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. 99-4991, 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.

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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: Hexachloroethane
CAS Number: 67-72-1
Date: September 1996
Profile Status: Draft 3 Post-public comments
Route: [x] Inhalation [ ] Oral
Duration: [x] Acute [ ] Intermediate [ ] Chronic
Graph Key: 4
Species: Rat

Minimal Risk Level: 6 [ ] mg/kg/day [x] ppm

Reference: Weeks et al. 1979

Experimental design:

Groups of 22 pregnant Sprague-Dawley rats were exposed to vapors of hexachloroethane (0, 15, 48, or 260 ppm) 6 hours/day on gestation days 6-16. Specific details of methods and results are not reported in this paper.

Effects noted in study and corresponding doses:

Hexachloroethane resulted in tremors at 260 ppm, with no neurological effects at 48 ppm. Transient mucopurulent nasal exudate in 85% of the animals and an unspecified decrease in maternal weight gain were noted in animals at 48 ppm. This effect was considered a result of an endemic mycoplasma infection and was not observed at 48 ppm in the 6-week study (Weeks et al. 1979). The 260-ppm concentration is a serious LOAEL for neurological effects and the 48-ppm concentration is a NOAEL.

Dose and end point used for MRL derivation:

[X] NOAEL [ ] LOAEL

48 ppm

Uncertainty Factors used in MRL derivation:

[ ] 3 for use of a minimal LOAEL
[x] 3 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? No.
If so, explain:

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

Human Equivalent Concentration was calculated using default values from EPA (1988a).
48 ppm [(0.22 m^3/day/0.204 kg) / (20 m^3/day/70 kg)] = 181 ppm

Other additional studies or pertinent information which lend support to this MRL:

Other than the study by Weeks et al. (1979), there are no inhalation studies useful for estimating an acute inhalation MRL.

Chemical Name: Hexachloroethane
CAS Number: 67-72-1
Date: September 1996
Profile Status: Draft 3 Post-public comments
Route: [x] Inhalation [ ] Oral
Duration: [ ] Acute [x] Intermediate [ ] Chronic
Graph Key: 14
Species: Rat

Minimal Risk Level: 6 [ ] mg/kg/day [x] ppm

Reference: Weeks et al. 1979

Experimental design:

Groups of 25 male and 25 female Sprague-Dawley rats were exposed to vapors of hexachloroethane (0, 15, 48 or 260 ppm) 6 hours/day, 5 days/week for 6 weeks. Half of the animals were sacrificed at the end of the exposure period while the remainder were sacrificed 12 weeks after the end of the study. Quantitative data are not reported in this paper.

Effects noted in study and corresponding doses:

One male and one female rat exposed at 260 ppm died. There was an increased incidence of mycoplasma infection at 260 ppm that the authors attributed to hexachloroethane-induced potentiation of an endemic infection. Histopathologic changes were not observed in the brain, lungs, heart, liver, kidneys, spleen, eyes, bone marrow, trachea, nasal turbinates, thymus, stomach, small intestines, large intestines, pancreas, adrenal glands, bladder, testes, skin, skeletal muscle, and bone. Body weights (quantitative data not given) were reduced, and eye irritation was noted at 260 ppm. The high concentration is a serious effect level associated with tremors and less serious effects, reduced resistance to infection, eye irritation, and reduced body weight. The 48-ppm concentration is a NOAEL.

Dose and end point used for MRL derivation:

[x] NOAEL [ ] LOAEL

48 ppm

Uncertainty Factors used in MRL derivation:

- [ ] 10 for use of a LOAEL
- [x] 3 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? No.
If so, explain:

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

Human Equivalent Concentration was calculated using default values from EPA (1988a).

Other additional studies or pertinent information which lend support to this MRL:

Other than the study by Weeks et al. (1979) there are no inhalation studies useful for estimating an intermediate inhalation MRL. Studies in guinea pigs and dogs confirm that 260 ppm hexachloroethane is a serious effect concentration; 4/10 guinea pigs, and 1/4 dogs died at this concentration. These studies do not clearly identify a less serious LOAEL that does not have some serious effects. The 48-ppm concentration is a NOAEL for the most sensitive toxicity endpoint in all three species.

