

US EPA ARCHIVE DOCUMENT

# Health Effects Information Used In Cancer and Noncancer Risk Characterization for the NATA 1996 National-Scale Assessment

## Sources of Information

Hazard identification and dose-response assessment information for the NATA national-scale assessment was obtained from various sources. Information was assigned greater weight if (1) it was conceptually consistency with the EPA risk assessment guidelines and (2) the level of review it received was high. This process of prioritizing information was aimed at ensuring the assessment was based on the best available science. The following sources were used.

### *US Environmental Protection Agency (EPA)*

The EPA has developed dose-response assessments for chronic exposure to many of the pollutants in this study. These assessments typically give a reference concentration (RfC) to protect against effects other than cancer, and/or a unit risk estimate (URE) to estimate the probability of contracting cancer as a result of exposure to a pollutant. The RfC is an estimate of a concentration in air to which a human population might be exposed (including sensitive subgroups) that is likely to be without appreciable risks of deleterious effects during a lifetime. The uncertainty in this concentration spans perhaps an order of magnitude. The URE is an upper-bound estimate of the excess cancer risk resulting from a lifetime of continuous exposure to an agent at a concentration of  $1 \mu\text{g}/\text{m}^3$  in air. In assessing a substance's carcinogenic potential, the EPA evaluates various types of toxicological data and develops a weight-of-evidence (WOE) determination. Current WOE assessments include a system of categorizing carcinogens (recommended by the EPA's 1986 guidelines for carcinogen risk assessment) and a paragraph of descriptive text (recommended by the current draft revisions to the 1986 guidelines).

The EPA disseminates dose-response assessment information in several forms, depending on the level of internal review. The EPA publishes dose-response assessments that have achieved full intra-agency consensus on its Integrated Risk Information System (IRIS), which is regularly updated and available on-line at <http://www.epa.gov/iris>. All IRIS assessments since 1996 have also undergone external scientific peer review.

### *Agency for Toxic Substances and Disease Registry (ATSDR)*

The ATSDR, which is part of the US Department of Health and Human Services, develops and publishes Minimal Risk Levels (MRLs) for many toxic substances. The MRL is defined as an estimate of daily human exposure to a substance that is likely to be without an appreciable risk of adverse effects (other than cancer) over a specified duration of exposure. MRLs can be derived for acute, intermediate, and chronic duration exposures following inhalation and ingestion. The ATSDR describes MRLs as concentrations to be used by health assessors in selecting environmental contaminants for further evaluation. MRLs are presented with only 1 significant figure and are considered concentrations below which contaminants are unlikely to pose a health threat. Concentrations above an MRL do not necessarily represent a threat, and MRLs are therefore not intended for use as predictors of adverse health effects or for setting cleanup levels.

Inhalation MRLs were used in the non-cancer portion of this assessment when IRIS RfCs were not available because the concept, definition, and derivation of MRLs and RfCs are philosophically consistent (though not identical). The ATSDR publishes MRLs as part of pollutant-specific toxicological profile documents, and also in a table of “comparison values” that the ATSDR regularly updates and distributes (available on-line at <http://www.atsdr.cdc.gov/mrls.html> ).

### ***California Environmental Protection Agency (CalEPA)***

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

The CalEPA’s quantitative dose-response information on carcinogenicity by inhalation exposure is expressed in terms of the URE, defined similarly to the EPA’s URE. This assessment uses specific CalEPA UREs in the same way as EPA’s when no IRIS URE values exist.

The CalEPA’s dose response information for carcinogens and noncarcinogens is available on-line at [http://www.oehha.ca.gov/air/hot\\_spots/index.html](http://www.oehha.ca.gov/air/hot_spots/index.html).

### ***International Agency for Research on Cancer (IARC)***

The IARC, a branch of the World Health Organization, coordinates and conducts research on the causes of human cancer and develops scientific strategies for cancer control. The IARC sponsors both epidemiological and laboratory research and disseminates scientific information through meetings, publications, courses, and fellowships.

As part of its mission, the IARC assembles evidence that substances cause cancer in humans and issues judgments on the strength of evidence. The IARC’s “degrees of evidence” categories are Group 1 (carcinogenic in humans), Group 2A (probably carcinogenic), Group 2B (possibly carcinogenic), Group 3 (not classifiable), and Group 4 (probably not carcinogenic). The categorization scheme may be applied to either single chemicals or mixtures. The IARC does not develop quantitative dose-response indices such as UREs.

