TOXICS RELEASE INVENTORY
RELATIVE RISK-BASED ENVIRONMENTAL INDICATORS:

INTERIM TOXICITY WEIGHTING SUMMARY DOCUMENT

Nicolaas W. Bouwes, Ph.D.
Steven M. Hassur, Ph.D.

Economics, Exposure and Technology Division
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency

June 1997

Contractor Support:

Abt Associates, Inc.
4800 Montgomery Lane
Bethesda, MD 20814

For further information or inquiries, please contact:

Nicolaas W. Bouwes, Ph.D.
(202) 260-1622
bouwes.nick@epamail.epa.gov

or

Steven M. Hassur, Ph.D.
(202) 260-1735
hassur.steven@epamail.epa.gov

Economics, Exposure and Technology Division (7406)
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
401 M St., SW
Washington, D.C. 20460

ACKNOWLEDGMENT

This supplemental report is one of several products of the TRI Relative Risk-Based Environmental Indicators Project. We wish to thank Dr. Elizabeth Margosches of the Risk Assessment Division in the Office of Pollution Prevention and Toxics for her careful review of the first draft of this document.

Project Managers: Nick Bouwes and Steve Hassur

Toxics Release Inventory Relative Risk-Based Environmental Indicators: Interim Toxicity Weighting Summary Document

ERRATA

The toxicity weights for a number of scored TRI chemicals found in Tables 7-1, 7-2, 7-3 and 7-5, and in Tables A-1, B-1, B-2, C-1 and C-2 of the Appendices have changed.

The scores for the following chemicals are affected:

Acrylic acid	Methanol
Allyl alcohol	Methoxone
Benomyl	Methoxychlor
Biphenyl	Nitro-o-toluidine
Butyl acrylate	Nitrobenzene
Carbofuran	Nitrosodimethylamine, –
Chlorosulfuron	Oryzalin
Cresol, —	Oxydiazon
Cresol, o-	Permethrin
Cresol, p-	Propanil
Cyhalothrin	Selenium & compounds
Dichlorvos	Silver & compounds
Heptachlor	Simazine
Isopropylidenediphenol, 4,4'-	Thiram
Maneb	Zineb

Copper and copper compounds were removed from the listing because they are no longer on IRIS and the toxicity data for HEAST was inadequate for deriving an RfD.

The following chemicals were inadvertently omitted from the listing and are now added:

Naphthalene
Trichloroethane, 1-,1-,1-

Information regarding uncertainty factors, modifying factors and confidence levels pertaining to interim and final derived scores were added to the listing.

Since the toxicity weights for various TRI chemicals are undergoing further review, and modifications of the scores and the addition of new chemicals are likely, the reader should consult the most recent listing of the toxicity weights used in the TRI Environmental Indicators. Please contact the authors to obtain the most recently published listing.

Table of Contents

List of Exhibits and Tables

Executive Summary

Section 313 of the Emergency Planning and Community Right to Know Act (EPCRA) requires annual reporting to the U.S. Environmental Protection Agency (EPA) and states of releases to the environment of specified toxic chemicals from certain manufacturing facilities. These data are collected by EPA and made available to the public through the Toxic Release Inventory (TRI) database.

Information reported in the TRI database includes data, in pounds, on releases of these chemicals to all environmental media, transfers of the chemicals in waste to off-site locations, on-site waste treatment methods and efficiency, on-site energy recovery and recycling processes, and source reduction and recycling activities. The database does not, however, contain information or methods by which human health or environmental risk-based impacts can be compared systematically. Such comparisons could be useful for tracking environmental progress, setting pollution prevention priorities, and identifying potential regulatory initiatives.

In 1989, EPA initiated an effort to focus resources on regulatory or other programs with the greatest potential to achieve reductions in health or environmental risks. As part of this effort, the Agency began to explore ways to evaluate its successes in reducing risks, an effort that includes the development of indicators of environmental progress. The Office of Pollution Prevention and Toxics (OPPT) was charged with developing indicators of the impacts of chemical emissions on human health and the environment over time, using the TRI database. One result of OPPT's efforts is the TRI Relative Risked-Based Environmental Indicators Project.

The Indicators combines release and transfer information from the TRI database with chemical- and pathway-specific toxicology, exposure potential and exposed population information. The Indicators provide EPA and other TRI database users with scientifically sound methods by which to judge relative risks pertaining to TRI chemicals in all media and set priorities and target for pollution prevention, regulation and remediation.

One of several inputs to the Indicators method is a set of chemical- and exposure-specific *toxicity weights*, which represent unitless measures of relative toxicity among TRI chemicals. This document provides the methodology and preliminary results for the chronic exposure human health toxicity weights used in the Indicators project. For many chemicals, the toxicity weights for the Indicator project are derived from Agency-published chronic exposure toxicity values: cancer potencies and weight of evidence (WOE) classifications for carcinogens, and Reference Doses (RfDs) and Reference Concentrations (RfDs) for non-carcinogens. For some chemicals that lack published values, other data sources were consulted to evaluate the relative toxicity of the chemicals.

For the 1995 reporting year, there are 578 discrete chemicals and 28 separate chemical categories (two of which are delimited categories including 39 additional chemicals). Published Agency toxicity values for 288 TRI chemicals and chemical categories are available from EPA's Integrated Risk Information System (IRIS) database and Health Effects Assessment Summary Tables (HEAST) (search date, April 1997). The IRIS and HEAST toxicity values were used directly to derive toxicity weights for these TRI chemicals, as described in Chapter 5, and are listed in Appendix

A. TRI chemicals and chemical categories lacking IRIS or HEAST toxicity values are categorized into high and low priority chemicals. Of those currently identified as high priority TRI chemicals (not including any unscored chemicals from those 245 chemicals added to the TRI list for the 1995 reporting year), toxicity value estimates and toxicity weights were derived for 48 based on expert review within OPPT, using data from secondary sources. Final and interim toxicity weights for these TRI chemicals are listed and discussed in Appendices B and C, respectively. The remaining high priority chemicals from the 1994 TRI List were not assigned toxicity weights, due to lack of sufficient data to assign a weight. Lower priority chemicals were also not assigned toxicity weights. Those TRI expansion chemicals lacking IRIS and HEAST data are not currently included in the model; however, it is anticipated that many of these chemicals will be included in the model in the future. Table 7.4 lists the TRI chemicals (270 total) from the 1994 TRI List and from the 1996 expansion that lack toxicity weights.

Chapters 1 and 2 provide the background and overview of the TRI Environmental Indicators Project. Chapter 3 describes the process for prioritizing data needs. Chapter 4 briefly describes the TRI Environmental Indicator model for chronic human health effects. Chapter 5 discusses the methods used to derive (1) toxicity weights from published toxicity values, and (2) toxicity weights derived from dose-response data found in the secondary literature. Chapter 6 describes how indicator toxicity weightings differ from EPCRA Section 313 Statutory Criteria. Finally, Chapter 7 provides summary tables of all toxicity weights calculated as of April 1997.

Appendix A provides a comprehensive listing of contains all chemicals and chemical categories on the 1995 TRI List with toxicity weights; providing all relevant data pertaining to the toxicity weighting of each chemical. Derived toxicity weights are listed in Appendices B (final derived) and C (interim derived); incorporating all relevant data pertaining to the toxicity weighting of each chemical. These last two appendices also have toxicological summaries for each chemical.

1. Overview and Methodology

Section 313 of the Emergency Planning and Community Right to Know Act (EPCRA), also known as Title III of the Superfund Amendments and Reauthorization Act, requires annual reporting to the U.S. Environmental Protection Agency (EPA) and states of releases to the environment of specified toxic chemicals from certain manufacturing facilities. These data are collected by EPA and are made available to the public through the Toxic Chemical Release Inventory (TRI) database.

The TRI database includes data, in pounds, on releases of these chemicals to all environmental media, transfers of chemicals in waste to off-site locations, on-site waste treatment methods and efficiency, on-site energy recovery and recycling processes, and source reduction and recycling activities. The TRI data are intended to inform the public about the presence and release of toxic chemicals in their communities, and about the waste management and pollution prevention practices being employed. The data also assist government agencies, researchers, and others in conducting research and data gathering, in evaluating pollution prevention opportunities, identifying hotspots of pollution, and developing targeted regulations, standards, and guidelines.

Although the TRI database does not capture all chemicals or industry sectors of concern to EPA or the public, the database is the Agency's single best source of consistently reported emissions data. The database does not, however, contain information or methods by which human health or environmental risk impacts can be compared systematically. A number of TRI database users within and outside the Agency have expressed a desire to have chemical-specific measures more directly related to health and environmental impacts linked to the release and transfer data contained in the TRI database.

2. Background and Purpose of TRI Environmental Indicators Project

In 1989, EPA initiated an effort to focus resources on regulatory or other programs with the greatest potential to achieve reductions in health or environmental risks. As part of this effort, the Agency began to explore ways to evaluate its successes in reducing risks, an effort that includes the development of indicators of environmental progress. The Office of Pollution Prevention and Toxics (OPPT) was charged with developing indicators of the impacts of chemical emissions on human health and the environment over time, using the TRI database. One of the results of OPPT's efforts is the TRI Relative Risked-Based Environmental Indicators Project.

The original goal of the Indicators project was to devise a measure reflecting the impacts of chemical releases, which can then be used to assess progress in reducing these impacts over time. Release and transfer information from the TRI database combined with chemical- and pathway-specific toxicology, exposure potential and exposed population information, the Indicators project provides EPA and other TRI database users with scientifically sound methods by which to measure progress, to judge relative risks pertaining to TRI chemicals in all media and set priorities for pollution prevention and remediation. The Indicators may eventually consist of a set of four indicators: human health impacts of chronic and acute exposure, and chronic and acute ecological

impacts. This document discusses only the toxicity component for chronic human health impacts, the first of the TRI Indicators to be developed.

One of the major components of the Indicators method is the assignment of chemical- and exposure pathway-specific toxicity weights. The *TRI Environmental Relative Risked-Based Indicators Project: Interim Toxicity Weighting Summary Document* provides the methodology and results for the first set of chronic human health toxicity weights for use in the Indicators project. This methodology is based upon EPA's Hazard Ranking System (EPA, 1990a). The Hazard Ranking System (HRS) is a multipathway scoring system "used to assess the threat associated with actual or potential releases of hazardous substances at sites" (EPA, 1990a). The HRS score determines whether a site will be included on the National Priorities List (NPL). Part of the HRS scoring system rates the inherent toxicity of chemicals based on Agency-published chronic toxicity values: cancer slope factors and weight of evidence (WOE) classifications for carcinogens, and Reference Doses (RfDs) for non-carcinogens.

3. Data Sources

3.1. Prioritizing Data Needs

Information regarding the human health effects data for the TRI chemicals is compiled from a number of sources. The primary source of these data is the Integrated Risk Information System (IRIS). This computerized data source includes information on EPA evaluations of chemical toxicity for both cancer and noncancer effects of chemicals.[1] IRIS provides both background information on the studies used to develop the toxicity evaluations and the numerical toxicity values used by EPA to characterize risks from these chemicals. These values include upper-bound slope factors (q_1^*) and unit risks for chemicals with carcinogenic effects as well as RfDs and RfCs for chemicals with noncancer effects. Data contained in IRIS have been peer-reviewed and represent Agency consensus. In the past, the peer-review process involved literature review and evaluation of a chemical by individual EPA program offices and intra-Agency work groups before inclusion in IRIS. However, the IRIS review process has undergone considerable change in the past several years. Generally, individual workgroups no longer conduct the reviews. Rather, as announced in the Federal Register several years ago, a pilot review of 11 chemicals was initiated; this review is ongoing. At that time public comment was solicited regarding this approach. As in the past, the public and industry may provide relevant information and toxicological studies to the review, but an IRIS submissions desk has also been established for these 11 reviews (as announced in the Federal Register notice). This submissions desk is maintained by the Risk Information Hotline in Cincinnati, Ohio (513/569-7254); the Hotline may be contacted for additional information. Each of these chemicals under review is assigned a manager and, after preliminary review of data relevant to both oral and inhalation exposures related to cancer and non-cancer health effects, the review is sent through an Agency

[1] The IRIS data base contains information comprised of comprehensive literature searches and utilizing primarily studies listed in the peer-reviewed literature. In some cases, data from other sources is consulted, as in the case of pesticide files which may include study data submitted by registrants.

consensus process. In some cases, the Agency has elected to conduct this consensus review through workshops, and industry and the public have been directly involved. It is anticipated that the TRI Relative Risk-Based Environmental Indicators Project will annually review IRIS/HEAST data to update the chemical toxicity weights.

When IRIS values are not available for TRI chemicals, an alternate source of toxicity data is the Health Effects Assessment Summary Tables (HEAST). These tables are constructed for use in both the Superfund program and the Resource Conservation and Recovery Program (RCRA) but do not generally represent overall Agency consensus. Exceptions are where HEAST reports National Ambient Air Quality Standards (NAAQS) or Drinking Water Criteria. The HEAST document is updated three times yearly and are publicly available from the Superfund program. The tables include slope factor estimates and WOE categorizations for chemicals with cancer effects, and RfDs for noncancer effects.

Of the TRI chemicals listed in 1994, toxicity values for many of the chemicals were extracted from IRIS, or lacking data in IRIS, from HEAST. These toxicity values were used directly to derive toxicity weights for these TRI chemicals, as described below in Chapter 5 and listed in Appendix A. A large number of chemicals lacked IRIS or HEAST toxicity values. With the assistance of reviewers from the Chemical Screening and Risk Assessment Division (CSRAD) and the Health Effects Review Division (HERD) within OPPT, high priority chemicals were chosen for toxicity weight calculation from those lacking IRIS or HEAST toxicity values. These chemicals were chosen based on two pieces of information. First, scores previously assigned to the chemicals by the Structure-Activity Team (SAT) of the Office of Pollution Prevention and Toxics were examined. These scores were assigned based on rapid assessment of limited data and the best professional judgment of the SAT members. Chemicals were rated in terms of high, medium-high, medium, low-medium, or low concern for human health; these categories were translated into unitless scores of 1, 10, 100, 1000, and 10,000.

Second, the total pounds released to all media, except underground injection (for the original prioritization), during TRI reporting year 1990 were determined for each chemical. Four benchmark levels of releases were established: less than 1000 pounds, 1001 to 10,000 pounds, 10,001 pounds to 100,000 pounds, and greater than 100,000 pounds. Finally, chemicals were categorized into two classes, high priority chemicals and low priority chemicals, based on their adjusted SAT score and their 1990 total releases as reported in the TRI database. The definitions of the two classifications are as follows:

High Priority Chemicals are those with:

1) an SAT score of 1 and releases greater than 1,000 pounds,
2) an SAT score of 10 or 100 and releases greater than 10,000 pounds, or
3) an SAT score of 1,000 or 10,000 and releases greater than 100,000 pounds.

Low Priority Chemicals are those with:

1) an SAT score of 1 and releases less than 1,000 pounds,
2) an SAT score of 10 or 100 and releases less than 10,000 pounds, or
3) an SAT score of 1,000 or 10,000 and releases less than 100,000 pounds.

The process of prioritizing chemicals for scoring the TRI-listed chemicals in 1994 is depicted in Exhibit 3.1 (this does not include the expansion chemicals added to the TRI in 1996). Resources were directed to evaluating and assigning toxicity weights to "high priority" chemicals. No further effort was made to evaluate the low priority chemicals, a number of which had no reported releases or were reported as zero pounds released. The low priority chemicals currently lack toxicity weights. In addition, during the course of this project, many additional chemicals were added to the TRI List. These chemicals have not yet been assigned toxicity weights unless they were listed in IRIS or HEAST. Toxicity weights were developed for 48 chemicals lacking IRIS and HEAST data for one or more routes of exposure. They are described in Appendices B and C.

Additional chemicals were added in recent years. Many of these have IRIS or HEAST data and are included in the indicators. Others that lack IRIS/HEAST data will go through a prioritization process similar to the one described above. A subset of those will undergo a toxicity evaluation and be assigned toxicity weights.

The current status of the 606 chemicals (including 28 chemical categories) on the TRI list is as follows:

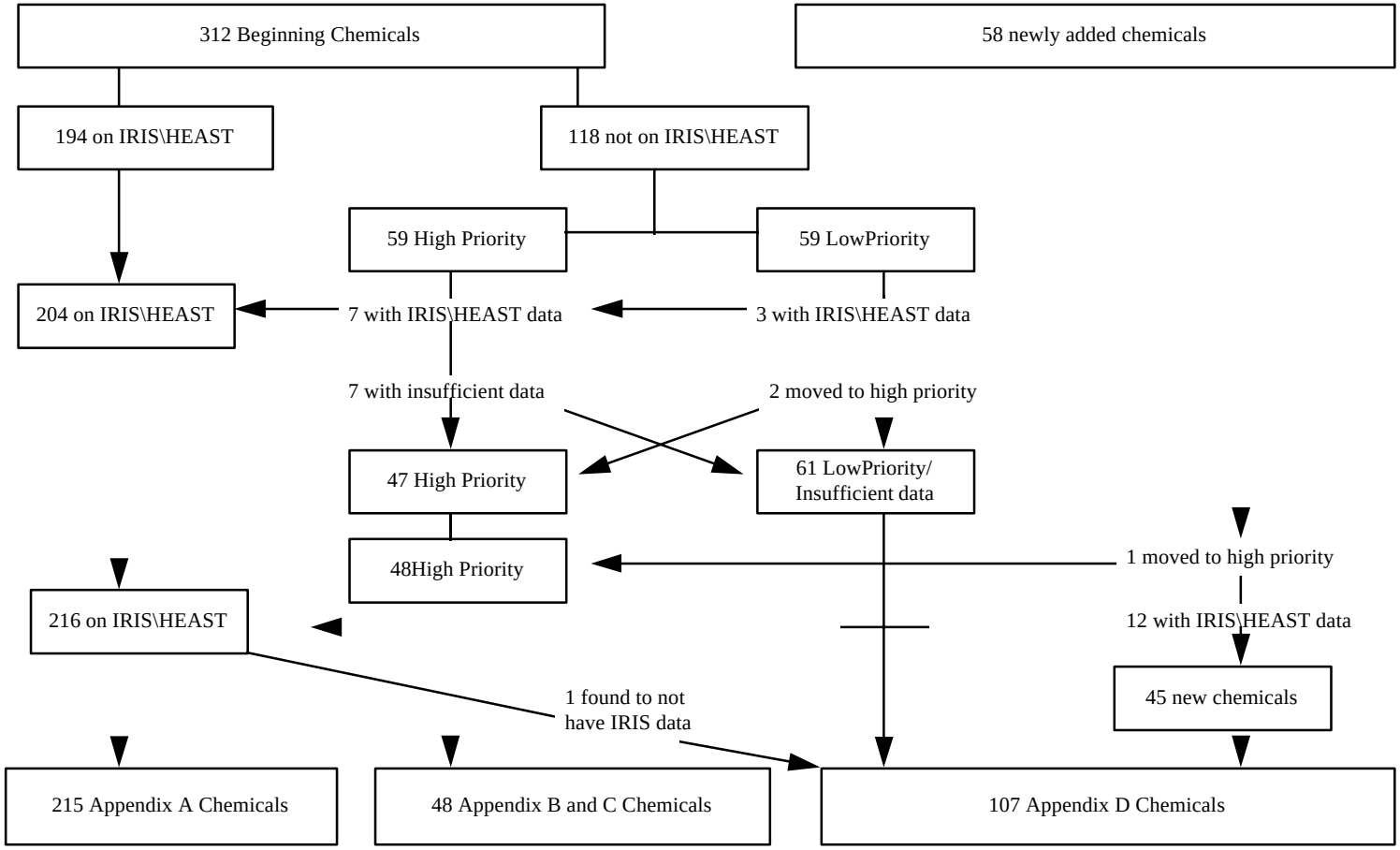
- 288 chemicals/chemical categories have toxicity scores based on IRIS or HEAST
- 48 chemicals/chemical categories have either final or interim toxicity scores based on a toxicity evaluation by OPPT health scientists (a few of these chemicals have a final toxicity value for one exposure pathway and an interim value for the other)
- 270 chemicals/chemical categories lack toxicity weights

3.2. Derived Toxicity Weights

In cases where IRIS or HEAST do not have toxicity values and WOE classifications, several other sources for data are relied upon from which to assign weights for use in the Indicators method.[2] Although individual literature searches for toxicological and epidemiological data for each chemical were beyond the scope of this project, data bases such as the Hazardous Substances Data Base (HSDB), as well as various EPA and Agency for Toxic Substances and Disease Registry (ATSDR) summary documents, provided succinct summaries of toxic effects and quantitative data,

[2] Although this document refers to values derived from IRIS or HEAST this does not imply that the sources are equally acceptable within the Agency. HEAST data do not have the same consensus standing as IRIS values; however, both are publicly available toxicity evaluations that are not specific to this project.

Exhibit 3.1 Process for Prioritizing Toxicity Scoring



toxicological and epidemiological studies, and, in some cases, regulatory status data. Summaries of these data, and suggested toxicity scores based on the summaries, were provided for selected chemicals to a group of OPPT health scientists charged with reviewing toxicity data. After their review, this group then approved or disapproved the suggested scores through the HERD Disposition Process.

As described above, the "derived" toxicity weights for certain high priority chemicals without IRIS or HEAST values were formally reviewed and approved by OPPT. For this purpose, scientists from the Chemical Screening and Risk Assessment Division (CSRAD) and the Health and Environmental Review Division (HERD) were briefed regarding the methods utilized to derive toxicity values for use with the TRI Environmental Indicators. The CSRAD/HERD Disposition Team, a long-standing, regular review process, was used for reviewing the available literature and the preliminary scores.

The CSRAD/HERD Disposition Team offers a weekly review of hazard and risk assessment issues for the Office of Pollution Prevention and Toxics within EPA. It is attended regularly by senior management (including the CSRAD and HERD Division Directors) and is staffed by experts in the human health field who represent a wide variety of disciplines. The goal of these meetings is to reach consensus regarding the technical issues under discussion using both professional judgment and interpretive analysis of health data. This process is a key component in the review of new and existing chemicals (with possible testing recommendations) under the Toxic Substances Control Act (TSCA) and the TRI petition process under EPCRA. Because of the historical programmatic perspective of this team, these health scientists are able to offer insightful comment on toxicological issues based on accepted standards for hazard and risk assessment within OPPT.

The team members were provided, in advance, with summaries of the available toxicological data pertaining to each high priority chemical obtained from secondary sources (no primary literature was reviewed). These summaries included WOE considerations appropriate to each case and the rationale for the proposed toxicity weight. The acquired data were used to address the most sensitive endpoints, but lack of generated data could potentially obscure the appropriate endpoints. The intent of this review was to rank these chemicals in order of magnitude categories, not to assign specific cancer slope factor or reference dose values. The conservative nature of the process was appropriate because, in fact, many of these chemicals were chosen for ranking due to their potentially greater hazard. The reviewers suggested specific and generic changes in the toxicological summaries, which were incorporated before a final consensus was achieved regarding the appropriate toxicity weight for each chemical.[3]

The toxicological and epidemiological information on chemicals is being continually updated and the understanding of underlying processes and pharmacokinetics is also increasing rapidly. Consequently, new data are being reviewed continually throughout EPA to determine their relevance and potential impact on human health toxicity evaluations. Some chemicals that have gone through

[3] EPA welcomes toxicological and epidemiological data relevant to human health on all TRI chemicals, and in particular on the chemicals for which quantitative IRIS and HEAST data are not available. Scientific articles in peer-reviewed journals of high quality that describe studies using generally accepted test protocols are typically required for use in evaluating such chemicals.

the Disposition Process are being reviewed again based on new data and/or the significance of their risk-related impacts. This process is also ongoing for chemicals listed on IRIS and HEAST. As new data become available and as chemicals are added to the TRI list, the toxicity weights for chemicals may change in keeping with the current scientific literature and upgraded as needed.

Chapter 4 briefly describes the TRI Environmental Indicator model for chronic human health effects. Chapter 5 discusses the methods used to derive 1) toxicity weights using Agency published toxicity values, and 2) toxicity value estimates for TRI chemicals lacking IRIS or HEAST toxicity values. Chapter 6 reports the process used by EPA to review derived toxicity value estimates for those chemicals lacking IRIS or HEAST values. Chapter 7 provides summary tables of all toxicity weights calculated as of April, 1997. Toxicity weights for all scored TRI chemicals (including those with IRIS or HEAST toxicity values, as well as those with derived values) are given in Appendix A. Final and interim toxicity weights for TRI chemicals with derived toxicity value estimates are given in Appendices B and C, respectively, along with discussions of the toxicological data and calculations used to derive the toxicity value estimates.

4. General Description of the TRI Relative Risk-Based Environmental Indicator Model for Chronic Human Health Effects

The objective of the TRI Relative Risk-Based Environmental Indicators is to calculate a unitless value that reflects the overall impacts, at a specified point in time, of releases and transfers of all included TRI chemicals by all facilities to each environmental medium. The Indicators improve on simple comparisons of pounds released and transferred, because they incorporate elements related to the risk impacts of the releases and transfers.

To construct Indicators related to risk, TRI releases and transfers must be adjusted in a manner that relates to the risks associated with each media-specific release or transfer of each chemical. The risk potentially posed by a chemical emission depends on the inherent toxicity of the chemical, the environmental fate and transport of the chemical in the medium to which it is released, the degree of contact between the contaminated medium and the human or ecological receptors, and the size of exposed populations. Differences in toxicity among chemicals, as well as differences in environmental fate and the size and characteristics of populations potentially exposed, influence the relative contribution that each emission makes to each Indicator. Transfers to offsite locations such as sewage treatment plants (POTWs) require an additional estimate of the impact of treatment technologies on the emissions.

To incorporate these factors into the Indicators when they are determined, three main components are used to compute each Indicator. These are:

- the quantity of chemicals released or transferred,
- adjustments for chemical-specific toxicity (described in Chapter 5), and
- adjustments for pathway-specific exposure potential (described in Chapter 5).

An additional adjustment is applied to the Chronic Human Health Indicator to reflect the size of the potentially exposed population in the location relevant to the release[4].

The TRI Chronic Human Health Indicator uses these components to perform a separate assessment for each unique combination of a chemical, facility, and release medium. Each of these releases or transfers results in a calculated Indicator "element," a unitless value proportional to the potential impact of each specific release or transfer. The value for the TRI Chronic Human Health Indicator is simply the sum of all the applicable Indicator elements. Similarly, for the TRI Chronic Ecological Indicator, a separate assessment is made for each unique chemical-facility combination affecting the water medium, yielding the Ecological Indicator elements. The overall TRI Chronic Ecological Indicator is the sum of these elements.

As a screening-level analytical tool Indicators can be used to examine trends. An example of trends analysis would be to select a "base year" to which later years' Indicator values are compared. This comparison allows assessment of the changes in estimated impacts of TRI releases and transfers from year to year. The Indicators can also be used to prioritize and target, and when linked with appropriate demographic information it can be used to investigate environmental justice issues.

Importantly, the TRI Indicators method offers unlimited combinations and views of the Indicators' subcomponents. Each facility-chemical-media Indicator element is retained by the computer program and thus can be evaluated by users wishing to investigate the makeup of the Indicators. Regions, states, or individuals could use these individual elements to create their own "subindicators" that examine the relative contribution of chemicals, industries, or geographic regions to the overall Indicator value.

It must be emphasized that the TRI Indicators method is not intended to be a quantitative risk assessment and does not calculate risk estimates. The method follows the same general paradigm often applied in quantitative assessments, but in a relative way. The TRI Indicators are by their nature intended only to reflect the direction and the general magnitude of the change in releases over time, scaled by factors (toxicity, exposure potential, receptor population size) that relate to potential

[4]The method is focused on general exposed populations: individuals, particularly highly exposed individuals, are not the focus of the Indicator. Additional Indicators based upon highly exposed subpopulations may be developed in the future.

risk. As such, an Indicator value has only relative rather than absolute meaning; it can be used only in comparisons to other values at different points in time, or in identifying the relative size of contributing factors.

4.1. The Use of Toxicity Weights in the TRI Chronic Human Health Indicator Calculation

A key element of the Chronic Human Health Indicator is the set of toxicity weights applied to the chemicals. A release could be weighted based upon a variety of factors and characteristics. The Emergency Planning and Community Right-to-Know Act of 1986 (EPCRA) Section 313 criteria list several human toxicity parameters that EPA must consider when evaluating a chemical for addition to TRI, including acute toxicity, cancer or teratogenic effects, serious or irreversible reproductive dysfunctions, neurological disorders, heritable genetic mutations, or other chronic health effects. Some chemicals have toxicity data for only one effect, while others will have evidence of effects within several of these toxicity categories. The definition of these parameters, as given in Section 313, are given in Exhibit 4.1.

Exhibit 4.1. Toxicity Endpoints

Endpoint	Definition
Carcinogenicity	This toxicity endpoint concerns the ability of a chemical to produce cancer in animals or humans.
Heritable Genetic and Chromosomal Mutation	Chemicals which affect this endpoint can cause at least three separate modes of failure to transmit genetic information: gain or loss of whole chromosomes (aneuploidization), rearrangement of parts of chromosomes (clastogenesis), and addition or deletion of a small number of base pairs (mutagenesis).
Developmental Toxicity	Any detrimental effect produced by exposures to developing organisms during embryonic stages of development, resulting in: prenatal or early postnatal death, structural abnormalities, altered growth, and functional deficits (reduced immunological competence, learning disorders, etc.).
Reproductive Toxicity	This endpoint concerns the development of normal reproductive capacity. Chemicals can affect gonadal function, the estrous cycle, mating behavior, conception, parturition, lactation, and weaning.
Acute Toxicity	Acute toxicity indicates the potential for a short-term exposure (typically hours or days) by inhalation, oral, or dermal routes to cause acute health effect or death.
Chronic Toxicity	Chronic toxicity indicates the potential for any adverse effects other than cancer observed in humans or animals resulting from long-term exposure (typically months or years) to a chemical.
Neurotoxicity	This endpoint concerns the central and/or peripheral nervous system. Changes to the system may be morphological (biochemical changes in the system or neurological diseases) or functional (behavioral, electrophysiological, or neurochemical effects).

A TRI emission could be weighted based upon the number of effects that it causes, the relative severity of the effects, the potency of the chemical for one or more of these effects and the uncertainty inherent in characterizing effects.

The TRI Relative Risk-Based Environmental Indicators method for developing chronic human health toxicity weights focuses on the latter two factors. It thus considers both qualitative and quantitative elements to judge the relative toxicity of chemicals. There is uncertainty inherent in both determining whether exposure to a chemical will cause an effect in humans, and the potency of the chemical. Quantitative potency data must be considered in the context of a qualitative classification of the uncertainty associated with that data. In the case of noncancer effects, this classification is considered in the development of the quantitative toxicity values (e.g., Reference Dose values). However, the Indicators method uses existing qualitative weight-of-evidence (WOE) measures in addition to quantitative toxicity values to assign toxicity weights based on carcinogenic effects.

Qualitative Data

Risk assessors use a variety of data to evaluate the potential toxicity of a chemical to humans, including epidemiological data, data from acute and chronic animal studies, and in vitro toxicity tests. Together, these data form a body of evidence regarding the potential for toxic chemicals to cause a particular health effect in humans. The risk assessor can judge qualitatively the strengths of this body of evidence when determining the probability of the occurrence of the effect in humans. Based on this judgment, the chemical is assigned a WOE classification. Weight-of-evidence schemes can be designed to indicate whether a chemical either causes a specific health effect in general, or specifically in humans. The carcinogenicity WOE system presented in this methodology relies on categorical definitions from the EPA Cancer Risk Assessment Guidelines (EPA, 1986a, currently being revised), which are related to the potential of a chemical's carcinogenicity in humans. These Guidelines define the following six WOE categories, as shown in Exhibit 4.2.

Exhibit 4.2. Weight of Evidence Categories for Carcinogenicity

Category	Weight of Evidence
A	Sufficient evidence from epidemiological studies to support a causal relationship between exposure to the agent and cancer.
B1	Limited evidence from epidemiological studies and sufficient animal data.
B2	Sufficient evidence from animal studies but inadequate or no evidence or no data from epidemiological studies.
C	Limited evidence of carcinogenicity in animals and an absence of evidence or data in humans.
D	Inadequate human and animal evidence for carcinogenicity or no data.
E	No evidence for carcinogenicity in at least two adequate animal tests in different species or in both adequate epidemiological and animal studies, coupled with no evidence or data in epidemiological studies.

For noncancer effects, weight-of-evidence is considered qualitatively in the hazard identification step of determining a Reference Dose (RfD) (see below for discussion of RfD). The WOE evaluation for noncancer effects is different from that for carcinogenic effects. For exposure to chemicals with potential carcinogenic effects, current EPA policy assumes no threshold exposure below which cancer risk is zero; thus, determining a chemical to be a known, probable, or possible human carcinogen implies some risk associated with any exposure. Therefore, the WOE determination focuses on whether the chemical may or may not cause cancer in humans. In contrast, the judgment that a chemical is a systemic toxicant is dose-dependent; the WOE evaluation focuses on the dose where chemical exposure would be relevant to humans (M. Dourson, EPA, ORD, personal correspondence). The focus of the WOE evaluation, and the expression of the level of confidence in the RfD, is a judgment of the accuracy with which the dose relevant to humans has been estimated. The WOE evaluation is included qualitatively in the RfD, but does not affect its numerical calculation. Since weight of evidence has been considered in developing RfDs, the Indicators method does not consider WOE separately for noncancer effects.

Quantitative Data

Quantitative data on the relative potencies of chemicals are needed for toxicity weighting. For **cancer risk assessment**, EPA has developed standard methods for predicting the incremental lifetime risk of cancer per dose of a chemical. EPA generally uses a linearized multistage model of carcinogenesis to quantitatively model the dose-response function of a potential carcinogen. The upper bound of the linear term of this model is called the q_1^*. This slope factor is a measure of cancer potency. Cancer risk can also be expressed as a unit risk factor, that is, the incremental lifetime risk of cancer per mg/m^3 in air or per mg/L in water. Although the level of conservatism inherent in these slope factors and unit risks varies by chemical, unit risks and q_1^*s nonetheless are the best readily available values that allow comparison of the relative cancer potency of chemicals.

For **noncancer risks,** data on dose-response are more limited; generally, a risk assessor evaluates dose compared to a Reference Dose (RfD) or Inhalation Reference Concentration (RfC). Both the RfD and RfC are defined as "an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime" (EPA, 1988). The units of RfD are mg of chemical/kg body weight-day, while the units of the Inhalation Reference Concentration are mg of chemical/m^3 of air.

A chemical's reference dose or reference concentration is based on a No Observable Adverse Effect Level or Lowest Observable Adverse Effect Level, combined with appropriate uncertainty factors to account for intraspecies variability in sensitivity, interspecies extrapolation, extrapolation from LOAELs to NOAELs, and extrapolation from subchronic to chronic data. In addition, a modifying factor can be applied to reflect EPA's best professional judgment on the quality of the entire toxicity database for the chemical. By definition, exposures below the RfD or RfC are unlikely to produce an adverse effect; above this value, an exposed individual may be at risk for the effect. Empirical evidence generally shows that as the dosage of a toxicant increases, the severity and/or incidence of effect increases (EPA, 1988), but for a given dose above the RfD or RfC, the specific

probability of an effect is not known, nor is its severity. For purposes of the TRI Relative Risk-based Environmental Indicator method, we assume that noncancer risk varies as the ratio of the estimated dose to the RfD or RfC.

Although non-carcinogens are assumed to have a threshold for response that is below the RfD or RfC, chemicals are included in the model whether or not the release is anticipated to generate exposures above the RfD or RfC. This is done because exposure may occur from a variety of sources in the environment, a single facility release represents only one source of exposure (exposures to the same chemical may also occur from other nearby facilities), the sum of exposures from all sources may exceed the threshold for toxicity, and many chemicals have similar mechanisms and types of toxicity and may act in an additive manner to increase toxicity (e.g., organophosphates, carbamates, some solvents).

4.1.1. General Format for Combining Weight of Evidence and Oral Slope Factors or Inhalation Unit Risks for Carcinogenic Effects

This method uses different schemes to weight the toxic effects of a chemical, depending on whether the effect is carcinogenic or noncarcinogenic. For carcinogenic effects, the method uses a matrix to evaluate a chemical based on WOE and carcinogenic potential simultaneously, as discussed below. For noncarcinogenic effects, WOE is considered in the development of RfDs or RfCs as discussed previously. For these chemicals, toxicity weights are directly based on ranges of RfD or RfC values.

Using categorical weights for toxicity has several advantages over calculating specific, unique numerical weights for chemical releases. First, unique weights would imply that we know the toxicity of the chemical with enough accuracy and precision to distinguish among relatively small differences in these values. In fact, there are significant uncertainties associated with the assessment of a chemical's slope factor and weight-of-evidence, as well as the RfD or RfC. IRIS values are an estimate with uncertainty spanning perhaps an order of magnitude. Weighting a release based on the broad categories of toxicity into which it falls avoids the impression of precision where such precision does not exist. Second, when general categories are used, chemicals are likely to remain in the broad toxicity category to which they are originally assigned, unless significant new and different toxicity data become available; lending stability to the Indicators over time. A third advantage to the use of categorical toxicity weights is that this is likely to be a more robust and flexible approach, which can be adapted to incorporate new methods for evaluating the toxicity of chemicals (such as new approaches to cancer risk assessment) that may develop over time. Finally, defining broad categories of weights allows EPA analysts to use both qualitative and quantitative toxicity information, including consideration of chemicals that are policy priorities for the Agency, to make approximate judgments about the relative level of concern with respect to toxicity for chemicals where specific oral slope factors (inhalation unit risks) and RfD (RfC) values have not yet

been developed by the Agency. This more flexible approach allows more chemicals to be included in the Indicator than would be possible if exact numeric risk values were required for the development of toxicity weights.

4.1.2. Weights Applied to the Categories

Either ordinal or proportional weights could be assigned to the categories defined by the matrix cells. Ordinal weights delineate the relative toxicity rank among emissions and are useful for setting priorities. They do not, however, provide information on the magnitude of the toxicity of chemicals relative to one another. For example, an ordinal rank of 3 for chemical A and 1 for chemical B does not mean chemical A is three times worse than chemical B. Since ordinal weights do not reflect proportional differences in toxicity, the ability of the Indicator to reflect changes in health and environmental impacts could be limited if ordinal weights are used. In fact, if ordinal weights are used, it is possible that the Indicator could decrease over a period when actual risk increases. Unlike ordinal systems, proportional scoring systems use numerical scores that reflect the magnitude of difference between the impacts associated with chemical releases. An example of the different Indicator values which might arise from these alternate approaches is demonstrated in Chapter III of the TRI Relative Risk-Based Environmental Indicators Methodology (EPA, 1997); which compares the different trends observed in a ordinal-based vs. proportional-based Indicator to the trend shown in a hypothetical quantitative risk assessment.

Because of these considerations, the method assigns proportional weights to matrix cells. Weights increase by an order of magnitude for each order of magnitude increase in toxicity and for each increase in WOE category, as described below.

4.1.3. Selecting the Final Human Health Toxicity Weight for a Chemical

Chemicals can cause several types of toxic effects. The TRI Environmental Indicator for Chronic Human Health Effects assigns weight a chemical based on the most sensitive adverse effect for a given exposure pathway. If a chemical exhibits both carcinogenic and noncarcinogenic effects, the higher of the cancer and noncancer weights is assigned as the final weight for the chemical for the given pathway.

The approach of weighting based on the most sensitive adverse effect does not consider differences in the severity of the effects posed by the chemicals. For example, reproductive toxicity is weighted with no greater or lesser severity than neurotoxicity is weighted. Also, chemicals with a broad range of adverse health effects are weighted the same as a chemical with only one effect. Applying additional weights reflecting severity of effect across categories of toxic endpoints would require a subjective evaluation of the relative severity of the health effects. In addition, a chemical may appear to demonstrate just one adverse effect only because there are no data on other effects;

thus, applying a weight based on the number of endpoints may undervalue some poorly studied but still risky chemicals. For these reasons, the options for applying additional weights based on number and severity of endpoints were rejected.[5]

Although choosing the most sensitive endpoint to weight a given substance does not consider severity of effects, whether carcinogenic or otherwise, the method of separately weighting compounds with carcinogenic effects and those with other than carcinogenic effects cannot avoid appearing to equate toxicity values between these groups. For example, the weighting scheme equates a q_1^* value of 0.1 risk per mg/kg-day with an RfD of 0.001 mg/kg-day, since both are assigned a weight of 1000. If one were to use this weighting scheme to evaluate actual doses, this weighting would imply that a cancer risk of 1×10^{-4} would be equated to a noncancer risk at the RfD.[6] At the low end of the toxicity spectrum, a cancer risk of less than 5 per thousand (0.005 per mg/kg-day) for a suspected (Class C) carcinogen is assigned the same toxicity weight (10) as the noncancer toxicity with a potency that generates an RfD greater than 0.05 mg/kg-day. Cancer and non-cancer weights are calculated separately, when data are available on both endpoints, and the higher weight predominates in assigning the toxicity score. Separate indicators were not developed for cancer and non-cancer effects because they both address the same overall concern of potential human health impacts. Cancers are often "severe" effects, although, in some cases, are not life-threatening in nature. Likewise, the various types of non-cancer effects may vary considerably in severity. With the recent emphasis on developmental effects, non-cancer effects now more frequently include potentially lethal effects. This project has the goal of evaluating the **relative** risk-related impacts of TRI emissions through the use of pathway-specific effects that address overall chronic human health concerns. Separately establishing different indicators to address each subset of the toxicity effect would be quite confusing to interpret, since the relative hazard of different effects are not directly comparable. However, the Indicator model does permit the user to identify subsets of chemicals which share a particular type of effect for separate analysis.

Inhalation and oral toxicity weights are calculated separately. In general, if values are available for only one route, the same toxicity weight is applied for both routes. In rare instances, toxicity studies are available to show that a given chemical causes no effects via one route; in these instances, toxicity weights are assigned only to the route that results in effects. Applying a toxicity weight from one route to another is a reasonable approach for the Indicators project because the Indicators do not require precise potency estimates or weighting, but rather focus on the relative toxicity of chemicals to each other. In the absence of route-specific data, it is not assumed that we know nothing regarding a reasonable estimation of the likely toxicity of chemicals because a specific exposure pathway has not been tested. It is necessary only to be cautious in applying toxicity scores where there is not evidence to the contrary (e.g., portal of entry effects). This procedure of adopting

---

[5]Although we do not apply subjective weights based on number and severity of effects, the assignment of weights based on the most sensitive effect is a subjective decision in itself.