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Chemical Name: Hexachloroethane
CAS Number: 67-72-1
Date: September 1996
Profile Status: Draft 3 Post-public comments
Route: [] Inhalation [x] Oral
Duration: [x] Acute [] Intermediate [ ] Chronic
Graph Key: 8
Species: Rabbit

Minimal Risk Level: 1 [x] mg/kg/day [] ppm

Reference: Weeks et al. 1979

Experimental design:

Groups of five male New Zealand rabbits were treated by gavage with hexachloroethane in methyl cellulose for 12 days at 0, 100, 320, or 1,000 mg/kg/day. Body weights were recorded daily, clinical signs were monitored, and serum chemistry parameters were evaluated (alanine aminotransferase, aspartate aminotransferase, blood urea nitrogen, alkaline phosphatase, bilirubin, total protein, potassium, and sodium). Necropsies were performed 4 days after the last dose and organs (lungs, liver, kidneys, spleen, testes) were weighed. Histopathological examinations of selected tissues and organs (eye, brain, lung, kidney, liver, spleen, heart, stomach, pancreas, small intestine, large intestine, skeletal muscle, bone, urinary bladder, testes) were also conducted.

Effects noted in study and corresponding doses:

Liver degeneration and necrosis occurred in a dose-related manner at 320 and 1,000 mg/kg/day. Effects were characterized as fatty degeneration, coagulative necrosis, hemorrhage, ballooning degeneration, eosinophilic change, and hemosiderin-laden macrophages and giant cells. Comparable effects were not seen in the 100-mg/kg/day dose group (lowest dose tested). Also, liver weights increased at the highest dose tested; however, quantitative data were not provided for evaluation. For the most part, serum clinical chemistry parameters were not significantly affected, except that levels of potassium and glucose were decreased significantly at dose levels of 320 mg/kg/day or greater. No quantitative data were provided for evaluation. Toxic tubular nephrosis of the convoluted tubules was seen at dose levels of 320 and 1,000 mg/kg/day; however, comparable effects were not observed at the lowest dose tested (100 mg/kg/day). Effects observed among treatment groups did not occur in a dose-dependent manner. Minimal tubular nephrocalcinosis occurred in a dose-related manner at dose levels of 320 mg/kg/day or greater. Also, kidney weights increased significantly ($p<0.05$) at the highest dose tested. Quantitative data were not provided for evaluation. No treatment-related gross or histopathological lesions of the urinary bladder were reported. Body weights were reduced significantly ($p<0.05$) at exposure levels of 320 and 1,000 mg/kg/day. Effects were seen within 7 days after compound exposure in the highest dose group and within 10 days at the intermediate dose. No changes in body weight were found at 100 mg/kg/day, the lowest dose tested. Quantitative data were not provided for evaluation.

Dose and end point used for MRL derivation:

[x] NOAEL [ ] LOAEL

100 mg/kg/day for lack of liver effects

Uncertainty Factors used in MRL derivation:

[ ] 10 for use of a 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? No.
If so, explain:

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

Other additional studies or pertinent information which lend support to this MRL:

There are no other acute oral studies of hexachloroethane which support this MRL. However, intermediate-duration oral studies of hexachloroethane in rats described further in the worksheet for the intermediate-duration oral MRL provide support that the liver is a target following oral exposure to hexachloroethane.

Chemical Name: Hexachloroethane
CAS Number: 67-72-1
Date: September 1996
Profile Status: Draft 3 Post-public comments
Route: [] Inhalation [x] Oral
Duration: [] Acute [x] Intermediate [ ] Chronic
Graph Key: 18
Species: Rat

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

Reference: Gorzinski et al. 1985

Experimental design:

Groups of 10 male and 10 female Fischer-344 rats were fed hexachloroethane in the diet for 16 weeks at levels that provided doses of 0, 1, 15, or 62 mg/kg/day. Procedures were taken to minimize volatilization from food, and the doses are actual doses rather than target doses. Body weights were monitored weekly and food consumption biweekly. At 13 weeks, blood samples were collected and analyzed for red cell count, hemoglobin concentration, and leukocyte counts. Urine specimens (13-week) were analyzed for pH, glucose, protein, ketones, occult blood, and urobilinogen. Blood samples taken at 16 weeks were analyzed for serum urea nitrogen, creatine, glutamate-pyruvate transaminase, and alkaline phosphatase. After sacrifice, the weights of the brain, heart, liver, kidneys, and testes were determined. The tissues of the organs were preserved and examined histologically.

