APPENDIX A

ATSDR MINIMAL RISK LEVEL

The Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) [42 U.S.C. 9601 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 (EPA), in order of priority, a list of hazardous substances most commonly found at facilities on the CERCLA National Priorities List (NPL); prepare toxicological profiles for each substance included on the priority list of hazardous substances; and assure the initiation of a research program to fill identified data needs associated with the substances.

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, Minimal Risk Levels (MRLs) are derived when reliable and sufficient data exist to identify the target organ(s) of effect or the most sensitive health effect(s) for a specific duration for a given route of exposure. 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. MRLs are based on noncancer health effects only and are not based on a consideration of cancer effects. These substance-specific estimates, which are intended to serve as screening levels, are used by ATSDR health assessors to identify contaminants and potential health effects that may be of concern at hazardous waste sites. It is important to note that MRLs are not intended to define clean-up or action levels.

MRLs are derived for hazardous substances using the no-observed-adverse-effect level/uncertainty factor approach. They are below levels that might cause adverse health effects in the people most sensitive to such chemical-induced effects. MRLs are derived for acute (1–14 days), intermediate (15–364 days), and chronic (365 days and longer) durations and for the oral and inhalation routes of exposure. Currently, MRLs for the dermal route of exposure are not derived because ATSDR has not yet identified a method suitable for this route of exposure. MRLs are generally based on the most sensitive chemical-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. Exposure to a level above the MRL does not mean that adverse health effects will occur.

MRLs are intended only 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 that are not expected to cause adverse health effects. Most MRLs contain a degree of uncertainty because of the lack of precise toxicological information on the people who might be most sensitive (e.g., infants, elderly, nutritionally or immunologically compromised) to the effects of hazardous substances. ATSDR uses a conservative (i.e., protective) approach to address this uncertainty consistent with the public health principle of prevention. Although human data are preferred, MRLs often must be based on animal studies because relevant human studies are lacking. In the absence of evidence to the contrary, ATSDR assumes that humans are more sensitive to the effects of hazardous substance than animals and that certain persons may be particularly sensitive. Thus, the resulting MRL may be as much as a hundredfold below levels that have been shown to be nontoxic in laboratory animals.

Proposed MRLs undergo a rigorous review process: Health Effects/MRL Workgroup reviews within the Division of Toxicology, expert panel peer reviews, and agencywide MRL Workgroup reviews, with participation from other federal agencies and comments from the public. They are subject to change as new information becomes available concomitant with updating the toxicological profiles. Thus, MRLs in the most recent toxicological profiles supersede previously published levels. For additional information regarding MRLs, please contact the Division of Toxicology, Agency for Toxic Substances and Disease Registry, 1600 Clifton Road, Mailstop E-29, Atlanta, Georgia 30333.
MINIMAL RISK LEVEL WORKSHEETS

Chemical Name: Carbon disulfide
CAS Number: 75-15-0
Date: July 1996
Profile Status: Second Draft
Route: [X] Inhalation [ ] Oral
Duration: [ ] Acute [ ] Intermediate [X] Chronic
Graph Key: 35
Species: Human

Minimal Risk Level: 0.3 [ ] mg/kg/day [X] ppm


Experimental design: (human study details or strain, number of animals per exposure/control groups, sex, dose administration details):