[6]At a dose of 0.001 mg/kg-day, a chemical with a q_1^* of 0.1 (kg-day/mg) would yield a risk of 1×10^{-4} (i.e., $0.001 \times 0.1 = 0.0001$).

scores from one exposure pathway to another is consistent with the Hazard Ranking System (HRS) methodology for toxicity factor scoring. In fact, the HRS scoring system is quite conservative in that it applies the highest toxicity weight to all exposure routes for a given chemical regardless of the toxicity data appropriate to the individual routes.

Metals pose a unique challenge in the evaluation of toxicity and determination of toxicity weights. Facilities are required only to report the metal fraction of their TRI releases of metal compound chemical categories. Consequently, specific data is not available on the identity of any metallic compounds released, or their valence state. These often play a critical role in determining toxicity. Toxicity data (usually from IRIS) on the metals is used to determine toxicity weights . This typically is based on the metallic form which has the most available toxicological and epidemiological data that is deemed relevant to human health and exposure. In most cases, the same toxicity weight is applied to both the metal and metal compounds. Generally, the toxicity weights used in the Indicators are based on IRIS when those data are available (or HEAST when IRIS data was not available). This is the best use of the available data that can be made at this time.

5. Derivation of Toxicity Weights

Depending on the availability of dose-response data, up to four separate preliminary chronic human health toxicity weights are developed for each TRI chemical: cancer oral, cancer inhalation and noncancer oral and noncancer inhalation. Where two (i.e., noncancer and cancer) toxicity weights are derived for the same exposure pathway, the more sensitive of the two (i.e., the one with the greater weight) is chosen for use as an overall toxicity weight for that pathway.[7] As noted above, when dose-response data are available for only one exposure pathway, the toxicity weight calculated for that pathway is usually assigned to both pathways. If evidence indicates the chemical is toxic through only one pathway then the other pathway is assigned no weight. Thus two final toxicity weights are calculated for most TRI chemicals: one oral toxicity weight, and one inhalation toxicity weight. Methods for deriving cancer and noncancer toxicity weights are described below.

EPA's Integrated Risk Information System (IRIS) and Health Effects Assessment Summary Tables (HEAST) contain noncancer Reference Doses (RfDs), cancer potencies, and/or WOE classifications for many of the chemicals currently on the TRI list. As described earlier, IRIS was first searched for data on the TRI chemicals. If data were not available from IRIS, HEAST information was used. For chemicals with at least one RfD, RfC, or slope factor contained in IRIS (or, if not in IRIS, in HEAST), toxicity weights were based on the available IRIS or HEAST toxicity values and no further review of the literature was done. These toxicity weights were not reviewed further because the toxicity values (cancer slope factors and reference doses) on which they are based are available in publicly available data sources, are not specific to this project and have already received review from at least one office within EPA. However, it must be noted again that the IRIS values

[7]This is consistent with the EPA RfD/RfC Workgroup practice of choosing the most sensitive (i.e., most protective) non-cancer health endpoint for use in deriving Reference Doses.

represent Agency consensus, whereas the HEAST values may be limited to review within one office and thus do not represent Agency consensus. Toxicity weights for chemicals with IRIS or HEAST toxicity values are listed in Chapter 7 and Appendix A.

For chemicals that lack IRIS or HEAST toxicity values, a review of the secondary toxicological literature was done (see the discussions of individual chemicals in Appendix B and C for the sources used). Wherever possible, interim toxicity values from these secondary sources were used to assign weights. Where interim toxicity values were lacking, available dose-response data were used to derive toxicity value estimates for the purpose of assigning toxicity weights to each chemical, as described below.

All toxicity values not found in IRIS or HEAST that were used to calculate chronic and cancer toxicity weights were reviewed by an OPPT Chemical Disposition Work Group (see Chapter 6 for details). Toxicity weights approved by the Work Group are given in Chapter 7 and Appendix B, along with summary descriptions of the data and calculations used to derive the toxicity values. Toxicity weights reviewed but not yet approved by the Work Group are listed in Chapter 7 and Appendix C, with summary descriptions of the data and calculations used to derive them.

The RfD/RfC-analogous values, WOE-analogous determinations, and slope factor-analogous estimates derived through the Disposition Process should be interpreted only as a means to allow consistent, systematic weighting of TRI chemicals. The toxicity values derived for the TRI Environmental Indicators project, though reviewed by EPA, do not represent Agency consensus and should not be used for other purposes. To distinguish between Agency-published toxicity values and toxicity values derived for this project, the terms "Slope Factor Estimate," "Reference Dose Estimate," and "WOE Estimate" are used to denote derived toxicity values.

The data summaries in Appendices B and C describe the data sources and specific calculations used to assign the toxicity weights for chemicals without published IRIS/HEAST values. In rare instances, the score was based upon professional judgment and specific programmatic emphasis on highlighting exposures to chemicals of concern. However, it is important to keep in mind that the assignment of a weight reflects an order-of-magnitude estimate of the relative toxicity of the chemical, not a specific toxicity value; as a result, qualitative, professional judgments can be appropriate for this exercise. For example, in the case of lead and lead compounds, due to the availability of strong human data, specific numerical calculations were not used to derive toxicity weight estimates; instead, maximum toxicity values were assigned.

In addition, the toxicity weights contained in this document are based on the data available to the authors during the time in which the toxicity weights were developed. Because new toxicological data and methods are constantly becoming available, the toxicity weights may change over time. Future revisions of this document will reflect those changes as resources permit.

5.1. Methods for Deriving Toxicity Weights for Carcinogenic Health Endpoints

The TRI Environmental Indicators project uses cancer slope factors (expressed as risk per mg/kg-d) as quantitative measures of a chemical's carcinogenicity. Cancer slope factors are combined with qualitative weight of evidence (WOE) classifications[8] to assign cancer toxicity weights to TRI chemicals. Table 5-1, with WOE categories on one axis and cancer slope factor value ranges on the other, represents the matrix used to assign cancer toxicity weights to each TRI chemical. For example, as Table 5-1 shows, this project would assign a cancer toxicity weight of 1000 to a substance with a cancer slope factor of 0.07 per mg/kg-d and a WOE classification of B2.

The particular ranges of cancer slope factor values selected were chosen to correspond to the ranges presented in EPA's Hazard Ranking System (55 Federal Register 51532, 40 CFR Part 300, December 14, 1990). The Hazard Ranking System (HRS) is a multipathway scoring system "used to assess the threat associated with actual or potential releases of hazardous substances at sites" (Federal Register, *op cit.*). Part of the HRS scoring system rates the inherent toxicity of chemicals based on cancer slope factors or Reference Doses. Ranges of toxicity values that differ by an order of magnitude are assigned weights that differ by an order of magnitude. The actual numerical weights assigned to the matrix cells in Table 5-1 correspond to the scores assigned in the HRS to these ranges. Inhalation unit risks are converted to risk per mg/kg-day to determine toxicity weightings using assumptions of inhalation of $20 m^3$/day of air and a body weight of 70 kg.

In certain cases, ranges presented in Table 5-1 extend beyond those presented in the HRS because the range of cancer potencies covered by the TRI chemicals is broader than the ranges included in the HRS. However, the basic logic of assigning the weights to these ranges remains the same: ranges that differ by an order of magnitude are assigned weights that differ by an order of magnitude.

[8]See U.S. Environmental Protection Agency. 1986a. Guidelines for Carcinogen Risk Assessment. 51 Federal Register 33992. September 24. The WOE classification scheme is currently being revised.

Table 5-1. Matrix for Assigning Toxicity Weights to Chemicals With Cancer Health Effects

Range of Oral Slope Factor (SF) (risk per mg/kg-day)	Range of Inhalation Unit Risk (UR) (risk per mg/m^3)	Weight of Evidence Category	
		A/B (Known/Probable)	C (Possible)
SF < 0.005	UR < 0.0014	10	1
0.005 ≤ SF < 0.05	0.0014 ≤ UR < 0.014	100	10
0.05 ≤ SF < 0.5	0.014 ≤ UR < 0.14	1000	100
0.5 ≤ SF < 5	0.14 ≤ UR < 1.4	10,000	1000
5 ≤ SF < 50	1.4 ≤ UR < 14	100,000	10,000
SF ≥ 50	UR ≥ 14	1,000,000	100,000

Carcinogens with a WOE of A, B1, or B2 ("known" or "probable" human carcinogens) were assigned toxicity weights based on the HRS scoring system, with a minimum (least toxic) toxicity weight of 10 and a maximum (most toxic) toxicity weight of 1,000,000. Carcinogens with a WOE of C ("possible" human carcinogens), were assigned toxicity weights one-tenth those of carcinogens with a WOE of A or B for the same range of cancer slope factor values, as shown in Table 5-1.[9] Possible toxicity weights for carcinogens with a WOE of C range from one (least toxic) to 100,000 (most toxic). Chemicals that have been demonstrated not to have carcinogenic potential, and are in classified "E" based on their negative cancer test results, are not assigned a cancer-based toxicity weight.

The combination of the A and B categories represents a modification of the HRS system, where A, B and C categories are scored separately. This modification and one other (see below) were made based upon comments received from two of the 1992 peer reviewers: Adam Finkel, Sc.D. (Resources for the Future) and John Graham, Ph.D. (Harvard Center for Risk Analysis). These reviewers felt that the combining of categories A and B may reduce the potential of a false dichotomy which would be inappropriate for quantitative potency adjustments of this type, and because it has the advantage of stabilizing the Indicator against changes induced by chemicals shuttling between the A and B categories.[10]

---

[9]For example, as Table 5-1 indicates, a carcinogen with a cancer oral slope factor of 0.2 and a WOE of B2 would be assigned a cancer toxicity weight of 1,000, while a carcinogen with a cancer oral slope factor of 0.2 and a WOE of C would be assigned a cancer toxicity weight one-tenth of 1000, or 100.

[10]This scoring system also differs from HRS methodology in that it does not assign the same default toxicity weight of 10,000 to asbestos and lead.

The cells in the first row of the matrix (that is, the column that corresponds to the "known/probable" WOE category) were assigned weights based on the HRS values for carcinogens in the A category. Weights in the other row (i.e., the "possible" WOE category) were assigned by dividing the weights in the first row by a factor of 10, because evidence that they cause cancer in humans is less certain. The choice of applying a factor of 10 is arbitrary, but reflects the concern of these same peer reviewers that the factor of 100 separating category A and C carcinogens in the HRS scoring matrices is too great.

For chemicals without calculated slope factor values available in IRIS or HEAST, and that lacked toxicity values from the secondary literature, available dose-response data were used to develop quantitative cancer slope factor estimates using a simplified approach, as described in Section 5.1.1.[11]

5.1.1. Methods Used for Deriving Slope Factor Estimates When Published Values are Unavailable

EPA and most risk assessors take a probabilistic approach to estimating carcinogenic risks based on the general assumption that any exposure to a carcinogen will generate some cancer risk. Consequently, carcinogens are not considered to have a safe threshold for exposure. The risk is proportional to the cumulative exposure, and at low exposure levels may be very small.[12]

EPA uses various methods to estimate carcinogenic risk for individuals and populations. For most chemicals, it is necessary to estimate risks at low exposures from data obtained from high exposure studies. The required extrapolation may be carried out using a variety of models. EPA generally uses a linearized multistage procedure, in the absence of information requiring other approaches (51 FR (185) 33997).[13] The use of this procedure generates a plausible upper limit risk estimate. The multistage model has the general form shown in Equation 1:

$$P(d) = 1 - \exp - (q_0 + q_1 d + q_2 d^2 \ldots q_k d^k) \qquad \text{Eqn. 1.}$$

where:

d = the dose

$P(d)$ = the lifetime risk of cancer at dose d

[11]Throughout this document, toxicity values derived through the Disposition Process for the purpose of deriving toxicity weights for TRI chemicals will be referred to as "estimates," i.e., cancer potency estimate, Reference Dose estimate, and WOE estimate.

[12]This position is currently being evaluated by EPA.

[13]Note that the methodology for calculating cancer risk is currently under review at EPA. Future revisions of this document will reflect the new methods once they are finalized.

Toxicological dose-response data are used to provide the dose and probability inputs to the model.[14] Using this model, an estimate of response is calculated. The dose is adjusted to estimate the human-equivalent dose when non-human studies are used. The q_1 value is often the only parameter estimate obtained from the equation. When using animal data, EPA typically calculates the 95th percentile upper confidence limit on this model parameter, termed the q_1^*. This animal upper bound value is usually referred to as the cancer slope factor. It estimates human upper bound risk per mg/kg-day. The methods used to estimate cancer risk are discussed in detail in the IRIS documentation (EPA, 1988) and EPA's *Guidelines for Carcinogen Risk Assessment* (51 FR (185) 33992-34003 (9/24/86)). Note that this method does not necessarily provide a realistic risk prediction. Rather, it provides an upper estimate of risk. The actual risk may be significantly lower and could be zero.

For the purposes of the Indicator project, the following simplified method was adopted to derive cancer slope factor estimates for use in calculating cancer toxicity weights. Although this approach differs from the one typically used by EPA with animal data (in that it uses a simpler mathematical calculation for the slope factor estimate), it follows the general concepts of the carcinogen risk assessment guidelines and is suitable for the purposes of assigning toxicity weights that vary by a full order of magnitude. Cancer slope factor estimates were calculated for both oral and inhalation exposure.

Calculation of cancer slope factor estimates involved four steps:

1. The most appropriate dose-response data were identified from available studies;
2. Dose levels were adjusted for interspecies differences;
3. The 95th percentile upper confidence bound on the dose-response data was calculated; and;
4. A linear equation describing the dose-response relationship was developed.

These steps are discussed in turn below.

1. Identifying the Most Appropriate Dose-Response Data

Various criteria were used to select appropriate dose-response data for carcinogenic risk estimates. The criteria generally applied were as follows:

[14]When epidemiological data are used to calculate the cancer slope factor, other models may be more appropriate to use. For example, the IRIS value for benzene inhalation cancer potency was calculated using the one hit model with data pooled from multiple human epidemiological studies (EPA, 1996). For the chemicals without IRIS or HEAST slope factors or interim slope factors, no calculations of cancer potency were made using human epidemiological data.

- Human data are preferred over animal data;
- Animal data from species whose biological responses are most like those of humans are preferred;
- In the absence of the previous two study subjects, data from the most sensitive species are preferred;
- The route of exposure resembling that being evaluated in humans is preferred;
- In cases where animals have more than one tumor, the total number of animals with tumors are considered, rather than the total number of tumors;
- Benign tumors with the potential to progress to malignant tumors of the same histogenic origin are combined with malignant tumors to quantify tumor incidence; and
- Consistency in response among studies provides qualitative support for the results.

These criteria are discussed in more detail in the IRIS documentation (EPA, 1988). In addition to these criteria, statistical significance was required of all data used to calculate cancer potencies, and was evaluated using standard statistical tests.

2. Modifying Dose Data for Interspecies Differences

When the dose-response data are not obtained from a human study, it is necessary to make adjustments to the dose to account for differences between animals and humans in their body weight and surface area ratios. Relative species surface area is thought to be a more appropriate scaling factor than relative body weights. Surface area can be approximated by body weight to the 2/3 power. For doses expressed as mg/day, the adjustment is carried out by raising the body weight of the study animal and an average human adult (estimated to be 70 kg) to the 2/3 power, and dividing the animal dose by the resulting ratio to estimate an equivalent human dose. For doses expressed as mg/kg-day, the adjustment requires raising the body weight of the average adult to the 1/3 and the body weight of the study animal to the 1/3. The animal dose is then divided by the resulting ratio to determine the human equivalent dose. EPA recommends using a scaling factor of 13 for mice and a scaling factor of 5.8 for rats in dose adjustments using doses expressed as mg/kg-day (e.g. the animal dose is divided by 13 to provide a human equivalent dose), based on standard weights for the animals (EPA, 1988).

For example, modifying a dose of 50 mg/kg-d administered to mice would yield a human equivalent dose of 3.9 mg/kg-d, as shown in Equation 2:

$$\frac{50\ mg/kg-d}{13} = 3.85 \approx 3.9\ mg/kg-d \qquad \text{Eqn. 2.}$$

3. Calculating an Upper 95th Percentile Confidence Bound on the Data

When calculating slope factor estimates using data from a single study, confidence bounds are related to the reliability of the data as determined by sample size. With a large number of study subjects, the confidence in the study results will be high and the confidence bounds around the actual observed responses will be relatively small. With a small number of subjects, the reverse will be true.[15] A Poisson distribution can be used to estimate the binomial distribution and obtain the upper 95th percentile confidence bound. The Poisson distribution (Pearson and Hartley, 1966) can be used in cases where the observed responses affect 20 percent or fewer of the study subjects and the population size is at least 50. Where these requirements were not met, the binomial equation was used directly to obtain the 95th percentile bound, as shown in Equation 3:

$$I = 1.96 \cdot \sqrt{\frac{\frac{r}{n} \cdot (1 - \frac{r}{n})}{n}} \qquad \text{Eqn. 3.}$$

where:

I = the fraction increase in r that provides a 95th percentile upper confidence bound;

r = the number of study respondents; and

n = the number of study subjects.

The value I obtained using the binomial equation is then used in Equation 4 to calculate the upper 95th percentile confidence bound on the response data:

$$UB_{95\%} = (r \cdot I) + r \qquad \text{Eqn. 4.}$$

where $UB_{95\%}$ is the upper 95th percentile confidence bound on the response data, and the other variables are as defined above.

The upper bound value is then converted to a ratio using the relationship described in Equation 5:

[15]The use of multiple independent studies to estimate a slope factor necessitates alternative approaches to data analysis, data aggregation, and statistical bounding. However, all slope factors calculated using the method presented in this section used data from single studies.

$$RR_{95\%} = \frac{UB_{95\%}}{n} \qquad \text{Eqn. 5.}$$

where $RR_{95\%}$ is the 95th percentile upper bound response ratio and the other variables are defined as above. This value represents the upper bound response for that dosed group, and indicates that there is a 95 percent chance that the calculated ratio would not be exceeded if the same experiment were repeated numerous times. The 95th percentile upper confidence bound value is used as the response data in the development of the linear equation which describes the dose-response relationship for carcinogens. This procedure will not give the same result as the EPA's linearized multi-stage procedure because it relies on each dose individually, not the variability in the experiment as a whole.

4. Develop an Equation Describing the Dose-response Relationship

A simple linear equation of the form $y = ax$ is calculated from the upper bound dose-response data. The equation is derived from the lowest statistically significant dose-response data and the control data from the critical study. The cancer slope factor estimate is obtained using the algebraic equation for a line between two points:

$$a = \frac{y_1 - y_2}{x_1 - x_2} \qquad \text{Eqn. 6.}$$

where:

a = the slope of the line (i.e., the cancer slope factor estimate);

x = the control dose (i.e., 0 mg/kg-d);

y_1 = the control response;

x_2 = the study dose level (in mg/kg-d); and

y_2 = the 95th percentile upper confidence bound on study response at x_2.

5.1.2. Methods Used for Assessing Weight Of Evidence Estimates When Published Values are Unavailable

During the process of hazard identification, risk assessors consider a variety of data in light of its significance to the potential carcinogenic effects of a chemical on humans. Information considered can include human epidemiology data, data from long-term animal studies, short-term mutagenicity tests, physicochemical properties and routes and patterns of exposure, structure activity

relationships, metabolism and pharmacokinetics, toxicological effects other than cancer (see carcinogen risk assessment guidelines, 51 FR 33992, Sept 24, 1986). The weight of evidence evaluation summarizes the judgment of the assessor regarding the likelihood of carcinogenicity in humans, based on the type and quality of available information. It is important to note that a weight-of-evidence judgment reflects only the likelihood that a chemical is carcinogenic in humans; it does not provide information regarding the slope factor of the chemical.

The 1986 carcinogen risk assessment guidelines present a system for classifying the weight of evidence, with special emphasis on the results of long-term animal and epidemiology studies.

The Indicators project followed the EPA's classification system as diagramed in Table 5-2 to derive WOE estimates for use in calculating cancer toxicity weights for TRI chemicals.

Table 5-2. EPA Weight of Evidence Classification System

Human Data	Animal Data				
	Sufficient	Limited	Insufficient	No Data	No Evidence
Sufficient	A	A	A	A	A
Limited	B1	B1	B1	B1	B1
Insufficient	B2	C	D	D	D
No data	B2	C	D	D	E
No evidence	B2	C	D	D	E

5.2. Methods for Deriving Toxicity Weights for Non-Cancer Health Endpoints

The TRI Environmental Indicators method derives weights for non-cancer endpoints using chronic Reference Doses (RfDs). Chemical-specific Reference Doses are based on the highest dose level at which no adverse effects are observed (NOAEL) or, in the absence of a satisfactory NOAEL, the lowest dose level at which an adverse effect is observed (LOAEL). A NOAEL or LOAEL is combined with appropriate uncertainty factors to account for variability in chemical sensitivity among humans, interspecies extrapolation, extrapolation from a LOAEL to a NOAEL, and extrapolation from subchronic to chronic data. A modifying factor can also be used to account for the quality of the database.

Unlike for potential carcinogens, no systematic weight of evidence classification is associated with values developed for chemicals with noncancer systemic health endpoints. Rather, a qualitative weight of evidence judgement, expressed as the level of confidence in the RfD, is used. The confidence level (i.e., low, medium, or high) is included with the RfD, but does not affect its numerical calculation per se.

Table 5-3 shows the matrix used to assign chronic toxicity weights to each TRI chemical. This weighting system is taken directly from the HRS (see Section 5.1), with the exception of the highest (most toxic) weighting category of 100,000. However, the toxicity weight of 100,000 assigned to RfDs less than 5×10^{-5} mg/kg-d is logically consistent with the HRS scoring system; as the RfD decreases by a factor of 10, the toxicity weight increases by a factor of 10. Reference concentrations were converted to risk per mg/kg-day to determine toxicity weightings using assumptions of inhalation of $20 m^3$/day of air and a body weight of 70 kg.

Table 5-3. Matrix for Assigning Toxicity Weights to Chemicals With Noncancer Health Effects

RfD Range (mg/kg-day)	RfC Range (mg/m^3)	Assigned Weight
RfD $\geq$ 0.5	RfC $\geq$ 1.8	1
0.05 $\leq$ RfD < 0.5	0.18 $\leq$ RfC < 1.8	10
0.005 $\leq$ RfD < 0.05	0.018 $\leq$ RfC < 0.18	100
0.0005 $\leq$ RfD < 0.005	0.0018 $\leq$ RfC < 0.018	1,000
0.00005 $\leq$ RfD < 0.0005	0.00018 $\leq$ RfC < 0.0018	10,000
RfD < 0.00005	RfC < 0.00018	100,000

Weight-of-evidence is considered only qualitatively since it is taken into account in the development of the RfD.

This weighting system is applied directly to TRI chemicals with RfDs listed in IRIS or HEAST. For substances with non-cancer effects without IRIS or HEAST RfDs, a review of the secondary literature was performed in order to calculate RfD estimates and assign toxicity weights. Whenever possible, interim risk values from secondary sources were used, as described in Appendices B and C. When these were unavailable, RfD estimates were derived following EPA methods, as described below in Section 5.2.1.

5.2.1. Methods Used for Deriving Reference Dose Estimates When Published Values are Unavailable

When calculating Reference Doses (RfDs) for chronic noncancer health effects, the EPA RfD/RfC Workgroup performs an extensive literature review to determine the highest "no observed adverse effects level" (NOAEL) or lowest "lowest observed adverse effects level" (LOAEL) available from toxicological studies of animals and humans or epidemiological studies of humans. The LOAEL or NOAEL is divided by the product of up to four Uncertainty Factors and a Modifying Factor to

derive the RfD in mg/kg-d for oral exposure, or RfC in mg/m^3 for inhalation exposure.[16] RfDs/RfCs represent daily exposure levels below which adverse noncancer health effects are not expected to occur. The Uncertainty Factors and Modifying Factor are used to provide a margin of safety when the RfD's/RfC's critical study is not based on the most sensitive human populations. The Uncertainty Factors and Modifying Factor used in calculating RfDs are listed in Table 5-4.

Table 5-4. Uncertainty Factors and Modifying Factor Used in Calculating RfDs/RfCs

Value	Name	Definition
3-10	Intraspecies Uncertainty Factor	Accounts for variation in sensitivity within the human population
3-10	Interspecies Uncertainty Factor	Accounts for uncertainty in extrapolating from animals to humans
3-10	Subchronic Data Uncertainty Factor	Accounts for uncertainty in extrapolating from subchronic to chronic (lifetime) exposure
3-10	LOAEL Uncertainty Factor	Accounts for uncertainty in extrapolating from a LOAEL to a NOAEL
1-10	Quality of Data Modifying Factor	Accounts for uncertainties such as data gaps, concordance of results, number of species tested, etc. The default value is 1.

The approach used in the TRI Environmental Indicators project parallels EPA's methodology for derivation of RfDs, as described below. The significant difference, however, is that the in-depth analysis of the epidemiological and toxicological literature conducted by EPA when developing its consensus risk values is not possible for this effort. To distinguish derived values from published values, the derived values are called *Reference Dose Estimates*. In addition, in calculating RfD/RfC Estimates, the term "Data Quality Factor" is used in place of "Modifying Factor", to further differentiate between EPA consensus values and toxicity value estimates calculated for the purpose of deriving toxicity weights for TRI chemicals.

Calculation of RfDs (and RfD estimates) involves two steps: 1) identifying the most appropriate NOAEL or LOAEL; and 2) applying relevant Uncertainty and Modifying Factors.

1. Identifying the Most Appropriate NOAEL or LOAEL

The hierarchy used to select a NOAEL or LOAEL is as follows (EPA, 1988):

- Human data are preferred over animal data;
- Animal data from species whose biological responses are most like those of humans are preferred;

[16]Reference Doses are usually referred to as Reference Concentrations (RfCs) for inhalation exposure, in units of mg/m^3.

- In the absence of the previous two study subjects, data from the most sensitive species are preferred;
- The route of exposure resembling that being evaluated in humans is preferred: oral or gavage for oral exposure, and inhalation for inhalation exposure;
- A chronic (lifetime) study is preferable to a subchronic study. An acute study cannot be used to quantify risks associated with chronic exposure;
- A study with sufficient subjects to obtain statistical significance at relatively low exposure levels is required;
- A recent study identifying adequately sensitive endpoints is required (e.g., not mortality);
- An adequate control population is required;
- In general, a NOAEL is preferable to a LOAEL. Usually, the LOAEL which generates the lowest exposure threshold (after the application of Uncertainty and Modifying Factors) is selected, if a NOAEL is not available.

Issues related to the quality of the study should also be considered in selecting the critical study. Additional information on selection criteria can be reviewed in the IRIS documentation (EPA, 1988).

In a number of studies, in order to obtain RfD estimates in units of mg/kg-d, study dose levels were converted to other units using reference inhalation rates, food intake rates, and body weights. The reference values used and their sources are listed in Table 5-5.

2. Apply Relevant Uncertainty and Modifying Factors

The NOAEL or LOAEL chosen from the literature review was divided by the product of the relevant Uncertainty and Modifying Factors shown in Table 5-4 to obtain a Reference Dose (or Reference Dose estimate) in mg/kg-d. While the Uncertainty Factors address specific concerns, the Modifying Factor covers a wider range of circumstances. The most common modifying factor adjustment results from insufficient data on a chemical. Often the dose-response data address a limited number of effects and do not adequately address effects of major concern.

In some cases there are a number of studies but the focus of analysis is narrow and insufficiently sensitive. In other cases there is not a sufficient number or breadth of studies.

Associated with RfD calculations are qualitative confidence levels (high, medium, or low) designed to advise the reader of the quality of the study data and the supporting database. EPA has recommended the following studies be available to warrant a high level of confidence in an RfD: two adequate mammalian chronic toxicity studies in different species, one adequate mammalian 2-generation reproductive toxicity study, and two adequate mammalian developmental toxicity studies in different species (Dourson et al., 1992).

Table 5-5. Reference Values Used in Calculating RfD/RfC Estimates			
Species	Reference Value	Value	Source
Dog	Body Weight	12.6 kg	Cicmanec, 1993
Dog	Respiration Rate	4.5 m3/d	Cicmanec, 1993
Human Adult	Respiration Rate	20 m^3/d	U.S. EPA OHEA, 1990b
Human Adult	Body Weight	70 kg	U.S. EPA OHEA, 1990b
Human Adult	Water Intake Rate	2 L/d	U.S. EPA OHEA, 1990b
Mice	Body Weight	0.03 kg	Hallenbeck and Cunningham, 1986
Mice	Water Intake Rate	0.005 L/d	Hallenbeck and Cunningham, 1986
Mice	Respiration Rate	0.04 m^3/d	Hallenbeck and Cunningham, 1986
Rabbit	Body Weight	2 kg	Crosfil and Widdecombe, 1961
Rabbit	Respiration Rate	0.9 m^3/d	Crosfil and Widdecombe, 1961
Rat	Body Weight	0.5 kg (males) 0.35 (females)	Hallenbeck and Cunningham, 1986
Rat	Food Intake Rate	20 g/d (males) 18 g/d (females)	Hallenbeck and Cunningham, 1986
Rat	Respiration Rate	0.2 m^3/d	Hallenbeck and Cunningham, 1986

Derived RfD/RfC estimates that have been reviewed and finalized for this project by EPA are listed in Appendix B, along with the critical studies, calculations, and literature sources used in deriving them. Appendix C contains the derived RfD estimates reviewed for this project by EPA but not yet finalized.

5.3. Selecting Overall Pathway-Specific Toxicity Weights

A number of TRI chemicals may cause both non-cancer systemic and cancer health endpoints. For the TRI Chronic Human Health Indicator project, up to four toxicity weights are derived for each TRI chemical: non-cancer systemic health effects for inhalation and oral exposure, and cancer health effects for inhalation and oral exposure. When data were lacking for one of the exposure pathways (i.e., oral or inhalation) for a certain health endpoint (i.e., cancer or noncancer effects), the toxicity weight calculated for one exposure pathway was applied to both pathways for that health endpoint, unless evidence specifically indicated that the chemical was toxic through only one pathway. Where data were lacking for one of the health endpoints (i.e., cancer or noncancer effects), no toxicity weight was calculated for that health endpoint.

The final step in the process of assigning toxicity weights to TRI chemicals was to determine an overall toxicity weight for each of the exposure pathways. First, the cancer and non-cancer systemic toxicity weights for a single exposure pathway were compared. Second, the higher (i.e., more sensitive) toxicity weight for a given pathway was designated as the overall toxicity weight for that exposure pathway. The process was repeated for the other exposure pathway, so that two overall toxicity weights were assigned to each TRI chemical: one for oral exposure, and one for inhalation exposure.

Inhalation and oral toxicity weights are developed separately. As discussed above, if values are available for each route, then separate values are assigned to each exposure route. If data are available for only one route, the same toxicity weight generally is applied for both routes. In rare instances, toxicity studies are available to show that a given chemical causes no effects via one route; in these instances, we assign the toxicity weight only to the route that results in effects. Although assigning the same weight to both routes is only an approximation of a chemical's toxicological potency, it is sufficient for the Indicators method, which relies on order-of-magnitude toxicity weights. In fact, the HRS scoring system is quite conservative in that it applies the highest toxicity weight to *all* exposure routes for a given chemical regardless of the toxicity data appropriate to the individual routes. The Indicators method attempts to evaluate the toxicological data independently for each exposure route; however, in those instances where toxicity data are unavailable, the Indicators adopts this more conservative approach of the HRS in applying the same toxicity weight to both pathways rather than assuming no health effects from the other route.

This approach does not take into consideration differences in the severity of the effects posed by the chemicals. For example, one RfD may be based on sensitization in humans, while another may be based on severe liver toxicity or fetal death in mice. The final toxicity weights do not indicate this difference, except to the extent that the difference is considered in the derivation of the RfD or estimated, through the use of a Modifying Factor. In addition, no distinction is made between chemicals with a broad range of adverse health effects and chemicals with only one reported adverse effect.

The TRI Environmental Indicator Work Group considered the option of applying an additional factor to toxicity weights, based on a subjective evaluation of the relative severity of the health effects. The Work Group also considered the option of applying an additional weight based on the number of endpoints for which the chemical demonstrates effects. However, a chemical may appear to demonstrate only one effect due to a lack of data on other effects; thus, applying a weight based on the number of endpoints may undervalue poorly-studied chemicals. Because the additional weights involved a high degree of subjectivity and possible error, the Work Group rejected these options. Pathway-specific overall toxicity weights are based on the single most sensitive health endpoint (i.e., highest toxicity weight) observed without applying additional weights for the severity of the health endpoint or the number of observed effects.

The final toxicity weights for each pathway are usually based on the above matrices, using either IRIS/HEAST data or values obtained through the Disposition Process based on chemical toxicity. However, the selection toxicity weights provide EPA with an opportunity to consider important policy issues in determining final weights. These include consideration of high priority chemicals such as lead. In some cases the Agency's desire to highlight potential relative risks associated with exposures to a specific chemical is incorporated into the weighting process to reflect a high level of concern regarding exposure to specific chemicals. This is consistent with the overall goals of the Indicators project, which is to prioritize and target those releases which are of particular concern to EPA.

6. How Indicator Toxicity Weightings Differ from EPCRA Section 313 Statutory Criteria

The TRI Relative Risk-Based Environmental Indicators utilize Toxics Release Inventory (TRI) chemical reporting data. All of the TRI chemicals included in the Indicators are listed on the TRI because they meet one or more statutory criteria regarding acute or chronic human toxicity, or environmental toxicity. The goal of the Indicators is to use data reported to the Agency to investigate the relative risk-based impacts of the releases and transfers of these chemicals on the general, non-worker population.

To do this, the Indicators must differentiate the relative toxicity of listed chemicals and rank them in a consistent manner. The ranking of each chemical reflects its toxicity only relative to other chemicals which are included in the Indicators; not to some benchmark or absolute value.

The TRI Relative Risk-Based Chronic Human Health Indicator addresses only the single, most sensitive chronic human health toxicity endpoint. Unlike the statutory criteria used for listing and delisting chemicals, the Indicator does not address the absolute chronic toxicity of chemicals on the TRI (e.g., multiple effects or the severity of effects); nor does it attempt to reflect the statutory criteria for these chemicals.

It is important that the public not confuse the use of the Indicator as a screening-level tool for investigating relative risk-based impacts related to the releases and transfers of TRI chemicals, with the very different and separate activity of listing/delisting chemicals on the TRI using statutory criteria. The toxicity weightings provided in the Indicator method cannot be used as a scoring system for evaluating listing/delisting decisions.

6.1. Emergency Planning and Community Right-to-Know Act Section 313 Statutory Criteria

The Emergency Planning and Community Right-to-Know Act of 1986 (EPCRA) section 313(d)(2) sets out criteria for adding chemicals to the list of chemicals subject to reporting under EPCRA section 313(a). For a chemical (or category of chemicals) to be added to the EPCRA section

313(c) list of toxic chemicals, the Administrator must judge whether there is sufficient evidence to establish any one of the following:

Acute Human Toxicity §313(d)(2)(A) - The chemical is known to cause or can reasonably be anticipated to cause significant adverse acute human health effects at concentration levels that are reasonably likely to exist beyond facility site boundaries as a result of continuous, or frequently recurring, releases.

Chronic Human Toxicity §313(d)(2)(B) - The chemical is known to cause or can reasonably be anticipated to cause in humans--

(i) cancer or teratogenic effects, or
(ii) serious or irreversible--
  (I) reproductive dysfunctions,
  (II) neurological disorders,
  (III) heritable genetic mutations, or
  (IV) other chronic health effects.

Environmental Toxicity §313(d)(2)(C) - The chemical is known to cause or can reasonably be anticipated to cause, because of--

(i) its toxicity,
(ii) its toxicity and persistence in the environment, or
(iii) its toxicity and tendency to bioaccumulate in the environment,

a significant adverse effect on the environment of sufficient seriousness, in the judgement of the Administrator, to warrant reporting under this section.

To remove a chemical from the section 313(c) list, the Administrator must determine that there is not sufficient evidence to establish any of the criteria described above as required by EPCRA section 313(d)(3).

The EPA examines all of the studies available for a chemical to decide if the chemical is capable of causing any of the adverse health effects or environmental toxicity in the criteria. Agency guidelines describe when a study shows such effects as cancer (EPA, 1986a), developmental toxicity (teratogenic effects) (EPA, 1991), or heritable genetic mutations (EPA, 1986b). The review makes a qualitative judgment regarding the potential of each chemical to meet at least one of the criteria and the chemical is added to the list if this judgment is positive. If a chemical is on the list and it is not possible to make a positive judgment regarding any of the criteria, then the chemical can be removed. There is no correlation between the toxicity criteria and methodology used to make listing decisions under EPCRA section 313 and the methodology used to rank chemicals for the Indicators.

6.2. Relative Toxicity Weighting of Chemicals in the TRI Relative Risk-Based Chronic Human Health Indicator

In order to help the Agency make decisions, comparisons can be made among chemicals once they are listed under EPCRA section 313. The TRI Chronic Human Health Indicator is based on aspects of the adverse health effects (cancer and noncancer) to permit the chemicals to be ranked relative to one another. These aspects are available in public Agency-generated databases. Uncertainty reflecting the quality and adequacy of the data is incorporated into a toxicity weighting each chemical receives. The approach is intended to differentiate the relative toxicity of these chemicals in a uniform manner, provide a clear and reproducible scoring system based upon easily accessible and publicly available information, and utilize EPA consensus opinion to the greatest extent possible.

7. Summary of Toxicity Weights by Classification

This section lists all of the chemicals and chemical categories on the 1995 TRI List and their toxicity weights, if they were calculated. Sections 7.1 to 7.4 provide tables of these TRI chemicals, arranged in alphabetical order. (More detailed tables, provided in the Appendices, present chemicals both alphabetically and by CAS number). Section 7.1 lists the toxicity weights for chemicals with IRIS or HEAST toxicity values. Section 7.2 lists the TRI chemicals with final toxicity weights calculated from derived toxicity value estimates. Section 7.3 provides interim toxicity weights for chemicals with derived toxicity value estimates that have been reviewed but not finalized by EPA. Section 7.4 lists those TRI chemicals for which no toxicity weights have been derived, and the reasons why no weights were derived. Section 7.5 provides a table of all TRI chemicals, sorted by toxicity weight categories.

7.1. Toxicity Weights for TRI Chemicals With IRIS or HEAST Toxicity Values

Table 7-1 contains the toxicity weights for all TRI chemicals with at least one IRIS or HEAST toxicity value (oral, inhalation or both exposure pathways), in alphabetical order by chemical name.