Effects noted in study and corresponding doses:

Liver weights were increased in male rats at the highest dose and there was swelling of the hepatocytes in males at the highest two doses. Differences were significant for absolute and relative liver weights at the highest dose. Increased relative liver weights were seen in females at the highest dose. The kidneys in the two highest male dose groups displayed tubular atrophy, hypertrophy, and dilation. At the highest dose, kidney weights were increased by 10% and relative kidney weight by 5.5%. These changes in the kidneys were not seen in females except at the highest dose. There were no differences in the urinalysis results for the controls and exposed animals. Histopathologic changes in other organs were not observed. The 15-mg/kg/day dose is considered a minimal LOAEL for swelling of hepatocytes, and the 1-mg/kg/day dose is a NOAEL.

Dose and end point used for MRL derivation:

[x] NOAEL [ ] LOAEL

1 mg/kg/day for lack of liver effects

Uncertainty Factors used in MRL derivation:

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

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

Other additional studies or pertinent information which lend support to this MRL:

Increased liver weights and an increase in the number of gamma glutamyl transpeptidase positive foci (dimethylnitrosoamine was used as an initiator), were reported in rats treated by gavage with hexachloroethane in corn oil at 497 mg/kg/day 5 days/week for 7 weeks (Milman et al. 1988; Story et al. 1986). No other doses were used in this study. Centrilobular necrosis was observed in female Fischer-344 rats treated by gavage with hexachloroethane in corn oil 5 days/week for 13 weeks (NTP 1989). No liver effects were observed at 94 mg/kg/day, suggesting that the LOAEL identified in the Gorzinski et al. (1985) study may be conservative. No liver effects were observed in female rats treated by gavage with hexachloroethane in corn oil 5 days/week for 2 years (NTP 1989) providing further support that the 15-mg/kg/day LOAEL observed in the Gorzinski et al. (1985) study may be conservative.

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-l 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-l and Figure 2-l 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-l) 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

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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 tigures 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-l).

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.

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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-l

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/m' 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 to 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 (q_1*).

19) Key to LSE Figure The Key explains the abbreviations and symbols used in the figure.

SAMPLE

1 →

TABLE 2-1. Levels of Significant Exposure to [Chemical x] – Inhalation

Key to figure[a]	Species	Exposure frequency/ duration	System	NOAEL (ppm)	LOAEL (effect) Less serious (ppm)		Reference
2 → INTERMEDIATE EXPOSURE							
	5 ↓	6 ↓	7 ↓	8 ↓	9 ↓		10 ↓
3 → Systemic							
4 → 18	Rat	13 wk 5d/wk 6hr/d	Resp	3 [b]	10 (hyperplasia)		Nitschke et al. 1981
CHRONIC EXPOSURE						11 ↓	
Cancer							
38	Rat	18 mo 5d/wk 7hr/d				20 (CEL, multiple organs)	Wong et al. 1982
39	Rat	89–104 wk 5d/wk 6hr/d				10 (CEL, lung tumors, nasal tumors)	NTP 1982
40	Mouse	79–103 wk 5d/wk 6hr/d				10 (CEL, lung tumors, hemangiosarcomas)	NTP 1982

[a] The number corresponds to entries in Figure 2-1.