The IARC’s WOE for substances are included as supporting information for this assessment as a backup to the EPA’s WOE determinations, which do not cover all substances and in some cases may be out-of-date. The list of IARC evaluations to date is available at <http://193.51.164.11/monoeval/grlist.html>.

## Prioritizing and Combining Information from Data Sources

Some substances have been subjected to dose-response assessments by several of the agencies used as sources for this assessment. Because different scientists developed these assessments at different times for purposes that were similar but not identical, the results are not totally consistent. In some cases interagency differences are substantial, especially between assessments done many years apart. To resolve these differences the EPA applied a consistent priority scheme to the available dose-response information.

Externally peer-reviewed draft RfCs and UREs under development for the IRIS process were given first priority. These assessments reflect the most recent available toxicity information and data analysis and were used in some cases to replace existing values on IRIS. This was only done for assessments that had already undergone peer review and subsequent revision to reflect peer comments. This assessment specifically did not use draft assessments that have not yet undergone such review because the EPA judged that the soundness of assessments should receive a higher priority than the date on which they were performed. In other words, an older assessment that had received strong scientific review was preferred to a more recent unreviewed assessment. This decision is fully consistent with the restructuring of the IRIS review process in 1996 to require such external peer review. The EPA believes that using unreviewed information in this study would undermine the quality of this assessment as well as the IRIS review process.

Where externally peer reviewed IRIS draft assessments were not available, this study relied on information currently in the EPA's IRIS database. For substances lacking IRIS assessments, ATSDR MRLs (for noncancer effects) received next preference, followed by CalEPA RELs and UREs.

For two carcinogenic substances (quinoline and 1,2-dichloropropane) that lack UREs for inhalation exposures, oral carcinogenic potency estimates were converted to inhalation UREs. The oral potency estimate for quinoline came from an older EPA assessment cited in the EPA's 1997 Health Effects Assessment Summary Tables (HEAST). The conversion from oral risk (probability of cancer per mg/kg/d oral intake) to inhalation risk (probability of cancer per  $\mu\text{g}/\text{m}^3$  inhaled) was based on the EPA's standard assumptions of a 70-kg body mass and 20  $\text{m}^3/\text{d}$  inhalation rate, as follows:

$$\left(\frac{\mu\text{g}}{\text{m}^3}\right)^{-1} = \left(\frac{\text{mg}}{\text{kg} \cdot \text{d}}\right)^{-1} \times \frac{1}{70(\text{kg})} \times 20\left(\frac{\text{m}^3}{\text{d}}\right) \times \frac{1}{1000}\left(\frac{\text{mg}}{\mu\text{g}}\right)$$

The EPA understands that conversion of oral dose-response information to inhalation exposure is a problematic risk assessment practice. However, the alternative to this would have been to omit these substances from quantitative risk estimates altogether, thereby making a *de facto* assumption of zero carcinogenic potency. The EPA regards this alternative as unacceptable for the purposes of the national-scale assessment.

## Assumptions on Speciation and Other Adjustments to Dose-Response Information

Following the prioritization of dose-response information, the EPA made the following adjustments based on professional judgment:

