Hazard Ranking System Issue Analysis: Toxicity as a Ranking Factor

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August 1987

MTR-86W128

SPONSOR:
U.S. Environmental Protection Agency
CONTRACT NO.:
EPA-68-01-7054

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ABSTRACT

This report, prepared for the Office of Emergency and Remedial Response (OERR) of the Environmental Protection Agency, recommends modifications to the toxicity factor of the EPA Hazard Ranking System (HRS) that incorporate: (1) an the assessment of the capacity of a substance to cause short- or long-term adverse effects, cancer, birth defects, or changes in genetic material; (2) a more accurate assessment of the potential hazard of substances by considering the toxicity of each substance for each expected mode of exposure to humans; and (3) more discrimination in the ranking of toxic substances and waste sites. This report critiques the current HRS toxicity factor and eight other ranking systems selected as representative of the methodologies used to discern the relative dangers of substances. This report then presents the rationale and derivation of the suggested modifications to the HRS toxicity factor and presents the evaluation of 30 substances found at National Priorities List (NPL) sites as examples of the proposed scoring methodology.

Suggested Keywords: Acute Toxicity, Chronic Toxicity, Carcinogenicity, Mutagenicity, Developmental Toxicity, and Carcinogenic Potency.

ACKNOWLEDGMENTS

The author is indebted to MITRE's toxicology staff for assistance in the preparation of early versions of this document. Drs. Maryce Jacobs, Michael Cunningham, Roman Pienta, Byong-Han Chin, and J. Michael Kelley contributed to preliminary asessments of other toxicity ranking methodologies and to discussions of the methodology proposed herein. Extraction of toxicity data and preliminary scoring of substances were performed by various members of the MITRE staff including Drs. Daniel Casagrande, Maryce Jacobs, Michael Cunningham, Roman Pienta, Byong-Han Chin, Miss Suzanne Locher, and Messrs. Gerald Goldgraben and Mack Skaggs. Dr. Barbara Fuller was instrumental in performing quality assurance of the toxicity data extracted for example, scoring of chemicals.

TABLE OF CONTENTS

TABLE OF CONTENTS (Continued)

TABLE OF CONTENTS (Concluded)

LIST OF TABLES

1.0 INTRODUCTION

1.1 Background

The Comprehensive Environmental Response, Compensation and Liability Act of 1980 (CERCLA) (PL 96-510) requires the President to identify national priorities for remedial action among releases or threatened releases of hazardous substances. These releases are to be identified based on criteria promulgated in the National Contingency Plan (NCP). On July 16, 1982, EPA promulgated the Hazard Ranking System (HRS) as Appendix A to the NCP (40 CFR 300; 47 FR 31180). The HRS comprises the criteria required under CERCLA and is used by EPA to estimate the relative potential hazard posed by releases or threatened releases of hazardous substances.

The HRS is a means for applying uniform technical judgment regarding the potential hazards presented by a release relative to other releases. The HRS is used in identifying releases as national priorities for further investigation and possible remedial action by assigning numerical values (according to prescribed guidelines) to factors that characterize the potential of any given release to cause harm. The values are manipulated mathematically to yield a single score that is designed to indicate the potential hazard posed by each release relative to other releases. This score is one of the criteria used by EPA in determining whether the release should be placed on the National Priorities List (NPL).

During the original NCP rulemaking process and the subsequent application of the HRS to specific releases, a number of technical issues have been raised regarding the HRS. These issues concern the desire for modifications to the HRS, to improve its capability, to estimate the relative potential hazard of releases. The issues include:

- Review of other existing ranking systems suitable for ranking hazardous waste sites for the NPL.
- Feasibility of considering ground water flow direction and distance, as well as defining "aquifer of concern," in determining potentially affected targets.
- Development of a human food chain exposure evaluation methodology.
- Development of a potential for air release factor category in the HRS air pathway.
- Review of the adequacy of the target distance specified in the air pathway.
- Feasibility of considering the accumulation of hazardous substances in indoor environments.
- Feasibility of developing factors to account for environmental attenuation of hazardous substances in ground and surface water.
- Feasibility of developing a more discriminating toxicity factor.
- Refinement of the definition of "significance" as it relates to observed releases.
- Suitability of the current HRS default value for an unknown waste quantity.
- Feasibility of determining and using hazardous substance concentration data.

- Feasibility of evaluating waste quantity on a hazardous constituent basis.
- Review of the adequacy of the target distance specified in the surface water pathway.
- Development of a sensitive environment evaluation methodology.
- Feasibility of revising the containment factors to increase discrimination among facilities.
- Review of the potential for future changes in laboratory detection limits to affect the types of sites considered for the NPL.

Each technical issue is the subject of one or more separate but related reports. These reports, although providing background, analysis, conclusions and recommendations regarding the technical issue, will not directly affect the HRS. Rather, these reports will be used by an EPA working group that will assess and integrate the results and prepare recommendations to EPA management regarding future changes to the HRS. Any changes will then be proposed in Federal notice and comment rulemaking as formal changes to the NCP. The following section describes the specific issue that is the subject of this report.

1.2 Toxicity as a Ranking Factor

As a result of both the NCP and NPL rulemaking and the subsequent application of the HRS to uncontrolled hazardous wastes sites, public comments have been received by EPA on the method used in the HRS to rank the toxicity of hazardous substances. The current HRS method is based on a rating scheme developed by

N. Irving Sax (1975, 1979 and 1984) and rates the toxicity of hazardous substances on a scale of 0 to 3 (see Section 3 for further discussion of the HRS toxicity factor).

Several technical issues were raised by commenters that suggest the possible need for modification of the HRS in order to improve its ability to discriminate among sites whose wastes have different toxicological characteristics. In particular, commenters raised the following issues: (1) better guidance or instructions for determination of HRS toxicity values should be given; (2) chronic toxicity and carcinogenic effects are not addressed adequately in the HRS; (3) mutagenic and teratogenic effects are not considered; and (4) the current HRS toxicity factor provides insufficient stratification in toxicity values for many toxic substances and consequently has little influence on the final ranking of sites. EPA also desires to evaluate modifications of the HRS that could improve its ability to estimate the relative dangers due to the toxicity of substances at uncontrolled hazardous wastes disposal sites.

1.3 Review of Other Ranking Systems

Many other systems for ranking the relative toxicities of hazardous substances or the relative dangers of hazardous wastes disposal sites have been developed. More than 55 systems were reviewed at the initiation of this project (Haus and Wolfinger, 1986). Eight of these systems were selected for further review and

analysis as representative of the spectrum of approaches to hazard ranking. These systems include the CERCLA Reportable Quantities (RQ) Methodology; the Superfund Public Health Evaluation (SPHE) Method; the Preliminary Pollutant Level Value (PPLV) Method; the State of Michigan Site Assessment System (SAS); the U.S. Air Force Hazard Assessment Rating Methodology II (HARM II); the RCRA Hazardous Waste Scheduling Methodology; the European Economic Community (EEC) Plan; and the Centers for Disease Control (CDC) System for Prevention, Assessment, and Control of Exposures (SPACE). Since each system was developed with a different set of objectives and has its own approach for addressing toxicity, it is possible that one or more of these systems could provide guidance for designing an approach to improve the ability of the HRS to estimate the relative dangers posed by hazardous substances present at wastes disposal sites. Descriptions and evaluations of these systems are found in Section 3 and Appendices A through H.

1.4 Objectives

The objective of this study is to determine if improvements can be made in the means of evaluating hazardous substances at hazardous wastes sites to better reflect the relative toxic hazard posed by these substances.

1.5 Scope and Approach

The scope of this project consisted of an evaluation of the method used by the current HRS for estimating the relative toxicity

of substances at hazardous wastes disposal sites as well as the methods employed by other ranking systems and (2) the presentation of suggested improvements to the HRS toxicity factor.

Three sets of characteristics were selected to evaluate the various systems. These characteristics address the range of toxic effects considered, the ability to account for variables that affect exposure, and the manner for using the available data, as discussed below.

Since human exposure to substances that are released from uncontrolled hazardous wastes sites may be of either an acute (short duration) or a chronic (long duration) nature, an appropriately designed ranking system should address the toxic effects resulting from both acute and chronic exposure. Therefore, one set of characteristics that must be evaluated, concerns the comprehensiveness of the toxic effects (i.e., acute toxicity, carcinogenicity, mutagenicity, teratogenicity and other chronic effects) that provide the basis for the hazard assessment.

Since the toxicity of a substance can be influenced by the duration of exposure to it, an appropriately designed ranking system should take into account factors that determine human exposure to a substance. Therefore, the second set of characteristics that require evaluation relates to the ability of the ranking system to account for variables that affect exposure, including modes of

exposure, persistence, and presence of incompatible or reactive mixtures.*

In order to ensure consistency and the appropriate application of a ranking methodology to a given hazardous wastes site, the methodology should be readily understood, simply designed, easy to use, and scientifically sound. Therefore, the third set of characteristics that require evaluation is the manner with which each ranking system uses the available data. This includes the number of hazardous substances considered in the toxicity ranking, the quantity of data required for scoring each hazardous substance, and the clarity of instructions and ease of use of the ranking system.

These three sets of characteristics are described in detail in Section 2. In order to ensure a consistent evaluation, each ranking system was evaluated according to these characteristics. In addition, each ranking system was assessed to determine the purpose for which it was designed, the toxicologic endpoints that were considered, and how the final toxicity score was calculated. This additional information is presented in Section 3 to provide a complete understanding of the various systems evaluated.

*Incompatible or reactive mixtures were considered within this category due to their potential to accelerate the release of substances via fires and/or explosions as well as their ability to create new toxic substances.

Based on the evaluation of the EPA HRS, its limitations in assessing toxicity were identified. Evaluation of the other eight ranking systems provided insight to the design of approaches to address the limitations in the HRS. Where possible, modifications are recommended to improve the capability of the HRS to assess toxicity, and a proposed scoring methodology is described. This information is presented in Section 4. The details of the evaluation of the other eight systems are presented in Appendices A through H.

Thirty substances have been ranked as examples using the methodology described in Section 4. Appendix I presents a summary of the ranking assigned to each substance.

Section 5 provides a glossary of terms and Section 6 is a bibliography of references used in this report.

2.0 CHARACTERISTICS EVALUATED

The EPA HRS and eight other ranking systems were evaluated using the characteristics described below. These characteristics include the type of toxic effect (e.g., acute and chronic), the determinants of exposure (e.g., persistence and mode of exposure), and the use of available data (e.g., number of substances considered).

2.1 Type of Toxic Effect

2.1.1 Acute Toxicity

The evaluation of acute toxicity includes a description of the types of toxic effects (lethality, sensitization, irritation, corrosion, etc.) which may result after short term exposure to hazardous substances. Assessment of acute toxicity potential is important to protect persons who may be exposed to hazardous substances accidentally, for a short period of time. In addition, acute toxicity data are generally available for most toxic materials, allowing a common ground for estimating the relative acute danger posed by the hazardous substances.

2.1.2 Chronic Toxicity

All types of chronic toxic effects may be important because substances escaping from hazardous wastes sites are likely to result in long term exposures at low doses. Therefore, a ranking system should be able to discriminate between hazardous substances which cause toxic effects after short exposure (acute toxicity) versus hazardous substances which cause toxic effects only after prolonged

exposure (chronic toxicity). In the latter case, it is implicit that the acute (short term) toxicity is relatively low, or else the chronic toxicity may not be seen because of the acute effects.

2.1.3 Carcinogenicity, Mutagenicity, and/or Teratogenicity (CMT) Potential

The potential for hazardous substances to cause CMT effects is important in ranking hazardous wastes sites because (1) carcinogenic effects are usually not observed in humans until 20 to 30 years after exposure, in which time large numbers of people may be exposed; (2) mutagenic effects may go undetected in humans for periods up to many years, and such effects may cause either heritable genetic damage that can be passed on from generation to generation or lethal effects that result in abortion or miscarriage; and (3) teratogenic effects may be undetected in pregnant women but may cause major structural malformations or mental retardation in offspring.

2.2 Determinants of Exposure

2.2.1 Persistence

Persistence describes the longevity of the hazardous substance in the environment. This characteristic of a hazardous substance is included because the more resistant a substance is to environmental degradation, the greater the potential period of exposure.

2.2.2 Routes of Release

The routes by which hazardous substances can be released from wastes sites are important because the route of release from a site dictates the mode of exposure to humans and the environment. Routes of release generally include ground water, surface water, and air, but may also include direct exposure to the waste without a release to the environment. The modes of exposure, therefore, are ingestion (oral), breathing (inhalational), and direct contact (dermal).

2.2.3 Presence of Incompatible or Reactive Mixtures

An assessment of the ability of multiple substances in a wastes site to react to produce either additional (new) hazardous substances or fires and/or explosions is important. These reactions may result in the danger of injury to persons in the immediate vicinity, the release of new hazardous substances, or a change in the rate of migration of hazardous substances from the site.

2.3 Use of Data

2.3.1 Number of Hazardous Substances Evaluated

The number of individual hazardous substances or chemical species that are used in ranking sites is important in order to understand how each system assesses the overall hazard of the site. Many wastes sites contain more than one hazardous substance or chemical species and the total hazard to health or the environment is dependent upon all hazardous substances to which exposure occurs.

2.3.2 Quantity of Data Required on Each Hazardous Substance

The amount and availability of data required for each hazardous substance assessed at a release site can greatly affect the ability of an individual to use the system. How problems, such as lack of sufficient data, are handled by the ranking system is very important because the toxicity data base is a central feature for assessing the hazards inherent in each substance. Easily available information is required; extensive data requirements can lead to an impractical system due to increased expenditures of time or money without commensurate benefits (i.e., ability to discriminate among sites).

2.3.3 Clarity and Ease of Use

Not only is the simplicity with which the toxicity factor(s) of each system is derived important, but also how clearly the directions and the rationale for their use are presented. Effective use of any ranking system requires consistency that must be based on an understanding of how the system functions. Misunderstanding or misinterpretation due to ambiguity in descriptions or directions may lead to inconsistent scores and improper ranking of sites or wastes.

3.0 EVALUATION OF THE EPA HAZARD RANKING SYSTEM AND COMPARATIVE OVERVIEW OF SELECTED OTHER SYSTEMS

3.1 Environmental Protection Agency Hazard Ranking System (EPA HRS)

The EPA HRS was designed to identify releases or threatened releases of hazardous substances as national priorities for further investigation and possible remedial action. The system was described and promulgated in the July 16, 1982 Federal Register (47 FR 31219).

3.1.1 Type of Toxic Effect

3.1.1.1 Acute Toxicity. In the EPA HRS, toxicity is evaluated using either the rating scheme developed by Sax (1975, 1979 and 1984) or the rating scheme developed by the National Fire Protection Association (1977). These toxicity rating schemes are, in general, based on the acute lethal dose (LD_{50})* of a substance. The Sax reference provides toxic hazard review (THR) values for the substances contained in the compendium. Each substance is assigned a THR value from 0 (no data or an LD_{50} above 40,000 mg/kg) to 3 (an LD_{50} less than 400 mg/kg). These criteria have changed over time with each new edition of the Sax reference (1975, 1979 and 1984). The toxicity value is combined with a persistence value (c.f. 3.2.1.5) in a matrix to provide a toxicity/persistence factor value.

*LD_{50} is the dose of a substance that causes 50 percent of the exposed experimental animals to die.

There are several shortcomings in the use of the Sax rating system for HRS purposes. The THR values in Sax are apparently based on the LD_{50} although other (chronic) criteria for assigning THR values are discussed in the introductory material. Often, the only THR values given in Sax are based on the most sensitive mode (route) of administration, including injections into the abdomen (intraperitoneal), directly into veins (intravenous), or beneath the skin (subcutaneous). These routes of administration are shortcomings for the assessment of the toxicity of substances from hazardous wastes sites because the expected human exposure routes at these sites are oral, inhalational, or dermal routes. In addition, it is not possible to verify the appropriateness and accuracy of the THR values presented in the Sax data base because the specific data used to evaluate the toxicity of a given substance are not indicated. (See Section 3.1.1.2 for a further discussion of the Sax evaluation system.)

In the EPA HRS, toxicity is evaluated for each environmental route of migration (ground water, surface water, and air) according to the toxicity and persistence of the most toxic substance identified at the site which is available to migrate via that migration route. (See Section 3.1.2.1 for a discussion of toxicity/persistence values.) Although data are not available to determine the actual distribution of toxicity/persistence values that have been assigned to all wastes sites ranked using the HRS, it is

apparent from data for NPL sites that there is little variation in the toxicity values assigned among NPL sites. Table 1 presents the distribution of toxicity/persistence values (for the ground and surface water migration routes) and toxicity values (for the air migration route) that have been assigned to 888 NPL sites. Nearly 90 percent of the NPL sites have had the maximum toxicity value assigned. (Toxicity/persistence values of 18 can result only from maximum toxicity values of 3. Toxicity/persistence values of 15, 12 or 9 may or may not result from a maximum toxicity value. For example, a toxicity/persistence value of 15 can result from a toxicity value of 3 and persistence value of 2 or vice versa.) Table 1 illustrates that the toxicity factor of the present EPA HRS provides little discrimination among NPL sites based on the toxicity of the substances present. These data do not, however, indicate the effect of toxicity values on the ability of the current HRS to discriminate between NPL and non-NPL sites. It is possible that low toxicity values do, in fact, assist in discriminating non-NPL from NPL sites. Data to prove or disprove this have not been compiled.

3.1.1.2 Chronic Toxicity. In effect, the EPA HRS does not consider chronic toxicity in the ranking of hazardous wastes sites. According to the scheme presented in Sax (1975, 1979 and 1984), chronic toxicity appears to be a consideration in the evaluation (by Sax) of the toxicity potential of a compound. In point of fact, the

TABLE 1

DISTRIBUTION OF HRS TOXICITY/PERSISTENCE FACTOR VALUES AT NPL FACILITIES*

Toxicity/Persistence Values for Water Routes	Number of NPL Facilities			
	Ground Water		Surface Water	
	No.	%	No.	%
18	776	84	641	87
15	80	9	40	5
12	65	7	50	7
9	1	0	2	0
6	0	0	0	0
3	0	0	0	0
0	--	--	--	--
Total:	922	100	733	100

Toxicity Value for Air Route	Number of NPL Facilities	
	Air	Air
	No.	%
3	130	98
2	3	2
1	0	0
0	--	--
Total:	133	100

*Represents data on 951 NPL facilities through Final Update 3/4.

values assigned to substances in the Sax compendium are derived primarily on the basis of LD_{50} values as stated in the Preface to that compendium and not on the basis of chronic toxicity considerations (Sax, 1984).

Thus, the values in Sax (and, therefore, the EPA HRS toxicity factor wherein the Sax THR values are used) are not generally based on information about chronic toxicity. This is a limitation for adequate assessment of the potential danger associated with substances released by any route of migration.

3.1.1.3 Carcinogenicity, Mutagenicity, and Teratogenicity (CMT) Potential. The EPA HRS does not consider the potential of a hazardous substance to produce CMT effects in the ranking of hazardous wastes sites. This is a shortcoming for adequate assessment of the potential danger associated with hazardous substances released by any route of migration.

3.1.2 Determinants of Exposure

3.1.2.1 Persistence. The EPA HRS assigns persistence values from 0 to 3 for hazardous substances based upon their resistance to biodegradation. Loss of substances from the site due to volatility or environmental degradation such as hydrolysis or photolysis, are not considered. Substances that are easily biodegraded receive a value of 0; those substances that are very persistent receive a value of 3. The EPA HRS provides a table of substances listed by resistance to biodegradation. If the substance in question is not

presented in the table, a set of persistence criteria are provided to help the individual evaluating a site to assign a persistence value based on chemical structure. The persistence value is used in a matrix with the toxicity value to provide a single toxicity/ persistence value, which ranges from 0 to 18, for use in the surface water and ground water migration routes of the EPA HRS, but not in the air route.* Although consideration of the persistence of a substance is an important feature of the EPA HRS, the persistence factor has limitations because only biodegradation is considered in the evaluation.

3.1.2.2 Routes of Release. The EPA HRS describes the possible migration routes by which substances can be released from hazardous wastes sites including releases to ground water, surface water, and the atmosphere. A hazard score for each migration route is calculated and the three migration route scores are combined to provide an index of the hazard to people or the environment due to migration of substances away from the site. Consideration of multiple routes of release of a chemical is a strong point of the EPA HRS.

3.1.2.3 Presence of Incompatible or Reactive Mixtures. This factor applies only to the HRS air route and is used to assess the potential of substances present in wastes sites to react, thereby

*Since persistence in the EPA HRS is based solely upon resistance to biodegradation (i.e., via microbial metabolism), it is not combined with the toxicity value in the air pathway.

producing either new toxic substances or explosions which further the release of toxicants. Incompatibility is assigned values from 0 to 3, where zero indicates that no incompatible substances are present and three indicates that incompatible substances are both present and pose an immediate hazard. Examples of both incompatible substances (designated Groups A and B) and their consequences include: (1) a mixture of metals such as sodium (Group A) with acids (Group B) which could generate flammable hydrogen gas, (2) a mixture of spent cyanide (Group A) with acids (Group B) which could generate toxic hydrogen cyanide, and (3) a mixture of chlorates or chlorites (Group A) with corrosive acids (Group B) which could generate chlorine gas.

The National Fire Protection Association (NFPA, 1977) rating for reactivity is used to evaluate the reactivity of materials at wastes sites. For example, reactivity values range from 0 for materials that are normally stable even when exposed to fire and that are not reactive with water, to a value of 3 for materials that are readily capable of detonation, explosive decomposition, or explosive reaction at normal temperatures. The larger of the assigned incompatibility value or the reactivity value is used for this factor in the HRS air migration route.