7-1. Toxicity Weights for TRI Chemicals with Published Reference Doses and Cancer Potencies, in Alphabetical Order

CAS Number	Chemical Name	Overall Toxicity Weight		Source
		Inhalation	Oral	
94-82-6	2,4-DB	100*	100	IRIS
30560-19-1	Acephate (Acetylphosphoramidothioic acid O,S-dimethyl ester)	1000*	1000	IRIS
75-07-0	Acetaldehyde	1000	1000*	IRIS
94-75-7	Acetic acid (2,4-D((2,4-dichlorophenoxy)))	100*	100	IRIS
75-05-8	Acetonitrile	100*	100	IRIS
98-86-2	Acetophenone	10*	10	IRIS
62476-59-9	Acifluorfen, sodium salt [5-(2-Chloro-4-(triflouromethyl)phenoxy)-2-nitrobenzoic acid, sodium salt]	100*	100	IRIS
107-02-8	Acrolein	100000	100000*	IRIS
79-06-1	Acrylamide	10000	10000	IRIS
79-10-7	Acrylic acid	10000	10	IRIS
107-13-1	Acrylonitrile	1000	10000	IRIS
15972-60-8	Alachlor	100*	100	IRIS
116-06-3	Aldicarb	1000*	1000	IRIS
309-00-2	Aldrin	100000	100000	IRIS
107-18-6	Allyl alcohol	1000*	1000	IRIS
107-05-1	Allyl chloride	10000	10000*	IRIS
319-84-6	alpha-Hexachlorocyclohexane	100000	100000	IRIS
20859-73-8	Aluminum phosphide	10000*	10000	IRIS
834-12-8	Ametryn (N-Ethyl-N'-(1-methylethyl)-6-(methylthio)-1,3,5,-triazine- 2,4 diamine)	100*	100	IRIS
33089-61-1	Amitraz	1000*	1000	IRIS

7-1. Toxicity Weights for TRI Chemicals with Published Reference Doses and Cancer Potencies, in Alphabetical Order				
CAS Number	Chemical Name	Overall Toxicity Weight		Source
		Inhalation	Oral	
7664-41-7	Ammonia	100	100*	IRIS
62-53-3	Aniline	10000	100	IRIS
120-12-7	Anthracene	10*	10	IRIS
7440-36-0	Antimony	10000*	10000	IRIS
N010	Antimony compounds	10000*	10000	IRIS
7440-38-2	Arsenic	100000	10000	IRIS
N020	Arsenic compounds	100000	10000	IRIS
1332-21-4	Asbestos (friable)	1000	n/a	IRIS
1912-24-9	Atrazine (6-Chloro-N-ethyl-N'-(1-methylethyl)-1,3,5,-triazine-2,4-diamine)	100*	100	IRIS
N040	Barium compounds	10*	10	IRIS
7440-39-3	Barium	10*	10	IRIS
1861-40-1	Benfluralin (N-Butyl-N-ethyl-2,6-dinitro-4-(trifluoromethyl)benzenamine)	10*	10	IRIS
17804-35-2	Benomyl	100*	100	IRIS
71-43-2	Benzene	100	100	IRIS
92-87-5	Benzidine	1000000	1000000	IRIS
98-07-7	Benzotrichloride	100000*	100000	IRIS
100-44-7	Benzyl chloride	1000*	1000	IRIS
7440-41-7	Beryllium	100000	10000	IRIS
N050	Beryllium compounds	100000	10000	IRIS
82657-04-3	Bifenthrin	100*	100	IRIS
92-52-4	Biphenyl	100*	100	IRIS
111-44-4	Bis(2-chloroethyl)ether	10000	10000	IRIS
542-88-1	Bis(chloromethyl)ether	1000000	1000000	IRIS
56-35-9	Bis(tributyltin) oxide	100000*	100000	IRIS
75-25-2	Bromoform (Tribromomethane)	10	100	IRIS

7-1. Toxicity Weights for TRI Chemicals with Published Reference Doses and Cancer Potencies, in Alphabetical Order				
CAS Number	Chemical Name	Overall Toxicity Weight		Source
		Inhalation	Oral	
74-83-9	Bromomethane (Methyl Bromide)	1000	1000	IRIS
1689-99-2	Bromoxynil octanoate (Octanoic acid,2,6-dibromo-4-cyanophenyl ester)	100*	100	IRIS
1689-84-5	Bromoxynil (3,5-Dibromo-4-hydroxybenzonitrile)	100*	100	IRIS
106-99-0	Butadiene, 1,3-	10000	10000*	IRIS
106-88-7	Butylene oxide, 1,2-	100	100*	IRIS
16071-86-6	C.I. Direct Brown 95	100000*	100000	HEAST
1937-37-7	C.I. Direct Black 38	100000*	100000	HEAST
2602-46-2	C.I. Direct Blue 6	100000*	100000	HEAST
7440-43-9	Cadmium	100000	10000	IRIS
N078	Cadmium compounds	100000	10000	IRIS
133-06-2	Captan	10*	10	IRIS
63-25-2	Carbaryl	10*	10	IRIS
1563-66-2	Carbofuran	1000*	1000	IRIS
56-23-5	Carbon tetrachloride	1000	1000	IRIS
75-15-0	Carbon disulfide	10	10	IRIS
5234-68-4	Carboxin (5,6-Dihydro-2-methyl-N-phenyl-1,4-oxathiin-3-carboxamide)	10*	10	IRIS
75-69-4	CFC-11	10*	10	IRIS
75-71-8	CFC-12	10*	10	IRIS
133-90-4	Chloramben	100*	100	IRIS
57-74-9	Chlordane	10000	10000	IRIS
90982-32-4	Chlorimuron ethyl (Ethyl-2-[[[(4-chloro-6-methoxyprimidin-2-yl)-carbonyl]-amino]sulfonyl]benzoate)	100*	100	IRIS
10049-04-4	Chlorine dioxide	10000	10000*	IRIS
7782-50-5	Chlorine	10*	10	IRIS
75-68-3	Chloro-1,1-difluoroethane, 1-	1	1*	IRIS

7-1. Toxicity Weights for TRI Chemicals with Published Reference Doses and Cancer Potencies, in Alphabetical Order				
CAS Number	Chemical Name	Overall Toxicity Weight		Source
		Inhalation	Oral	
79-11-8	Chloroacetic acid	1000*	1000	HEAST
532-27-4	Chloroacetophenone, 2-	100000	100000*	IRIS
108-90-7	Chlorobenzene	100*	100	IRIS
510-15-6	Chlorobenzilate	100*	100	IRIS
75-00-3	Chloroethane (Ethyl chloride)	1	1*	IRIS
67-66-3	Chloroform	1000	100	IRIS
74-87-3	Chloromethane	10	10	HEAST
1897-45-6	Chlorothalonil	100*	100	IRIS
64902-72-3	Chlorsulfuron (2-Chloro-N-[[(4-methoxy-6-methyl-1,3,5-triazin-2-yl)amino]carbonyl]benzenesulfonamide)	100*	100	IRIS
7440-50-8	Copper	1*	1	HEAST
98-82-8	Cumene	100*	100	IRIS
N106	Cyanide compounds	100*	100	IRIS
68359-37-5	Cyfluthrin (3-(2,2-Dichloroethenyl)-2,2-dimethylcyclopropanecarboxylic acid,cyano(4-fluoro-3-phenoxyphenyl)methy	100*	100	IRIS
68085-85-8	Cyhalothrin (3-(2-Chloro-3,3,3-trifluoro-1-propenyl)-2,2-Dimethylcyclopropanecarboxylic acidcyano(3-phenoxypheny	1000*	1000	IRIS
1163-19-5	Decabromodiphenyl oxide	100*	100	IRIS
117-81-7	Di(2-ethylhexyl) phthalate	100*	100	IRIS
2303-16-4	Diallate	1000*	1000	HEAST
95-80-7	Diaminotoluene, 2,4-	10000*	10000	HEAST
96-12-8	Dibromo-3-chloropropane (DBCP), 1,2-	10000	10000*	IRIS
106-93-4	Dibromoethane, 1,2-	10000	1000000	IRIS
84-74-2	Dibutyl phthalate	10*	10	IRIS
1918-00-9	Dicamba (3,6-Dichloro-2-methyoxybenzoicacid)	100*	100	IRIS
764-41-0	Dichloro-2-butene, 1,4-	100000	100000*	HEAST

7-1. Toxicity Weights for TRI Chemicals with Published Reference Doses and Cancer Potencies, in Alphabetical Order				
CAS Number	Chemical Name	Overall Toxicity Weight		Source
		Inhalation	Oral	
95-50-1	Dichlorobenzene, 1,2	10*	10	IRIS
106-46-7	Dichlorobenzene, 1,4-	10	10*	IRIS
91-94-1	Dichlorobenzidine, 3,3'-	1000*	1000	IRIS
75-27-4	Dichlorobromomethane	1000*	1000	IRIS
107-06-2	Dichloroethane, 1,2-	1000	1000	IRIS
540-59-0	Dichloroethylene, 1,2-	100*	100	HEAST
75-09-2	Dichloromethane	10	100	IRIS
120-83-2	Dichlorophenol, 2,4-	1000*	1000	IRIS
78-87-5	Dichloropropane, 1,2-	1000	1000*	IRIS
542-75-6	Dichloropropylene, 1,3-	100	10000	IRIS
62-73-7	Dichlorvos	10000	10000	IRIS
35367-38-5	Diflubenzuron	100*	100	IRIS
55290-64-7	Dimethipin (2,3,-Dihydro-5,6-dimethyl-1,4-dithiin 1,1,4,4-tetraoxide)	100*	100	IRIS
60-51-5	Dimethoate	10000*	10000	IRIS
119-90-4	Dimethoxybenzidine, 3,3'-	100*	100	HEAST
119-93-7	Dimethylbenzidine, 3,3'-	100000*	100000	HEAST
576-26-1	Dimethylphenol, 2,6-	1000*	1000	IRIS
105-67-9	Dimethylphenol, 2,4-	100*	100	IRIS
88-85-7	Dinitrobutyl phenol (Dinoseb)	1000*	1000	IRIS
51-28-5	Dinitrophenol, 2,4-	1000*	1000	IRIS
121-14-2	Dinitrotoluene, 2,4-	1000*	1000	IRIS
606-20-2	Dinitrotoluene, 2,6-	10000*	10000	IRIS
123-91-1	Dioxane, 1,4-	100*	100	IRIS
957-51-7	Diphenamid	100*	100	IRIS
122-39-4	Diphenylamine	100*	100	IRIS
122-66-7	Diphenylhydrazine, 1,2-	10000	10000	IRIS

7-1. Toxicity Weights for TRI Chemicals with Published Reference Doses and Cancer Potencies, in Alphabetical Order				
CAS Number	Chemical Name	Overall Toxicity Weight		Source
		Inhalation	Oral	
330-54-1	Diuron	1000*	1000	IRIS
2439-10-3	Dodine (Dodecylguanidine monoacetate)	1000*	1000	IRIS
106-89-8	Epichlorohydrin	10000	100	IRIS
110-80-5	Ethoxyethanol, 2-	10	10*	IRIS
759-94-4	Ethyl dipropylthiocarbamate (EPTC)	100*	100	IRIS
140-88-5	Ethyl acrylate	100*	100	HEAST
100-41-4	Ethylbenzene	10	10	IRIS
96-45-7	Ethylene thiourea	10000*	10000	IRIS
75-21-8	Ethylene oxide	10000*	10000	HEAST
107-21-1	Ethylene glycol	1*	1	IRIS
39515-41-8	Fenpropathrin (2,2,3,3-Tetramethylcyclopropane carboxylicacid cyano(3-phenoxyphenyl)methylester)	100*	100	IRIS
51630-58-1	Fenvalerate (4-Chloro-alpha-(1-methylethyl)benzeneacetic acid cyano(3-phenoxyphenyl)methyl ester)	100*	100	IRIS
2164-17-2	Fluometuron	100*	100	IRIS
7782-41-4	Fluorine	10*	10	IRIS
69409-94-5	Fluvalinate (N-[2-Chloro-4-(trifluoromethyl)phenyl]-DL-valine(+)-cyano (3-phenoxyphenyl)methyl ester)	100*	100	IRIS
133-07-3	Folpet	10*	10	IRIS
72178-02-0	Fomesafen (5-(2-Chloro-4-(trifluoromethyl)phenoxy)-Nmethylsulfonyl)-2-nitrobenzamide)	100*	100	IRIS
50-00-0	Formaldehyde	100	10	IRIS
64-18-6	Formic acid	1*	1	HEAST
76-13-1	Freon 113	1*	1	IRIS
76-44-8	Heptachlor	10000	10000	IRIS
87-68-3	Hexachloro-1,3-butadiene	100	100	IRIS
118-74-1	Hexachlorobenzene	10000	10000	IRIS
77-47-4	Hexachlorocyclopentadiene	100*	100	IRIS

7-1. Toxicity Weights for TRI Chemicals with Published Reference Doses and Cancer Potencies, in Alphabetical Order				
CAS Number	Chemical Name	Overall Toxicity Weight		Source
		Inhalation	Oral	
67-72-1	Hexachloroethane	10	1000	IRIS
70-30-4	Hexachlorophene	10000*	10000	IRIS
51235-04-2	Hexazinone	100*	100	IRIS
67485-29-4	Hydramethylnon (Tetrahydro-5,5-di-methyl-2(1H)-pyrimidinone[3-[4-(trifluoromethyl)phenyl]-1-[2-[4-(trifluoromet	10000*	10000	IRIS
302-01-2	Hydrazine	100000	10000	IRIS
7647-01-0	Hydrochloric acid	100	100*	IRIS
74-90-8	Hydrogen cyanide	1000	100	IRIS
123-31-9	Hydroquinone	100*	100	HEAST
35554-44-0	Imazalil (1-[2-(2,4-Dichlorophenyl)-2-(2-propenyloxy)ethyl]-1H-imidazole)	100*	100	IRIS
80-05-7	Isopropylidenediphenol, 4,4'-	100*	100	IRIS
77501-63-4	Lactofen (5-(2-Chloro-4-(trifluoromethyl)phenoxy)-2-nitro-2-ethoxy-1-methyl-2-oxoethyl ester)	1000*	1000	IRIS
58-89-9	Lindane	10000*	10000	IRIS
330-55-2	Linuron	1000*	1000	IRIS
108-39-4	m-Cresol	100*	100	IRIS
99-65-0	m-Dinitrobenzene	10000*	10000	IRIS
108-38-3	m-Xylene	1*	1	HEAST
121-75-5	Malathion	100*	100	IRIS
108-31-6	Maleic anhydride	10*	10	IRIS
109-77-3	Malonitrile	100000*	100000	HEAST
12427-38-2	Maneb	1000*	1000	IRIS
7439-96-5	Manganese	100000	10	IRIS
N450	Manganese compounds	100000	10	IRIS
93-65-2	Mecoprop	1000*	1000	IRIS
7439-97-6	Mercury	10000	10000*	IRIS

7-1. Toxicity Weights for TRI Chemicals with Published Reference Doses and Cancer Potencies, in Alphabetical Order				
CAS Number	Chemical Name	Overall Toxicity Weight		Source
		Inhalation	Oral	
N458	Mercury compounds	10000	10000*	IRIS
150-50-5	Merphos	100000*	100000	IRIS
126-98-7	Methacryonitrile	10000*	10000	IRIS
67-56-1	Methanol	10*	10	IRIS
94-74-6	Methoxone ((4-Chloro-2-methylphenoxy)acetic acid) (MCPA)	10000*	10000	IRIS
72-43-5	Methoxychlor	1000*	1000	IRIS
109-86-4	Methoxyethanol, 2-	100	100*	IRIS
78-93-3	Methyl ethyl ketone	10	1	IRIS
1634-04-4	Methyl tert-butyl ether	1	1*	IRIS
96-33-3	Methyl acrylate	100*	100	HEAST
298-00-0	Methyl parathion	10000*	10000	IRIS
108-10-1	Methyl isobutyl ketone	10*	10	HEAST
80-62-6	Methyl methacrylate	10*	10	HEAST
74-95-3	Methylene bromide	100*	100	HEAST
101-14-4	Methylenebis(2-chloroaniline), 4,4'-	1000	1000	HEAST
101-61-1	Methylenebis(N,N-dimethylbenzenamine), 4,4'-	100*	100	IRIS
21087-64-9	Metribuzin	100*	100	IRIS
2212-67-1	Molinate (1H-Azepine-1 carbothioicacid, hexahydro-S-ethyl ester)	1000*	1000	IRIS
88671-89-0	Myclobutanil (.alpha.-Butyl-.alpha.-(4-chlorophenyl)-1H-1,2,4-triazole-1-propanenitrile)	100*	100	IRIS
68-12-2	N,N-Dimethylformamide	100	100*	IRIS
121-69-7	N,N-Dimethylaniline	1000*	1000	IRIS
71-36-3	n-Butyl alcohol	10*	10	IRIS
110-54-3	n-Hexane	10	10*	IRIS
759-73-9	N-Nitroso-N-ethylurea	1000000*	1000000	HEAST
924-16-3	N-Nitrosodi-n-butylamine	100000	100000	IRIS

7-1. Toxicity Weights for TRI Chemicals with Published Reference Doses and Cancer Potencies, in Alphabetical Order				
CAS Number	Chemical Name	Overall Toxicity Weight		Source
		Inhalation	Oral	
621-64-7	N-Nitrosodi-n-propylamine	100000*	100000	IRIS
55-18-5	N-Nitrosodiethylamine	1000000	1000000	IRIS
62-75-9	N-Nitrosodimethylamine	100000	1000000	IRIS
86-30-6	N-Nitrosodiphenylamine	10*	10	IRIS
300-76-5	Naled	1000*	1000	IRIS
No CASRNa	Nitrate compounds (water dissociable)	1*	1	IRIS
99-59-2	Nitro-o-anisidine, 5-	100*	100	HEAST
99-55-8	Nitro-o-toluidine	100*	100	HEAST
98-95-3	Nitrobenzene	10000*	10000	IRIS
79-46-9	Nitropropane, 2-	100	100*	IRIS
27314-13-2	Norflurazon (4-Chloro-5-(methylamino)-2-[3-(trifluoromethyl)phenyl]-3(2H)-pyridazinone)	100*	100	IRIS
95-48-7	o-Cresol	100*	100	IRIS
528-29-0	o-Dinitrobenzene	10000*	10000	HEAST
95-53-4	o-Toluidine	1000*	1000	HEAST
636-21-5	o-Toluidine hydrochloride	1000*	1000	HEAST
95-47-6	o-Xylene	1*	1	HEAST
19044-88-3	Oryzalin (4-(Dipropylamino)-3,5-dinitrobenzenesulfonamide)	100*	100	IRIS
19666-30-9	Oxydiazon (3-[2,4-Dichloro-5-(1-methylethoxy)phenyl]-5-(1,1-dimethylethyl)-1,3,4-oxadiazol-2(3H)-one)	1000*	1000	IRIS
42874-03-3	Oxyfluorfen	1000*	1000	IRIS
106-47-8	p-Chloroaniline	1000*	1000	IRIS
106-44-5	p-Cresol	1000*	1000	HEAST
100-25-4	p-Dinitrobenzene	10000*	10000	HEAST
106-50-3	p-Phenylenediamine	10*	10	HEAST
1910-42-5	Paraquat dichloride	1000*	1000	IRIS
56-38-2	Parathion	100*	100	HEAST

7-1. Toxicity Weights for TRI Chemicals with Published Reference Doses and Cancer Potencies, in Alphabetical Order				
CAS Number	Chemical Name	Overall Toxicity Weight		Source
		Inhalation	Oral	
40487-42-1	Pendimethalin (N-(1-Ethylpropyl)-3,4-dimethyl-2,6-dinitrobenzenamine)	100*	100	IRIS
87-86-5	Pentachlorophenol	1000*	1000	IRIS
52645-53-1	Permethrin (3-(2,2-Dichloroethenyl)-2,2-dimethylcyclopropanecarboxylic acid,(3-phenoxyphenyl)methyl ester)	100*	100	IRIS
108-95-2	Phenol	1*	1	IRIS
108-45-2	Phenylenediamine, 1,3-	100*	100	IRIS
90-43-7	Phenylphenol, 2-	1*	1	HEAST
7803-51-2	Phosphine	10000	10000	IRIS
7664-38-2	Phosphoric acid	1000	See Table 7-2	IRIS
7723-14-0	Phosphorus (yellow or white)	100000*	100000	IRIS
85-44-9	Phthalic anhydride	1*	1	IRIS
1918-02-1	Picloram	10*	10	IRIS
29232-93-7	Pirimiphos methyl (O-(2-(Diethylamino)-6-methyl-4-pyrimidinyl)-O,O-dimethylphosphorothioate)	100*	100	IRIS
N575	Polybrominated Biphenyls (PBBs)	100000*	100000	HEAST
1336-36-3	Polychlorinated biphenyls	1000	100000	IRIS
7287-19-6	Prometryn (N,N'-Bis(1-methylethyl)-6-methylthio-1,3,5-triazine-2,4-diamine)	1000*	1000	IRIS
23950-58-5	Pronamide	10*	10	IRIS
1918-16-7	Propachlor (2-Chloro-N-(1-methylethyl)-N-phenylacetamide)	100*	100	IRIS
709-98-8	Propanil (N-(3,4-Dichlorophenyl)propanamide)	1000*	1000	IRIS
2312-35-8	Propargite	100*	100	IRIS
107-19-7	Propargyl alcohol	1000*	1000	IRIS
60207-90-1	Propiconazole (1-[2-(2,4-Dichlorophenyl)-4-propyl-1,3-dioxolan-2-yl]-methyl-1H-1,2,4,-triazole)	100*	100	IRIS
114-26-1	Propoxur	1000*	1000	IRIS

7-1. Toxicity Weights for TRI Chemicals with Published Reference Doses and Cancer Potencies, in Alphabetical Order				
CAS Number	Chemical Name	Overall Toxicity Weight		Source
		Inhalation	Oral	
75-56-9	Propylene oxide	100	1000	IRIS
110-86-1	Pyridine	1000*	1000	IRIS
91-22-5	Quinoline	10000*	10000	HEAST
82-68-8	Quintozene	1000*	1000	IRIS
76578-14-8	Quizalofop-ethyl (2-[4-[(6-Chloro-2-quinoxalinyl)oxy]phenoxy] propanoicacid ethyl ester)	100*	100	IRIS
10453-86-8	Resmethrin ([5-(Phenylmethyl)-3-furanyl]methyl 2,2-dimethyl-3-(2-methyl-1-propenyl)cyclopropanecarboxylate])	100*	100	IRIS
7782-49-2	Selenium	1000*	1000	IRIS
N725	Selenium compounds	1000*	1000	IRIS
74051-80-2	Sethoxydim (2-[1-(Ethoxyimino)butyl]-5-[2-(ethylthio)propyl]-3-hydroxyl-2-cyclohexen-1-one)	10*	10	IRIS
7440-22-4	Silver	1000*	1000	IRIS
N740	Silver compounds	1000*	1000	IRIS
122-34-9	Simazine	1000*	1000	IRIS
26628-22-8	Sodium azide	1000*	1000	IRIS
62-74-8	Sodium fluoroacetate	100000*	100000	IRIS
No CASRNb	Strychnine and salts	10000*	10000	IRIS
100-42-5	Styrene	10	10	IRIS
34014-18-1	Tebuthiuron (N-[5-(1,1-Dimethylethyl)-1,3,4-thiadiazol-2-yl)- N,N'-dimethylurea)	10*	10	IRIS
5902-51-2	Terbacil (5-Chloro-3-(1,1-dimethylethyl)-6-methyl- 2,4 (1H,3H)-pyrimidinedione)	100*	100	IRIS
79-34-5	Tetrachloroethane, 1,1,2,2-	100	100	IRIS
630-20-6	Tetrachloroethane, 1,1,1,2-	10	100	IRIS
127-18-4	Tetrachloroethylene (Perchlorethyle	100*	100	IRIS
961-11-5	Tetrachlorvinphos	100*	100	IRIS

7-1. Toxicity Weights for TRI Chemicals with Published Reference Doses and Cancer Potencies, in Alphabetical Order				
CAS Number	Chemical Name	Overall Toxicity Weight		Source
		Inhalation	Oral	
28249-77-6	Thiobencarb (Carbamic acid, diethylthio-, S-(p-chlorobenzyl))	100*	100	IRIS
23564-05-8	Thiophanate-methyl	10*	10	IRIS
137-26-8	Thiram	1000*	1000	IRIS
108-88-3	Toluene	10	10	IRIS
26471-62-5	Toluenediisocyanate	100000	See Table 7-3	IRIS
8001-35-2	Toxaphene	10000	10000	IRIS
43121-43-3	Triadimefon (1-(4-Chlorophenoxy)-3,3-dimethyl-1-(1H-1,2,4-triazol-1-yl)-2-butanone)	100*	100	IRIS
2303-17-5	Triallate	100*	100	IRIS
101200-48-0	Tribenuron methyl (2-(4-Methoxy-6-methyl-1,3,5-triazin-2-yl)-methylamino)carbonyl)amino)sulfonyl)-,methyl ester)	100*	100	IRIS
78-48-8	Tributyltrithiophosphate (DEF), S,S,S-	100000*	100000	IRIS
120-82-1	Trichlorobenzene, 1,2,4-	100*	100	IRIS
79-00-5	Trichloroethane, 1,1,2-	100	1000	IRIS
95-95-4	Trichlorophenol, 2,4,5-	10*	10	IRIS
88-06-2	Trichlorophenol, 2,4,6-	100	100	IRIS
96-18-4	Trichloropropane, 1,2,3-	100*	100	IRIS
121-44-8	Triethylamine	1000	1000*	IRIS
1582-09-8	Trifluralin	100*	100	IRIS
7440-62-2	Vanadium (fume or dust)	100*	100	HEAST
50471-44-8	Vinclozolin (3-(3,5-Dichlorophenyl)-5-ethenyl-5-methyl-2,4-oxazolidinedione)	100*	100	IRIS
108-05-4	Vinyl acetate	10	10*	IRIS
593-60-2	Vinyl bromide	1000	1000*	IRIS
75-01-4	Vinyl chloride	10000*	10000	HEAST
75-35-4	Vinylidene chloride	100	1000	IRIS

7-1. Toxicity Weights for TRI Chemicals with Published Reference Doses and Cancer Potencies, in Alphabetical Order				
CAS Number	Chemical Name	Overall Toxicity Weight		Source
		Inhalation	Oral	
81-81-2	Warfarin and salts	10000*	10000	IRIS
1330-20-7	Xylene (mixed isomers)	1*	1	IRIS
7440-66-6	Zinc (fume or dust)	10*	10	IRIS
12122-67-7	Zineb	100*	100	IRIS

*Toxicity weight is adopted from the other exposure pathway.

7.2. Toxicity Weights for TRI Chemicals With Final Derived Toxicity Values

Table 7-2 contains the finalized toxicity weights for all TRI chemicals with derived toxicity value estimates, in alphabetical order by chemical name.

Table 7-2. Toxicity Weights for TRI Chemicals with Final Derived Toxicity Values, in Alphabetical Order

CAS #	Chemical Name	Overall Toxicity Weight	
		Inhalation	Oral
6484-52-2	Ammonium Nitrate	1*	1
90-04-0	Anisidine, o-	10,000[a]	1,000
156-62-7	Calcium Cyanamide	1,000*	1,000
80-15-9	Cumene Hydroperoxide	1,000	1,000*
135-20-6	Cupferron	1,000*	1,000
101-80-4	Diaminodiphenylether, 4,4-	1,000*	1,000
25321-22-6	Dichlorobenzene (mixed isomers)	10[a]	100
541-73-1	Dichlorobenzene, 1,3-[b]	10[a]	100
64-67-5	Diethyl Sulfate	10,000*	10,000
74-85-1	Ethylene	1	1*
624-83-9	Methyl Isocyanate	100,000	100,000*
90-94-8	Michlers Ketone	1,000*	1,000
91-20-3	Napththalene	1000	1000*
7697-37-2	Nitric Acid	100	100*
100-02-7	Nitrophenol, 4-	1,000	1,000
7664-38-2	Phosphoric Acid	1000	1
88-89-1	Picric Acid (2,4,6-Trinitrophenol)	10,000	10,000
115-07-1	Propylene (Propene)	1	1*
75-55-8	Propylenimine	1,000,000*	1,000,000
7664-93-9	Sulfuric Acid	10,000	1
62-56-6	Thiourea	10,000*	10,000
1314-20-1	Thorium Dioxide	10,000	1,000,000
71-55-6	Trichloroethane, 1,1,1-	10	10*

Table 7-2. Toxicity Weights for TRI Chemicals with Final Derived Toxicity Values, in Alphabetical Order			
CAS #	Chemical Name	Overall Toxicity Weight	
		Inhalation	Oral
95-63-6	Trimethylbenzene, 1,2,4-	1,000	1,000
106-42-3	Xylene, p-	1*	1

*Toxicity weight is adopted from the other exposure pathway.
[a]Interim derived weight; see Appendix C.
[b]Data gap exists for this chemical; data taken from isomer listed above.

7.3. Toxicity Weights for TRI Chemicals With Interim Derived Toxicity Values

Table 7-3 contains the interim toxicity weights for all TRI chemicals with derived toxicity value estimates, in alphabetical order by chemical name.

Table 7-3. Toxicity Weights For TRI Chemicals with Interim Derived Toxicity Values, in Alphabetical Order

CAS Number	Chemical Name	Overall Toxicity Weights	
		Inhalation	Oral
7429-90-5	Aluminum (fume or dust)	100,000	
90-04-0	Anisidine, o-	10,000	1,000[a]
141-32-2	Butyl Acrylate	10	10,000
463-58-1	Carbonyl Sulfide	100	100*
120-80-9	Catechol (1,2-Dihydroxybenzene)	100	100*
7440-48-4	Cobalt	100,000	100,000*
N096	Cobalt Compounds[b]	100,000	100,000*
120-71-8	Cresidine, p-	1,000*	1,000
110-82-7	Cyclohexane	1	1*
25376-45-8	Diaminotoluene (mixed isomers)	100,000*	100,000
2532-12-26	Dichlorobenzene (mixed isomers)	10	100[a]
54-17-31	Dichlorobenzene, 1,3-	10	100[a]
111-42-2	Diethanolamine	100*	100
77-78-1	Dimethyl Sulfate	1,000,000	1,000,000*
534-52-1	Dinitro-o-cresol, 4,6-	10,000	10,000
78-84-2	Isobutyraldehyde	100,000	100,000*
67-63-0	Isopropyl Alcohol	10,000	1
7439-92-1	Lead	100,000	100,000
N420	Lead Compounds[b]	100,000	100,000
74-88-4	Methyl Iodide	1,000*	1,000
1313-27-5	Molybdenum Trioxide	10,000	1,000

Table 7-3. Toxicity Weights For TRI Chemicals with Interim Derived Toxicity Values, in Alphabetical Order			
CAS Number	Chemical Name	Overall Toxicity Weights	
		Inhalation	Oral
139-13-9	Nitrilotriacetic Acid	100*	100
55-63-0	Nitroglycerin	10,000*	10,000
79-21-0	Peracetic Acid	1,000	1,000*
7550-45-0	Titanium Tetrachloride	100,000	100,000*
26471-62-5	Toluene Diisocyanate (mixed isomers)	100,000	100
91-08-7	Toluene Diisocyanate, 2,6-[c]	100,000	100
584-84-9	Toluene Diisocyanate, 2,4-[c]	100,000	100

*Toxicity weight is adopted from the other exposure pathway.
[a]Final derived weight; see Appendix B.
[b]Toxicity weight for metal compounds is assumed to be the same as for the parent metal.
[c]Data gap exists for this chemical; data are taken from another isomer.

7.4. TRI Chemicals With No Toxicity Weights

Table 7-4 contains a list of the chemicals and chemical categories on the 1995 TRI List with no toxicity weights, in alphabetical order by chemical name.

Table 7-4. TRI Chemicals Without Toxicity Weights, in Alphabetical Order

CAS Number	Chemical Name	Reason for no Toxicity Weight
71751412	Abamectin (Avermectin B1)	new chemical, not derived
60-35-5	Acetamide	low priority chemical
53-96-3	Acetylaminofluorene, 2-	low priority chemical
107119	Allylamine	new chemical, not derived
134-32-7	alpha-Naphthylamine	low priority chemical
1344-28-1	Aluminum oxide (fibrous forms)	new chemical, derived, not reviewed
82-28-0	Amino-2-methyl-anthraquinone, 1-	low priority chemical
117-79-3	Aminoanthraquinone, 2-	low priority chemical
60-09-3	Aminoazobenzene, 4-	low priority chemical
92-67-1	Aminodiphenyl, 4-	low priority chemical
61-82-5	Amitrole	new chemical, not derived
101053	Anilazine (4,6-Dichloro-N-(2-chlorophenyl)-1,3,5-triazin-2-amine)	new chemical, not derived
492-80-8	Auramine	low priority chemical
22781233	Bendiocarb (2,2-Dimethyl-1,3-benzodioxol-4-ol methylcarbamate)	new chemical, not derived
98-87-3	Benzal chloride	insufficient data
55-21-0	Benzamide	low priority chemical
94-36-0	Benzoyl Peroxide	insufficient data
98-88-4	Benzoyl chloride	insufficient data
91-59-8	beta-Naphthylamine	new chemical, not derived
57-57-8	beta-Propiolactone	low priority chemical
108-60-1	Bis(2-chloro-1-methethyl)ether	new chemical, not derived
111-91-1	Bis(2-chloroethoxy)methane	new chemical, not derived
7637072	Boron trifluoride	new chemical, not derived

Table 7-4. TRI Chemicals Without Toxicity Weights, in Alphabetical Order		
CAS Number	Chemical Name	Reason for no Toxicity Weight
10294345	Boron trichloride	new chemical, not derived
314409	Bromacil (5-Bromo-6-methyl-3-(1-methylpropyl)-2,4(1H,3H)-pyrimidinedione)	new chemical, not derived
53404196	Bromacil lithium salt (2,4(1H,3H)-Pyrimidinedione, 5-bromo-6-methyl-3 (1-methylpropyl), lithium salt)	new chemical, not derived
7726956	Bromine	new chemical, not derived
35691657	Bromo-1-(bromomethyl)-1,3-propanedicarbonitrile, 1-	new chemical, not derived
52517	Bromo-2-nitropropane-1,3-diol(Bronopol), 2-	new chemical, not derived
353-59-3	Bromochlorodifluoromethane (Halon 1	new chemical, derived, not reviewed
75-63-8	Bromotrifluoromethane (Halon 1301)	new chemical, not derived
357573	Brucine	new chemical, not derived
1929733	butoxyethyl ester, 2,4-D	new chemical, not derived
94804	butyl ester, 2,4-D	new chemical, not derived
123-72-8	Butyraldehyde	insufficient data
989-38-8	C.I. Basic Red 1	low priority chemical
128-66-5	C.I. Vat Yellow 4	low priority chemical
97-56-3	C.I. Solvent Yellow 3	low priority chemical
6459945	C.I. Acid Red 114	new chemical, not derived
4680-78-8	C.I. Acid Green 3	low priority chemical
3118-97-6	C.I. Solvent Orange 7	low priority chemical
28407376	C.I. Direct Blue 218	new chemical, not derived
2832-40-8	C.I. Disperse Yellow 3	low priority chemical
81-88-9	C.I. Food Red 15	low priority chemical
842-07-9	C.I. Solvent Yellow 14	low priority chemical
569-64-2	C.I. Basic Green 4	low priority chemical
3761-53-3	C.I. Food Red 5	low priority chemical
76-15-3	CFC 115	new chemical, not derived
76-14-2	CFC 114	new chemical, not derived

Table 7-4. TRI Chemicals Without Toxicity Weights, in Alphabetical Order		
CAS Number	Chemical Name	Reason for no Toxicity Weight
2439012	Chinomethionat (6-Methyl-1,3-dithiolo[4,5-b]quinoxalin-2-one)	new chemical, not derived
115286	Chlorendic acid	new chemical, not derived
75887	Chloro-1,1,1-trifluoroethane (HCFC-133a), 2-	new chemical, not derived
354-25-6	Chloro-1,1,2,2-tetrafluoroethane, 1-	new chemical, not derived
460355	Chloro-1,1,1-trifluoropropane(HCFC-253fb), 3-	new chemical, not derived
2837-89-0	Chloro-1,1,1,2-tetrafluoroethane, 2-	new chemical, not derived
563473	Chloro-2-methyl-1-propene, 3-	new chemical, not derived
4080313	Chloroallyl)-3,5,7-triaza-1-azoniaadamantane chloride, 1-(3-	new chemical, not derived
2971382	chlorocrotyl ester, 2,4-D	new chemical, not derived
74-45-6	Chlorodifluoromethane (HCFC-22)	new chemical, not derived
107-30-2	Chloromethyl methyl ether	insufficient data
N084	Chlorophenols	new chemical, not derived
76062	Chloropicrin	new chemical, not derived
126-99-8	Chloroprene	insufficient data
542767	Chloropropionitrile, 3-	new chemical, not derived
63938-10-3	Chlorotetrafluoroethane	new chemical, not derived
75729	Chlorotrifluoromethane (CFC-13)	new chemical, not derived
5598130	Chlorpyrifos methyl (O,O-Dimethyl-O-(3,5,6-trichloro-2-pyridyl)phosphorothioate)	new chemical, not derived
7440-47-3	Chromium	insufficient data
N090	Chromium compounds	insufficient data
N100	Copper compounds	insufficient data
8001-58-9	Creosote, coal tar	new chemical, not derived
1319-77-3	Cresol (mixed isomers)	insufficient data
4170303	Crotonaldehyde	new chemical, not derived
21725462	Cyanazine	new chemical, not derived
1134232	Cycloate	new chemical, not derived

Table 7-4. TRI Chemicals Without Toxicity Weights, in Alphabetical Order		
CAS Number	Chemical Name	Reason for no Toxicity Weight
108930	Cyclohexanol	new chemical, not derived
28057489	d-trans-Allethrin [d-trans-Chrysanthemic acid of d-allethrone]	new chemical, not derived
53404607	Dazomet sodium salt (2H-1,3,5-Thiadiazine-2-thione, tetrahydro-3,5-dimethyl-, ion(1-), sodium)	new chemical, not derived
533744	Dazomet (Tetrahydro-3,5-dimethyl-2H-1,3,5-thiadiazine-2-thione)	new chemical, not derived
13684565	Desmedipham	new chemical, not derived
39156-41-7	Diaminoanisole sulfate, 2,4-	low priority chemical
615-05-4	Diaminoanisole, 2,4-	low priority chemical
333415	Diazinon	new chemical, not derived
334-88-3	Diazomethane	low priority chemical
132-64-9	Dibenzofuran	insufficient data
124-73-2	Dibromotetrafluoromethane (Halon 24	new chemical, derived, not reviewed
99309	Dichloran (2,6-Dichloro-4-nitroaniline)	new chemical, not derived
136013791	Dichloro-1,1,2,3,3-pentafluoropropane (HCFC-225ea), 1,3-	new chemical, not derived
90454-18-5	Dichloro-1,1,2-trifluoroethane	insufficient data
812-04-4	Dichloro-1,2,2-trifluoroethane (HCFC-123b), 1,1-	new chemical, not derived
13474889	Dichloro-1,2,2,3,3-pentafluoropropane (HCFC-225cc), 1,1-	new chemical, not derived
1649087	Dichloro-1,1-difluoroethane (HCFC-132b), 1,2-	new chemical, not derived
128903219	Dichloro-1,1,1,3,3-pentafluoropropane (HCFC-225aa), 2,2-	new chemical, not derived
306-83-2	Dichloro-1,1,1-trifluoroethane, 2,2-	new chemical, not derived
111512562	Dichloro-1,2,3,3,3-pentafluoropropane (HCFC-225eb), 1,1-	new chemical, not derived
422560	Dichloro-1,1,1,2,2-pentafluoropropane (HCFC-225ca), 3,3-	new chemical, not derived
431867	Dichloro-1,1,3,3,3-pentafluoropropane (HCFC-225da), 1,2-	new chemical, not derived
354-23-4	Dichloro-1,1,2-trifluoroethane, 1,2-	new chemical, not derived
422480	Dichloro-1,1,1,2,3-pentafluoropropane (HCFC-225ba), 2,3-	new chemical, not derived
422446	Dichloro-1,1,2,3,3-pentafluoropropane (HCFC-225bb), 1,2-	new chemical, not derived
507551	Dichloro-1,1,2,2,3-pentafluoropropane (HCFC-225cb), 1,3-	new chemical, not derived

Table 7-4. TRI Chemicals Without Toxicity Weights, in Alphabetical Order		
CAS Number	Chemical Name	Reason for no Toxicity Weight
1717-00-6	Dichloro-1-fluoroethane, 1,1-	new chemical, not derived
612839	Dichlorobenzidine dihydrochloride, 3,3'-	new chemical, not derived
64969342	Dichlorobenzidine sulfate, 3,3'-	new chemical, not derived
75434	Dichlorofluoromethane (HCFC-21)	new chemical, not derived
127564925	Dichloropentafluoropropane	new chemical, not derived
97234	Dichlorophene (2,2'-Methylenebis(4-chlorophenol)	new chemical, not derived
78-88-6	Dichloropropene, 2,3-	new chemical, not derived
34077-87-7	Dichlorotrifluoroethane	new chemical, not derived
51338273	Diclofop methyl (2-[4-(2,4-Dichlorophenoxy)phenoxy]propanoicacid, methyl ester)	new chemical, not derived
115-32-2	Dicofol	low priority chemical
77736	Dicyclopentadiene	new chemical, not derived
1464-53-5	Diepoxybutane	low priority chemical
38727558	Diethatyl ethyl	new chemical, not derived
101906	Diglycidyl resorcinol ether	new chemical, not derived
94-58-6	Dihydrosafrole	new chemical, not derived
No CASRN	Diisocyantates	new chemical, not derived
111984099	Dimethoxybenzidine hydrochloride(o-Dianisidine hydrochloride), 3,3'-	new chemical, not derived
20325400	Dimethoxybenzidine dihydrochloride(o-Dianisidine dihydrochloride), 3,3'-	new chemical, not derived
131-11-3	Dimethyl phthalate	insufficient data
2524030	Dimethyl chlorothiophosphate	new chemical, not derived
57-14-7	Dimethyl Hydrazine, 1,1-	insufficient data
2300665	Dimethylamine dicamba	new chemical, not derived
124403	Dimethylamine	new chemical, not derived
60-11-7	Dimethylaminoazobenzene, 4-	low priority chemical
41766750	Dimethylbenzidine dihydrofluoride(o-Tolidine dihydrofluoride), 3,3'-	new chemical, not derived

Table 7-4. TRI Chemicals Without Toxicity Weights, in Alphabetical Order		
CAS Number	Chemical Name	Reason for no Toxicity Weight
612828	Dimethylbenzidine dihydrochloride(o-Tolidine dihydrochloride), 3,3'-	new chemical, not derived
79-44-7	Dimethylcarbamyl chloride	low priority chemical
25321-14-6	Dinitrotoluene (mixed isomers)	new chemical, not derived
39300453	Dinocap	new chemical, not derived
2164070	Dipotassium endothall (7-Oxabicyclo(2.2.1)heptane-2,3-dicarboxylic acid, dipotassium salt)	new chemical, not derived
136458	Dipropyl isocinchomeronate	new chemical, not derived
138932	Disodium cyanodithioimidocarbonate	new chemical, not derived
541537	Dithiobiuret, 2,4-	new chemical, not derived
120365	DP (Dichlorprop), 2,4-	new chemical, not derived
13194484	Ethoprop (Phosphorodithioic acid O-ethyl S,S-dipropyl ester)	new chemical, not derived
541-41-3	Ethyl chloroformate	low priority chemical
53404378	ethyl-4-methylpentyl ester, 2,4-D 2-	new chemical, not derived
N1000	Ethylenebisdithiocarbamic acid, salts and esters	insufficient data
151-56-4	Ethyleneimine (Aziridine)	low priority chemical
1928434	ethylhexyl ester, 2,4-D 2-	new chemical, not derived
75-34-3	Ethylidene dichloride	insufficient data
52857	Famphur	new chemical, not derived
60168889	Fenarimol (.alpha.-(2-Chlorophenyl)-.alpha.-4-chlorophenyl)-5-pyrimidinemethanol)	new chemical, not derived
13356086	Fenbutatin oxide (hexakis(2-methyl-2-phenylpropyl)distannoxane)	new chemical, not derived
66441234	Fenoxaprop ethyl (2-(4-((6-Chloro-2-benzoxazolylen)oxy)phenoxy)propanoicacid,ethyl ester)	new chemical, not derived
72490018	Fenoxycarb (2-(4-Phenoxyphenoxy)ethyl]carbamic acidethyl ester)	new chemical, not derived
55389	Fenthion (O,O-Dimethyl O-[3-methyl-4-(methylthio) phenyl] ester,phosphorothioic acid)	new chemical, not derived
14484641	Ferbam (Tris(dimethylcarbamodithioato-S,S')iron)	new chemical, not derived

Table 7-4. TRI Chemicals Without Toxicity Weights, in Alphabetical Order		
CAS Number	Chemical Name	Reason for no Toxicity Weight
69806504	Fluazifop butyl (2-[4-[[5-(Trifluoromethyl)-2-pyridinyl]oxy]-phenoxy]propanoic acid, butyl ester)	new chemical, not derived
51218	Fluorouracil (5-Fluorouracil)	new chemical, not derived
N230	Glycol Ethers	insufficient data
1335-87-1	Hexachloronaphthalene	low priority chemical
680-31-9	Hexamethylphosphoramide	low priority chemical
10034-93-2	Hydrazine sulfate	insufficient data
7664-39-3	Hydrogen fluoride	insufficient data
55406536	Iodo-2-propynyl butylcarbamate, 3-	new chemical, not derived
13463406	Iron pentacarbonyl	new chemical, not derived
465736	Isodrin	new chemical, not derived
25311711	Isofenphos (2-[[Ethoxyl[(1-methylethyl)amino]phosphinothioyl]oxy]benzoic acid 1-methylethyl ester)	new chemical, not derived
94111	isopropyl ester, 2,4-D	new chemical, not derived
120-58-1	Isosafrole	new chemical, not derived
554132	Lithium carbonate	new chemical, not derived
149304	Mercaptobenzothiazole (MBT), 2-	new chemical, not derived
137428	Metham sodium (Sodiummethyldithiocarbamate)	new chemical, not derived
20354261	Methazole (2-(3,4-Dichlorophenyl)-4-methyl-1,2,4-oxadiazolidine-3,5-dione)	new chemical, not derived
2032657	Methiocarb	new chemical, not derived
3653483	Methoxone sodium salt ((4-Chloro-2-methylphenoxy) acetate sodium salt)	new chemical, not derived
556616	Methyl isothiocyanate	new chemical, not derived
60-34-4	Methyl hydrazine	insufficient data
79-22-1	Methyl chlorocarbonate	new chemical, not derived
101-77-9	Methylenedianiline, 4,4'-	insufficient data
75865	Methyllactonitrile, 2-	new chemical, not derived