1. Chromium. For chromium compounds, the IRIS RfC for particulate hexavalent chromium was used in preference to the RfC for chromic acid mists and dissolved aerosols. Both the RfC and the URE for hexavalent chromium shown in Tables 1 and 2 below were then adjusted to reflect an assumption that 34% of all atmospheric chromium is hexavalent. This represents the best judgment of EPA staff based on limited data on species of chromium emitted from five significant source categories. The total chromium mass in these emissions ranged from 0.4% to 70% hexavalent. Because the high end of the range was associated exclusively with electroplating sources the EPA chose 34%, the upper end of the range for utility boilers. It is likely that most sources of chromium emissions in the US contain lesser amounts of hexavalent chromium.
2. Nickel. The IRIS URE for nickel inhalation shown in Table 1 below was derived from evidence of the carcinogenic effects of insoluble nickel compounds in crystalline form. Soluble nickel species, and insoluble species in amorphous form, do not appear to produce genotoxic effects by the same mode of action as insoluble crystalline nickel. Nickel speciation information for some of the largest nickel-emitting sources (including oil combustion, coal combustion, and others) suggests that at least 35% of total nickel emissions may be soluble compounds. The remaining insoluble nickel emissions are not well-characterized, however. Consistent with this limited information, this analysis has conservatively assumed that 65% of emitted nickel is insoluble, and that all insoluble nickel is crystalline. On this basis, the nickel URE (based on nickel subsulfide, and representative of pure insoluble crystalline nickel) was adjusted to reflect an assumption that 65% of the total mass of nickel may be carcinogenic. The ATSDR MRL in Table 2 was not adjusted, however, because the noncancer effects of nickel are not thought to be limited to the crystalline, insoluble form.
3. Polycyclic Organic Matter. The assessment considered polycyclic organic matter (POM) emissions reported in the 1996 NTI as “total POM.” Total POM reported as a group were assumed to have a carcinogenic potency equal to 5% of that for pure benzo[a]pyrene. Details of the derivation of these relative potency estimates are presented in [Appendix H](#) of the 2001 Science Advisory Board draft of this study. The draft version of the assessment also included a separate dose-response value for a subgroup of seven carcinogenic polynuclear aromatic hydrocarbon (PAH) compounds within the POM category, because these compounds were tracked as a group in the 1996 NTI and their emissions were more completely characterized than those of the rest of the POM category. The “7-PAH” compounds as a group were assumed to have a carcinogenic potency equal to 18% of that for pure benzo[a]pyrene. However, risks associated with 7-PAH alone were found to be an order-of-magnitude lower than risks from total POM, and 7-PAH was dropped from the final assessment.

**Table 1: Dose-Responses Values for Cancer.**

This table lists quantitative cancer risk potency estimates (summarized as a Unit Risk Estimate or URE) used in the initial 1996 national-scale assessment. The EPA and IARC weight-of-evidence (WOE) categories characterize the extent to which available data support the hypothesis that a pollutant causes cancer in humans. The EPA carcinogen categories are: Group A—known carcinogen; Group B1—probable carcinogen, based on incomplete human data; Group B2—probable carcinogen, based on adequate animal data; Group C—possible carcinogen; Group D—not classifiable; and Group E—evidence of non-carcinogenicity. The IARC categories are Group 1—carcinogenic in humans; Group 2A—probably carcinogenic; Group 2B—possibly carcinogenic; Group 3—not classifiable; and Group 4—probably not carcinogenic. The URE is the upper bound risk estimate of cancer risk from a lifetime exposure to a concentration of 1 microgram per cubic meter. The source of the URE, date of the assessment, and a description of confidence in the assessment are provided, along with information about the EPA’s IRIS schedule. Internet links to the sources for assessments are provided where possible. Other information such as conformance with the revised cancer guidelines, use of UCL rather than MLE, existence of URE ranges, etc., is shown in footnotes.

Pollutant	Weight of Evidence		Unit Risk Estimate (per ug/m <sup>3</sup> )	Source	Date of Assessment	Outside Peer Review?	Confidence in URE <sup>1</sup>	EPA IRIS Reassessment Expected	Citation for Current Assessment
	EPA	IARC							
Acetaldehyde	B2	2B	2.2E-06	IRIS <sup>2</sup>	1988	No	Low	2002	<a href="http://www.epa.gov/iris/subst/0290.htm">www.epa.gov/iris/subst/0290.htm</a>
Acrylonitrile	B1	2A	6.8E-05	IRIS <sup>2</sup>	1987	No	Medium	--	<a href="http://www.epa.gov/iris/subst/0206.htm">www.epa.gov/iris/subst/0206.htm</a>
Arsenic compounds	A	1	4.3E-03	IRIS <sup>3</sup>	1994	No	High	2002	<a href="http://www.epa.gov/iris/subst/0278.htm">www.epa.gov/iris/subst/0278.htm</a>
Benzene	A	1	7.8E-06	IRIS <sup>3,4,5</sup>	1998	Yes	High	--	<a href="http://www.epa.gov/iris/subst/0276.htm">www.epa.gov/iris/subst/0276.htm</a>
Beryllium compounds	B1	1	2.4E-03	IRIS <sup>2,5</sup>	1998	Yes	Medium	--	<a href="http://www.epa.gov/iris/subst/0012.htm">www.epa.gov/iris/subst/0012.htm</a>
1,3-Butadiene	A	2A	3.0E-05	EPA NCEA <sup>2,5,6</sup>	2001	Yes	Medium	2001	US EPA, 2001. Health Risk Assessment of 1,3-Butadiene. IRIS consensus review draft, January, 2001.
Cadmium compounds	B1	1	1.8E-03	IRIS <sup>2</sup>	1986	No	Medium	2002	<a href="http://www.epa.gov/iris/subst/0141.htm">www.epa.gov/iris/subst/0141.htm</a>
Carbon tetrachloride	B2	2B	1.5E-05	IRIS <sup>2</sup>	1986	No	Low	2002	<a href="http://www.epa.gov/iris/subst/0020.htm">www.epa.gov/iris/subst/0020.htm</a>