3.1.3 Use of Data

3.1.3.1 Number of Substances Evaluated. The EPA HRS selects the substance with the highest toxicity/persistence value (discussed

above) for the ground and surface water routes or the substance with the highest toxicity value for the air route in scoring a migration route. This approach provides a conservative estimate of the potential hazard presented by wastes sites that contain more than one substance. It is apparent that this approach has resulted in a NPL where many sites receive a maximum toxicity/persistence value and, therefore, where discrimination based on toxicity among sites ranking high enough to be placed on the NPL is low.

The combined toxicity/persistence values for 16 substances most frequently used to score the migration routes at 951 NPL facilities are presented in Table 2. A total of 13 of the 16 substances have an assigned toxicity/persistence value of 18; the remaining three substances have toxicity/persistence values of 15 or 12. The data distribution is similar for the air migration route. The result of this skewed distribution is that nearly 90 percent of NPL sites received the highest possible toxicity/persistence value (Table 1). Consequently, there is virtually no discrimination among NPL sites based on the toxicity/persistence values. However, this does not imply that the toxicity/persistence values do not discriminate between NPL and non-NPL sites. Data to prove or disprove this are not currently available.

3.1.3.2 Quantity of Data on Each Substance. The EPA HRS depends primarily upon the rating system and toxicity data base developed by Sax. The current edition (Sax, 1984) contains

TABLE 2

SUBSTANCES MOST FREQUENTLY* USED TO ASSIGN TOXICITY/PERSISTENCE FACTOR VALUES AT NPL FACILITIES

Substance	Frequency of Use			Tox/Per for Water Routes**	Toxicity for Air Route***
	Ground Water	Surface Water	Air		
Lead and Compounds, NOS	180	153	8	18	3
Polychlorinated Biphenyls, NOS	126	117	15	18	3
Chloroform	119	79	8	18	3
Chromium and Compounds, NOS	93	75	0	18	3
Arsenic and Compounds, NOS	86	67	6	18	3
Cadmium and Compounds, NOS	55	47	5	18	3
Pentachlorophenol	37	34	2	18	3
Carbon Tetrachloride	46	23	2	18	3
Mercury and Compounds, NOS	34	31	3	18	3
Benzene	13	13	23	12	3
1,1,2-Trichloroethylene	27	20	1	12	2
1,1-Dichloroethene	32	6	3	15	3
Zinc and Compounds, NOS	22	19	0	18	3
Copper and Compounds, NOS	21	17	0	18	3
Chromium, Hexavalent	17	14	0	18	3
DDT	12	14	2	18	3
Vinyl Chloride	16	6	6	15	3

*Most frequently is determined by the sum of the total number of migration routes of the 951 NPL facilities (through Final Update 3/4) for which each substance was used to assign an HRS rating factor value for toxicity. Only those substances used at least 25 times are shown.

**Toxicity/persistence rating factor value for ground and surface water migration routes.

***Toxicity rating factor value for air migration route. This is combined with a multiplier (3).

information on approximately 18,000 substances. In the event no data are available for a substance, that substance is assigned a value of 0. This allows substances with known toxicity to receive higher rating values than those for which it is unknown. The consequence is that sites are rated based on known hazards rather than on unknowns.

3.1.3.3 Clarity. The EPA HRS clearly describes how wastes sites are evaluated for their potential to cause adverse human health or ecological effects for the purpose of priority ranking. Detailed instructions are provided, as are definitions and descriptions of the components contained in the EPA HRS. References, graphics, and examples are included, which guide the reader through the use of the system. Worksheets for the routes of exposure are provided.

3.2 Comparative Review of Selected Ranking Systems

A detailed description and analysis of eight other ranking systems is provided in Appendices A through H. The following paragraphs summarize that information. Although each of the eight other ranking systems that were evaluated is designed to protect people from the dangers associated with hazardous substances, there are important differences in the kinds of substances to be evaluated and the immediate objective of the hazard ranking. For instance, the plan developed by the European Economic Community (EEC) (Schmidt-Bleek et al., 1982) is designed to predict the dangers to

public health from new chemicals that might be produced by chemical companies prior to their being manufactured on a large scale. The Preliminary Pollutant Limit Value (PPLV) Method (Rosenblatt et al., 1980, 1982) is designed to determine the acceptable level of cleanup at a contaminated site. The EPA HRS and Michigan's Site Assessment System (SAS) (Michigan, 1983) are designed to assign priorities for further investigation and possible cleanup of hazardous wastes sites. The RCRA Hazardous Waste Scheduling Methodology (RCRA) (Environ, 1985) is designed to schedule substances for further study as to whether they should be banned from land disposal. The CERCLA Reportable Quantities (RQ) Methodology (Environmental Monitoring and Services, 1985) is designed to identify those quantities of released substances that require mandatory notification so that the need for Federal removal or remedial action can be assessed. Due to the differences in purpose of each of the systems, there are differences in the ways in which the relative danger to people is assessed. These differences include consideration of different aspects of toxicity of substances, differences in toxicity data requirements, and differences in both the required expertise of the individuals doing the evaluation and the extent of professional judgment permitted. Table 3 presents a comparative summary of each of the ranking systems reviewed in this document. The following paragraphs present an overview of the findings. Details are discussed in Appendices A through H.

TABLE 3

COMPARATIVE EVALUATION OF TOXICITY FACTORS
AMONG SELECTED HAZARDOUS WASTE RANKING SYSTEMS

Parameter Evaluated	Ranking System*								
	HRS	SAS	HARM II	RCRA	EEC	SPACE	RQ	PPLV	SPHE
Acute Toxicity	+	+	+	+	-	+a	+	-	-
Chronic Toxicity	-	+	-	+	b	-	+	+	+
CMT	-	CMT	-	C	M	-	CT	-	C
Persistence	+c	+	+c	-	+	+a,c	+	+?	+
Routes of Release	+	+	-e	-	+	+	-	+	+
Incompatible Mixtures	+	-d	-	-	-	+?	-d	-	-
Number of Chemicals Used in Ranking	1	all	all	1	1?	5	individual	individual	10-15
Quantity of Data	Mod	Mod	High	Low	N/A	Mod	Low	High	High
Clarity/Ease of Use	High	High	Low	Mod	Low	High	High	Low	Low

+ = present in ranking system
- = absent from ranking system
? = discussed but no guidance for use is provided
a = uses HRS methods
b = based on subchronic (28 day) NOEL
c = considers only biodegradability
d = addresses reactivity and ignitability of individual chemicals
e = includes ground and surface water routes only
N/A = not applicable
CMT = Carcinogenicity, Mutagenicity, Teratogenicity

*HRS = Hazard Ranking System (EPA, 1982)
SAS = Site Assessment System (Michigan, 1983)
HARM II = Hazard Assessment Rating Methodology (Barnthouse, 1986)
RCRA = Resource Conservation and Recovery Act Hazardous Waste Scheduling Methodology (Environ, 1985)
EEC = European Economic Community (Schmidt-Bleck et al., 1982)
SPACE = System for Prevention, Assessment and Control of Exposure (CDC, 1984)
RQ = Reportable Quantities (Environmental Monitoring and Services, 1985)
PPLV = Preliminary Pollutant Limit Values (Rosenblatt et al., 1980, 1982)
SPHE = Superfund Public Health Evaluation Method (ICF, 1985)

3.2.1 Types of Toxic Effect

3.2.1.1 Acute Toxicity. Six of the systems evaluated (HRS, SAS, HARM II, RCRA, SPACE and RQ) include consideration of acute toxicity. All of these systems use LD_{50} or LC_{50} data from experimental animals as a basis for scoring. Although the EEC plan does not assess acute toxicity per se, it is the only system that evaluates substances based upon dermal sensitization.

3.2.1.2 Chronic Toxicity. Six of the systems evaluated (SAS, RCRA, EEC, RQ, PPLV and SPHE) assess the chronic toxicity of substances by one of two methods. The SAS, RQ, SPHE and EEC systems use either the magnitude of the lowest dose that caused an irreversible toxic effect or the magnitude of the highest dose that caused no toxic effect in groups of experimental animals during chronic (SAS, RQ and SPHE) or subchronic (EEC) tests to obtain a score. In the case of the RQ method, the toxicity score is the product of a value based on the dosages and a severity index score which describes the seriousness of the observed effect. Reproductive and teratogenic effects are considered as chronic effects. In contrast to the four systems mentioned above, the RCRA and PPLV systems assess chronic toxicity based upon modifications of a technique used to calculate the acceptable daily intake (ADI) of toxic substances. (This technique is described in Section 4.1.2.)

Of these two methods of assessing chronic toxicity, the ADI method is more rigorous because it systematically uses the most

appropriate toxicity data that are available. If human data are available, they are used to determine the ADI. If human data are not available, chronic animal data are used. If chronic animal data are not available, subchronic data may be used. If subchronic data are unavailable, acute data may be used. With each type of data, a different safety factor (discussed in Section 4.3.2) is applied according to a predetermined set of rules. The other method (used by SAS, RQ, SPHE and EEC) has no such hierarchy of data use.

3.2.1.3 Carcinogenicity, Mutagenicity, and Teratogenicity (CMT) Potential. Among the nine systems evaluated, only SAS considers all three CMT effects. SAS scores chemicals for CMT effects based upon the weight-of-evidence. If a substance is a proven human carcinogen, mutagen, or teratogen, it receives the highest score. Decreasing scores are assigned based on decreasing strength of evidence (e.g., proven animal carcinogen; suspected animal carcinogen; mutagenic in short term test). Although the weight-of-evidence method does not discriminate between strong and weak carcinogens, it has the advantage of a predetermined, objective set of criteria by which substances are scored. This makes the weight-of-evidence approach easy to apply.

The EEC plan considers the mutagenicity of substances. Scores are assigned based on the weight-of-evidence from short term mutagenicity tests. Carcinogenicity and teratogenicity are not addressed.

Both the SPHE and RCRA methods score substances for carcinogenic potential based upon animal test data. The SPHE method requires calculation of the ED_{50} (the dose which causes a 10 percent increase in cancer incidence among treated animals). The RCRA method entails calculation of carcinogenic potencies and unit cancer risks (see Appendix F for details). The RCRA approach depends upon good animal data and the choice of the appropriate mathematical model to obtain low-dose extrapolations from high-dose test data. There are several models available for such extrapolations including linear extrapolation to the origin (zero dose), probit (Mantel and Bryan, 1961), single hit (Turner, 1975), multi-hit (Turner, 1975), multi-hit multistage (Armitage and Doll, 1961), and multistage with dependent dose patterns (Crump and Howe, 1984) models. All have different assumptions and give different results at low doses.

The RQ system considers both teratogenic and carcinogenic effects. Teratogenic effects are defined as chronic toxicity effects and, therefore, are included under consideration of chronic toxicity scoring. For carcinogenic effects, the RQ system combines the qualitative weight-of-evidence scores in a matrix with relative carcinogenic potencies derived from animal data to arrive at a relative hazard score for potential carcinogens (Cogliano, 1986). Mutagenic effects are not considered.

Of the approaches outlined above, the combined weight-of-evidence with ED_{10} approach (RQ methodology) appears most appropriate for hazard ranking of potential carcinogens. This methodology is objective, easy to apply, and it provides a measure of carcinogenic potency while avoiding much of the scientific controversy currently surrounding topics like the choice of appropriate low-dose extrapolation models for calculating carcinogenic potency.

3.2.2 Determinants of Exposure

3.2.2.1 Persistence. All of the systems evaluated except the RCRA method consider the environmental persistence of chemicals. However, three of the systems (HRS, HARM II, and SPACE) consider only biodegradation; the EEC plan gives only vague guidelines for assessing persistence; and the PPLV method states that persistence is an important consideration, but gives no guidance at all. The RQ method restricts persistence to loss from the environment by biodegradation, hydrolysis, or photochemical decomposition. The SPHE and SAS methods score persistence based on the half-life of the substance in various environmental media regardless of the mechanism of loss. (The SPHE document contains a table of half-lives of many substances in an appendix.)

Among the systems, the most appealing method is that used by SAS and SPHE because several types of degradation (e.g., hydrolysis in water and photolysis in air) are considered. However, SAS does

not identify data sources for this information. SPHE provides a look-up table for scores for selected chemicals, but it does not consider volatility. Thus, there is no system which has satisfactorily outlined criteria or data sources for scoring persistence for a wide range of substances from all types of environmental degradation.

3.2.2.2 Routes of Release. Seven systems consider routes of release of hazardous substances from the sites. The two systems which do not consider routes of release (RCRA and RQ) were designed to consider the danger associated with a particular substance, independent of the route of release.

3.2.2.3 Presence of Incompatible or Reactive Mixtures. The EPA HRS is the only system that gives guidance concerning the reactivity and incompatibility of mixtures of substances since it provides guidance in terms of classes of substances (e.g., alcohols mixed with metal hydrides). SPACE instructs individuals using the system to determine whether or not there are incompatible substances, and if so, whether they are safe distances apart; however, SPACE provides no guidelines for performing this type of assessment.

Both the SAS and RQ methods present criteria to help assess the reactivity and ignitability of individual substances, but not of mixtures of substances.

3.2.3 Use of Data

3.2.3.1 Number of Substances Evaluated. Five of the systems evaluate either "the most toxic" substance (HRS, RCRA) or are designed to evaluate one substance at a time (EEC, RQ and PPLV). Two systems (SAS and HARM II) evaluate all substances identified. Of the other two systems, SPACE evaluates the five most toxic substances; and SPHE evaluates 10 to 15 substances. Thus, seven of the nine systems consider one extreme or the other in numbers of substances per site (i.e., one or all).

In order to get a more characteristic toxicity profile of a site, it would be more appropriate to evaluate more than one substance per site. Although evaluation of all substances at a site would provide the most complete toxicity profile, the methodology becomes unwieldy due to the potentially large number of calculations necessary. The formula prescribed by SPACE, which evaluates the five most toxic substances, appears to be a reasonable compromise while still providing a toxicity profile.

3.2.3.2 Quantity of Data on Each Substance. Only three of the methodologies (HARM II, PPLV and SPHE) require extensive amounts of data to score the substances in question. These systems require additional information and calculations, such as the tabulation of multiple physical and chemical characteristics (e.g., vapor pressure, solubilities in various solvents and partition coefficients), or tabulation of the results of multiple toxicity

tests in multiple species of laboratory animals, or the selection of "structural analogues" of the substance under consideration and the tabulation of data for those analogues.

3.2.3.3 Clarity. Among the nine systems evaluated, five (HRS, SAS, RCRA, SPACE and RQ) are straightforward, logical, and easy to use. The EEC plan provides too little guidance to evaluate many factors. Both the PPLV and HARM II systems require many data manipulations and calculations that make the systems difficult to use. Both the SPHE and PPLV systems leave many aspects of the assessment to the "professional judgment" of the individual doing the assessment. This allows results derived using those methods to be subjective and less consistent than the other systems.

4.0 RECOMMENDATIONS FOR IMPROVEMENT TO THE HRS TOXICITY FACTOR

Both public comments on the EPA HRS and the present evaluation of how the EPA HRS toxicity factor is scored have called attention to the limitations of the system in assessing toxicity. The EPA HRS toxicity factor is based primarily on information contained in Sax (1975, 1979 and 1984), which generally uses acute toxicity data (the lowest mammalian LD_{50}). The toxicity factor is combined with environmental persistence by means of a matrix to provide a toxicity/persistence value which is used in the calculation of surface water and ground water migration route scores. The toxicity value is not combined with persistence in the air route.

As discussed in the preceding sections of this report, the major limitations of the EPA HRS with respect to the toxicity factor include the following:

- The evaluation of toxic effects relies heavily on Sax to assign toxic hazard ratings. Since Sax does not specify the rationale for each assigned value, it is not possible to verify his values.
- Chronic toxicity is not usually considered.
- CMT effects are not considered.
- There is little discrimination among the most toxic substances.

Although the overall objective of modifying the HRS toxicity factor is to design a system that would address these limitations and would thereby better reflect the relative hazards posed by the toxic substances at waste sites, some important constraints were

identified. In particular, the methodology must be easy to apply (i.e., a low level of toxicological expertise should be required); the system should use methodologies that have been approved by the scientific community; and where possible, the system should use readily available toxicity data.

In order to address the limitations and conform to the constraints, the following sections present several recommended modifications to the EPA HRS and the rationale underlying them.

4.1 Framework for Considering Toxicity

Prior to discussing the methodologies which are available for the assessment of the various aspects of toxicity, a framework is presented within which the toxicity of a substance may be considered. Since systemic toxicity is, to a large extent, dependent upon both rate and amount of a substance which enters the body, the toxicity of a substance can be affected by its mode of entry into the body. The major routes by which substances enter the body are via the lungs, the gastrointestinal tract, and the skin. Each of these routes differs in the efficiency with which it will absorb a substance and the time that it takes for absorption to occur. For instance, many substances that are absorbed well via the gastrointestinal route are not absorbed (or are absorbed extremely slowly and to a small extent) via the skin. Such substances could exert toxic effects if ingested, but toxicity would not be observed

if the exposure were only via the percutaneous route. Therefore, it seems appropriate to assess toxicity factors based upon the expected mode of entry into the body. If substances are expected to be ingested, a toxicity factor based upon the oral toxicity is appropriate, whereas if substances are expected to be inhaled, a toxicity factor based upon inhalational toxicity is appropriate.

The capacity of a substance to cause damage can be either acute in nature, that is, occurring shortly after the agent has been applied to the organism, or the effects may be chronic in nature. For the purposes of the present analysis, chronic effects are considered as those that are generally manifested after long-term, low-level exposure to a chemical. Chronic effects can be divided into two broad categories: non-neoplastic chronic effects* and carcinogenic and mutagenic (CM) effects. This framework is displayed schematically below.

$$\text{Toxicity}_{\text{route}} = f\,[\text{acute toxicity} + \text{chronic toxicity} + \text{CM}]$$

4.2 Type of Toxic Effect

4.2.1 Acute Toxicity

Toxic effects subsequent to acute exposure are of special relevance to people who may be exposed accidentally to high concentrations of substances for a brief period at or near hazardous wastes sites. For the purposes of this analysis, an acute exposure

*For reasons to be discussed below, developmentally toxic effects (including teratogenic effects) will be considered as non-neoplastic chronic effects.

is defined as exposure to a single dose over a short period (24 hours or less). The acute toxicity of hazardous substances is generally assessed through the use of LD_{50} or LC_{50} tests in laboratory rodents. Indeed, the most frequently determined index of toxicity is the LD_{50}. An LD_{50} may be calculated for oral, dermal, subcutaneous, intravenous, intraperitoneal, or other routes of exposure (LC_{50} for inhalational route). The EPA HRS toxicity factor is based on the LD_{50} appropriate for the route of exposure (e.g., LD_{50} [oral] for drinking water) when it is available. If the pathway-specific LD_{50} is unavailable, the factor is based on the lowest LD_{50} value available, regardless of mode of exposure.

Since exposure to substances present at wastes sites generally occurs only via oral, dermal, and inhalational modes, it is inappropriate to assign acute toxicity scores based on data from other than these modes of exposure (e.g., intraperitoneal, intravenous or subcutaneous injection data are not appropriate). It is recommended, therefore, that three acute toxicity values be assigned to a substance, one for each relevant mode of exposure (oral, dermal and inhalational). For oral or dermal exposures, LD_{50} data should be used; for substances which will be inhaled (including vapors, gases, dusts or mists) LC_{50} data should be used.

The lowest reported mammalian LD_{50} or LC_{50} for the appropriate mode of exposure should be used. This assumes that humans will respond to the hazardous substances in the same way as

the most sensitive test mammal. Such an assumption is conservative in that it may overstate risk. If a mammalian LD_{50} (LC_{50}) is not available, use of an LD_{lo} (LC_{lo}) is recommended. In the case of substances for which oral, dermal or inhalational LD_{50} (LC_{50}) data are not available, guidelines for establishing toxicity values based upon either dermal or ocular irritation are presented in Table 4. The assigned acute toxicity values range from 0 to 3 and are based upon EPA toxicology guidelines, including break points, as summarized by Ashton (1982). In the event that no acute toxicity data are available, use of the toxicity value obtained for chronic toxicity (discussed in Section 4.2.2) for the same route of administration is recommended. In the above scheme, the LD_{50} (LC_{50}) of the most sensitive mammal listed in the NIOSH Registry of the Toxic Effects of Chemical Substances is used to assign a toxicity value.

In the event that inhalational or dermal data are not available, the toxicity value for the dermal or inhalational route defaults to the toxicity value obtained via the oral route. Defaulting to that value does not imply a physiologic or mechanistic rationale for assigning an equivalent LC_{50} or dermal LD_{50} from orally derived data. Rather, the default to the oral toxicity value is used instead of defaulting to 0.

In the absence of toxicity data, a default to a score of 0 is the procedure that is followed in the current HRS. The rationale for this default value is that sites would then be scored on the

TABLE 4
PROPOSED ACUTE TOXICITY VALUES FOR ORAL, DERMAL AND INHALATIONAL EXPOSURES*

Acute Toxic Effects						
		Inhalational LC_{50}**				
Oral LD_{50} (mg/kg)	Dermal LD_{50} (mg/kg)	Dust or Mist (mg/liter)	Gas or Vapor (ppm)	Dermal Irritation	Ocular Irritation	Acute Toxicity Value***
>5,000	>20,000	>200	>20,000	No irritation within 72 hours	No irritation within 72 hours	0
>500-5,000	>2,000-20,000	>20-200	>2,000-20,000	Mild or slight irritation within 72 hours	No corneal opacity; irritation reversible within 72 hours	1
>50 500	>200-2,000	>2-20	>200 2,000	Moderate irritation within 72 hours	Corneal opacity reversible within 7 days, or irritation persisting for 7 days	2
≤50	≤200	≤2	≤200	Severe irritation or damage within 72 hours	Corneal opacity irreversible within 7 days	3

*Adapted from U.S. EPA Toxicology Guidelines, summarized by Ashton, 1982.

