

# Health Effects Information Used In Cancer and Noncancer Risk Characterization for the 2005 National-Scale Assessment

## Introduction

Hazard identification and dose-response assessment information for the 2005 national-scale assessment was obtained from various sources and prioritized according to (1) conceptual consistency with EPA risk assessment guidelines and (2) the level of review received. The prioritization process was aimed at incorporating into our assessment the best available science with respect to dose-response information. The following sources were used.

## US Environmental Protection Agency (EPA)

EPA has developed dose-response assessments for chronic exposure to many of the pollutants in this study. These assessments typically specify a reference concentration, or RfC (to protect against effects other than cancer) and/or a unit risk estimate, or URE (to estimate the probability of contracting cancer). The RfC is an estimate, with uncertainty spanning perhaps an order of magnitude, of an inhalation exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risks of deleterious effects during a lifetime. The URE is the upper-bound excess cancer risk estimated to result 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, EPA evaluates various types of toxicological data and develops a weight-of-evidence (WOE) determination. Older WOE assessments use an alphanumeric categorization (recommended by EPA's 1986 guidelines for carcinogen risk assessment); assessments developed since the 2005 revisions to the cancer guidelines (see: <http://cfpub.epa.gov/ncea/raf/recordisplay.cfm?deid=116283>) characterize the WOE with a paragraph of descriptive text.

EPA disseminates dose-response assessment information in several forms, depending on the level of internal review. 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)

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 by the inhalation and oral routes. ATSDR describes MRLs as media-specific concentrations to be used by health assessors to select 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 noncancer portion of this assessment when IRIS RfCs were not available because their concept, definition, and derivation are philosophically consistent (though not identical) with the basis for EPA's RfCs. ATSDR MRLs are reviewed by an expert panel of external peers and also by an interagency workgroup that includes EPA. MRLs are published in pollutant-specific toxicological profile documents, and also in a table of "comparison values" that ATSDR regularly updates and distributes (available on-line at <http://www.atsdr.cdc.gov/mrls.html> ).

### **California Office of Environmental Health Hazard Assessment (OEHHA)**

The California OEHHA 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 incorporates significant external scientific peer review. The non-cancer information includes available inhalation health risk guidance values expressed as chronic inhalation reference exposure levels (RELs). OEHHA defines the REL as a concentration level at (or below) which no health effects are anticipated, a concept that is substantially similar to EPA's non-cancer dose-response assessment perspective. This assessment uses chronic RELs in the same way as RfCs when no IRIS or ATSDR values exist.

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

### **US EPA Health Effects Assessment Tables (HEAST)**

HEAST is a comprehensive listing consisting almost entirely of provisional UREs, RfCs, and other risk assessment information for chemicals of interest. Although the assessments summarized in HEAST have undergone review and have the concurrence of individual EPA program offices, and each is supported by an agency reference, they have not had enough review to be recognized as high-quality, EPA-wide consensus information. Because of these limitations, and the fact that HEAST has not been updated since 1997 and exists only in hard copy (PB97-921199), this assessment uses HEAST information only when no values from the other sources described above are available.

### **Prioritization of Data Sources**

Some substances have been assessed for dose-response by more than one of the agencies used as sources for this analysis. Because different scientists developed these assessments at different times for purposes that were similar but not identical, it is inevitable that the results are not totally consistent. In some cases interagency differences were substantial, especially among assessments done many years apart. To resolve interagency discrepancies for this analysis, EPA applied a consistent priority scheme to the universe of dose-response information.

Externally peer-reviewed assessments 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 supersede existing values on IRIS. Where externally peer reviewed IRIS draft assessments were not available, the next preferred source was EPA's IRIS database. For substances lacking IRIS assessments, ATSDR MRLs (available only for noncancer effects) received next preference, followed by OEHHA RELs and UREs.

