US EPA ARCHIVE DOCUMENT

US EPA ARCHIVE DOCUMENT

Health Effects Information Used In Cancer and Noncancer Risk Characterization For the 1999 National-Scale Assessment

Introduction

Hazard identification and dose-response assessment information for the 1999 national-scale assessment was obtained from various sources and prioritized according to (1) conceptual consistency with EPA risk assessment guidelines and (2) 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 $\mu g/m^3$ 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 2002 characterize the WOE with a paragraph of descriptive text (recommended by the current draft revisions to the 1986 guidelines).

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.

US EPA ARCHIVE DOCUMENT

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.

US EPA ARCHIVE DOCUMENT

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.

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. 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, however.

IARC's degrees of evidence for substances are included as supporting information for this assessment as a backup to 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://monographs.iarc.fr/monoeval/grlist.html.

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

US EPA ARCHIVE DOCUMENT

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 13 carcinogenic substances, (benzotrichloride, captan, DDE, dichlorvos, 3,3'-dimethoxy benzidine, 3,3'-dimethylbenzidine, 1,4-dioxane, ethyl acrylate, 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 $\mu g/m^3$ inhaled) was based on EPA's standard assumptions of a 70-kg body mass and 20 m^3/d inhalation rate, as follows:

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

Where: URE = Unit risk estimate for inhalation (risk per $\mu g/m^3$)
CPS = Carcinogenic potency slope for ingestion (risk per mg oral intake per kg body mass per day)

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 inhalation risk estimates altogether, thereby making a *de facto* assumption of zero carcinogenic potency. For the purposes of the national-

US EPA ARCHIVE DOCUMENT

scale assessment, EPA 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*. EPA no longer considers the formaldehyde URE reported in IRIS, which is based on a 1987 study, to represent the best available science in the peer-reviewed literature. Since that time, significant new data and analyses have become available. Accordingly, the 1999 risk estimates for formaldehyde are based on a dose-response value developed by the CIIT Centers for Health Research (formerly the Chemical Industry Institute of Toxicology) and published in 1999. This assessment incorporates mechanistic and dosimetric information on formaldehyde that had been accumulated over the past decade, and developed a URE using approaches that are consistent with EPA's guidelines for carcinogenic risk assessment. EPA had judged that this CIIT modeling effort currently represents the best application of available mechanistic and dosimetric science on the dose-response for portal of entry cancers due to formaldehyde exposures. EPA is currently reviewing the CIIT analysis and other recent information, including recently published epidemiological studies, in our reassessment of our formaldehyde unit risk estimate (URE).

- *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 1999 national-scale assessment, as with the 1996 assessment, does 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 (which was not available for the 1996 assessment).

US EPA ARCHIVE DOCUMENT

- *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 x 10-6 per ug/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 unspeciated 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.

US EPA ARCHIVE DOCUMENT

- 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 1999 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, Group B1—probable, based on incomplete human data, Group B2—probable, based on adequate animal data, Group C—possible, 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 "RfC" column lists reference concentrations and similar values (i.e., RELs, MRLs) that were used in the initial 1996 national-scale 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.