Table 7-4. TRI Chemicals Without Toxicity Weights, in Alphabetical Order		
CAS Number	Chemical Name	Reason for no Toxicity Weight
109-06-8	Methylpyridine, 2-	new chemical, not derived
9006422	Metiram	new chemical, not derived
7786347	Mevinphos	new chemical, not derived
150685	Monuron	new chemical, not derived
505-60-2	Mustard gas	low priority chemical
872504	N-Methyl-2-pyrrolidone	new chemical, not derived
924425	N-Methylolacrylamide	new chemical, not derived
684-93-5	N-Nitroso-N-methylurea	low priority chemical
4549-40-0	N-Nitrosomethylvinylamine	low priority chemical
59-89-2	N-Nitrosomorpholine	low priority chemical
16543-55-8	N-Nitrosonornicotine	low priority chemical
100-75-4	N-Nitrosopiperidine	low priority chemical
142596	Nabam	new chemical, not derived
N495	Nickel compounds	insufficient data
7440-02-0	Nickel	insufficient data
No CASRN	Nicotine and salts	new chemical, not derived
1929824	Nitrapyrin (2-Chloro-6-(trichloromethyl)pyridine)	new chemical, not derived
92-93-3	Nitrobiphenyl, 4-	low priority chemical
1836-75-5	Nitrofen	low priority chemical
51-75-2	Nitrogen mustard	low priority chemical
88-75-5	Nitrophenol, 2-	insufficient data
134-29-2	o-Anisidine hydrochloride	low priority chemical
2234-13-1	Octachloronaphtahlene	low priority chemical
20816-12-0	Osmium tetroxide	low priority chemical
301122	Oxydemeton methyl (S-(2-(Ethylsulfinyl)ethyl) O,O-dimethylester phosphorothioic acid)	new chemical, not derived
10028156	Ozone	new chemical, not derived
104-94-9	p-Anisidine	low priority chemical

Table 7-4. TRI Chemicals Without Toxicity Weights, in Alphabetical Order		
CAS Number	Chemical Name	Reason for no Toxicity Weight
95692	p-Chloro-o-toluidine	new chemical, not derived
104121	p-Chlorophenyl isocyanate	new chemical, not derived
100016	p-Nitroaniline	new chemical, not derived
156-10-5	p-Nitrosodiphenylamine	low priority chemical
123-67-7	Paraldehyde	new chemical, not derived
1114712	Pebulate (Butylethylcarbamothioic acidS-propyl ester)	new chemical, not derived
76-01-7	Pentachloroethane	new chemical, not derived
57330	Pentobarbital sodium	new chemical, not derived
594423	Perchloromethyl mercaptan	new chemical, not derived
85018	Phenanthrene	new chemical, not derived
26002802	Phenothrin (2,2-Dimethyl-3-(2-methyl-1-propenyl) cyclopropanecarboxylic acid(3-phenoxyphenyl)methyl ester)	new chemical, not derived
624180	Phenylenediamine dihydrochloride, 1,4-	new chemical, not derived
615281	Phenylenediamine dihydrochloride, 1,2-	new chemical, not derived
95545	Phenylenediamine, 1,2-	new chemical, not derived
57410	Phenytoin	new chemical, not derived
75-44-5	Phosgene	low priority chemical
51036	Piperonyl butoxide	new chemical, not derived
No CASRN	Polychlorinated alkanes	new chemical, not derived
No CASRN	Polycyclic aromatic compounds	new chemical, not derived
7758012	Potassium bromate	new chemical, not derived
128030	Potassium dimethyldithiocarbamate	new chemical, not derived
137417	Potassium N-methyldithiocarbamate	new chemical, not derived
41198087	Profenofos (O-(4-Bromo-2-chlorophenyl)-O-ethyl-S-propyl phosphorothioate)	new chemical, not derived
1120-71-4	Propane sultone	new chemical, not derived
31218834	Propetamphos (3-[(Ethylamino)methoxyphosphinothioyl]oxy]-2-butenoic acid, 1-methylethylester)	new chemical, not derived
123-38-6	Propionaldehyde	insufficient data

Table 7-4. TRI Chemicals Without Toxicity Weights, in Alphabetical Order		
CAS Number	Chemical Name	Reason for no Toxicity Weight
1320189	propylene glycol butyl etherester, 2,4-D	new chemical, not derived
106-51-4	Quinone	low priority chemical
81-07-2	Saccharin (manufacturing)	low priority chemical
94-59-7	Safrole	low priority chemical
78-92-2	sec-Butyl alcohol	insufficient data
2702729	sodium salt, 2,4-D	new chemical, not derived
1982690	Sodium dicamba (3,6-Dichloro-2-methoxybenzoic acid, sodium salt)	new chemical, not derived
131522	Sodium pentachlorophenate	new chemical, not derived
128041	Sodium dimethyldithiocarbamate	new chemical, not derived
7632000	Sodium nitrite	new chemical, not derived
132274	Sodium o-phenylphenoxide	new chemical, not derived
96-09-3	Styrene oxide	low priority chemical
2699798	Sulfuryl fluoride (Vikane)	new chemical, not derived
35400432	Sulprofos (O-Ethyl O-[4-(methylthio)phenyl]phosphorodithioicacid S propyl ester)	new chemical, not derived
3383968	Temephos	new chemical, not derived
75-65-0	tert-Butyl Alcohol	insufficient data
354143	Tetrachloro-1-fluoroethane(HCFC-121), 1,1,2,2-	new chemical, not derived
354110	Tetrachloro-2-fluoroethane(HCFC-121a), 1,1,1,2-	new chemical, not derived
64755	Tetracycline hydrochloride	new chemical, not derived
7696120	Tetramethrin (2,2-Dimethyl-3-(2-methyl-1-propenyl) cyclopropanecarboxylicacid (1,3,4,5,6,7-hexahydro-1,3-dioxo-2	new chemical, not derived
7440-28-0	Thallium	insufficient data
N760	Thallium comounds	insufficient data
148798	Thiabendazole (2-(4-Thiazolyl)-1H-benzimidazole)	new chemical, not derived
62-55-5	Thioacetamide	low priority chemical
139-65-1	Thiodianiline, 4,4'-	low priority chemical

Table 7-4. TRI Chemicals Without Toxicity Weights, in Alphabetical Order		
CAS Number	Chemical Name	Reason for no Toxicity Weight
59669260	Thiodicarb	new chemical, not derived
23564069	Thiophanate ethyl ([1,2-Phenylenebis(iminocarbonothioyl)]biscarbamic acid diethyl ester)	new chemical, not derived
79196	Thiosemicarbazide	new chemical, not derived
10061026	trans-1,3-Dichloropropene	new chemical, not derived
110576	trans-1,4-Dichloro-2-butene	new chemical, not derived
68-76-8	Triaziquone	low priority chemical
2155706	Tributyltin methacrylate	new chemical, not derived
1983104	Tributyltin fluoride	new chemical, not derived
52-68-6	Trichlorfon	new chemical, not derived
76028	Trichloroacetyl chloride	new chemical, not derived
79-01-6	Trichloroethylene	insufficient data
57213691	Triclopyr triethylammonium salt	new chemical, not derived
26644462	Triforine (N,N'-[1,4-Piperazinediylbis-2,2,2-trichloroethylidene)]bisformamide)	new chemical, not derived
2655154	Trimethylphenyl methylcarbamate, 2,3,5-	new chemical, not derived
76879	Triphenyltin hydroxide	new chemical, not derived
639587	Triphenyltin chloride	new chemical, not derived
126-72-7	Tris(2,3-dibromopropyl)phosphate	new chemical, not derived
72-57-1	Trypan blue	new chemical, not derived
51-79-6	Urethane (Ethyl Carbamate)	new chemical, not derived
87-62-7	Xylidine, 2,6-	low priority chemical
N982	Zinc Compounds	insufficient data

7.5. Sorted Compilation of Toxicity Weights for All TRI Chemicals

Table 7-5 contains all chemicals and chemical categories on the 1995 TRI List, by sorted toxicity weight category. Chemicals without toxicity weights are listed alphabetically below weighted chemicals.

Table 7-5. Toxicity Weights for all TRI Chemicals, by Toxicity Weight Category

CAS Number	Chemical Name	Toxicity Weight		Source
		Inhalation	Oral	
Chemicals With One or More Toxicity Weights of 1,000,000				
92-87-5	Benzidine	1000000	1000000	IRIS
542-88-1	Bis(chloromethyl)ether	1000000	1000000	IRIS
106-93-4	Dibromoethane, 1,2-	10000	1000000	IRIS
77-78-1	Dimethyl sulfate	1000000	1000000*	interim derived
759-73-9	N-Nitroso-N-ethylurea	1000000*	1000000	HEAST
55-18-5	N-Nitrosodiethylamine	1000000	1000000	IRIS
62-75-9	N-Nitrosodimethylamine	100000	1000000	IRIS
75-55-8	Propyleneimine	1000000*	1000000	final derived
1314-20-1	Thorium dioxide	10000	1000000	final derived
Chemicals With One or More Toxicity Weights of 100,000				
107-02-8	Acrolein	100000	100000*	IRIS
309-00-2	Aldrin	100000	100000	IRIS
319-84-6	alpha-Hexachlorocyclohexane	100000	100000	IRIS
7429-90-5	Aluminum (fume or dust)	100000		interim derived
7440-38-2	Arsenic	100000	10000	IRIS
N020	Arsenic compounds	100000	10000	IRIS
98-07-7	Benzotrichloride	100000*	100000	IRIS
N050	Beryllium compounds	100000	10000	IRIS
7440-41-7	Beryllium	100000	10000	IRIS
56-35-9	Bis(tributyltin) oxide	100000*	100000	IRIS
2602-46-2	C.I. Direct Blue 6	100000*	100000	HEAST

Table 7-5. Toxicity Weights for all TRI Chemicals, by Toxicity Weight Category				
CAS Number	Chemical Name	Toxicity Weight		Source
		Inhalation	Oral	
1937-37-7	C.I. Direct Black 38	100000*	100000	HEAST
16071-86-6	C.I. Direct Brown 95	100000*	100000	HEAST
7440-43-9	Cadmium	100000	10000	IRIS
N078	Cadmium compounds	100000	10000	IRIS
532-27-4	Chloroacetophenone, 2-	100000	100000*	IRIS
7440-48-4	Cobalt	100000	100000*	interim derived
N096	Cobalt compounds	100000	100000*	interim derived
25376-45-8	Diaminotoluene (mixed isomers)	100000*	100000	interim derived
764-41-0	Dichloro-2-butene, 1,4-	100000	100000*	HEAST
119-93-7	Dimethylbenzidine, 3,3'-	100000*	100000	HEAST
302-01-2	Hydrazine	100000	10000	IRIS
78-84-2	Isobutyraldehyde	100000	100000*	interim derived
N420	Lead compounds	100000	100000	interim derived
7439-92-1	Lead	100000	100000	interim derived
109-77-3	Malonitrile	100000*	100000	HEAST
7439-96-5	Manganese	100000	10	IRIS
N450	Manganese compounds	100000	10	IRIS
150-50-5	Merphos	100000*	100000	IRIS
624-83-9	Methyl isocyanate	100000	100000*	final derived
924-16-3	N-Nitrosodi-n-butylamine	100000	100000	IRIS
621-64-7	N-Nitrosodi-n-propylamine	100000*	100000	IRIS
7723-14-0	Phosphorus (yellow or white)	100000*	100000	IRIS
N575	Polybrominated Biphenyls (PBBs)	100000*	100000	HEAST
1336-36-3	Polychlorinated biphenyls	1000	100000	IRIS
62-74-8	Sodium fluoroacetate	100000*	100000	IRIS
7550-45-0	Titanium tetrachloride	100000	100000*	interim derived

Table 7-5. Toxicity Weights for all TRI Chemicals, by Toxicity Weight Category				
CAS Number	Chemical Name	Toxicity Weight		Source
		Inhalation	Oral	
584-84-9	Toluene-2,4-diisocyanate	100000	100	final derived
91-08-7	Toluene-2,6-Diisocyanate	100000	100	final derived
26471-62-5	Toluenediisocyanate	100000	100	IRIS
78-48-8	Tributyltrithiophosphate (DEF), S,S,S-	100000*	100000	IRIS
Chemicals With One or More Toxicity Weights of 10,000				
79-06-1	Acrylamide	10000	10000	IRIS
79-10-7	Acrylic acid	10000	10	IRIS
107-13-1	Acrylonitrile	1000	10000	IRIS
107-05-1	Allyl chloride	10000	10000*	IRIS
20859-73-8	Aluminum phosphide	10000*	10000	IRIS
62-53-3	Aniline	10000	100	IRIS
7440-36-0	Antimony	10000*	10000	IRIS
N010	Antimony compounds	10000*	10000	IRIS
111-44-4	Bis(2-chloroethyl)ether	10000	10000	IRIS
106-99-0	Butadiene, 1,3-	10000	10000*	IRIS
141-32-2	Butyl acrylate	10	10000	interim derived
57-74-9	Chlordane	10000	10000	IRIS
10049-04-4	Chlorine dioxide	10000	10000*	IRIS
95-80-7	Diaminotoluene, 2,4-	10000*	10000	HEAST
96-12-8	Dibromo-3-chloropropane (DBCP), 1,2-	10000	10000*	IRIS
542-75-6	Dichloropropylene, 1,3-	100	10000	IRIS
62-73-7	Dichlorvos	10000	10000	IRIS
64-67-5	Diethyl sulfate	10000*	10000	final derived
60-51-5	Dimethoate	10000*	10000	IRIS
534-52-1	Dinitro-o-cresol, 4,6-	10000	10000	interim derived
606-20-2	Dinitrotoluene, 2,6-	10000*	10000	IRIS

Table 7-5. Toxicity Weights for all TRI Chemicals, by Toxicity Weight Category				
CAS Number	Chemical Name	Toxicity Weight		Source
		Inhalation	Oral	
122-66-7	Diphenylhydrazine, 1,2-	10000	10000	IRIS
106-89-8	Epichlorohydrin	10000	100	IRIS
96-45-7	Ethylene thiourea	10000*	10000	IRIS
75-21-8	Ethylene oxide	10000*	10000	HEAST
76-44-8	Heptachlor	10000	10000	IRIS
118-74-1	Hexachlorobenzene	10000	10000	IRIS
70-30-4	Hexachlorophene	10000*	10000	IRIS
67485-29-4	Hydramethylnon (Tetrahydro-5,5-di-methyl-2(1H)- pyrimidinone[3-[4-(trifluoromethyl)phenyl]-1-[2-[4-(trifluoromet	10000*	10000	IRIS
58-89-9	Lindane	10000*	10000	IRIS
99-65-0	m-Dinitrobenzene	10000*	10000	IRIS
7439-97-6	Mercury	10000	10000*	IRIS
N458	Mercury compounds	10000	10000*	IRIS
126-98-7	Methacryonitrile	10000*	10000	IRIS
94-74-6	Methoxone ((4-Chloro-2-methylphenoxy)acetic acid) (MCPA)	10000*	10000	IRIS
298-00-0	Methyl parathion	10000*	10000	IRIS
1313-27-5	Molybdenum trioxide	10000	1000	interim derived
98-95-3	Nitrobenzene	10000*	10000	IRIS
55-63-0	Nitroglycerin	10000*	10000	interim derived
90-04-0	o-Anisidine	10000	1000	interim derived
528-29-0	o-Dinitrobenzene	10000*	10000	HEAST
100-25-4	p-Dinitrobenzene	10000*	10000	HEAST
7803-51-2	Phosphine	10000	10000	IRIS
88-89-1	Picric acid	10000	10000	final derived
91-22-5	Quinoline	10000*	10000	HEAST
No CASRNb	Strychnine and salts	10000*	10000	IRIS

Table 7-5. Toxicity Weights for all TRI Chemicals, by Toxicity Weight Category				
CAS Number	Chemical Name	Toxicity Weight		Source
		Inhalation	Oral	
7664-93-9	Sulfuric acid	10,000	1	final derived
62-56-6	Thiourea	10000*	10000	final derived
8001-35-2	Toxaphene	10000	10000	IRIS
75-01-4	Vinyl chloride	10000*	10000	HEAST
81-81-2	Warfarin and salts	10000*	10000	IRIS
Chemicals With One or More Toxicity Weights of 1,000				
30560-19-1	Acephate (Acetylphosphoramidothioic acid O,S-dimethyl ester)	1000*	1000	IRIS
75-07-0	Acetaldehyde	1000	1000*	IRIS
116-06-3	Aldicarb	1000*	1000	IRIS
107-18-6	Allyl alcohol	1000*	1000	IRIS
33089-61-1	Amitraz	1000*	1000	IRIS
1332-21-4	Asbestos (friable)	1000	n/a	IRIS
100-44-7	Benzyl chloride	1000*	1000	IRIS
74-83-9	Bromomethane (Methyl Bromide)	1000	1000	IRIS
156-62-7	Calcium cyanamide	1000*	1000	final derived
1563-66-2	Carbofuran	1000*	1000	IRIS
56-23-5	Carbon tetrachloride	1000	1000	IRIS
79-11-8	Chloroacetic acid	1000*	1000	HEAST
67-66-3	Chloroform	1000	100	IRIS
80-15-9	Cumene hydroperoxide	1000	1000*	final derived
135-20-6	Cupferron	1000*	1000	final derived
68085-85-8	Cyhalothrin (3-(2-Chloro-3,3,3-trifluoro-1-propenyl)-2,2-Dimethylcyclopropanecarboxylic acidcyano(3-phenoxypheny	1000*	1000	IRIS
2303-16-4	Diallate	1000*	1000	HEAST
101-80-4	Diaminodiphenylether, 4,4'-	1000*	1000	final derived
91-94-1	Dichlorobenzidine, 3,3'-	1000*	1000	IRIS

Table 7-5. Toxicity Weights for all TRI Chemicals, by Toxicity Weight Category				
CAS Number	Chemical Name	Toxicity Weight		Source
		Inhalation	Oral	
75-27-4	Dichlorobromomethane	1000*	1000	IRIS
107-06-2	Dichloroethane, 1,2-	1000	1000	IRIS
120-83-2	Dichlorophenol, 2,4-	1000*	1000	IRIS
78-87-5	Dichloropropane, 1,2-	1000	1000*	IRIS
576-26-1	Dimethylphenol, 2,6-	1000*	1000	IRIS
88-85-7	Dinitrobutyl phenol (Dinoseb)	1000*	1000	IRIS
51-28-5	Dinitrophenol, 2,4-	1000*	1000	IRIS
121-14-2	Dinitrotoluene, 2,4-	1000*	1000	IRIS
330-54-1	Diuron	1000*	1000	IRIS
2439-10-3	Dodine (Dodecylguanidine monoacetate)	1000*	1000	IRIS
67-72-1	Hexachloroethane	10	1000	IRIS
74-90-8	Hydrogen cyanide	1000	100	IRIS
77501-63-4	Lactofen (5-(2-Chloro-4-(trifluoromethyl)phenoxy)-2-nitro-2-ethoxy-1-methyl-2-oxoethyl ester)	1000*	1000	IRIS
330-55-2	Linuron	1000*	1000	IRIS
12427-38-2	Maneb	1000*	1000	IRIS
93-65-2	Mecoprop	1000*	1000	IRIS
72-43-5	Methoxychlor	1000*	1000	IRIS
74-88-4	Methyl iodide	1000*	1000	interim derived
101-14-4	Methylenebis(2-chloroaniline), 4,4'-	1000	1000	HEAST
90-94-8	Michlers Ketone	1000*	1000	final derived
2212-67-1	Molinate (1H-Azepine-1 carbothioicacid, hexahydro-S-ethyl ester)	1000*	1000	IRIS
121-69-7	N,N-Dimethylaniline	1000*	1000	IRIS
300-76-5	Naled	1000*	1000	IRIS
100-02-7	Nitrophenol, 4-	1000	1000	final derived
95-53-4	o-Toluidine	1000*	1000	HEAST

Table 7-5. Toxicity Weights for all TRI Chemicals, by Toxicity Weight Category				
CAS Number	Chemical Name	Toxicity Weight		Source
		Inhalation	Oral	
636-21-5	o-Toluidine hydrochloride	1000*	1000	HEAST
19666-30-9	Oxydiazon (3-[2,4-Dichloro-5-(1-methylethoxy)phenyl]-5-(1,1-dimethylethyl)-1,3,4-oxadiazol-2(3H)-one)	1000*	1000	IRIS
42874-03-3	Oxyfluorfen	1000*	1000	IRIS
106-47-8	p-Chloroaniline	1000*	1000	IRIS
120-71-8	p-Cresidine	1000*	1000	interim derived
106-44-5	p-Cresol	1000*	1000	HEAST
1910-42-5	Paraquat dichloride	1000*	1000	IRIS
87-86-5	Pentachlorophenol	1000*	1000	IRIS
79-21-0	Peracetic acid	1000	1000*	interim derived
7664-38-2	Phosphoric acid	1000	1	IRIS; final derived
7287-19-6	Prometryn (N,N'-Bis(1-methylethyl)-6-methylthio-1,3,5-triazine-2,4-diamine)	1000*	1000	IRIS
709-98-8	Propanil (N-(3,4-Dichlorophenyl)propanamide)	1000*	1000	IRIS
107-19-7	Propargyl alcohol	1000*	1000	IRIS
114-26-1	Propoxur	1000*	1000	IRIS
75-56-9	Propylene oxide	100	1000	IRIS
110-86-1	Pyridine	1000*	1000	IRIS
82-68-8	Quintozene	1000*	1000	IRIS
7782-49-2	Selenium	1000*	1000	IRIS
N725	Selenium compounds	1000*	1000	IRIS
7440-22-4	Silver	1000*	1000	IRIS
N740	Silver compounds	1000*	1000	IRIS
122-34-9	Simazine	1000*	1000	IRIS
26628-22-8	Sodium azide	1000*	1000	IRIS
137-26-8	Thiram	1000*	1000	IRIS
79-00-5	Trichloroethane, 1,1,2-	100	1000	IRIS

Table 7-5. Toxicity Weights for all TRI Chemicals, by Toxicity Weight Category				
CAS Number	Chemical Name	Toxicity Weight		Source
		Inhalation	Oral	
121-44-8	Triethylamine	1000	1000*	IRIS
95-63-6	Trimethylbenzene, 1,2,4	1000	1000	final derived
593-60-2	Vinyl bromide	1000	1000*	IRIS
75-35-4	Vinylidene chloride	100	1000	IRIS
Chemicals With One or More Toxicity Weights of 100				
94-82-6	2,4-DB	100*	100	IRIS
94-75-7	Acetic acid (2,4-D((2,4-dichlorophenoxy)))	100*	100	IRIS
75-05-8	Acetonitrile	100*	100	IRIS
62476-59-9	Acifluorfen, sodium salt [5-(2-Chloro-4-(triflouromethyl)phenoxy)-2-nitrobenzoic acid, sodium salt]	100*	100	IRIS
15972-60-8	Alachlor	100*	100	IRIS
834-12-8	Ametryn (N-Ethyl-N'-(1-methylethyl)-6-(methylthio)-1,3,5,-triazine- 2,4 diamine)	100*	100	IRIS
7664-41-7	Ammonia	100	100*	IRIS
1912-24-9	Atrazine (6-Chloro-N-ethyl-N'-(1-methylethyl)-1,3,5,-triazine-2,4-diamine)	100*	100	IRIS
17804-35-2	Benomyl	100*	100	IRIS
71-43-2	Benzene	100	100	IRIS
82657-04-3	Bifenthrin	100*	100	IRIS
92-52-4	Biphenyl	100*	100	IRIS
75-25-2	Bromoform (Tribromomethane)	10	100	IRIS
1689-99-2	Bromoxynil octanoate (Octanoic acid,2,6-dibromo-4-cyanophenyl ester)	100*	100	IRIS
1689-84-5	Bromoxynil (3,5-Dibromo-4-hydroxybenzonitrile)	100*	100	IRIS
106-88-7	Butylene oxide, 1,2-	100	100*	IRIS
463-58-1	Carbonyl sulfide	100	100*	interim derived
120-80-9	Catechol	100	100	interim derived

Table 7-5. Toxicity Weights for all TRI Chemicals, by Toxicity Weight Category				
CAS Number	Chemical Name	Toxicity Weight		Source
		Inhalation	Oral	
133-90-4	Chloramben	100*	100	IRIS
90982-32-4	Chlorimuron ethyl (Ethyl-2-[[[(4-chloro-6-methoxyprimidin-2-yl)-carbonyl]-amino]sulfonyl]benzoate)	100*	100	IRIS
108-90-7	Chlorobenzene	100*	100	IRIS
510-15-6	Chlorobenzilate	100*	100	IRIS
1897-45-6	Chlorothalonil	100*	100	IRIS
64902-72-3	Chlorsulfuron (2-Chloro-N-[[(4-methoxy-6-methyl-1,3,5-triazin-2-yl)amino]carbonyl]benzenesulfonamide)	100*	100	IRIS
98-82-8	Cumene	100*	100	IRIS
N106	Cyanide compounds	100*	100	IRIS
68359-37-5	Cyfluthrin (3-(2,2-Dichloroethenyl)-2,2-dimethylcyclopropanecarboxylic acid,cyano(4-fluoro-3-phenoxyphenyl)methy	100*	100	IRIS
1163-19-5	Decabromodiphenyl oxide	100*	100	IRIS
117-81-7	Di(2-ethylhexyl) phthalate	100*	100	IRIS
1918-00-9	Dicamba (3,6-Dichloro-2-methyoxybenzoicacid)	100*	100	IRIS
541-73-1	Dichlorobenzene, 1,3-	10	100	interim derived
25321-22-6	Dichlorobenzene (mixed isomers)	10	100	interim derived
540-59-0	Dichloroethylene, 1,2-	100*	100	HEAST
75-09-2	Dichloromethane	10	100	IRIS
111-42-2	Diethanolamine	100*	100	interim derived
35367-38-5	Diflubenzuron	100*	100	IRIS
55290-64-7	Dimethipin (2,3,-Dihydro-5,6-dimethyl-1,4-dithiin 1,1,4,4-tetraoxide)	100*	100	IRIS
119-90-4	Dimethoxybenzidine, 3,3'-	100*	100	HEAST
105-67-9	Dimethylphenol, 2,4-	100*	100	IRIS
123-91-1	Dioxane, 1,4-	100*	100	IRIS

Table 7-5. Toxicity Weights for all TRI Chemicals, by Toxicity Weight Category				
CAS Number	Chemical Name	Toxicity Weight		Source
		Inhalation	Oral	
957-51-7	Diphenamid	100*	100	IRIS
122-39-4	Diphenylamine	100*	100	IRIS
759-94-4	Ethyl dipropylthiocarbamate (EPTC)	100*	100	IRIS
140-88-5	Ethyl acrylate	100*	100	HEAST
39515-41-8	Fenpropathrin (2,2,3,3-Tetramethylcyclopropane carboxylicacid cyano(3-phenoxyphenyl)methylester)	100*	100	IRIS
51630-58-1	Fenvalerate (4-Chloro-alpha-(1-methylethyl)benzeneacetic acid cyano(3-phenoxyphenyl)methyl ester)	100*	100	IRIS
2164-17-2	Fluometuron	100*	100	IRIS
69409-94-5	Fluvalinate (N-[2-Chloro-4-(trifluoromethyl)phenyl]-DL-valine(+)-cyano (3-phenoxyphenyl)methyl ester)	100*	100	IRIS
72178-02-0	Fomesafen (5-(2-Chloro-4-(trifluoromethyl)phenoxy)-Nmethylsulfonyl)-2-nitrobenzamide)	100*	100	IRIS
50-00-0	Formaldehyde	100	10	IRIS
87-68-3	Hexachloro-1,3-butadiene	100	100	IRIS
77-47-4	Hexachlorocyclopentadiene	100*	100	IRIS
51235-04-2	Hexazinone	100*	100	IRIS
7647-01-0	Hydrochloric acid	100	100*	IRIS
123-31-9	Hydroquinone	100*	100	HEAST
35554-44-0	Imazalil (1-[2-(2,4-Dichlorophenyl)-2-(2-propenyloxy)ethyl]-1H-imidazole)	100*	100	IRIS
80-05-7	Isopropylidenediphenol, 4,4'-	100*	100	IRIS
108-39-4	m-Cresol	100*	100	IRIS
121-75-5	Malathion	100*	100	IRIS
109-86-4	Methoxyethanol, 2-	100	100*	IRIS
96-33-3	Methyl acrylate	100*	100	HEAST

Table 7-5. Toxicity Weights for all TRI Chemicals, by Toxicity Weight Category				
CAS Number	Chemical Name	Toxicity Weight		Source
		Inhalation	Oral	
74-95-3	Methylene bromide	100*	100	HEAST
101-61-1	Methylenebis(N,N-dimethylbenzenamine), 4,4'-	100*	100	IRIS
21087-64-9	Metribuzin	100*	100	IRIS
88671-89-0	Myclobutanil (.alpha.-Butyl-.alpha.-(4-chlorophenyl)-1H-1,2,4-triazole-1-propanenitrile)	100*	100	IRIS
68-12-2	N,N-Dimethylformamide	100	100*	IRIS
7697-37-2	Nitric acid	100	100*	final derived
139-13-9	Nitrilotriacetic acid	100*	100	interim derived
99-59-2	Nitro-o-anisidine, 5-	100*	100	HEAST
99-55-8	Nitro-o-toluidine	100*	100	HEAST
79-46-9	Nitropropane, 2-	100	100*	IRIS
27314-13-2	Norflurazon (4-Chloro-5-(methylamino)-2-[3-(trifluoromethyl)phenyl]-3(2H)-pyridazinone)	100*	100	IRIS
95-48-7	o-Cresol	100*	100	IRIS
19044-88-3	Oryzalin (4-(Dipropylamino)-3,5-dinitrobenzenesulfonamide)	100*	100	IRIS
56-38-2	Parathion	100*	100	HEAST
40487-42-1	Pendimethalin (N-(1-Ethylpropyl)-3,4-dimethyl-2,6-dinitrobenzenamine)	100*	100	IRIS
52645-53-1	Permethrin (3-(2,2-Dichloroethenyl)-2,2-dimethylcyclopropanecarboxylic acid,(3-phenoxyphenyl)methyl ester)	100*	100	IRIS
108-45-2	Phenylenediamine, 1,3-	100*	100	IRIS
29232-93-7	Pirimiphos methyl (O-(2-(Diethylamino)-6-methyl-4- pyrimidinyl)-O,O-dimethylphosphorothioate)	100*	100	IRIS
1918-16-7	Propachlor (2-Chloro-N-(1-methylethyl)-N-phenylacetamide)	100*	100	IRIS
2312-35-8	Propargite	100*	100	IRIS

Table 7-5. Toxicity Weights for all TRI Chemicals, by Toxicity Weight Category				
CAS Number	Chemical Name	Toxicity Weight		Source
		Inhalation	Oral	
60207-90-1	Propiconazole (1-[2-(2,4-Dichlorophenyl)-4-propyl-1,3-dioxolan-2-yl]-methyl-1H-1,2,4,-triazole)	100*	100	IRIS
76578-14-8	Quizalofop-ethyl (2-[4-[(6-Chloro-2-quinoxalinyl)oxy]phenoxy] propanoicacid ethyl ester)	100*	100	IRIS
10453-86-8	Resmethrin ([5-(Phenylmethyl)-3-furanyl]methyl 2,2-dimethyl-3-(2-methyl-1-propenyl)cyclopropanecarboxylate])	100*	100	IRIS
5902-51-2	Terbacil (5-Chloro-3-(1,1-dimethylethyl)-6-methyl- 2,4 (1H,3H)-pyrimidinedione)	100*	100	IRIS
630-20-6	Tetrachloroethane, 1,1,1,2-	10	100	IRIS
79-34-5	Tetrachloroethane, 1,1,2,2-	100	100	IRIS
127-18-4	Tetrachloroethylene (Perchlorethyle	100*	100	IRIS
961-11-5	Tetrachlorvinphos	100*	100	IRIS
28249-77-6	Thiobencarb (Carbamic acid, diethylthio-, S-(p-chlorobenzyl))	100*	100	IRIS
43121-43-3	Triadimefon (1-(4-Chlorophenoxy)-3,3-dimethyl-1-(1H-1,2,4-triazol-1-yl)-2-butanone)	100*	100	IRIS
2303-17-5	Triallate	100*	100	IRIS
101200-48-0	Tribenuron methyl (2-(4-Methoxy-6-methyl-1,3,5-triazin-2-yl)-methylamino)carbonyl)amino)sulfonyl)-,methyl ester)	100*	100	IRIS
120-82-1	Trichlorobenzene, 1,2,4-	100*	100	IRIS
88-06-2	Trichlorophenol, 2,4,6-	100	100	IRIS
96-18-4	Trichloropropane, 1,2,3-	100*	100	IRIS
1582-09-8	Trifluralin	100*	100	IRIS
7440-62-2	Vanadium (fume or dust)	100*	100	HEAST
50471-44-8	Vinclozolin (3-(3,5-Dichlorophenyl)-5-ethenyl-5-methyl-2,4-oxazolidinedione)	100*	100	IRIS
12122-67-7	Zineb	100*	100	IRIS

Table 7-5. Toxicity Weights for all TRI Chemicals, by Toxicity Weight Category				
CAS Number	Chemical Name	Toxicity Weight		Source
		Inhalation	Oral	
Chemicals With One or More Toxicity Weights of 10				
98-86-2	Acetophenone	10*	10	IRIS
120-12-7	Anthracene	10*	10	IRIS
N040	Barium compounds	10*	10	IRIS
7440-39-3	Barium	10*	10	IRIS
1861-40-1	Benfluralin (N-Butyl-N-ethyl-2,6-dinitro-4-(trifluoromethyl)benzenamine)	10*	10	IRIS
133-06-2	Captan	10*	10	IRIS
63-25-2	Carbaryl	10*	10	IRIS
75-15-0	Carbon disulfide	10	10	IRIS
5234-68-4	Carboxin (5,6-Dihydro-2-methyl-N-phenyl-1,4-oxathiin-3-carboxamide)	10*	10	IRIS
75-69-4	CFC-11	10*	10	IRIS
75-71-8	CFC-12	10*	10	IRIS
7782-50-5	Chlorine	10*	10	IRIS
74-87-3	Chloromethane	10	10	HEAST
84-74-2	Dibutyl phthalate	10*	10	IRIS
106-46-7	Dichlorobenzene, 1,4-	10	10*	IRIS
95-50-1	Dichlorobenzene, 1,2	10*	10	IRIS
110-80-5	Ethoxyethanol, 2-	10	10*	IRIS
100-41-4	Ethylbenzene	10	10	IRIS
7782-41-4	Fluorine	10*	10	IRIS
133-07-3	Folpet	10*	10	IRIS
108-31-6	Maleic anhydride	10*	10	IRIS
67-56-1	Methanol	10*	10	IRIS
80-62-6	Methyl methacrylate	10*	10	HEAST
78-93-3	Methyl ethyl ketone	10	1	IRIS

Table 7-5. Toxicity Weights for all TRI Chemicals, by Toxicity Weight Category				
CAS Number	Chemical Name	Toxicity Weight		Source
		Inhalation	Oral	
108-10-1	Methyl isobutyl ketone	10*	10	HEAST
71-36-3	n-Butyl alcohol	10*	10	IRIS
110-54-3	n-Hexane	10	10*	IRIS
86-30-6	N-Nitrosodiphenylamine	10*	10	IRIS
106-50-3	p-Phenylenediamine	10*	10	HEAST
1918-02-1	Picloram	10*	10	IRIS
23950-58-5	Pronamide	10*	10	IRIS
74051-80-2	Sethoxydim (2-[1-(Ethoxyimino)butyl]-5-[2-(ethylthio)propyl]-3-hydroxyl-2-cyclohexen-1-one)	10*	10	IRIS
100-42-5	Styrene	10	10	IRIS
34014-18-1	Tebuthiuron (N-[5-(1,1-Dimethylethyl)-1,3,4-thiadiazol-2-yl)- N,N'-dimethylurea)	10*	10	IRIS
23564-05-8	Thiophanate-methyl	10*	10	IRIS
108-88-3	Toluene	10	10	IRIS
95-95-4	Trichlorophenol, 2,4,5-	10*	10	IRIS
108-05-4	Vinyl acetate	10	10*	IRIS
7440-66-6	Zinc (fume or dust)	10*	10	IRIS
Chemicals with Toxicity Weights of 1 for Both Exposure Pathways				
6484-52-2	Ammonium nitrate (solution)	1*	1	final derived
75-68-3	Chloro-1,1-difluoroethane, 1-	1	1*	IRIS
75-00-3	Chloroethane (Ethyl chloride)	1	1*	IRIS
7440-50-8	Copper	1*	1	HEAST
110-82-7	Cyclohexane	1	1*	interim derived
107-21-1	Ethylene glycol	1*	1	IRIS
74-85-1	Ethylene	1	1*	final derived
64-18-6	Formic acid	1*	1	HEAST
76-13-1	Freon 113	1*	1	IRIS

Table 7-5. Toxicity Weights for all TRI Chemicals, by Toxicity Weight Category				
CAS Number	Chemical Name	Toxicity Weight		Source
		Inhalation	Oral	
108-38-3	m-Xylene	1*	1	HEAST
1634-04-4	Methyl tert-butyl ether	1	1*	IRIS
No CASRNa	Nitrate compounds (water dissociable)	1*	1	IRIS
95-47-6	o-Xylene	1*	1	HEAST
108-95-2	Phenol	1*	1	IRIS
90-43-7	Phenylphenol, 2-	1*	1	HEAST
85-44-9	Phthalic anhydride	1*	1	IRIS
115-07-1	Propylene (Propene)	1	1*	final derived
1330-20-7	Xylene (mixed isomers)	1*	1	IRIS
Chemicals with No Toxicity Weights				
71751412	Abamectin (Avermectin B1)			new chemical, not derived
60-35-5	Acetamide			low priority chemical
53-96-3	Acetylaminofluorene, 2-			low priority chemical
107119	Allylamine			new chemical, not derived
134-32-7	alpha-Naphthylamine			low priority chemical
1344-28-1	Aluminum oxide (fibrous forms)			new chemical, derived, not reviewed
82-28-0	Amino-2-methyl-anthraquinone, 1-			low priority chemical
117-79-3	Aminoanthraquinone, 2-			low priority chemical
60-09-3	Aminoazobenzene, 4-			low priority chemical
92-67-1	Aminodiphenyl, 4-			low priority chemical
61-82-5	Amitrole			new chemical, not derived
101053	Anilazine (4,6-Dichloro-N-(2-chlorophenyl)-1,3,5-triazin-2-amine)			new chemical, not derived
492-80-8	Auramine			low priority chemical
22781233	Bendiocarb (2,2-Dimethyl-1,3-benzodioxol-4-ol methylcarbamate)			new chemical, not derived
98-87-3	Benzal chloride			insufficient data

Table 7-5. Toxicity Weights for all TRI Chemicals, by Toxicity Weight Category				
CAS Number	Chemical Name	Toxicity Weight		Source
		Inhalation	Oral	
55-21-0	Benzamide			low priority chemical
98-88-4	Benzoyl chloride			insufficient data
94-36-0	Benzoyl Peroxide			insufficient data
91-59-8	beta-Naphthylamine			new chemical, not derived
57-57-8	beta-Propiolactone			low priority chemical
108-60-1	Bis(2-chloro-1-methethyl)ether			new chemical, not derived
111-91-1	Bis(2-chloroethoxy)methane			new chemical, not derived
7637072	Boron trifluoride			new chemical, not derived
10294345	Boron trichloride			new chemical, not derived
314409	Bromacil (5-Bromo-6-methyl-3-(1-methylpropyl)-2,4(1H,3H)-pyrimidinedione)			new chemical, not derived
53404196	Bromacil lithium salt (2,4(1H,3H)-Pyrimidinedione, 5-bromo-6-methyl-3 (1-methylpropyl), lithium salt)			new chemical, not derived
7726956	Bromine			new chemical, not derived
35691657	Bromo-1-(bromomethyl)-1,3-propanedicarbonitrile, 1-			new chemical, not derived
52517	Bromo-2-nitropropane-1,3-diol(Bronopol), 2-			new chemical, not derived
353-59-3	Bromochlorodifluoromethane (Halon 1			new chemical, derived, not reviewed
75-63-8	Bromotrifluoromethane (Halon 1301)			new chemical, not derived
357573	Brucine			new chemical, not derived
1929733	butoxyethyl ester, 2,4-D			new chemical, not derived
94804	butyl ester, 2,4-D			new chemical, not derived
123-72-8	Butyraldehyde			insufficient data
842-07-9	C.I. Solvent Yellow 14			low priority chemical
97-56-3	C.I. Solvent Yellow 3			low priority chemical
128-66-5	C.I. Vat Yellow 4			low priority chemical

Table 7-5. Toxicity Weights for all TRI Chemicals, by Toxicity Weight Category				
CAS Number	Chemical Name	Toxicity Weight		Source
		Inhalation	Oral	
989-38-8	C.I. Basic Red 1			low priority chemical
569-64-2	C.I. Basic Green 4			low priority chemical
3761-53-3	C.I. Food Red 5			low priority chemical
6459945	C.I. Acid Red 114			new chemical, not derived
81-88-9	C.I. Food Red 15			low priority chemical
2832-40-8	C.I. Disperse Yellow 3			low priority chemical
4680-78-8	C.I. Acid Green 3			low priority chemical
28407376	C.I. Direct Blue 218			new chemical, not derived
3118-97-6	C.I. Solvent Orange 7			low priority chemical
76-14-2	CFC 114			new chemical, not derived
76-15-3	CFC 115			new chemical, not derived
2439012	Chinomethionat (6-Methyl-1,3-dithiolo[4,5-b]quinoxalin-2-one)			new chemical, not derived
115286	Chlorendic acid			new chemical, not derived
75887	Chloro-1,1,1-trifluoroethane (HCFC-133a), 2-			new chemical, not derived
354-25-6	Chloro-1,1,2,2-tetrafluoroethane, 1-			new chemical, not derived
460355	Chloro-1,1,1-trifluoropropane(HCFC-253fb), 3-			new chemical, not derived
2837-89-0	Chloro-1,1,1,2-tetrafluoroethane, 2-			new chemical, not derived
563473	Chloro-2-methyl-1-propene, 3-			new chemical, not derived
4080313	Chloroallyl)-3,5,7-triaza-1-azoniaadamantane chloride, 1-(3-			new chemical, not derived
2971382	chlorocrotyl ester, 2,4-D			new chemical, not derived
74-45-6	Chlorodifluoromethane (HCFC-22)			new chemical, not derived
107-30-2	Chloromethyl methyl ether			insufficient data
N084	Chlorophenols			new chemical, not derived
76062	Chloropicrin			new chemical, not derived
126-99-8	Chloroprene			insufficient data