### Adjustments to Dose-Response Information

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

- *Oral carcinogens lacking inhalation assessments.* For 12 carcinogenic substances, (benzotrichloride, captan, DDE, dichlorvos, 3,3'-dimethoxybenzidine, 3,3'-dimethylbenzidine, 1,4-dioxane, isophorone, pentachloronitrobenzene, propylene dichloride, quinoline, and trifluralin) that currently lack inhalation assessments from the sources described above, oral carcinogenic potency estimates were converted to inhalation UREs. The conversion from oral risk (per mg/kg/d oral intake) to inhalation risk (per  $\mu\text{g}/\text{m}^3$  inhaled) was based on EPA's standard assumptions of a 70-kg body mass and 20  $\text{m}^3/\text{d}$  inhalation rate, as follows:

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

Where: URE = Unit risk estimate for inhalation (risk per  $\mu\text{g}/\text{m}^3$ )

CPS = Carcinogenic potency slope for ingestion (risk per mg oral intake per kg body mass per day)

OAQPS understands that method used for the 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 inhalation risk estimates altogether, thereby making a *de facto* assumption of zero carcinogenic potency. For the purposes of the national-scale assessment, OAQPS prefers to use the approach described above to screen these carcinogens for their potential contributions to risk. If a substance is determined to be a potentially important contributor to risk, it will be prioritized for further dose-response development through EPA's IRIS process.

- *Hexavalent chromium compounds.* The IRIS RfC for particulate hexavalent chromium was used in preference to the RfC for chromic acid mists and dissolved aerosols.
- *Formaldehyde.* In recent NATA analyses (1999 and 2002), EPA utilized a cancer potency for inhalation exposure to formaldehyde derived from modeling sponsored by what was then the Chemical Industry Institute for Toxicology (CIIT), now called the Hamner Institutes for Health Sciences. Based on more recent publications, the EPA's Office of Research and Development (ORD) now believes there is sufficient published,

peer reviewed research to advise against the continued use of the CIIT potency estimate. EPA is currently updating the Integrated Risk Information System (IRIS) file for formaldehyde to consider new science published in the peer-reviewed and epidemiologic literature. This study is not expected to be completed in time for the release of the 2005 NATA. Therefore, for this assessment and in the near term, EPA is using the existing IRIS URE value for formaldehyde. That URE is  $1.3 \times 10^{-5}$  per  $\mu\text{g}/\text{m}^3$ .

- *Glycol ethers.* Most of the emission inventory information for the glycol ether category reports only the total mass for the entire group without distinguishing between individual glycol ether compounds. These individual compounds, however, vary substantially in toxicity. In order to avoid underestimating the health hazard associated with glycol ethers, EPA has protectively applied the RfC for ethylene glycol methyl ether (the most toxic for which an assessment exists) to the entire group.
- *Diesel emissions.* The national-scale assessments do not include quantitative cancer risk estimates for diesel emissions because EPA has judged that toxicological data are not yet sufficient to develop a URE. However, diesel emissions have been assessed for effects other than cancer, using the 2003 IRIS RfC.
- *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 toxic 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.
- *2-Nitropropane.* The assessment used a URE of  $5.6 \times 10^{-6}$  per  $\mu\text{g}/\text{m}^3$  for 2-nitropropane. This value was derived in 1999 by the Health Council of the Netherlands (available at: <http://www.gr.nl/pdf.php?ID=423&p=1>), based on induction of hepatocellular nodules in rats, and is consistent with weight-of-evidence determinations by the U.S. National Toxicology Program (“reasonably anticipated to be a human carcinogen”) and the IARC (“possibly carcinogenic to humans”).
- *Polycyclic organic matter (POM).* The assessment divided POM emissions into eight categories. The first two categories were assigned a URE equal to 5% of that for pure benzo[a]pyrene (the same assumption that the 1996 assessment used for all POM data). Categories 3-7 were composed of emissions that were reported as individual compounds. These compounds were placed in the category with an appropriate URE. Category 8, composed of unspiciated carcinogenic polynuclear aromatic hydrocarbons (a subset of

POM called 7-PAH), was assigned a URE equal to 18% of that for pure benzo[a]pyrene. Details on the development of the 5% and 18% URE estimates are available here: <http://www.epa.gov/ttn/atw/sab/appendix-h.pdf>.