**The exposure period for acute inhalational studies is normalized to 4 hours using Haber's law which states that the product of exposure concentration and period of exposure is a constant ($Ct=K$).

***If LD_{50} or LC_{50} data are unavailable, dermal or ocular irritation data can be used as indicated above. If no acute data are available, the chronic toxicity value for same mode of exposure is used. If no toxicity data are available, assign a value of 0.

basis of known toxic effects. The issue of the appropriate default value is one that could be revisited. It is possible that a default to the highest value (3) could be assigned. Such a value would tend to overstate most dangers. If the HRS were to be used in a regulatory decision to establish allowable levels of a substance in the environment, the appropriate default seems to be one of a higher toxicity value in order to be conservative and to protect the public from unknown, potential danger. However, since the HRS is used as a screening tool to decide where additional resources should be allocated for further study (remedial investigation), a default to a score of 0 appears more appropriate because the sites would be scored on the basis of known dangers.

In addition to considering how acute toxicity may be assessed, it is appropriate to consider to what extent the acute toxicity value should affect the total value for assessment of toxicity for a particular substance. For instance, it is not expected that members of the general public would be exposed to large single doses of substances from abandoned hazardous waste sites; however, this is the exposure regime for acute toxicity studies in animals. This could be the basis for an argument to remove acute toxicity from consideration in determining the HRS toxicity value that is assigned to a hazardous substance. On the other hand, acute toxicity data are the most commonly available data and may provide the best common ground on which to compare chemicals. It is recommended that acute

toxicity be included in the determination of the toxicity factor value; however, acute toxicity should not carry as much weight as chronic toxicity in that determination.

4.2.2 Chronic Toxicity

It is recommended that chronic toxicity parameters for each mode of exposure (oral, dermal and inhalational) be added to the EPA HRS. The chronic toxicity parameters should be based upon the maximum daily dose of a substance that is anticipated to not pose a risk to adult (70 kg) humans after lifetime (70 years) exposure. The ADI method has been used to recommend regulatory limits and safety standards for maximum daily exposure to toxic substances in human food supplies and drinking water by various national and international scientific advisory and regulatory agencies including the U.S. EPA, the U.S. Food and Drug Administration, the Food and Agriculture Organization, and the World Health Organization (Kilgore and Li, 1980). The method is usually restricted to noncarcinogenic substances because it assumes there is a threshold dose for each substance below which there is no adverse effect. The assumption of a threshold is not widely accepted for carcinogens.

The ADI is based on a No Observed Effect Level (NOEL) and a Margin of Safety (MOS). The NOEL is obtained from chronic or subchronic experiments in laboratory animals. The NOEL is the highest dose of a substance, in a series of dose levels tested, at which no adverse effect is detected in treated animals compared to

untreated control animals. The ADI is calculated from the NOEL by dividing by the MOS; i.e.,

$$ADI = NOEL/MOS$$

The MOS is a factor that converts an apparently safe daily dose in laboratory animals to a presumed safe daily dose for humans. The MOS is the product of several safety factors and ranges from 10^1 to 10^5. The safety factors (e.g., f_1, f_2, . . . f_n) are commonly, but not always, each equal to 10. A summary of the justification for using safety factors of 10 is presented in Kushner et al. (1983), although other authors have suggested the use of safety factors of alternative (usually smaller) magnitudes (Zielhuis and van der Kreek, 1979). In calculating the MOS, safety factors are multiplicative ($f_1 \times f_2 \ldots \times f_n$), and can account for such uncertainties as (Klaassen, 1986):

- Variation in susceptibility among humans.
- Difference between the sensitivity of the test species and humans.
- Lack of confidence in the experimental data or less than ideal conditions (e.g., conversion of LOEL* to NOEL or using subchronic rather than chronic lifetime tests).

Recently, the Office of Research and Development (ORD) of EPA has assessed the chronic toxicity of substances through the establishment of reference dose (RfD) values. RfDs are established for noncarcinogenic effects. The RfD methodology is similar in

*LOEL = The lowest observed effect level.

concept to the ADI methodology. The primary difference between ADI and RfD methodologies is that RfDs are never calculated based on acute data. About 200 RfDs have been subjected to Agency-wide verification (DeRosa, 1987), most of which have been based on oral exposures.

Although MITRE concurs with the scientific underpinnings of the RfD methodology, the relatively small number of currently available RfDs and the paucity of chronic data for substances listed at hazardous waste sites require that a more flexible method be used to evaluate the relative chronic toxicity of substances. In cases where the only toxicity data available for a substance are acute toxicity data, it is a mistake for a screening tool (such as the HRS) to postpone assessing the hazard until appropriate data become available or to use an arbitrary default value. Therefore, it is recommended that in cases where RfDs are available they be used as described in Section 4.2.2.4, and that when they are not available, an ADI be calculated to assess the relation chronic toxicity.

The recommended methods for calculating ADIs for substances based upon exposure via ingestion, direct contact, or inhalation are presented below.

The great strength of the ADI is that it uses the best toxicity data that are available. Thus, if human data are available, they may be used in the calculation of an ADI. In the event that human data are not available, animal data are used. Chronic and subchronic data are preferred but, if necessary, acute toxicity data can be used. Note that calculation of an ADI by this method is not presumed to be

anything more than a means to derive a relative toxicity value for use in the HRS. It is not intended to actually set Acceptable Daily Intakes.

4.2.2.1 Calculation of an ADI: Ingestion. Calculation of an ADI for ingestion uses toxicity data derived from studies of laboratory animals exposed via the oral route when data for human exposure are not available. Studies which can be used to identify a NOEL or LOEL (i.e., chronic or subchronic studies) are preferred for this calculation because of the long term nature of the studies used to calculate the NOEL or LOEL as opposed to the acute nature of the studies used to determine other toxicity indices (e.g., LD_{50}).

The following guidelines (adapted from U.S. EPA, 1980) are recommended as a means of calculating an ADI for oral exposure from data derived from a variety of experimental designs.

A. NOEL Available

If a $NOEL_{oral}$ is available:

$$ADI_{oral} = NOEL_{oral}/MOS$$

The MOS is calculated as follows:

- If human data are available, MOS = 10 (human variability)
- If only data for laboratory animals are available, MOS = [10 (species extrapolation) x 10 (human variability)] = 10^2

B. LOEL Available

If a $NOEL_{oral}$ is not available but a $LOEL_{oral}$ is available:

$$ADI_{oral} = LOEL_{oral}/MOS$$

The MOS is calculated as follows:

- If human data are available, MOS = [10 (human variability) x 10 (conversion of LOEL to NOEL)] = 10^2
- If only data for laboratory animals are available, MOS = [10 (species extrapolation) x 10 (human variability) x 10 (conversion of LOEL to NOEL)] = 10^3

C. TD_{lo}* Available

If only TD_{lo} oral data are available:

$$ADI_{oral} = TD_{lo}/MOS$$

The MOS is calculated as follows:

- If human data are available, MOS = [10 (human variability) x 100 (conversion of TD_{lo} to NOEL)] = 10^3
- If only data for laboratory animals are available, MOS = [10 (species extrapolation) x 10 (human variability) x 100 (conversion of TD_{lo} to NOEL)] = 10^4

D. LD_{lo}** or LD_{50} Available

If only LD_{lo} or LD_{50} data are available:

$$ADI_{oral} = LD_{lo}/MOS \text{ or } LD_{50}/MOS$$

The MOS is calculated as follows:

- If human data are available, MOS = [10 (human variability) x 1000 (conversion of LD_{lo} or LD_{50} to NOEL)]*** = 10^4
- If only data for laboratory animals are available, MOS = [10 (species extrapolation) x 10 (human variability) x 1000 (conversion of LD_{lo} or LD_{50} to NOEL)] = 10^5

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*TD_{lo} = The lowest dose which causes a toxic effect in any animal in the test group.

**LD_{lo} = The lowest dose which causes the death of any animal in the test group.

***The LD_{lo} of a substance is generally 1/10 the LD_{50} value. However, since the LD_{lo} is a single observed mortality, confidence in its value is weaker than in the LD_{50} (which is calculated from statistical analysis). Thus, an additional factor of 10 in the MOS (for conversion of LD_{lo} to LD_{50}) is effectively cancelled out by the difference in magnitude between the two values.

4.2.2.2 Calculation of an ADI: Dermal. Calculation of an ADI for exposure to substances by direct contact (dermal exposure) uses toxicity data derived from studies of humans or laboratory animals exposed via the dermal route over their lifetime. Studies which can be used to identify a NOEL or LOEL (i.e., chronic or subchronic studies) are preferred for this calculation because of the long term nature of the studies conducted to calculate the NOEL or LOEL as opposed to the acute nature of the studies which provide other toxicity indices (e.g., LD_{50}).

The following guidelines (adapted from EPA, 1980) may be used to calculate an ADI for dermal exposure from data derived from a variety of experimental designs.

A. NOEL Available

If a $NOEL_{dermal}$ is available:

$$ADI_{dermal} = NOEL_{dermal}/MOS$$

The MOS is calculated as follows:

- If human data are available, MOS = 10 (human variability)
- If only data for laboratory animals are available, MOS = [10 (species extrapolation) x 10 (human variability)] = 10^2

B. LOEL Available

If a $NOEL_{dermal}$ is not available but a $LOEL_{dermal}$ is available:

$$ADI_{dermal} = LOEL_{dermal}/MOS$$

The MOS is calculated as follows:

- If human data are available, MOS = [10 (human variability) x 10 (conversion of LOEL to NOEL)] = 10^2
- If only data from laboratory animals are available, MOS = [10 (species extrapolation) x 10 (human variability) x 10 (conversion of LOEL to NOEL)] = 10^3

C. TD_{1o} Available

If only TD_{1o} dermal data are available:

$$ADI_{dermal} = TD_{1o}/MOS$$

The MOS is calculated as follows:

- If human data are available, MOS = [10 (human variability) x 100 (conversion of TD_{1o} to NOEL)] = 10^3
- If only data from laboratory animals are available, MOS = [10 (species extrapolation) x 10 (human variability) x 100 (conversion of TD_{1o} to NOEL)] = 10^4

D. LD_{1o} or LD_{50} Available

If only LD_{1o} dermal or LD_{50} dermal data are available:

$$ADI_{dermal} = LD_{1o}/MOS \text{ or } LD_{50}/MOS$$

The MOS is calculated as follows:

- If human data are available, MOS = [10 (human variability) x 1000 (conversion of LD_{1o} or LD_{50} to NOEL)] = 10^4
- If only data from laboratory animals are available, MOS = [10 (species extrapolation) x 10 (human variability) x 1000 (conversion of LD_{1o} or LD_{50} to NOEL)] = 10^5

4.2.2.3 Calculation of an ADI: Inhalation. Calculation of an ADI inhalation uses toxicity data derived from studies of laboratory animals exposed via inhalation. The Threshold Limit Value-Time Weighted Average (TLV-TWA)*, as defined by the American Conference of Governmental Industrial Hygienists (ACGIH, 1985), is usually used as the basis for the inhalational ADI calculation. TLV-CL values

*Threshold Limit Value-Time Weighted Average (TLV-TWA) is defined as the maximum average concentration for a normal 8-hour workday and a 40-hour workweek, to which nearly all workers may be repeatedly exposed, day after day, without adverse effect.

are not to be used because they are not designed to protect people from long term exposure, but rather to set a upper bound on exposure levels which should not be exceeded. If a TLV-TWA is not available, the OSHA standard air TWA may be used. TLV-TWA or OSHA standard air TWA values are preferred for the calculation over data from nonhuman laboratory studies using LC_{50}, NOEL, or LOEL data because TLV-TWAs and OSHA standard air TWAs are human estimates.

The following guidelines (adapted from U.S. EPA, 1980) may be used to calculate an ADI for inhalational exposure from data derived from a variety of sources.

A. TLV-TWA Available

If a TLV-TWA is available:

$$ADI_{inhalation} = TLV\text{-}TWA(mg/m^3) \times 10\ (m^3/day) \times 8/24 \times 5/7 \times (0.5)/MOS = 1.19 \times TLV\text{-}TWA/MOS$$

where:

10 m^3/day = Estimated amount of air breathed per workday

8/24 = Conversion of an 8 hour workday to a 24 hour day

5/7 = Conversion of a 5 day/week exposure to a 7 day/week exposure

0.5/1.0 = Efficiency of absorption of airborne chemicals from air exposure (0.5) and from oral exposure (1.0)*

MOS = 10 to account for human variability

*Although many scientists believe that the efficiency of pulmonary absorption may be equal to that of gastrointestinal absorption, the assumption of 50 percent absorption decreases the magnitude of the calculated ADI and is, therefore, conservative in that it may overestimate risk.

B. Animal Data Available

If only animal toxicity data are available, the following formula may be used to calculate an $ADI_{inhalation}$:

$ADI_{inhalation}$ = CA x DE x d x (0.5) x BRA x 70 kg/(BWA x MOS)

where:

CA = Lowest reported concentration of chemical in the air (in mg/m^3) that caused an effect

DE = Duration of exposure (hours/day)

d = Number of days exposed/number of days observed

0.5/1.0 = Efficiency of absorption of airborne chemicals from air exposure (0.5) and from oral exposure (1.0)

BRA = Volume of air breathed by the animal in one day (m^3)

70 kg = Assumed human body weight

BWA = Body weight of experimental animals (kg)

MOS = [10 (species extrapolation) x 10 (human variability)] = 10^2

4.2.2.4 Use of RfDs or ADIs to Evaluate Chronic Toxicity. It is recommended that the magnitude of the RfD or calculated ADI be used as the basis for evaluating the relative chronic toxicity potential of a substance. The chronic toxicity value may be assigned based on the RfD or ADI, as presented in Table 5. The assigned values range from 0 to 3 and are the same as to the range of values of the proposed acute toxicity factor.

The break points for chronic toxicity values were selected to provide a reasonable distribution of values among the substances to

TABLE 5

PROPOSED CHRONIC TOXICITY VALUES BASED ON REFERENCE DOSES OR ACCEPTABLE DAILY INTAKES FOR ORAL, DERMAL AND INHALATIONAL EXPOSURES

RfD or ADI Oral (mg/kg/day)	RfD or ADI Dermal (mg/kg/day)	RfD or ADI Inhalational (mg/kg/day)		Assigned Toxicity Value
		Dust or Mist	Gas or Vapor	
>5.0	>20	>0.2	>20	0
>0.5-5.0	>2.0-20	>0.02-0.2	>2.0-20	1
>0.05-0.5	>0.2-2.0	>0.002-0.02	>0.2-2.0	2
≤0.05	≤0.2	≤0.002	≤0.2	3

be assessed. In the event chronic toxicity data are not available for dermal or inhalational routes, the pathway-specific acute toxicity value may be used (except when based on irritation). In the event no toxicity data are available for either the inhalational or dermal modes of exposure, the assigned oral chronic toxicity value is to be used as the default value for the inhalational or dermal chronic toxicity value. If no toxicity data are available at all, a value of 0 is assigned. The discussion of the issues surrounding default values is the same as that presented previously for the acute toxicity assessment (see Section 4.2.1).

4.2.3 Carcinogenicity, Mutagenicity, and Teratogenicity (CMT) Potential

The EPA HRS does not consider the possible carcinogenic, mutagenic, or teratogenic actions of substances. It is recommended that the toxicity factor be modified to account for the possible carcinogenicity, mutagenicity and teratogenicity of substances. Although CMT effects are frequently considered together in regulatory toxicology, the grouping of the effects is for convenience. There is no clear mechanistic linkage among the three types of effects. Indeed, many investigators believe that environmental agent-induced teratogenesis demonstrates a threshold (Wilson, 1977; Beckman and Brent, 1986), whereas the concept of a threshold is not believed to apply to carcinogenesis or mutagenesis. Since agents that induce teratogenesis exhibit a threshold, it is recommended that they be assessed under the

methodology described for chronic toxicity (Section 4.2.2). Since carcinogenesis and mutagenesis are considered to be stochastic events (i.e., they do not exhibit thresholds), it is suggested that they be assessed together as described below.

A combined weight-of-evidence and relative potency approach is suggested for determination of the CM factor. This type of approach combines qualitative assessment of the reliability of carcinogenicity data for a given substance with a quantitative assessment of the relative potency of that substance to induce cancer.

A weight-of-evidence approach is a method for assigning values based upon a set of predetermined guidelines. For the proposed CM factor, the first step is to determine the weight-of-evidence. Those substances for which epidemiological studies indicate the substances produce carcinogenic effects in humans or for which laboratory tests demonstrate carcinogenic effects in multiple species of test mammals are assigned to Category III. Substances which produce carcinogenic effects in one species of test mammal or mutagenic effects in one or more whole animal tests, but for which there are no relevant human data, are assigned to Category II. Substances which are mutagenic in cellular systems, but have not yet been proven to produce carcinogenic effects in humans or animals, are assigned to Category I. Substances which have been tested in any of the above systems but were found to be inactive are assigned to Category 0. Guidelines for assigning the CM weight-of-evidence

categories, based on the weight-of-evidence approach (adapted from Squire, 1981 and U.S. EPA, 1986), are presented in Table 6.

The sources of data acceptable for evaluation of the CM weight-of-evidence categories are the Registry of Toxic Effects of Chemical Substances (RTECS) (Tatken and Lewis, 1982; Lewis and Sweet, 1985), the International Agency for Research on Cancer (IARC), the National Toxicology Program (NTP), and the National Cancer Institute (NCI). If no data exist from any of the above sources, the substance is assigned to Category 0. The discussion surrounding default values is the same as discussed under acute toxicity (Section 4.2.2).

The second step in determining the CM factor is to estimate the relative carcinogenic potency (i.e., the efficacy) of the substance. The carcinogenic potency of a substance is usually determined through low dose extrapolations using sophisticated mathematical models that have theoretical bases in the presumed mechanism of carcinogenic action. The most commonly used of these models is Crump's Global 82. Use of such mathematical models requires access to high quality laboratory animal data. In addition, a high level of expertise is required in deciding the appropriate model to use since for some carcinogens (e.g., amitrole) multistage models such as Global 82 are not appropriate in determining carcinogenic potency.

TABLE 6

PROPOSED CM* WEIGHT-OF-EVIDENCE CATEGORIES

Evidence	CM Weight-of-Evidence Category
Available information demonstrates the substance is carcinogenic to humans or to multiple mammalian test species.	III
Available information demonstrates the substance is carcinogenic in a single mammalian test species and/or mutagenic in one or more whole animal tests (human evidence is not available).	II
Available information demonstrates the substance is mutagenic in cellular systems but information for whole animals is not available.	I
Available data demonstrate the substance to be neither carcinogenic nor mutagenic in humans, animals, or cellular systems.	0
No data are available.	0

*CM = carcinogenicity and mutagenicity.

An alternative method to the low dose extrapolation approach uses the ED_{10}. The ED_{10} methodology estimates the lifetime daily dose of a substance which causes 10 percent of the animals to have a particular lesion, in this case, cancer. Most studies published in peer reviewed journals and/or studies conducted by the National Toxicology Program or National Cancer Institute have a sufficient number of treated and control groups to allow the incidence of tumors to be plotted as a function of dose. Generally, the ED_{10} level is in the linear range of the dose response curve and consequently, sophisticated modeling procedures such as are used in the Global 82 method are not necessary. The magnitude of the estimated ED_{10} (in mg/kg/day) can be used as an indicator of the carcinogenic potency of a substance. The proposed relative carcinogenic potency groups, based on the magnitude of the ED_{10}, are presented in Table 7. Substances for which an ED_{10} is not available or for which inadequate data exist to calculate an ED_{10} are assigned a relative carcinogenic potency of low.

The final step in determining the proposed CM value for a substance is accomplished by combining the weight-of-evidence category with the relative carcinogenic potency group according to the matrix in Table 8. The proposed CM values range from 0 to 3.

4.2.4 Toxicity of Metals

One class of hazardous substances which is particularly difficult to assess toxicologically is the metals. Metals exist in

TABLE 7

PROPOSED RELATIVE CARCINOGENIC POTENCY GROUPS BASED ON THE CARCINOGENIC ED_{10}

ED_{10} (mg/kg/day)	Carcinogenic Potency Group
0.01	High
1.0-0.01	Medium
1.0	Low

TABLE 8

PROPOSED CM* VALUES BASED ON WEIGHT-OF-EVIDENCE AND RELATIVE POTENCY

Weight-of-Evidence Category	Relative Potency Group		
	Low	Medium	High
0	0	0	0
I	1	1	2
II	1	2	3
III	2	3	3

*CM = Carcinogenicity and Mutagenicity.

various forms in the environment, including inorganic metal salts (e.g., nickel chloride and zinc sulfate), organometallic compounds (e.g., methylmercury), and other covalently bound metals (e.g., zinc sulfide and iron oxide). When metals have been identified at NPL sites, analytical data are reported as total metal without specifying the type of metal compound. For example, lead chloride, lead sulfate, lead oxide, lead sulfide, and tetraethyl lead each have their own toxicity characteristics, CAS numbers, and can be assigned toxicity factor values using the EPA HRS. However, analytical results would report the sum of these substances as simply lead. Unless an inventory or other means of identifying the individual lead compounds is available, they would be listed under a common heading of "lead, NOS" (Not Otherwise Specified).