<sup>1</sup> High – URE incorporates high-quality human data. Medium – URE considers human data of lower quality. Low – URE does not incorporate human data.

<sup>2</sup> Upper confidence limit URE (assessments that did not specify method were assumed to use UCL).

<sup>3</sup> Maximum likelihood URE.

<sup>4</sup> Higher of two recommended UREs used.

<sup>5</sup> Consistent with 1996 proposed cancer guidelines.

<sup>6</sup> Peer-reviewed draft IRIS assessment, expected to be finalized shortly.

Pollutant	Weight of Evidence		Unit Risk Estimate (per ug/m <sup>3</sup> )	Source	Date of Assessment	Outside Peer Review?	Confidence in URE <sup>1</sup>	EPA IRIS Reassessment Expected	Citation for Current Assessment
	EPA	IARC							
Chloroform	B2	2B	2.3E-05	IRIS <sup>2</sup>	1987	No	Low	2002	<a href="http://www.epa.gov/iris/subst/0025.htm">www.epa.gov/iris/subst/0025.htm</a>
Chromium compounds	A	1	1.2E-02	IRIS <sup>3,5,7</sup>	1998	Yes	High	--	<a href="http://www.epa.gov/iris/subst/0144.htm">www.epa.gov/iris/subst/0144.htm</a>
Coke Oven Emissions	A	-	6.2E-04	IRIS <sup>2</sup>	1989	No	High	--	<a href="http://www.epa.gov/iris/subst/0395.htm">www.epa.gov/iris/subst/0395.htm</a>
1,3-Dichloropropene	B2	2B	4.0E-06	IRIS <sup>2,5</sup>	2000	Yes	Low	--	<a href="http://www.epa.gov/iris/subst/0224.htm">www.epa.gov/iris/subst/0224.htm</a>
Ethylene dibromide (1,2-dibromoethane)	B2	2A	2.2E-04	IRIS <sup>2</sup>	1987	No	Low	2002	<a href="http://www.epa.gov/iris/subst/0361.htm">www.epa.gov/iris/subst/0361.htm</a>
Ethylene dichloride (1,2-dichloroethane)	B2	2B	2.6E-05	IRIS <sup>2</sup>	1986	No	Low	2002	<a href="http://www.epa.gov/iris/subst/0149.htm">www.epa.gov/iris/subst/0149.htm</a>
Ethylene oxide	B1	1	8.8E-05	CAL EPA	1999	Yes	Low	2002	<a href="http://www.oehha.ca.gov/pdf/HSCA2.pdf">www.oehha.ca.gov/pdf/HSCA2.pdf</a> , pg. 290
Formaldehyde	B1	2A	1.3E-05	IRIS <sup>2</sup>	1991	Yes	Medium	2002	<a href="http://www.epa.gov/iris/subst/0419.htm">www.epa.gov/iris/subst/0419.htm</a>
Hexachlorobenzene	B2	2B	4.6E-04	IRIS <sup>2</sup>	1989	No	Low	2002	<a href="http://www.epa.gov/iris/subst/0374.htm">www.epa.gov/iris/subst/0374.htm</a>
Hydrazine, hydrazine sulfate	B2	2B	4.9E-03	IRIS <sup>2</sup>	1987	No	Low	--	<a href="http://www.epa.gov/iris/subst/0352.htm">www.epa.gov/iris/subst/0352.htm</a>
Lead compounds	B2	2B	1.2E-05	CAL EPA	1999	Yes	Low	--	<a href="http://www.oehha.ca.gov/pdf/HSCA2.pdf">www.oehha.ca.gov/pdf/HSCA2.pdf</a> , pg. 331
Methylene chloride (dichloromethane)	B2	2B	4.7E-07	IRIS <sup>2</sup>	1989	No	Low	2002	<a href="http://www.epa.gov/iris/subst/0070.htm">www.epa.gov/iris/subst/0070.htm</a>
Nickel compounds	A	2B	4.8E-04	IRIS <sup>2,7</sup>	1987	No	High	2002	<a href="http://www.epa.gov/iris/subst/0272.htm">www.epa.gov/iris/subst/0272.htm</a>
Polychlorinated biphenyls (PCBs)	B2	2A	1.0E-04	IRIS <sup>2</sup>	1996	Yes	Low	--	<a href="http://www.epa.gov/iris/subst/0294.htm">www.epa.gov/iris/subst/0294.htm</a>
Polycyclic Organic Matter	<sup>8</sup>	<sup>8</sup>	5.5E-05	OAQPS <sup>9</sup>	2001	Yes	Low	--	Appendix H
Carcinogenic PAHs: 7-PAH	B2	<sup>8</sup>	2.0E-04	OAQPS <sup>9</sup>	2001	Yes	Low	2003 <sup>10</sup>	Appendix H

