MINIMAL RISK LEVELS (MRLs) FOR HAZARDOUS SUBSTANCES

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The Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) [42 U.S.C. 9604 et seq.], as amended by the Superfund Amendments and Reauthorization Act (SARA) [Pub. L. 99-499], requires that the Agency for Toxic Substances and Disease Registry (ATSDR) develop jointly with the U.S. Environmental Protection Agency (USEPA), in order of priority, a list of hazardous substances most commonly found at facilities on the CERCLA National Priorities List (NPL) (42 U.S.C. 9604(i)(2)); prepare toxicological profiles for each substance included on the priority list of hazardous substances, and ascertain in the toxicological profiles, significant human exposure levels (SHELs) for hazardous substances in the environment, and the associated acute, subacute, and chronic health effects (42 U.S.C. 9604(i)(3)); and assure the initiation of a research program to fill identified data needs associated with the substances (42 U.S.C. 9604(i)(5)). The ATSDR Minimal Risk Levels (MRLs) were developed as an initial response to the mandate and to provide screening levels for health assessors and other responders to identify contaminants and potential health effects that may be of concern at hazardous waste sites and releases. An MRL is an estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk of adverse noncancer health effects over a specified duration of exposure. In this paper, we describe ATSDR's current approach for deriving MRLs for priority hazardous substances. The MRLs for a particular substance are published in the toxicological profile for that substance. A listing of the current published MRLs as of December 1997 is also provided.

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2. Abbreviations: ATSDR, Agency for Toxic Substances and Disease Registry; CERCLA, The Comprehensive Environmental Response, Compensation, and Liability Act; DHHS, U.S. Department of Health and Human Services; ESADDIs, Estimated Safe and Adequate Daily Dietary Intakes; LOAEL, Lowest Observable Adverse Effect Level; MF, modifying factor; mg/m^3, milligrams per cubic meter; MRLs, minimal risk levels; NIEHS, National Institute of Environmental Health Sciences; NOAEL, No Observable Adverse Effects Level; NPL, National Priorities List; ppm, parts per million; RDAs, Recommended Daily Allowances; RfCs, reference concentrations; RfDs, reference doses; SARA, Superfund Amendments and Reauthorization Act; SHELs, significant human exposure levels; SGOT, serum aspartate aminotransferase; SGPT, serum alanine aminotransferase; UFs, uncertainty factors; USEPA, U.S. Environmental Protection Agency.

3. Key words: Health Guidance Values, non-cancer risk assessment.

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INTRODUCTION

The Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) requires that the Agency for Toxic Substances and Disease Registry (ATSDR) prepare toxicological profiles for priority hazardous substances, and ascertain significant human exposure levels for these substances in the environment, and the associated acute, subacute, and chronic health effects (42 U.S.C. 9604(i)(3)). Minimal Risk Levels (MRLs) were developed as an initial response to the mandate. Following discussions with scientists within the Department of Health and Human Service (DHHS) and the United States Environmental Proetection Agency (USEPA), ATSDR chose to adopt a practice similar to that of the USEPA's Reference Dose (RfD) and Reference Concentration (RfC) methodology for deriving substance-specific health guidance levels for non-neoplastic end points. An MRL is an estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk of adverse noncancer health effects over a specified duration of exposure. These substance-specific estimates, which are intended to serve as screening levels, are used by ATSDR health assessors and other responders to identify contaminants and potential health effects that may be of concern at hazardous waste sites and releases. The MRLs are not intended to define clean-up or action levels.

The toxicological profiles include an examination, summary, and interpretation of available toxicological information and epidemiologic evaluations of a hazardous substance. During the development of toxicological profiles, MRLs are derived when reliable and sufficient data are available to identify the target organ(s) of effect, or the most sensitive health effect(s) for acute (1–14 days), intermediate (15–364 days), and chronic (365 days and longer) exposure durations and for the oral and inhalation routes of exposure to the substance. MRLs are based on noncancer health effects only and are not based on a consideration of cancer effects.

MRLs are derived using the no-observed-adverse-effect level/uncertainty factor (NOAEL/UF) approach that ensures that they are below levels that might cause detectable adverse health effects in the people most sensitive to such effects. In the absence of a complete database, uncertainty factors are used to account for extrapolation from lowest-observed-adverse-effect levels (LOAELs) to NOAELs, for extrapolation from animals to humans, for intrahuman variability, and for extrapolation from subchronic to chronic exposure durations.

METHODS

The NOAEL/UF approach is used to derive MRLs for hazardous substances. MRLs are derived for acute (1–14 days), intermediate (15–364 days), and chronic (365 days and longer) exposure durations and for the oral and inhalation routes of exposure. MRLs are generally based on the most sensitive substance-induced end point considered to be of relevance to humans. Serious health effects (such as irreparable damage to the liver or kidneys, or birth defects) are not used as a basis for establishing MRLs. Inhalation MRLs are exposure concentrations expressed in units of parts per million (ppm) for gases and volatiles, or milligrams per cubic meter (mg/m^3) for particles. Oral MRLs are expressed as daily human doses in units of milligrams per kilogram per day (mg/kg/day). Currently, MRLs for the dermal route of exposure are not derived because methodology suitable for this route of exposure has not been devised.

Categories Used to Derive MRLs

The following health effect end points can be used to derive MRLs:

- Systemic
  - Respiratory
  - Cardiovascular
  - Gastrointestinal
  - Hematological
  - Musculoskeletal
  - Hepatic
  - Renal
  - Endocrine
  - Dermal
  - Ocular
  - Metabolic
  - Body weight change
  - Other systemic effects
- Immunological and Lymphoreticular
- Neurological
- Reproductive
- Developmental

To provide a better analysis of the toxic potential of the profiled substance, the same effect can be considered under more than one system category; for example, behavioral effects in the offspring can be either neurological or developmental. However, only one system category per exposure route and duration could be chosen as the basis for deriving the MRL. When two different effects within two different systems would result in the same MRL value, the MRL was derived from the one that is best supported by data from all exposure routes and durations.

Classification of End Points as NOAELs, Less Serious LOAELs or Serious LOAELs

MRLs are derived from NOAELs. In the absence of NOAELs, MRLs can be derived from less serious LOAELs. MRLs are not derived from serious LOAELs. The distinction between less serious and serious LOAEL is intended to help the users of the toxicological profiles see at what levels of exposure "major" effects begin to appear, and whether the less serious effects occur at approximately the same levels as serious effects or at substantially lower levels of exposure. In general, a dose that evokes failure in a biological system and can lead to morbidity or mortality (e.g., acute respiratory distress or death) is referred to as a serious LOAEL. In its 1986–1988 Biennial Report, Volume II, ATSDR defines an adverse health effect as a harmful or potentially harmful change in the physiologic function, psychologic state, or organ structure that may result in an observed deleterious health outcome. Adverse health effects may be manifested in pathophysiologic changes in target organs, psychologic effects, or overt disease. This definition is interpreted to indicate that any effect that enhances the susceptibility of an organism to the deleterious effects of other chemical, physical, microbiological, or environmental influences should be considered adverse.