A cohort of male viscose rayon workers exposed to carbon disulfide (n=145) were compared to a group of non-exposed artificial fiber plant workers (n=212) located on the same premises. The mean exposure period was 12.1 ± 6.9 years (mean ± SD), and individuals were divided into three groups based on previous exposure histories, job descriptions, and current carbon disulfide levels established on the basis of 8-hour personal monitors. The median carbon disulfide level for the comparison group was 0.2 ppm (0.6 mg/cu.m, duration adjusted to 0.1 mg/cu.m; while the median carbon disulfide levels of exposed individuals was 1.4, 4.1, and 7.6 ppm (3, 13, and 24 mg/cu.m; duration adjusted to 0.7, 3.0, and 5.6 mg/cu.m). The mean exposure concentration of all groups considered together was 7.3 ± 17.2 ppm (mean ± SD) (23 mg/cu.m), ranging from 0.6 to 16 ppm (1.9 to 50 mg/cu.m). Workers were excluded on the basis of excess alcohol consumption, diabetes, or elevated blood lead levels. Surface electrodes were used to measure maximum motor conduction velocity (MCV) in the ulnar and peroneal nerves, and sensory nerve conduction velocity (SCV) in the sural nerve. Both latency, and amplitude ratios were calculated. Data were presented after they adjusted for temperature and terminal distance. In addition, participant’s responses to a medical questionnaire with questions relevant to both central and peripheral nervous system symptoms were tabulated. Neurophysiological test results from the comparison group were compared to the overall exposure group, as well as to the low, medium, and high exposure groups.

Effects noted in study and corresponding doses:

Peroneal MCV decreased in a dose-dependent manner with increasing carbon disulfide exposure levels. This decrease was statistically significantly in the high concentration exposure group vs. the comparison group. When MCV was stratified according to the cumulative exposure index (ppm months), a significant association was made between this index and decreased MCV. The peroneal nerve amplitude ratio was also significantly decreased in the highest exposure group. Sural SCV was decreased in exposed vs. comparison groups; however there was no dose response relationship in the three groups. The sural sensory amplitude was significantly greater in the high exposure group than in the low exposure group, however the value for the comparison group was midway between the medium and high exposure values. Therefore, the significance of this finding is unclear. No differences in the number of self-reported symptoms related to the peripheral nervous system were
found. Study limitations included the use of only one sex (not enough women to permit valid statistical analysis were identified), failure to use a biomarker (such as carbon disulfide in blood or urine), the variability of exposure concentrations, the use of median exposure concentrations for comparison that were based on job history and air and personal monitoring, and potential concurrent exposure in the workplace to hydrogen sulfide, tin oxide, zinc oxide and sulfate, sodium hydroxide, and sulfuric acid. Hydrogen sulfide levels were determined not to exceed 1 ppm. There were brief periods of high carbon disulfide exposures due to infrequent periods of breakdown in production. An appropriate exclusion of confounding factors (diabetes, alcohol consumption, blood lead levels) was used. The decrease in MCV constitutes a LOAEL of 7.6 ppm (24 mg/cu.m) which was considered minimal because the MCVs, although reduced compared to controls, were still within a range of clinically normal values. The study authors and the MRL workgroup considered these effects indicative of minimal neurotoxicity.

Dose and endpoint used for MRL derivation:

- [X] 3 for use of a minimal LOAEL
- [ ] 10 for extrapolation from animals to humans
- [X] 10 for human variability

Was a conversion used from ppm in food or water to a mg/body weight dose? If so explain: NA

If an inhalation study in animals, list the conversion factors used in determining human equivalent dose: N/A

MRL Calculation:

LOAEL: 7.6 ppm
MRL = LOAEL /UF = 7.6/30 = 0.25 ppm, rounded to 0.3 ppm

Agency Contact (Chemical Manager): Henry Abadin, MSPH
Chemical Name: Carbon disulfide  
CAS Number: 75-15-0  
Date: July 1996  
Profile Status: Second Draft  
Route: [ ] Inhalation [X] Oral  
Duration: [X] Acute [ ] Intermediate [ ] Chronic  
Graph Key: 2  
Species: Mice  

Minimal Risk Level: 0.01 [X] mg/kg/day [ ] ppm  


Experimental design: (human study details or strain, number of animals per exposure/control groups, sex, dose administration details):