Table 7-5. Toxicity Weights for all TRI Chemicals, by Toxicity Weight Category				
CAS Number	Chemical Name	Toxicity Weight		Source
		Inhalation	Oral	
542767	Chloropropionitrile, 3-			new chemical, not derived
63938-10-3	Chlorotetrafluoroethane			new chemical, not derived
75729	Chlorotrifluoromethane (CFC-13)			new chemical, not derived
5598130	Chlorpyrifos methyl (O,O-Dimethyl-O-(3,5,6-trichloro-2-pyridyl)phosphorothioate)			new chemical, not derived
7440-47-3	Chromium			insufficient data
N090	Chromium compounds			insufficient data
N100	Copper compounds			insufficient data
8001-58-9	Creosote, coal tar			new chemical, not derived
1319-77-3	Cresol (mixed isomers)			insufficient data
4170303	Crotonaldehyde			new chemical, not derived
21725462	Cyanazine			new chemical, not derived
1134232	Cycloate			new chemical, not derived
108930	Cyclohexanol			new chemical, not derived
28057489	d-trans-Allethrin [d-trans-Chrysanthemic acid of d-allethrone]			new chemical, not derived
533744	Dazomet (Tetrahydro-3,5-dimethyl-2H-1,3,5-thiadiazine-2-thione)			new chemical, not derived
53404607	Dazomet sodium salt (2H-1,3,5-Thiadiazine-2-thione, tetrahydro-3,5-dimethyl-, ion(1-), sodium)			new chemical, not derived
13684565	Desmedipham			new chemical, not derived
39156-41-7	Diaminoanisole sulfate, 2,4-			low priority chemical
615-05-4	Diaminoanisole, 2,4-			low priority chemical
333415	Diazinon			new chemical, not derived
334-88-3	Diazomethane			low priority chemical
132-64-9	Dibenzofuran			insufficient data
124-73-2	Dibromotetrafluoromethane (Halon 24			new chemical, derived, not reviewed

Table 7-5. Toxicity Weights for all TRI Chemicals, by Toxicity Weight Category				
CAS Number	Chemical Name	Toxicity Weight		Source
		Inhalation	Oral	
99309	Dichloran (2,6-Dichloro-4-nitroaniline)			new chemical, not derived
422560	Dichloro-1,1,1,2,2-pentafluoropropane (HCFC-225ca), 3,3-			new chemical, not derived
1649087	Dichloro-1,1-difluoroethane (HCFC-132b), 1,2-			new chemical, not derived
507551	Dichloro-1,1,2,2,3-pentafluoropropane (HCFC-225cb), 1,3-			new chemical, not derived
111512562	Dichloro-1,2,3,3,3-pentafluoropropane (HCFC-225eb), 1,1-			new chemical, not derived
422480	Dichloro-1,1,1,2,3-pentafluoropropane (HCFC-225ba), 2,3-			new chemical, not derived
90454-18-5	Dichloro-1,1,2-trifluoroethane			insufficient data
812-04-4	Dichloro-1,2,2-trifluoroethane (HCFC-123b), 1,1-			new chemical, not derived
136013791	Dichloro-1,1,2,3,3-pentafluoropropane (HCFC-225ea), 1,3-			new chemical, not derived
13474889	Dichloro-1,2,2,3,3-pentafluoropropane (HCFC-225cc), 1,1-			new chemical, not derived
431867	Dichloro-1,1,3,3,3-pentafluoropropane (HCFC-225da), 1,2-			new chemical, not derived
422446	Dichloro-1,1,2,3,3-pentafluoropropane (HCFC-225bb), 1,2-			new chemical, not derived
128903219	Dichloro-1,1,1,3,3-pentafluoropropane (HCFC-225aa), 2,2-			new chemical, not derived
354-23-4	Dichloro-1,1,2-trifluoroethane, 1,2-			new chemical, not derived
306-83-2	Dichloro-1,1,1-trifluoroethane, 2,2-			new chemical, not derived
1717-00-6	Dichloro-1-fluoroethane, 1,1-			new chemical, not derived
612839	Dichlorobenzidine dihydrochloride, 3,3'-			new chemical, not derived
64969342	Dichlorobenzidine sulfate, 3,3'-			new chemical, not derived
75434	Dichlorofluoromethane (HCFC-21)			new chemical, not derived
127564925	Dichloropentafluoropropane			new chemical, not derived

Table 7-5. Toxicity Weights for all TRI Chemicals, by Toxicity Weight Category				
CAS Number	Chemical Name	Toxicity Weight		Source
		Inhalation	Oral	
97234	Dichlorophene (2,2'-Methylenebis(4-chlorophenol)			new chemical, not derived
78-88-6	Dichloropropene, 2,3-			new chemical, not derived
34077-87-7	Dichlorotrifluoroethane			new chemical, not derived
51338273	Diclofop methyl (2-[4-(2,4-Dichlorophenoxy)phenoxy]propanoicacid, methyl ester)			new chemical, not derived
115-32-2	Dicofol			low priority chemical
77736	Dicyclopentadiene			new chemical, not derived
1464-53-5	Diepoxybutane			low priority chemical
38727558	Diethatyl ethyl			new chemical, not derived
101906	Diglycidyl resorcinol ether			new chemical, not derived
94-58-6	Dihydrosafrole			new chemical, not derived
No CASRN	Diisocyanates			new chemical, not derived
20325400	Dimethoxybenzidine dihydrochloride(o-Dianisidine dihydrochloride), 3,3'-			new chemical, not derived
111984099	Dimethoxybenzidine hydrochloride(o-Dianisidine hydrochloride), 3,3'-			new chemical, not derived
2524030	Dimethyl chlorothiophosphate			new chemical, not derived
57-14-7	Dimethyl Hydrazine, 1,1-			insufficient data
131-11-3	Dimethyl phthalate			insufficient data
2300665	Dimethylamine dicamba			new chemical, not derived
124403	Dimethylamine			new chemical, not derived
60-11-7	Dimethylaminoazobenzene, 4-			low priority chemical
612828	Dimethylbenzidine dihydrochloride(o-Tolidine dihydrochloride), 3,3'-			new chemical, not derived
41766750	Dimethylbenzidine dihydrofluoride(o-Tolidine dihydrofluoride), 3,3'-			new chemical, not derived
79-44-7	Dimethylcarbamyl chloride			low priority chemical

Table 7-5. Toxicity Weights for all TRI Chemicals, by Toxicity Weight Category				
CAS Number	Chemical Name	Toxicity Weight		Source
		Inhalation	Oral	
25321-14-6	Dinitrotoluene (mixed isomers)			new chemical, not derived
39300453	Dinocap			new chemical, not derived
2164070	Dipotassium endothall (7-Oxabicyclo(2.2.1)heptane-2,3-dicarboxylic acid, dipotassium salt)			new chemical, not derived
136458	Dipropyl isocinchomeronate			new chemical, not derived
138932	Disodium cyanodithioimidocarbonate			new chemical, not derived
541537	Dithiobiuret, 2,4-			new chemical, not derived
120365	DP (Dichlorprop), 2,4-			new chemical, not derived
13194484	Ethoprop (Phosphorodithioic acid O-ethyl S,S-dipropyl ester)			new chemical, not derived
541-41-3	Ethyl chloroformate			low priority chemical
53404378	ethyl-4-methylpentyl ester, 2,4-D 2-			new chemical, not derived
N1000	Ethylenebisdithiocarbamic acid, salts and esters			insufficient data
151-56-4	Ethyleneimine (Aziridine)			low priority chemical
1928434	ethylhexyl ester, 2,4-D 2-			new chemical, not derived
75-34-3	Ethylidene dichloride			insufficient data
52857	Famphur			new chemical, not derived
60168889	Fenarimol (.alpha.-(2-Chlorophenyl)-.alpha.-4-chlorophenyl)-5-pyrimidinemethanol)			new chemical, not derived
13356086	Fenbutatin oxide (hexakis(2-methyl-2-phenylpropyl)distannoxane)			new chemical, not derived
66441234	Fenoxaprop ethyl (2-(4-((6-Chloro-2-benzoxazolylen)oxy)phenoxy)propanoicacid,ethyl ester)			new chemical, not derived
72490018	Fenoxycarb (2-(4-Phenoxyphenoxy)ethyl]carbamic acidethyl ester)			new chemical, not derived
55389	Fenthion (O,O-Dimethyl O-[3-methyl-4-(methylthio) phenyl] ester,phosphorothioic acid)			new chemical, not derived
14484641	Ferbam (Tris(dimethylcarbamodithioato-S,S')iron)			new chemical, not derived

Table 7-5. Toxicity Weights for all TRI Chemicals, by Toxicity Weight Category				
CAS Number	Chemical Name	Toxicity Weight		Source
		Inhalation	Oral	
69806504	Fluazifop butyl (2-[4-[[5-(Trifluoromethyl)-2-pyridinyl]oxy]-phenoxy]propanoic acid, butyl ester)			new chemical, not derived
51218	Fluorouracil (5-Fluorouracil)			new chemical, not derived
N230	Glycol Ethers			insufficient data
1335-87-1	Hexachloronaphthalene			low priority chemical
680-31-9	Hexamethylphosphoramide			low priority chemical
10034-93-2	Hydrazine sulfate			insufficient data
7664-39-3	Hydrogen fluoride			insufficient data
55406536	Iodo-2-propynyl butylcarbamate, 3-			new chemical, not derived
13463406	Iron pentacarbonyl			new chemical, not derived
465736	Isodrin			new chemical, not derived
25311711	Isofenphos (2-[[Ethoxyl[(1-methylethyl)amino]phosphinothioyl]oxy]benzoic acid 1-methylethyl ester)			new chemical, not derived
94111	isopropyl ester, 2,4-D			new chemical, not derived
67-63-0	Isopropyl alcohol			interim derived
120-58-1	Isosafrole			new chemical, not derived
554132	Lithium carbonate			new chemical, not derived
149304	Mercaptobenzothiazole (MBT), 2-			new chemical, not derived
137428	Metham sodium (Sodiummethyldithiocarbamate)			new chemical, not derived
20354261	Methazole (2-(3,4-Dichlorophenyl)-4-methyl-1,2,4-oxadiazolidine-3,5-dione)			new chemical, not derived
2032657	Methiocarb			new chemical, not derived
3653483	Methoxone sodium salt ((4-Chloro-2-methylphenoxy) acetate sodium salt)			new chemical, not derived
556616	Methyl isothiocyanate			new chemical, not derived
60-34-4	Methyl hydrazine			insufficient data
79-22-1	Methyl chlorocarbonate			new chemical, not derived

Table 7-5. Toxicity Weights for all TRI Chemicals, by Toxicity Weight Category				
CAS Number	Chemical Name	Toxicity Weight		Source
		Inhalation	Oral	
101-77-9	Methylenedianiline, 4,4'-			insufficient data
75865	Methyllactonitrile, 2-			new chemical, not derived
109-06-8	Methylpyridine, 2-			new chemical, not derived
9006422	Metiram			new chemical, not derived
7786347	Mevinphos			new chemical, not derived
150685	Monuron			new chemical, not derived
505-60-2	Mustard gas			low priority chemical
872504	N-Methyl-2-pyrrolidone			new chemical, not derived
924425	N-Methylolacrylamide			new chemical, not derived
684-93-5	N-Nitroso-N-methylurea			low priority chemical
4549-40-0	N-Nitrosomethylvinylamine			low priority chemical
59-89-2	N-Nitrosomorpholine			low priority chemical
16543-55-8	N-Nitrosonornicotine			low priority chemical
100-75-4	N-Nitrosopiperidine			low priority chemical
142596	Nabam			new chemical, not derived
91-20-3	Naphthalene			new chemical, not derived
7440-02-0	Nickel			insufficient data
N495	Nickel compounds			insufficient data
No CASRN	Nicotine and salts			new chemical, not derived
1929824	Nitrapyrin (2-Chloro-6-(trichloromethyl)pyridine)			new chemical, not derived
92-93-3	Nitrobiphenyl, 4-			low priority chemical
1836-75-5	Nitrofen			low priority chemical
51-75-2	Nitrogen mustard			low priority chemical
88-75-5	Nitrophenol, 2-			insufficient data
134-29-2	o-Anisidine hydrochloride			low priority chemical
2234-13-1	Octachloronaphtahlene			low priority chemical

Table 7-5. Toxicity Weights for all TRI Chemicals, by Toxicity Weight Category				
CAS Number	Chemical Name	Toxicity Weight		Source
		Inhalation	Oral	
20816-12-0	Osmium tetroxide			low priority chemical
301122	Oxydemeton methyl (S-(2-(Ethylsulfinyl)ethyl) O,O-dimethylester phosphorothioic acid)			new chemical, not derived
10028156	Ozone			new chemical, not derived
104-94-9	p-Anisidine			low priority chemical
95692	p-Chloro-o-toluidine			new chemical, not derived
104121	p-Chlorophenyl isocyanate			new chemical, not derived
100016	p-Nitroaniline			new chemical, not derived
156-10-5	p-Nitrosodiphenylamine			low priority chemical
106-42-3	p-Xylene			new chemical, not derived
123-67-7	Paraldehyde			new chemical, not derived
1114712	Pebulate (Butylethylcarbamothioic acidS-propyl ester)			new chemical, not derived
76-01-7	Pentachloroethane			new chemical, not derived
57330	Pentobarbital sodium			new chemical, not derived
594423	Perchloromethyl mercaptan			new chemical, not derived
85018	Phenanthrene			new chemical, not derived
26002802	Phenothrin (2,2-Dimethyl-3-(2-methyl-1-propenyl) cyclopropanecarboxylic acid(3-phenoxyphenyl)methyl ester)			new chemical, not derived
615281	Phenylenediamine dihydrochloride, 1,2-			new chemical, not derived
624180	Phenylenediamine dihydrochloride, 1,4-			new chemical, not derived
95545	Phenylenediamine, 1,2-			new chemical, not derived
57410	Phenytoin			new chemical, not derived
75-44-5	Phosgene			low priority chemical
51036	Piperonyl butoxide			new chemical, not derived
No CASRN	Polychlorinated alkanes			new chemical, not derived
No CASRN	Polycyclic aromatic compounds			new chemical, not derived

Table 7-5. Toxicity Weights for all TRI Chemicals, by Toxicity Weight Category				
CAS Number	Chemical Name	Toxicity Weight		Source
		Inhalation	Oral	
7758012	Potassium bromate			new chemical, not derived
137417	Potassium N-methyldithiocarbamate			new chemical, not derived
128030	Potassium dimethyldithiocarbamate			new chemical, not derived
41198087	Profenofos (O-(4-Bromo-2-chlorophenyl)-O-ethyl-S-propyl phosphorothioate)			new chemical, not derived
1120-71-4	Propane sultone			new chemical, not derived
31218834	Propetamphos (3-[(Ethylamino)methoxyphosphinothioyl]oxy]-2-butenoic acid, 1-methylethylester)			new chemical, not derived
123-38-6	Propionaldehyde			insufficient data
1320189	propylene glycol butyl etherester, 2,4-D			new chemical, not derived
106-51-4	Quinone			low priority chemical
81-07-2	Saccharin (manufacturing)			low priority chemical
94-59-7	Safrole			low priority chemical
78-92-2	sec-Butyl alcohol			insufficient data
2702729	sodium salt, 2,4-D			new chemical, not derived
132274	Sodium o-phenylphenoxide			new chemical, not derived
7632000	Sodium nitrite			new chemical, not derived
1982690	Sodium dicamba (3,6-Dichloro-2-methoxybenzoic acid, sodium salt)			new chemical, not derived
128041	Sodium dimethyldithiocarbamate			new chemical, not derived
131522	Sodium pentachlorophenate			new chemical, not derived
96-09-3	Styrene oxide			low priority chemical
2699798	Sulfuryl fluoride (Vikane)			new chemical, not derived
35400432	Sulprofos (O-Ethyl O-[4-(methylthio)phenyl]phosphorodithioicacid S propyl ester)			new chemical, not derived
3383968	Temephos			new chemical, not derived
75-65-0	tert-Butyl Alcohol			insufficient data

Table 7-5. Toxicity Weights for all TRI Chemicals, by Toxicity Weight Category				
CAS Number	Chemical Name	Toxicity Weight		Source
		Inhalation	Oral	
354143	Tetrachloro-1-fluoroethane(HCFC-121), 1,1,2,2-			new chemical, not derived
354110	Tetrachloro-2-fluoroethane(HCFC-121a), 1,1,1,2-			new chemical, not derived
64755	Tetracycline hydrochloride			new chemical, not derived
7696120	Tetramethrin (2,2-Dimethyl-3-(2-methyl-1-propenyl) cyclopropanecarboxylicacid (1,3,4,5,6,7-hexahydro-1,3-dioxo-2			new chemical, not derived
7440-28-0	Thallium			insufficient data
N760	Thallium comounds			insufficient data
148798	Thiabendazole (2-(4-Thiazolyl)-1H-benzimidazole)			new chemical, not derived
62-55-5	Thioacetamide			low priority chemical
139-65-1	Thiodianiline, 4,4'-			low priority chemical
59669260	Thiodicarb			new chemical, not derived
23564069	Thiophanate ethyl ([1,2-Phenylenebis(iminocarbonothioyl)]biscarbamic acid diethyl ester)			new chemical, not derived
79196	Thiosemicarbazide			new chemical, not derived
10061026	trans-1,3-Dichloropropene			new chemical, not derived
110576	trans-1,4-Dichloro-2-butene			new chemical, not derived
68-76-8	Triaziquone			low priority chemical
2155706	Tributyltin methacrylate			new chemical, not derived
1983104	Tributyltin fluoride			new chemical, not derived
52-68-6	Trichlorfon			new chemical, not derived
76028	Trichloroacetyl chloride			new chemical, not derived
71-55-6	Trichloroethane, 1,1,1-			new chemical, not derived
79-01-6	Trichloroethylene			insufficient data
57213691	Triclopyr triethylammonium salt			new chemical, not derived

Table 7-5. Toxicity Weights for all TRI Chemicals, by Toxicity Weight Category				
CAS Number	Chemical Name	Toxicity Weight		Source
		Inhalation	Oral	
26644462	Triforine (N,N'-[1,4-Piperazinediylbis-2,2,2-trichloroethylidene)]bisformamide)			new chemical, not derived
2655154	Trimethylphenyl methylcarbamate, 2,3,5-			new chemical, not derived
76879	Triphenyltin hydroxide			new chemical, not derived
639587	Triphenyltin chloride			new chemical, not derived
126-72-7	Tris(2,3-dibromopropyl)phosphate			new chemical, not derived
72-57-1	Trypan blue			new chemical, not derived
51-79-6	Urethane (Ethyl Carbamate)			new chemical, not derived
87-62-7	Xylidine, 2,6-			low priority chemical
N982	Zinc Compounds			insufficient data

*Toxicity weight is adopted from the other exposure pathway.

8. References Cited

Cicmanec, J. U.S. EPA OHEA. Personal communication, November 16, 1993.

Crosfil and Widdicombe, 1961. *Journal of Physiology.* 151:1.

Dourson, M.L., Knauf, L.A., Swartout, J.C. 1992. *On Reference Dose (RfD) and Its Underlying Toxicity Data Base.* Toxicology and Industrial Health. 8(3).

Hallenbeck, W. and Cunningham, K. 1986. *Quantitative Risk Assessment for Environmental and Occupational Health.* Ann Arbor, MI: Lewis Press.

Pearson and Hartley, eds. 1966. *Biometrika Tables for Statisticians.* Vol. 1. Cambridge University Press.

U.S. EPA. 1986a. *Cancer Risk Assessment Guidelines.* Federal Register 51 (185): 33992-34003. September 24.

U.S. EPA. 1986b. *Guidelines for Mutagenicity Risk Assessment.* Federal Register 51 (185): 34006-34012. September 24.

U.S. EPA. 1988. *Integrated Risk Information System (IRIS).* Background Documents. Washington, D.C.

U.S. EPA. 1990a. *Hazard Ranking System; Final Rule.* Federal Register 55: 51532-51667. December 14.

U.S. EPA OHEA. 1990b. *Exposure Factors Handbook.* Washington, DC. EPA 600/8-89/043.

U.S. EPA. 1991. *Guidelines for Developmental Toxicity Risk Assessment.* Federal Register 56 (234), 63798-63826. December 5.

U.S. EPA. *Hazardous Substances Data Bank.* Accessed via TOXNET.

U.S. EPA. 1996. *Integrated Risk Information System (IRIS).* On-line toxicity information for Benzene.

U.S. EPA. 1997. *TRI Relative Risk-Based Environmental Indicators Methodology.*

Appendix A.
Toxicity Weights for All Scored TRI Chemicals and Chemical Categories

Appendix A. Toxicity Weights for All Scored TRI Chemicals and Chemical Categories

A.1. Introduction

Appendix A contains the 288 TRI chemicals and chemical categories of for which at least one published toxicity value was available. Toxicity weights for the chemicals and chemical categories listed in Appendix A were derived from toxicity values listed in the Integrated Risk Information System (IRIS) database or the 1995 Health Effects Assessment Summary Tables (HEAST). The review of IRIS and HEAST was performed on April 1, 1997 (the IRIS search was done on the IRIS electronic database (version 1.0) with the April 1997 updates). Toxicity values used included Reference Doses (RfDs) and Reference Concentrations (RfCs) for noncancer effects, and Oral Slope Factors and Inhalation Unit Risks, as well as weight of evidence (WOE) classifications, for cancer effects. Methods for deriving toxicity weights from these data are described in Chapter 1. This listing also includes the toxicity weights and type of health effect for all chemicals and chemical categories with derived values through the Office of Pollution Prevention and Toxics (OPPT) Dispositon Process.

Generally, for chemicals with at least one IRIS or HEAST noncancer RfD or RfC and/or cancer Oral Slope Factor or Inhaltion Unit Risk, toxicity weights were based on the published toxicity values and no further review was done. For chemicals with no IRIS or HEAST values, a review of the secondary literature was performed, and toxicity values were derived or obtained from other sources. The basis for the derived toxicity weights is provided in Appendices B (final derived) and C (interim derived).

A.2. Table of Toxicity Weights For All Scored TRI Chemicals and Chemical Categories

Table A-1 contains all chemicals and chemical categories on the 1995 TRI List with toxicity weights. This listing provides a detailed listing of all relevant data pertaining to the toxicity weighting of each chemical or chemical category.

Table A-1. Toxicity Weights for All Scored TRI Chemicals and Chemical Categories, in Alphabetical Order

CAS No.	Chemical Name	Source[1]	Non-Cancer										Cancer				Overall Toxicity Weights			
		IRIS, HEAST or Derived[2]	Reference Concentration (mg/m^3)					Reference Dose (mg/kg-d)					Inhalation Unit Risk (Risk per mg/m^3)	Oral Slope Factor (risk per mg/kg-d)	WOE[3]	Listing Date	Inhalation		Oral	
			Inhalation	UF[4]	MF[5]	LOC[6]	Listing Date	Oral	UF[4]	MF[5]	LOC[6]	Listing Date					Weight	Effect[7]	Weight	Effect[7]
94-82-6	2,4-DB	IRIS						0.008	1000	1	L	08/01/92					100*	Non-cancer*	100	Non-cancer
30560-19-1	Acephate (Acetylphosphoramidothioic acid O,S-dimethyl ester)	IRIS						0.004	30	1	H	02/01/90		0.0087	C	10/01/93	1000*	Non-cancer*	1000	Non-cancer
75-07-0	Acetaldehyde	IRIS	0.009	1000	1	L	10/01/91						2.2e-06		B2	01/01/91	1000	Non-cancer	1000*	Non-cancer*
94-75-7	Acetic acid (2,4-D((2,4-dichlorophenoxy)))	IRIS						0.01	100	1	M	05/05/88					100*	Non-cancer*	100	Non-cancer
75-05-8	Acetonitrile	IRIS						0.006	3000	1	L	02/01/96					100*	Non-cancer*	100	Non-cancer
98-86-2	Acetophenone	IRIS					08/01/92	0.1	3000	1	L	01/01/89			D	02/01/91	10*	Non-cancer*	10	Non-cancer
62476-59-9	Acifluorfen, sodium salt [5-(2-Chloro-4-(triflouromethyl)phenoxy)-2-nitrobenzoic acid, sodium salt]	IRIS						0.013	100	1	M	12/01/88				11/01/93	100*	Non-cancer*	100	Non-cancer
107-02-8	Acrolein	IRIS	0.00002	1000	1	M	07/01/93								C	02/01/94	100000	Non-cancer	100000*	Non-cancer*
79-06-1	Acrylamide	IRIS					11/01/90	0.0002	1000	1	M	03/01/91	0.0013	4.5	B2	07/01/93	10000	Cancer	10000	Both
79-10-7	Acrylic acid	IRIS	0.001	300	1	M	05/01/95	0.5	100	1	H	05/01/94					10000	Non-cancer	10	Non-cancer
107-13-1	Acrylonitrile	IRIS	0.002	1000	1	M	12/01/91					07/01/93	6.8e-05	0.54	B1	01/01/91	1000	Both	10000	Cancer

Table A-1. Toxicity Weights for All Scored TRI Chemicals and Chemical Categories, in Alphabetical Order

CAS No.	Chemical Name	Source[1]	Non-Cancer										Cancer				Overall Toxicity Weights			
		IRIS, HEAST or Derived[2]	Reference Concentration (mg/m^3)					Reference Dose (mg/kg-d)					Inhalation Unit Risk (Risk per mg/m^3)	Oral Slope Factor (risk per mg/kg-d)	WOE[3]	Listing Date	Inhalation		Oral	
			Inhalation	UF[4]	MF[5]	LOC[6]	Listing Date	Oral	UF[4]	MF[5]	LOC[6]	Listing Date					Weight	Effect[7]	Weight	Effect[7]
15972-60-8	Alachlor	IRIS						0.01	100	1	H	09/01/93					100*	Non-cancer*	100	Non-cancer
116-06-3	Aldicarb	IRIS						0.001	10	1	M	11/01/93			D	03/01/91	1000*	Non-cancer*	1000	Non-cancer
309-00-2	Aldrin	IRIS						3e-05	1000	1	M	03/01/88	0.0049	17	B2	07/01/93	100000	Cancer	100000	Both
107-05-1	Allyl chloride	IRIS	0.001	3000	1	L	05/01/95								C	08/01/94	10000	Non-cancer	10000*	Non-cancer*
107-18-6	Allyl alcohol	IRIS						0.005	1000	1	L	08/01/89					1000*	Non-cancer*	1000	Non-cancer
319-84-6	alpha-Hexachlorocyclohexane	IRIS											0.0018	6.3	B2	07/01/93	100000	Cancer	100000	Cancer
20859-73-8	Aluminum phosphide	IRIS						0.0004	100	1	M	03/01/88					10000*	Non-cancer*	10000	Non-cancer
7429-90-5	Aluminum (fume or dust)	interim derived															100000	Non-cancer		
834-12-8	Ametryn (N-Ethyl-N'-(1-methylethyl)-6-(methylthio)-1,3,5,-triazine- 2,4 diamine)	IRIS						0.009	1000	1	L	11/01/89					100*	Non-cancer*	100	Non-cancer
33089-61-1	Amitraz	IRIS						0.0025	100	1	M	12/01/88					1000*	Non-cancer*	1000	Non-cancer
7664-41-7	Ammonia	IRIS	0.1	30	1	M	05/01/91										100	Non-cancer	100*	Non-cancer*
6484-52-2	Ammonium nitrate (solution)	final derived															1*	Non-cancer*	1	Non-cancer

Table A-1. Toxicity Weights for All Scored TRI Chemicals and Chemical Categories, in Alphabetical Order

CAS No.	Chemical Name	Source[1]	Non-Cancer										Cancer				Overall Toxicity Weights			
		IRIS, HEAST or Derived[2]	Reference Concentration (mg/m^3)					Reference Dose (mg/kg-d)					Inhalation Unit Risk (Risk per mg/m^3)	Oral Slope Factor (risk per mg/kg-d)	WOE[3]	Listing Date	Inhalation		Oral	
			Inhalation	UF[4]	MF[5]	LOC[6]	Listing Date	Oral	UF[4]	MF[5]	LOC[6]	Listing Date					Weight	Effect[7]	Weight	Effect[7]
62-53-3	Aniline	IRIS	0.001	3000	1	L	12/01/93							0.0057	B2	02/01/94	10000	Non-cancer	100	Cancer
120-12-7	Anthracene	IRIS					09/01/94	0.3	3000	1	L	07/01/93			D	01/01/91	10*	Non-cancer*	10	Non-cancer
N010	Antimony compounds	IRIS						0.0004	1000	1	L	02/01/91					10000*	Non-cancer*	10000	Non-cancer
7440-36-0	Antimony	IRIS						0.0004	1000	1	L	02/01/91					10000*	Non-cancer*	10000	Non-cancer
7440-38-2	Arsenic	IRIS						0.0003	3	1	M	03/01/93	0.0043	1.5	A	07/01/95	100000	Cancer	10000	Both
N020	Arsenic compounds	IRIS						0.0003	3	1	M	03/01/93	0.0043	1.5	A	07/01/95	100000	Cancer	10000	Both
1332-21-4	Asbestos (friable)	IRIS											0.23		A	07/01/93	1000	Cancer	n/a	
1912-24-9	Atrazine (6-Chloro-N-ethyl-N'-(1-methylethyl)-1,3,5,-triazine-2,4-diamine)	IRIS						0.035	100	1	H	10/01/93					100*	Non-cancer*	100	Non-cancer
7440-39-3	Barium	IRIS					12/01/91	0.07	3	1	M	08/01/90					10*	Non-cancer*	10	Non-cancer
N040	Barium compounds	IRIS					12/01/91	0.07	3	1	M	08/01/90					10*	Non-cancer*	10	Non-cancer
1861-40-1	Benfluralin (N-Butyl-N-ethyl-2,6-dinitro-4-(trifluoromethyl)benzenamine)	IRIS						0.3	100	1	M	03/01/88					10*	Non-cancer*	10	Non-cancer
17804-35-2	Benomyl	IRIS						0.05	100	1	H	03/01/89					100*	Non-cancer*	100	Non-cancer

Table A-1. Toxicity Weights for All Scored TRI Chemicals and Chemical Categories, in Alphabetical Order

CAS No.	Chemical Name	Source[1]	Non-Cancer										Cancer				Overall Toxicity Weights			
		IRIS, HEAST or Derived[2]	Reference Concentration (mg/m^3)					Reference Dose (mg/kg-d)					Inhalation Unit Risk (Risk per mg/m^3)	Oral Slope Factor (risk per mg/kg-d)	WOE[3]	Listing Date	Inhalation		Oral	
			Inhalation	UF[4]	MF[5]	LOC[6]	Listing Date	Oral	UF[4]	MF[5]	LOC[6]	Listing Date					Weight	Effect[7]	Weight	Effect[7]
71-43-2	Benzene	IRIS											8.3e-06	0.029	A	02/01/94	100	Cancer	100	Cancer
92-87-5	Benzidine	IRIS					07/01/91	0.003	1000	1	M	02/01/95	0.067	230	A	08/01/92	1000000	Cancer	1000000	Cancer
98-07-7	Benzotrichloride	IRIS												13	B2	07/01/93	100000*	Cancer*	100000	Cancer
100-44-7	Benzyl chloride	IRIS					07/01/95							0.17	B2	08/01/94	1000*	Cancer*	1000	Cancer
7440-41-7	Beryllium	IRIS						0.005	100	1	L	02/01/93	0.0024	4.3	B2	09/01/92	100000	Cancer	10000	Cancer
N050	Beryllium compounds	IRIS						0.005	100	1	L	02/01/93	0.0024	4.3	B2	09/01/92	100000	Cancer	10000	Cancer
82657-04-3	Bifenthrin	IRIS						0.015	100	1	H	08/22/88					100*	Non-cancer*	100	Non-cancer
92-52-4	Biphenyl	IRIS					11/01/90	0.05	100	10	M	08/01/89			D	03/01/91	100*	Non-cancer*	100	Non-cancer
111-44-4	Bis(2-chloroethyl)ether	IRIS					10/01/91						0.00033	1.1	B2	02/01/94	10000	Cancer	10000	Cancer
542-88-1	Bis(chloromethyl)ether	IRIS					07/01/91						0.062	220	A	01/01/91	1000000	Cancer	1000000	Cancer
56-35-9	Bis(tributyltin) oxide	IRIS						3e-05	1000	1	L	09/01/93					100000*	Non-cancer*	100000	Non-cancer
75-25-2	Bromoform (Tribromomethane)	IRIS					12/01/93	0.02	1000	1	M	03/01/91	1.1e-06	0.0079	B2	01/01/91	10	Cancer	100	Both
74-83-9	Bromomethane (Methyl Bromide)	IRIS	0.005	100	1	H	10/01/92	0.0014	1000	1	M	07/01/91			D	08/01/90	1000	Non-cancer	1000	Non-cancer
1689-84-5	Bromoxynil (3,5-Dibromo-4-hydroxybenzonitrile)	IRIS						0.02	300	1	M	06/30/88					100*	Non-cancer*	100	Non-cancer

Table A-1. Toxicity Weights for All Scored TRI Chemicals and Chemical Categories, in Alphabetical Order

CAS No.	Chemical Name	Source[1]	Non-Cancer										Cancer				Overall Toxicity Weights			
		IRIS, HEAST or Derived[2]	Reference Concentration (mg/m^3)					Reference Dose (mg/kg-d)					Inhalation Unit Risk (Risk per mg/m^3)	Oral Slope Factor (risk per mg/kg-d)	WOE[3]	Listing Date	Inhalation		Oral	
			Inhalation	UF[4]	MF[5]	LOC[6]	Listing Date	Oral	UF[4]	MF[5]	LOC[6]	Listing Date					Weight	Effect[7]	Weight	Effect[7]
1689-99-2	Bromoxynil octanoate (Octanoic acid,2,6-dibromo-4-cyanophenyl ester)	IRIS						0.02	300	1	M	09/07/88					100*	Non-cancer*	100	Non-cancer
106-99-0	Butadiene, 1,3-	IRIS											0.00028		B2	02/01/91	10000	Cancer	10000*	Cancer*
141-32-2	Butyl acrylate	interim derived															10	Non-cancer	10000	Non-cancer
106-88-7	Butylene oxide, 1,2-	IRIS	0.02	300	1	M	05/01/92										100	Non-cancer	100*	Non-cancer*
1937-37-7	C.I. Direct Black 38	HEAST												8.6	A		100000*	Cancer*	100000	Cancer
2602-46-2	C.I. Direct Blue 6	HEAST												8.1	A		100000*	Cancer*	100000	Cancer
16071-86-6	C.I. Direct Brown 95	HEAST												9.3			100000*	Cancer*	100000	Cancer
N078	Cadmium compounds	IRIS						0.0005	10	1	H	02/01/94	0.0018		B1	06/01/92	100000	Cancer	10000	Non-cancer
7440-43-9	Cadmium	IRIS						0.0005	10	1	H	02/01/94	0.0018		B1	06/01/92	100000	Cancer	10000	Non-cancer
156-62-7	Calcium cyanamide	final derived															1000*	Non-cancer*	1000	Non-cancer
133-06-2	Captan	IRIS					07/01/92	0.13	100	1	H	03/01/89					10*	Non-cancer*	10	Non-cancer
63-25-2	Carbaryl	IRIS					11/01/91	0.1	100	1	M	03/01/88					10*	Non-cancer*	10	Non-cancer
1563-66-2	Carbofuran	IRIS						0.005	100	1	H	09/30/87					1000*	Non-cancer*	1000	Non-cancer

Table A-1. Toxicity Weights for All Scored TRI Chemicals and Chemical Categories, in Alphabetical Order

CAS No.	Chemical Name	Source[1]	Non-Cancer										Cancer				Overall Toxicity Weights			
		IRIS, HEAST or Derived[2]	Reference Concentration (mg/m^3)					Reference Dose (mg/kg-d)					Inhalation Unit Risk (Risk per mg/m^3)	Oral Slope Factor (risk per mg/kg-d)	WOE[3]	Listing Date	Inhalation		Oral	
			Inhalation	UF[4]	MF[5]	LOC[6]	Listing Date	Oral	UF[4]	MF[5]	LOC[6]	Listing Date					Weight	Effect[7]	Weight	Effect[7]
75-15-0	Carbon disulfide	IRIS	0.7	30	1	M	08/01/95	0.1	100	1	M	09/01/90					10	Non-cancer	10	Non-cancer
56-23-5	Carbon tetrachloride	IRIS						0.0007	1000	1	M	06/01/91	1.5e-05	0.13	B2	10/01/92	1000	Cancer	1000	Both
463-58-1	Carbonyl sulfide	interim derived															100	Non-cancer	100*	Non-cancer*
5234-68-4	Carboxin (5,6-Dihydro-2-methyl-N-phenyl-1,4-oxathiin-3-carboxamide)	IRIS						0.1	100	1	H	07/01/89					10*	Non-cancer*	10	Non-cancer
120-80-9	Catechol	interim derived															100*	Cancer*	100	Cancer
75-69-4	CFC-11	IRIS						0.3	1000	1	M	08/01/92					10*	Non-cancer*	10	Non-cancer
75-71-8	CFC-12	IRIS						0.2	100	1	M	11/01/95					10*	Non-cancer*	10	Non-cancer
133-90-4	Chloramben	IRIS					09/01/92	0.015	1000	1	M	03/01/88					100*	Non-cancer*	100	Non-cancer
57-74-9	Chlordane	IRIS						6e-05	1000	1	L	07/01/89	0.00037	1.3	B2	07/01/93	10000	Cancer	10000	Both
90982-32-4	Chlorimuron ethyl (Ethyl-2-[[[(4-chloro-6-methoxyprimidin-2-yl)-carbonyl]-amino]sulfonyl]benzoate)	IRIS						0.02	300	1	M	11/01/89					100*	Non-cancer*	100	Non-cancer
10049-04-4	Chlorine dioxide	IRIS	0.0002	3000	1	L	11/01/90					01/01/94			D	11/01/95	10000	Non-cancer	10000*	Non-cancer*

Table A-1. Toxicity Weights for All Scored TRI Chemicals and Chemical Categories, in Alphabetical Order

CAS No.	Chemical Name	Source[1]	Non-Cancer										Cancer				Overall Toxicity Weights			
		IRIS, HEAST or Derived[2]	Reference Concentration (mg/m^3)					Reference Dose (mg/kg-d)					Inhalation Unit Risk (Risk per mg/m^3)	Oral Slope Factor (risk per mg/kg-d)	WOE[3]	Listing Date	Inhalation		Oral	
			Inhalation	UF[4]	MF[5]	LOC[6]	Listing Date	Oral	UF[4]	MF[5]	LOC[6]	Listing Date					Weight	Effect[7]	Weight	Effect[7]
7782-50-5	Chlorine	IRIS						0.1	100	1	M	06/01/94				01/01/93	10*	Non-cancer*	10	Non-cancer
75-68-3	Chloro-1,1-difluoroethane, 1-	IRIS	50	300	1	M	07/01/95										1	Non-cancer	1*	Non-cancer*
79-11-8	Chloroacetic acid	HEAST						0.002	10000								1000*	Non-cancer*	1000	Non-cancer
532-27-4	Chloroacetophenone, 2-	IRIS	0.00003	1000	1	L	10/01/91										100000	Non-cancer	100000*	Non-cancer*
108-90-7	Chlorobenzene	IRIS						0.02	1000	1	M	07/01/93			D	03/01/91	100*	Non-cancer*	100	Non-cancer
510-15-6	Chlorobenzilate	IRIS					03/01/93	0.02	300	1	M	12/01/89					100*	Non-cancer*	100	Non-cancer
75-00-3	Chloroethane (Ethyl chloride)	IRIS	10	300	1	M	04/01/91									01/01/95	1	Non-cancer	1*	Non-cancer*
67-66-3	Chloroform	IRIS						0.01	1000	1	M	09/01/92	2.3e-05	0.0061	B2	07/01/92	1000	Cancer	100	Both
74-87-3	Chloromethane	HEAST											1.8e-06	0.013	C		10	Cancer	10	Cancer
1897-45-6	Chlorothalonil	IRIS						0.015	100	1	M	03/01/88					100*	Non-cancer*	100	Non-cancer
64902-72-3	Chlorsulfuron (2-Chloro-N-[[(4-methoxy-6-methyl-1,3,5-triazin-2-yl)amino]carbonyl]benzenesulfonamide)	IRIS						0.05	100	1	H	01/01/90					100*	Non-cancer*	100	Non-cancer
7440-48-4	Cobalt	interim derived															100000	Non-cancer	100000*	Non-cancer*

Table A-1. Toxicity Weights for All Scored TRI Chemicals and Chemical Categories, in Alphabetical Order

CAS No.	Chemical Name	Source[1]	Non-Cancer										Cancer				Overall Toxicity Weights			
		IRIS, HEAST or Derived[2]	Reference Concentration (mg/m^3)					Reference Dose (mg/kg-d)					Inhalation Unit Risk (Risk per mg/m^3)	Oral Slope Factor (risk per mg/kg-d)	WOE[3]	Listing Date	Inhalation		Oral	
			Inhalation	UF[4]	MF[5]	LOC[6]	Listing Date	Oral	UF[4]	MF[5]	LOC[6]	Listing Date					Weight	Effect[7]	Weight	Effect[7]
N096	Cobalt compounds	interim derived															100000	Non-cancer	100000*	Non-cancer*
7440-50-8	Copper	HEAST						1.3									1*	Non-cancer*	1	Non-cancer
98-82-8	Cumene	IRIS						0.04	3000	1	L	04/01/91					100*	Non-cancer*	100	Non-cancer
80-15-9	Cumene hydroperoxide	final derived															1000	Non-cancer	1000*	Non-cancer*
135-20-6	Cupferron	final derived															1000*	Cancer*	1000	Cancer
N106	Cyanide compounds	IRIS						0.02	100	5	M	02/01/93					100*	Non-cancer*	100	Non-cancer
110-82-7	Cyclohexane	interim derived															1	Non-cancer	1*	Non-cancer*
68359-37-5	Cyfluthrin (3-(2,2-Dichloroethenyl)-2,2-dimethylcyclopropanecarboxylic acid,cyano(4-fluoro-3-phenoxyphenyl)methy	IRIS						0.025	100	1	H	03/01/88					100*	Non-cancer*	100	Non-cancer