A considerable amount of judgment is required in this process and in some cases, the data will be insufficient to decide whether an effect will lead to significant dysfunction. An MRL generally will not be derived if no adverse health effect has been reported in the published peer reviewed literature in any target organ (e.g., all free standing NOAELs) for a given duration. However, data from other durations and routes of exposure may lend support for selecting an appropriate end point to derive an MRL.

Deciding whether an end point is a NOAEL or a LOAEL depends in part upon the toxicity that occurs at other doses in the studies evaluated, and in part upon knowledge regarding the mechanism of toxicity of the substance. A more specific classification scheme is as follows.

No Adverse Effects

- ❑ Weight loss or decrease in body weight gain of less than 10%.
- ❑ Changes in organ weight of nontarget organ tissues not associated with abnormal morphologic or biochemical changes.
- ❑ Increased mortality over controls that is not statistically significant ($p > 0.05$).
- ❑ Some adaptive responses.

Less Serious Adverse Effects

- ❑ Reversible cellular alterations at the ultrastructural level (e.g., dilated endoplasmic reticulum) and at the light-microscopy level (e.g., cloudy swelling, fatty change).
- ❑ Necrosis (dependent upon location, distribution, reversibility, or the degree of associated dysfunction), metaplasia, or atrophy with no apparent decrement of organ function.
- ❑ Serum chemistry changes, e.g., moderate elevations of serum aspartate aminotransferase (SGOT), serum alanine aminotransferase (SGPT).
- ❑ Weight loss or decrease in body weight gain of 10–19%.
- ❑ Some adaptive responses.

Serious Effects

- ❑ Death
- ❑ Clinical effects of significant organ impairment (e.g., convulsions, icterus, cyanosis).

- ❑ Morphologic changes in organ tissues that potentially could result in severe dysfunction (e.g., marked necrosis of hepatocytes or renal tubules).
- ❑ Weight loss or decrease in body weight gain of 20% or greater.
- ❑ Serum chemistry changes (e.g., major elevations of SGOT, SGPT)
- ❑ Major metabolic effects (e.g., ketosis, acidosis, alkalosis).
- ❑ Cancer

Adequacy of the Database for Derivation of an MRL

It is difficult to provide strict rules governing this determination. Each profiled substance presents its own unique situation. The following key points should be considered:

- ❑ Good quality human data are generally preferred over animal data.
- ❑ Only one MRL is derived per exposure period (acute, intermediate, or chronic) for each route of exposure.
- ❑ The MRL is generally based on the highest NOAEL (that does not exceed a LOAEL) or the lowest LOAEL for the most sensitive end point for that route and exposure period.
- ❑ Although not a preferred end point for MRL derivation, decreased body weight gain can be used when the decrease is greater than 10% and when the study provides some indication that weight loss is due to a systemic effect of toxicant and not reduced food or water intake.
- ❑ It is preferable to derive MRLs using data for each exposure duration. However, when this is not possible because of limitations of the database for a given duration, an MRL derived for one duration may sometimes be applicable to MRL(s) for other duration(s) of the same route based on consideration of the overall database.

Selection of Most Sensitive Effect

The MRLs are based on the concept that a threshold level of exposure exists below which no noncancer health effect is likely to occur, and, therefore, an exposure level protective against the most sensitive effect would also be protective against all other effects. The most sensitive effect is the first adverse effect that occurs or that is expected to occur in humans as dose increases. However, information on the mechanisms of action should be considered when assessing the significance of the effects. Where the target organ of effect is not clearly identified, an MRL is usually not derived. However, the lack of quantitative data for a particular system category does not preclude derivation of an MRL if other evidence, such as information from human case studies, toxicokinetics, and other exposure routes, indicates that this system would be expected to be most sensitive to the substance for the exposure route and duration of concern.

Toxicokinetics data enter into consideration when comparing information across species, routes, and durations for determination of the most sensitive effect. Comparison of the metabolism of the compound exhibiting the toxic effect in animals with its metabolism in humans may affect the choice of the most sensitive end point. Toxicokinetic differences among species and for various chemical forms of the compound may help to explain an apparent inconsistency among studies. Differences across routes of exposure can also be explained by different rates of absorption, metabolism (both detoxication and activation), and excretion.

Selection of a Representative, Quality Study for MRL Derivation

Data from humans are preferred whenever such data are reliable and appropriate for MRL derivation. However, human studies must be of sufficient duration and contain an adequate number of documented exposed individuals to be useful in risk assessment. In the absence of adequate human studies, animal studies are used. The author(s) of the study must provide enough information on the oral dose or inhalation exposure concentration administered to the treated animals to allow for estimation of an equivalent human oral dose or inhalation exposure. For both oral and inhalation studies, the data presented in the study should at least include the air, water, or food concentration, the duration of exposure, the frequency of exposure (i.e., per day and per week), the age of the animals, and evidence that the food and water consumption rates were not abnormal (e.g., from weight gain data) for an animal of similar age. Other general principles that have been accepted in practice when evaluating studies include:

- ❑ Considerations to the exposure scenario more likely to occur in environmental exposures. For example, drinking water or feeding studies are preferred over gavage oil studies for oral exposures.

- ❑ Determination whether the study data show a dose-response consistent with other studies.

The following effects are not used for MRL derivation:

- ❑ Increased incidence of mortality.

- ❑ Serious LOAELs.

- ❑ Health effects that occur in test species as a result of mechanisms or metabolic processes that are not found in humans (e.g., 2μ-globulin nephropathy in male rats).

- ❑ Spontaneously occurring disorders that are species and gender related (e.g., chronic progressive nephropathy in male rats).

- ❑ Effects of unknown biological significance, based on mechanism of action, that do not affect known target organs.

- ❑ Cancer effects.

Computation of Inhalation MRLs

1. Extrapolating from animals to humans. When animal data are used in the absence of adequate quantitative human data, exposure concentrations should be converted to human equivalent concentrations by using dosimetry adjustment in accordance with USEPA (1990), "Interim Methods for Development of Inhalation Reference Concentrations" (USEPA/600/8-90/066A, August 1990). Standard reference values should be obtained from USEPA (1988): "Recommendations for and Documentation of Biological Values for Use in Risk Assessment" (USEPA 600-6-87/008, February 1988).

For inhalation exposures to gases or vapors, it may be necessary to convert to human equivalent exposures for respiratory effects (e.g., using the regional gas dose ratio for the targeted region of the respiratory tract) or extra-respiratory effects (e.g., using the blood to air partition coefficient ratio).

For inhalation exposure to particles, it may also be necessary to convert to human equivalent exposures for respiratory effects (e.g., using the regional deposited dose ratio for the targeted region of the respiratory tract), or extrarespiratory effects (e.g., using the regional deposited dose ratio and uptake from the entire respiratory system).