The effects of carbon disulfide on the liver microsomal drug-metabolizing enzyme system and other enzyme activities were examined one hour after the oral administration of 0, 3, 30, 300 mg/kg carbon disulfide in SPF-grade male mice of the ddY-strain. Carbon disulfide was administered in olive oil. Control animals received only the vehicle. Microsomal enzyme assays included cytochrome P-450, cytochrome b5, total heme content, NADPH-P-450 reductase, NADPH-cytochrome c reductase, NADH-cytochrome c reductase, P-450 dependent peroxidase activity (aniline hydroxylation and N,N-dimethyl p-phenylene diamine oxidation, 7-ethoxycoumarin and 7-ethoxyresorufin-O-deethylase, phenylthiourea S-oxidase, N,N-dimethylaniline N-oxidase, N-demethylase, UDP-glucuronyltransferase, glucose-6-phosphatase, glutathione S-transferase, heme oxygenase, liver glutathione content, and conjugated diene levels. The hepatotoxic potential of carbon disulfide was examined in mice following oral administration of 500, 1000, 1500, or 2000 mg/kg carbon disulfide. Plasma glutamic pyruvic transaminase activity and liver calcium content were measured as an indicator of potential hepatotoxicity. The time-course of changes in drug-metabolizing enzyme activities was studied in mice following the oral administration of 3 and 30 mg/kg carbon disulfide.

Effects noted in study and corresponding doses:

There was no evidence of hepatotoxicity in mice administered up to 2000 mg/kg carbon disulfide. Following the oral administration of 3 or 30 mg/kg carbon disulfide, the hepatic microsomal cytochrome P-450 content and drug metabolizing enzyme activities decreased rapidly, reaching their lowest levels at 1 hour, and then gradually returning to control levels by 24 hours. The following enzyme activities were decreased: hydroxylation of aniline, O-dealkylation of p-nitroanisole, 7-ethoxycoumarin and 7-ethoxyresorufin, N-demethylation of N,N-dimethylaniline, NADPH-cytochrome P-450 reductase activity, and P-450-associated peroxidase activity. A dose-dependent decrease in total heme content and cytochrome P-450 content was observed at 30 and 300 mg/kg carbon disulfide. There were no effects on the activities of NADPH-ferricyanide reductase, NADPH-cytochrome c reductase, flavin-containing monoxygenase, UDP-glucuronyltransferase, glucose-6-phosphatase, heme oxygenase, and glutathione S-transferase. Also, the content of cytochrome b5 was not altered. The decrease in liver microsomal drug-metabolizing enzymes constitutes a minimal LOAEL of
3 mg/kg/day. The effect was considered to be minimal since the inhibition of enzyme activities was selective and reversible.

**Dose and endpoint used for MRL derivation:**

3 mg/kg/day, dose-dependent decreases in the activities of hepatic microsomal drug-metabolizing enzyme.

[ ] NOAEL  [X] LOAEL

**Uncertainty Factors used in MRL derivation:**

[X] 3 for use of a minimal LOAEL
[X] 10 for extrapolation from animals to humans
[X] 10 for human variability

**Was a conversion used from ppm in food or water to a mg/body weight dose?**

If so, explain: N/A

**If an inhalation study in animals, list the conversion factors used in determining human equivalent dose:** N/A

**MRL Calculation:**

LOAEL: 3 mg/kg/day

\[
MRL = \frac{LOAEL}{UF} = \frac{3}{300} = 0.01 \text{ mg/kg/day}
\]

**Agency Contact (Chemical Manager):** Henry Abadin, MSPH
APPENDIX B

USER'S GUIDE

Chapter 1

Public Health Statement

This chapter of the profile is a health effects summary written in non-technical language. Its intended audience is the general public especially people living in the vicinity of a hazardous waste site or chemical release. If the Public Health Statement were removed from the rest of the document, it would still communicate to the lay public essential information about the chemical.

The major headings in the Public Health Statement are useful to find specific topics of concern. The topics are written in a question and answer format. The answer to each question includes a sentence that will direct the reader to chapters in the profile that will provide more information on the given topic.