Table A-1. Toxicity Weights for All Scored TRI Chemicals and Chemical Categories, in Alphabetical Order

CAS No.	Chemical Name	Source[1]	Non-Cancer										Cancer				Overall Toxicity Weights			
		IRIS, HEAST or Derived[2]	Reference Concentration (mg/m^3)					Reference Dose (mg/kg-d)					Inhalation Unit Risk (Risk per mg/m^3)	Oral Slope Factor (risk per mg/kg-d)	WOE[3]	Listing Date	Inhalation		Oral	
			Inhalation	UF[4]	MF[5]	LOC[6]	Listing Date	Oral	UF[4]	MF[5]	LOC[6]	Listing Date					Weight	Effect[7]	Weight	Effect[7]
68085-85-8	Cyhalothrin (3-(2-Chloro-3,3,3-trifluoro-1-propenyl)-2,2-Dimethylcyclopropanecarboxylic acidcyano(3-phenoxypheny	IRIS						0.005	100	1	H	06/30/88					1000*	Non-cancer*	1000	Non-cancer
1163-19-5	Decabromodiphenyl oxide	IRIS						0.01	100	1	L	02/01/95			C	01/01/90	100*	Non-cancer*	100	Non-cancer
117-81-7	Di(2-ethylhexyl) phthalate	IRIS						0.02	1000	1	M	05/01/91		0.014	B2	02/01/93	100*	Both*	100	Both
2303-16-4	Diallate	HEAST												0.061	B2		1000*	Cancer*	1000	Cancer
101-80-4	Diaminodiphenylether, 4,4'-	final derived															1000*	Cancer*	1000	Cancer
25376-45-8	Diaminotoluene (mixed isomers)	interim derived															100000*	Cancer*	100000	Cancer
95-80-7	Diaminotoluene, 2,4-	HEAST												3.2	B2		10000*	Cancer*	10000	Cancer
96-12-8	Dibromo-3-chloropropane (DBCP), 1,2-	IRIS	0.0002	1000	1	M	10/01/91									07/01/92	10000	Non-cancer	10000*	Non-cancer*
106-93-4	Dibromoethane, 1,2-	IRIS					12/01/92						0.00022	85	B2	01/01/91	10000	Cancer	1000000	Cancer
84-74-2	Dibutyl phthalate	IRIS					10/01/90	0.1	1000	1	L	08/01/90			D	02/01/93	10*	Non-cancer*	10	Non-cancer

Table A-1. Toxicity Weights for All Scored TRI Chemicals and Chemical Categories, in Alphabetical Order

CAS No.	Chemical Name	Source[1]	Non-Cancer										Cancer				Overall Toxicity Weights			
		IRIS, HEAST or Derived[2]	Reference Concentration (mg/m^3)					Reference Dose (mg/kg-d)					Inhalation Unit Risk (Risk per mg/m^3)	Oral Slope Factor (risk per mg/kg-d)	WOE[3]	Listing Date	Inhalation		Oral	
			Inhalation	UF[4]	MF[5]	LOC[6]	Listing Date	Oral	UF[4]	MF[5]	LOC[6]	Listing Date					Weight	Effect[7]	Weight	Effect[7]
1918-00-9	Dicamba (3,6-Dichloro-2-methyoxybenzoicacid)	IRIS						0.03	100	1	H	07/01/92				11/01/93	100*	Non-cancer*	100	Non-cancer
764-41-0	Dichloro-2-butene, 1,4-	HEAST											0.0026		B2		100000	Cancer	100000*	Cancer*
541-73-1	Dichlorobenzene, 1,3-	interim derived															10	Non-cancer	100	Cancer
95-50-1	Dichlorobenzene, 1,2	IRIS						0.09	1000	1	L	03/01/91			D	01/01/91	10*	Non-cancer*	10	Non-cancer
25321-22-6	Dichlorobenzene (mixed isomers)	interim derived															10	Non-cancer	100	Cancer
106-46-7	Dichlorobenzene, 1,4-	IRIS	0.8	100	1	M	11/01/96										10	Non-cancer	10*	Non-cancer*
91-94-1	Dichlorobenzidine, 3,3'-	IRIS					11/01/91							0.45	B2	07/01/93	1000*	Cancer*	1000	Cancer
75-27-4	Dichlorobromomethane	IRIS						0.02	1000	1	M	03/01/91		0.062	B2	03/01/93	1000*	Cancer*	1000	Cancer
107-06-2	Dichloroethane, 1,2-	IRIS											2.6e-05	0.091	B2	07/01/93	1000	Cancer	1000	Cancer
540-59-0	Dichloroethylene, 1,2-	HEAST						0.009	1000								100*	Non-cancer*	100	Non-cancer
75-09-2	Dichloromethane	IRIS					09/01/91	0.06	100	1	M	03/01/88	4.7e-07	0.0075	B2	02/01/95	10	Cancer	100	Cancer
120-83-2	Dichlorophenol, 2,4-	IRIS						0.003	100	1	L	06/30/88					1000*	Non-cancer*	1000	Non-cancer
78-87-5	Dichloropropane, 1,2-	IRIS	0.004	300	1	M	12/01/91										1000	Non-cancer	1000*	Non-cancer*

Table A-1. Toxicity Weights for All Scored TRI Chemicals and Chemical Categories, in Alphabetical Order

CAS No.	Chemical Name	Source[1]	Non-Cancer										Cancer				Overall Toxicity Weights			
		IRIS, HEAST or Derived[2]	Reference Concentration (mg/m^3)					Reference Dose (mg/kg-d)					Inhalation Unit Risk (Risk per mg/m^3)	Oral Slope Factor (risk per mg/kg-d)	WOE[3]	Listing Date	Inhalation		Oral	
			Inhalation	UF[4]	MF[5]	LOC[6]	Listing Date	Oral	UF[4]	MF[5]	LOC[6]	Listing Date					Weight	Effect[7]	Weight	Effect[7]
542-75-6	Dichloropropylene, 1,3-	IRIS	0.02	30	1	H	01/01/91	0.0003	10000	1	L	10/01/90			B2	10/01/93	100	Non-cancer	10000	Non-cancer
62-73-7	Dichlorvos	IRIS	0.0005	100	1	M	06/01/94	0.0005	100	1	M	11/01/93		0.29	B2	06/01/95	10000	Non-cancer	10000	Non-cancer
111-42-2	Diethanolamine	interim derived															100*	Non-cancer*	100	Non-cancer
64-67-5	Diethyl sulfate	final derived															10000*	Cancer*	10000	Cancer
35367-38-5	Diflubenzuron	IRIS						0.02	100	1	H	09/01/90					100*	Non-cancer*	100	Non-cancer
55290-64-7	Dimethipin (2,3,-Dihydro-5,6-dimethyl-1,4-dithiin 1,1,4,4-tetraoxide)	IRIS						0.02	100	1	H	05/01/90			C	10/01/93	100*	Non-cancer*	100	Non-cancer
60-51-5	Dimethoate	IRIS						0.0002	300	1	M	09/01/90					10000*	Non-cancer*	10000	Non-cancer
119-90-4	Dimethoxybenzidine, 3,3'-	HEAST												0.014	B2		100*	Cancer*	100	Cancer
77-78-1	Dimethyl sulfate	interim derived															1000000	Cancer	1000000*	Cancer*
119-93-7	Dimethylbenzidine, 3,3'-	HEAST												9.2	B2		100000*	Cancer*	100000	Cancer
576-26-1	Dimethylphenol, 2,6-	IRIS						0.0006	1000	1	L	09/07/88					1000*	Non-cancer*	1000	Non-cancer
105-67-9	Dimethylphenol, 2,4-	IRIS						0.02	3000	1	L	11/01/90					100*	Non-cancer*	100	Non-cancer

Table A-1. Toxicity Weights for All Scored TRI Chemicals and Chemical Categories, in Alphabetical Order

CAS No.	Chemical Name	Source[1]	Non-Cancer										Cancer				Overall Toxicity Weights			
		IRIS, HEAST or Derived[2]	Reference Concentration (mg/m^3)					Reference Dose (mg/kg-d)					Inhalation Unit Risk (Risk per mg/m^3)	Oral Slope Factor (risk per mg/kg-d)	WOE[3]	Listing Date	Inhalation		Oral	
			Inhalation	UF[4]	MF[5]	LOC[6]	Listing Date	Oral	UF[4]	MF[5]	LOC[6]	Listing Date					Weight	Effect[7]	Weight	Effect[7]
534-52-1	Dinitro-o-cresol, 4,6-	interim derived															10000	Non-cancer	10000	Non-cancer
88-85-7	Dinitrobutyl phenol (Dinoseb)	IRIS						0.001	1000	1	L	08/01/89			D	07/01/93	1000*	Non-cancer*	1000	Non-cancer
51-28-5	Dinitrophenol, 2,4-	IRIS					10/01/91	0.002	1000	1	L	07/01/91					1000*	Non-cancer*	1000	Non-cancer
606-20-2	Dinitrotoluene, 2,6-	IRIS												0.68	B2	09/01/90	10000*	Cancer*	10000	Cancer
121-14-2	Dinitrotoluene, 2,4-	IRIS					03/01/91	0.002	100	1	H	04/01/93					1000*	Non-cancer*	1000	Non-cancer
123-91-1	Dioxane, 1,4-	IRIS												0.011	B2	09/01/90	100*	Cancer*	100	Cancer
957-51-7	Diphenamid	IRIS						0.03	100	1	M	03/01/91					100*	Non-cancer*	100	Non-cancer
122-39-4	Diphenylamine	IRIS						0.025	100	1	M	04/01/93				07/01/92	100*	Non-cancer*	100	Non-cancer
122-66-7	Diphenylhydrazine, 1,2-	IRIS					11/01/91						0.00022	0.8	B2	01/01/91	10000	Cancer	10000	Cancer
330-54-1	Diuron	IRIS						0.002	300	1	L	08/22/88					1000*	Non-cancer*	1000	Non-cancer
2439-10-3	Dodine (Dodecylguanidine monoacetate)	IRIS						0.004	300	1	L	09/01/90					1000*	Non-cancer*	1000	Non-cancer
106-89-8	Epichlorohydrin	IRIS	0.001	300	1	M	04/01/92		0	0		04/01/92	1.2e-06	0.0099	B2	02/01/94	10000	Non-cancer	100	Cancer
110-80-5	Ethoxyethanol, 2-	IRIS	0.2	300	1	M	05/01/91										10	Non-cancer	10*	Non-cancer*

Table A-1. Toxicity Weights for All Scored TRI Chemicals and Chemical Categories, in Alphabetical Order

CAS No.	Chemical Name	Source[1]	Non-Cancer										Cancer				Overall Toxicity Weights			
		IRIS, HEAST or Derived[2]	Reference Concentration (mg/m^3)					Reference Dose (mg/kg-d)					Inhalation Unit Risk (Risk per mg/m^3)	Oral Slope Factor (risk per mg/kg-d)	WOE[3]	Listing Date	Inhalation		Oral	
			Inhalation	UF[4]	MF[5]	LOC[6]	Listing Date	Oral	UF[4]	MF[5]	LOC[6]	Listing Date					Weight	Effect[7]	Weight	Effect[7]
759-94-4	Ethyl dipropylthiocarbamate (EPTC)	IRIS						0.025	100	1	M	09/01/90					100*	Non-cancer*	100	Non-cancer
140-88-5	Ethyl acrylate	HEAST												0.048	B2		100*	Cancer*	100	Cancer
100-41-4	Ethylbenzene	IRIS	1	300	1	L	03/01/91	0.1	1000	1	L	06/01/91			D	08/01/91	10	Non-cancer	10	Non-cancer
74-85-1	Ethylene	final derived															1	Cancer	1*	Cancer*
75-21-8	Ethylene oxide	HEAST												1.02	B1		10000*	Cancer*	10000	Cancer
107-21-1	Ethylene glycol	IRIS						2	100	1	H	09/01/89					1*	Non-cancer*	1	Non-cancer
96-45-7	Ethylene thiourea	IRIS					09/01/92	8e-05	3000	1	M	11/01/96				09/01/93	10000*	Non-cancer*	10000	Non-cancer
39515-41-8	Fenpropathrin (2,2,3,3-Tetramethylcyclopropane carboxylicacid cyano(3-phenoxyphenyl)methylester)	IRIS						0.025	100	1	H	10/01/94					100*	Non-cancer*	100	Non-cancer
51630-58-1	Fenvalerate (4-Chloro-alpha-(1-methylethyl)benzene acetic acid cyano(3-phenoxyphenyl)methyl ester)	IRIS						0.025	100	1	H	01/01/92					100*	Non-cancer*	100	Non-cancer
2164-17-2	Fluometuron	IRIS						0.013	1000	1	L	09/01/90					100*	Non-cancer*	100	Non-cancer

Table A-1. Toxicity Weights for All Scored TRI Chemicals and Chemical Categories, in Alphabetical Order

CAS No.	Chemical Name	Source[1]	Non-Cancer										Cancer				Overall Toxicity Weights			
		IRIS, HEAST or Derived[2]	Reference Concentration (mg/m^3)					Reference Dose (mg/kg-d)					Inhalation Unit Risk (Risk per mg/m^3)	Oral Slope Factor (risk per mg/kg-d)	WOE[3]	Listing Date	Inhalation		Oral	
			Inhalation	UF[4]	MF[5]	LOC[6]	Listing Date	Oral	UF[4]	MF[5]	LOC[6]	Listing Date					Weight	Effect[7]	Weight	Effect[7]
7782-41-4	Fluorine	IRIS						0.06	1	1	H	06/01/89					10*	Non-cancer*	10	Non-cancer
69409-94-5	Fluvalinate (N-[2-Chloro-4-(trifluoromethyl)phenyl]-DL-valine(+)-cyano (3-phenoxyphenyl)methyl ester)	IRIS						0.01	100	1	H	03/01/91					100*	Non-cancer*	100	Non-cancer
133-07-3	Folpet	IRIS						0.1	100	1	H	03/01/91		0.0035	B2	10/01/93	10*	Both*	10	Both
72178-02-0	Fomesafen (5-(2-Chloro-4-(trifluoromethyl)phenoxy)-Nmethylsulfonyl)-2-nitrobenzamide)	IRIS												0.19	C	10/01/93	100*	Cancer*	100	Cancer
50-00-0	Formaldehyde	IRIS						0.2	100	1	M	09/01/90	1.3e-05		B1	05/01/91	100	Cancer	10	Non-cancer
64-18-6	Formic acid	HEAST						2	100								1*	Non-cancer*	1	Non-cancer
76-13-1	Freon 113	IRIS						30	10	1	L	02/01/96					1*	Non-cancer*	1	Non-cancer
76-44-8	Heptachlor	IRIS						0.0005	300	1	L	03/01/91	0.0013	4.5	B2	07/01/93	10000	Cancer	10000	Both
87-68-3	Hexachloro-1,3-butadiene	IRIS							0	0		05/01/93	2.2e-05	0.078	C	04/01/91	100	Cancer	100	Cancer
118-74-1	Hexachlorobenzene	IRIS					03/01/91	0.0008	100	1	M	04/01/91	0.00046	1.6	B2	11/01/96	10000	Cancer	10000	Cancer

Table A-1. Toxicity Weights for All Scored TRI Chemicals and Chemical Categories, in Alphabetical Order

CAS No.	Chemical Name	Source[1]	Non-Cancer										Cancer				Overall Toxicity Weights			
		IRIS, HEAST or Derived[2]	Reference Concentration (mg/m^3)					Reference Dose (mg/kg-d)					Inhalation Unit Risk (Risk per mg/m^3)	Oral Slope Factor (risk per mg/kg-d)	WOE[3]	Listing Date	Inhalation		Oral	
			Inhalation	UF[4]	MF[5]	LOC[6]	Listing Date	Oral	UF[4]	MF[5]	LOC[6]	Listing Date					Weight	Effect[7]	Weight	Effect[7]
77-47-4	Hexachlorocyclopentadiene	IRIS						0.007	1000	1	L	09/01/90			D	09/01/90	100*	Non-cancer*	100	Non-cancer
67-72-1	Hexachloroethane	IRIS					12/01/92	0.001	1000	1	M	04/01/91	4e-06	0.014	C	02/01/94	10	Cancer	1000	Non-cancer
70-30-4	Hexachlorophene	IRIS						0.0003	3000	1	M	04/01/91					10000*	Non-cancer*	10000	Non-cancer
51235-04-2	Hexazinone	IRIS						0.033	300	1	M	09/01/90					100*	Non-cancer*	100	Non-cancer
67485-29-4	Hydramethylnon (Tetrahydro-5,5-dimethyl-2(1H)-pyrimidinone[3-[4-(trifluoromethyl)phenyl]-1-[2-[4-(trifluoromet	IRIS						0.0003	1000	1	H	09/30/87					10000*	Non-cancer*	10000	Non-cancer
302-01-2	Hydrazine	IRIS											0.0049	3	B2	04/01/91	100000	Cancer	10000	Cancer
7647-01-0	Hydrochloric acid	IRIS	0.02	300	1	L	07/01/95										100	Non-cancer	100*	Non-cancer*
74-90-8	Hydrogen cyanide	IRIS	0.003	1000	1	L	11/01/94	0.02	100	5	M	02/01/93					1000	Non-cancer	100	Non-cancer
123-31-9	Hydroquinone	HEAST						0.04	100								100*	Non-cancer*	100	Non-cancer
35554-44-0	Imazalil (1-[2-(2,4-Dichlorophenyl)-2-(2-propenyloxy)ethyl]-1H-imidazole)	IRIS						0.013	100	1	M	09/01/90					100*	Non-cancer*	100	Non-cancer

Table A-1. Toxicity Weights for All Scored TRI Chemicals and Chemical Categories, in Alphabetical Order

CAS No.	Chemical Name	Source[1]	Non-Cancer										Cancer				Overall Toxicity Weights			
		IRIS, HEAST or Derived[2]	Reference Concentration (mg/m^3)					Reference Dose (mg/kg-d)					Inhalation Unit Risk (Risk per mg/m^3)	Oral Slope Factor (risk per mg/kg-d)	WOE[3]	Listing Date	Inhalation		Oral	
			Inhalation	UF[4]	MF[5]	LOC[6]	Listing Date	Oral	UF[4]	MF[5]	LOC[6]	Listing Date					Weight	Effect[7]	Weight	Effect[7]
78-84-2	Isobutyraldehyde	interim derived															100000	Non-cancer	100000*	Non-cancer*
67-63-0	Isopropyl alcohol	interim derived															0	Non-cancer	0	Non-cancer
80-05-7	Isopropylidenediphenol, 4,4'-	IRIS						0.05	1000	1	H	07/01/93					100*	Non-cancer*	100	Non-cancer
77501-63-4	Lactofen (5-(2-Chloro-4-(trifluoromethyl)phenoxy)-2-nitro-2-ethoxy-1-methyl-2-oxoethyl ester)	IRIS						0.002	1000	1	H	04/01/91					1000*	Non-cancer*	1000	Non-cancer
N420	Lead compounds	interim derived															100000	Cancer	100000	Cancer
7439-92-1	Lead	interim derived															100000	Cancer	100000	Cancer
58-89-9	Lindane	IRIS					07/01/92	0.0003	1000	1	M	03/01/88				10/01/93	10000*	Non-cancer*	10000	Non-cancer
330-55-2	Linuron	IRIS						0.002	300	1	H	08/01/90			C	10/01/93	1000*	Non-cancer*	1000	Non-cancer
108-39-4	m-Cresol	IRIS					04/01/92	0.05	1000	1	M	09/01/90			C	08/01/91	100*	Non-cancer*	100	Non-cancer
99-65-0	m-Dinitrobenzene	IRIS						0.0001	3000	1	L	08/22/88			D	02/01/93	10000*	Non-cancer*	10000	Non-cancer
108-38-3	m-Xylene	HEAST						2	100								1*	Non-cancer*	1	Non-cancer

Table A-1. Toxicity Weights for All Scored TRI Chemicals and Chemical Categories, in Alphabetical Order

CAS No.	Chemical Name	Source[1]	Non-Cancer										Cancer				Overall Toxicity Weights			
		IRIS, HEAST or Derived[2]	Reference Concentration (mg/m^3)					Reference Dose (mg/kg-d)					Inhalation Unit Risk (Risk per mg/m^3)	Oral Slope Factor (risk per mg/kg-d)	WOE[3]	Listing Date	Inhalation		Oral	
			Inhalation	UF[4]	MF[5]	LOC[6]	Listing Date	Oral	UF[4]	MF[5]	LOC[6]	Listing Date					Weight	Effect[7]	Weight	Effect[7]
121-75-5	Malathion	IRIS					08/01/91	0.02	10	1	M	01/01/92					100*	Non-cancer*	100	Non-cancer
108-31-6	Maleic anhydride	IRIS						0.1	100	1	M	07/01/93					10*	Non-cancer*	10	Non-cancer
109-77-3	Malonitrile	HEAST						2e-05	10000								100000*	Non-cancer*	100000	Non-cancer
12427-38-2	Maneb	IRIS						0.005	1000	1	L	01/01/92					1000*	Non-cancer*	1000	Non-cancer
N450	Manganese compounds	IRIS	0.00005	1000	1	M	12/01/93	0.14	1	1	M	05/01/96			D	12/01/96	100000	Non-cancer	10	Non-cancer
7439-96-5	Manganese	IRIS	0.00005	1000	1	M	12/01/93	0.14	1	1	M	05/01/96			D	12/01/96	100000	Non-cancer	10	Non-cancer
93-65-2	Mecoprop	IRIS						0.001	3000	1	M	08/01/90					1000*	Non-cancer*	1000	Non-cancer
7439-97-6	Mercury	IRIS	0.0003	30	1	M	06/01/95								D	05/01/95	10000	Non-cancer	10000*	Non-cancer*
N458	Mercury compounds	IRIS	0.0003	30	1	M	06/01/95								D	05/01/95	10000	Non-cancer	10000*	Non-cancer*
150-50-5	Merphos	IRIS					11/01/92	3e-05	3000	1	L	04/01/91					100000*	Non-cancer*	100000	Non-cancer
126-98-7	Methacryonitrile	IRIS						0.0001	3000	1	L	02/01/96					10000*	Non-cancer*	10000	Non-cancer
67-56-1	Methanol	IRIS						0.5	1000	1	M	07/01/93					10*	Non-cancer*	10	Non-cancer

Table A-1. Toxicity Weights for All Scored TRI Chemicals and Chemical Categories, in Alphabetical Order

CAS No.	Chemical Name	Source[1]	Non-Cancer										Cancer				Overall Toxicity Weights			
		IRIS, HEAST or Derived[2]	Reference Concentration (mg/m^3)					Reference Dose (mg/kg-d)					Inhalation Unit Risk (Risk per mg/m^3)	Oral Slope Factor (risk per mg/kg-d)	WOE[3]	Listing Date	Inhalation		Oral	
			Inhalation	UF[4]	MF[5]	LOC[6]	Listing Date	Oral	UF[4]	MF[5]	LOC[6]	Listing Date					Weight	Effect[7]	Weight	Effect[7]
94-74-6	Methoxone ((4-Chloro-2-methylphenoxy)acetic acid) (MCPA)	IRIS						0.0005	300	1	M	01/01/91					10000*	Non-cancer*	10000	Non-cancer
72-43-5	Methoxychlor	IRIS					12/01/93	0.005	1000	1	L	08/01/91			D	10/01/90	1000*	Non-cancer*	1000	Non-cancer
109-86-4	Methoxyethanol, 2-	IRIS	0.02	1000	1	M	05/01/91					04/01/92					100	Non-cancer	100*	Non-cancer*
1634-04-4	Methyl tert-butyl ether	IRIS	3	100	1	M	09/01/93					03/01/93					1	Non-cancer	1*	Non-cancer*
78-93-3	Methyl ethyl ketone	IRIS	1	1000	3	L	08/01/92	0.6	3000	1	L	05/01/93			D	06/01/93	10	Non-cancer	1	Non-cancer
74-88-4	Methyl iodide	interim derived															1000*	Cancer*	1000	Cancer
96-33-3	Methyl acrylate	HEAST						0.03	100								100*	Non-cancer*	100	Non-cancer
108-10-1	Methyl isobutyl ketone	HEAST						0.08	3000								10*	Non-cancer*	10	Non-cancer
80-62-6	Methyl methacrylate	HEAST						0.08	100								10*	Non-cancer*	10	Non-cancer
624-83-9	Methyl isocyanate	final derived															100000	Non-cancer	100000*	Non-cancer*
298-00-0	Methyl parathion	IRIS						0.00025	100	1	M	03/01/91					10000*	Non-cancer*	10000	Non-cancer
74-95-3	Methylene bromide	HEAST						0.01	1000								100*	Non-cancer*	100	Non-cancer

Table A-1. Toxicity Weights for All Scored TRI Chemicals and Chemical Categories, in Alphabetical Order

CAS No.	Chemical Name	Source[1]	Non-Cancer										Cancer				Overall Toxicity Weights			
		IRIS, HEAST or Derived[2]	Reference Concentration (mg/m^3)					Reference Dose (mg/kg-d)					Inhalation Unit Risk (Risk per mg/m^3)	Oral Slope Factor (risk per mg/kg-d)	WOE[3]	Listing Date	Inhalation		Oral	
			Inhalation	UF[4]	MF[5]	LOC[6]	Listing Date	Oral	UF[4]	MF[5]	LOC[6]	Listing Date					Weight	Effect[7]	Weight	Effect[7]
101-14-4	Methylenebis(2-chloroaniline), 4,4'-	HEAST						0.0007	10000				3.7e-05	0.13	B2		1000	Cancer	1000	Both
101-61-1	Methylenebis(N,N-dimethylbenzenamine), 4,4'-	IRIS												0.046	B2	07/01/93	100*	Cancer*	100	Cancer
21087-64-9	Metribuzin	IRIS						0.025	100	1	M	01/01/95			D	12/01/96	100*	Non-cancer*	100	Non-cancer
90-94-8	Michlers Ketone	final derived															1000*	Cancer*	1000	Cancer
2212-67-1	Molinate (1H-Azepine-1 carbothioicacid, hexahydro-S-ethyl ester)	IRIS						0.002	100	1	L	02/01/91					1000*	Non-cancer*	1000	Non-cancer
1313-27-5	Molybdenum trioxide	interim derived															10000	Non-cancer	1000	Non-cancer
88671-89-0	Myclobutanil (.alpha.-Butyl-.alpha.-(4-chlorophenyl)-1H-1,2,4-triazole-1-propanenitrile)	IRIS						0.025	100	1	H	01/01/95					100*	Non-cancer*	100	Non-cancer
68-12-2	N,N-Dimethylformamide	IRIS	0.03	300	1	M	10/01/90										100	Non-cancer	100*	Non-cancer*
121-69-7	N,N-Dimethylaniline	IRIS						0.002	10000	1	L	03/01/88					1000*	Non-cancer*	1000	Non-cancer
71-36-3	n-Butyl alcohol	IRIS						0.1	1000	1	L	09/01/90			D	03/01/91	10*	Non-cancer*	10	Non-cancer

Table A-1. Toxicity Weights for All Scored TRI Chemicals and Chemical Categories, in Alphabetical Order

CAS No.	Chemical Name	Source[1]	Non-Cancer										Cancer				Overall Toxicity Weights			
		IRIS, HEAST or Derived[2]	Reference Concentration (mg/m^3)					Reference Dose (mg/kg-d)					Inhalation Unit Risk (Risk per mg/m^3)	Oral Slope Factor (risk per mg/kg-d)	WOE[3]	Listing Date	Inhalation		Oral	
			Inhalation	UF[4]	MF[5]	LOC[6]	Listing Date	Oral	UF[4]	MF[5]	LOC[6]	Listing Date					Weight	Effect[7]	Weight	Effect[7]
110-54-3	n-Hexane	IRIS	0.2	300	1	M	07/01/93									09/01/91	10	Non-cancer	10*	Non-cancer*
759-73-9	N-Nitroso-N-ethylurea	HEAST												140	B2		1000000*	Cancer*	1000000	Cancer
924-16-3	N-Nitrosodi-n-butylamine	IRIS											0.0016	5.4	B2	07/01/93	100000	Cancer	100000	Cancer
621-64-7	N-Nitrosodi-n-propylamine	IRIS												7	B2	07/01/93	100000*	Cancer*	100000	Cancer
55-18-5	N-Nitrosodiethylamine	IRIS											0.043	150	B2	07/01/93	1000000	Cancer	1000000	Cancer
62-75-9	N-Nitrosodimethylamine	IRIS					09/01/92						0.014	51	B2	07/01/93	100000	Cancer	1000000	Cancer
86-30-6	N-Nitrosodiphenylamine	IRIS												0.0049	B2	07/01/93	10*	Cancer*	10	Cancer
300-76-5	Naled	IRIS						0.002	100	1	M	01/01/95					1000*	Non-cancer*	1000	Non-cancer
No CASRNa	Nitrate compounds (water dissociable)	IRIS						1.6	1	1	H	10/01/1901					1*	Non-cancer*	1	Non-cancer
7697-37-2	Nitric acid	final derived															100	Non-cancer	100*	Non-cancer*
139-13-9	Nitrilotriacetic acid	interim derived															100*	Cancer*	100	Cancer
99-59-2	Nitro-o-anisidine, 5-	HEAST												0.046	B2		100*	Cancer*	100	Cancer
99-55-8	Nitro-o-toluidine	HEAST												0.046	B2		100*	Cancer*	100	Cancer

Table A-1. Toxicity Weights for All Scored TRI Chemicals and Chemical Categories, in Alphabetical Order

CAS No.	Chemical Name	Source[1]	Non-Cancer										Cancer				Overall Toxicity Weights			
		IRIS, HEAST or Derived[2]	Reference Concentration (mg/m^3)					Reference Dose (mg/kg-d)					Inhalation Unit Risk (Risk per mg/m^3)	Oral Slope Factor (risk per mg/kg-d)	WOE[3]	Listing Date	Inhalation		Oral	
			Inhalation	UF[4]	MF[5]	LOC[6]	Listing Date	Oral	UF[4]	MF[5]	LOC[6]	Listing Date					Weight	Effect[7]	Weight	Effect[7]
98-95-3	Nitrobenzene	IRIS						0.0005	10000	1	L	01/01/91			D	02/01/95	10000*	Non-cancer*	10000	Non-cancer
55-63-0	Nitroglycerin	interim derived															10000*	Cancer*	10000	Cancer
100-02-7	Nitrophenol, 4-	final derived															1000	Non-cancer	1000	Non-cancer
79-46-9	Nitropropane, 2-	IRIS	0.02	1000	1	L	03/01/91										100	Non-cancer	100*	Non-cancer*
27314-13-2	Norflurazon (4-Chloro-5-(methylamino)-2-[3-(trifluoromethyl)phenyl]-3(2H)-pyridazinone)	IRIS						0.04	100	1	H	04/01/91					100*	Non-cancer*	100	Non-cancer
90-04-0	o-Anisidine	interim derived															10000	Non-cancer	1000	Non-cancer
95-48-7	o-Cresol	IRIS					04/01/92	0.05	1000	1	M	09/01/90			C	08/01/91	100*	Non-cancer*	100	Non-cancer
528-29-0	o-Dinitrobenzene	HEAST						0.0004	1000								10000*	Non-cancer*	10000	Non-cancer
95-53-4	o-Toluidine	HEAST												0.24	B2		1000*	Cancer*	1000	Cancer
636-21-5	o-Toluidine hydrochloride	HEAST												0.18	B2		1000*	Cancer*	1000	Cancer
95-47-6	o-Xylene	HEAST						2	100								1*	Non-cancer*	1	Non-cancer

Table A-1. Toxicity Weights for All Scored TRI Chemicals and Chemical Categories, in Alphabetical Order

CAS No.	Chemical Name	Source[1]	Non-Cancer										Cancer				Overall Toxicity Weights			
		IRIS, HEAST or Derived[2]	Reference Concentration (mg/m^3)					Reference Dose (mg/kg-d)					Inhalation Unit Risk (Risk per mg/m^3)	Oral Slope Factor (risk per mg/kg-d)	WOE[3]	Listing Date	Inhalation		Oral	
			Inhalation	UF[4]	MF[5]	LOC[6]	Listing Date	Oral	UF[4]	MF[5]	LOC[6]	Listing Date					Weight	Effect[7]	Weight	Effect[7]
19044-88-3	Oryzalin (4-(Dipropylamino)-3,5-dinitrobenzenesulfonamide)	IRIS						0.05	100	1	H	02/01/91			C	10/01/93	100*	Non-cancer*	100	Non-cancer
19666-30-9	Oxydiazon (3-[2,4-Dichloro-5-(1-methylethoxy)phenyl]-5-(1,1-dimethylethyl)-1,3,4-oxadiazol-2(3H)-one)	IRIS						0.005	100	1	M	03/01/91					1000*	Non-cancer*	1000	Non-cancer
42874-03-3	Oxyfluorfen	IRIS						0.003	100	1	H	03/01/91					1000*	Non-cancer*	1000	Non-cancer
106-47-8	p-Chloroaniline	IRIS						0.004	3000	1	L	02/01/95					1000*	Non-cancer*	1000	Non-cancer
120-71-8	p-Cresidine	interim derived															1000*	Cancer*	1000	Cancer
106-44-5	p-Cresol	HEAST						0.005	1000								1000*	Non-cancer*	1000	Non-cancer
100-25-4	p-Dinitrobenzene	HEAST						0.0004	1000								10000*	Non-cancer*	10000	Non-cancer
106-50-3	p-Phenylenediamine	HEAST						0.19	100								10*	Non-cancer*	10	Non-cancer
1910-42-5	Paraquat dichloride	IRIS						0.0045	100	1	H	02/01/91			C	10/01/93	1000*	Non-cancer*	1000	Non-cancer
56-38-2	Parathion	HEAST						0.006	10								100*	Non-cancer*	100	Non-cancer

Table A-1. Toxicity Weights for All Scored TRI Chemicals and Chemical Categories, in Alphabetical Order

CAS No.	Chemical Name	Source[1]	Non-Cancer										Cancer				Overall Toxicity Weights			
		IRIS, HEAST or Derived[2]	Reference Concentration (mg/m^3)					Reference Dose (mg/kg-d)					Inhalation Unit Risk (Risk per mg/m^3)	Oral Slope Factor (risk per mg/kg-d)	WOE[3]	Listing Date	Inhalation		Oral	
			Inhalation	UF[4]	MF[5]	LOC[6]	Listing Date	Oral	UF[4]	MF[5]	LOC[6]	Listing Date					Weight	Effect[7]	Weight	Effect[7]
40487-42-1	Pendimethalin (N-(1-Ethylpropyl)-3,4-dimethyl-2,6-dinitrobenzenamine)	IRIS						0.04	300	1	M	02/01/91					100*	Non-cancer*	100	Non-cancer
87-86-5	Pentachlorophenol	IRIS						0.03	100	1	M	02/01/93		0.12	B2	07/01/93	1000*	Cancer*	1000	Cancer
79-21-0	Peracetic acid	interim derived															1000	Non-cancer	1000*	Non-cancer*
52645-53-1	Permethrin (3-(2,2-Dichloroethenyl)-2,2-dimethylcyclopropanecarboxylic acid,(3-phenoxyphenyl)methyl ester)	IRIS						0.05	100	1	H	01/01/92					100*	Non-cancer*	100	Non-cancer
108-95-2	Phenol	IRIS					03/01/91	0.6	100	1	L	02/01/90			D	11/01/90	1*	Non-cancer*	1	Non-cancer
108-45-2	Phenylenediamine, 1,3-	IRIS						0.006	1000	1	L	08/01/91					100*	Non-cancer*	100	Non-cancer
90-43-7	Phenylphenol, 2-	HEAST												0.00194	C		1*	Cancer*	1	Cancer
7803-51-2	Phosphine	IRIS	0.0003	1000	1	L	07/01/95	0.0003	100	1	M	12/01/93			D	12/01/96	10000	Non-cancer	10000	Non-cancer
7664-38-2	Phosphoric acid	IRIS, derived	0.01	300	1	M	08/01/95										1000	Non-cancer	1	Non-cancer
7723-14-0	Phosphorus (yellow or white)	IRIS					11/01/93	2e-05	1000	1	L	02/01/93			D	07/01/93	100000*	Non-cancer*	100000	Non-cancer
85-44-9	Phthalic anhydride	IRIS						2	1000	1	M	09/07/88				05/01/92	1*	Non-cancer*	1	Non-cancer

Table A-1. Toxicity Weights for All Scored TRI Chemicals and Chemical Categories, in Alphabetical Order

CAS No.	Chemical Name	Source[1]	Non-Cancer										Cancer				Overall Toxicity Weights			
		IRIS, HEAST or Derived[2]	Reference Concentration (mg/m^3)					Reference Dose (mg/kg-d)					Inhalation Unit Risk (Risk per mg/m^3)	Oral Slope Factor (risk per mg/kg-d)	WOE[3]	Listing Date	Inhalation		Oral	
			Inhalation	UF[4]	MF[5]	LOC[6]	Listing Date	Oral	UF[4]	MF[5]	LOC[6]	Listing Date					Weight	Effect[7]	Weight	Effect[7]
1918-02-1	Picloram	IRIS						0.07	100	1	M	05/01/92					10*	Non-cancer*	10	Non-cancer
88-89-1	Picric acid	final derived															10000	Non-cancer	10000	Non-cancer
29232-93-7	Pirimiphos methyl (O-(2-(Diethylamino)-6-methyl-4-pyrimidinyl)-O,O-dimethylphosphorothioate)	IRIS						0.01	25	1	H	01/01/92					100*	Non-cancer*	100	Non-cancer
N575	Polybrominated Biphenyls (PBBs)	HEAST						7e-06	10000					8.9	B2		100000*	Both*	100000	Both
1336-36-3	Polychlorinated biphenyls	IRIS						2e-05	300	1	m	11/01/96	0.0001	2	B2	11/01/96	1000	Cancer	100000	Non-cancer
7287-19-6	Prometryn (N,N'-Bis(1-methylethyl)-6-methylthio-1,3,5-triazine-2,4-diamine)	IRIS						0.004	1000	1	L	07/01/92					1000*	Non-cancer*	1000	Non-cancer
23950-58-5	Pronamide	IRIS						0.075	100	1	M	01/01/94					10*	Non-cancer*	10	Non-cancer
1918-16-7	Propachlor (2-Chloro-N-(1-methylethyl)-N-phenylacetamide)	IRIS						0.013	1000	1	L	01/01/92					100*	Non-cancer*	100	Non-cancer
709-98-8	Propanil (N-(3,4-Dichlorophenyl)propanamide)	IRIS						0.005	1000	1	M	01/01/92					1000*	Non-cancer*	1000	Non-cancer

Table A-1. Toxicity Weights for All Scored TRI Chemicals and Chemical Categories, in Alphabetical Order

CAS No.	Chemical Name	Source[1]	Non-Cancer										Cancer				Overall Toxicity Weights			
		IRIS, HEAST or Derived[2]	Reference Concentration (mg/m^3)					Reference Dose (mg/kg-d)					Inhalation Unit Risk (Risk per mg/m^3)	Oral Slope Factor (risk per mg/kg-d)	WOE[3]	Listing Date	Inhalation		Oral	
			Inhalation	UF[4]	MF[5]	LOC[6]	Listing Date	Oral	UF[4]	MF[5]	LOC[6]	Listing Date					Weight	Effect[7]	Weight	Effect[7]
2312-35-8	Propargite	IRIS						0.02	1000	1	M	05/01/90					100*	Non-cancer*	100	Non-cancer
107-19-7	Propargyl alcohol	IRIS						0.002	3000	1	L	01/01/94					1000*	Non-cancer*	1000	Non-cancer
60207-90-1	Propiconazole (1-[2-(2,4-Dichlorophenyl)-4-propyl-1,3-dioxolan-2-yl]-methyl-1H-1,2,4,-triazole)	IRIS						0.013	100	1	H	01/01/92					100*	Non-cancer*	100	Non-cancer
114-26-1	Propoxur	IRIS						0.004	100	1	M	07/01/92					1000*	Non-cancer*	1000	Non-cancer
75-56-9	Propylene oxide	IRIS	0.03	100	1	M	11/01/90						3.7e-06	0.24	B2	04/01/94	100	Both	1000	Cancer
115-07-1	Propylene (Propene)	final derived															1	Non-cancer	1*	Non-cancer*
75-55-8	Propyleneimine	final derived															1000000*	Cancer*	1000000	Cancer
110-86-1	Pyridine	IRIS						0.001	1000	1	M	06/01/89					1000*	Non-cancer*	1000	Non-cancer
91-22-5	Quinoline	HEAST												12	C		10000*	Cancer*	10000	Cancer
82-68-8	Quintozene	IRIS						0.003	300	1	M	04/01/92					1000*	Non-cancer*	1000	Non-cancer
76578-14-8	Quizalofop-ethyl (2-[4-[(6-Chloro-2-quinoxalinyl)oxy]phenoxy] propanoicacid ethyl ester)	IRIS						0.009	100	1	H	09/26/88			D	10/01/93	100*	Non-cancer*	100	Non-cancer

Table A-1. Toxicity Weights for All Scored TRI Chemicals and Chemical Categories, in Alphabetical Order