US EPA ARCHIVE DOCUMENT

Chemical Name	CAS No.	EPA WOE	IARC WOE	URE ($\mu g/m^3)^{-1}$	URE Source	URE Date	RfC[1] (mg/m^3)	RfC Source	RfC Date	Target System 1	Target System 2	Target System 3
Acetaldehyde[2]	75070	B2	2B	0.000002	IRIS	1997	0.009	IRIS	1991	Respiratory		
Acetamide	60355		2B	0.00002	CAL	1999						
Acetonitrile	75058	D					0.06	IRIS	1999	Whole body		
Acrolein[2]	107028		3				0.00002	IRIS	2003	Respiratory		
Acrylamide[2]	79061	B2	2A	0.0013	IRIS	1997	0.0007	PCAL[3]	1997	Neurological		
Acrylic acid	79107						0.001	IRIS	1995	Respiratory		
Acrylonitrile[2]	107131	B1	2A	0.000068	IRIS	1991	0.002	IRIS	1997	Respiratory		
Allyl chloride	107051	C	3	0.000006	CAL	1999	0.001	IRIS	1991	Neurological		
Aniline	62533	B2	3	0.000001	CAL	1999	0.001	IRIS	1991	Spleen		
Antimony compounds							0.0002	IRIS	1995	Respiratory		
Arsenic[2]	7440382	A	1	0.0043	IRIS[4]	1997	0.00003	CAL	2000	Developmental		
Arsine	7784421						0.00005	IRIS	1994	Hematological		
Benzene	71432	A	1	0.000007	IRIS[4]	2000	0.03	IRIS	2003	Immunological		
Benzidine	92875	A		0.067	IRIS	1992	0.01	PCAL[3]	1997	Neurological	Liver	
Benzotrichloride	98077	B2	2B	0.0037	Conv. Oral[5]	2004						
Benzyl chloride	100447	B2	2B	0.000049	CAL	1999						
Beryllium compounds[2]		B1	1	0.0024	IRIS	1998	0.00002	IRIS	1998	Respiratory		
Bis(2-ethylhexyl) phthalate[2]	117817	B2	2B	0.000002	CAL	1999	0.01	CAL	1999	Respiratory	Liver	
Bis(chloromethyl) ether	542881	A	1	0.062	IRIS	1997						
Bromoform[2]	75252	B2	3	0.000001	IRIS	1997						
1,3-Butadiene	106990	A	2A	0.00003	IRIS	2002	0.002	IRIS	2002	Reproductive		
Cadmium compounds[2]		B1	1	0.0018	IRIS	1992	0.00002	CAL	2000	Kidney		
Captan	133062	B2	3	0.000001	Conv. Oral[5]	2004						
Carbon disulfide	75150						0.7	IRIS	1995	Neurological		
Carbon tetrachloride[2]	56235	B2	2B	0.000015	IRIS	1991	0.04	CAL	2000	Liver		
Chlordane	57749	B2	2B	0.0001	IRIS	1998	0.0007	IRIS	1998	Liver		

[1] Includes EPA reference concentrations (RfCs) and similar values, i.e., California OEHHA reference exposure levels (RELs), and ATSDR minimum risk levels (MRLs).
[2] EPA is currently developing a new dose-response assessment for this chemical. This situation will change as these assessments are completed and EPA begins assessments for other substances. A current status report for all EPA assessments is available at http://cfpub.epa.gov/iristrac/index.cfm.
[3] Proposed by California OEHHA; not yet adopted in final form.
[4] Maximum likelihood URE.
[5] 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.