2. Adjusting from intermittent to continuous dosing. An MRL is defined as "an estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk of adverse noncancer health effects over a specified duration of exposure." The ideal study would involve continuous dosing over the course of the study. If a study did not involve continuous dosing over the entire exposure period, an adjustment is usually made. The "intermittent exposure dose" (either the NOAEL or LOAEL of the critical effect selected to be used for MRL derivation) is multiplied by correction factors to adjust for full day and week exposures. For example, in intermediate (longer than 14 days) or chronic (longer than 364 days) studies in which the experimental animals were dosed for 6 hours a day for 5 days a week, the estimated "adjusted dose" becomes:

$$\text{Adjusted dose} = \text{Intermittent dose} \times (6 \text{ hours}/24 \text{ hours}) \times (5 \text{ days}/7 \text{ days})$$

Intermediate and chronic duration inhalation studies are usually dose-adjusted for day and week exposures; acute duration inhalation studies can be duration adjusted from intermittent exposures to 24 hours continuous exposure, but are not adjusted to 1 week. For example, acute studies in which animals were exposed for 6 hours/day for 3 days can be adjusted as follows:

$$\text{Adjusted dose} = \text{Intermittent dose} \times (6 \text{ hours}/24 \text{ hours})$$

However, making duration adjustments may not be appropriate in every instance. The toxicokinetics and mechanism of action should be examined to the fullest extent possible before a determination is made to adjust for intermittent exposures. The following are other factors to consider in adjusting for dose and duration.

- When the critical effects are mainly dependent on the exposure concentrations and the substance being tested is rapidly metabolized or excreted, dose adjustment is inappropriate.

- If the effects being examined are mainly duration dependent (e.g., longer periods of exposure increase the severity of the effects being studied) and metabolism/excretion is moderate to slow, or the study identifies a cumulative effect, duration adjustment may be appropriate.

3. Converting from salt to parent substance. Salt concentrations or doses are converted to equivalent concentrations or doses of the parent substance by multiplying by the molecular weight ratio of parent to salt.

Computation of Oral MRLs

1. Converting from concentration to dose. For feeding studies, the equation for the conversion from food concentrations is:

(ppm in food) × (f/kg body weight) = mg/kg/day

The food consumption factor (f) is kg of food consumed per day. Unless the food consumption rate and body weights are available, standard reference values should be obtained from USEPA (1988).

For drinking water studies, the equation for the conversion from water concentrations is:

(ppm in water) × (C/kg body weight) = mg/kg/day

The water consumption rate (C) is liters of water consumed per day. Unless C and body weights are provided in the study, standard reference values should be obtained from USEPA (1988) or USEPA (1986), as appropriate.

2. Converting from intermittent to daily dosing. If the principal study did not involve daily dosing over the entire exposure period, an adjustment is usually made. The "intermittent dose" is multiplied by the fraction of the study days over which the test animals were actively dosed. Acute oral studies are not adjusted to 1 week; intermediate and chronic oral studies are usually dose-adjusted to full week exposures. For example, for animals orally dosed weekly 5 days a week, the estimated "continuous dose" becomes:

adjusted dose = intermittent dose × (5 days/7 days)

Uncertainty Factors and Modifying Factor

When sufficient human data are not available to allow an accurate assessment of noncancer health risks, ATSDR may extrapolate from available information using uncertainty factors (UFs) to account for different areas of uncertainty in the database to derive MRLs. In addition, a modifying factor (MF) may be applied to reflect additional scientific judgement on the database.

MRLs are derived from human equivalent no-observed-adverse-effect levels and are calculated as follows:

$$MRL = (NOAEL)_{HEC} / (UF \times MF)$$

When an appropriate NOAEL does not exist, the lowest LOAEL should be used and a UF is applied for the use of a LOAEL. Additional uncertainty factors for human variability to protect sensitive subpopulations, for interspecies extrapolation when animal studies are used for derivation of MRLs, and for extrapolation across exposure durations are also used.

The default value for each individual UF is 10; if complete certainty in data exists, a value of 1 can be used; and an intermediate value is 3. By multiplying these individual uncertainty factors, a combined UF is obtained. The use of UFs and MFs should be based on scientific judgement on a case-by-case basis. General guidelines are as follows:

Intrahuman Variation
A UF of 10 is generally used to account for intrahuman variation. However, a UF of 3 or 1 may be applied when a large epidemiologic study or a study of the sensitive population was used.

Interspecies Extrapolation
In the absence of adequate human data, animal data are used; a UF of 10 is generally used to account for extrapolation from animals to humans. However, a UF of 3 or 1 may also be used when comparative toxicological data indicate that similar effects are expected in humans at comparable exposure levels. For inhalation MRLs, when dosimetry adjustment is made for converting animal exposure levels to human equivalent concentrations, a UF of 3 is generally applied to account for any remaining uncertainty (Jarabek and Segal, 1994).

LOAEL to NOAEL Extrapolation
MRLs are derived from NOAELs. In the absence of a NOAEL, the lowest LOAEL that causes less serious adverse health effects is used, and a UF of 10 is generally applied. When the less serious LOAEL approaches the threshold level, that is, only minimal effects are observed representing an early indication of toxicity, the effect level is considered to be a "minimal LOAEL", and a UF of 3 may be used.

Extrapolation Across Durations
It is preferable to derive MRLs using data for each exposure duration. However, when the database supports extrapolation across acute, intermediate, or chronic exposure durations, a UF may be applied based on scientific judgement. For example, the chronic inhalation MRL for chlordane was derived from the intermediate inhalation MRL with an additional UF of 10 to account for across duration extrapolation; the chronic inhalation MRL was supported by the limited data on chronic exposure as well as the data on oral exposure.

Modifying Factor (MF)

An MF greater than zero and up to 10 may be applied to reflect additional concerns about the database not covered by the UFs. The default value for MF is 1. An example is the use of an MF of 3 to account for the incomplete database in deriving the chronic oral MRL for 4,4'-methylenebis(2-chloroaniline). Another possible consideration is that if a test substance is known to bioaccumulate, some studies may overestimate the dose needed to cause effects. In such cases, a modifying factor may be applied.

USEPA RfDs and ATSDR MRLs

The current approach for MRL derivation by ATSDR is similar to the methods used by USEPA to derive RfDs and RfCs for chronic exposures. Table 1 shows the difference in methodology used by ATSDR and USEPA in deriving MRLs and RfDs/RfCs, respectively.

TABLE 1. Comparison of Methodogy Used in Deriving ATSDR MRLS and USEPA RfDs/RfCs

	MRL	RfD/RfC
Exposure duration	Acute Intermediate Chronic	Chronic
Route of exposure	Oral, Inhalation	Oral, Inhalation
Uncertainty Factors (UFs) used:		
Human variability	Yes	Yes
Animals to humans extrapolation	Yes	Yes
Extrapolation from a LOAEL to a NOAEL	Yes	Yes
Extrapolation across exposure durations	Yes	Yes
Incomplete database	No	Yes
Across exposure route extrapolation	No	Yes
Modifying Factor (MF)	Yes	Yes

As with RfD methodology, in deriving MRLs, ATSDR uses UFs and MF to account for extrapolation from animals to humans and from LOAEL to NOAEL, for intrahuman variability, for across duration extrapolation, and for professional judgement on the database. In addition, USEPA uses a UF for an incomplete database (USEPA, 1990) whereas ATSDR incorporates scientific judgement, including an incomplete database in the MF. However, ATSDR does not extrapolate across route of exposure at this time. It is recognized that USEPA derives RfDs as part of its regulatory decision-making process. Extrapolation across route of exposure (most commonly using data from inhalation studies to estimate levels by the oral route) is sometimes used to develop an RfD where there is inadequate route-specific information.