Chapter 2

Tables and Figures for Levels of Significant Exposure (LSE)

Tables (2-1, 2-2, and 2-3) and figures (2-1 and 2-2) are used to summarize health effects and illustrate graphically levels of exposure associated with those effects. These levels cover health effects observed at increasing dose concentrations and durations, differences in response by species, minimal risk levels (MRLs) to humans for noncancer end points, and EPA's estimated range associated with an upper-bound individual lifetime cancer risk of 1 in 10,000 to 1 in 10,000,000. Use the LSE tables and figures for a quick review of the health effects and to locate data for a specific exposure scenario. The LSE tables and figures should always be used in conjunction with the text. All entries in these tables and figures represent studies that provide reliable, quantitative estimates of No-Observed-Adverse-Effect Levels (NOAELs), Lowest-Observed-Adverse-Effect Levels (LOAELs), or Cancer Effect Levels (CELs).

The legends presented below demonstrate the application of these tables and figures. Representative examples of LSE Table 2-1 and Figure 2-1 are shown. The numbers in the left column of the legends correspond to the numbers in the example table and figure.

LEGEND

See LSE Table 2-1

(1) **Route of Exposure** One of the first considerations when reviewing the toxicity of a substance using these tables and figures should be the relevant and appropriate route of exposure. When sufficient data exists, three LSE tables and two LSE figures are presented in the document. The three LSE tables present data on the three principal routes of exposure, i.e., inhalation, oral, and dermal (LSE Table 2-1, 2-2, and 2-3, respectively). LSE figures are limited to the inhalation (LSE Figure 2-1) and oral (LSE Figure 2-2) routes. Not all substances will have data on each route of exposure and will not therefore have all five of the tables and figures.
(2) **Exposure Period** Three exposure periods - acute (less than 15 days), intermediate (15–364 days), and chronic (365 days or more) are presented within each relevant route of exposure. In this example, an inhalation study of intermediate exposure duration is reported. For quick reference to health effects occurring from a known length of exposure, locate the applicable exposure period within the LSE table and figure.

(3) **Health Effect** The major categories of health effects included in LSE tables and figures are death, systemic, immunological, neurological, developmental, reproductive, and cancer. NOAELs and LOAELs can be reported in the tables and figures for all effects but cancer. Systemic effects are further defined in the "System" column of the LSE table (see key number 18).

(4) **Key to Figure** Each key number in the LSE table links study information to one or more data points using the same key number in the corresponding LSE figure. In this example, the study represented by key number 18 has been used to derive a NOAEL and a Less Serious LOAEL (also see the 2 "18r" data points in Figure 2-1).

(5) **Species** The test species, whether animal or human, are identified in this column. Section 2.5, "Relevance to Public Health," covers the relevance of animal data to human toxicity and Section 2.3, "Toxicokinetics," contains any available information on comparative toxicokinetics. Although NOAELs and LOAELs are species specific, the levels are extrapolated to equivalent human doses to derive an MRL.

(6) **Exposure Frequency/Duration** The duration of the study and the weekly and daily exposure regimen are provided in this column. This permits comparison of NOAELs and LOAELs from different studies. In this case (key number 18), rats were exposed to 1,1,2,2-tetrachloroethane via inhalation for 6 hours per day, 5 days per week, for 3 weeks. For a more complete review of the dosing regimen refer to the appropriate sections of the text or the original reference paper, i.e., Nitschke et al. 1981.

(7) **System** This column further defines the systemic effects. These systems include: respiratory, cardiovascular, gastrointestinal, hematological, musculoskeletal, hepatic, renal, and dermal/ocular. "Other" refers to any systemic effect (e.g., a decrease in body weight) not covered in these systems. In the example of key number 18, 1 systemic effect (respiratory) was investigated.

(8) **NOAEL** A No-Observed-Adverse-Effect Level (NOAEL) is the highest exposure level at which no harmful effects were seen in the organ system studied. Key number 18 reports a NOAEL of 3 ppm for the respiratory system which was used to derive an intermediate exposure, inhalation MRL of 0.005 ppm (see footnote "b").