<sup>7</sup> Number shown is derived from indicated data source, but risk estimates also include subsequent speciation assumptions. Details are provided in text above.

<sup>8</sup> WOE varies among individual compounds.

<sup>9</sup> Development by OAQPS staff of UREs for total POM and 7-PAH is described in Appendix H. These composite UREs are based on CalEPA estimates for various polycyclic organic compounds using a toxic equivalency approach in which the potency of individual compounds is estimated based on relative activity rather than individual assessments of bioassay data.

<sup>10</sup> Assessment will be limited to polynuclear aromatic hydrocarbons, an important subset of POM.

Pollutant	Weight of Evidence		Unit Risk Estimate (per ug/m <sup>3</sup> )	Source	Date of Assessment	Outside Peer Review?	Confidence in URE <sup>1</sup>	EPA IRIS Reassessment Expected	Citation for Current Assessment
	EPA	IARC							
Propylene dichloride (1,2-dichloropropane)	B2	3	1.9E-05	HEAST oral <sup>2,11</sup>	1991	No	Low	--	US EPA, 1997. Health Effects Assessment Summary Tables, EPA-540-R-97-036, FY 1997 Update.
Quinoline	C	-	3.4E-03	HEAST oral <sup>2,11</sup>	1985	No	Low	2001	US EPA, 1997. Health Effects Assessment Summary Tables, EPA-540-R-97-036, FY 1997 Update.
1,1,2,2-Tetrachloroethane	C	3	5.8E-05	IRIS <sup>2</sup>	1986	No	Low	--	<a href="http://www.epa.gov/iris/subst/0193.htm">www.epa.gov/iris/subst/0193.htm</a>
Tetrachloroethylene (perchloroethylene)	B2-C	2A	5.6E-06	CAL EPA	1999	Yes	Low	2002	<a href="http://www.oehha.ca.gov/pdf/HSCA2.pdf">www.oehha.ca.gov/pdf/HSCA2.pdf</a> , pg. 465
Trichloroethylene (TCE)	B2-C	2A	2.0E-06	CAL EPA	1999	Yes	Low	2002	<a href="http://www.oehha.ca.gov/pdf/HSCA2.pdf">www.oehha.ca.gov/pdf/HSCA2.pdf</a> , pg. 507
Vinyl chloride	A	1	8.8E-06	IRIS <sup>2,5,12</sup>	2000	Yes	High	--	<a href="http://www.epa.gov/iris/subst/1001.htm">www.epa.gov/iris/subst/1001.htm</a>

<sup>11</sup> Conversion or oral potency slope to inhalation unit risk estimate was based on the following assumptions: (1) whole-life, continuous exposure, (2) inhalation rate of 20 cubic meters of air per day, and (3) body mass of 70 kg. Details are provided in the text.