Because MRLs may be based on more recent data and are derived using a slightly different methodology, or because MRLs are derived as a result of different scientific judgment, MRLs and RfDs (or RfCs) for the same substance are not necessarily of the same value.

MRLs for Essential Trace Elements

Since many nutritionally essential elements have been found to be common contaminants at some toxic waste sites, consideration was given to both essentiality and toxicity when deriving MRLs for these substances. Special reference was given to background levels and levels that have been published as Recommended Dietary Allowances (RDAs) or Estimated Safe and Adequate Daily Dietary Intakes (ESADDIs) by the Food and Nutrition Board of the National Research Council. MRLs should not be in conflict with the corresponding RDAs and should be protective for all age groups.

MRLs vs Ambient Levels

Since MRLs serve as screening tools for health assessors, it is important to compare MRLs with ambient levels reported in environmental monitoring studies. When MRLs are lower than ambient levels, the relevance of the MRLs is in question, and special consideration is warranted.

RESULTS AND DISCUSSION

The first toxicological profiles were published in 1989. The MRLs were derived using default methodology that employed standard UFs of 10 to account for extrapolations from a LOAEL to a NOAEL and from animal to human, and for intrahuman variability. In October 1992, the agency wide MRL Workgroup was formally chartered; observers from two other federal agencies, USEPA and the National Institute of Environmental Health Sciences (NIEHS) were also invited to attend the workgroup meetings. The MRL derivation methodology was expanded and revised to reflect current risk assessment approaches. In July 1994, ATSDR sponsored a peer review workshop, "Guidance for Derivation of MRLs." An expert panel of peer reviewers reviewed and commented on the updated methodology for MRL derivation. Evidence of the application of the revised guidance is reflected in MRLs for substances in the new and updated toxicological profiles published since 1993.

In addition to the standard default UFs of 10, 3 or 1 may also be used on a case-by-case basis when the database supports it. For example, a UF of 3 is applied for the use of a minimal LOAEL; a UF of 3 is applied for animal to human extrapolation when using human equivalent concentrations converted from animal inhalation exposure concentrations. Extrapolation across exposure durations is also allowed with the use of a UF. MFs may also be used to account for any remaining uncertainties in the database. Table 2 contains a listing of the current published MRLs as of December 1997 and the associated information such as route and duration of exposure, total UF and MF applied and the health effect end point used for derivation of the MRL. As the MRLs are published in the substance-specific toxicological profiles, the status of the toxicological profile, draft or final, and the toxicological profile publication cover date are also included. A total of 273 MRLs for 134 substances have been derived. Analysis of the health end points among the listed MRLs showed that hepatic effects and neurological effects were most frequently used as the basis for MRLs, followed by developmental effects and respiratory effects. Because MRLs are derived from NOAELs and less serious LOAELs, but not serious LOAELs, interpretation and catagorization of health effects is very important. Individual helath effects end-point assessments and their application in deriving MRLs will be presented elsewhere.

TABLE 2. ATSDR Minimal Risk Levels (MRLs)

Name	Route	Duration	MRL	Factors	Endpoint	Draft / Final	Cover Date	CAS Number
ACENAPHTHENE	Oral	Int.	0.6 mg/kg/day	300	Hepatic	Final	08/95	000083-32-9
ACETONE	Inh.	Acute	26 ppm	9	Neurol.	Final	05/94	000067-64-1
		Int.	13 ppm	100	Neurol.			
		Chr.	13 ppm	100	Neurol.			
	Oral	Int.	2 mg/kg/day	100	Hemato.			
ACROLEIN	Inh.	Acute	0.00005 ppm	100	Ocular	Final	12/90	000107-02-8
		Int.	0.000009 ppm	1000	Resp.			
	Oral	Chr.	0.0005 mg/kg/day	100	Hemato.			
ACRYLONITRILE	Inh.	Acute	0.1 ppm	10	Neurol.	Final	12/90	000107-13-1
	Oral	Acute	0.1 mg/kg/day	100	Develop.			
		Int.	0.01 mg/kg/day	1000	Repro.			
		Chr.	0.04 mg/kg/day	100	Hemato.			
ALDRIN	Oral	Acute	0.002 mg/kg/day	1000	Develop.	Final	04/93	000309-00-2
		Chr.	0.00003 mg/kg/day	1000	Hepatic			
AMMONIA	Inh.	Acute	0.5 ppm	100	Resp.	Final	12/90	007664-41-7
		Chr.	0.3 ppm	10	Resp.			
	Oral	Int.	0.3 mg/kg/day	100	Other			
ANTHRACENE	Oral	Int.	10 mg/kg/day	100	Hepatic	Final	08/95	000120-12-7
AROCLOR 1254	Oral	Chr.	0.02 mg/kg/day	300	Imuno.	Final	09/97	011097-69-1
ARSENIC	Oral	Chr.	0.0003 mg/kg/day	3	Dermal	Final	04/93	007440-38-2
BENZENE	Inh.	Acute	0.05 ppm	300	Imuno	Final	09/97	000071-43-2
		Int.	0.004 ppm	90	Neurol.			
BIS(CHLOROMETHYL) ETHER	Inh.	Int.	0.0003 ppm	100	Resp.	Final	12/89	000542-88-1
BIS(2-CHLOROMETHYL) ETHER	Inh.	Int.	0.02 ppm	1000	Body Wt.	Final	12/89	000111-44-4
BORON	Oral	Int.	0.01 mg/kg/day	1000	Develop.	Final	07/92	007440-42-8
BROMODICHLOROMETHANE	Oral	Acute	0.04 mg/kg/day	1000	Hepatic	Final	12/89	000072-27-4
		Chr.	0.02 mg/kg/day	1000	Renal			

TABLE 2. ATSDR Minimal Risk Levels (MRLs) (cont'd)