(9) **LOAEL** A Lowest-Observed-Adverse-Effect Level (LOAEL) is the lowest dose used in the study that caused a harmful health effect. LOAELs have been classified into "Less Serious" and "Serious" effects. These distinctions help readers identify the levels of exposure at which adverse health effects first appear and the gradation of effects with increasing dose. A brief description of the specific endpoint used to quantify the adverse effect accompanies the LOAEL. The respiratory effect reported in key number 18 (hyperplasia) is a Less serious LOAEL of 10 ppm. MRLs are not derived from Serious LOAELs.

(10) **Reference** The complete reference citation is given in chapter 8 of the profile.
(11) **CEL.** A Cancer Effect Level (CEL) is the lowest exposure level associated with the onset of carcinogenesis in experimental or epidemiologic studies. CELs are always considered serious effects. The LSE tables and figures do not contain NOAELs for cancer, but the text may report doses not causing measurable cancer increases.

(12) **Footnotes.** Explanations of abbreviations or reference notes for data in the LSE tables are found in the footnotes. Footnote "b" indicates the NOAEL of 3 ppm in key number 18 was used to derive an MRL of 0.005 ppm.

**LEGEND**

See Figure 2-1

LSE figures graphically illustrate the data presented in the corresponding LSE tables. Figures help the reader quickly compare health effects according to exposure concentrations for particular exposure periods.

(13) **Exposure Period.** The same exposure periods appear as in the LSE table. In this example, health effects observed within the intermediate and chronic exposure periods are illustrated.

(14) **Health Effect.** These are the categories of health effects for which reliable quantitative data exists. The same health effects appear in the LSE table.

(15) **Levels of Exposure.** Concentrations or doses for each health effect in the LSE tables are graphically displayed in the LSE figures. Exposure concentration or dose is measured on the log scale "y" axis. Inhalation exposure is reported in mg/m³ or ppm and oral exposure is reported in mg/kg/day.

(16) **NOAEL.** In this example, 18r NOAEL is the critical endpoint for which an intermediate inhalation exposure MRL is based. As you can see from the LSE figure key, the open-circle symbol indicates a NOAEL for the test species-rat. The key number 18 corresponds to the entry in the LSE table. The dashed descending arrow indicates the extrapolation from the exposure level of 3 ppm (see entry 18 in the Table) to the MRL of 0.005 ppm (see footnote "b" in the LSE table).

(17) **CEL.** Key number 38r is 1 of 3 studies for which Cancer Effect Levels were derived. The diamond symbol refers to a Cancer Effect Level for the test species-mouse. The number 38 corresponds to the entry in the LSE table.

(18) **Estimated Upper-Bound Human Cancer Risk Levels.** This is the range associated with the upper-bound for lifetime cancer risk of 1 in 10,000 to 1 in 10,000,000. These risk levels are derived from the EPA’s Human Health Assessment Group’s upper-bound estimates of the slope of the cancer dose response curve at low dose levels (q₁*).

(19) **Key to LSE Figure.** The Key explains the abbreviations and symbols used in the figure.
# TABLE 2-1. Levels of Significant Exposure to [Chemical x] – Inhalation

<table>
<thead>
<tr>
<th>Key to figure</th>
<th>Species</th>
<th>Exposure frequency/ duration</th>
<th>System</th>
<th>NOAEL (ppm)</th>
<th>LOAEL (effect)</th>
<th>Less serious (ppm)</th>
<th>Serious (ppm)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
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<tr>
<td>2</td>
<td>INTERMEDIATE EXPOSURE</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>3</td>
<td>Systemic</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>18 Rat</td>
<td>13 wk</td>
<td>Resp</td>
<td>3&lt;sup&gt;b&lt;/sup&gt;</td>
<td>10 (hyperplasia)</td>
<td></td>
<td></td>
<td>Nitschke et al. 1981</td>
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</tbody>
</table>