A scientifically defensible, reasonable approach would evaluate such substances on the basis of the most toxic chemical that contains the metal in question. Due to the large number of entries in RTECS for any given metal (e.g., lead), a method must be found to reduce the number of substances to be assessed. It would be appropriate to confine the toxicity factor evaluation to substances that have been defined as "hazardous substances" by the EPA. A list of 717 hazardous substances has been compiled under CERCLA. Therefore, it is recommended that the assignment of toxicity values to metals, NOS or unspecified metal compounds be accomplished in the following manner. First, obtain the identities of all species of

that metal which are found in the CERCLA list of hazardous substances. Then, identify the most toxic species for which there are toxicity data and which contain a single moiety that is expected to be active in causing toxicity. The most toxic species in that list is denoted by the species with the smallest reportable quantity (RQ). The current list of RQs is presented in the March 16, 1987 Federal Register (52 FR 8140).

As an example, the selection of the appropriate compound for assigning a toxicity value to "lead and compounds, NOS" follows. According to the CERCLA RQ list, there are 12 lead-containing compounds. The lead compound with the smallest RQ (1) is lead arsenate. Since that substance is comprised of two metals, it is not used to assign a toxicity value. Two lead-containing substances have RQs of 10: lead acetate and tetraethyl lead. Since tetraethyl lead has both more and better toxicity data (including an oral RfD and a TLV-TWA), it would be selected as the lead compound to use for assigning a toxicity factor value to all unspecified lead compounds.

4.3 Determinants of Exposure

4.3.1 Persistence

Exposure to a substance depends, in part, on its persistence in the environment. Since the chance of long-term exposure to a toxic substance in the environment is directly related to the stability of the substance in the environment, substances which are easily degraded present less chance of chronic exposure than those which

are resistant to degradation. The current EPA HRS presents guidelines for evaluating persistence based upon biodegradation. Although the criteria for assigning a persistence value were not analyzed in depth by the present study, it is apparent that other types of physical and chemical processes can cause a substance to be lost from the environment (e.g., photolysis by sunlight; hydrolysis in aqueous environment; volatilization from soil or water). Other HRS-related studies have indicated that biodegradation is not an important loss mechanism within the context of the HRS. Efforts are underway to modify or replace the current, biodegradation-based persistence factor. It is recommended that EPA continue its effort to review the current persistence factor but to separate this consideration from the toxicity factor.

4.3.2 Routes of Release

It is recommended that the EPA HRS continue to evaluate the hazard from hazardous substances which have been or may be released from hazardous wastes sites by any of the migration pathways. Pathway-specific toxicity values should be used in the calculation of the different pathway scores. For each pathway, a pathway-specific toxicity value should be calculated that incorporates measures of acute toxicity, as well as chronic toxicity and CM effects. As described below, it is recommended that the toxicity factor value be calculated from an equation that adds terms for acute toxicity, chronic toxicity and CM effects. The additive

nature of this scheme allows the chronic toxicity and CM effects to be weighted more heavily than the acute effects and it prevents a very low value (e.g., zero) for any one toxic effect from negating the effects in others. A multiplicative scheme would be undesirable for this reason.

The $toxicity_{oral}$ value should be used as the toxicity factor value in the surface water and ground water pathways. The $toxicity_{oral}$ value is calculated as follows:

$$toxicity_{oral} = \text{acute } toxicity_{oral} \text{ value} + \text{chronic } toxicity_{oral} \text{ value} + CM$$

As an example, the $toxicity_{oral}$ value for chloroform is calculated in Table 9. The $toxicity_{inhalational}$ (for the air pathway) and $toxicity_{dermal}$ (for direct contact) values are calculated in a similar manner.

The pathway-specific toxicity values range from 0 to 9 (in unit increments) in this recommended change to the HRS compared to a range of 0 to 3 for the toxicity rating factor of the current HRS. Note that the current HRS also uses a multiplier of 3 for the toxicity factor, yielding an effective range of values from 0 to 9 in increments of 3.

4.3.3 Presence of Incompatible or Reactive Mixtures

The current HRS does an adequate job of assessing incompatibility/reactivity for the purposes of toxicological assessment; therefore, no changes are recommended in this part of the system.

TABLE 9

EXAMPLE CALCULATION OF $TOXICITY_{ORAL}$ VALUE (CHLOROFORM)

Type of Toxicity	Basis	Value
Acute	LD_{50} = 36 mg/kg (mouse)	3
Chronic	RfD = 0.01 mg/kg/day	3
CM	a. Weight-of-Evidence Category III (+ rat; + mouse)	
	b. Potency Group Medium (ED_{10} = 0.508 mg/kg/day)	
	c. III x Medium from Matrix*	3
$Toxicity_{oral}$ Value	Acute + Chronic + CM	9

*See Table 8.

4.4 Use of Data

4.4.1 Number of Substances Evaluated

The current EPA HRS assigns a toxicity value for a pathway based upon "the substance with the highest score (toxicity/persistence)." As has been shown in Tables 1 and 2, this practice results in little discrimination among NPL sites based on toxicity. This occurs because the majority of NPL site migration pathways are assigned toxicity values on a very limited number of substances receiving high factor values, at least one of which can be found among the multiple substances identified at most sites. The proposed revision to the EPA HRS toxicity factor will provide increased discrimination among substances. However, if only the single "most toxic" substance is used for the site evaluation, it is likely that many sites (most of which contain multiple substances) will be evaluated on the same "most toxic" substance as is currently done. This, once again, is expected to provide little discrimination among NPL sites. To provide a better profile of the combined estimated toxicity of the substances at a site, and to provide additional discrimination among sites, it is recommended that each site be rated for toxicity for each relevant pathway by combining toxicity values of the five "most toxic" substances (defined below) found at the site and available for migration. The toxicity values of multiple substances will provide a better toxicity assessment of the hazard posed by a site than will the toxicity value of a single

substance. Although the assessment of the potential hazard from all substances present at a site would give the best toxicity assessment for a site, such an assessment would be time-consuming and could possibly understate the danger associated with very toxic substances if a large number of weakly toxic substances were also present. The assessment of the potential hazard associated with a site based on the five highest ranking substances is a reasonable compromise. The toxicity values can be combined in a variety of ways. For example, the average of the toxicity values assigned could be used as a convenient method to normalize the value. Alternatively, the geometric mean of the toxicity values for the five most toxic substances could be used. Whichever method is used must account for the possibility of a site with fewer than five substances. This is to ensure that the combined toxicity value is not less at a site with few substances than that at a site with the same plus additional substances.

It is recommended that "most toxic" be defined by the numerical designations of the toxicity values assigned to of substances available for migration in a given pathway. For each pathway, at each site, the five substances (potentially) available for migration by that pathway, with the highest appropriate $\text{toxicity}_{\text{route}}$ values, would be used. Thus, the selection of the most toxic substances would be migration pathway-specific. For example, to evaluate the pathway water route, substances present in the ground water (or available to migrate to ground water) would be evaluated

to determine their $toxicity_{oral}$ values. The five substances with the highest values would be used to assign a value to the toxicity factor in the ground water pathway.

The increased discrimination among the values assigned to 30 selected substances is demonstrated in Table 10. The data supporting these values are presented in Appendix J. Under the current HRS toxicity factor evaluation method, possible values range from 0 to 3. Ten of the substances are assigned toxicity values of 2, the remaining 20 substances are assigned a 3. Under the proposed pathway-specific methodology, the substances have possible values that range from 0 to 9 for each of the 3 pathways. The substances were assigned values that ranged from 3 to 9 for the oral and dermal pathways; and from 1 to 9 for the inhalational pathway. The toxicity values of a particular substance differ according to the underlying data, as is exemplified by chloroform which has a $toxicity_{oral}$ value of 9, $toxicity_{dermal}$ value of 7, and a $toxicity_{inhalational}$ value of 5.

4.4.2 Quantity of Data on Each Substance

The preferred source of toxicity data for use in the proposed methodology is RTECS because it contains all of the toxicity data required to assess a substance. RTECS is intended to be a single data source. It presents toxicity data concerning the lowest reported dose of a substance to cause toxic effects by several routes of exposure in various species. The RTECS data base is

TABLE 10

COMPARISON OF TOXICITY VALUES USING THE CURRENT EPA HRS WITH THE PROPOSED PATHWAY-SPECIFIC TOXICITY FACTOR METHODOLOGY

	Current HRS Toxicity Value	Proposed Pathway-Specific Toxicity Values		
		Oral	Dermal	Inhalational
Acetone	2	4	4	2
Arsenic and Compounds, NOS	3	9	9	9
Benzene	3	4	5	4
Benzo(a)pyrene	3	7	6	7
Cadmium and Compounds, NOS	3	8	8	9
Carbon Tetrachloride	3	7	7	5
Chlorobenzene	2	4	4	2
Chloroform	3	9	7	5
Chromium and Compounds, NOS	3	8	8	9
Chromium, Hexavalent	3	8	8	9
Chromium, Trivalent	2	3	3	5
Copper and Compounds, NOS	3	7	7	5
Creosote	2	5	5	7
DDT	3	8	8	9
1,1-Dichloroethylene	3	8	8	6
Lead and Compounds, NOS	3	7	6	7
Lindane	3	7	8	8
Mercury and Compounds, NOS	3	6	6	6
Methyl Ethyl Ketone	2	3	4	1
Naphthalene	2	5	5	3
PCBs (Arochlor), NOS	3	7	7	9
Pentachlorophenol	3	5	7	7
Phenanthrene	3	5	5	5
Phenol	3	5	6	5
Tetrachloroethylene	2	4	7	4
Toluene	2	4	5	2
1,1,1-Trichloroethane	2	3	6	3
1,1,2-Trichloroethylene	2	6	8	4
Vinyl Chloride	3	7	7	6
Zinc and Compounds, NOS	3	6	6	6

updated annually; the last hard copy editions (Tatken and Lewis, 1982; Lewis and Sweet, 1985) contain entries for a total of 57,599 substances. Updates are available on-line. TLVs are listed in RTECS; alternatively, they may be obtained from the American Council of Governmental and Industrial Hygienists. RfDs and ED_{10} are available on-line on EPA's IRIS system. Alternatively, they are listed in the appendices of the Superfund Public Health Evaluation Manual (ICF, 1986).

4.4.3 Clarity

Details of the recommended method for assessing acute and chronic toxicity and CM effects have been described in Sections 4.2.1 to 4.2.3. The recommended methodology provides a logical evaluation method and allows the toxicity potential of substances to be assessed independently for each potential mode of exposure. In addition, pathway-specific toxicity values can be calculated for substances in advance and be provided as guidance (a look-up table) for the substances commonly identified at NPL. The supporting data from which the values were derived and further description of the methodology (including an example) are presented in Appendix I.

5.0 GLOSSARY

Acute Toxicity	Acute toxicity is the capacity of a substance to cause adverse effects occurring within a short time (usually 4 days or less, but up to 14 days) following administration of a single exposure or multiple exposures of that substance within a 24-hour period.
ADI	The acceptable daily intake is the maximum daily dose of a substance that is anticipated to be without risk to adult (70 kg) humans after a lifetime (70 years) of exposure. Calculated by dividing the NOEL by a MOS. Substitutions for the NOEL, such as an LD_{50}, LC_{50}, LOEL or TLV-TWA, can be made with appropriate adjustments in the MOS.
Bioaccumulation	Bioaccumulation is the uptake of a substance from the environment, via a biological process, to be incorporated into and stored within tissue.
CM	CM is an abbreviation for carcinogencity and mutagenicity.
CMT	CMT is an abbreviation for carcinogenicity, mutagenicity, and teratogenicity.
Carcinogens	Carcinogens are agents that induce cancer.
Carcinogenicity	Carcinogenicity is the ability of an agent to cause cancer.
Chronic Toxicity	Chronic toxicity is the capacity of a substance either to cause adverse effects resulting from repeated exposures to that substance throughout a long period of time, for instance, greater than 50 percent of the lifespan of a laboratory rodent (e.g., 12 to 15 months in rat strains), or to cause adverse effects that appear much later in time than the initial exposure.

EC_{50}	The effective concentration, 50 percent, is the concentration in air or water (any fluid) of a chemical that elicits a measurable effect within a specified period of time in 50 percent of a group of treated animals above the background incidence (in control animals) of that effect.
ED_{10}	The effective dose, 10 percent, is the dose that elicits any measurable effect in 10 percent of a group of treated animals above the background incidence (in control animals) of that effect.
EDE	The equivalent dose estimate is that dose at which the estimated risk associated with a compound is comparable among all compounds being evaluated.
Incompatible Substances	Substances which, when commingled under uncontrolled conditions, produce heat or pressure; fires or explosions; violent reactions; toxic dusts, mists or gases; or flammable fumes or gases.
Intraperitoneal	Intraperitoneal means within the abdominal cavity.
LC_{50}	The lethal concentration, 50 percent, is the concentration in air or water of a substance that kills 50 percent of a group of treated animals within a specified period of time.
LC_{50}	The lethal concentration, low, is the concentration in air or water of a substance that kills at least one of a group of treated animals within a specified period of time.
LD_{50}	The lethal dose, 50 percent, is the dose of a substance that kills 50 percent of a group of treated animals within a specified period of time.
LD_{lo}	The lethal dose, low, is the lowest dose of a substance that kills at least one of a group of treated animals within a specified period of time.

LOEL (or LEL)	The lowest observed effect level (LOEL) is the lowest dose, in a series of doses tested in long term (chronic or subchronic) studies, at which an adverse effect is observed in the species tested.
Log P	The logarithm of P is the logarithm of the ratio of the concentration of a substance in octanol to the concentration of the substance in water. It is considered to be a measure of lipophilicity and to be directly proportional to the ease with which a substance can cross biological membranes and thereby enters the body. It is used to estimate bioaccumulation potential.
MCL	The maximum concentration limit is the maximum permissible level of a contaminant in water that may be delivered to a user of a public water system serving a minimum of 25 people. The maximum concentration limits are promulgated pursuant to Section 1412 of the Safe Drinking Water Act.
MED	The minimum effective dose is the minimum dose of a substance that elicits a statistically significant incidence of an effect above the background incidence (in controls).
MOS	The margin of safety is a factor used to convert a no observed effect level (NOEL) derived from laboratory animal toxicity data to a presumed safe lifetime daily dose for humans. The conversion factor accounts for variability in sensitivity within and among species and for varying confidence in the quality of the data.
Multistage Model	The multistage model is a mathematical model that describes the dose-response relationship for carcinogens at very low doses. The model assumes that a tumor can be induced from a single cell only after that cell has undergone several heritable changes caused by a substance.
Mutagens	Mutagens are substances that cause heritable alterations in genetic material.

Mutagenicity	Mutagenicity is the ability of an agent to cause mutations.
Mutation	A mutation is an alteration in genetic material that is potentially heritable (i.e., able to be transmitted to offspring).
NOEL	The no observed effect level (NOEL) is the highest dose, in a series of dose levels tested, at which no adverse effect is observed in the species tested.
Ocular Irritation	Ocular irritation is a local inflammatory reaction of tissues of the eye following direct instillation of a substance in the eye.
One-hit Model	The one-hit model is a mathematical model that describes the dose-response relationship for carcinogens at very low doses. The model is based on the concept that a tumor can be induced when a single cell has undergone a single heritable change caused by a substance.
Partition Coefficient	Partition coefficient is the ratio of the concentration of a substance in one solvent (phase) to the concentration of the substance in a second solvent (phase). For biological studies, the solvents are usually octanol/water.
Percutaneous	Percutaneous is the transfer of a substance through the skin into the body.
Reactive Substances	Substances that are normally unstable and readily undergo violent change without detonating; that react violently with water; that form potentially explosive mixtures with water; that generate toxic gases, vapors, or fumes when mixed with water; that are capable of detonation or explosive reaction if subjected to a strong initiating source or if heated under confinement; or that are readily capable of detonation or explosive decomposition or reaction at normal (ambient) temperatures and pressures.

Reportable Quantity (RQ)	Reportable quantity is the quantity of a substance, as specified in 40 CFR 302, that, when released into the environment, may present substantial danger to public health or welfare or the environment. Therefore, the release of a substance into the environment must be reported if it exceeds an expressed quantity.
Subchronic Toxicity	Subchronic toxicity is the capacity of a substance to cause adverse effects resulting from repeated exposure to a substance throughout a limited period of time, for instance, less than 10 percent of the lifespan of laboratory rodents (e.g., 3 months in rat strains).
Subcutaneous	Subcutaneous refers to beneath the skin.
TC_{50}	The toxic concentration, 50 percent, is the concentration in air of a chemical that elicits a measurable adverse effect in 50 percent of a group of treated animals above the background incidence (in control animals) of that effect.
TD_{lo}	The toxic dose, low, is the lowest dose of a substance that is toxic to at least one of a group of treated animals.
Teratogen	A teratogen is a substance that causes birth defects.
Teratogenicity	Teratogenicity is the ability of an agent to cause birth defects.
TLV-TWA	The threshold limit value--time-weighted average (TLV-TWA) is the concentration of a substance in air averaged over a normal 8-hour workday and a 40-hour work week, which causes an adverse effect in "nearly all" workers (except the most sensitive). The TLV-TWA is expressed in units of ppm and mg/m^3.
UCR	The unit cancer risk is defined as the upper limit on the lifetime probability that a chemical will cause cancer at a dose of 1 mg/kg body weight/day.

Weight-of-Evidence	A ranking or weighting of data for substances to predict their potential for toxicity in humans according to a defined set of rules.

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APPENDIX A

ENVIRONMENTAL PROTECTION AGENCY NOTIFICATION REQUIREMENTS: CERCLA REPORTABLE QUANTITIES (RQ)

Sections 103(a) and 103(b) of CERCLA require that persons in charge of vessels or facilities from which hazardous substances have been released in quantities that are equal to or greater than statutory reportable quantities (RQs) immediately notify the National Response Center of the release. The RQ levels, which may be 1, 10, 100, 1,000, or 5,000 pounds, reflect EPA's judgment of which releases should trigger mandatory notification so that the need for Federal removal or remedial action may be assessed. They do not reflect a determination that a release of a substance will be hazardous at, or above, the RQ level or not hazardous below that level. It should be noted that EPA has also promulgated RQs for radioactive substances (radionuclides). Although the radionuclide RQs are considerably smaller than those mentioned above, they are not pertinents to the present discussion.

A.1 Type of Toxic Effect

Each designated CERCLA hazardous substance is assessed in the following six categories: reactivity, ignitability, acute toxicity, chronic toxicity, carcinogenicity, and aquatic toxicity. For each of the five categories, a substance receives a tentative RQ level based on its intrinsic physical, chemical, and toxicological properties; the lowest RQ for each of the six categories becomes the

"primary criteria RQ" for that substance. The primary criteria RQ may be raised one level (adjusted) before being set as a statutory RQ based on the susceptibility of the substance to biodegradation, hydrolysis, and photolysis. Details of the system used to establish and adjust RQ values are published in the May 25, 1983 Federal Register (48 FR 12552), the April 4, 1985 Federal Register (50 FR 13456), the March 16, 1987 Federal Register (52 FR 8140), and in the Technical Background Document to Support Rulemaking Pursuant to CERCLA Section 102 (Environmental Monitoring and Services, Inc., 1985).

A.1.1 Acute Toxicity

The acute toxicity of a substance is assessed based on the LD_{50} or LC_{50} of a substance administered by the oral, dermal, or inhalational route. Each of the five RQ levels has an LD_{50} value range for both acute oral and acute dermal toxicity, and an LC_{50} range for inhalation toxicity. For example, an RQ of 1 pound is set for substances with an oral LD_{50} less than 0.1 mg/kg, a dermal LD_{50} below 0.04 mg/kg, or an inhalational LC_{50} below 0.4 ppm. An RQ of 5,000 pounds is set for substances with an oral LD_{50} between 100 and 500 mg/kg, a dermal LD_{50} between 40 and 200 mg/kg, or an inhalational LC_{50} between 400 and 2,000 ppm. The RQ level chosen for the acute toxicity category is the lowest of the RQs derived from the available acute toxicity data by the modes of administration listed above.

A.1.2 Chronic Toxicity

The chronic toxicity RQ is determined by a composite score assigned to a substance based on both minimum effective dose (MED) levels (oral, dermal and inhalational) and the severity of the effects caused by repeated or continuous exposure. Teratogenic effects are considered as chronic effects. MED levels are assigned a score from 1 to 10 that is inversely proportional to the logarithm of the MED. The type and severity of adverse effect caused by the agent is scored on a scale from 1 to 10 with minor effects, such as enzyme induction, being assigned a score of 1 while scores of 9 and 10 are assigned to pronounced pathological changes. The composite score for a substance is the product of the MED score and the effects score. The composite scores, which range from 1 to 100, are divided into five tiers, 81 to 100, 41 to 80, 21 to 40, 6 to 20, and 1 to 5, that are associated with RQ values of 1, 10, 100, 1,000, and 5,000 pounds, respectively.

A.1.3 Carcinogenicity, Mutagenicity, Teratogenicity (CMT) Potential

The RQ method considers teratogenic effects under chronic toxicity (see above). The severity index scores for substances which cause teratogenic effects are very high. Substances which cause birth defects in offspring in the absence of maternal toxicity are assigned a score of 10; if maternal toxicity is present, the severity index score is 9.

The RQ method ranks carcinogenic potential through a two-stage, combined weight-of-evidence and carcinogenic potency approach. During the first stage, a qualitative assessment of the available epidemiological and experimental data is conducted according to the weight-of-evidence classification method presented in the EPA "Guidelines for Carcinogen Risk Assessment" (Federal Register of September 24, 1986; 51 FR 33992 through 34003). Evidence from animal and human studies are evaluated and the substance is assigned to a category according to set of prescribed rules. The weight-of-evidence categories, include Group A (known human carcinogen—evidence in humans is sufficient), Group B (probable human carcinogen—evidence in humans is limited or inadequate, but animal evidence is sufficient), Group C (possible human carcinogen—inadequate or no evidence in humans and animal evidence is limited), Group D (not classifiable), or Group E (evidence of noncarcinogenicity for humans).