Name	Route	Duration	MRL	Factors	Endpoint	Draft / Final	Cover Date	CAS Number
BROMOFORM	Oral	Acute	0.6 mg/kg/day	100	Neurol.	Final	12/90	000075-25-2
		Chr.	0.2 mg/kg/day	100	Hepatic			
BROMOMETHANE	Inh.	Acute	0.05 ppm	100	Neurol.	Final	09/92	000074-83-9
		Int.	0.05 ppm	100	Neurol.			
		Chr.	0.005 ppm	100	Neurol.			
	Oral	Int.	0.003 mg/kg/day	100	Gastro.			
CADMIUM	Oral	Chr.	0.0002 mg/kg/day	10	Renal	Draft	09/97	007440-43-9
CARBON DISULFIDE	Inh.	Chr.	0.3 ppm	30	Neurol.	Final	08/96	000075-15-0
	Oral	Acute	0.01 mg/kg/day	300	Hepatic			
CARBON TETRACHLORIDE	Inh.	Acute	0.2 ppm	300	Hepatic	Final	05/94	000056-23-5
		Int.	0.05 ppm	100	Hepatic			
	Oral	Acute	0.02 mg/kg/day	300	Hepatic			
		Int.	0.007 mg/kg/day	100	Hepatic			
CHLORDANE	Inh.	Int.	0.002 mg/m^3	100	Hepatic	Final	05/94	000057-74-9
		Chr.	0.00002 mg/m^3	1000	Hepatic			
	Oral	Acute	0.001 mg/kg/day	1000	Develop.			
		Int.	0.0006 mg/kg/day	100	Hepatic			
		Chr.	0.0006 mg/kg/day	100	Hepatic			
CHLORDECONE	Oral	Acute	0.01 mg/kg/day	100	Neurol.	Final	08/95	000143-50-0
		Int.	0.0005 mg/kg/day	100	Renal			
		Chr.	0.0005 mg/kg/day	100	Renal			
CHLORFENVINPHOS	Oral	Acute	0.002 mg/kg/day	1000	Neurol.	Final	09/97	000470-90-6
		Int.	0.002 mg/kg/day	1000	Immuno.			
		Chr.	0.0007 mg/kg/day	1000	Neurol.			
CHLOROBENZENE	Oral	Int.	0.4 mg/kg/day	100	Hepatic	Final	12/90	000108-90-7
CHLORODIBROMOMETHANE	Oral	Acute	0.04 mg/kg/day	1000	Renal	Final	12/90	000124-48-1
		Chr.	0.03 mg/kg/day	1000	Hepatic			

TABLE 2. ATSDR Minimal Risk Levels (MRLs) (cont'd)

Name	Route	Duration	MRL	Factors	Endpoint	Draft / Final	Cover Date	CAS Number
CHLOROETHANE	Inh.	Acute	15 ppm	100	Develop.	Draft	09/97	000075-00-3
CHLOROFORM	Inh.	Acute	0.1 ppm	30	Hepatic	Final	09/97	000067-66-3
		Int.	0.05 ppm	100	Hepatic			
		Chr.	0.02 ppm	100	Hepatic			
	Oral	Acute	0.3 mg/kg/day	100	Hepatic			
		Int.	0.1 mg/kg/day	100	Hepatic			
		Chr.	0.01 mg/kg/day	1000	Hepatic			
CHLOROMETHANE	Inh.	Acute	0.5 ppm	100	Neurol.	Draft	09/97	000074-87-3
		Int.	0.2 ppm	300	Hepatic			
		Chr.	0.05 ppm	1000	Neurol.			
CHLORPYRIFOS	Oral	Acute	0.003 mg/kg/day	10	Neurol.	Final	09/97	002921-88-2
		Int.	0.003 mg/kg/day	10	Neurol.			
		Chr.	0.001 mg/kg/day	100	Neurol.			
CHROMIUM, HEXAVALENT	Inh.	Int.	0.00002 mg/m^3	10	Resp.	Final	04/93	018540-29-9
		Chr.	0.00002 mg/m^3	10	Resp.			
COBALT	Inh.	Int.	0.00003 mg/m^3	1000	Resp.	Final	07/92	007440-48-4
CRESOL, META-	Oral	Acute	0.05 mg/kg/day	100	Resp.	Final	07/92	000108-39-4
CRESOL, ORTHO-	Oral	Acute	0.05 mg/kg/day	100	Neurol.	Final	07/92	000095-48-7
CRESOL, PARA-	Oral	Acute	0.05 mg/kg/day	100	Neurol.	Final	07/92	000106-44-5
CYANIDE, SODIUM	Oral	Int.	0.05 mg/kg/day	100	Repro.	Final	09/97	000143-33-9
CYCLOTETRAMETHYLENE TETRANITRAMINE (HMX)	Oral	Acute	0.06 mg/kg/day	100	Neurol.	Final	09/97	002691-41-0
		Int.	0.03 mg/kg/day	300	Hepatic			
CYCLOTRIMETHYLENETRINITRAMINE (RDX)	Oral	Acute	0.06 mg/kg/day	100	Neurol.	Final	06/95	000121-82-4
		Int.	0.03 mg/kg/day	300	Repro.			
DDT, P, P'-	Oral	Acute	0.0005 mg/kg/day	1000	Develop.	Final	05/94	000050-29-3
		Int.	0.0005 mg/kg/day	100	Hepatic			
DI (2-ETHYLHEXYL) PHTHALATE	Oral	Acute	1 mg/kg/day	100	Repro.	Final	04/93	000117-81-7
		Int.	0.4 mg/kg/day	100	Develop.			
DI-N-BUTYL PHTHALATE	Oral	Int.	0.6 mg/kg/day	100	Develop.	Final	12/90	000084-74-2

TABLE 2. ATSDR Minimal Risk Levels (MRLs) (cont'd)

Name	Route	Duration	MRL	Factors	Endpoint	Draft / Final	Cover Date	CAS Number
DI-N-OCTYL PHTHALATE	Oral	Acute	3 mg/kg/day	300	Hepatic	Final	09/97	000117-84-0
		Int.	0.4 mg/kg/day	100	Hepatic			
DIAZINON	Inh.	Int.	0.009 mg/m^3	30	Neurol.	Final	08/96	000333-41-5
	Oral	Int.	0.0002 mg/kg/day	100	Neurol.			
DICHLORVOS	Inh.	Acute	0.002 ppm	100	Neurol.	Final	09/97	000062-73-7
		Int.	0.0003	100	Neurol.			
		Chr.	0.00006 ppm	100	Neurol.			
	Oral	Acute	0.004 mg/kg/day	1000	Neurol.			
		Int.	0.003 mg/kg/day	10	Neurol.			
		Chr.	0.0005 mg/kg/day	100	Neurol.			
DIELDRIN	Oral	Acute	0.00007 mg/kg/day	1000	Immuno.	Final	04/93	000060-57-1
DIETHYL PHTHALATE	Oral	Acute	7 mg/kg/day	300	Repro.	Final	06/95	000084-66-2
		Int.	6 mg/kg/day	300	Hepatic			
DIISOPROPHYL METHYL PHOSPHONATE	Oral	Int.	0.8 mg/kg/day	100	Hemato.	Draft	08/96	001445-75-6
DISULFOTON	Inh.	Acute	0.006 mg/m^3	30	Neurol.	Final	08/95	000298-04-4
		Int.	0.0002 mg/m^3	30	Neurol.			
	Oral	Acute	0.001 mg/kg/day	100	Neurol.			
		Int.	0.00009 mg/kg/day	100	Develop.			
		Chr.	0.00006 mg/kg/day	1000	Neurol.			
ENDOSULFAN	Oral	Int.	0.002 mg/kg/day	100	Immuno.	Final	04/93	000115-29-7
		Chr.	0.002 mg/kg/day	100	Hepatic			
ENDRIN	Oral	Int.	0.002 mg/kg/day	100	Neurol.	Final	08/96	000072-20-8
		Chr.	0.0003 mg/kg/day	100	Neurol.			
ETHYLBENZENE	Inh.	Int.	0.2 ppm	100	Develop.	Draft	09/97	000100-41-4
ETHYLENE GLYCOL	Inh.	Acute	0.5 ppm	100	Renal	Final	09/97	000107-21-1
	Oral	Acute	2.0 mg/kg/day	100	Develop.			
		Chr.	2.0 mg/kg/day	100	Renal			