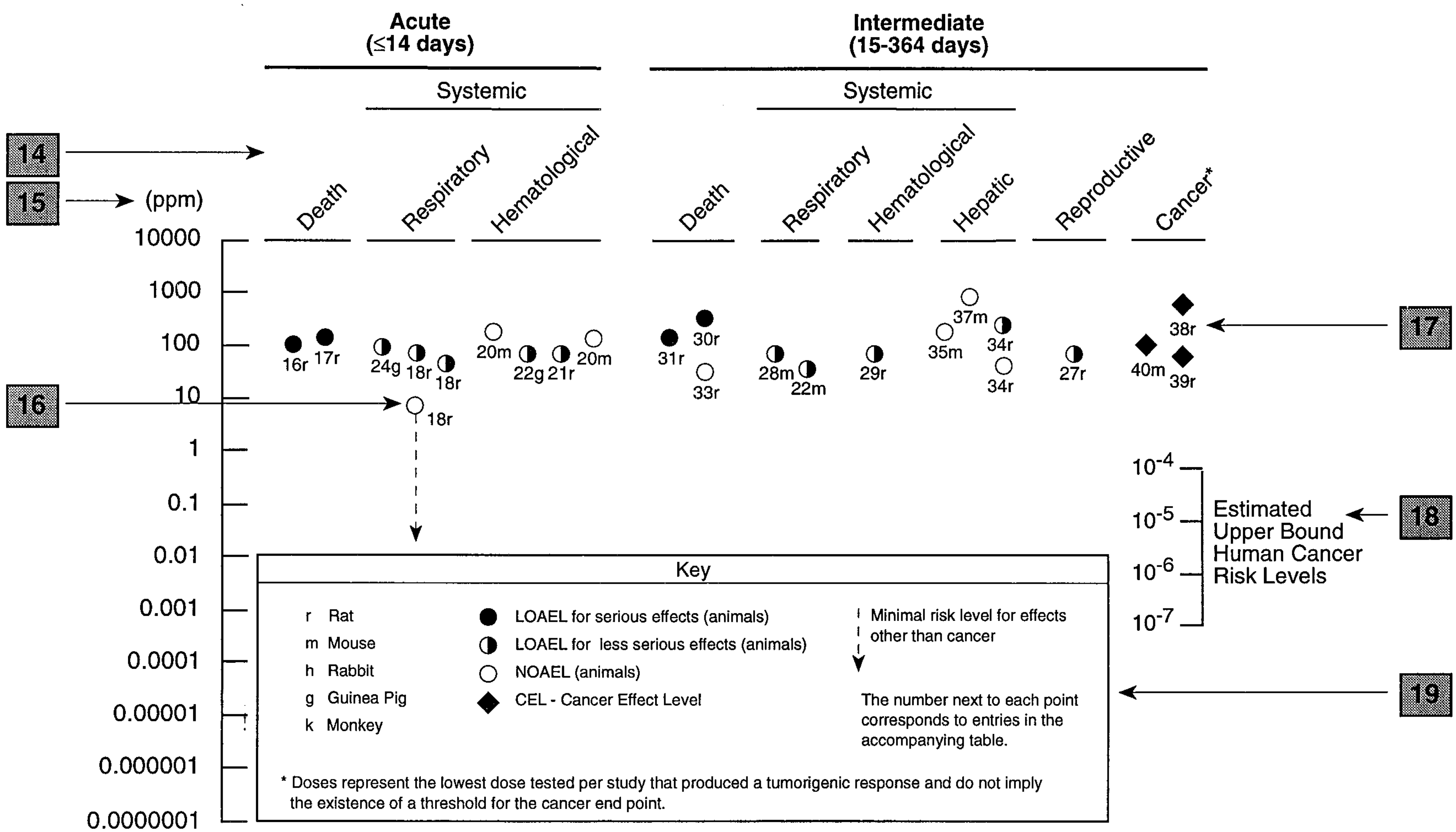
12 → [b]

by an uncertainty factor of 100 (10 for extrapolation from animal to humans, 10 for human variability).

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)

SAMPLE

13 → Figure 2-1. Levels of Significant Exposure to [Chemical X] – Inhalation



APPENDIX B

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).

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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

ACGIH	American Conference of Governmental Industrial Hygienists
ADME	Absorption, Distribution, Metabolism, and Excretion
AML	acute myeloid leukemia
atm	atmosphere
ATSDR	Agency for Toxic Substances and Disease Registry
BCF	bioconcentration factor
BEI	Biological Exposure Index
BSC	Board of Scientific Counselors
C	Centigrade
CDC	Centers for Disease Control
CEL	Cancer Effect Level
CERCLA	Comprehensive Environmental Response, Compensation, and Liability Act
CFR	Code of Federal Regulations
Ci	curie
CLP	Contract Laboratory Program
cm	centimeter
CML	chronic myeloid leukemia
CNS	central nervous system
d	day
DHEW	Department of Health, Education, and Welfare
DHHS	Department of Health and Human Services
DOL	Department of Labor
ECG	electrocardiogram
EEG	electroencephalogram
EPA	Environmental Protection Agency
EKG	see ECG
F	Fahrenheit
F_1	first filial generation
FAO	Food and Agricultural Organization of the United Nations
FEMA	Federal Emergency Management Agency
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
fpm	feet per minute
ft	foot
FR	*Federal Register*
g	gram
GC	gas chromatography
gen	generation
HPLC	high-performance liquid chromatography
hr	hour
IDLH	Immediately Dangerous to Life and Health
IARC	International Agency for Research on Cancer
ILO	International Labor Organization
in	inch
Kd	adsorption ratio

kg	kilogram
kkg	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
NIOSHTIC	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
≥	greater than or equal to
=	equal to
<	less than
≤	less than or equal to
%	percent
α	alpha
β	beta
δ	delta
γ	gamma
μm	micrometer
μg	microgram