/m³ was converted to an internal dose assuming a mouse ventilation rate of 1 m³/h, 6 hr/day, pulmonary absorption of 30%, and a human BW of 70 kg.

²³⁷ Using the IRIS RfD of 2 mg/kg-day and assuming 70 kg body weight, 2 liters water intake per day, a DWEL of 70 mg/L can be derived. This would result in a new MCLG of 14 mg/L based on a RSC of 20%.

²³⁸ Significant data limitations precluded the evaluation of potential concern for reproductive or developmental toxicity.

²³⁹ Using the RfD of 0.2 mg/kg-day and assuming 70 kg body weight, 2 liters water intake per day, a DWEL of 7 mg/L can be derived. Assuming a RSC of 20% would result in a new MCLG of 1 mg/L. This value is 10% the current value.

Abbreviations: AADI = - Adjusted acceptable daily intake or adjusted average daily intake; ADI = average daily intake; Adj. = adjusted for intermittent exposure; BMDL = lower 95% confidence limit on the benchmark dose; DWEL = drinking water equivalent level; HED = Human equivalent dose; IRIS = Integrated Risk Information System; MCL = maximum contaminant level; MCLG = maximum contaminant level goal; NOAEL = no observed adverse effect level; LEL = lowest effect level; LOAEL = lowest observed adverse effect level; NA = not applicable; OPP = Office of Pesticide Programs; ORIA = Office of Radiation and Indoor Air; OW = Office of Water; PQL = practical quantitation limit, also termed “analytical feasibility”; RfD = Reference dose; RSC = relative source contribution; SAB = Science Advisory Board; TBD = to be determined; UF = uncertainty factor (with H = intraspecies UF; A = interspecies UF; L = UF for LOAEL to NOAEL; S = UF for subchronic to chronic extrapolation; D = database UF)

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