US EPA ARCHIVE DOCUMENT

Chemical Name	CAS No.	EPA WOE	IARC WOE	URE $(\mu g/m^3)^{-1}$	URE Source	URE Date	RfC[1] (mg/m^3)	RfC Source	RfC Date	Target System 1	Target System 2	Target System 3
Chlorine	7782505						0.0002	CAL	2000	Respiratory		
2-Chloroacetophenone	532274						0.00003	IRIS	1991	Respiratory		
Chlorobenzene	108907						1	CAL	2000	Reproductive	Kidney	Liver
Chlorobenzilate	510156	B2		0.000078	HEAST	1997						
Chloroform[2]	67663	B2	2B				0.098	ATSDR	1998	Liver		
Chloroprene[2]	126998						0.007	HEAST	1997	Respiratory		
Chromium VI compounds		A	1	0.012	IRIS[4]	1998	0.0001	IRIS	1998	Respiratory		
Cobalt compounds[2]	7440484						0.0001	ATSDR	2001	Respiratory		
Coke Oven Emissions	8007452	A		0.00062	IRIS	1991						
Cresols (mixed)	1319773	C					0.6	CAL	2000	Neurological	Whole body	
Cumene	98828	D					0.4	IRIS	1997	Kidney	Endocrine	
Cyanide compounds[2]		D					0.003	IRIS	1994	Neurological	Thyroid	
1,2-Dibromo-3-chloropropane	96128	B2		0.002	CAL	1999	0.0002	IRIS	1991	Reproductive		
p-Dichlorobenzene[2]	106467	C	2B	0.000011	CAL	1999	0.8	IRIS	1994	Liver		
3,3'-Dichlorobenzidine	91941	B2	2B	0.00034	CAL	1999						
Dichloroethyl ether	111444	B2		0.00033	IRIS	1997						
1,3-Dichloropropene	542756	B2	2B	0.000004	IRIS	2000	0.02	IRIS	2000	Respiratory		
Dichlorvos	62737	B2	2B	0.000083	Conv. Oral[5]	2004	0.0005	IRIS	1994	Neurological		
Diesel emissions		B1					0.005	IRIS	2003	Respiratory		
Diethanolamine	111422						0.003	CAL	2001	Respiratory		
3,3'-Dimethoxy benzidine	119904	B2	2B	0.000004	Conv. Oral[5]	2004						
p-Dimethylamino azobenzene	60117		2B	0.0013	CAL	1999						
3,3'-Dimethylbenzidine	119937	B2		0.0026	Conv. Oral[5]	2004						
Dimethyl formamide	68122		2B				0.03	IRIS	1999	Liver		
2,4-Dinitrotoluene	121142	B2	2B	0.000089	CAL	1997	0.007	PCAL[3]	1997	Liver	Neurological	
1,4-Dioxane[2]	123911	B2	2B	0.000003	Conv. Oral[5]	2004	3	CAL	2000	Liver	Hematological	Kidney
1,2-Diphenylhydrazine	122667	B2		0.00022	IRIS	1991						
Epichlorohydrin	106898	B2	2A	0.000001	IRIS	1997	0.001	IRIS	1992	Respiratory		
1,2-Epoxybutane	106887						0.02	IRIS	1992	Respiratory		
Ethyl acrylate	140885	B2	2B	0.000014	Conv. Oral[5]	2004						

US EPA ARCHIVE DOCUMENT

Chemical Name	CAS No.	EPA WOE	IARC WOE	URE $(\mu g/m^3)^{-1}$	URE Source	URE Date	RfC[1] (mg/m^3)	RfC Source	RfC Date	Target System 1	Target System 2	Target System 3
Ethylbenzene[2]	100414	D					1	IRIS	1991	Developmental		
Ethyl carbamate	51796		2B	0.00029	CAL	1999						
Ethyl chloride	75003						10	IRIS	1991	Developmental		
Ethylene dibromide	106934	B2	2A	0.00022	IRIS	1997	0.0008	CAL	2001	Reproductive		
Ethylene dichloride[2]	107062	B2	2B	0.000026	IRIS	1997	2.4	ATSDR	2001	Liver		
Ethylene glycol	107211						0.4	CAL	2000	Respiratory		
Ethylene oxide[2]	75218	B1	1	0.000088	CAL	2004	0.03	CAL	2000	Neurological		
Ethylene thiourea	96457	B2	2B	0.000013	CAL	1999	0.003	PCAL[3]	1997	Endocrine		
Ethylidene dichloride	75343	C		0.000001	CAL	1999	0.5	HEAST	1992	Kidney		
Formaldehyde[2]	50000	B1	2A	5.5e-9	EPA OAQPS	2004	0.0098	ATSDR	1999	Respiratory		
Glycol ether compounds[2]							0.02	EPA OAQPS	2000	Reproductive		
Hexachlorobenzene	118741	B2	2B	0.00046	IRIS	1997	0.003	PCAL[3]	1997	Liver		
Hexachlorobutadiene[2]	87683	C	3	0.000022	IRIS	1997	0.09	PCAL[3]	1997	Reproductive		
Hexachlorocyclopentadiene[2]	77474	E					0.0002	IRIS	2001	Respiratory		
Hexachloroethane	67721	C	3	0.000004	IRIS	1997	0.08	PCAL[3]	1997	Kidney	Liver	Neurological
Hexamethylene-1,6-diisocyanate	822060						0.00001	IRIS	1994	Respiratory		
n-Hexane[2]	110543						0.2	IRIS	1991	Neurological	Respiratory	
Hydrazine	302012	B2	2B	0.0049	IRIS	1997	0.0002	CAL	2000	Liver	Thyroid	
Hydrochloric acid	7647010						0.02	IRIS	1995	Respiratory		
Hydrofluoric acid	7664393						0.03	CAL	1999	Skeletal		
Isophorone	78591	C		2.7e-7	Conv. Oral[5]	2004	2	CAL	2001	Liver	Developmental	
Lead[2]	7439921	B2	2B				0.0015	EPA OAQPS[6]	2003	Developmental		
Lindane (all isomers)			2B	0.00053	IRIS	1988	0.0003	PCAL[3]	1997	Kidney	Liver	Reproductive
Maleic anhydride	108316						0.0007	CAL	2001	Respiratory		
Manganese compounds		D					0.00005	IRIS	1993	Neurological		
Mercury compounds		C					0.00009	CAL	2000	Neurological		
Methanol[2]	67561						4	CAL	2000	Developmental		