The process of URE estimation includes the following important sources of uncertainty:

- Many of the substances in this assessment were classified as probable carcinogens, indicating that data were not sufficient to prove these substances definitely cause cancer in humans. It is possible that some of these substances are not human carcinogens at environmentally relevant doses, and that the true risk associated with them is zero.
- All UREs used in this assessment were based on linear extrapolation from high to low doses. To the extent that true dose-response relationships for some substances are nonlinear, this assumption may result in significant over- or underestimates of risk.
- UREs for most of these substances were developed from animal data using conservative methods to extrapolate between species. Actual human responses may differ from the predicted ones.
- Most UREs used in this assessment (typically, those based on animal data) were based on the statistical upper confidence limit (UCL) of the fitted dose-response curve. That means true risk would probably be less, but could be greater. A few (typically, those based on human data) were based on the statistical best fit (“maximum likelihood estimate,” or MLE). UREs based on the MLE are identified in a footnote to Table 1. This difference between UCL- and MLE-based assessments results in some UREs that are somewhat less conservative than the rest.

### **Table 1: Dose-Responses Values**

This table lists includes dose-response values and supporting information for both cancer and noncancer effects used in the 2005 national-scale assessment. The EPA 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 Carcinogenic to Humans, Likely to be Carcinogenic to Humans, Suggestive Evidence of Carcinogenic Potential,, Inadequate Information to Assess Carcinogenic Potential, and Not Likely to Be Carcinogenic to Humans . 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 “RfC” column lists reference concentrations and similar values (i.e., RELs, MRLs) that were used in this assessment. The reference concentration (RfC) is an estimate, with uncertainty spanning perhaps an order of magnitude, of an inhalation exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risks of deleterious effects during a lifetime. The “target system” columns show up to three organs or organ system adversely affected at the lowest dose in human or animal studies. Other information on individual substances is shown in footnotes.

Chemical Name	CAS No.	EPA WOE	URE ( $\mu\text{g}/\text{m}^3\text{-}^1$ )	URE Source	RfC <sup>1</sup> ( $\text{mg}/\text{m}^3$ )	RfC Source	Target System 1 <sup>14</sup>	Target System 2 <sup>14</sup>	Target System 3 <sup>14</sup>
Acetaldehyde	75070	B2	0.0000022	IRIS	0.009	IRIS	Respiratory		
Acetamide	60355		0.00002	CAL					
Acetonitrile	75058	D			0.06	IRIS	Whole body		
Acetophenone	98862								
2-Acetylaminofluorene	53963								
Acrolein	107028				0.00002	IRIS	Respiratory		
Acrylamide	79061	B2	0.00016 <sup>3</sup>	IRIS	0.006	IRIS	Neurological		
Acrylic acid	79107				0.001	IRIS	Respiratory		
Acrylonitrile	107131	B1	0.000068	IRIS	0.002	IRIS	Respiratory		
Allyl chloride	107051	C	0.000006	CAL	0.001	IRIS	Neurological		
4-Aminobiphenyl	92671								
Aniline	62533	B2	0.0000016	CAL	0.001	IRIS	Spleen		
o-Anisidine	90040								
Antimony compounds	7440360				0.0002 <sup>2</sup>	IRIS	Respiratory		
Arsenic compounds	7440382	A	0.0043	IRIS	0.000015	CAL	Developmental		
Arsine	7784421				0.00005	IRIS	Hematological		
Benzene	71432	A	0.0000078	IRIS	0.03	IRIS	Immunological		
Benzidine	92875	A	0.1072 <sup>3</sup>	IRIS	0.01	PCAL <sup>15</sup>	Neurological	Liver	
Benzo[trichloride	98077	B2	0.0037	Conv. Oral <sup>4</sup>					
Benzyl chloride	100447	B2	0.000049	CAL					
Biphenyl	92524	D							
Beryllium compounds	7440417	B1	0.0024	IRIS	0.00002	IRIS	Respiratory		
Bis(2-ethylhexyl) phthalate	117817	B2	0.0000024	CAL	0.01	PCAL <sup>15</sup>	Respiratory	Liver	
Bis(chloromethyl) ether	542881	A	0.062	IRIS					
Bromoform	75252	B2	0.0000011	IRIS					
1,3-Butadiene	106990	A	0.00003	IRIS	0.002	IRIS	Reproductive		
Calcium cyanamide	156627								
Cadmium compounds	7440439	B1	0.0018	IRIS	0.00001	D_ATSDR	Kidney		

<sup>1</sup> Includes EPA reference concentrations (RfCs) and similar values, i.e., California OEHHA reference exposure levels (RELs), and ATSDR minimum risk levels (MRLs). Many of these chemicals are under review for the development of RfCs. A current status report for all EPA assessments is available at <http://cfpub.epa.gov/irisstrac/index.cfm>.