CAS No.	Chemical Name	Source[1]	Non-Cancer										Cancer				Overall Toxicity Weights			
		IRIS, HEAST or Derived[2]	Reference Concentration (mg/m^3)					Reference Dose (mg/kg-d)					Inhalation Unit Risk (Risk per mg/m^3)	Oral Slope Factor (risk per mg/kg-d)	WOE[3]	Listing Date	Inhalation		Oral	
			Inhalation	UF[4]	MF[5]	LOC[6]	Listing Date	Oral	UF[4]	MF[5]	LOC[6]	Listing Date					Weight	Effect[7]	Weight	Effect[7]
10453-86-8	Resmethrin ([5-(Phenylmethyl)-3-furanyl]methyl 2,2-dimethyl-3-(2-methyl-1-propenyl)cyclopropanecarboxylate])	IRIS						0.03	1000	1	H	09/26/88					100*	Non-cancer*	100	Non-cancer
7782-49-2	Selenium	IRIS						0.005	3	1	H	09/01/91			D	07/01/93	1000*	Non-cancer*	1000	Non-cancer
N725	Selenium compounds	IRIS						0.005	3	1	H	09/01/91			D	07/01/93	1000*	Non-cancer*	1000	Non-cancer
74051-80-2	Sethoxydim (2-[1-(Ethoxyimino)butyl]-5-[2-(ethylthio)propyl]-3-hydroxyl-2-cyclohexen-1-one)	IRIS						0.09	100	1	H	11/01/89					10*	Non-cancer*	10	Non-cancer
N740	Silver compounds	IRIS						0.005	3	1	L	12/01/96			D	06/01/89	1000*	Non-cancer*	1000	Non-cancer
7440-22-4	Silver	IRIS						0.005	3	1	L	12/01/96			D	06/01/89	1000*	Non-cancer*	1000	Non-cancer
122-34-9	Simazine	IRIS						0.005	100	1	H	09/01/93					1000*	Non-cancer*	1000	Non-cancer
62-74-8	Sodium fluoroacetate	IRIS						2e-05	3000	1	L	07/01/93					100000*	Non-cancer*	100000	Non-cancer
26628-22-8	Sodium azide	IRIS						0.004	1000	1	M	03/01/88					1000*	Non-cancer*	1000	Non-cancer
No CASRNb	Strychnine and salts	IRIS						0.0003	10000	1	L	03/01/88					10000*	Non-cancer*	10000	Non-cancer

Table A-1. Toxicity Weights for All Scored TRI Chemicals and Chemical Categories, in Alphabetical Order

CAS No.	Chemical Name	Source[1]	Non-Cancer										Cancer				Overall Toxicity Weights			
		IRIS, HEAST or Derived[2]	Reference Concentration (mg/m^3)					Reference Dose (mg/kg-d)					Inhalation Unit Risk (Risk per mg/m^3)	Oral Slope Factor (risk per mg/kg-d)	WOE[3]	Listing Date	Inhalation		Oral	
			Inhalation	UF[4]	MF[5]	LOC[6]	Listing Date	Oral	UF[4]	MF[5]	LOC[6]	Listing Date					Weight	Effect[7]	Weight	Effect[7]
100-42-5	Styrene	IRIS	1	30	1	M	07/01/93	0.2	1000	1	M	09/01/90					10	Non-cancer	10	Non-cancer
7664-93-9	Sulfuric acid	final derived															10000	Non-cancer	1	Non-cancer
34014-18-1	Tebuthiuron (N-[5-(1,1-Dimethylethyl)-1,3,4-thiadiazol-2-yl)- N,N'-dimethylurea)	IRIS						0.07	100	1	H	07/01/92					10*	Non-cancer*	10	Non-cancer
5902-51-2	Terbacil (5-Chloro-3-(1,1-dimethylethyl)-6-methyl- 2,4 (1H,3H)-pyrimidinedione)	IRIS						0.013	100	1	M	09/01/89					100*	Non-cancer*	100	Non-cancer
630-20-6	Tetrachloroethane, 1,1,1,2-	IRIS						0.03	3000	1	L	12/01/96	7.4e-06	0.026	C	01/01/91	10	Cancer	100	Non-cancer
79-34-5	Tetrachloroethane, 1,1,2,2-	IRIS											5.8e-05	0.2	C	02/01/94	100	Cancer	100	Cancer
127-18-4	Tetrachloroethylene (Perchlorethyle	IRIS						0.01	1000	1	M	03/01/88					100*	Non-cancer*	100	Non-cancer
961-11-5	Tetrachlorvinphos	IRIS						0.03	100	1	M	01/01/92					100*	Non-cancer*	100	Non-cancer
28249-77-6	Thiobencarb (Carbamic acid, diethylthio-, S-(p-chlorobenzyl))	IRIS						0.01	100	1	M	01/01/92					100*	Non-cancer*	100	Non-cancer
23564-05-8	Thiophanate-methyl	IRIS						0.08	100	1	H	01/01/92					10*	Non-cancer*	10	Non-cancer

Table A-1. Toxicity Weights for All Scored TRI Chemicals and Chemical Categories, in Alphabetical Order

CAS No.	Chemical Name	Source[1]	Non-Cancer										Cancer				Overall Toxicity Weights			
		IRIS, HEAST or Derived[2]	Reference Concentration (mg/m^3)					Reference Dose (mg/kg-d)					Inhalation Unit Risk (Risk per mg/m^3)	Oral Slope Factor (risk per mg/kg-d)	WOE[3]	Listing Date	Inhalation		Oral	
			Inhalation	UF[4]	MF[5]	LOC[6]	Listing Date	Oral	UF[4]	MF[5]	LOC[6]	Listing Date					Weight	Effect[7]	Weight	Effect[7]
62-56-6	Thiourea	final derived															10000*	Cancer*	10000	Cancer
137-26-8	Thiram	IRIS						0.005	1000	1	L	07/01/92				09/01/91	1000*	Non-cancer*	1000	Non-cancer
1314-20-1	Thorium dioxide	final derived															10000	Non-cancer	1000000	Cancer
7550-45-0	Titanium tetrachloride	interim derived															100000	Non-cancer	100000*	Non-cancer*
108-88-3	Toluene	IRIS	0.4	300	1	M	08/01/92	0.2	1000	1	M	04/01/94			D	02/01/94	10	Non-cancer	10	Non-cancer
584-84-9	Toluene-2,4-diisocyanate	final derived															100000	Non-cancer	100	Cancer
91-08-7	Toluene-2,6-Diisocyanate	final derived															100000	Non-cancer	100	Cancer
26471-62-5	Toluenediisocyanate	IRIS	0.00007	30	1	M	09/01/95										100000	Non-cancer	100	Non-cancer*
8001-35-2	Toxaphene	IRIS											0.00032	1.1	B2	01/01/91	10000	Cancer	10000	Cancer
43121-43-3	Triadimefon (1-(4-Chlorophenoxy)-3,3-dimethyl-1-(1H-1,2,4-triazol-1-yl)-2-butanone)	IRIS						0.03	100	1	H	03/01/88					100*	Non-cancer*	100	Non-cancer
2303-17-5	Triallate	IRIS						0.013	100	1	H	01/01/92					100*	Non-cancer*	100	Non-cancer

Table A-1. Toxicity Weights for All Scored TRI Chemicals and Chemical Categories, in Alphabetical Order

CAS No.	Chemical Name	Source[1]	Non-Cancer										Cancer				Overall Toxicity Weights			
		IRIS, HEAST or Derived[2]	Reference Concentration (mg/m^3)					Reference Dose (mg/kg-d)					Inhalation Unit Risk (Risk per mg/m^3)	Oral Slope Factor (risk per mg/kg-d)	WOE[3]	Listing Date	Inhalation		Oral	
			Inhalation	UF[4]	MF[5]	LOC[6]	Listing Date	Oral	UF[4]	MF[5]	LOC[6]	Listing Date					Weight	Effect[7]	Weight	Effect[7]
101200-48-0	Tribenuron methyl (2-(4-Methoxy-6-methyl-1,3,5-triazin-2-yl)-methylamino)carbonyl)amino)sulfonyl)-,methyl ester)	IRIS						0.008	100	1	H	04/01/90					100*	Non-cancer*	100	Non-cancer
78-48-8	Tributyltrithiophosphate (DEF), S,S,S-	IRIS					11/01/92	3e-05	3000	1	L	04/01/91					100000*	Non-cancer*	100000	Non-cancer
120-82-1	Trichlorobenzene, 1,2,4-	IRIS					08/01/93	0.01	1000	1	M	11/01/96			D	07/01/93	100*	Non-cancer*	100	Non-cancer
79-00-5	Trichloroethane, 1,1,2-	IRIS					12/01/92	0.004	1000	1	M	02/01/95	1.6e-05	0.057	C	02/01/94	100	Cancer	1000	Non-cancer
95-95-4	Trichlorophenol, 2,4,5-	IRIS					07/01/91	0.1	1000	1	L	03/01/88					10*	Non-cancer*	10	Non-cancer
88-06-2	Trichlorophenol, 2,4,6-	IRIS					07/01/91						3.1e-06	0.011	B2	02/01/94	100	Cancer	100	Cancer
96-18-4	Trichloropropane, 1,2,3-	IRIS						0.006	1000	1	L	08/01/90				11/01/93	100*	Non-cancer*	100	Non-cancer
121-44-8	Triethylamine	IRIS	0.007	3000	1	L	04/01/91									03/01/93	1000	Non-cancer	1000*	Non-cancer*
1582-09-8	Trifluralin	IRIS						0.0075	100	1	H	07/01/89		0.0077	C	10/01/93	100*	Non-cancer*	100	Non-cancer
95-63-6	Trimethylbenzene, 1,2,4	final derived															1000	Non-cancer	1000	Non-cancer
7440-62-2	Vanadium (fume or dust)	HEAST						0.007	100								100*	Non-cancer*	100	Non-cancer

Table A-1. Toxicity Weights for All Scored TRI Chemicals and Chemical Categories, in Alphabetical Order

CAS No.	Chemical Name	Source[1]	Non-Cancer										Cancer				Overall Toxicity Weights			
		IRIS, HEAST or Derived[2]	Reference Concentration (mg/m^3)					Reference Dose (mg/kg-d)					Inhalation Unit Risk (Risk per mg/m^3)	Oral Slope Factor (risk per mg/kg-d)	WOE[3]	Listing Date	Inhalation		Oral	
			Inhalation	UF[4]	MF[5]	LOC[6]	Listing Date	Oral	UF[4]	MF[5]	LOC[6]	Listing Date					Weight	Effect[7]	Weight	Effect[7]
50471-44-8	Vinclozolin (3-(3,5-Dichlorophenyl)-5-ethenyl-5-methyl-2,4-oxazolidinedione)	IRIS						0.025	100	1	H	01/01/92					100*	Non-cancer*	100	Non-cancer
108-05-4	Vinyl acetate	IRIS	0.2	30	1	H	10/01/90										10	Non-cancer	10*	Non-cancer*
593-60-2	Vinyl bromide	IRIS	0.003	3000	1	L	11/01/94										1000	Non-cancer	1000*	Non-cancer*
75-01-4	Vinyl chloride	HEAST												1.9	A		10000*	Cancer*	10000	Cancer
75-35-4	Vinylidene chloride	IRIS						0.009	1000	1	M	04/01/89	5e-05	0.6	C	02/01/91	100	Cancer	1000	Cancer
81-81-2	Warfarin and salts	IRIS						0.0003	100	1	L	03/01/88					10000*	Non-cancer*	10000	Non-cancer
1330-20-7	Xylene (mixed isomers)	IRIS						2	100	1	M	09/30/87			D	03/01/91	1*	Non-cancer*	1	Non-cancer
7440-66-6	Zinc (fume or dust)	IRIS						0.3	3	1	M	10/01/92			D	02/01/91	10*	Non-cancer*	10	Non-cancer
12122-67-7	Zineb	IRIS						0.05	500	1	M	03/01/88					100*	Non-cancer*	100	Non-cancer

*Toxicity weight adopted from the other exposure pathway.

[1]IRIS searches performed April 1997. HEAST values from 1995 Health Effects Assessment Summary Tables.

[2]Derived values are those determined by the Disposition Process. See text.

[3]WOE = weight of evidence. See text.

[4]UF = Uncertainty factors. See text.

[5]MF = Modifying factor. See text.

[6]LOC = Level of confidence. See text.

[7]Types of effects (cancer, non-cancer or both, i.e. either effect has the same toxicity weight).

Appendix B.
Toxicity Information for TRI Chemicals and Chemical Categories with Final Derived Toxicity Weights

Appendix B. Toxicity Information for TRI Chemicals and Chemical Categories with Final Derived Toxicity Weights

B.1. Tables of Toxicity Weights for TRI Chemicals and Chemical Categories with Final Derived Toxicity Values

Appendix B contains summary descriptions of the sources used and the additional calculations required to derive cancer and noncancer toxicity weights pertaining to chronic exposures to TRI chemicals and chemical categories that lack published noncancer RfDs or RfCs and cancer Oral Slope Factors and Inhalation Unit Risks and which have been finalized by the Office of Pollution Prevention and Toxics (OPPT). Table B-1 lists these chemicals in alphabetical order. Table B-2 lists the same chemicals sorted by ascending CAS number. In Section B.2, summary discussions of the relevant toxicological information are ordered alphabetically by chemical name, with the CAS number of each chemical following the chemical name in each section heading. Note that each pathway-specific toxicity weight discussion for both chronic and cancer effects is divided into two subsections: *Basis of toxicity weight* and *Further calculations*. The *Basis of toxicity weight* subsections contain the relevant published dose-response data used to estimate toxicity weights for each chemical. The *Further calculations* subsections contain all the additional data manipulations used in deriving the calculated toxicity weights. The section entitled *Sources* for each discussion provides the relevant references.

All of the toxicity weights contained in Appendix B have been finalized by the OPPT Disposition Process. Interim toxicity weights that have been reviewed but not finalized by the Disposition Process appear in Appendix C. The methods used to calculate the toxicity weights given below are described in Chapters 5 of the TRI Relative Risk-Based Environmental Indicators: Interim Toxicity Weighting Summary Document.

Table B-1. Toxicity Weights for TRI Chemicals and Chemical Categories with Final Derived Toxicity Values, in Alphabetical Order

CAS #	Chemical Name		Toxicity Weight Calculations					Overall Toxicity Weight
			Cancer		Chronic			
			Basis of Weight	Toxicity Weight	Basis of Weight	Critical Effect	Toxicity Weight	
6484-52-2	Ammonium Nitrate	Oral	--	--	RfD of 1.6 mg/kg-d from nitrate	hematological	1	1
		Inhalation	--	--	--	--	--	1*
90-04-0	Anisidine, o-	Oral	cancer potency estimate of 0.80 per mg/kg-d WOE estimate of C	1,000	LOAEL of 41 mg/kg-d	thyroid, kidney, spleen	1,000	1,000
		Inhalation	--	--	--	--	See App. C	10,000
156-62-7	Calcium Cyanamide	Oral	negative 2-yr NTP study	1	LOAEL of 10 mg/kg-d	thyroid	1,000	1,000
		Inhalation	--	--	--	--	--	1,000*
80-15-9	Cumene Hydroperoxide	Oral	--	--	--	--	--	1,000*
		Inhalation	--	--	NOAEL of 2.2 mg/m^3		1,000	1,000
135-20-6	Cupferron	Oral	cancer potency of 0.22 per mg/kg-d WOE estimate of B2	1,000	--	--	--	1,000
		Inhalation	--	--	--	--	--	1,000*

Table B-1. Toxicity Weights for TRI Chemicals and Chemical Categories with Final Derived Toxicity Values, in Alphabetical Order

CAS #	Chemical Name		Toxicity Weight Calculations					Overall Toxicity Weight
			Cancer		Chronic			
			Basis of Weight	Toxicity Weight	Basis of Weight	Critical Effect	Toxicity Weight	
101-80-4	Diaminodiphenyl ether, 4,4-	Oral	cancer potency of 0.14 per mg/kg-d IARC Group 2B	1,000	--	--	--	1,000
		Inhalation	--	--	--	--	--	1,000*
25321-22-6	Dichlorobenzene (mixed isomers)	Oral	cancer potency of 0.024 per mg/kg-d WOE of B2	100	RfD of 0.09 mg/kg-d	renal	10	100
		Inhalation	--	--	--	--	See App. C	10
541-73-1	Dichlorobenzene, 1,3-[a]	Oral	cancer potency of 0.024 per mg/kg-d WOE of B2	100	RfD of 0.09 mg/kg-d	renal	10	100
		Inhalation	--	--	--	--	See App. C	10
64-67-5	Diethyl Sulfate	Oral	cancer potency of 1.2 mg/kg-d IARC Group 2A	10,000	--	--	--	10,000
		Inhalation	--	--	--	--	--	10,000*
74-85-1	Ethylene	Oral	--	--	--	--	--	1*
		Inhalation	negative 2 yr NTP study	1	NOAEL of 3000 ppm	gross and microscopic physiological changes	1	1

Table B-1. Toxicity Weights for TRI Chemicals and Chemical Categories with Final Derived Toxicity Values, in Alphabetical Order

CAS #	Chemical Name		Toxicity Weight Calculations					Overall Toxicity Weight
			Cancer		Chronic			
			Basis of Weight	Toxicity Weight	Basis of Weight	Critical Effect	Toxicity Weight	
624-83-9	Methyl Isocyanate	Oral	--	--	--	--	--	100,000*
		Inhalation	--	--	LOAEL of 1 ppm	developmental	100,000	100,000
90-94-8	Michlers Ketone	Oral	potency factor of 0.86 per mg/kg-d IARC Group 3	1,000	--	--	--	1,000
		Inhalation	--	--	--	--	--	1,000*
91-20-3	Naphthalene	Oral	--	--	--	--	--	1,000*
		Inhalation	--	--	LOAEL of 3.6 mg/kg/day	respiratory	1,000	1,000
7697-37-2	Nitric Acid	Oral	--	--	--	--	--	100*
		Inhalation	--	--	LOAEL of 0.013 mg/L	benign bone lesions	100	100
100-02-7	Nitrophenol, 4-	Oral	--	--	NOAEL of 25 mg/kg-d	early mortality	1,000	1,000
		Inhalation	--	--	NOAEL of 26 mg/m^3	hematological	1,000	1,000
7664-38-2	Phosphoric Acid	Oral	--	--	ADI of 221 mg/kg-d	--	1	1
		Inhalation	--	--	RfC of 0.01 mg/m^3	fibrosis	See App. A.	1000

Table B-1. Toxicity Weights for TRI Chemicals and Chemical Categories with Final Derived Toxicity Values, in Alphabetical Order

CAS #	Chemical Name		Toxicity Weight Calculations					Overall Toxicity Weight
			Cancer		Chronic			
			Basis of Weight	Toxicity Weight	Basis of Weight	Critical Effect	Toxicity Weight	
88-89-1	Picric Acid (2,4,6-Trinitrophenol)	Oral	--	--	RfD of 6×10^{-5} mg/kg-d	renal	10,000	10,000
		Inhalation	--	--	RfD of 3×10^{-4} mg/kg-d	TLV-TWA	10,000	10,000
115-07-1	Propylene (Propene)	Oral	--	--	--	--	--	1*
		Inhalation	--	--	LOAEL of 5,000 ppm	benign nasal lesions	1	1
75-55-8	Propylenimine	Oral	cancer potency of 150 per mg/kg-d WOE of B2	1,000,000	--	--	--	1,000,000
		Inhalation	--	--	--	--	--	1,000,000*
7664-93-9	Sulfuric Acid	Oral			estimated NOAEL of 500 mg/L	laxative effect	1	1
		Inhalation			LOAEL of 0.38 mg/m^3	respiratory	10,000	10,000
62-56-6	Thiourea	Oral	cancer potency of 1.05 per mg/kg-d WOE of B2	10,000	--	--	--	10,000
		Inhalation	--	--	--	--	--	10,000*

Table B-1. Toxicity Weights for TRI Chemicals and Chemical Categories with Final Derived Toxicity Values, in Alphabetical Order

CAS #	Chemical Name		Toxicity Weight Calculations					Overall Toxicity Weight
			Cancer		Chronic			
			Basis of Weight	Toxicity Weight	Basis of Weight	Critical Effect	Toxicity Weight	
1314-20-1	Thorium Dioxide	Oral	qualitative based on human data	1,000,000	--	--	--	1,000,000
		Inhalation	--	--	LOAEL of 10 mg/m^3	hematological	10,000	10,000
71-55-6	Trichloroethane, 1,1,1-	Oral	--	--	LOAEL of 500 mg/kg/day	weight gain reduction	10	10
		Inhalation	--	--	NOAEL of 382 mg/m^3	neurological	10	10
95-63-6	Trimethyl-benzene, 1,2,4-	Oral	--	--	5×10^{-4} mg/kg-d	CNS, respiratory, hematological	1,000	1,000
		Inhalation	--	--	6×10^{-3} mg/m^3	CNS, respiratory, hematological	1,000	1,000
106-42-3	xylene, p-	Oral	--	--	RfD of 2 mg/kg/day	mortality, weight reductions	1	1
		Inhalation	--	--	--	--		1*

*Toxicity weight is adopted from the other exposure pathway due to a lack of dose-response data.
[a]Data gap exists for this chemical; data taken from isomer listed above.

Table B-2. Toxicity Weights for TRI Chemicals and Chemical Categories with Final Derived Toxicity Values, by CAS Number

CAS #	Chemical Name		Toxicity Weight Calculation					Overall Toxicity Weight
			Cancer		Chronic Oral			
			Basis of Weight	Toxicity Weight	Basis of Weight	Critical Effect	Toxicity Weight	
62-56-6	Thiourea	Oral	cancer potency of 1.05 per mg/kg-d WOE of B2	10,000	--	--	--	10,000
		Inhalation	--	--	--	--	--	10,000*
64-67-5	Diethyl Sulfate	Oral	cancer potency estimate of 1,2 per mg/kg-d IARC Group 2A	10,000	--	--	--	10,000
		Inhalation	--	--	--	--	--	10,000*
71-55-6	Trichloroethane, 1,1,1-	Oral	--	--	LOAEL of 500 mg/kg/day	weight gain reduction	10	10
		Inhalation	--	--	NOAEL of 382 mg/m^3	neurological	10	10
74-85-1	Ethylene	Oral	--	--	--	--	--	1*
		Inhalation	negative 2 year NTP study	1	NOAEL of 3,000 ppm	gross and microscopic physiology	1	1

Table B-2. Toxicity Weights for TRI Chemicals and Chemical Categories with Final Derived Toxicity Values, by CAS Number

CAS #	Chemical Name		Toxicity Weight Calculation					Overall Toxicity Weight
			Cancer		Chronic Oral			
			Basis of Weight	Toxicity Weight	Basis of Weight	Critical Effect	Toxicity Weight	
75-55-8	Propylenimine	Oral	cancer potency of 150 WOE of B2	1,000,000	--	--	--	1,000,000*
		Inhalation	--	--	--	--	--	1,000,000
80-15-9	Cumene Hydroperoxide	Oral	--	--	--	--	--	1,000
		Inhalation	--	--	NOAEL of 2.2 mg/m^3		1,000	1,000*
88-89-1	Picric Acid (2,4,6-Trinitrophenol)	Oral	--	--	RfD of 6×10^{-5} mg/kg-d	renal	10,000	10,000
		Inhalation	--	--	RfD of 3×10^{-4} mg/kg-d	TLV-TWA	10,000	10,000
90-04-0	Anisidine, o-	Oral	cancer potency estimate of 0.80 per mg/kg-d WOE estimate of C	1,000	LOAEL of 41 mg/kg-d	thyroid, kidney, spleen	1,000	1,000
		Inhalation	--	--	--	--	See App. C	10,000

Table B-2. Toxicity Weights for TRI Chemicals and Chemical Categories with Final Derived Toxicity Values, by CAS Number

CAS #	Chemical Name		Toxicity Weight Calculation					Overall Toxicity Weight
			Cancer		Chronic Oral			
			Basis of Weight	Toxicity Weight	Basis of Weight	Critical Effect	Toxicity Weight	
90-94-8	Michlers Ketone	Oral	potency factor of 0.86 per mg/kg-d IARC Group 3	1,000	--	--	--	1,000
		Inhalation	--	--	--	--	--	1,000*
91-20-3	Naphthalene	Oral	--	--	--	--	--	1,000*
		Inhalation	--	--	LOAEL of 3.6 mg/kg/day	respiratory	1,000	1,000
95-63-6	Trimethylbenzene, 1,2,4-	Oral	--	--	5×10^{-4} mg/kg-d	CNS, respiratory, hematological	1,000	1,000
		Inhalation	--	--	6×10^{-3} mg/m^3	CNS, respiratory, hematological	1,000	1,000
100-02-7	Nitrophenol, 4-	Oral	--	--	NOAEL of 25 mg/kg-d	early mortality	1,000	1,000
		Inhalation	--	--	NOAEL of 26 mg/m^3	hematological	1,000	1,000

Table B-2. Toxicity Weights for TRI Chemicals and Chemical Categories with Final Derived Toxicity Values, by CAS Number

CAS #	Chemical Name		Toxicity Weight Calculation					Overall Toxicity Weight
			Cancer		Chronic Oral			
			Basis of Weight	Toxicity Weight	Basis of Weight	Critical Effect	Toxicity Weight	
101-80-4	Diaminodiphenylether, 4,4-	Oral	cancer potency of 0.14 per mg/kg-d IARC Group 2B	1,000	--	--	--	1,000
		Inhalation	--	--	--	--	--	1,000*
106-42-3	xylene, p-	Oral	--	--	RfD of 2 mg/kg/day	mortality, weight reduction	1	1
		Inhalation	--	--	--	--	--	1*
115-07-1	Propylene (Propene)	Oral	--	--	--	--	--	1*
		Inhalation	--	--	LOAEL of 5,000 ppm	benign nasal lesions	1	1
135-20-6	Cupferron	Oral	cancer potency of 0.22 per mg/kg-d WOE estimate of B2	1,000	--	--	--	1,000
		Inhalation	--	--	--	--	--	1,000*

Table B-2. Toxicity Weights for TRI Chemicals and Chemical Categories with Final Derived Toxicity Values, by CAS Number

CAS #	Chemical Name		Toxicity Weight Calculation					Overall Toxicity Weight
			Cancer		Chronic Oral			
			Basis of Weight	Toxicity Weight	Basis of Weight	Critical Effect	Toxicity Weight	
156-62-7	Calcium Cyanamide	Oral	negative 2 year NTP study	1	LOAEL of 10 mg/k-d	thyroid	1,000	1,000
		Inhalation	--	--	--	--	--	1,000*
541-73-1	Dichlorobenzene,1,3-[a]	Oral	cancer potency of 0.024 per mg/kg-d WOE of B2	100	RfD of 0.09 mg/kg-d	renal	10	100
		Inhalation	--	--	--	--	See App. C	10
624-83-9	Methyl Isocyanate	Oral	--	--	--	--	--	100,000*
		Inhalation	--	--	LOAEL of 1 ppm for dev. effects	developmental	100,000	100,000
1314-20-1	Thorium Dioxide	Oral	qualitative based on human data	1,000,000	--	--	--	1,000,000
		Inhalation	--	--	LOAEL of 10 mg/m^3	hematological	10,000	10,000
6484-52-2	Ammonium Nitrate	Oral	--	--	RfD of 1.6 mg/kg-d for nitrate	hematological	1	1
		Inhalation	--	--	--	--	--	1*

Table B-2. Toxicity Weights for TRI Chemicals and Chemical Categories with Final Derived Toxicity Values, by CAS Number

CAS #	Chemical Name		Toxicity Weight Calculation					Overall Toxicity Weight
			Cancer		Chronic Oral			
			Basis of Weight	Toxicity Weight	Basis of Weight	Critical Effect	Toxicity Weight	
7664-38-2	Phosphoric Acid	Oral	--	--	ADI of 221 mg/kg-d	--	1	1
		Inhalation	--	--	RfC of 0.01 mg/m^3	fibrosis	See App. A	1000
7664-93-9	Sulfuric Acid	Oral			estimated NOAEL of 500 mg/L	laxative effect	1	1
		Inhalation			LOAEL of 0.38 mg/m^3	respiratory	10,000	10,000
7697-37-2	Nitric Acid	Oral	--	--	--	--	--	100*
		Inhalation	--	--	LOAEL of 26 mg/m^3	benign bone lesions	100	100
25321-22-6	Dichlorobenzene (mixed isomers)	Oral	cancer potency of 0.024 per mg/kg-d WOE of B2	100	RfD of 0.09 mg/kg-d	renal	10	100
		Inhalation	--	--	--	--	See App. C	10

*Toxicity weight adopted from the other exposure pathway due to a lack of dose-response data.
[a]Data gap exists for this chemical; data taken from another isomer.

B.2. Data Summaries Used as Bases for Final Toxicity Weights

B.2.1. Ammonium Nitrate (6484-52-2)

Although no data were found for ammonium nitrate from which to derive toxicity weights, the Hazardous Substances Data Bank (HSDB) reports that ammonium nitrate dissociates in water and that the nitrate ion is more persistent than the ammonium ion. Toxicity values for nitrate were therefore used to derive a toxicity weight for ammonium nitrate.

Chronic Oral

Basis of toxicity weight

The Integrated Risk Information System (IRIS) reports that "nitrate toxicity is primarily caused by its conversion to nitrite" in the gastrointestinal tract, leading to cyanosis and methemoglobinemia ("blue baby syndrome"). Infants are particularly at risk of methemoglobinemia, since the infant gastrointestinal system normally has a high pH that favors the growth of nitrate reducing-bacteria. A chronic oral RfD of 1.6 mg/kg-d for nitrate is reported in IRIS. The RfD was derived from two chronic epidemiology studies of infants fed formula prepared from nitrate-contaminated water. The first study by Bosch et al. (1950) evaluated 139 cases of infant cyanosis due to methemoglobinemia caused by well-water containing 10 to 100 mg nitrate-nitrogen/L. The second study (Walton, 1960) identified 278 clinical cases of infant methemoglobinemia associated with ingestion of nitrate-contaminated water. In both studies there were no reported cases of methemoglobinemia in infants that consumed water with nitrate-nitrogen levels below 10 mg/L. IRIS used a NOAEL of 1.6 mg/kg-d (10 mg/L × 0.64 L/day / 4 kg) and an uncertainty factor of 1 (since the NOAEL represented the critical toxic effect in the sensitive human population) to derive the RfD of 1.6 mg/kg-d. Several other studies support this NOAEL (Cornblath and Hartmann, 1948; Simon et al., 1964; Toussaint and Selenka, 1970; Cruan et al., 1981). IRIS reports that confidence in the database is high.

Further calculations

Following TRI Environmental Indicator methods, the RfD of 1.6 mg/kg-d yielded a chronic oral toxicity weight of 1. Confidence in the toxicity value is high because confidence in the underlying data is high.

Chronic Inhalation

No dose-response data were found to support the calculation of an chronic inhalation toxicity weight. Following TRI Environmental Indicator methods, the chronic oral toxicity weight of 1 was applied to both exposure pathways.

Cancer Oral and Inhalation

No data were found to support the calculation of a cancer toxicity weight for ammonium nitrate.

Sources

NIOSH. 1993. Registry of Toxic Effects of Chemical Substances. Accessed via TOXNET.

U.S. EPA. 1993. Hazardous Substances Data Bank. Accessed via TOXNET.

U.S. EPA. 1993. Integrated Risk Information System. Accessed via TOXNET.

No other sources were found.

B.2.2. o-Anisidine (90-04-0)

The Integrated Risk Information System (IRIS) reports that health effects data for chronic inhalation was reviewed by the EPA RfD/RfC Work Group and determined to be inadequate for the derivation of an inhalation RfD for o-anisidine. The Hazardous Substances Data Bank (HSDB), however, contained studies from which to calculate chronic toxicity weights for o-anisidine. In addition, only the chronic oral and the cancer toxicity weights have been finalized by EPA. The interim chronic inhalation toxicity weight for o-anisidine is given in Appendix C.

Chronic Oral

Basis of toxicity weight

HSDB reported a study by IARC (1982) in which male Fisher 344 rats administered a total dose of 1000 mg/kg over seven weeks developed granular spleens; no adverse effects were observed in females given the same dose. Males and females fed 5000 or 10,000 mg/kg o-anisidine over seven weeks developed non-neoplastic lesions of the thyroid gland and kidney, and males and females fed more than 10,000 mg/kg showed severe reductions in weight gain (more than 50 percent in males) and had dark and granular spleens.

Further calculations

A LOAEL of 41 mg/kg-d was calculated from this study using a reference rat body weight of 0.5 kg, and was divided by an uncertainty factor of 10,000 (10 each for inter- and intraspecific extrapolation, 10 for the use of a LOAEL, and 10 for the use of a subchronic study) to obtain a chronic oral RfD estimate of 0.004 mg/kg-d. Following TRI Environmental Indicator methods, the RfD estimate of 0.004 mg/kg-d yielded a chronic oral toxicity weight of 1,000. Confidence in the toxicity weight is low due to the poor quality of the database.

Chronic Inhalation

See Appendix C.

Cancer Oral and Inhalation

Basis of toxicity weight

IARC classified o-anisidine a Group 2B carcinogen, based on inadequate or no evidence for carcinogenicity in humans and limited evidence for carcinogenicity in animals.

HSDB reported a study cited by IARC (1982), which evaluated the effects of o-anisidine on rats. Fifty-five/sex Fisher 344 rats were fed a total dose of 0 or 5000 mg/kg o-anisidine over 103 weeks (equivalent to a constant dose of 6.9 mg/kg-d). Transitional-cell carcinomas were found in 50/54 dosed males (0/51 controls) and in 41/49 dosed females (0/49 controls). Thyroid follicular cell tumors (carcinomas, adenomas, and other tumor types) were found in 7/40 dosed males (0/53 controls); no significant increase was noted in the females. Other tumors and carcinomas observed in dosed rats in statistically insignificant numbers were transitional-cell carcinomas of the renal pelvis, transitional-cell papillomas of the bladder, hydronephrosis, epithelial hyperplasia of the urinary tract, and renal papillary necrosis.

Further calculations

Following simplified methods outlined in Chapter 1, the results for incidence of transitional cell carcinomas in males and females combined were used to calculate an oral cancer potency estimate of 0.80 per mg/kg-d. The data used by IARC to classify o-anisidine a Group 2B carcinogen suggest a possible EPA weight of evidence classification of C. Following TRI Environmental Indicator methods, the cancer potency estimate of 0.80 per mg/kg-d was combined with the EPA WOE classification estimate of C to obtain an oral cancer toxicity weight of 1,000 for o-anisidine. Confidence in the toxicity weight is medium due to the high quality of the study but the lack of supporting data.

No data were found to support the calculation of a cancer toxicity weight for inhalation exposure to o-anisidine. Following TRI Environmental Indicator methods, the cancer oral toxicity value was applied to both exposure pathways.

Sources

IARC. 1993. *Monographs on the Evaluation of Carcinogenic Risk to Humans*. Lyon, France.

NIOSH. 1993. Registry of Toxic Effects of Chemical Substances. Accessed via TOXNET.

U.S. EPA. 1993. Hazardous Substances Data Bank. Accessed via TOXNET.

U.S. EPA. 1993. Integrated Risk Information System. Accessed via TOXNET.

No other sources were found.

B.2.3. Calcium Cyanamide (156-62-7)

Chronic Oral

Basis of toxicity weight

The *Technical Background Document to Support Rulemaking Pursuant to the Clean Air Act Section 112(g): Ranking of Pollutants With Respect to Hazard to Human Health* (U.S. EPA OHEA, 1993) cites a study by Kramer et al. (1967) in which rats were administered 10 mg/kg-d calcium cyanamide in their diet for three months. Dosed rats showed increased relative and absolute thyroid weights compared to controls.

Further calculations

The LOAEL of 10 mg/kg-d was divided by an uncertainty factor of 10,000 (10 each for intra- and interspecific extrapolation, for the use of a LOAEL, and for the use of a subchronic study) to derive an RfD estimate of 0.001 mg/kg-d. Following TRI Environmental Indicator methods, the RfD estimate yielded a chronic oral toxicity weight of 1,000 to calcium cyanamid. Confidence in the toxicity weight is low, due to the incomplete database.

Chronic Inhalation

No data were found to support the calculation of a chronic inhalation toxicity weight for calcium cyanamide. Following TRI Environmental Indicator methods, the chronic oral toxicity weight of 1,000 was applied to both pathways.

Cancer Oral and Inhalation

Basis of toxicity weight

The *Environmental Health Perspectives Supplements: Compendium of Abstracts From Long-Term Cancer Studies Reported by the National Toxicology Program From 1976 to 1992* (NTP, 1993) reports that a 107-week bioassay with rats and mice dosed at levels of 100 to 400 ppm (rats) or 500 to 2,000 ppm (mice) in the diet showed no evidence of carcinogenicity.

Further calculations

Based on the high quality of the study showing no evidence of carcinogenicity, the minimum cancer toxicity weight of 1 was assigned to oral exposure to calcium cyanamide. Confidence in the toxicity weight is medium, due to the high quality of the study but the lack of supporting data.

Following TRI Environmental Indicator methods, due to an absence of data on inhalation exposure to calcium cyanamide, the cancer oral toxicity weight of 1 was assigned to both

exposure pathways.

Sources

National Toxicology Program. 1993. *Environmental Health Perspectives Supplements: Compendium of Abstracts from Long-Term Cancer Studies Reported by the National Toxicology Program from 1976 to 1992*. Vol 101, Suppl. 1. April.

U.S. EPA. 1993. Hazardous Substances Data Bank. Accessed via TOXNET.

U.S. EPA. 1993. Integrated Risk Information System. Accessed via TOXNET.

U.S. EPA OHEA. 1993. *Technical Background Document to Support Rulemaking Pursuant to the Clean Air Act Section 112(g): Ranking of Pollutants With Respect to Hazard to Human Health*.

No other sources of information were found.

B.2.4. Cumene Hydroperoxide (CASRN 80-15-9)

Organic peroxides are generally nonvolatile, very reactive oxidizing agents and are used industrially as catalyzers in the production of plastics (Anonymous, 1964; Sax and Lewis, 1989). Cumene hydroperoxide is acutely irritating to eyes, skin and nasal passages (Floyd and Stokinger, 1958; Gage, 1970).

Computer searches of the TOXLINE, CANCERLINE, TSCATS and HSDB databases were conducted on cumene hydroperoxide in August 1996 for the time period 1965-August 1996 utilizing both the chemical name and CASRN. The literature search strategy was designed to identify oral and inhalation toxicity and cancer information.

Chronic Oral

Basis of toxicity weight

No data were located on the chronic oral toxicity of cumene hydroperoxide in humans or animals from which to derive a chronic oral toxicity weight. Following TRI Environmental Indicator methods, the chronic oral toxicity weight of 1,000 was applied to both exposure pathways.

Chronic Inhalation

Basis of toxicity weight

No data were located on the chronic toxicity of cumene hydroperoxide in humans by the inhalation route. Information on the inhalation toxicity of cumene hydroperoxide in animals is limited to one subchronic inhalation study that identifies a NOAEL and a FEL (frank effect level), and which is an appropriate basis for deriving a chronic inhalation toxicity weight.

Groups of Fischer 344 rats (10/sex) were exposed to nominal concentrations of 1, 6, 31 or 124 mg/m^3 (0.16, 1, 5 or 20 ppm) aerosolized cumene hydroperoxide (purity= 80%) for 6 hr/day, 5 days/week for approximately 3 months (total of 50, 61, 61 or 5 exposures, respectively) (Watanabe et al., 1979). A control group, consisting of 10/sex, was held in an animal holding room. The highest dose group was sacrificed on Day 12 of the study because the rats were moribund or had died. A group exposed to 1 mg/m^3 was started 15 days after the 6 and 31 mg/m^3 groups. Median particle size diameter for the 3 lower exposures ranged from 0.48-0.51 µm, suggesting to the authors that the exposure approximated a vapor phase (low concentrations, vapor pressure of cumene hydroperoxide= 0.9 mm Hg at 70C). Body weight was measured weekly. At study termination, organ weights, hematology, clinical chemistry, urinalysis, and gross necropsy with examinations of the animals' eyes were conducted on all animals. Comprehensive histopathologic examination was conducted on 5/sex of the 31-mg/m^3 and control groups. While there were statistically significant alterations in heart, liver and kidney absolute and relative weights, they were not dose-related, nor were there concomitant, dose-related alterations in body weight, organ histology, or hematologic or clinical chemistry parameters. Based on the judgment that the organ weight changes do not represent an adverse toxicologic effect but are most likely physiologically-adaptive, the NOAEL for rats in this study is 31 mg/m^3 (subchronic exposure) and 124 mg/m^3 is a FEL (acute exposure).

Further calculations

The NOAEL for intermittent subchronic exposure was adjusted to a continuous exposure concentration as follows:

$$NOAEL_{ADJ} = 31 \text{ mg/m}^3 \times (6 \text{ hr}/24 \text{ hr}) \times (5 \text{ d}/7 \text{ d}) = 5.5 \text{ mg/m}^3.$$

The $NOAEL_{ADJ}$ was converted to a mg/kg-day equivalent dose using the reference rat inhalation rate of 0.2 m^3/day and body weight of 0.5 kg (in TRI Table 5-5), as follows:

$$NOAEL_{ADJ} \text{ (mg/kg-day)} = 5.5 \text{ mg/m}^3 \times 0.2 \text{ m}^3/\text{d} \times (0.5 \text{ kg})^{-1} = 2.2 \text{ mg/kg-day}.$$

An uncertainty factor of 1000 (10 for intraspecies variability, 10 for interspecies variability and 10 for database deficiencies) was applied to the $NOAEL_{ADJ}$ to derive an RfD equivalent of 0.0022 mg/kg-day. An uncertainty factor of 10 was used for database deficiencies as there is only one subchronic study in one species, and no chronic or reproductive or developmental studies are

available. Confidence in the RfD equivalent is low because there were deficiencies in the principal study and database. In the principal study, there were small groups of animals tested, and not all animals were examined for histopathology. Furthermore, the experimental NOAEL (31 mg/m^3) was the highest concentration tested of subchronic duration in the principal study (i.e., animals exposed to the highest concentration, 124 mg/m^3, died or became moribund within 12 days). The database lacks supporting animal toxicity studies of similar or longer duration, as well as developmental or reproductive toxicity studies.

Following TRI Environmental Indicator methods, a toxicity weight of 1,000 is assigned to the RfD equivalent of 0.0022 mg/kg-day. Reflecting low confidence in the principal study and database, confidence in the toxicity weight is also low.

Cancer Oral and Inhalation

Basis of toxicity weight

No data were found regarding the carcinogenicity of cumene hydroperoxide in humans. Animal carcinogenicity studies of cumene hydroperoxide include skin painting and subcutaneous injection studies. There are several genotoxicity studies of cumene hydroperoxide, with equivocal results. No data were found to support the calculation of cancer toxicity weights for cumene hydroperoxide.

Kotin and Falk (1963) treated 50 C57Bl mice (sex not specified) with 50 µM of cumene hydroperoxide, but they did not clearly specify the dose, exposure route, or duration of exposure. A subcutaneous tumor was found in 1 mouse and malignant lymphomas were found in 11 of 38 surviving mice. The first tumor was noted at 14 months. Neither control data nor criteria for tumor diagnosis are detailed in the report.