[6] 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.

US EPA ARCHIVE DOCUMENT

Chemical Name	CAS No.	EPA WOE	IARC WOE	URE $(\mu g/m^3)^{-1}$	URE Source	URE Date	RfC[1] (mg/m^3)	RfC Source	RfC Date	Target System 1	Target System 2	Target System 3
Methyl bromide	74839	D					0.005	IRIS	1992	Respiratory		
Methyl chloride	74873	D					0.09	IRIS	2001	Neurological		
Methyl ethyl ketone	78933						5	IRIS	2003	Developmental		
Methyl isobutyl ketone	108101						3	IRIS	2003	Developmental		
Methyl isocyanate	624839						0.001	CAL	2001	Respiratory	Whole body	
Methyl methacrylate	80626	E					0.7	IRIS	1998	Respiratory		
Methyl tert-butyl ether[2]	1634044						3	IRIS	1993	Liver	Kidney	Ocular
4,4'-Methylene bis(2-chloroaniline)	101144	B2	2A	0.00043	CAL	1999						
Methylene chloride[2]	75092	B2	2B	4.7e-7	IRIS	1997	1	ATSDR	2000	Liver		
Methylene diphenyl diisocyanate	101688	D					0.0006	IRIS	1998	Respiratory		
4,4'-Methylenedianiline	101779		2B	0.00046	CAL	1999	0.02	CAL	2002	Ocular		
Naphthalene[2]	91203	C	2B	0.000034	CAL	2004	0.003	IRIS	1998	Respiratory		
Nickel compounds[2]		A	2B	0.00016	EPA OAQPS	2004	0.000065	CAL	2000	Respiratory	Immunological	
Nitrobenzene[2]	98953	D	2B				0.03	PCAL[3]	1997	Respiratory		
2-Nitropropane	79469	B2	2B	0.000005	EPA OAQPS	2003	0.02	IRIS	1991	Liver		
Nitrosodimethylamine	62759	B2	2A	0.014	IRIS	1997						
N-Nitrosomorpholine	59892		2B	0.0019	CAL	1999						
PCB Group	1336363	B2	2A	0.0001	IRIS	1999						
Pentachloronitrobenzene	82688	C	3	0.000074	Conv. Oral[5]	2004						
Pentachlorophenol[2]	87865	B2	2B	0.000005	CAL	1999	0.1	PCAL[3]	1997	Liver	Kidney	
Phenol	108952	D	3				0.2	CAL	2000	Liver		
Phosgene[2]	75445						0.0003	PCAL[3]	1997	Respiratory		
Phosphine	7803512	D					0.0003	IRIS	1995	Whole body		
Phthalic anhydride	85449						0.02	CAL	2000	Respiratory	Ocular	
Polycyclic organic matter[7] group 1[2]		[8]		0.000055	OAQPS	2004						
Polycyclic organic matter group 2[2]		[8]		0.000055	OAQPS	2004						

[7] A full discussion of the risk assessment for polycyclic organic matter is available at: http://www.epa.gov/ttn/atw/sab/appendix-h.pdf.
[8] EPA WOE varies among individual compounds.