<sup>12</sup> URE based on whole life exposure was selected over a URE based on adult exposure only.



**Table 2: Dose-Response Values for Effects Other Than Cancer.**

This table lists reference concentrations (RfCs) and similar values (i.e., RELs, MRLs) that were used in the initial 1996 national-scale assessment. The RfC is an estimate of a concentration in air that is likely to be without appreciable risks of deleterious effects during a lifetime (including in sensitive subpopulations). Where the EPA RfCs were absent, similar values developed by other agencies were used. The UF and MF are the uncertainty factor and modifying factor used in the development of the RfC. The source of the RfC, date of the assessment, and a description of confidence in the assessment are provided, along with information about the EPA’s IRIS schedule. Internet links to the sources for assessments are provided where possible. The target organ for critical effects is the organ or organ system adversely affected at the lowest dose in human or animal studies. The target organs for other effects are those organs or systems adversely affected at higher doses. Other information on individual substances is shown in footnotes.

Pollutant	RfC <sup>13</sup> (mg/m3)	Target Organ for Chronic Critical Effect <sup>14</sup>	Severity <sup>15</sup> of Critical Effect	Target Organs for Other Chronic Effects	Source	Date of Assmnt.	Outside Peer Review?	Confidence in RfC <sup>16</sup>	UF(MF) <sup>17</sup>	EPA IRIS Reassmnt. Expected	Citation for Current Assessment
Acetaldehyde	9.0E-03	Degeneration of nasal epithelium in rats	Severe	Growth retardation in rats	IRIS	1991	No	Medium	1000	2002	<a href="http://www.epa.gov/iris/subst/0290.htm">www.epa.gov/iris/subst/0290.htm</a>
Acrolein	2.0E-05	Degeneration of nasal epithelium in rats	Severe	Lung lesions in rats	IRIS	1991	No	Medium	1000	2002	<a href="http://www.epa.gov/iris/subst/0364.htm">www.epa.gov/iris/subst/0364.htm</a>
Acrylonitrile	2.0E-03	Degeneration of nasal epithelium in rats	Severe	Central nervous system depression in humans	IRIS	1991	No	Medium	100(10)	--	<a href="http://www.epa.gov/iris/subst/0206.htm">www.epa.gov/iris/subst/0206.htm</a>

<sup>13</sup> Includes EPA reference concentrations (RfCs) and similar values, i.e., Cal EPA reference exposure levels (RELs), and ATSDR minimum risk levels (MRLs).

<sup>14</sup> The critical effect is the adverse effect upon which the RfC or similar value is based.

<sup>15</sup> Severe – substantial AND irreversible. Medium – substantial OR irreversible. Mild – not substantial AND not irreversible.

<sup>16</sup> For IRIS values, this column shows confidence statement from IRIS. For other sources: High – value incorporates high-quality human data. Medium – value considers human data of lower quality. Low – value does not incorporate human data.

<sup>17</sup> UF – uncertainty factor. MF -- modifying factor. MFs are shown in parentheses. MF values of 1 are not shown.