During the second stage, a quantitative assessment of the animal data (for Group A, B and C) is made by estimating the dose of the substance that causes a 10 percent increase in tumor incidence above control levels. This estimated dose is termed the ED_{10}. A potency factor (F) is calculated from the reciprocal of the ED_{10} according to the equation:

$$F = \frac{1}{ED_{10}}$$

Substances are assigned to potency groups of 1 (high), 2, or 3 depending on the magnitude of F. Substances for which F is greater than 100 are assigned to potency group 1 (highest), substances for which F is greater than 1 but less than 100 are assigned to potency group 2; substances for which F is less than 1 are assigned to potency group 3 (Cogliano, 1986).

The weight-of-evidence and potency classifications for a given substance are combined through the use of a matrix that allows a designation of potential carcinogens into hazardous categories of high, medium or low.

A.2 Modifiers of Exposure

A.2.1 Persistence

RQs are adjusted based on the susceptibility of the substance bring evaluated to the natural degradation processes of biodegradation, hydrolysis, and photolysis (BHP). The effects of oxidation and volatilization are not considered. If a substance is susceptible to BHP, the RQ value is raised one level from that assigned by the primary criteria analysis to compensate for the reduction in relative toxicity of the degraded products. BHP criteria are not used to lower the RQ values in the event that substances are transformed to more toxic agents by BHP.

A.2.2 Routes of Release

The RQ system does not address specific routes of release because it is only intended to trigger mandatory notification of the

National Response Center when a release to any medium exceeds a given level.

A.2.3 Presence of Incompatible or Reactive Mixtures

The RQ system has categories that address the ignitability and the reactivity of individual substances but the system does not address reactivity of mixtures (since mixtures are not addressed under the RQ system). The ignitability and reactivity categories each have only four RQ levels, 10, 100, 1,000, and 5,000 pounds. Ignitibility RQs are associated with flash point and boiling point characteristics of substances and range from 10, for substances that are pyrolytic or self-ignitable, up to 5,000 for substances with a flash point of 100 to 140°F. Reactivity RQs are assessed based on the ability of a substance to react with water and/or itself and range from 10, for substances that react with water and/or have extreme self-reaction, to 5,000 for substances that have slight self-reaction (e.g., polymerization with low heat release).

A.3 Use of Data

A.3.1 Number of Substances Evaluated

The RQ system assesses individual substances and not sites containing groups or mixtures of substances.

A.3.2 Quantity of Data on Each Substance

The RQ system requires acute toxicity data (oral and dermal LD_{50}s and/or inhalational LC_{50}s), chronic toxicity data (MED levels and severity of toxic effects), aquatic toxicity data (LC_{50}

values), ignitability data, and reactivity data (reactivity with water and self-reactivity). Criteria for BHP are used to assess the need to adjust (raise) the RQ values one level, if appropriate. Incomplete data on a substance may result in the elimination of an RQ category or default to available data. The consequence is that substances receive RQs that are based on known hazards or properties rather than unknowns.

A.3.3 Clarity

The EPA RQ system itself is clearly described in the Technical Background Document and the May 25, 1983; April 4, 1985, and March 16, 1987 Federal Registers; however, the methods for applying some components of the system are somewhat vague. For instance, the specific criteria for raising an RQ one level based on BHP are not presented. Also, no guidance is provided with respect to preferred sources of toxicity data and physical parameters; therefore, it is assumed that LD_{50} and LC_{50} values published in any source may be used.

APPENDIX B

SUPERFUND PUBLIC HEALTH EVALUATION SYSTEM (SPHE)

The Superfund Public Health Evaluation (SPHE) system (ICF Incorporated, 1985) is a method for estimating public health risks at hazardous waste sites and developing goals for remedial alternatives. The SPHE system is not intended to rank toxic waste sites. Rather, it addresses the fourth phase of the five-step remedial response process set forth in the National Oil and Hazardous Substances Pollution Contingency Plan (40 CFR 300). After the priorities for remedial study have been established, the fourth phase of the remedial response process calls for the identification, evaluation, and selection of appropriate cleanup alternatives, and for the analysis of these alternatives to identify the most appropriate, cost-effective solution at a site. The SPHE system provides detailed guidance on how to conduct this fourth phase.

The SPHE system calculates "Indicator Scores" (IS) for the hazardous substances found at a site. The IS is the product of the measured concentration of a substance times a "toxicity constant." Toxicity constants are pathway-specific (i.e., water, air and soil) and are derived separately for carcinogens (T_c) and noncarcinogens (T_n). Subsequent to the calculation of the IS for both carcinogens and noncarcinogens, the topscoring 10 to 15 substances from each of the two groups are designated as the initial indicator substances. From those two initial lists, the final indicator

substances (unspecified number) are selected for use in a risk assessment for the site.

B.1 Type of Toxic Effect

B.1.1 Acute Toxicity

The acute toxicity, per se, of substances found at hazardous waste sites is not addressed by the SPHE system.

B.1.2 Chronic Toxicity

The SPHE system discriminates between the chronic toxicity produced by nononcogenic substances and that produced by carcinogenic substances (discussed in the following section). For noncarcinogenic substances, a toxicity constant (T_n) is calculated for each route of release (water, soil and air). T_n is calculated for a reference human (who weighs 70 kg, breathes 20 m^3/day, drinks 2 liters of water/day, and consumes 100 mg soil/day). T_n is based on the minimum effective dose (MED) of substance (in mg/day)* that causes an irreversible effect and a severity factor (RV_e) that ranges from 1 to 10 (and is identical to the scale described for the RQ method in Appendix A).

Thus, for water, $^{w}T_n = 2 \text{ liter/day} \cdot RV_e/MED_{(oral)}$

for soil, $^{s}T_n = 0.0001 \text{ kg/day} \cdot RV_e/MED_{(oral)}$

and for air, $^{a}T_n = 20 \text{ m}^3\text{/day} \cdot RV_e/MED_{(inhalation)}$

*If MED is given in mg/kg/day, it must be multiplied by 70 kg before substituting it into the equation.

The units for T_n are the inverse of concentration. Consequently, the IS (which is the product of a substance's toxicity constant (T_n) and its concentration) is a unitless number.

The selection of the final indicator substances involves the magnitude of the IS scores and consideration of five physical and chemical properties for each substance (water solubility, vapor pressure, Henry's Law Constant, organic carbon partition coefficient, and persistence); however, the SPHE manual provides no "set of precise decision rules on which to base the selection." This allows a great potential for inconsistency in the selection of final indicator substances.

B.1.3 Carcinogenicity, Mutagenicity, and Teratogenicity (CMT) Potential

The SPHE system requires the determination of toxicity constants for carcinogenic substances by a method similar to that described for chronic toxicants. For carcinogenic substances, a toxicity constant (T_c) is calculated from data for a reference human for each route of exposure (water, soil and air). T_c is based upon the ED_{10} (the dose to experimental animals in mg/kg/day that causes a particular tumor to occur at 10 percent greater incidence than in controls).

Thus, for water, $^{w}T_c = 2 \text{ liter/day}/70 \text{ kg} \cdot ED_{10}$

for soil, $^{s}T_c = 0.0001 \text{ kg/day}/70 \text{ kg} \cdot ED_{10}$

and for air, $^{a}T_c = 20 \text{ m}^3\text{/day}/70 \text{ kg} \cdot ED_{10}$

The units for T_c are also the inverse of concentration.

In addition to calculation of T_c, each potential carcinogen is qualitatively classified according to the weight-of-evidence criteria published by the International Agency for Research on Cancer (IARC). The SPHE manual clearly states that this classification does not directly affect the IS; however, it is implied that the weight-of- evidence classification should be considered along with the physical and chemical properties (discussed in chronic toxicity) in the selection of final indicator substances.

B.2 Determinants of Exposure

B.2.1 Persistence The SPHE system allows the analyst to consider environmental persistence as one factor in the selection of the final list of substances which are used to estimate public health risks resulting from exposure to toxic substances escaping from waste sites. The overall half-lives of many substances in air, soil, and water are provided in an appendix. The half-life for each substance is to be used along with other physical data and, if appropriate, the IARC weight-of-evidence carcinogenicity rating in the final scoring of substances at a site. The procedure for assessing the relative importance of these factors is not specified. Rather, it is left to the judgment of the individual analyst involved in the site scoring as to what weight persistence should have in determining the final score of a substance.

B.2.2 Routes of Release

The SPHE system offers comprehensive analysis of exposure to substances via air (due to volatilization and fugitive dust emission), surface water (due to runoff, episodic overland flows, and ground water seepage), ground water (due to seepage), onsite soil (due to leaching), and offsite soil (due to runoff, episodic overland flows, deposition of fugitive dust and tracking of contaminated soil from a site to a previously uncontaminated site). The frequency (i.e., whether chronic or episodic) and amount of each type of release is also estimated and categorized. However, the SPHE system is not clear on how this information is to be used.

B.2.3 Presence of Incompatible or Reactive Mixtures

The SPHE system does not assess the hazard resulting from incompatible or reactive wastes at a site.

B.3 Use of Data

B.3.1 Number of Substances Evaluated

The SPHE system selects a list of "initial indicator" substances from all substances identified at a waste site. The 10 to 15 compounds with the highest IS from each category of potential carcinogens and noncarcinogens comprise the "initial indicator" substances.

B.3.2 Quantity of Data on Each Substance

The SPHE system requires a variety of biological and physical data on each substance identified at a waste site. For the

selection of the list of "initial indicator" substances, toxicity data such as the human minimum effective dose (MED) for noncarcinogens and the animal ED_{10} for carcinogens are required for the calculation of toxicity constants. In addition, rating constants for the severity of effects caused by noncarcinogens must be assigned. The organic carbon partition coefficient is also needed for the ranking of the initial list of indicator substances. There are no instructions concerning how to proceed in the absence of such information.

For the list of "final indicator" substances, physical data including water solubility, vapor pressure, Henry's Law constant, organic carbon partition coefficient, and persistence are also required. Information from IARC concerning the weight-of-evidence relative to the carcinogenicity of each substance is also required. Much of these data are not readily available, and little guidance is presented in the SPHE documentation concerning how to proceed in the absence of data.

B.3.3 Clarity

The SPHE system clearly presents the directions with which to score substances in waste sites. Details are provided for the ranking of carcinogenic and noncarcinogenic substances, quantification of human exposure characteristics, calculation of toxicity factors for each substance, and the assessment of human risk resulting from the release of substances from waste sites.

Worksheets and examples are provided which are useful in working through this system.

Ambiguity arises at several places in the SPHE system where the analyst is directed to several air, water, and soil release models and is required to choose the appropriate one based on the professional judgment of the analyst. Throughout the SPHE system, numerous important decisions rely on the judgment of the site analyst. This leads to a hazard assessment system which may be affected by personal biases of individual analysts leading to possible inconsistency in the scoring of sites.

B.4 Other Considerations

A list of the "final indicator" substances is selected from the list of "initial indicator" substances. There is no set number of "final indicator" substances, nor is there a set of precise decision rules for their selection. However, various chemical and physical properties of each substance are to be used for ranking the final indicator substances at each site.

Each "final indicator" substance is subjected to a risk characterization which is the ratio of the estimated exposure level of the substance by all routes of exposure and the acceptable exposure level according to the EPA's proposed guidelines for Health Risk Assessment of Chemical Mixtures. For each "final indicator" the sum of the ratios for each route of exposure is the hazard index. Changes in the magnitude of the hazard index by various

remedial alternatives are utilized to determine which alternatives would provide acceptable public exposures.

The risk assessment calculations are based on many assumptions, use of environmental models, and estimates. The accuracy of the estimates of the expected changes in constituent concentration in release streams from a site depends on the models and data used to make the estimates. Throughout the risk estimation process, the SPHE system relies upon the professional judgment of the analyst. Simultaneously, a record of all assumptions and their "biases" is to be kept. The ultimate result is a strong potential for a lack of consistency in the scoring among sites.

APPENDIX C

PRELIMINARY POLLUTANT LIMIT VALUE (PPLV) METHOD

The preliminary pollutant limit value (PPLV) method is designed to predict (probable) acceptable environmental limits for pollutants with respect to their ability to cause human health effects. Details of the PPLV system are contained in Rosenblatt, Dacre and Cogley (1980 and 1982).

C.1 Type of Toxic Effect

The PPLV method provides a preliminary estimate of acceptable levels of a given contaminant in various media (soil, water and air). The steps involved in calculating a PPLV include:

- Determination of an acceptable lifetime, daily dose (DT) of the contaminant for humans.
- For each medium (soil, water and air), identification of the possible medium-to-human pathways or routes of exposure (e.g., for soil some of the pathways include 1) root crops, 2) other crops, 3) food chain animals eating contaminated plants, 4) contaminated runoff to waters to fish to man, and 5) leachate to groundwater to man).
- Determination or estimation of relevant partition coefficients for the contaminant through all pathways, (e.g., between the media and food chain, within the food chain, between the media and humans, and between the food chain and humans).
- Calculation of the maximum concentration of a contaminant in each pathway that would result in the delivery of exactly D_T (this is the single pathway PPLV which is also called the SPPPLV).

- Identification of "critical pathways" for each medium.
- Calculation of the PPLV for each medium (or over all media) by "normalizing" the SPPPLVs; normalization adjusts the contaminant concentration for each pathway so that the target organism, man, receives a total daily dose of exactly D_T; normalization is necessary when there are several pathways within a medium or when pathways from different medium intersect; normalization is done as follows:

$$PPLV = \sum_{i=1}^{n} \frac{1}{(SPPPLV)_i}^{-1}$$

C.1.1 Acute Toxicity

The PPLV method does not include a factor which addresses the acute toxicity, per se, of a substance. Acute toxicity data is utilized for calculation of the acceptable daily dose (D_T) of a toxicant only if chronic data is not available, as discussed under chronic toxicity.

C.1.2 Chronic Toxicity

Chronic toxicity is assessed in the PPLV method through the determination of D_T. Essentially, this is a modification of the ADI approach. If ADI values are available from the World Health Organization, they are recommended for use as the D_T. If ADIs are not available, the recommendation is that the maximum concentration level (MCL) in drinking water, as established by EPA, be converted to a D_T by dividing the MCL by 35 (to adjust for daily water intake and body weight). If a TLV is available, the recommendation is that it be converted to D_T by multiplying by 0.0004 (to adjust for breathing rate, exposure time, and a safety factor of 100). If

animal data must be used, it is recommended that the NOEL from a lifetime study in animals be used by dividing it by a safety factor of 100; if a NOEL from a subchronic (90 day) study is used, the recommended safety factor is 1,000; if the LD_{50} must be used, the recommended safety factor is 86,950. Additional safety factors may also be applied in determining the D_T to protect exceptionally sensitive individuals such as embryos, infants, and aged individuals.

C.1.3 Carcinogenicity, Mutagenicity, and Teratogenicity (CMT) Potential

Although the PPLV system mentions the "special challenge" posed by determining the D_T for carcinogens, exact instructions for how to proceed are lacking. Rather, it is suggested that a D_T be calculated based on several types of concentrations including:

- The limit of detectability for easily detected toxic substances in general.
- The concentration at which a "variety of potent but ubiquitious carcinogens" are found in drinking water.
- The lowest available water quality criterion promulgated by the EPA.

There is no further guidance for the calculation of PPLV for carcinogens. No additional consideration is given to the potential effects resulting from exposure to mutagens. Teratogenicity is considered only as a possible additional safety factor to be applied to the determination of the D_T, as mentioned under chronic toxicity.

C.2 Determinants of Exposure

C.2.1 Persistence

The PPLV system refers to the persistence of a chemical as the resistance of the chemical to photochemical, hydrolytic, oxidative, and biodegradative loss. Although persistence is recognized as a factor that affects the probability of exposure to a contaminant, the PPLV method largely ignores it. According to the authors, persistence is "only estimated when the particular circumstances warrant such consideration." However, they do not explain what are the circumstances that warrant consideration of persistence, nor how persistence data should be used.

C.2.2 Routes of Release

The PPLV system categorizes the release of toxicants from waste sites by their release to various media (soil, surface water, ground water, or air). Transport of toxicants through various pathways within and between media (e.g., food chain to humans) are also included, although percutaneous exposure is not considered.

C.2.3 Presence of Incompatible or Reactive Mixtures

The PPLV system does not include a factor for scoring the hazard resulting from reactive or incompatible wastes present at a site.

C.3 Use of Data

C.3.1 Number of Substances Evaluated

The "limiting pollutant level" (i.e., the smallest SPPPLV) for each toxicant at a waste site is calculated for each relevant pathway and included in the calculation of the final PPLV for that toxicant. However, it is not clear exactly how each SPPPLV is included in the final calculation of the PPLV because "subjective judgments are made of the most likely among the significant pathways for the site under consideration."

C.3.2 Quantity of Data on Each Substance

Calculation of the PPLVs used in this system requires an extensive amount of data, much of which may not be available. In particular, intercompartmental partition coefficients (K) for each chemical for each route of transport (e.g., soil to water, water to plants, water to animals, plants to animals, plants to humans, and animals to humans) are required for the calculation of PPLVs. Values for such partition coefficients are presently available only for a very limited number of substances. In addition, physical data on each substance, such as aqueous solubility and vapor pressure, are required for the calculation of some SPPPLVs. Such extensive data are available for relatively few substances found at toxic waste sites; the extensive data requirements, therefore, severely limit the use of the PPLV system.

C.3.3 Clarity

In order to properly assess the hazard resulting from release of substances from toxic waste sites, the analyst needs to be proficient in using up to 38 equations comprised of up to 43 components. The complexity of this system makes the calculation of PPLVs untenable for widespread use by individuals who are not highly trained.

Although the underlying scientific concept and numerical calculations used to derive PPLVs, SPPPLVs, and D_T appear to be reasonable, the method for obtaining many of the factors in the equations (e.g., dietary intake factors, and intercompartmental partition coefficients) often relies heavily on professional intuition and assumptions that are based upon varying amounts and quality of experimental evidence. Thus, the resulting PPLVs must often be regarded as tenuous. In addition, the extensive need for professional judgment on the part of the analysts using the PPLV system is expected to result in inconsistent scores between sites. As the authors state: "One should not be surprised, therefore, if two environmental engineers obtain different results from analysis of the identical situation. This may be the result of valid differences in judgment."

APPENDIX D

SITE ASSESSMENT SYSTEM (SAS), STATE OF MICHIGAN

The Site Assessment System (SAS; Michigan, 1983) was modified from the EPA HRS by the State of Michigan for the purpose of assigning priorities to wastes sites, in terms of relative risk, for further investigation and possible remedial action. The methodology used for the hazard ranking of substances was originally published in the Michigan Critical Materials Register (Michigan, 1980). That method was modified for incorporation into the SAS.

D.1 Type of Toxic Effect

In the SAS methodology for the hazard ranking of substances, each substance is scored for environmental concern based on six factors: acute toxicity, genotoxicity (including carcinogenicity and mutagenicity), subchronic/chronic toxicity (including teratogenicity), bioaccumulation, persistence, and ecotoxicity. The values for each factor are added and the sum is multiplied by a "data uncertainty multiplier" (to correct for the quality of the data) to provide the potential toxicity score.

D.1.1 Acute Toxicity

SAS assesses acute toxicity by assigning scores for substances based upon the lowest mammalian oral or dermal LD_{50} or inhalational LC_{50}. For the oral and dermal modes of exposure, if the LD_{50} is less than 5 mg/kg, the score is 10; if the LD_{50} is 5 to 500 mg/kg, the score is 5; and if the LD_{50} is greater than 500

mg/kg, the score is 0. For the inhalational mode of exposure, if the LC_{50} is less than 0.5 mg/l, the score is 10; if the LC_{50} is 0.5 to 20 mg/l, the score is 5; if the LC_{50} is greater than 20 mg/l, the score is 0.

D.1.2 Chronic Toxicity

SAS assigns scores for subchronic/chronic toxicity by all modes of exposure based upon both the magnitude of the lowest dose which causes an "irreversible adverse effect" in the most sensitive mammal and whether the substance is teratogenic in mammals. A score of 20 is assigned if the substance causes irreversible adverse effects at doses lower than 0.5 mg/kg/day for oral or dermal exposure or 0.05 mg/l for inhalational exposure and if it is teratogenic. A score of 10 is assigned if only one of the two preceding criteria are met. A score of 5 is assigned if irreversible adverse effects are caused at "low" doses. Guidance as to the definition of "low" dose is not given.

D.1.3 Carcinogenicity, Mutagenicity, and Teratogenicity (CMT) Factor

SAS includes teratogenic effects as a part of the chronic toxicity assessment. Carcinogenicity and mutagenicity are scored on a weight-of-evidence basis. If the substance has been demonstrated to be both a positive or potential carcinogen in humans or animals and a hereditary mutagen in a multicellular organism, it is assigned a score of 20. If only one of the two preceding criteria are met, it receives a score of 10. If the substance is positive in

bacterial mutagenicity tests, cell transformation assays, or tumor promotion studies, it receives a score of 5.

D.2 Determinants of Exposure

D.2.1 Persistence

SAS assesses the environmental persistence of a substance by assigning a persistence score of 5 if the half-life of the substance in soil, air or water is longer than six months (26 weeks). If it is less than six months, it receives a score of 0.

D.2.2 Routes of Release

The routes of release in the SAS include ground water, surface water, direct contact, and the atmosphere. The consideration of all routes, including the atmosphere, is a strong point.