TABLE 2. ATSDR Minimal Risk Levels (MRLs) (cont'd)

Name	Route	Duration	MRL	Factors	Endpoint	Draft / Final	Cover Date	CAS Number
ETHYLENE OXIDE	Inh.	Int.	0.09 ppm	100	Renal	Final	12/90	000075-21-8
FLUORANTHENE	Oral	Int.	0.4 mg/kg/day	300	Hepatic	Final	08/95	000206-44-0
FLUORENE	Oral	Int.	0.4 mg/kg/day	300	Hepatic	Final	08/95	000086-73-7
FLUORIDE, SODIUM	Oral	Chr.	0.05 mg/kg/day	10	Musculo.	Final	04/93	007681-49-4
FORMALDEHYDE	Inh.	Acute	0.05 ppm	9	Resp.	Draft	09/97	000050-00-0
		Int.	0.01 ppm	100	Resp.			
		Chr.	0.003 ppm	30	Resp.			
	Oral	Int.	0.3 mg/kg/day	100	Gastro.			
		Chr.	0.2 mg/kg/day	100	Gastro.			
FUEL OIL NO. 2	Inh.	Acute	0.02 mg/m^3	1000	Neurol.	Final	06/95	068476-30-2
HEXACHLOROBENZENE	Oral	Acute	0.008 mg/kg/day	300	Develop.	Final	08/96	000118-74-1
		Int.	0.0003 mg/kg/day	300	Repro.			
		Chr.	0.00002 mg/kg/day	1000	Develop.			
HEXACHLOROBUTADIENE	Oral	Int.	0.0002 mg/kg/day	1000	Renal	Final	05/94	000087-68-3
HEXACHLOROCYCLOHEXANE, ALPHA-	Oral	Int.	0.01 mg/kg/day	100	Hepatic	Draft	09/97	000319-84-6
HEXACHLOROCYCLOHEXANE, BETA-	Oral	Acute	0.2 mg/kg/day	100	Neurol.	Draft	09/97	000319-85-7
		Int.	0.0006 mg/kg/day	300	Hepatic			
HEXACHLOROCYCLOPENTADIENE	Inh.	Int.	0.0001 ppm	100	Resp.	Draft	09/97	000077-47-4
		Chr.	0.00003 ppm	300	Resp.			
	Oral	Int.	0.1 mg/kg/day	100	Renal			
HEXACHLOROCYCLOHEXANE, GAMMA-	Oral	Acute	0.01 mg/kg/day	100	Neurol.	Draft	09/97	000058-89-9
		Int.	0.00001 mg/kg/day	1000	Immuno.			
HEXACHLOROETHANE	Inh.	Acute	6 ppm	30	Neurol.	Final	09/97	000067-72-1
		Int.	6 ppm	30	Neurol.			
	Oral	Acute	1 mg/kg/day	100	Hepatic			
		Int.	0.01 mg/kg/day	100	Hepatic			

TABLE 2. ATSDR Minimal Risk Levels (MRLs) (cont'd)

Name	Route	Duration	MRL	Factors	Endpoint	Draft / Final	Cover Date	CAS Number
HEXAMETHYLENE DIISOCYANATE	Inh.	Int.	0.00003 ppm	30	Resp.	Draft	08/96	000067-72-1
		Chr.	0.00001 ppm	90	Resp.			
HEXANE, N-	Inh.	Chr.	0.6 ppm	100	Neurol.	Draft	09/97	000110-54-3
HYDRAZINE	Inh.	Int.	0.004 ppm	300	Hepatic	Final	09/97	000302-01-2
HYDROGEN SULFIDE	Inh.	Acute	0.5 ppm	10	Resp.	Draft	09/97	007783-06-4
		Int.	0.09 ppm	100	Resp.			
ISOPHORONE	Oral	Int.	3 mg/kg/day	100	Other	Final	12/89	000078-59-1
		Chr.	0.2 mg/kg/day	1000	Hepatic			
JP-4	Inh.	Int.	9 mg/m^3	300	Hepatic	Final	06/95	050815-00-4
JP-5/JP-8/FUEL	Inh.	Int.	3 mg/m^3	300	Hepatic	Draft	08/96	HZ0600-26-T
JP-7	Inh.	Chr.	0.3 ,g/m^3	300	Hepatic	Final	06/95	HZ0600-22-T
KEROSENE	Inh.	Int.	0.01 mg/m^3	1000	Hepatic	Final	06/95	008008-20-6
MANGANESE	Inh.	Chr.	0.00004 mg/m^3	900	Neurol.	Draft	09/97	007439-96-5
MERCURIC CHLORIDE	Oral	Acute	0.007 mg/kg/day	100	Renal	Draft	09/97	007487-94-7
		Int.	0.002 mg/kg/day	100	Renal			
MERCURY	Inh.	Chr.	0.0002 mg/m^3	30	Neurol.	Draft	09/97	007439-97-6
METHOXYCHLOR	Oral	Acute	0.02 mg/kg/day	1000	Repro.	Final	05/94	000072-43-5
		Int.	0.02 mg/kg/day	1000	Repro.			
METHYL PARATHION	Oral	Chr.	0.0003 mg/kg/day	100	Neurol.	Final	09/92	000298-00-0
METHYL T-BUTYL ETHER	Inh.	Acute	2 ppm	100	Neurol.	Final	08/96	001634-04-4
		Int.	0.7 ppm	100	Neurol.			
		Chr.	0.7 ppm	100	Renal			
	Oral	Acute	0.4 mg/kg/day	100	Neurol.			
		Int.	0.3 mg/kg/day	300	Hepatic			
METHYLENE CHLORIDE	Inh.	Acute	0.4 ppm	100	Neurol.	Final	04/93	000075-09-2
		Int.	0.03 ppm	1000	Hepatic			
	Oral	Chr.	0.06 mg/kg/day	100	Hepatic			

TABLE 2. ATSDR Minimal Risk Levels (MRLs) (cont'd)