Pollutant	RfC <sup>13</sup> (mg/m3)	Target Organ for Chronic Critical Effect <sup>14</sup>	Severity of Critical Effect <sup>15</sup>	Target Organs for Other Chronic Effects	Source	Date of Assmnt.	Outside Peer Review?	Confidence in RfC <sup>16</sup>	UF(MF) <sup>17</sup>	EPA IRIS Reassmnt. Expected	Citation for Current Assessment
Arsenic compounds	3.0E-05	Fetal malformation in mice	Severe	Irritation of mucous membranes in humans	CAL EPA	2000	Yes	Medium	1000	2002	<a href="http://www.oehha.ca.gov/air/chronic_rels/pdf/acrol-cresol.pdf">www.oehha.ca.gov/air/chronic_rels/pdf/acrol-cresol.pdf</a> , pg. A-8
Benzene	8.0E-02	Depressed lymphocyte count in humans	Medium	Central nervous system depression in humans	EPA NCEA <sup>6</sup>	2001	Yes	Medium	100	2001 <sup>18</sup>	US EPA, 2001. Toxicological review of benzene (noncancer effects). Consensus review draft, July 2001.
Beryllium compounds	2.0E-05	Chronic inflammatory lung lesions in humans	Severe	Proliferation of lymphocytes in human lung	IRIS	1998	Yes	Medium	10	--	<a href="http://www.epa.gov/iris/subst/0012.htm">www.epa.gov/iris/subst/0012.htm</a>
1,3-Butadiene	2.0E-03	Ovarian atrophy in mice	Severe	Mutation of germ cells leading to fetal death in mice	EPA NCEA <sup>6</sup>	2001	Yes	Low	100(3)	2001	US EPA, 2001. Health Risk Assessment of 1,3-Butadiene. IRIS consensus review draft, January, 2001.
Cadmium compounds	2.0E-05	Kidney damage (proteinuria) in humans	Severe	Reduction in respiratory capacity in humans	CAL EPA	2000	Yes	High	30	2002	<a href="http://www.oehha.ca.gov/air/chronic_rels/pdf/acrol-cresol.pdf">www.oehha.ca.gov/air/chronic_rels/pdf/acrol-cresol.pdf</a> , pg. A-40.
Carbon tetrachloride	4.0E-02	Fatty infiltration in liver of guinea pigs	Medium	Central nervous system depression in humans	CAL EPA	2000	Yes	Low	300	2002	<a href="http://www.oehha.ca.gov/air/chronic_rels/pdf/acrol-cresol.pdf">www.oehha.ca.gov/air/chronic_rels/pdf/acrol-cresol.pdf</a> , pg. A-47.
Chloroform	9.8E-02	Enlarged liver in humans	Medium	Enlarged spleen in humans	ATSDR	1997	Yes	High	100	2002	ATSDR, 1997. Toxicological profile for chloroform. US Dept. of HHS.
Chromium compounds	1.0E-04 <sup>7</sup>	Lung injury in rats	Medium	Immune system effects in rats	IRIS	1998	Yes	Low	90	--	<a href="http://www.epa.gov/iris/subst/0144.htm">www.epa.gov/iris/subst/0144.htm</a>

<sup>18</sup> IRIS assessment to include noncancer effects only.

Pollutant	RfC <sup>13</sup> (mg/m3)	Target Organ for Chronic Critical Effect <sup>14</sup>	Severity <sup>15</sup> of Critical Effect	Target Organs for Other Chronic Effects	Source	Date of Assmnt.	Outside Peer Review?	Confidence in RfC <sup>16</sup>	UF(MF) <sup>17</sup>	EPA IRIS Reassmnt. Expected	Citation for Current Assessment
1,3-Dichloropropene	2.0E-02	Degeneration of nasal epithelium in rats	Medium	Cell proliferation in mouse bladder	IRIS	2000	Yes	High	30	--	<a href="http://www.epa.gov/iris/subst/0224.htm">www.epa.gov/iris/subst/0224.htm</a>
Ethylene dibromide (1,2-dibromoethane)	8.0E-04	Reduced sperm count in humans	Medium	Degeneration of respiratory epithelium in mice and rats	CAL EPA <sup>19</sup>	1997	Yes	Medium	100	2002	California EPA, 1997. Technical Support Document for the Determination of Noncancer Chronic Reference Exposure Levels.
Ethylene dichloride (1,2-dichloroethane)	2.4E+00	Liver and kidney lesions in rats	Severe	Cardiac lesions in several animal species	ATSDR	1999	Yes	Low	90	2002	ATSDR, 1999. Toxicological profile for 1,2-dichloroethane (update). US Dept. of HHS.
Ethylene oxide	3.0E-02	Neurobehavioral effects (CNS) in mice	Severe	Effects on blood in humans and mice	CAL EPA	2000	Yes	Low	100	2002	<a href="http://www.oehha.ca.gov/air/chronic_rels/pdf/Dichlbenz-Hydr.pdf">www.oehha.ca.gov/air/chronic_rels/pdf/Dichlbenz-Hydr.pdf</a> , pg. A-125.
Formaldehyde	9.8E-03	Abnormalities in nasal mucosa in humans	Mild	--	ATSDR	1997	Yes	High	30	2002	ATSDR, 1999. Toxicological profile for formaldehyde. US Dept. of HHS.
Hexachlorobenzene	3.0E-03	Liver (developmental) effects in animal studies	Severe	--	CAL EPA <sup>19</sup>	1997	Yes	Low	100	2002	California EPA, 1997. Technical Support Document for the Determination of Noncancer Chronic Reference Exposure Levels.
Hydrazine, hydrazine sulfate	2.0E-04	Abnormal protein deposits in hamster liver	Severe	Inflammation of respiratory tissues in rats	CAL EPA	2000	Yes	Low	300	--	<a href="http://www.oehha.ca.gov/air/chronic_rels/pdf/302012.pdf">www.oehha.ca.gov/air/chronic_rels/pdf/302012.pdf</a>
Lead compounds <sup>20</sup>	1.5E-03	Neurobehavioral effects (CNS) in humans	Severe	Blood, cardiovascular, and kidney effects in humans	NAAQS	1978	Yes	High	1	--	40 CFR 50.12