<p>| |</p>
<table>
<thead>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>CHRONIC EXPOSURE</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cancer</th>
<th>38 Rat</th>
<th>18 mo</th>
<th>20 (CEL, multiple organs)</th>
<th>Wong et al. 1982</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>5d/wk</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>7hr/d</td>
<td></td>
<td></td>
</tr>
<tr>
<td>39 Rat</td>
<td>89–104 wk</td>
<td>5d/wk</td>
<td>10 (CEL, lung tumors, nasal tumors)</td>
<td>NTP 1982</td>
</tr>
<tr>
<td></td>
<td>6hr/d</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>40 Mouse</td>
<td>79–103 wk</td>
<td>5d/wk</td>
<td>10 (CEL, lung tumors, hemangiosarcomas)</td>
<td>NTP 1982</td>
</tr>
<tr>
<td></td>
<td>6hr/d</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

<sup>a</sup> The number corresponds to entries in Figure 2-1.

<sup>b</sup> Used to derive an intermediate inhalation Minimal Risk Level (MRL) of $5 \times 10^{-3}$ ppm; dose adjusted for intermittent exposure and divided by an uncertainty factor of 100 (10 for extrapolation from animal to humans, 10 for human variability).

**Primary**

- **CEL**: cancer effect level; **d**: days(s); **hr**: hour(s); **LOAEL**: lowest-observed-adverse-effect level; **mo**: month(s); **NOAEL**: no-observed-adverse-effect level; **Resp**: respiratory; **wk**: week(s)
Figure 2-1. Levels of Significant Exposure to [Chemical X] – Inhalation

Key:
- r Rat
- m Mouse
- h Rabbit
- g Guinea Pig
- k Monkey
- O LOAEL for serious effects (animals)
- • LOAEL for less serious effects (animals)
- O NOAEL (animals)
- © CEL - Cancer Effect Level
- ••••• Minimal risk level for effects other than cancer

* Doses represent the lowest dose tested per study that produced a tumorigenic response and do not imply the existence of a threshold for the cancer end point.

Estimated Upper Bound Human Cancer Risk Levels:
- $10^{-4}$
- $10^{-5}$
- $10^{-6}$
- $10^{-7}$

Human Cancer Risk Levels:
- 0.01
- 0.001
- 0.0001
- 0.00001
- 0.000001
- 0.0000001
Chapter 2 (Section 2.5)

Relevance to Public Health

The Relevance to Public Health section provides a health effects summary based on evaluations of existing toxicologic, epidemiologic, and toxicokinetic information. This summary is designed to present interpretive, weight-of-evidence discussions for human health end points by addressing the following questions.

1. What effects are known to occur in humans?
2. What effects observed in animals are likely to be of concern to humans?
3. What exposure conditions are likely to be of concern to humans, especially around hazardous waste sites?

The section covers end points in the same order they appear within the Discussion of Health Effects by Route of Exposure section, by route (inhalation, oral, dermal) and within route by effect. Human data are presented first, then animal data. Both are organized by duration (acute, intermediate, chronic). In vitro data and data from parenteral routes (intramuscular, intravenous, subcutaneous, etc.) are also considered in this section. If data are located in the scientific literature, a table of genotoxicity information is included.

The carcinogenic potential of the profiled substance is qualitatively evaluated, when appropriate, using existing toxicokinetic, genotoxic, and carcinogenic data. ATSDR does not currently assess cancer potency or perform cancer risk assessments. Minimal risk levels (MRLs) for noncancer end points (if derived) and the end points from which they were derived are indicated and discussed.

Limitations to existing scientific literature that prevent a satisfactory evaluation of the relevance to public health are identified in the Data Needs section.

Interpretation of Minimal Risk Levels

Where sufficient toxicologic information is available, we have derived minimal risk levels (MRLs) for inhalation and oral routes of entry at each duration of exposure (acute, intermediate, and chronic). These MRLs are not meant to support regulatory action; but to acquaint health professionals with exposure levels at which adverse health effects are not expected to occur in humans. They should help physicians and public health officials determine the safety of a community living near a chemical emission, given the concentration of a contaminant in air or the estimated daily dose in water. MRLs are based largely on toxicological studies in animals and on reports of human occupational exposure.