<sup>2</sup> RfC used for antimony compounds is derived from RfC for antimony trioxide.

<sup>3</sup> Includes age-related adjustment factor (1.6 x) to account for early childhood exposures to a known mutagenic agent. See document at [http://www.epa.gov/ttn/atw/childrens\\_supplement\\_final.pdf](http://www.epa.gov/ttn/atw/childrens_supplement_final.pdf) for further details.

<sup>4</sup> Conversion of 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. Further details are provided in the text above.

Chemical Name	CAS No.	EPA WOE	URE ( $\mu\text{g}/\text{m}^3$ ) <sup>-1</sup>	URE Source	RfC <sup>1</sup> ( $\text{mg}/\text{m}^3$ )	RfC Source	Target System 1 <sup>14</sup>	Target System 2 <sup>14</sup>	Target System 3 <sup>14</sup>
Captan	133062	B2	0.000001	Conv. Oral <sup>4</sup>					
Carbaryl	63252								
Carbon disulfide	75150				0.7	IRIS	Neurological		
Carbon tetrachloride	56235	B2	0.000006	IRIS	0.1	IRIS	Liver		
Carbonyl sulfide	463581								
Catechol	120809								
Chlordane	57749	B2	0.0001	IRIS	0.0007	IRIS	Liver		
Chlorine	7782505				0.00015	D-ATSDR	Respiratory		
Chloroacetic acid	79118								
2-Chloroacetophenone	532274				0.00003	IRIS	Respiratory		
Chlorobenzene	108907				1	CAL	Reproductive	Kidney	Liver
Chlorobenzilate	510156	B2	0.000078	HEAST					
Chloroform	67663	B2			0.098	ATSDR	Liver		
Chloromethyl methyl ether	107302	A							
Chloroprene	126998				0.007	HEAST	Respiratory		
Chromium VI compounds	18540299	A	0.012	IRIS	0.0001	IRIS	Respiratory		
Cobalt compounds	7440484				0.0001	ATSDR	Respiratory		
Coke Oven Emissions	8007452	A	0.00062	IRIS					
Cresols (mixed)	1319773	C			0.6	CAL	Neurological	Whole body	
0-cresol <sup>5</sup>	95487				0.6	OAQPS	Neurological		
m-cresol <sup>5</sup>	108394				0.6	OAQPS	Neurological		
p-cresol <sup>5</sup>	106445				0.6	OAQPS	Neurological		
Cumene	98828	D			0.4	IRIS	Kidney	Endocrine	
2,4-d, salts and esters	94757								
DDE	72559	B2	0.000097	Conv. Oral <sup>4</sup>					
Diazomethane	334883								
Dibenzofurans	132649	D							
Cyanide compounds	57125	D			0.003 <sup>6</sup>	IRIS	Neurological	Thyroid	
1,2-Dibromo-3-chloropropane	96128	B2	0.002	CAL	0.0002	IRIS	Reproductive		
Dibutylphthalate	84742	D							
p-Dichlorobenzene	106467	C	0.000011	CAL	0.8	IRIS	Liver		
3,3'-Dichlorobenzidine	91941	B2	0.00034	CAL					

<sup>5</sup> The individual cresol and xylene isomers were modeled separately if their emissions were reported separately, and hazard quotients were generated for each isomer using the RfC for their mixture. The final NATA results present their results combined under the HAP category of 'cresol or xylene mixture'.

<sup>6</sup> The RfC used is from the HAP, hydrogen cyanide.