<sup>19</sup> Proposed by Cal EPA in 1997; not yet adopted in final form.

<sup>20</sup> EPA has not developed an RfC for lead. The NSA uses the National Ambient Air Quality Standard for lead, which was developed using the EPA Integrated Exposure, Uptake, Biokinetic Model, and did not use the UF/MF method. Because sensitive human subpopulations were modeled, the effective UF is 1.

Pollutant	RfC <sup>13</sup> (mg/m <sup>3</sup> )	Target Organ for Chronic Critical Effect <sup>14</sup>	Severity <sup>15</sup> of Critical Effect	Target Organs for Other Chronic Effects	Source	Date of Assmnt.	Outside Peer Review?	Confidence in RfC <sup>16</sup>	UF(MF) <sup>17</sup>	EPA IRIS Reassmnt. Expected	Citation for Current Assessment
Manganese compounds	5.0E-05	Neurobehavioral effects (CNS) in humans	Medium	Cough, bronchitis in humans	IRIS	1993	No	Medium	1000	--	<a href="http://www.epa.gov/iris/subst/0373.htm">www.epa.gov/iris/subst/0373.htm</a>
Mercury compounds <sup>21</sup>	3.0E-04	Neurobehavioral effects (CNS) in humans	Medium	Altered kidney function in humans	IRIS	1990	No	Medium	30	2001 <sup>22</sup>	<a href="http://www.epa.gov/iris/subst/0370.htm">www.epa.gov/iris/subst/0370.htm</a>
Methylene chloride	1.0E+00	Pathological changes in liver cells in rats	Medium	Effects on blood chemistry in humans	ATSDR	2000	Yes	Low	30	2002	ATSDR, 2000. Toxicological profile for methylene chloride. US Dept. of HHS.
Nickel compounds	2.0E-04	Respiratory tract inflammation in rats	Mild	Immune system effects in humans	ATSDR	1997	Yes	Low	30	2002	ATSDR, 1997. Toxicological profile for nickel. US Dept. of HHS.
Propylene dichloride (1,2-dichloropropane)	4.0E-03	Increase in cell growth of nasal epithelium in rat	Mild	Anemia in rabbits	IRIS	1991	No	Medium	300	--	<a href="http://www.epa.gov/iris/subst/0601.htm">www.epa.gov/iris/subst/0601.htm</a>
Tetrachloroethylene (perchloroethylene)	2.7E-01	Neurobehavioral effects (CNS) in humans	Medium	Liver and kidney damage in humans	ATSDR	1997	Yes	High	100	2002	ATSDR, 1997. Toxicological profile for tetrachloroethylene. US Dept. of HHS.
Trichloroethylene (TCE)	6.0E-01	Central nervous system depression in humans	Medium	Respiratory irritation in humans	CAL EPA	2000	Yes	High	100	2002	<a href="http://www.oehha.ca.gov/air/chronic_rels/pdf/79016.pdf">www.oehha.ca.gov/air/chronic_rels/pdf/79016.pdf</a>
Vinyl chloride	1.0E-01	Cellular changes and cysts in rat liver	Severe	Testicular damage in rats, CNS depression in humans	IRIS	2000	Yes	Medium	30	--	<a href="http://www.epa.gov/iris/subst/1001.htm">www.epa.gov/iris/subst/1001.htm</a>

<sup>21</sup> Hazard calculations for mercury compounds were based on the RfC for elemental mercury.

<sup>22</sup> This IRIS assessment includes methyl mercury only, and would not have impacted the NATA national-scale assessment.