D.2.3 Presence of Incompatible or Reactive Mixtures

All substances present in quantities greater than 100 kilograms are rated for flammability, based either on the National Fire Prevention Association method (see Section 3.1.2.3) or on chemical flash point, and for their ability to react with themselves. However, the reactivity of mixtures of chemicals is not assessed.

D.3 Use of Data

D.3.1 Number of Substances Evaluated

All substances identified at a site are scored for toxicity.

D.3.2 Quantity of Data on Each Substance

SAS employs a variety of toxicity endpoints and physical/chemical data from which to calculate the final hazard score used in

the ranking of waste sites. It requires extensive amounts of data per substance to evaluate the six factors discussed above. The information required may be obtained from a variety of sources including the International Agency for Research on Cancer (IARC), the National Cancer Institute (NCI), the National Institute for Occupational Safety and Health (NIOSH), the National Toxicology Program (NTP), and the Michigan Critical Materials Register (MCMR). If data for a given category of toxicity are not available, a score of 0 is given. A score of 0 due to absence of data is offset by the multiplication of the toxicity score by a "data uncertainty multiplier" which increases from 1.2 to 1.8 as more toxicity characteristics have no data.

D.3.3 Clarity

SAS is a modification of the EPA HRS, and is similar in clarity. Step-by-step instructions, flow diagrams, worksheets, and examples provide adequate information for understanding the scoring process. However, SAS is complicated by the high level of professional judgment required to evaluate each component of the hazard characterization. The scorer must be able to locate and assess the data to support the scores. For instance, only "well conducted" mammalian teratogenicity tests are to be used, but what is meant by "well conducted" is not specified.

D.4 Other Considerations

SAS also considers ecotoxicity and bioaccumulation in its hazard score for a substance. Ecotoxicity is scored based on the magnitude of the most sensitive indicator among either the avian LD_{50} levels, fish 96-hour LC_{50} levels, or the chronic EC_{50} (effective concentration) to aquatic organisms. Bioaccumulation of the substance is scored based on the more sensitive of the following two indicators of bioaccumulation: (1) the bioaccumulation factors for fish and (2) the logarithm of the octanol/water partition coefficient of the substance.

APPENDIX E

HAZARD ASSESSMENT RATING METHODOLOGY II (HARM II)

The Hazard Assessment Rating Methodology II (HARM II) was developed by the Environmental Sciences Division of Oak Ridge National Laboratory (1986) for use by the U.S. Air Force in evaluating hazardous material disposal sites. Details are contained in Oak Ridge National Laboratory Publication No. 2582.

E.1 Type of Toxic Effect

E.1.1 Acute Toxicity

The toxicity factor in HARM II is unique among the systems reviewed. It incorporates "benchmark" health hazard scores for each "significant" substance identified at a waste site. The benchmark health hazard scores are defined on the basis of "permissible concentrations" for the following three classes of substances: carcinogens, regulated substances, and nonregulated substances.

The definition of permissible concentration of a substance in HARM II as a concentration that will not cause adverse health effects "under typical exposure conditions" is vague and could lead to inconsistent interpretations. For regulated substances, the HARM II system uses the drinking water standards (permissible concentrations of those substances) promulgated by EPA or NIOSH. For carcinogens for which drinking water standards have not been set, HARM II uses "permissible concentrations" as estimated by the Carcinogen Assessment Group (CAG) of the EPA Office of Health and

Environmental Assessment. For unregulated substances, HARM II uses a relative potency approach to define a benchmark. In this approach, a series of relative potency estimates for the substance in question is prepared. Each relative potency estimate is the ratio of acute toxicity data (e.g., LD_{50} or LD_{1o}*) for the substance in question to the acute toxicity data for a single, well-studied, structurally related substance. The data used to construct the series of ratios may come from any species of mammal and may mix the types of waste toxicity. The median ratio determined from the above series of ratios is the "median potency." The potency of the structural analogue used in the above exercise relative to benzo(a)pyrene, the primary standard, is multiplied by the median potency to derive the relative potency of the substance in question. The benchmark for an unregulated substance is the product of its relative potency and the drinking water standard for benzo(a)pyrene. The toxicity data base for the chemicals is found in the Registry of the Toxic Effects of Chemical Substances (RTECS, Lewis and Tatken, 1982).

The assessment of relative acute toxicity potential through the use of "permissible concentrations" in the HARM II system involves inconsistencies because the assumptions and formulae used by the EPA Office of Drinking Water, NIOSH, and CAG are not identical. Further

*LD_{1o} = the lowest dose of a chemical that causes at least one death among a group of exposed experimental animals.

inconsistencies can arise from the choice of structural analogues and the calculation of median potency values for unregulated chemicals. These opportunities for lack of consistency are a weakness which detracts from the usefulness of this method for ranking sites.

E.1.2 Chronic Toxicity

Chronic toxicity, per se, is not evaluated by HARM II, although some of the relative potency ratios may use chronic toxicity data. This is a shortcoming for adequate assessment of the potential danger associated with substances released slowly, over a prolonged period of time.

E.1.3 Carcinogenicity, Mutagenicity, and Teratogenicity (CMT) Potential

The HARM II ranking system does not assess carcinogenicity except for those carcinogens which have either drinking water standards or permissible concentrations estimated by CAG. HARM II does not assess mutagenic and teratogenic effects. This is a shortcoming for adequate assessment of the potential danger associated with substances released over a long period of time.

E.2 Determinants of Exposure

E.2.1 Persistence

The HARM II system assesses the resistance of a substance to environmental degradation by the same criteria as the HRS. In HARM II, however, persistence is used in calculating the hazard quotients of only those substances which have not been released from

the site. Each persistence category is assigned a multiplier that varies from 0.4 to 1.0 and operates on the sum of the toxicity and bioaccumulation indices (c.f. E.4 Other Considerations).

E.2.2 Routes of Release

Surface water and ground water contamination are included in the HARM II system; however, the airborne route of release is omitted. According to the authors, direct contact and fire and explosion routes of release are also omitted because HARM II is intended for use at protected Air Force installations which are secure from the general public.

E.2.3 Presence of Incompatible or Reactive Mixtures

The HARM II system does not include a factor for scoring the hazard resulting from incompatible or reactive wastes present at a site.

E.3 Use of Data

E.3.1 Number of Substances Evaluated

The HARM II system scores all "significantly toxic" substances identified at a waste site. However, it is not clear upon what basis the decision of "significantly toxic" is made.

E.3.2 Quantity of Data on Each Substance

All the types of data necessary to calculate the median and relative potency estimates for a substance are available in RTECS. Potentially, 10 or more toxicity values per substance may be needed. The large amount of data required and the scientific

expertise needed to select structural analogues contribute to the cumbersome nature of HARM II. Furthermore, no guidance is provided for the evaluation of substances that are not listed in RTECS, even though it appears that LD_{50} values or other toxicity data published in any source may be used to calculate potency estimates. A substance without either a "permissible concentration" or an LD_{50} cannot be evaluated using the HARM II methodology.

E.3.3 Clarity

The HARM II system assesses many of the same factors as the EPA HRS. It also includes flow diagrams for the calculation of site scores, extensive discussion of the parameters contained in each scoring component, and numerous examples describing the application of the system in simulated and real life case studies. However, the number and complexity of operations required to establish "benchmark" health hazard scores make HARM II cumbersome.

E.4 Other Considerations

The HARM II system ranks sites through the calculation of a normalized human health hazard subscore. The method for calculating the normalized human health hazard subscore differs depending on whether or not monitoring has detected the release of contaminants from the waste site. If contaminants have been detected, a hazard quotient for each contaminant identified is calculated. The hazard quotient for a contaminant is derived by dividing the sum of the estimated total intake of the contaminant from drinking

(concentration in ground water x 2 liters) plus the total estimated intake from eating fish (concentration in surface water x fish bioaccumulation factor x 6.5 grams) by the health effects benchmark for the contaminant. The hazard quotients for all contaminants are added and a human health hazard index is assigned based on the magnitude of the logarithm of the sum of the quotients. The human health hazard index ranges from 0 to 6. The health hazard index is then normalized (i.e., divided by 6 and multiplied by 100). A human health subscore is calculated by multiplying the normalized health hazard index by a waste quantity factor.

If contaminants have not migrated from the disposal site, a health hazard index is calculated for each contaminant present at the site. The health hazard index is determined by multiplying the persistence multiplier by the sum of the toxicity index of the contaminant (based on the magnitude of the logarithm of the benchmark for health effects) and the bioaccumulation index. This human health hazard index ranges from 0 to 9. The highest value calculated for any single contaminant is taken as the health hazard index for the site. This index is then normalized. A human health subscore is calculated by multiplying the normalized health hazard index by a waste quantity factor.

APPENDIX F

RCRA HAZARDOUS WASTE SCHEDULING METHODOLOGY

The RCRA Hazardous Waste Scheduling Methodology (RCRA Method) was developed to assist EPA in scheduling RCRA (Resource Conservation and Recovery Act) hazardous wastes for further study as to whether they should be banned from land disposal (e.g., landfill, surface impoundment and landfarm). To accomplish this, the RCRA Method ranks RCRA waste streams based on both the toxic potential of the waste stream and the total volume of the waste stream that is land disposed (Environ Corporation, 1985).

F.1 Type of Toxic Effect

F.1.1 Acute Toxicity

The RCRA Method scores acute toxicity based on the lowest LD_{50} in any mammal via oral, dermal, or inhalational* exposure. If the lowest LD_{50} is less than 50 mg/kg, the substance is considered to have high acute toxicity and is assigned a score of 1. If the lowest LD_{50} is greater than 50 mg/kg, the substance receives a score of 0. If LD_{50} data are unavailable, the lowest LD_{lo} value is used. If no data are available, acute data for appropriate structural analogues to the substance in question are used.

*Acute toxicity data from inhalation studies are usually reported as LC_{50} (the concentration of a test substance in the air which causes the death of 50 percent of exposed experimental animals). If the LC_{50} is the only data available, it is converted to an LD_{50} using standard values for body weight and respiratory volumes.

F.1.2 Chronic Toxicity

For chronic toxicity, the RCRA Method computes an Equivalent Dose Estimate (EDE). The EDE is defined as that dose "at which the estimated risk associated with a compound is comparable among all compounds being evaluated." For noncarcinogens, the EDE is the acceptable daily intake (ADI) as established by either the EPA Environmental Criteria and Assessment Office, the EPA Office of Pesticide Programs, or the National Academy of Science (NAS). In the event the ADI has not been established by EPA or NAS, the EDE can be calculated (1) by dividing the No Observable Effect Level (NOEL)* from a chronic study by a "standardization factor" or by dividing the product of the Lowest Observable Effect Level (LOEL)** times a "severity factor" by a standardization factor or (2) by dividing the LD_{50} by 105. The standardization factors correspond to the uncertainty factors utilized in deriving ADIs (i.e., 10 for intraspecies variability; 100 for intra-and interspecies variability; 1,000 for the uncertainty associated with extrapolating from subchronic to chronic exposures as well as intra- and interspecies variability). Severity factors were assigned as 2.14 for mild effects, such as biochemical changes and potentially reversible, mild organ changes, or 4.68 for more severe effects, such as teratogenicity, reproductive or

*NOEL = the highest dose of a substance that did not cause toxic effects when administered to a group of experimental animals.

**LOEL = the lowest dose of a substance that caused toxic effects when administered to a group of experimental animals.

neurological dysfunction, or istologically described organ necrosis. Based upon the magnitude of the EDE, a chronic toxicity score of 1 to 9 is assigned (the score ranges from 1, if EDE is equal to or greater than 1, to a score of 9, if EDE is less than 10^{-7}). For noncarcinogens, the acute toxicity score is added to the chronic toxicity score to give a final toxicity score. The toxicity score of a waste stream is considered to be the score of its most toxic constituent.

F.1.3 Carcinogenicity, Mutagenicity, and Teratogenicity Factor for Carcinogenic Chemicals

The RCRA Method utilizes the unit carcinogenic risk (UCR)* factor for the calculation of EDE for carcinogens. The UCR is defined as the "upper limit" of the probability that the substance will cause cancer at a dose of 1 mg/kg body weight/day over a lifetime. The UCR factor has been calculated by CAG for a substantial number of carcinogens. For other carcinogens that have been designated by either the U.S. Department of Health and Human Services (HHS) or the IARC, the UCR can be calculated from animal data using either the multistage (when there are sufficient data) or the one-hit model.** For carcinogenesis, the EDE is calculated as

*UCR = the slope of the carcinogenicity dose-response curve at low levels of exposure.

**The multistage and one-hit models are linear extrapolation equations that are used to project the risk associated with a dose of a carcinogen which is lower than any of the tested doses. Both models assume that there is no threshold dose (i.e., all doses are associated with some risk). In both models, the shape of the dose-response curve, between the lowest dose tested and the origin, approaches linearity at very low doses.

a "standardization factor" (10-6) divided by the UCR. For carcinogens, the chronic toxicity score is assigned based upon the magnitude of the EDE according to the same range of scores (1 to 9) described for noncarcinogens. The final toxicity score of a substance is the sum of the acute and chronic toxicity scores. The toxicity of a waste stream is considered to be the score of its most toxic constituent.

Mutagenic and teratogenic effects are not considered in the RCRA Method.

F.2 Determinants of Exposure

F.2.1 Persistence

The RCRA Method does not assess the environmental persistence of substances.

F.2.2 Routes of Release

While the RCRA Method is directed at waste streams that are land disposed, it does not consider pathway-specific factors. It is based solely on the toxicity and quantity of the waste stream. It does not consider the release of the waste stream.

F.2.3 Presence of Incompatible or Reactive Mixtures

The RCRA Method contains no factor for evaluating incompatible or reactive mixtures at wastes sites.

F.3 Use of Data

F.3.1 Number of Substances Evaluated

The RCRA Method scores waste streams based on the one constituent that has the highest toxicity score multiplied by the total volume of the waste stream land disposed in the U.S.

F.3.2 Quantity of Data on Each Substance

The data required for assigning the toxicity factor in the RCRA Method have already been compiled, the calculations completed, and toxicity factors assigned for 363 constituents hazardous under RCRA. For other constituents, toxicity data for assigning a toxicity score may be available from EPA, HHS, or IARC. In the case of substances for which insufficient toxicity data exist, data from structural analogues (presumably selected by the scorer) may be used in combination with appropriate uncertainty factors.

F.3.3 Clarity

The RCRA Method is a straightforward scheme that ranks waste streams on the basis of the toxicity of the single most toxic constituent and the total volume to be land disposed. Although the specific calculations used to estimate toxicity and volume factors are complex, the calculation of the final score used for ranking purposes is simply the product of these two factors. The RCRA Method report is well referenced and contains detailed appendices that demonstrate how to calculate toxicity and volume factors. In addition, it presents the actual ranking of 363 constituents hazardous under RCRA.

APPENDIX G

EUROPEAN ECONOMIC COMMUNITY (EEC) PLAN

The EEC Plan was developed in order to classify "new chemicals" with respect to their potential hazard to humans and the environment, and to provide guidelines for developing a ranking system for hazardous wastes sites. Details were published by Schmidt-Bleek et al., (1982).

G.1 Type of Toxic Effect

According to the EEC Plan, hazard scores are assigned for each of three media: air, water, and soil/sediment. In each case the hazard score is the product of an exposure score times an "effects" score. The effects score takes into account mammalian oral and inhalational subchronic toxicities, aquatic toxicity, mutagenicity and dermal sensitization. Subscores for each of these aspects of toxicity are based upon data as described in the following sections. The subscores are combined as described below.

For soil/sediment, the effects score is the mammalian oral toxicity subscore plus one half of the score of the mutagenicity and dermal sensitization subscores. For air, the effects score is the mammalian inhalational toxicity subscore plus one half the scores of the mutagenicity and dermal sensitization subscores. The effects score for water is based upon the aquatic toxicity subscore (derived from data on fish and daphnia) plus one half the score of the mutagenicity and dermal sensitization subscores.

G.1.1 Acute Toxicity

Acute toxicity, per se, is not addressed by the EEC Plan. However, a score of 1.0 to 1.5 is assigned based upon the skin sensitization activity of the chemical. In the event of insufficient data, the highest possible score is assigned for sensitization. The use of dermal sensitization as a surrogate for acute systemic toxicity is a shortcoming of this method because many dermal sensitizers (e.g., nickel) are not acute systemic toxicants when applied topically and vice versa (National Academy of Sciences, 1975).

G.1.2 Chronic Toxicity

The EEC Plan does not directly consider chronic toxicity; instead, subchronic toxicity is evaluated. The EEC Plan assigns a score of 1 to 3 for mammalian toxicity based upon the NOEL observed in either a subchronic (28-day) oral study or a subchronic (4 hours of exposure/day) inhalation study. In the event of insufficient data, the highest possible score is assigned.

G.1.3 Carcinogenicity, Mutagenicity, and Teratogenicity (CMT) Factor

Mutagenicity effects are assigned a score of 1 to 3 in the EEC Plan, although the specific test organisms (bacterial, mammalian, etc.) or tests that are acceptable are not specified. A total of 2 tests are scored; if both tests are negative, a score of 1 is assigned. For each positive test, 1 point is added. Carcinogenicity and teratogenicity effects are not included in the system. The

omission of carcinogenicity and teratogenicity data from the EEC Plan is a shortcoming when attempting to rank hazardous wastes sites.

G.2 Determinants of Exposure

G.2.1 Persistence

The EEC Plan scores the environmental persistence of chemicals by summing the scores assigned for biodegradability and those assigned for abiotic degradability. A total of 2 points is scored for compounds that are resistant to biodegradation in soil or water; one point is scored for "readily biodegradable" compounds. (The criteria for assignment of scores are not specified.) For abiotic degradation, scores are assigned based on either hydrolysis half-life (shorter than 1 year = 1; 1 year or longer = 2) or photodegradability ("good evidence for instability" = 1; "no good evidence for instability" = 2). The persistence subscore is a term in the calculation of the exposure score. Assessment of this characteristic is especially difficult for the EEC Plan because guidance concerning the requisite data bases or references are lacking.

G.2.2 Routes of Release

Three routes of release are included in the EEC Plan: release into the air, water, and soil/sediment. However, water releases are not classified with regard to surface or ground water, and the meaning of release to soil/sediment is not defined. No assessment of toxicity due to accidental direct contact of people is presented.

G.2.3 Presence of Incompatible or Reactive Mixtures

The EEC Plan does not contain a factor which considers the hazard due to incompatible or reactive mixtures.

G.3 Use of Data

G.3.1 Number of Substances Evaluated

The EEC Plan is designed to assess the potential risks due to exposure to new chemicals prior to their disposal at wastes sites. Therefore, it evaluates one chemical at a time, often using only its physical and chemical properties. It is not clear from the description of the Plan whether only one chemical or all chemicals would be evaluated for ranking a wastes site.

G.3.2 Quantity of Data on Each Substance

Numerous data are required on each chemical. Several physical and chemical properties for each chemical, such as log P, vapor pressure, water solubility, and molecular weight are needed for the proposed hazard scoring, as well as the following toxicity data: subchronic toxicity for mammals, dermal sensitization, mutagenicity tests, and acute toxicity to fish and daphnids. For chemicals on which there are insufficient data, the maximum score for that particular element is assigned.

G.3.3 Clarity

The EEC Plan does not actually rank hazardous wastes sites, but rather presents theoretical guidelines that could be followed to develop a hazard ranking system. It describes, in general, how a

decision-tree may be constructed for the purpose of regulating wastes sites. The overall system is based on hazard assessments for individual chemicals which are combined using a series of formulas (few of which are clearly explained or derived) to achieve a final score. The overall Plan is not clearly presented. The terminology is often ill-defined or imprecisely used, making the EEC Plan open to wide variation in interpretation. These deficiencies result in a somewhat confusing and ambiguous system.

APPENDIX H

SYSTEM FOR PREVENTION, ASSESSMENT, AND CONTROL OF EXPOSURES AND HEALTH EFFECTS FROM HAZARDOUS SITES (SPACE)

The SPACE for Health system was developed by the Centers for Disease Control for State health agencies to prevent or control human health problems related to exposure to hazardous wastes (Centers for Disease Control, 1984).

H.1 Type of Toxic Effect

H.1.1 Acute Toxicity

The SPACE system uses the same evaluation methodology as the EPA HRS for toxicity assessments; however, it scores the five most toxic substances per site as opposed to the single most toxic substance.

H.1.2 Chronic Toxicity

Since this system utilizes the same methodology as the EPA HRS toxicity factor, in general, it does not consider chronic effects.

H.1.3 Carcinogenicity, Mutagenicity, and Teratogenicity (CMT) Factor

The SPACE system does not consider CMT effects.

H.2 Determinants of Exposure

H.2.1 Persistence

The SPACE system utilizes the same criteria as the EPA HRS for assignment of the environmental persistence of substances. Consequently, its persistence score takes into account only resistance to biodegradation.

H.2.2 Routes of Exposure

The SPACE system includes factors which consider contamination of soil and food chains in addition to ground water, surface water and air.

H.2.3 Presence of Incompatible or Reaction Mixtures

Although the SPACE system instructs assessors to determine whether or not reactive mixtures are present (and if so whether they are sufficiently separated to be safe), it does not provide guidance for identifying substances that will react/ignite when mixed.

H.3 Use of Data

H.3.1 Number of Substances Evaluated

The toxicity, quantity, and concentration of the five most hazardous substances at a wastes site are included in the scoring of a wastes site by the SPACE system.

H.3.2 Quantity of Data on Each Substance

Since the SPACE system utilizes the methodology described in the EPA HRS for its toxicity assessments, its data requirements are the same as those for the EPA HRS.