Chemical Name	CAS No.	EPA WOE	URE ( $\mu\text{g}/\text{m}^3$ ) <sup>-1</sup>	URE Source	RfC <sup>1</sup> (mg/m <sup>3</sup> )	RfC Source	Target System 1 <sup>14</sup>	Target System 2 <sup>14</sup>	Target System 3 <sup>14</sup>
Dichloroethyl ether	111444	B2	0.00033	IRIS					
1,3-Dichloropropene	542756	B2	0.000004	IRIS	0.02	IRIS	Respiratory		
Dichlorvos	62737	B2	0.000083	Conv. Oral <sup>4</sup>	0.0005	IRIS	Neurological		
Diesel emissions					0.005	IRIS	Respiratory		
Diethanolamine	111422				0.003	CAL	Respiratory		
N,N-Dimethyl aniline	121697								
Diethyl sulfate	64675								
3,3'-Dimethoxybenzidine	119904	B2	0.000004	Conv. Oral <sup>4</sup>					
p-Dimethylaminoazobenzene	60117		0.0013	CAL					
3,3'-Dimethylbenzidine	119937	B2	0.0026	Conv. Oral <sup>4</sup>					
Dimethyl carbamoyl chloride	79447								
Dimethylformamide	68122				0.03	IRIS	Liver		
1,1-Dimethylhydrazine	57147								
Dimethyl phthalate	131113	D							
Dimethyl sulfate	77781	B2							
4,6-Dinitro-o-cresol and salts	534521								
2,4-Dinitrophenol	51285								
2,4-Dinitrotoluene	121142	B2	0.000089	CAL	0.007	PCAL <sup>15</sup>	Liver	Neurological	
1,4-Dioxane	123911	B2	0.0000077	CAL	3.6	D-ATSDR	Liver	Hematol	Kidney
Epichlorohydrin	106898	B2	0.0000012	IRIS	0.001	IRIS	Respiratory		
1,2-Epoxybutane	106887				0.02	IRIS	Respiratory		
Ethyl acrylate	140885	B2							
Ethylbenzene	100414	D	0.000002.5	CAL	1	IRIS	Developmental		
Ethyl carbamate	51796		0.00046 <sup>3</sup>	CAL					
Ethyl chloride	75003				10	IRIS	Developmental		
Ethylene dibromide	106934	B2	0.0006	IRIS	0.009	IRIS	Respiratory		
Ethylene dichloride	107062	B2	0.000026	IRIS	2.4	ATSDR	Liver		
Ethylene glycol	107211				0.4	CAL	Respiratory		
Ethylene imine	151564								
Ethylene oxide	75218	B1	0.000088	CAL	0.03	CAL	Neurological		
Ethylene thiourea	96457	B2	0.000013	CAL	0.003	PCAL <sup>15</sup>	Endocrine		
Ethylidene dichloride	75343	C	0.0000016	CAL	0.5	HEAST	Kidney		
Formaldehyde	50000	B1	0.000013	IRIS	0.0098	ATSDR	Respiratory		
Heptachlor	76448	B2	0.0013	IRIS					