MRL users should be familiar with the toxicologic information on which the number is based. Chapter 2.5, "Relevance to Public Health," contains basic information known about the substance. Other sections such as 2.7, "Interactions with Other Substances," and 2.8, "Populations that are Unusually Susceptible" provide important supplemental information.

MRL users should also understand the MRL derivation methodology. MRLs are derived using a modified version of the risk assessment methodology the Environmental Protection Agency (EPA) provides (Barnes and Dourson 1988) to determine reference doses for lifetime exposure (RfDs).
To derive an MRL, ATSDR generally selects the most sensitive endpoint which, in its best judgement, represents the most sensitive human health effect for a given exposure route and duration. ATSDR cannot make this judgement or derive an MRL unless information (quantitative or qualitative) is available for all potential systemic, neurological, and developmental effects. If this information and reliable quantitative data on the chosen endpoint are available, ATSDR derives an MRL using the most sensitive species (when information from multiple species is available) with the highest NOAEL that does not exceed any adverse effect levels. When a NOAEL is not available, a lowest-observed-adverse-effect level (LOAEL) can be used to derive an MRL, and an uncertainty factor (UF) of 10 must be employed. Additional uncertainty factors of 10 must be used both for human variability to protect sensitive subpopulations (people who are most susceptible to the health effects caused by the substance) and for interspecies variability (extrapolation from animals to humans). In deriving an MRL, these individual uncertainty factors are multiplied together. The product is then divided into the inhalation concentration or oral dosage selected from the study. Uncertainty factors used in developing a substance-specific MRL are provided in the footnotes of the LSE Tables.
# APPENDIX C