H.3.3 Clarity

The SPACE system outlines steps to be followed for the inspection, monitoring, and assigning priorities for cleanup of hazardous wastes sites. A flow diagram allows one to see at a glance the entire process from identification of wastes sites to the assignment of priorities and performance of the requisite health

studies. This system is intended for use by State health officials to rank a wide diversity of wastes sites but lacks specific details. However, there is extensive referral to literature sources where the reader may acquire in-depth information. Although the scoring of many of the individual components of a waste site is abstracted directly from the EPA HRS, it is not clear how the overall site score is calculated.

H.4 Other Considerations

Although the SPACE system utilizes many of the same criteria and methods for assessing toxicity as the EPA HRS, it goes beyond the EPA HRS in several aspects of human health effect assessments. For instance, in determining the potential for exposure to a hazardous substance, the SPACE system requires that samples be obtained not only from ground water, surface water, soil, and air for contamination, but also that the food chain be monitored for the possible presence of the hazardous substances. Scores of 0 to 3 are assigned based upon whether the substance is absent, present above background levels, present at or near the food tolerance level promulgated by the Food and Drug Administration (FDA), or present significantly above the FDA tolerance levels.

The SPACE system can also extend the basis upon which human exposure can be verified by monitoring the potentially exposed population through sampling of biological fluids (blood and urine) for the presence of the contaminant. In the absence of the ability

to perform biological assays, or in the case of allegations of past (but not current) exposure, the SPACE system can utilize epidemiological data. These data may be gathered both from current interviews, questionnaires, or retrospective studies via review of hospital clinical data or death records/birth defects registries and the like. Positive findings from the aforementioned types of studies can be used to raise the priority assigned a site. However, the overall impact of these scores on a site's priority is not clear because, as mentioned previously, the exact way to devise an overall site score is not clearly defined.

APPENDIX I

EXAMPLE OF PROPOSED SCORING METHODOLOGY

Toxicity values have been assigned to 30 hazardous substances based on the methodology presented in Section 4. This appendix presents the supporting data and provides guidance on how the methodology should be applied in order to assign toxicity values for one organic chemical (1,1,2-trichloroethylene; TCE). The data for all of the substances are provided in tabular form in Appendix J (n.b., one sheet is used per substance).*

I.1 Illustration of Methodology-TCE

Table I-1 presents the supporting data for assigning the pathway-specific toxicity values to 1,1,2-trichloroethylene. The pathway-specific toxicity values are derived by adding together the assigned oral, dermal, inhalational, and CM values as described in Section 4 and in this section.

I.2 CM

CM potential is assessed and incorporated into the pathway-specific toxicity values. Entries of CM data in the table are as follows. First, for weight-of-evidence, the positive responses (based on the definition of a positive response in RTECS), are a positive oral test in mice and positive inhalational tests in rats and hamsters. Thus, TCE has been shown to induce cancer in more

*For purposes of this paper, data tables are provided for only 30 selected substances. These substances are identified in Table 10.

TABLE I-1

SUPPORTING DATA FOR 1,1,2-TRICHLOROETHYENE

CM

Weight-of-Evidence
Basis: Positive, Mouse, Oral — Category: III
Positive, Hamster, Rat, Inhalation

Potency
Basis: ED_{10} = 6.67 mg/kg/day — Group: Low

Matrix: III x Low — CM Value: 2

ORAL TOXICITY

Acute Basis: LD_{50} = 2402 mg/kg (mouse) — Acute Value: 1

Chronic Basis: ADI = $2402/10^5$ = 0.024 — Chronic Value: 3

CM (from above): — CM Value: 2

$Toxicity_{ORAL}$ 6

DERMAL TOXICITY

Acute Basis: Dermal Irritation = Severe — Acute Value: 3

Chronic Basis: Default to Chronic Oral — Chronic Value: 3

CM (from above): — CM Value: 2

$Toxicity_{DERMAL}$ 8

INHALATION TOXICITY

Acute Basis: LC_{LO} = 3000 ppm/2H (mouse) — Acute Value: 2
ppm/4H: 1500 ppm/4H

Chronic Basis: TLV-TWA = 50 ppm = 270 mg/m^3 — Chronic Value: 0
ADI*: 32.13

CM (from above): — CM Value: 2

$Toxicity_{INHALATION}$ 4

*ADI = (TLV-TWA)(0.119).

than two animal species and is assigned to Category III according to the rules presented in Table 6. If no data had been available regarding carcinogenicity or mutagenicity, the weight-of-evidence value would have been 0. Second, for potency, the EPA has determined the ED_{10} for TCE to be 6.67 mg/kg/day. Since the ED_{10} is greater than 1.0 mg/kg/day, TCE is assigned to a low potency group following the rules presented in Table 7. Following the matrix presented in Table 8, substances in weight-of-evidence Category III with a low potency are assigned a CM value of 2.

I.3 Oral Toxicity

The oral toxicity of TCE is assessed in the following manner. The lowest mammalian oral LD_{50} listed in RTECS is 2,402 mg/kg in mice. Following the rules presented in Table 4, the LD_{50} is between 500 to 5,000 mg/kg resulting in an assigned acute oral value of 1. No chronic toxicity information is in listed RTECS and a RfD has not been assigned. Thus, the chronic value is determined by using the magnitude of $(LD_{50})(10^{-5})$ = 0.024 mg/kg. Following the rules in Table 5, this value is less than 0.5 mg/kg and thus a chronic oral value of 3 is assigned. The $toxicity_{oral}$ value is the sum of the $acute_{oral}$, $chronic_{oral}$, and CM values. Thus, the $toxicity_{oral}$ value for TCE is 6.

I.4 Dermal Toxicity

The dermal toxicity of TCE is assessed in the following manner. No dermal LD_{50} data are listed in RTECS, however, TCE is

reported to be a severe dermal irritant. Based on the irritation criteria in Table 4, TCE is assigned an acute dermal value of 3. No chronic dermal data are listed in RTECS. Since a dermal LD_{50} is not available, the chronic dermal value defaults to the chronic oral value of 3. The $toxicity_{dermal}$ value is the sum of the acute dermal, chronic dermal, and CM values. Thus, the $toxicity_{dermal}$ value is 8.

I.5 Inhalational Toxicity

The inhalation toxicity of TCE is assessed in the following manner. A mammalian LC_{50} value is not available, however, the lowest mammalian LC_{lo} is 3,000 ppm for a 2-hour exposure to mice. Since LC_{50} data are not available, the LC_{lo} may be used. The value reported is for a 2-hour exposure and must be converted to a 4-hour exposure using Haber's law which states that the product of exposure concentration and duration of exposure is a constant. Thus, the concentration for a 4-hour exposure period is calculated from the equation:

$$\text{concentration}_{4\text{-hour}} = \frac{(2\text{-hour})(3{,}000 \text{ ppm})}{4\text{-hours}} = 1{,}500 \text{ ppm}$$

According to Table 4, the acute inhalational value is 2, because 1,500 ppm is between 200 and 2,000 ppm. Since a TLV-TWA is available for TCE, a chronic inhalational score can be calculated by the formula:

$$ADI = (\text{TLV-TWA})(0.119)$$

Since the TLV-TWA for TCE is 270 mg/m^3, the ADI is 32.13 mg/m^3.

A chronic inhalational value of 0 is assigned because the calculated ADI is greater than 20 mg/m^3. The $toxicity_{inhalational}$ value is the sum of the $acute_{inhalational}$ + $chronic_{inhalation}$ + CM values. Thus, the $toxicity_{inhalational}$ value for TCE is 4.

APPENDIX J

SUPPORTING DATA FOR ASSIGNING TOXICITY VALUES TO HAZARDOUS SUBSTANCES

SUBSTANCE NAME: 1,1-Dichloroethylene CAS NO: 00075-35-4

CM

Weight-of-Evidence
Basis: Positive, Mouse, Inhalation Category: III
Positive, Rat, Inhalation

Potency
Basis: ED_{10} = 0.233 mg/kg/day Group: Med

Matrix: III x Med CM Value: 3

ORAL TOXICITY

Acute Basis: LD_{50} = 200 mg/kg (rat) Acute Value: 2

Chronic Basis: RfD = 0.009 mg/kg/day Chronic Value: 3

CM (from above): CM Value: 3

$Toxicity_{ORAL}$ 8

DERMAL TOXICITY

Acute Basis: Default to Acute Oral Acute Value: 2

Chronic Basis: Default to Chronic Oral Chronic Value: 3

CM (from above): CM Value: 3

$Toxicity_{DERMAL}$ 8

INHALATION TOXICITY

Acute Basis: LC_{50} = 539 ppm/4H (mouse) Acute Value: 2

Chronic Basis: TLV-TWA = 5 ppm = 20 mg/m^3 Chronic Value: 1
ADI* 2.38

CM (from above): CM Value: 3

$Toxicity_{INHALATIONAL}$ 6

*ADI = (TLV-TWA)(0.119).

SUBSTANCE NAME: 1,1,1-Trichloroethane CAS NO: 00071-55-6

CM

Weight-of-Evidence Basis: In Vitro, Mutagenicity Category: I

Potency Basis: Default Group: Low

Matrix: I x Low CM Value: 1

ORAL TOXICITY

Acute Basis: LD_{50} = 5660 mg/kg (rabbit) Acute Value: 0

Chronic Basis: TD_{LO}=43 mg/kg (rat cardiovascular anomalies) ADI=43/1000=0.043 mg/kg/day Chronic Value: 2

CM (from above): CM Value: 1

$Toxicity_{ORAL}$ 3

DERMAL TOXICITY

Acute Basis: LD_{50} = 1000 mg/kg (rabbit) Acute Value: 2

Chronic Basis: ADI=1000/10^5=0.1 mg/kg/day Chronic Value: 3

CM (from above): CM Value: 1

$Toxicity_{DERMAL}$ 6

INHALATION TOXICITY

Acute Basis: LC_{LO} = 1000 ppm/4H (rat) Acute Value: 2

Chronic Basis: TLV-TWA = 350 ppm = 1900 mg/m^3 Chronic Value: 0

ADI* 226.1

CM (from above): CM Value: 1

$Toxicity_{INHALATIONAL}$ 3

*ADI = (TLV-TWA)(0.119).

SUBSTANCE NAME: 1,1,2-Trichloroethylene CAS NO: 00079-01-6

CM

Weight-of-Evidence
Basis: Positive, Mouse, Oral Category: III
Positive, Hamster, Rat, Inhalation

Potency
Basis: ED_{10} = 6.67 mg/kg/day Group: Low

Matrix: III x Low CM Value: 2

ORAL TOXICITY

Acute Basis: LD_{50} = 2402 mg/kg (mouse) Acute Value: 1

Chronic Basis: ADI = $2402/10^5$ = 0.024 Chronic Value: 3

CM (from above): CM Value: 2

$Toxicity_{ORAL}$ 6

DERMAL TOXICITY

Acute Basis: Dermal Irritation - Severe Acute Value: 3

Chronic Basis: Default to Chronic Oral Chronic Value: 3

CM (from above): CM Value: 2

$Toxicity_{DERMAL}$ 8

INHALATION TOXICITY

Acute Basis: LC_{LO} = 3000 ppm/2H (mouse) Acute Value: 2
ppm/4H: 1500 ppm/4H

Chronic Basis: TLV-TWA = 50 ppm = 270 mg/m^3 Chronic Value: 0
ADI* 32.13

CM (from above): CM Value: 2

$Toxicity_{INHALATIONAL}$ 4

*ADI = (TLV-TWA)(0.119).

SUBSTANCE NAME: Acetone CAS NO: 00067-64-1

CM

Weight-of-Evidence Basis: In Vitro, Mutagenicity Category: I

Potency Basis: Default Group: Low

Matrix: I x Low CM Value: 1

ORAL TOXICITY

Acute Basis: LD_{50} = 3000 mg/kg (mouse) Acute Value: 1

Chronic Basis: RfD = 0.1 mg/kg/day Chronic Value: 2

CM (from above): CM Value: 1

$Toxicity_{ORAL}$ 4

DERMAL TOXICITY

Acute Basis: LD_{50} = 20000 mg/kg (rabbit) Acute Value: 1

Chronic Basis: ADI=20000/10^5=0.2 mg/kg/day Chronic Value: 2

CM (from above): CM Value: 1

$Toxicity_{DERMAL}$ 4

INHALATION TOXICITY

Acute Basis: LC_{50} = 110000 mg/m^3/62M Acute Value: 1
ppm/4H: 11985 ppm/4H (mouse)

Chronic Basis: TLV-TWA = 750 ppm = 1780 mg/m^3 Chronic Value: 0
ADI* 211.82

CM (from above): CM Value: 1

$Toxicity_{INHALATIONAL}$ 2

*ADI = (TLV-TWA)(0.119).

SUBSTANCE NAME: Arsenic (as Arsenic Trioxide) CAS NO: 01327-53-3

CM

Weight-of-Evidence Basis: Positive, Human Category: III

Potency Basis: ED_{10} = 0.00703 mg/kg/day Group: High

Matrix: III x High CM Value: 3

ORAL TOXICITY

Acute Basis: LD_{50} = 15.1 mg/kg (rat) Acute Value: 3

Chronic Basis: RfD = 0.0004 Chronic Value: 3

CM (from above): CM Value: 3

$Toxicity_{ORAL}$ 9

DERMAL TOXICITY

Acute Basis: Default to Acute Oral Acute Value: 3

Chronic Basis: Default to Chronic Oral Chronic Value: 3

CM (from above): CM Value: 3

$Toxicity_{DERMAL}$ 9

INHALATION TOXICITY

Acute Basis: Default to Chronic Inhalation Acute Value: 3

Chronic Basis: TWA = 10 ug (As)/m^3 = 13.2 ug/m^3 (of Arsenic trioxide) Chronic Value: 3

ADI* 0.00157

CM (from above): CM Value: 3

$Toxicity_{INHALATIONAL}$ 9

*ADI = (OSHA Air Standard-TWA)(0.119)

SUBSTANCE NAME: Benzene CAS NO: 00071-43-2

CM

Weight-of-Evidence Basis: Positive, Human Category: III

Potency Basis: ED_{10} = 3.7 mg/kg/day Group: Low

Matrix: III x Low CM Value: 2

ORAL TOXICITY

Acute Basis: LD_{50} = 4700 mg/kg (mouse) Acute Value: 1

Chronic Basis: TD_{LO} = 900 mg/kg (reduced (fetal weights) ADI=900/1000=0.9 mg/kg/day Chronic Value: 1

CM (from above): CM Value: 2

$Toxicity_{ORAL}$ 4

DERMAL TOXICITY

Acute Basis: Dermal Irritation - Moderate Acute Value: 2

Chronic Basis: Default to Chronic Oral Chronic Value: 1

CM (from above): CM Value: 2

$Toxicity_{DERMAL}$ 5

INHALATION TOXICITY

Acute Basis: LC_{50} = 9980 ppm (mouse) LC_{50} = 17500 ppm/4H (rat) Acute Value: 1

Chronic Basis: TLV-TWA = 10 ppm = 30 mg/m^3 ADI* 3.57 Chronic Value: 1

CM (from above): CM Value: 2

$Toxicity_{INHALATIONAL}$ 4

*ADI = (TLV-TWA)(0.119).

SUBSTANCE NAME: Benzo(a)pyrene CAS NO: 00050-32-8

CM

Weight-of-Evidence
Basis: Positive, Rat; Positive, Mouse Category: III

Potency
Basis: ED_{10} = 0.00628 mg/kg/day Group: High

Matrix: III x High CM Value: 3

ORAL TOXICITY

Acute Basis: Default to Chronic Oral Acute Value: 2

Chronic Basis: TD_{LO} 100 mg/kg, mouse (decreased male/female indices; decreased liveborn) ADI=100/1000=0.1 mg/kg/day Chronic Value: 2

CM (from above): CM Value: 3

$Toxicity_{ORAL}$ 7

DERMAL TOXICITY

Acute Basis: Dermal Irritation, Mild Acute Value: 1

Chronic Basis: Default to Chronic Oral Chronic Value: 2

CM (from above): CM Value: 3

$Toxicity_{DERMAL}$ 6

INHALATION TOXICITY

Acute Basis: Default to Acute Oral Acute Value: 2

Chronic Basis: Default to Chronic Oral Chronic Value: 2

CM (from above): CM Value: 3

$Toxicity_{INHALATIONAL}$ 7

SUBSTANCE NAME: Cadmium (as Cadmium Chloride) CAS NO: 10108-64-2

CM

Weight-of-Evidence Basis: Positive, Rat, Inhalation; Positive, Mouse, Subcutaneous — Category: III

Potency Basis: ED_{10} = 0.0173 mg/kg/day — Group: Med

Matrix: III x Med — CM Value: 3

ORAL TOXICITY

Acute Basis: LD_{50} = 60 mg/kg (mouse) — Acute Value: 2

Chronic Basis: TD_{LO} = 17 mg/kg (musculoskeletal anomalies); ADI = 17/1000 = 0.017 mg — Chronic Value: 3

CM (from above): — CM Value: 3

$Toxicity_{ORAL}$ 8

DERMAL TOXICITY

Acute Basis: LD_{LO}=233 mg/kg (guinea pig) — Acute Value: 2

Chronic Basis: ADI = $233/10^5$ = 0.00233 — Chronic Value: 3

CM (from above): — CM Value: 3

$Toxicity_{DERMAL}$ 8

INHALATION TOXICITY

Acute Basis: LC_{90}=420 mg/m^3/30M (dog); ppm/4H: 7 ppm/4H — Acute Value: 3

Chronic Basis: TLV-TWA = 50 ug(Cd)/m^3 = 81.53 ug/m^3 (of Cadmium chloride); ADI*: 0.00097 — Chronic Value: 3

CM (from above): — CM Value: 3

$Toxicity_{INHALATIONAL}$ 9

*ADI = (TLV-TWA)(0.119).

SUBSTANCE NAME: Carbon Tetrachloride CAS NO: 00056-23-5

CM

Weight-of-Evidence
Basis: Positive, Mouse, Oral
Positive, Hamster, Oral
Positive, Rat, Subcutaneous
Category: III

Potency
Basis: ED_{10} = 0.0152 mg/kg/day
Group: Med

Matrix: III x Med
CM Value: 3

ORAL TOXICITY

Acute Basis: LD_{50} = 2800 mg/kg (rat)
Acute Value: 1

Chronic Basis: ADI=2800/10^5=0.28 mg/kg/day
Chronic Value: 3

CM (from above):
CM Value: 3

$Toxicity_{ORAL}$ 7

DERMAL TOXICITY

Acute Basis: LD_{50} = 5070 mg/kg (rat)
Acute Value: 1

Chronic Basis: ADI=5070/10^5=0.0507 mg/kg
Chronic Value: 3

CM (from above):
CM Value: 3

$Toxicity_{DERMAL}$ 7

INHALATION TOXICITY

Acute Basis: LC_{50} = 9526 ppm/8H (rat)
ppm/4H: 19052 ppm/4H
Acute Value: 1

Chronic Basis: TLV-TWA = 5 ppm = 30 mg/m^3
ADI* 3.57
Chronic Value: 1

CM (from above):
CM Value: 3

$Toxicity_{INHALATIONAL}$ 5

*ADI = (TLV-TWA)(0.119).

SUBSTANCE NAME: Chlorobenzene CAS NO: 00108-90-7

CM

Weight-of-Evidence Basis: In Vitro, Mutagenicity Category: I

Potency Basis: Default Group: Low

Matrix: I x Low CM Value: 1

ORAL TOXICITY

Acute Basis: LD_{50} 2830 mg/kg (rabbit) Acute Value: 1

Chronic Basis: ADI=2830/10^5=0.0283 mg/kg/day Chronic Value: 2

CM (from above): CM Value: 1

$Toxicity_{ORAL}$ 4

DERMAL TOXICITY

Acute Basis: Default to Acute Oral Acute Value: 1

Chronic Basis: Default to Chronic Oral Chronic Value: 2

CM (from above): CM Value: 1

$Toxicity_{DERMAL}$ 4

INHALATION TOXICITY

Acute Basis: LC_{LO}=15000 mg/m^3=3265 ppm Acute Value: 1

Chronic Basis: TLV-TWA = 75 ppm = 350 mg/m^3 ADI* 41.65 Chronic Value: 0

CM (from above): CM Value: 1

$Toxicity_{INHALATIONAL}$ 2

*ADI = (TLV-TWA)(0.119).

SUBSTANCE NAME: Chloroform CAS NO: 00067-66-3

CM

Weight-of-Evidence
Basis: Positive, Rat, Oral Category: III
Positive, Mouse, Oral

Potency
Basis: ED_{10} = 0.508 mg/kg/day Group: Med

Matrix: III x Med CM Value: 3

ORAL TOXICITY

Acute Basis: LD_{50} = 36 mg/kg (mouse) Acute Value: 3

Chronic Basis: RfD = 0.01 mg/kg/day Chronic Value: 3

CM (from above): CM Value: 3

$Toxicity_{ORAL}$ 9

DERMAL TOXICITY

Acute Basis: Dermal Irritation - Mild Acute Value: 1

Chronic Basis: Default to Chronic Oral Chronic Value: 3

CM (from above): CM Value: 3

$Toxicity_{DERMAL}$ 7

INHALATION TOXICITY

Acute Basis: LC_{50} = 5747 ppm (mouse) Acute Value: 1

Chronic Basis: TLV-TWA = 10 ppm = 50 mg/m^3 Chronic Value: 1
50 mg/m^3

ADI* 5.95

CM (from above): CM Value: 3

$Toxicity_{INHALATIONAL}$ 5

*ADI = (TLV-TWA)(0.119).