Chemical Name	CAS No.	EPA WOE	URE ( $\mu\text{g}/\text{m}^3$ ) <sup>-1</sup>	URE Source	RfC <sup>1</sup> ( $\text{mg}/\text{m}^3$ )	RfC Source	Target System 1 <sup>14</sup>	Target System 2 <sup>14</sup>	Target System 3 <sup>14</sup>
Glycol ether compounds					0.02 <sup>7</sup>	OAQPS	Reproductive		
Hexachlorobenzene	118741	B2	0.00046	IRIS	0.003	PCAL <sup>15</sup>	Liver		
Hexachlorobutadiene	87683	C	0.000022	IRIS	0.09	PCAL <sup>15</sup>	Reproductive		
Hexachlorocyclopentadiene	77474	E			0.0002	IRIS	Respiratory		
Hexachloroethane	67721	C	0.000004	IRIS	0.08	PCAL <sup>15</sup>	Kidney	Liver	Neurological
Hexamethylene-1,6-diisocyanate	822060				0.00001	IRIS	Respiratory		
n-Hexane	110543				0.7	IRIS	Neurological	Respiratory	
Hydrazine	302012	B2	0.0049	IRIS	0.0002	CAL	Liver	Thyroid	
Hydrochloric acid	7647010				0.02	IRIS	Respiratory		
Hydrofluoric acid	7664393				0.014	CAL	Skeletal		
Hydroquinone	123319								
Isophorone	78591	C	2.7e-7	Conv. Oral <sup>4</sup>	2	CAL	Liver	Develop	
Lead compounds	7439921	B2			0.00015 <sup>8</sup>	OAQPS	Neurological		
Lindane (all isomers)			0.00031	IRIS	0.0003	PCAL <sup>15</sup>	Kidney	Liver	Reproductive
Maleic anhydride	108316				0.0007	CAL	Respiratory		
Manganese compounds	7439965	D			0.00005	IRIS	Neurological		
Mercury compounds		C			0.0003	IRIS	Neurological		
Methanol	67561				4	CAL	Developmental		
Methoxychlor	72435	D							
Methyl bromide	74839	D			0.005	IRIS	Respiratory		
Methyl chloride	74873	D			0.09	IRIS	Neurological		
Methyl isobutyl ketone	108101				3	IRIS	Developmental		
Methyl iodide	74884								
Methyl Hydrazine	60344								
Methyl isocyanate	624839				0.001	CAL	Respiratory	Whole body	
Methyl methacrylate	80626	E			0.7	IRIS	Respiratory		
Methyl tert-butyl ether	1634044		2.6e-7	CAL	3	IRIS	Liver	Kidney	Ocular
4,4'-Methylene bis(2-chloroaniline)	101144	B2	0.00043	CAL					
Methylene chloride	75092	B2	4.7e-7	IRIS	1	ATSDR	Liver		
Methylene diphenyl diisocyanate	101688	D			0.0006	IRIS	Respiratory		
4,4'-Methylenedianiline	101779		0.00046	CAL	0.02	CAL	Ocular		

<sup>7</sup> This RfC is for ethylene glycol methyl ether, the most toxic of this group for which an assessment exists. See note in text above for a more complete explanation.

<sup>8</sup> EPA has not developed an RfC for lead. The value shown is the quarterly National Ambient Air Quality Standard for lead, which EPA believes to be without significant adverse effects.

Chemical Name	CAS No.	EPA WOE	URE ( $\mu\text{g}/\text{m}^3$ ) <sup>-1</sup>	URE Source	RfC <sup>1</sup> (mg/m <sup>3</sup> )	RfC Source	Target System 1 <sup>14</sup>	Target System 2 <sup>14</sup>	Target System 3 <sup>14</sup>
Naphthalene	91203	C	0.000034	CAL	0.003	IRIS	Respiratory		
Nickel compounds		A	0.000312 <sup>9</sup>	OAQPS	0.00009	ATSDR	Respiratory	Immuno	
Nitrobenzene	98953	C	0.00004	IRIS	0.009	IRIS	Respiratory		
4-Nitrobiphenyl	92933								
4-Nitrophenol	100027								
2-Nitropropane	79469	B2	0.0000056	OAQPS	0.02	IRIS	Liver		
Nitrosodimethylamine	62759	B2	0.014	IRIS					
N-Nitrosomorpholine	59892		0.0019	CAL					
PCB Group	1336363	B2	0.0001	IRIS					
Pentachloronitrobenzene	82688	C	0.000074	Conv. Oral <sup>4</sup>					
Pentachlorophenol	87865	B2	0.0000051	CAL	0.1	PCAL <sup>15</sup>	Liver	Kidney	
Phenol	108952	D			0.2	CAL	Liver		
p-Phenylenediamine	106503								
Phosgene	75445								
Phosphine	7803512	D			0.0003	IRIS	Respiratory		
Phosphorus	7723140				0.0003	IRIS	Whole body		
Phthalic anhydride	85449				0.02	CAL	Respiratory	Ocular	
Polycyclic organic matter <sup>10</sup> Gp1		"	0.000088 <sup>3</sup>	OAQPS					
Polycyclic organic matter Gp2		"	0.000088 <sup>3</sup>	OAQPS					
Polycyclic organic matter Gp3		"	0.16 <sup>3</sup>	OAQPS					
Polycyclic organic matter Gp4		"	0.016 <sup>3</sup>	OAQPS					
Polycyclic organic matter Gp5		"	0.0016 <sup>3</sup>	OAQPS					
Polycyclic organic matter Gp6		"	0.00016 <sup>3</sup>	OAQPS					
Polycyclic organic matter Gp7		"	0.000016 <sup>3</sup>	OAQPS					
Polycyclic organic matter Gp8		"	0.00032 <sup>3</sup>	OAQPS					
1,3-Propane sulfone	1120714		0.00069	CAL					
Propionaldehyde	123386				0.008	IRIS	Respiratory		
Propoxur	114261								
Propylene dichloride	78875	B2	0.000019	Conv. Oral <sup>4</sup>	0.004	IRIS	Respiratory		
Propylene oxide	75569	B2	0.0000037	IRIS	0.03	IRIS	Respiratory		
1,2-Propylenimine	75558								
Quinoline	91225	B2							