Name	Route	Duration	MRL	Factors	Endpoint	Draft / Final	Cover Date	CAS Number
METHYLMERCURY	Oral	Chr.	0.5 µg/kg/day	1	Develop.	Draft	09/97	022967-92-6
MIREX	Oral	Chr.	0.0008 mg/kg/day	100	Hepatic	Final	08/95	002385-85-5
N-NITROSODI-N-PROPYLAMINE	Oral	Acute	0.095 mg/kg/day	100	Hepatic	Final	12/89	000621-64-7
NAPHTHALENE	Inh.	Chr.	0.002 ppm	1000	Resp.	Final	08/95	000091-20-3
	Oral	Acute	0.05 mg/kg/day	1000	Neurol.			
		Int.	0.02 mg/kg/day	300	Hepatic			
NICKEL	Inh.	Chr.	0.0002 mg/m^3	30	Resp.	Final	09/97	007440-02-0
PENTACHLOROPHENOL	Oral	Acute	0.005 mg/kg/day	1000	Develop.	Final	05/94	000087-86-5
		Int.	0.001 mg/kg/day	1000	Hepatic			
PHENOL	Oral	Int.	0.0003 mg/kg/day	10	Gastro.	Draft	09/97	000108-95-2
PHOSPHORUS, WHITE	Inh.	Acute	0.02 mg/m^3	30	Resp.	Final	09/97	007723-14-0
	Oral	Int.	0.0002 mg/kg/day	100	Repro.			
POLYBROMINATED BIPHENYLS	Oral	Acute	0.01 mg/kg/day	100	Endocr.	Final	08/95	067774-32-7
PROPYLENE GLYCOL DINITRATE	Inh.	Acute	0.003 ppm	10	Neurol.	Final	06/95	006423-43-4
		Int.	0.00004 ppm	1000	Hemato.			
		Chr.	0.00004 ppm	1000	Hemato.			
PROPYLENE GLYCOL	Inh.	Int.	0.009 ppm	1000	Resp.	Final	09/97	000057-55-6
SELENIUM	Oral	Chr.	0.005 mg/kg/day	3	Dermal	Final	08/96	007782-49-2
STYRENE	Inh.	Chr.	0.06 ppm	100	Neurol.	Final	09/92	000100-42-5
	Oral	Int.	0.2 mg/kg/day	1000	Hepatic			
SULFUR DIOXIDE	Inh.	Acute	0.01 ppm	9	Resp.	Draft	09/97	007446-09-5
TETRACHLOROETHYLENE	Inh.	Acute	0.2 ppm	10	Neurol.	Final	09/97	000127-18-4
		Chr.	0.04 ppm	100	Neurol.			
	Oral	Acute	0.05 mg/kg/day	100	Develop.			
TITANIUM TETRACHLORIDE	Inh.	Int.	0.01 mg/m^3	90	Resp.	Final	09/97	007550-45-0
		Chr.	0.0001 mg/m^3	90	Resp.			

TABLE 2. ATSDR Minimal Risk Levels (MRLs) (cont'd)

Name	Route	Duration	MRL	Factors	Endpoint	Draft / Final	Cover Date	CAS Number
TOLUENE	Inh.	Acute	3 ppm	30	Neurol.	Final	05/94	000108-88-3
		Chr.	1 ppm	30	Neurol.			
	Oral	Acute	0.8 mg/kg/day	300	Neurol.			
		Int.	0.02 mg/kg/day	300	Neurol.			
TOXAPHENE	Oral	Acute	0.005 mg/kg/day	1000	Hepatic	Final	08/96	008001-35-2
		Int.	0.001 mg/kg/day	300	Hepatic			
TRICHLOROETHYLENE	Inh.	Acute	2 ppm	30	Neurol.	Final	09/97	000079-01-6
		Int.	0.1 ppm	300	Neurol.			
	Oral	Acute	0.2 mg/kg/day	300	Develop.			
URANIUM	Inh.	Chr.	0.001 mg/m^3	30	Renal	Draft	09/97	007440-61-1
	Oral	Int.	0.001 mg/kg/day	900	Renal			
VANDIUM	Inh.	Acute	0.0002 mg/m^3	100	Resp.	Final	07/92	007440-62-2
	Oral	Int.	0.003 mg/kg/day	100	Renal			
VINYL ACETATE	Inh.	Int.	0.01 ppm	100	Resp.	Final	07/92	000108-05-4
VINYL CHLORIDE	Inh.	Acute	0.5 ppm	100	Develop.	Final	09/97	000075-01-4
		Int.	0.03 ppm	300	Hepatic			
	Oral	Chr.	0.00002 mg/kg/day	1000	Hepatic			
XYLENE, M-	Oral	Int.	0.6 mg/kg/day	1000	Hepatic	Final	08/95	000108-38-3
XYLENE, P-	Oral	Acute	1 mg/kg/day	100	Neurol.	Final	08/95	000106-42-3
XYLENES, TOTAL	Inh.	Acute	1 ppm	100	Neurol.	Final	08/95	001330-20-7
		Int.	0.7 ppm	300	Develop.			
		Chr.	0.1 ppm	100	Neurol.			
	Oral	Int.	0.2 mg/kg/day	1000	Renal			
ZINC	Oral	Int.	0.3 mg/kg/day	3	Hemato.	Final	05/94	007440-66-6
		Chr.	0.3 mg/kg/day	3	Hemato.			
1-METHYLNAPHTHALENE	Oral	Chr.	0.07 mg/kg/day	1000	Resp.	Final	08/95	000090-12-0

TABLE 2. ATSDR Minimal Risk Levels (MRLs) (cont'd)

Name	Route	Duration	MRL	Factors	Endpoint	Draft / Final	Cover Date	CAS Number
1,1-DICHLOROETHENE	Inh.	Int.	0.02 ppm	100	Hepatic	Final	05/94	000075-35-4
	Oral	Chr.	0.009 mg/kg/day	1000	Hepatic			
1,1-DIMETHYLHYDRAZINE	Inh.	Int.	0.0002 ppm	300	Hepatic	Final	09/97	000057-14-7
1,1,1-TRICHLOROETHANE	Inh.	Acute	2 ppm	100	Neurol.	Final	08/95	000071-55-6
		Int.	0.7 ppm	100	Neurol.			
1,1,2-TRICHLOROETHANE	Oral	Acute	0.3 mg/kg/day	100	Neurol.	Final	12/89	000079-00-5
		Int.	0.04 mg/kg/day	100	Hepatic			
1,1,2,2-TETRACHLOROETHANE	Inh.	Int.	0.4 ppm	300	Hepatic	Final	08/96	000079-34-5
	Oral	Int.	0.6 mg/kg/day	100	Body Wt.			
		Chr.	0.04 mg/kg/day	1000	Resp.			
1,2-DIBROMO-3-CHLOROPROPANE	Inh.	Int.	0.0002 ppm	100	Repro.	Final	09/92	000096-12-8
	Oral	Int.	0.002 mg/kg/day	1000	Repro.			
1,2-DICHLOROETHENE, CIS-	Oral	Acute	1 mg/kg/day	100	Hemato.	Final	08/96	000156-59-2
		Int.	0.3 mg/kg/day	100	Hemato.			
1,2-DICHLOROETHANE	Inh.	Acute	0.2 ppm	10	Immuno.	Final	05/94	000107-06-2
		Chr.	0.2 ppm	300	Hepatic			
	Oral	Int.	0.2 mg/kg/day	300	Renal			
1,2-DICHLOROPROPANE	Inh.	Acute	0.05 ppm	1000	Resp.	Final	12/89	000078-87-5
		Int.	0.007 ppm	1000	Resp.			
	Oral	Acute	0.1 mg/kg/day	1000	Neurol.			
		Int.	0.07 mg/kg/day	1000	Hemato.			
		Chr.	0.09 mg/kg/day	1000	Hepatic			
1,2-DICHLOROETHENE, TRANS-	Inh.	Acute	0.2 ppm	1000	Hepatic	Final	08/96	000156-60-5
		Int.	0.2 ppm	1000	Hepatic			
	Oral	Int.	0.2 mg/kg/day	100	Hepatic			
1,2-DIMETHYLHYDRAZINE	Oral	Int.	0.0008 mg/kg/day	1000	Hepatic	Final	09/97	000540-73-8