SUBSTANCE NAME: Chromium (see Chromium, Hexavalent) CAS NO: 13765-19-0

CM

Weight-of-Evidence Basis: Positive, Human Category: III

Potency Basis: ED_{10} = 0.00257 mg/kg/day Group: High

Matrix: III x High CM Value: 3

ORAL TOXICITY

Acute Basis: LD_{50} = 327 mg/kg (rat) (as dihydrate) Acute Value: 2

Chronic Basis: ADI = $327/10^5$ = 0.00327 Chronic Value: 3

CM (from above): CM Value: 3

$Toxicity_{ORAL}$ 8

DERMAL TOXICITY

Acute Basis: Default to Acute Oral Acute Value: 2

Chronic Basis: Default to Chronic Oral Chronic Value: 3

CM (from above): CM Value: 3

$Toxicity_{DERMAL}$ 8

INHALATION TOXICITY

Acute Basis: Default to Chronic Inhalation Acute Value: 3

Chronic Basis: TLV-TWA = 50 ug(Cu)/m^3 = 150.6 ug/m^3 (chromic acid, calcium) Chronic Value: 3

ADI* 0.018

CM (from above): CM Value: 3

$Toxicity_{INHALATIONAL}$ 9

*ADI = (TLV-TWA)(0.119).

SUBSTANCE NAME: Chromium, Trivalent (as Chromium Sulfate) CAS NO: 10101-53-8

CM

Weight-of-Evidence Basis: In Vitro, Mutagenicity Category: I

Potency Basis: Default Group: Low

Matrix: I x Low CM Value: 1

ORAL TOXICITY

Acute Basis: Default to Chronic Oral Acute Value: 1

Chronic Basis: RfD = 1.0 mg/kg/day Chronic Value: 1

CM (from above): CM Value: 1

$Toxicity_{ORAL}$ 3

DERMAL TOXICITY

Acute Basis: Default to Acute Oral Acute Value: 1

Chronic Basis: Default to Chronic Oral Chronic Value: 1

CM (from above): CM Value: 1

$Toxicity_{DERMAL}$ 3

INHALATION TOXICITY

Acute Basis: Default to Chronic Inhalation Acute Value: 2

Chronic Basis: TLV-TWA = 500 ug(Cr)/m^3 = 1.885 mg/m^3 (of Chromium sulfate) Chronic Value: 2

ADI* 0.224

CM (from above): CM Value: 1

$Toxicity_{INHALATIONAL}$ 5

*ADI = (TLV-TWA)(0.119).

SUBSTANCE NAME: Copper (as Cupric Chloride) CAS NO: 07447-39-4

CM

Weight-of-Evidence Basis: In Vitro, Mutagenicity Category: I

Potency Basis: Default Group: Low

Matrix: I x Low CM Value: 1

ORAL TOXICITY

Acute Basis: LD_{50}=31 mg/kg (guinea pig) Acute Value: 3

Chronic Basis: ADI = $31/10^5$ = 0.00031 mg Chronic Value: 3

CM (from above): CM Value: 1

$Toxicity_{ORAL}$ 7

DERMAL TOXICITY

Acute Basis: Default to Acute Oral Acute Value: 3

Chronic Basis: Default to Chronic Oral Chronic Value: 3

CM (from above): CM Value: 1

$Toxicity_{DERMAL}$ 7

INHALATION TOXICITY

Acute Basis: Default to Chronic Inhalation Acute Value: 2

Chronic Basis: TLV-TWA = 0.2 mg/m^3 (Cu) = 0.423 mg/m^3 (of Cupric chloride) Chronic Value: 2

ADI* 0.05035

CM (from above): CM Value: 1

$Toxicity_{INHALATIONAL}$ 5

*ADI = (TLV-TWA)(0.119).

SUBSTANCE NAME: Creosote CAS NO: 08001-58-9

CM

Weight-of-Evidence Basis: In Vitro, Mutagenicity Category: I

Potency Basis: Default Group: Low

Matrix: I x Low CM Value: 1

ORAL TOXICITY

Acute Basis: LD_{50} = 433 mg/kg (mouse) Acute Value: 2

Chronic Basis: TD_{LO} = 210 mg/kg/day (testicular, epidydimal degeneration) ADI=$210/10^3$=0.21 mg/kg/day Chronic Value 2

CM (from above): CM Value: 1

$Toxicity_{ORAL}$ 5

DERMAL TOXICITY

Acute Basis: Default to Acute Oral Acute Value: 2

Chronic Basis: Default to Chronic Oral Chronic Value: 2

CM (from above): CM Value: 1

$Toxicity_{DERMAL}$ 5

INHALATION TOXICITY

Acute Basis: Default to Chronic Inhalation Acute Value: 3

Chronic Basis: TWA = 0.1 mg/m^3 ADI* 0.0119 Chronic Value: 3

CM (from above): CM Value: 1

$Toxicity_{INHALATIONAL}$ 7

*ADI = (OSHA Air Standard - TWA)(0.119)

SUBSTANCE NAME: DDT CAS NO: 00050-29-3

CM

Weight-of-Evidence
Basis: Positive, Mouse
Positive, Rat
Positive, Hamster
Category: III

Potency
Basis: ED_{10} = 0.179 mg/kg/day
Group: Med

Matrix: III x Med
CM Value: 3

ORAL TOXICITY

Acute Basis: LD_{50} = 87 mg/kg (rat)
Acute Value: 2

Chronic Basis: RfD = 0.0005 mg/kg/day
Chronic Value: 3

CM (from above):
CM Value: 3

$Toxicity_{ORAL}$ 8

DERMAL TOXICITY

Acute Basis: LD_{50} = 300 mg/kg (rabbit)
Acute Value: 2

Chronic Basis: ADI=300/10^5=0.003 mg/kg/day
Chronic Value: 3

CM (from above):
CM Value: 3

$Toxicity_{DERMAL}$ 8

INHALATION TOXICITY

Acute Basis: Default to Chronic Inhalation
Acute Value: 3

Chronic Basis: TLV-TWA = 1 mg/m^3
ADI* 0.119
Chronic Value: 3

CM (from above):
CM Value: 3

$Toxicity_{INHALATIONAL}$ 9

*ADI = (TLV-TWA)(0.119).

SUBSTANCE NAME: Lead (as Tetraethyl Lead) CAS NO: 00078-00-2

CM

Weight-of-Evidence Basis: Positive, Mouse, Subcutaneous Category: II

Potency Basis: Default Group: Low

Matrix: II x Low CM Value: 1

ORAL TOXICITY

Acute Basis: LD_{50} = 12.3 mg/kg (rat) Acute Value: 3

Chronic Basis: RfD = 1.0×10^{-7} Chronic Value: 3

CM (from above): CM Value: 1

$Toxicity_{ORAL}$ 7

DERMAL TOXICITY

Acute Basis: LD_{LO} = 547 mg/kg (dog) Acute Value: 2

Chronic Basis: ADI = $547/10^5$ = 0.00547 Chronic Value: 3

CM (from above): CM Value: 1

$Toxicity_{DERMAL}$ 6

INHALATION TOXICITY

Acute Basis: LC_{50} = 850 mg/m^3/60M (rat) Acute Value: 3

ppm/4H: 16 ppm/4H

Chronic Basis: TLV-TWA = 100 ug(Pb)/m^3 Chronic Value: 3

156 ug/m^3 (tetraethyl lead)

ADI* 0.0186

CM (from above): CM Value: 1

$Toxicity_{INHALATIONAL}$ 7

*ADI = (TLV-TWA)(0.119).

SUBSTANCE NAME: Lindane CAS NO: 00058-89-9

CM

Weight-of-Evidence Basis: Positive, Mouse Category: II

Potency Basis: ED_{10} = 0.546 mg/kg/day Group: Med

Matrix: II x Med CM Value: 2

ORAL TOXICITY

Acute Basis: LD_{50} = 60 mg/kg (rabbit) Acute Value: 2

Chronic Basis: RfD = 0.0003 mg/kg/day Chronic Value: 3

CM (from above): CM Value: 2

$Toxicity_{ORAL}$ 7

DERMAL TOXICITY

Acute Basis: LD_{50} = 50 mg/kg (rabbit) Acute Value: 3

Chronic Basis: ADI=50/10^5=0.0005 mg/kg/day Chronic Value: 3

CM (from above): CM Value: 2

$Toxicity_{DERMAL}$ 8

INHALATION TOXICITY

Acute Basis: Default to Chronic Inhalation Acute Value: 3

Chronic Basis: TLV-TWA = 0.5 mg/m^3 Chronic Value: 3
ADI* 0.0595

CM (from above): CM Value: 2

$Toxicity_{INHALATIONAL}$ 8

*ADI = (TLV-TWA)(0.119).

SUBSTANCE NAME: Mercury (as Mercuric Sulfate) CAS NO: 07783-35-9

CM

Weight-of-Evidence Basis: No Data Category: 0

Potency Basis: Default Group: Low

Matrix: 0 x Low CM Value: 0

ORAL TOXICITY

Acute Basis: LD_{50} = 40 mg/kg (mouse) Acute Value: 3

Chronic Basis: RfD = 0.002 mg (inorganic Mercuric Compounds) Chronic Value: 3

CM (from above): CM Value: 0

$Toxicity_{ORAL}$ 6

DERMAL TOXICITY

Acute Basis: Default to Acute Oral Acute Value: 3

Chronic Basis: Default to Chronic Oral Chronic Value: 3

CM (from above): CM Value: 0

$Toxicity_{DERMAL}$ 6

INHALATION TOXICITY

Acute Basis: Default to Chronic Inhalation Acute Value: 3

Chronic Basis: TLV-TWA = 100 ug(Hg)/m^3 = 147.9 ug/m^3 (of Mercuric Sulfate) Chronic Value: 3

ADI* 0.0176

CM (from above): CM Value: 0

$Toxicity_{INHALATIONAL}$ 6

*ADI = (TLV-TWA)(0.119).

SUBSTANCE NAME: Methyl Ethyl Ketone CAS NO: 00078-93-3

CM

Weight-of-Evidence Basis: No Data Category: 0

Potency Basis: Default Group: Low

Matrix: 0 x Low CM Value: 0

ORAL TOXICITY

Acute Basis: LD_{50} = 2737 mg/kg (rat) Acute Value: 1

Chronic Basis: RfD = 0.05 mg/kg/day Chronic Value: 2

CM (from above): CM Value: 0

$Toxicity_{ORAL}$ 3

DERMAL TOXICITY

Acute Basis: LD_{50} = 13000 mg/kg (rabbit) Acute Value: 1

Chronic Basis: ADI=13000/10^5=0.13 mg/kg/day Chronic Value: 3

CM (from above): CM Value: 0

$Toxicity_{DERMAL}$ 4

INHALATION TOXICITY

Acute Basis: LC_{50} = 40 g/m^3/2H (mouse) Acute Value: 1
ppm/4H: 6794 ppm/4H

Chronic Basis: TLV-TWA=200 ppm=590 mg/m^3 Chronic Value: 0
ADI* 70.21

CM (from above): CM Value: 0

$Toxicity_{INHALATIONAL}$ 1

*ADI = (TLV-TWA)(0.119).

SUBSTANCE NAME: Naphthalene CAS NO: 00091-20-3

CM

Weight-of-Evidence
Basis: Positive, Rat, Subcutaneous Whole animal, Mutagenicity Category: II

Potency
Basis: Default Group: Low

Matrix: II x Low CM Value: 1

ORAL TOXICITY

Acute Basis: LD_{50} = 580 mg/kg (mouse) Acute Value: 1

Chronic Basis: ADI=580/10^5=0.0058 mg/kg/day Chronic Value: 3

CM (from above): CM Value: 1

$Toxicity_{ORAL}$ 5

DERMAL TOXICITY

Acute Basis: Dermal Irritation, Mild Acute Value: 1

Chronic Basis: Default to Chronic Oral Chronic Value: 3

CM (from above): CM Value: 1

$Toxicity_{DERMAL}$ 5

INHALATION TOXICITY

Acute Basis: Default to Chronic Inhalation Acute Value: 1

Chronic Basis: TLV-TWA = 10 ppm = 50 mg/m^3 Chronic Value: 1
ADI* 5.95

CM (from above): CM Value: 1

$Toxicity_{INHALATIONAL}$ 3

*ADI = (TLV-TWA)(0.119).

SUBSTANCE NAME: Polychlorinated Biphenyls (Arochlor 1254) CAS NO: 11097-69-1

CM

Weight-of-Evidence
Basis: Positive, Rat Category: III
Positive, Mouse

Potency
Basis: ED_{10} = 0.05 mg/kg/day Group: Med

Matrix: III x Med CM Value: 3

ORAL TOXICITY

Acute Basis: LD_{50} = 1010 mg/kg (rat) Acute Value: 1

Chronic Basis: TD_{LO} = 350 mg/kg (rabbit) Chronic Value: 3
(resorptions, abortion, fetal death)
ADI=350/1000 = 0.035 mg/kg/day

CM (from above): CM Value: 3

$Toxicity_{ORAL}$ 7

DERMAL TOXICITY

Acute Basis: Default to Acute Oral Acute Value: 1

Chronic Basis: Default to Chronic Oral Chronic Value: 3

CM (from above): CM Value: 3

$Toxicity_{DERMAL}$ 7

INHALATION TOXICITY

Acute Basis: Default to Chronic Inhalation Acute Value: 3

Chronic Basis: TLV-TWA = 500 ug/m^3 Chronic Value: 3
ADI* 0.0595

CM (from above): CM Value: 3

$Toxicity_{INHALATIONAL}$ 9

*ADI = (TLV-TWA)(0.119).

SUBSTANCE NAME: Pentachlorophenol (PCP) CAS NO: 00087-86-5

CM

Weight-of-Evidence Basis: Positive, Mouse, Subcutaneous Category: II

Potency Basis: Default Group: Low

Matrix: II x Low CM Value: 1

ORAL TOXICITY

Acute Basis: LD_{50} = 50 mg/kg (rat) Acute Value: 2

Chronic Basis: RfD = 0.03 mg/kg/day Chronic Value: 2

CM (from above): CM Value: 1

$Toxicity_{ORAL}$ 5

DERMAL TOXICITY

Acute Basis: LD_{50} = 105 mg/kg (rat) Acute Value: 3

Chronic Basis: ADI=105/10^5=0.00105 mg/kg/day Chronic Value: 3

CM (from above): CM Value: 1

$Toxicity_{DERMAL}$ 7

INHALATION TOXICITY

Acute Basis: Default to Chronic Inhalation Acute Value: 3

Chronic Basis: TLV-TWA = 500 ug/m^3 Chronic Value: 3
ADI* 0.0595

CM (from above): CM Value: 1

$Toxicity_{INHALATIONAL}$ 7

*ADI = (TLV-TWA)(0.119).

SUBSTANCE NAME: Phenanthrene CAS NO: 00085-01-8

CM

Weight-of-Evidence
Basis: Positive, Mouse, Dermal Category: II

Potency
Basis: Default Group: Low

Matrix: II x Low CM Value: 1

ORAL TOXICITY

Acute Basis: LD_{50} = 700 mg/kg (mouse) Acute Value: 1

Chronic Basis: ADI=700/10^5=0.007 mg/kg/day Chronic Value: 3

CM (from above): CM Value: 1

$Toxicity_{ORAL}$ 5

DERMAL TOXICITY

Acute Basis: Default to Acute Oral Acute Value: 1

Chronic Basis: Default to Chronic Oral Chronic Value: 3

CM (from above): CM Value: 1

$Toxicity_{DERMAL}$ 5

INHALATION TOXICITY

Acute Basis: Default to Acute Oral Acute Value: 1

Chronic Basis: Default to Chronic Oral Chronic Value: 3

CM (from above): CM Value: 1

$Toxicity_{INHALATIONAL}$ 5

SUBSTANCE NAME: Phenol CAS NO: 00108-95-2

CM

Weight-of-Evidence Basis: Positive, Mouse, Dermal Category: II

Potency Basis: Default Group: Low

Matrix: II x Low CM Value: 1

ORAL TOXICITY

Acute Basis: LD_{50} = 282 mg/kg/day (mouse) Acute Value: 2

Chronic Basis: RfD = 0.1 mg/kg/day Chronic Value: 2

CM (from above): CM Value: 1

$Toxicity_{ORAL}$ 5

DERMAL TOXICITY

Acute Basis: LD_{50} = 669 mg/kg (rat) Acute Value: 2

Chronic Basis: ADI=669/10^5=0.00669 mg/kg/day Chronic Value: 3

CM (from above): CM Value: 1

$Toxicity_{DERMAL}$ 6

INHALATION TOXICITY

Acute Basis: LD_{50}=177 mg/m^3=46.07 ppm Acute Value: 3

Chronic Basis: TLV-TWA = 5 ppm = 19 mg/m^3 Chronic Value: 1
ADI* 2.26

CM (from above): CM Value: 1

$Toxicity_{INHALATIONAL}$ 5

*ADI = (TLV-TWA)(0.119).

SUBSTANCE NAME: Tetrachloroethylene CAS NO: 00127-18-4

CM

Weight-of-Evidence
Basis: Positive, Mouse (NTP Bioassay) Category: III
Positive, Rat (NTP Bioassay)

Potency
Basis: ED_{10} = 3.23 mg/kg/day Group: Low

Matrix: III x Low CM Value: 2

ORAL TOXICITY

Acute Basis: LD_{50} = 8100 mg/kg (mouse) Acute Value: 0

Chronic Basis: RfD = 0.02 mg/kg/day Chronic Value: 2

CM (from above): CM Value: 2

$Toxicity_{ORAL}$ 4

DERMAL TOXICITY

Acute Basis: Dermal Irritation - Severe Acute Value: 3

Chronic Basis: Default to Chronic Oral Chronic Value: 2

CM (from above): CM Value: 2

$Toxicity_{DERMAL}$ 7

INHALATION TOXICITY

Acute Basis: LC_{LO} = 23000 mg/m^3/2H (mouse) Acute Value: 2
ppm/4H: 1699.13 ppm/4H

Chronic Basis: TLV-TWA = 50 ppm = 335 mg/m^3 Chronic Value: 0
ADI* 39.87

CM (from above): CM Value: 2

$Toxicity_{INHALATIONAL}$ 4

*ADI = (TLV-TWA)(0.119).

SUBSTANCE NAME: Toluene CAS NO: 00108-88-3

CM

Weight-of-Evidence Basis: Whole animal, Mutagenicity Category: II

Potency Basis: Default Group: Low

Matrix: II x Low CM Value: 1

ORAL TOXICITY

Acute Basis: LD_{50} = 5000 mg/kg (rat) Acute Value: 1

Chronic Basis: RfD = 0.3 mg/kg/day Chronic Value: 2

CM (from above): CM Value: 1

$Toxicity_{ORAL}$ 4

DERMAL TOXICITY

Acute Basis: LD_{50} = 12124 mg/kg (rabbit) Acute Value: 1

Chronic Basis: ADI=12124/10^5=0.121 mg/kg/day Chronic Value: 3

CM (from above): CM Value: 1

$Toxicity_{DERMAL}$ 5

INHALATION TOXICITY

Acute Basis: LC_{50} = 10640 ppm/4H (mouse) Acute Value: 1

Chronic Basis: TLV-TWA = 100 ppm = 375 mg/m^3 Chronic Value: 0
ADI* 44.625

CM (from above): CM Value: 1

$Toxicity_{INHALATIONAL}$ 2

*ADI = (TLV-TWA)(0.119).

SUBSTANCE NAME: Vinyl Chloride CAS NO: 00075-01-4

CM

Weight-of-Evidence
Basis: Positive, Rat, Oral; Positive, Mouse, Inhalation; Positive, Human — Category: III

Potency
Basis: ED_{10} = 6.67 mg/kg/day — Group: Low

Matrix: III x Low — CM Value: 2

ORAL TOXICITY

Acute Basis: LD_{50} = 500 mg/kg (rat) — Acute Value: 2

Chronic Basis: ADI=500/10^5=0.005 mg/kg/day — Chronic Value: 3

CM (from above): — CM Value: 2

$Toxicity_{ORAL}$ 7

DERMAL TOXICITY

Acute Basis: Default to Acute Oral — Acute Value: 2

Chronic Basis: Default to Chronic Oral — Chronic Value: 3

CM (from above): — CM Value: 2

$Toxicity_{DERMAL}$ 7

INHALATION TOXICITY

Acute Basis: LC_{LO} = 20 ppm/30M (guinea pig) — Acute Value: 3
ppm/4H: 2.5 ppm/4H

Chronic Basis: TLV-TWA = 5 ppm = 20 mg/m^3 — Chronic Value: 1
ADI* 2.38

CM (from above): — CM Value: 2

$Toxicity_{INHALATIONAL}$ 6

*ADI = (TLV-TWA)(0.119).

SUBSTANCE NAME: Zinc (as Zinc Phosphide) CAS NO: 01314-84-7

CM

Weight-of-Evidence
Basis: No Data Category: 0

Potency
Basis: Default Group: Low

Matrix: 0 x Low CM Value: 0

ORAL TOXICITY

Acute Basis: LD_{50} = 25 mg/kg (rat) Acute Value: 3

Chronic Basis: RfD = 0.0003 mg Chronic Value: 3

CM (from above): CM Value: 0

$Toxicity_{ORAL}$ 6

DERMAL TOXICITY

Acute Basis: Default to Acute Oral Acute Value: 3

Chronic Basis: Default to Chronic Oral Chronic Value: 3

CM (from above): CM Value: 0

$Toxicity_{DERMAL}$ 6

INHALATION TOXICITY

Acute Basis: Default to Acute Oral Acute Value: 3

Chronic Basis: Default to Chronic Oral Chronic Value: 3

CM (from above): CM Value: 0

$Toxicity_{INHALATIONAL}$ 6