<sup>9</sup> The URE used is derived by assuming 65% of the nickel subsulfide URE. See note in text above for a more complete explanation.

<sup>10</sup> A full discussion of the risk assessment for polycyclic organic matter is available at: <http://www.epa.gov/ttn/atw/sab/appendix-h.pdf>.

<sup>11</sup> EPA WOE varies among individual compounds.

Chemical Name	CAS No.	EPA WOE	URE ( $\mu\text{g}/\text{m}^3$ ) <sup>-1</sup>	URE Source	RfC <sup>1</sup> ( $\text{mg}/\text{m}^3$ )	RfC Source	Target System 1 <sup>14</sup>	Target System 2 <sup>14</sup>	Target System 3 <sup>14</sup>
Quinone	106514								
Selenium compounds	7782492	D			0.02	CAL	Neurological	Liver	Hematological
Styrene	100425				1	IRIS	Neurological		
Styrene oxide	96093				0.006	PCAL <sup>15</sup>	Respiratory		
1,1,2,2-Tetrachloroethane	79345	C	0.000058	IRIS					
Perchloroethylene	127184	B2C	0.0000059	CAL	0.27	ATSDR	Neurological		
Titanium tetrachloride	7550450				0.0001	ATSDR	Respiratory		
Toluene	108883	D			5.0	IRIS	Respiratory	Neurological	
2,4-Toluene diamine	95807	B2	0.0011	CAL					
2,4-Toluene diisocyanate	26471625		0.000011	CAL	0.00007	IRIS	Respiratory		
o-Toluidine	95534	B2	0.000051	CAL					
Toxaphene	8001352	B2	0.00032	IRIS					
1,2,4-Trichlorobenzene	120821	D			0.2	HEAST	Liver		
1,1,2-Trichloroethane	79005	C	0.000016	IRIS	0.4	PCAL <sup>15</sup>	Liver		
1,1,1-Trichloroethane	71556	D			5	IRIS	Neurological		
Trichloroethylene	79016	B2C	0.000002	CAL	0.6	CAL	Neurological	Ocular	
2,4,5-Trichlorophenol	95954								
2,4,6-Trichlorophenol	88062	B2	0.0000031	IRIS					
Triethylamine	121448				0.007	IRIS	Respiratory		
Trifluralin	1582098	C	0.0000022	Conv. Oral <sup>4</sup>					
2,2,4-Trimethylpentane	540841								
Vinyl acetate	108054				0.2	IRIS	Respiratory		
Vinyl bromide	593602	B2	0.000032	HEAST	0.003	IRIS	Liver		
Vinyl chloride	75014	A	0.0000088	IRIS <sup>12</sup>	0.1	IRIS	Liver		
Vinylidene chloride	75354	C			0.2	IRIS	Liver		
Xylenes (mixed)	1330207				0.1	IRIS	Neurological		
o-Xylene <sup>3</sup>	95476				0.1	IRIS	Neurological		
m-Xylene <sup>5</sup>	108383				0.1	IRIS	Neurological		
p-Xylene <sup>5</sup>	106423				0.1	IRIS	Neurological		

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

<sup>14</sup> Multiple target organs listed if the concentration at the “critical effect” is the same at all targets.

<sup>15</sup> PCAL is a preliminary value from CAL