## ACRONYMS, ABBREVIATIONS, AND SYMBOLS

<table>
<thead>
<tr>
<th>ACGIH</th>
<th>American Conference of Governmental Industrial Hygienists</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADME</td>
<td>Absorption, Distribution, Metabolism, and Excretion</td>
</tr>
<tr>
<td>AML</td>
<td>acute myeloid leukemia</td>
</tr>
<tr>
<td>atm</td>
<td>atmosphere</td>
</tr>
<tr>
<td>ATSDR</td>
<td>Agency for Toxic Substances and Disease Registry</td>
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<tr>
<td>BCF</td>
<td>bioconcentration factor</td>
</tr>
<tr>
<td>BEI</td>
<td>Biological Exposure Index</td>
</tr>
<tr>
<td>BSC</td>
<td>Board of Scientific Counselors</td>
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<tr>
<td>C</td>
<td>Centigrade</td>
</tr>
<tr>
<td>CDC</td>
<td>Centers for Disease Control</td>
</tr>
<tr>
<td>CEL</td>
<td>Cancer Effect Level</td>
</tr>
<tr>
<td>CERCLA</td>
<td>Comprehensive Environmental Response, Compensation, and Liability Act</td>
</tr>
<tr>
<td>CFR</td>
<td>Code of Federal Regulations</td>
</tr>
<tr>
<td>Ci</td>
<td>curie</td>
</tr>
<tr>
<td>CLP</td>
<td>Contract Laboratory Program</td>
</tr>
<tr>
<td>cm</td>
<td>centimeter</td>
</tr>
<tr>
<td>CML</td>
<td>chronic myeloid leukemia</td>
</tr>
<tr>
<td>CNS</td>
<td>central nervous system</td>
</tr>
<tr>
<td>d</td>
<td>day</td>
</tr>
<tr>
<td>DHEW</td>
<td>Department of Health, Education, and Welfare</td>
</tr>
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<td>DHHS</td>
<td>Department of Health and Human Services</td>
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<td>Department of Labor</td>
</tr>
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<td>ECG</td>
<td>electrocardiogram</td>
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<td>electroencephalogram</td>
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<td>EKG</td>
<td>see ECG</td>
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<tr>
<td>F</td>
<td>Fahrenheit</td>
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<tr>
<td>F&lt;sub&gt;1&lt;/sub&gt;</td>
<td>first filial generation</td>
</tr>
<tr>
<td>FAO</td>
<td>Food and Agricultural Organization of the United Nations</td>
</tr>
<tr>
<td>FEMA</td>
<td>Federal Emergency Management Agency</td>
</tr>
<tr>
<td>FIFRA</td>
<td>Federal Insecticide, Fungicide, and Rodenticide Act</td>
</tr>
<tr>
<td>fpm</td>
<td>feet per minute</td>
</tr>
<tr>
<td>ft</td>
<td>foot</td>
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<tr>
<td>FR</td>
<td>Federal Register</td>
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<tr>
<td>g</td>
<td>gram</td>
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<tr>
<td>GC</td>
<td>gas chromatography</td>
</tr>
<tr>
<td>gen</td>
<td>generation</td>
</tr>
<tr>
<td>HPLC</td>
<td>high-performance liquid chromatography</td>
</tr>
<tr>
<td>hr</td>
<td>hour</td>
</tr>
<tr>
<td>IDLH</td>
<td>Immediately Dangerous to Life and Health</td>
</tr>
<tr>
<td>IARC</td>
<td>International Agency for Research on Cancer</td>
</tr>
<tr>
<td>ILO</td>
<td>International Labor Organization</td>
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<tr>
<td>in</td>
<td>inch</td>
</tr>
<tr>
<td>Kd</td>
<td>adsorption ratio</td>
</tr>
</tbody>
</table>
kg  kilogram
kg  metric ton
K_{oc}  organic carbon partition coefficient
K_{ow}  octanol-water partition coefficient
L  liter
LC  liquid chromatography
LC_{lo}  lethal concentration, low
LC_{50}  lethal concentration, 50% kill
LD_{lo}  lethal dose, low
LD_{50}  lethal dose, 50% kill
LOAEL  lowest-observed-adverse-effect level
LSE  Levels of Significant Exposure
m  meter
MA  trans,trans-muconic acid
mCi  millicurie
mg  milligram
min  minute
mL  milliliter
mm  millimeter
mm Hg  millimeters of mercury
mmol  millimole
mo  month
mppcf  millions of particles per cubic foot
MRL  Minimal Risk Level
MS  mass spectrometry
NCE  normochromatic erythrocytes
NIEHS  National Institute of Environmental Health Sciences
NIOSH  National Institute for Occupational Safety and Health
NIOSHIC  NIOSH’s Computerized Information Retrieval System
ng  nanogram
nm  nanometer
NHANES  National Health and Nutrition Examination Survey
nmol  nanomole
NOAEL  no-observed-adverse-effect level
NOES  National Occupational Exposure Survey
NOHS  National Occupational Hazard Survey
NPL  National Priorities List
NRC  National Research Council
NTIS  National Technical Information Service
NTP  National Toxicology Program
OSHA  Occupational Safety and Health Administration
PEL  permissible exposure limit
PCE  polychromatic erythrocytes
pg  picogram
pmol  picomole
PHS  Public Health Service
PMR  proportionate mortality ratio
ppb  parts per billion
ppm  parts per million
ppt parts per trillion
REL recommended exposure limit
RfD Reference Dose
RTECS Registry of Toxic Effects of Chemical Substances
sec second
SCE sister chromatid exchange
SIC Standard Industrial Classification
SMR standard mortality ratio
STEL short term exposure limit
STORET STORAGE and RETRIEVAL
TLV threshold limit value
TSCA Toxic Substances Control Act
TRI Toxics Release Inventory
TWA time-weighted average
UMDNJ University of Medicine and Dentistry New Jersey
U.S. United States
UF uncertainty factor
yr year
WHO World Health Organization
wk week

> greater than
\geq greater than or equal to
= equal to
< less than
\leq less than or equal to
\% percent
\alpha alpha
\beta beta
\delta delta
\gamma gamma
\mu micrometer
\mu g microgram