TABLE 2. ATSDR Minimal Risk Levels (MRLs) (cont'd)

Name	Route	Duration	MRL	Factors	Endpoint	Draft / Final	Cover Date	CAS Number
1,2,3-TRICHLOROPROPANE	Inh.	Acute	0.0003 ppm	100	Resp.	Final	09/92	000096-18-4
	Oral	Int.	0.06 mg/kg/day	100	Hepatic			
1,3-DICHLOROPROPENE	Inh.	Int.	0.003 ppm	100	Resp.	Final	09/92	000542-75-6
		Chr.	0.002 ppm	100	Resp.			
1,3-DINITROBENZENE	Oral	Acute	0.008 mg/kg/day	100	Repro.	Final	06/95	000099-65-0
		Int.	0.0005 mg/kg/day	1000	Hemato.			
1,4-DICHLOROBENZENE	Inh.	Acute	0.8 ppm	100	Develop.	Draft	09/97	000106-46-7
		Int.	0.2 ppm	100	Hepatic			
		Chr.	0.1 ppm	100	Hepatic			
	Oral	Int.	0.1 mg/kg/day	100	Hepatic			
2-BUTOXYETHANOL	Inh.	Acute	7 ppm	30	Hemato.	Draft	08/96	000111-76-2
		Int.	3 ppm	30	Hemato.			
	Oral	Acute	0.4 mg/kg/day	90	Hemato.			
		Int.	0.07 mg/kg/day	1000	Hepatic			
2,3,4,7,8-PENTACHLORODIBENZOFURAN	Oral	Acute	0.000001 mg/kg/day	3000	Immuno.	Final	05/94	057117-31-4
		Int.	0.0000003 mg/kg/d	3000	Hepatic			
2,3,7,8-TETRACHLORODIBENZO-P-DIOXIN	Oral	Acute	0.0002 µg/kg/day	21	Immuno.	Draft	09/97	001746-01-6
		Int.	0.00002 µg/kg/day	30	Lympho.			
		Chr.	0.000001 µg/kg/day	90	Develop.			
2,4-DICHLOROPHENOL	Oral	Int.	0.003 mg/kg/day	100	Immuno.	Draft	09/97	000120-83-2
2,4-DINITROPHENOL	Oral	Acute	0.01 mg/kg/day	100	Bdy. Wt.	Final	08/95	000051-28-5
2,4-DINITROTOLUENE	Oral	Acute	0.05 mg/kg/day	100	Neurol.	Draft	09/97	000121-14-2
		Chr.	0.002 mg/kg/day	100	Hemato.			
2,4,6-TRINITROTOLUENE	Oral	Int.	0.0005 mg/kg/day	1000	Hepatic	Final	06/95	000118-96-7
2,6-DINITROTOLUENE	Oral	Int.	0.004 mg/kg/day	1000	Hemato.	Draft	09/97	000606-20-2
4-CHLOROPHENOL	Oral	Acute	0.01 mg/kg/.day	100	Hepatic	Draft	09/97	000106-48-9
4,4'-METHYLENEBIS (2-CHLOROANILINE)	Oral	Chr.	0.003 mg/kg/day	3000	Hepatic	Final	05/94	000101-14-4

TABLE 2. ATSDR Minimal Risk Levels (MRLs) (cont'd)

Name	Route	Duration	MRL	Factors	Endpoint	Draft / Final	Cover Date	CAS Number
4,4'-METHYLENEDIANILINE	Oral	Acute	0.2 mg/kg/day	300	Hepatic	Draft	08/96	000101-77-9
		Int.	0.08 mg/kg/day	100	Hepatic			
4,6-DINITRO-O-CRESOL	Oral	Acute	0.004 mg/kg/day	100	Neurol.	Final	08/95	000534-52-1
		Int.	0.004 mg/kg/day	100	Neurol.			
		Total Number of MRLs:		273				

Proposed MRLs undergo a rigorous review process. They are reviewed by the Health Effects/ MRL Workgroup within the Division of Toxicology; an expert panel of external peer reviewers; and the agency-wide MRL Workgroup, with participation from other federal agencies, including USEPA; The MRLs are also submitted for public comment through the toxicological profile public comment period. Each MRL is subject to change as new information becomes available concomitant with updating the toxicological profile for the substance.

MRLs are intended to serve as a screening tool to help public health professionals decide where to look more closely. They may also be viewed as a mechanism to identify those hazardous waste sites or other hazardous substance exposures that are not expected to cause adverse health effects. The MRLs are set below levels that, based on current information, might cause adverse health effects in the people most sensitive to such substance-induced effects (Barnes and Dourson, 1988; USEPA, 1990). Most MRLs contain some degree of uncertainty because of the lack of precise toxicological information on the people who might be most sensitive (e.g., infants, elderly, and nutritionally or immunologically compromised) to the effects of hazardous substances. A conservative (i.e., protective) approach is used to address these uncertainties, consistent with the public health principle of prevention. Although human data are preferred, MRLs often must be based on results of animal studies because relevant human studies are lacking. In the absence of evidence to the contrary, it is assumed that humans are more sensitive than animals to the effects of hazardous substances, and that certain persons may be particularly sensitive. Thus, the resulting MRL may be as much as a hundredfold below levels shown to be nontoxic in laboratory animals. Exposure to a level above the MRL does not mean that adverse health effects will occur.

The guidance for MRL derivation is continually evolving to reflect the current risk assessment methodology. ATSDR is currently evaluating the application of physiologically based pharmacokinetic modeling and quantitative structure-activity relationship to enhance understanding of dose and across-route extrapolations. In addition, ATSDR is evaluating the utility of Benchmark Dose modeling, to obtain low-incidence response exposure levels calculated from mathematically fitted dose-response curves, as an adjunct to the current NOAEL/LOAEL approach in deriving MRLs.

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REFERENCES

BARNES, D.G. and DOURSON, M. (1988). "Reference dose (RfD): Description and use in health risk assessments." Regulatory Toxicol. Pharmacol. 8:471–486.

JARABEK, A.M. and SEGAL, S.A. (1994). "Noncancer toxicity of inhaled air pollutants: Available approaches for risk assessment and risk management." In: Toxic Air Pollution Handbook. (D.R. Patrick, ed.) Van Nostrand Reinhold, New York, NY. pp. 529–541.

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA) (1986). Research and Development: Reference Values for Risk Assessment. (ECAO-CIN-477, September 1986).

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA) (1988). Recommendations for and Documentation of Biological Values for Use in Risk Assessment. (USEPA 600-6-87/008, February 1988).

U.S. ENVIRONMENTAL PROTECTION AGENCY (USEPA) (1990). Interim Methods for Development of Inhalation Reference Concentrations. (USEPA/600/8-90/066A, August 1990).