US EPA ARCHIVE DOCUMENT

Chemical Name	CAS No.	EPA WOE	IARC WOE	URE ($\mu g/m^3)^{-1}$	URE Source	URE Date	RfC[1] (mg/m^3)	RfC Source	RfC Date	Target System 1	Target System 2	Target System 3
Polycyclic organic matter group 3[2]		[8]		0.1	OAQPS	2004						
Polycyclic organic matter group 4[2]		[8]		0.01	OAQPS	2004						
Polycyclic organic matter group 5[2]		[8]		0.001	OAQPS	2004						
Polycyclic organic matter group 6[2]		[8]		0.0001	OAQPS	2004						
Polycyclic organic matter group 7[2]		[8]		0.00001	OAQPS	2004						
Polycyclic organic matter group 8[2]		[8]		0.0002	OAQPS	2004						
1,3-Propane sultone	1120714		2B	0.00069	CAL	1999						
Propylene dichloride	78875	B2		0.000019	Conv. Oral[5]	2004	0.004	IRIS	1991	Respiratory		
Propylene oxide	75569	B2	2B	0.000003	IRIS	1997	0.03	IRIS	1992	Respiratory		
Quinoline	91225	B2		0.0034	Conv. Oral[5]	2004						
Selenium compounds		D					0.02	CAL	2001	Neurological	Liver	Hematological
Styrene[2]	100425		2B				1	IRIS	1992	Neurological		
Styrene oxide	96093		2A				0.006	PCAL[3]	1997	Respiratory		
1,1,2,2-Tetrachloroethane	79345	C	3	0.000058	IRIS	1997						
Perchloroethylene[2]	127184	B2C	2A	0.000005	CAL	1999	0.27	ATSDR	1999	Neurological		
Titanium tetrachloride	7550450					2001	0.0001	ATSDR	1999	Respiratory		
Toluene[2]	108883	D	3				0.4	IRIS	1995	Respiratory	Neurological	
2,4-Toluene diamine	95807	B2		0.0011	CAL	1999						
2,4-Toluene diisocyanate	26471625		2B	0.000011	CAL	1999	0.00007	IRIS	1995	Respiratory		
o-Toluidine	95534	B2	2B	0.000051	CAL	1999						
Toxaphene	8001352	B2	2B	0.00032	IRIS	1997						
1,2,4-Trichlorobenzene	120821	D					0.2	HEAST	1993	Liver		
1,1,2-Trichloroethane	79005	C	3	0.000016	IRIS	1997	0.4	PCAL[3]	1997	Liver		
1,1,1-Trichloroethane[2]	71556	D					1	CAL	2000	Neurological		
Trichloroethylene[2]	79016	B2C	2A	0.000002	CAL	1999	0.6	CAL	2000	Ocular		
2,4,6-Trichlorophenol	88062	B2		0.000003	IRIS	1997						
Triethylamine	121448						0.007	IRIS	1991	Respiratory		

US EPA ARCHIVE DOCUMENT

Chemical Name	CAS No.	EPA WOE	IARC WOE	URE ($\mu g/m^3)^{-1}$	URE Source	URE Date	RfC[1] (mg/m^3)	RfC Source	RfC Date	Target System 1	Target System 2	Target System 3
Trifluralin	1582098	C	3	0.000002	Conv. Oral[5]	2004						
Vinyl acetate[2]	108054		2B				0.2	IRIS	1990	Respiratory		
Vinyl bromide	593602	B2	2A	0.000032	HEAST	1997	0.003	IRIS	1993	Liver		
Vinyl chloride	75014	A	1	0.000008	IRIS[9]	2000	0.1	IRIS	2000	Liver		
Vinylidene chloride[2]	75354	C					0.2	IRIS	2002	Liver		
Xylenes (mixed)	1330207						0.1	IRIS	2003	Neurological		

[9] URE based on whole life exposure was selected over a URE based on adult exposure only.