Van Duuren et al. (1966) administered 0.1 mg/week cumene hydroperoxide in tricaprylin subcutaneously to 30 female ICR/Ha Swiss mice (3.3 mg cumulative dose) for up to their lifetime (535 days). Controls consisted of two groups of 39-50 untreated mice on test for 519-599 days and 3 groups of 30-50 mice injected subcutaneously with 0.05 ml tricaprylin for 532-581 days. An injection site fibrosarcoma was noted in one treated animal at 16 months; no injection site tumors were reported in untreated or tricaprylin controls. An adenocarcinoma of the breast was noted in one treated mouse; untreated and vehicle controls showed other distant site tumors. Median survival was 415-431, 368-535, and 472 days for untreated control, vehicle control and cumene hydroperoxide-treated groups, respectively. The authors considered cumene hydroperoxide "weakly active".

Van Duuren et al. (1967) injected 20 female SD rats with 100mg/week cumene hydroperoxide in tricaprylin for up to their lifetime (541 days). Controls consisted of an untreated group and 2 groups injected with tricaprylin for 554-559 days. Median survival was 537, 483-537, and 532 days for untreated control, vehicle control and treated groups, respectively. No injection site subcutaneous sarcomas were reported in the control or treatments

groups. Distant site tumors did not differ significantly in type or frequency in treated or untreated control groups (data not shown).

Earlier studies by Van Duuren and colleagues showed 1% cumene hydroperoxide did not induce papillomas following skin application in mice (Van Duuren et al., 1963; Van Duuren et al., 1965).

Genotoxicity tests of cumene peroxide show increased revertants in *S. typhimurium, E. coli* (Chevallier and Luzatti, 1960; Dillon et al., 1992; Levin et al., 1982, 1984; NTP, 1996; Seed et al., 1981; Wilcox et al., 1990), and *Neurospora* (Jensen et al., 1951). Callen and Larson (1978) reported negative results for mitotic gene conversion in *S. Cerevisiae* strain D4. Cumene hydroperoxide did not induce dominant lethal mutations in mice (Epstein and Shafner, 1968; Epstein et al., 1972).

There are no human studies of cumene hydroperoxide carcinogenicity. Available animal studies wherein cumene hydroperoxide was administered by skin painting or subcutaneous injection show equivocal results, or were inadequately reported, making these data suggestive but inadequate to draw conclusions as to the potential carcinogenicity of cumene hydroperoxide. Genotoxicity studies indicate cumene peroxide is mutagenic in bacterial systems and yeast. An *in vivo* test for dominant lethal mutations was negative. Since the weight-of-evidence as to the carcinogenicity of cumene hydroperoxide is inadequate, the chemical is appropriately placed in EPA weight-of-evidence group D- not classifiable as to human carcinogenicity, precluding calculation of cancer toxicity weights.

Sources (critical studies are marked with *)

Anonymous. 1964. "Organic peroxides." In: *Industrial Toxicology and Dermatology in the Production and Processing of Plastics*. Elsevier Publishing Co., Amsterdam, pages 211-217.

Callen, D.F. and R.A. Larson. 1978. *J. Toxicol. Environ. Health*. 4: 913-917. (cited in Zimmermann et al., 1984)

Chevallier, M.R. and D. Luzatti. 1960. "The specific mutagenic action of 3 organic peroxides on reverse mutations of 2 loci in E. coli." *Compt. Rend.* 250: 1572. (cited in Fishbein, 1984).

Dillon, D.M., D.B. McGregor, R.D. Combes and E. Zeiger. 1992. "Detection of mutagenicity in Salmonella of some aldehydes and peroxides." *Environ. Molec. Mutag.* 19(20):15.

Epstein, S.S., E. Arnold, J. Andrea, W. Bass and Y. Bishop. 1972. "Detection of chemical mutagens by the Dominant Lethal Assay in the mouse." *Toxicol. Appl. Pharmacol.* 23: 288-325.

Epstein, S.S. and H. Shafner. 1968. "Chemical mutagens in the human environment." *Nature*. 29: 385-387.

Fishbein, L. 1984. "Toxicity of the components of Styrene polymers: polystyrene, acrylonitrile-butadiene-styrene (ABS) and styrene-butadiene-rubber (SBR). Reactants and additives." In: *Industrial Hazards of Plastics and Synthetic Elastomers*. Jarvisalo, J., P. Pfaffli and H. Vainio, editors. Alan R. Liss, Inc., New York. Pages 239-262.

Floyd, E.P. and H.E. Stokinger. 1958. "Toxicity Studies of Certain Organic Peroxides and Hydroperoxides." *Amer. Indus. Hyg. Assoc. J.* 19: 205-212.

Gage, J.C. 1970. "The subacute inhalation toxicity of 109 industrial chemicals." *Brit. J. Indus. Med.* 27: 1-18.

Jensen, K.A., I. Kirk, G. Kolmark and M. Westergaard. 1951. "Chemically-induced mutations in Neurospora." *Cold Springs Harbor Quant. Biol.* 16: 245. (cited in Fishbein, 1984)

Kotin, P. and H.L. Falk. 1963. "Organic peroxides, hydrogen peroxide, epoxides, and neoplasia." *Rad. Res. Suppl.* 3: 193-211.

Levin, D.E., M. Hollstein, M.F. Christman, E.A. Schwiers and B.N. Ames. 1982. "A new Salmonella tester strain (TA102) with AT base pairs at the site of mutation detects oxidative mutagens." *Proc. Natl. Acad. Sci.* USA 79: 7445-7449. (cited in Wilcox et al., 1990).

Levin, D.E., M. Hollstein, M.F. Christman and B.N. Ames. 1984. "Detection of oxidative mutagens with a new Salmonella tester strain (TA102)." *Methods Enzymol.* 105: 249-255. (cited in Wilcox et al., 1990).

Mortelmans, K., S. Haworth, T. Lawlor, W. Speck, B. Tainer and E. Zeiger. 1986. "Salmonella mutagenicity tests. 2. Results from the testing of 270 chemicals." *Environ. Mutagen.* 8: (Suppl. 7): 1-119.

NTP (National Toxicology Program). 1996. *NTP Results Report*. 08/08/96.

Sax, N.I. and R.J. Lewis, Sr. 1989. *Dangerous Properties of Industrial Materials*. Seventh edition. Van Nostrand Reinhold, New York.

Seed, J.L., J. Cader, T. Nagamatsu, S.Y. Wang and E. Bueding. 1981. "The mutagenic activity of cumene, thymine and thymidine hydroperoxides and their derivatives." *Environ. Mutag.* 3: 335.

Van Duuren, B.L., N. Nelson, L. Orris, E.D. Palmes, and F.L. Schmitt. 1963. "Carcinogenicity of epoxides, lactones and peroxy compounds." *J.NCI.* 31: 41-55. (cited in Van Duuren et al., 1966)

Van Duuren, B.L., L. Orris and N. Nelson. 1965. "Carcinogenicity of epoxides, lactones and

peroxy compounds. Part II." *J. NCI.* 35: 707-717. (cited in Van Duuren et al., 1966)

Van Duuren, B.L., L. Langseth, L. Orris, G. Teebor, N. Nelson and M. Kuschner. 1966. "Carcinogenicity of epoxides, lactones and peroxy compounds. IV. Tumor response in epithelial and connective tissue in mice and rats." *J. NCI.* 37: 825-838.

Van Duuren, B.L., L. Langseth, L. Orris, M. Baden and M. Kuschner. 1967. "Carcinogenicity of epoxides, lactones, and peroxy compounds. V. Subcutaneous injection in rats." *J. NCI.* 39: 1213-1216.

*Wantanabe, P.G., D.G. Pegg, J.D. Burek, H.O. Yakel and L.W. Rampy. 1979. *A 90-day repeated inhalaltion toxicity study of cumene hydroperoxide in rats*. Dow Chemical USA Toxicology Research Laboratory. EPA Document No. 868600016, Fiche No. OTS0510168.

Wilcox, P., A. Naidoo, D.J. Wedd and D.G. Gatehouse. 1990. "Comparison of *Salmonella typhimurium* TA102 with *Escherichia coli* WP2 tester strains." *Mutag.* 5: 285-291.

Zimmermann, F.K., R.C. von Borstel, E.S. von Halle, J.M. Parry, D. Siebert, G. Zetterberg, R. Barale and N. Loprieno. 1984. "Testing of chemicals for genetic activity with *Saccharomyces cervisiae*: a report of the U.S. Environmental Protection Agency Gene-Tox Program." *Mutat. Res.* 133: 199-244.

B.2.5. Cupferron (135-20-6)

Chronic Oral and Inhalation

No data from which to calculate chronic toxicity weights for cupferron were found.

Cancer Oral and Inhalation

Basis of toxicity weight

The California EPA Office of Environmental Health Hazard Assessment (OEHHA) derived a cancer potency of 0.22 per mg/kg-d for cupferron based on a National Cancer Institute 1978 dietary study in rats and mice. Forty-nine or 50 male and 50 female Fischer 344 rats and B6C3F1 mice were given 0, 0.15, or 0.30 percent (rats) or 0, 0.2, or 0.4 percent (mice) cupferron in their feed for 78 weeks, then observed for an additional 28 weeks (rats) or 18 weeks (mice). Cupferron was carcinogenic in both sexes of both species. Using the Crump linearized multistage polynomial (Crump et al., 1977), OEHHA calculated the cancer potency factor based on the data for vascular tumors in low dose male rats (38/49 versus 0/50 in controls), the most sensitive group tested.

Further calculations

The Sixth Annual Report on Carcinogens Summary 1991 (National Institute of Environmental Health Sciences, 1991) reports that sufficient evidence exists for the carcinogenicity of cupferron in experimental animals, but that no data were available to evaluate the carcinogenicity of cupferron in humans. These data suggest a possible EPA weight of evidence of B2 for cupferron. Following TRI Environmental Indicator methods, the WOE estimate of B2 was combined with the potency factor of 0.22 per mg/kg-d calculated by OEHHA to obtain a cancer toxicity weight of 1,000 for cupferron. Confidence in the toxicity weight is medium due to the high quality of the cancer potency, but the lack of supporting data and a calculated EPA WOE classification.

Sources

California EPA OEHHA. 1992. *Expedited Cancer Potency Values and Proposed Regulatory Levels for Certain Proposition 65 Carcinogens.*

National Cancer Institute. 1978. *Bioassay of Cupferron for Possible Carcinogenicity.*

National Institute of Environmental Health Sciences. 1991. *Sixth Annual Report on Carcinogens Summary 1991.*

National Toxicology Program. 1993. *Environmental Health Perspectives Supplements: Compendium of Abstracts from Long-Term Cancer Studies Reported by the National Toxicology Program from 1976 to 1992.* Vol 101, Suppl. 1. April.

U.S. EPA. 1993. Hazardous Substances Data Bank. Accessed via TOXNET.

No other sources of information were found.

B.2.6. 4,4-Diaminodiphenyl Ether (101-80-4)

Chronic Oral and Inhalation

No dose-response data were found from which to calculate chronic toxicity weights for 4,4-diaminodiphenyl ether.

Cancer Oral and Inhalation

Basis of toxicity weight

The California EPA Office of Environmental Health Hazard Assessment (OEHHA; 1992) derived a cancer potency of 0.14 per mg/kg-d for 4,4-diaminodiphenyl ether, based on a 104-week 1980 National Cancer Institute study. NCI fed 50/sex F344 rats 0, 200, 400, or 500 ppm 4,4-diaminodiphenyl ether and 50/sex B6C3F1 mice 0, 150, 300, or 800 ppm

4,4-diaminodiphenyl ether in their diet. Both sexes of both species showed dose-related liver tumors, and rats showed dose-related thyroid tumors. Using the Crump linearized multistage polynomial (Crump et al., 1977), OEHHA based the potency factor on dose-response data for benign and malignant liver tumors in male rats (1/50, 13/50, 41/50, and 39/50 for the 0, 200, 400, and 500 ppm dosed groups, respectively), the most sensitive dosed group.

The International Agency for Research on Cancer (IARC) has ranked 4,4-diaminodiphenyl ether a Group 2B carcinogen (possible human carcinogen) based to sufficient animal data (including the above study) and no human data.

Further calculations

The data used by IARC to rank 4,4-diaminodiphenyl ether a Group 2B carcinogen suggest a possible U.S. EPA weight of evidence (WOE) classification of B2 (probable human carcinogen). Following TRI Environmental Indicator methods, the potency factor of 0.14 per mg/kg-d calculated by OEHHA and the WOE estimate of B2 were used to derive a cancer toxicity weight of 1,000. Confidence in the toxicity weight is medium due to the high quality of the study but the lack of a calculated EPA WOE classification.

Sources

California EPA OEHHA. 1992. *Expedited Cancer Potency Values and Proposed Regulatory Level for Certain Proposition 65 Carcinogens.* April.

IARC. 1982. *IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans*. Lyon, France.

IARC. 1993. *IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans*. Lyon, France.

National Cancer Institute. 1980. *Bioassay of 4,4-Oxydianiline for Possible Carcinogenicity*.

National Toxicology Program. 1993. *Environmental Health Perspectives Supplements: Compendium of Abstracts from Long-Term Cancer Studies Reported by the National Toxicology Program from 1976 to 1992.* Vol 101, Suppl. 1. April.

U.S. EPA. 1993. Hazardous Substances Data Bank. Accessed via TOXNET.

No other sources of information were found.

B.2.7. Dichlorobenzene (mixed isomers and 1,3-) (25321-22-6 and 541-73-1)

The toxicity weights derived here represent all mixed isomers of dichlorobenzene (DCB),

and the individual isomer 1,3-DCB (541-73-1). IRIS or HEAST values exist for the individual isomers 1,2-DCB and 1,4-DCB, and are given in Appendix A. Chronic toxicity weights for mixed isomers and 1,3-DCB are based on 1,2-DCB, and cancer toxicity weights for mixed isomers and 1,3-DCB are based on 1,4-DCB. The isomer 1,2-DCB was used to represent mixed isomers of dichlorobenzene for chronic effects because available data show it to be the most toxic of the three isomers (1,2-, 1,3-, and 1,4-) for chronic health endpoints. The isomer 1,4-DCB is used to represent mixed isomers of dichlorobenzene due to a lack of data on the other two isomers.

Only the chronic oral and cancer toxicity weights for mixed isomers of DCB and 1,3-DCB have been finalized by EPA. An interim chronic inhalation weight has also been calculated, and is listed in Appendix C

Chronic Oral

Basis of toxicity weight

IRIS reports a chronic oral RfD of 0.09 mg/kg-d for 1,2-DCB, based on a two-year gavage study in mice and rats (NTP, 1985). Fifty/sex B6C3F1 mice and F344/N rats were administered 0, 60, or 120 mg/kg-d 1,2-dichlorobenzene in corn oil for five days per week for 103 weeks. Although a statistically significant increase in the incidence of renal tube regeneration was shown in male mice at a dose rate of 120 mg/kg-d, IRIS reports that there was no other evidence of treatment-related lesions in either species, and that the incidence of this lesion in male control mice was below that of three similar control groups studied at approximately the same time at the research facility. Because the observed effect was judged to be of questionable significance, the EPA RfD/RfC workgroup established a NOAEL of 120 mg/kg-d for the study. The NOAEL was multiplied by 5/7 days to yield a constant dose of 85.7 mg/kg-d, and divided by an uncertainty factor of 1,000 (10 each for intra- and interspecific extrapolation, and 10 for the lack of reproductive studies and adequate chronic toxicity studies) and a modifying factor of 1 to derive the RfD of 0.09 mg/kg-d. IRIS reports that confidence in the study is medium and in the database is low, for an overall low confidence level in the RfD.

Further calculations

Following TRI Environmental Indicator methods, the RfD for 1,2-DCB yielded a chronic oral toxicity weight of 10 for 1,2-dichlorobenzene, and therefore also for the mixed isomers of DCB. This toxicity weight will be applied to 1,2-DCB, mixed isomers of DCB, and, due to the absence of data from which to calculate a chronic oral toxicity weight, 1,3-DCB. Confidence in the toxicity weight is low, based on low confidence in the RfD.

Chronic Inhalation

See Appendix C.

Cancer Oral and Inhalation

Basis of toxicity weight

IRIS reports that both 1,2-DCB and 1,3-DCB are unclassifiable as to human carcinogenicity (WOE of D). The HEAST (EPA ORD, 1993) and the Health Effects Assessment document (HEA; EPA OHEA, 1987) for dichlorobenzenes both report a human oral cancer potency of 0.024 per mg/kg-d for 1,4-dichlorobenzene, based on a 103-week NTP (1986) gavage study. This study showed a significantly increased incidence of hepatocellular carcinoma or adenoma in male and female B6C3F1 mice and renal tubular cell adenoma or adenocarcinoma in male F344/N rats. The cancer potency is based on the results in male mice exposed to 212.2 mg/kg-d 1,4-DCB (22/40 in dosed mice, 17/44 in controls) and 424.5 mg/kg-d 1,4-DCB (40/42 in dosed mice, 17/44 in controls).

The HEA document reports that the International Agency on Research in Cancer (IARC) cited five case studies described by Girard et al. (1969), which suggest a possible association between leukemia and inhalation and perhaps percutaneous exposure to dichlorobenzenes. HEAST (1993) reported a Weight of Evidence (WOE) classification of B2 (probable human carcinogen) for 1,4-dichlorobenzene.

Further calculations

Following TRI Environmental Indicator methods, a cancer oral toxicity weight of 100 was assigned to 1,4-dichlorobenzene based on a cancer potency of 0.024 per mg/kg-d and a WOE of B2. This toxicity weight was assigned to mixed isomers of dichlorobenzene and, due to a lack of data, 1,3-DCB also. Confidence in the toxicity weight is medium, based on high confidence in the NTP study and low confidence in the database.

Following TRI Environmental Indicator methods, due to a lack of data concerning the carcinogenic effects of inhalation exposure to dichlorobenzenes, the cancer toxicity weight of 100 derived for oral exposure was assigned to both pathways.

Sources

IARC. 1978. *IARC Monographs on the Evaluation of the Carcinogenicity of Chemicals to Man*. Vol. 7. Lyon, France.

IARC. 1978. *IARC Monographs on the Evaluation of the Carcinogenicity of Chemicals to Man*. Vol. 29. Lyon, France.

U.S. EPA. 1993. Hazardous Substances Data Bank. Accessed via TOXNET.

U.S. EPA. 1995. Integrated Risk Information System. Accessed via TOXNET.

U.S. EPA OHEA. 1989. *Ambient Water Quality Criteria Document Addendum for Dichlorobenzenes*.

U.S. EPA OHEA. 1987. *Health Effects Assessment for Dichlorobenzenes.*

U.S. EPA ORD. 1993. *Health Effects Assessment Summary Tables*. March.

U.S. EPA ORD Superfund Health Risk Technical Support Center. n.d. *Risk Assessment Issue Papers for: Evaluation of the Carcinogenicity of 1,4-Dichlorobenzene (106-46-7).*

U.S. EPA ORD Superfund Health Risk Technical Support Center. n.d. *Risk Assessment Issue Papers for: Evaluation of the Inhalation Concentration for 1,2-Dichlorobenzene (95-50-1)*

U.S. EPA ORD Superfund Health Risk Technical Support Center. n.d. *Risk Assessment Issue Papers for: Derivation of Provisional Oral RfD for 1,3-Dichlorobenzene (541-73-1).*

No other sources of information were found.

B.2.8. Diethyl Sulfate (64-67-6)

Chronic Oral and Inhalation

The Reportable Quantity Document for Diethyl Sulfate (EPA, 1991) reported that as of 1991, no oral or inhalation studies had been conducted to determine the chronic or subchronic effects of exposure to diethyl sulfate. The *Technical Background Document to Support Rulemaking Pursuant to the Clean Air Act Section 112(g): Ranking of Pollutants with Respect to Hazard to Human Health* (Draft; EPA, 1993), however, gave diethyl sulfate a composite score of A on the RQ list of "High Concern" pollutants because of severe acute toxicity. No chronic toxicity weight was derived for diethyl sulfate.

Cancer Oral and Inhalation

The data available for diethyl sulfate are of sufficiently poor quality as to prohibit successful assignment of a cancer toxicity weight for the chemical. One study was cited in the *Reportable Quantity Document for Diethyl Sulfate* (EPA, 1991) from which a possible toxicity weight was calculated, though adoption of this toxicity weight is not recommended.

Basis of toxicity weight

Lynch et al. (1979) found a significant increase in laryngeal cancer among alcohol process workers in Baton Rouge, Louisiana who were exposed to diethyl sulfate for at least one month from 1950 to 1976. No dose-response data were available from the study.

The *Reportable Quantity Document for Diethyl Sulfate* (EPA, 1991) reports a study by Druckrey et al. (1970) in which two groups of 12 BD rats were given weekly doses of 25 or 50 mg/kg (3.6 or 7.1 mg/kg-d constant dose) diethyl sulfate by gavage for 81 weeks and observed

until death. Each group showed one squamous cell carcinoma. In both groups combined, 6/24 rats developed a number of benign papillomas of the forestomach. Controls were not described.

In the IARC Monographs 1972-Present (International Agency for Research on Cancer, 1987), IARC based their determination that diethyl sulfate is carcinogenic to animals on this study and on a subcutaneous injection study. In addition, the IARC text indicates that all tumors occurred in the low dose group. The authors of the RQ document commented that "the lack of controls precluded a definite conclusion, but the results were suggestive of a response (EPA, 1991)." IARC ranks diethyl sulfate as a Group 2A carcinogen (probable human carcinogen) based on limited evidence in humans and sufficient evidence in animals.

Further calculations

In order to use this study to derive a cancer potency estimate and a toxicity weight, it was assumed that controls developed no carcinomas or papillomas. Using the results of carcinomas and papillomas combined, and following the simplified method described in Chapter 1, the calculated cancer potency estimate for diethyl sulfate was 1.2 per mg/kg-d. The lack of information on controls, however, may cause the cancer potency calculated to be overly conservative.

The data on which IARC based its ranking of diethyl sulfate as a Group 2A carcinogen (limited evidence in humans and sufficient evidence in animals) suggest a possible U.S. EPA weight of evidence (WOE) classification of B1 (probable human carcinogen).

Following TRI Environmental Indicator methods, the combination of a cancer potency estimate of 1.2 per mg/kg-d and a WOE estimate of B1 yielded a cancer toxicity weight of 10,000. Given the incomplete reporting of results of the critical study, and the small sample size used, confidence in the toxicity weight is low.

Sources

U.S. EPA. 1993. Hazardous Substances Data Bank. Accessed via TOXNET.

U.S. EPA Office of Air Quality Planning and Standards. 1993. *Technical Background Document to Support Rulemaking Pursuant to the Clean Air Act Section 112(g): Ranking of Pollutants with Respect to Hazard to Human Health.* Draft.

U.S. EPA OHEA. 1991. *Reportable Quantity Document for Diethyl Sulfate.* Final Draft. ECAO-CIN-R615A. November.

No other sources of information were found.

B.2.9. Ethylene (74-85-1)

In 1989, EPA denied a petition to remove ethylene from the TRI list of chemicals based primarily on its contribution to the formation of tropospheric ozone, formaldehyde, and other hazardous air pollutants. For the purposes of this exercise, however, only the direct human health effects of exposure to ethylene are discussed.

Chronic Oral

No data were found to support the calculation of a chronic oral toxicity weight for ethylene. Following TRI Environmental Indicator methods, the toxicity weight calculated for chronic inhalation of 1 were used for both exposure pathways (see below).

Chronic Inhalation

Basis of toxicity weight

A memorandum entitled, "Contractor Documents on Propylene and Ethylene" (EPA OPPT, 1988) cites data from a study by Hamm et al. (1984, reported in Dynamac, 1988) in which 120/sex/dose Fischer 344 rats were exposed to doses of 0, 300, 1,000, or 3,000 ppm ethylene for 6 hrs/d, 5 d/wk for 24 months. No gross or microscopic adverse effects were observed. These results are supported by a subchronic study by Rhudy et al. (1978) in which rats exposed to 10,000 ppm ethylene for 6 hrs/d, 5 d/wk for 14 weeks also showed no ethylene-induced adverse effects.

Further calculations

The NOAEL of 3,000 ppm (3448 mg/m^3) was converted to a constant dose of 246 mg/kg-d by multiplying by a reference rat respiration rate of 0.2 m^3/d and 6/24 hrs/d and 5/7 d/wk and dividing by a reference rat body weight of 0.5 kg. The NOAEL of 246 mg/kg-d was divided by an uncertainty factor of 100 (10 each for intra- and interspecific extrapolation) to yield an RfD estimate of 2.5 mg/kg-d. Following TRI Environmental Indicator methods, this RfD estimate yielded a chronic inhalation toxicity weight of 1. Because of the high quality of the 2-year bioassay and the supporting database, confidence in the chronic inhalation toxicity weight is high.

Cancer Oral and Inhalation

Basis of toxicity weight

The International Agency for Research in Cancer (1979) reported finding no data indicating the carcinogenicity or mutagenicity of ethylene and assigned ethylene a ranking of Group 3 (not classifiable as to human carcinogenicity). The two-year study by Hamm et al. (1984) described above, however, found no lesions associated with exposure to up to 3,000 ppm (3448 mg/m^3) ethylene.

Further calculations

Because no cancer was found after two years of very high exposure rates, ethylene was assigned a cancer toxicity weight of 1 for exposure via inhalation. Following TRI Environmental

Indicator methods, in the absence of data on oral exposure to ethylene, the cancer inhalation toxicity weight was assigned to both exposure pathways.

Sources

IARC. 1979. *IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans*. Vol. 19. Lyon, France.

U.S. EPA. 1989. TSCA Docket #400023 (Chemical Manufacturers Association petition to delist ethylene and propylene from TRI reporting requirements).

U.S. EPA OPPT. 1988. TSCA Docket 400023: Memorandum entitled "Contractor Documents on Propylene and Ethylene."

U.S. EPA. 1993. Hazardous Substances Data Bank. Accessed via TOXNET.

No other sources of information were found.

B.2.10. Methyl Isocyanate (624-83-9)

Chronic Oral and Inhalation

No data were located to support the calculation of chronic toxicity weights for methyl isocyanate (MIC). There are, however, substantial data on acute effects and developmental effects resulting from prenatal exposure to MIC in both humans and animals (see below).

Cancer Oral and Inhalation

No information was available from which to calculate a cancer toxicity weight for MIC.

Developmental Oral and Inhalation

Basis of toxicity weight

The Integrated Risk Information System (IRIS) contains RfDs based on prenatal exposure and resulting developmental toxicity for a number of chemicals. Developmental toxicity data from two animal inhalation studies are available, which could be used to develop an inhalation RfD for MIC based on developmental effects. One study cited in HSDB that employed single prenatal dosing contained insufficient information to determine the NOAEL or LOAEL (Bucher et al., 1989). A second study by Schwetz et al. (1986) reported in the *Health and Environmental Effects Profile for Methyl Isocyanate* (OHEA, 1986) exposed CD-1 mice to 1 or 3 ppm MIC on gestational days 14-17 for six hours per day. The observed effects, decreased litter size and neonatal survival, are consistent with observations in exposed human populations of increased

miscarriage, increases in numerous types of chromosomal abnormalities, and decreased infant survival. Maternal survival was not affected, which may indicate that MIC has a greater toxicity for developing individuals than for adults.

Further calculations

The LOAEL of 1 ppm (2.3 mg/m^3) was converted to a constant dose of 0.58 mg/kg-d by multiplying by a reference mouse respiration rate of 0.04 m^3/d and 6/24 hours/day and dividing by a reference mouse body weight of 0.03 kg. The LOAEL of 0.58 mg/kg-d was divided by an uncertainty factor of 1,000 (10 each for inter- and intraspecies variability and 10 for the use of a LOAEL) to yield an RfD estimate of 5.8×10^{-4} mg/kg-d for developmental effects. Using TRI Environmental Indicator methods, this RfD estimate yielded a developmental inhalation toxicity weight of 1,000 for MIC. An additional data quality factor of 10 (to account for an incomplete database) was used, giving an RfD estimate of 5.8×10^{-5} mg/kg-d and a toxicity weight of 10,000.

The use of an RfD estimate based on brief prenatal exposure is problematic due to issues related to the timing of exposure and to the type of information available on TRI chemicals. The TRI exposure data are provided as yearly averages. Toxicity resulting from prenatal exposure is related to the level of exposure occurring over a brief period of time (usually a few days). Peak exposures during a year, rather than average yearly exposures, are critical for prenatally-induced developmental toxicity. Consequently, an estimated RfD based on this type of toxicity is not optimal for generating TRI indicators, despite its significance to human populations exposed to MIC. Because of the lack of adequate data and the use of a developmental study, an additional safety factor of 10 was used to result in a final toxicity weight of 100,000. Confidence in the toxicity weight is low.

Following TRI Environmental Indicator methods, due to a lack of information on oral exposure to MIC, the developmental inhalation toxicity weight of 100,000 for inhalation exposure was assigned to both exposure pathways.

Sources

U.S. EPA. 1993. Hazardous Substances Data Bank. Accessed via TOXNET.

U.S. EPA. 1993. Integrated Risk Information System. Accessed via TOXNET.

U.S. EPA OHEA. 1986. *Health and Environmental Effects Profile for Methyl Isocyanate*.

U.S. EPA OSWER. 1992. *Technical Background Document to Support Rulemaking Pursuant to CERCLA Section 102 Volume 6*.

No other sources of information were found.

B.2.11. Michler's Ketone (90-94-8)

Chronic Oral and Inhalation

No dose-response data were found from which to calculate chronic toxicity weights for Michler's ketone (4,4-bis (dimethylamino) benzophenone).

Cancer Oral and Inhalation

Basis of toxicity weight

The Office of Environmental Health Hazard Assessment (OEHHA) of the California EPA has derived a cancer potency of 0.86 per mg/kg-d for Michler's ketone, based on a 1979 National Cancer Institute dietary study with 50/sex Fischer 344 rats and 50/sex B6C3F1 mice (20/sex/species for controls). (This study was also cited in the PMN Analogue Profile on Michler's ketone without a cancer potency derived.) Male rats were fed 0, 250, and 500 ppm Michler's ketone, female rats 0, 500, and 1000 ppm, and male and female mice 0, 1250, and 2500 ppm. All dosed groups showed evidence of carcinogenicity; rats were more sensitive than mice, and males and females were similarly sensitive. Tumor incidence (hepatocellular carcinomas) in male rats was 0/20, 9/50, and 40/50 in controls and low and high dose groups, respectively. Tumor incidence (hepatocellular carcinomas) in female rats was 0/20, 41/47, and 44/49 for controls, low, and high dose groups, respectively. Incidence of hepatocellular carcinomas in mice were 0/19, 6/49, and 3/48 (male controls, low- and high-dose groups), and 0/19, 16/49, and 38/50 (female controls, low- and high-dose groups respectively). Incidence of hemangiosarcomas in mice were 0/19, 5/50, and 20/50 (male controls, low- and high dose groups), and 2/19, 0/49, and 2/50 (female control, low- and high-dose groups).

OEHHA reported that they used the Crump linearized multistage polynomial (Crump, 1977) to derive the cancer potency based on the values for liver tumors in female rats (0/20, 41/47, and 44/49 for controls, low, and high doses, respectively). No further comments were made by OEHHA.

The Hazardous Substances Data Bank (HSDB) reported that the International Agency for Research on Cancer (1987) ranks Michler's ketone as a Group 3 carcinogen (not classifiable as to its carcinogenicity to humans) based on 1) no human data, and 2) limited animal data.

Further calculations

The data used by IARC to rank Michler's ketone a Group 3 carcinogen (no human data and limited animal data) suggest a possible U.S. EPA weight of evidence (WOE) classification of C (possible human carcinogen). Following TRI Environmental Indicator methods, the WOE estimate of C and the potency factor of 0.86 per mg/kg-d calculated by Cal EPA OEHHA yielded a cancer toxicity weight of 1,000. Confidence in the toxicity weight is medium due to high confidence in the study and low confidence in the supporting database.

Sources

California EPA OEHHA. 1992. *Expected Cancer Potency Values and Proposed Regulatory Levels for Certain Proposition 65 Carcinogens*. April.

National Cancer Institute. 1989. *Bioassay of Michler's Ketone for Possible Carcinogenicity*.

National Toxicology Program. 1993. *Environmental Health Perspectives Supplements: A Compendium of Abstracts form Long-Term Cancer Studies Reported by the National Toxicology Program from 1976 to 1992*.

U.S. EPA. 1989. *PMN Analogue Profile on Michler's Ketone*. Working Draft.

U.S. EPA. 1993. Hazardous Substances Data Bank. Accessed via TOXNET.

No other sources of information were found.

B.2.12. Naphthalene (91-20-3)

Chronic Oral

The ATSDR did not find adequate data to calculate a chronic Minimum Risk Level (MRL) for naphthalene via the oral route (ATSDR, 1995). "One chronic study was located that documented the [chronic] toxicity of naphthalene in rats (Schmahl 1955, [as cited in ATSDR, 1995]). No treatment-related effects were reported at a [single] dose level of 41 mg/kg/day for 700 days. The study was not suitable as the basis for deriving a chronic MRL because only one dose level was evaluated, histopathological examination was limited, and dosing was not precisely controlled" (ATSDR, 1995).

Following TRI Environmental Indicator methods, the toxicity weight of 1,000 derived for chronic inhalation exposure was applied to both exposure pathways (see below).

Chronic Inhalation

Basis for toxicity weight

A chronic inhalation MRL for naphthalene was derived by ATSDR (1995) based on a chronic (2-year) inhalation study in mice using exposures of 0, 10, or 30 ppm (NTP, 1992a, as cited in ATSDR, 1995). Groups of mice were exposed for 5 days per week and 6 hours per day. Body weights, clinical signs, and mortality were monitored daily. Hematological measurements were made at 14 weeks, but not thereafter; ophthalmic examinations were performed at 6-month intervals. At sacrifice, gross necropsy of all animals was performed.

Histological examination of the tissues was conducted for both the control and high dose animals. Tumor incidence was evaluated in all organs.

This study identified a LOAEL of 10 ppm. A dose-related incidence of chronic inflammation of the epithelium of the nasal passages and lungs was observed. There was metaplasia of the olfactory epithelium and hyperplasia of the respiratory epithelium, but there was no treatment-related gross or histopathological lesions of the organs examined. The data suggest that the observed responses represented a respiratory inflammation and regeneration mechanism. There was an increased incidence of combined alveolar/bronchiolar adenomas and carcinomas in the lungs of females at the high dose (ATSDR, 1995).

Further calculations

The LOAEL of 10 ppm was used to derive the chronic inhalation MRL of 0.002 ppm. This concentration (10 ppm) was normalized by adjusting for the 6-hour-per-day and 5-day-per-week exposure pattern. An uncertainty factor of 1,000 (10 for the use of the LOAEL, 10 for extrapolation from animals to humans, and 10 for human variability) was applied to obtain the MRL.

To determine the toxicity weight for naphthalene for chronic inhalation, the MRL of 0.002 ppm was converted to mg/kg/day by multiplying the ppm by the molecular weight/24.5 (a gas and pressure constant), a standard mouse ventilation rate of 0.04 m^3/d, 6 hrs/24 hrs, 5 days/7 days, and dividing by a standard mouse body weight of 0.03 kg. A dose of 0.0036 mg/kg/day yielded a toxicity weight of 1,000.

Cancer Oral and Inhalation

EPA is currently reviewing the carcinogenicity classification for naphthalene.

Sources

ATSDR 1995. *Toxicological Profile for Naphthalene (Update)*. Agency for Toxic Substances and Disease Registry.

B.2.13. Nitric Acid (7697-37-2)

Chronic Oral

No dose-response data were found to support the calculation of an oral toxicity weight for nitric acid. Following TRI Environmental Indicator methods, the chronic inhalation toxicity weight of 100 (see below) was assigned to both exposure pathways.

Chronic Inhalation

Basis of toxicity weight

The Hazardous Substances Data Bank (HSDB) reports that Ballou et al. (1978) exposed rats to 0.013 to 0.049 mg/l nitric acid aerosol for 375 to 650 days. Mortality ranged from 9 to 25 percent. Benign bone lesions (osteoarthritis) were observed in both controls and acid-exposed animals.

Further calculations

The LOAEL of 0.013 mg/l was converted to a LOAEL of 5.2 mg/kg-d by multiplying by 1,000 l/m^3 and by a reference rat respiration rate of 0.2 m^3/d, and dividing by a reference rat body weight of 0.5 kg. The LOAEL of 5.2 mg/kg-d was divided by an uncertainty factor of 1,000 (10 each for intra- and interspecific extrapolation, and 10 for the use of a LOAEL) to yield an RfD estimate of 5.2×10^{-3}. This RfD estimate yielded a chronic inhalation toxicity weight of 100 for nitric acid. Confidence in the toxicity weights is low due to the severity of the critical effect and the lack of supporting data.

Cancer Oral and Inhalation

No dose-response data were located to support the calculation of cancer toxicity weights for nitric acid.

Sources

U.S. EPA. 1993. Hazardous Substances Data Bank. Accessed via TOXNET.

No other sources of information were found.

B.2.14. 4-Nitrophenol (100-02-7)

IRIS reports that the EPA RfD/RfC Workgroup is currently in the process of deriving an oral RfD, but has determined that insufficient health data exist to calculate an inhalation RfC.

Chronic Oral

Basis of toxicity weight

Of the studies reported in the ATSDR Toxicological Profile for 2-Nitrophenol and 4-Nitrophenol (1992), the critical study chosen to calculate a toxicity weight was done by Hazleton (1989), who reported early mortality in rats administered 70 mg/kg-d or more by gavage in water for 13 weeks. The NOAEL for the study was 25 mg/kg-d. Prior to death, prostration, wheezing, and dyspnea were noted. The cause of death was not indicated.

Further calculations

The NOAEL of 25 mg/kg-d was divided by an uncertainty factor of 1,000 (10 each for intra- and interspecific variability, and 10 for the use of a subchronic study) to derive an RfD estimate of 0.025 mg/kg-d. Following TRI Environmental Indicator methods, this RfD estimate yielded a chronic oral toxicity weight of 100. A data quality factor of 10 was used to account for the lack of adequate chronic mammalian studies and the severity of the endpoint, to result in an RfD estimate of 0.025 mg/kg-d and a toxicity weight of 1,000. Because of the lack of subchronic or chronic oral studies reporting less serious effects than death, confidence in the toxicity weight is low.

Chronic Inhalation

Basis of toxicity weight

No chronic or subchronic studies of longer than four weeks were found from which to calculate a chronic inhalation toxicity weight. The ATSDR Toxicological Profile for 4-Nitrophenol (1992) reports a four-week study (Hazelton 1989) reported a NOAEL of 30 mg/m^3, but did not report a LOAEL. Evidence of methemoglobinemia at the higher dose level was found, however, when Smith et al. (1988) exposed rats to 0, 26 mg/m^3, or 112 mg/m^3 4-nitrophenol for 6 hrs/d, 5 d/wk for two weeks. Despite the short duration of the two-week study, it was chosen as the critical study to calculate a inhalation toxicity weight for 4-nitrophenol because it indicated the lowest NOAEL of any study reported by ATSDR.

Further calculations

The NOAEL of 26 mg/m^3 was converted to a constant dose of 1.8 mg/kg-d by multiplying by a reference rat respiration rate of 0.2 m^3/d, 5/7 days/wk, and 6/24 hrs/d, and dividing by a reference rat body weight of 0.5 kg. The NOAEL of 1.8 mg/kg-d was divided by an uncertainty factor of 1,000 (10 each to account for intra- and interspecific extrapolation, and 10 for the use of a subchronic study) to derive an RfD estimate of 1.8×10^{-3} mg/kg-d. This RfD estimate yielded a toxicity weight of 1,000. Because of the lack of adequate subchronic or chronic inhalation studies, confidence in the toxicity weight is low.

Cancer Oral and Inhalation

The Health Effects Assessment for Nitrophenols (U.S. EPA OHEA, 1987) and the Superfund Health Risk Technical Support Center (U.S. EPA ORD) both reported a classification of Group D (not classifiable as to human carcinogenicity). No cancer toxicity weight for 4-nitrophenol was calculated.

Sources

ATSDR. 1992. *Toxicological Profile for 2-nitrophenol and 4-nitrophenol*.

U.S. EPA. 1993. Integrated Risk Information System. Accessed via TOXNET.

U.S. EPA OHEA. 1987. *Health Effects Assessment for Nitrophenols*. PB88-176967. July.

U.S. EPA ORD Superfund Health Risk Technical Support Center. n.d. *Risk Assessment Issue Paper for 4-Nitrophenol*. Draft.

No other sources of information were used, though the existence of a 1983 RQTox document was noted.

B.2.15. Phosphoric Acid (7664-38-2)

Chronic Oral

Basis of toxicity weight

Phosphoric acid is a multiple purpose GRAS (generally recognized as safe) food substance, when used in accordance with good manufacturing practice (FDA, 1989, 1991). U.S. EPA (1989) reported that no information was located regarding toxicity in animals from subchronic or chronic oral exposure to phosphoric acid.

Phosphoric acid is used as an acidulating agent in beverages at concentrations of 500-1000 mg/L (Schrödter et al., 1991). It is listed as an ingredient in some nonalcoholic carbonated beverages, such as Coca Cola (Coke). Daily consumption of one 12 oz (355 ml) can of carbonated beverage could thus provide up to 355 mg/day of phosphoric acid (5.1 mg H_3O_4P/kg-day, assuming 70 kg body weight).

The Food and Drug Administration (FDA, 1991) listed health effects studies that were not available and that it would want to see if phosphoric acid were newly submitted for approval as follows: chronic toxicity studies in two animal species (rodent and nonrodent), oncogenicity studies in two species (rat and another rodent), 2-generation reproduction study and teratology study. This list constitutes a list of database deficiencies.

Updated computer searches of the literature (through 1996) identified only one new study regarding potentially adverse health effects in animals or humans after subchronic or chronic oral exposure to phosphoric acid. In a case-control study of 57 children with serum calcium concentrations < 2.2 mmol/L and 171 referent children with serum calcium concentrations > 2.2 mmol/L, Mazariegos-Ramos et al. (1995) reported that a statistically significant association was found between the intake of phosphoric acid-containing soft drinks (at least 1.5 L/week) and hypocalcemia.

The World Health Organization (WHO, 1974) and Food and Agriculture Organization of the United Nations/World Health Organization (FAO/WHO, 1971) considered phosphoric acid, phosphates, and polyphosphates during a toxicological evaluation of food additives. Based on effects seen in rats fed mono and diphosphates in the diet, FAO/WHO (1971) concluded that renal

damage (calcification and necrosis of the tubular epithelium) is the critical effect of overexposure to this class of chemicals. The WHO (1974) estimated an ADI (Acceptable Daily Intake) of 0-70 mg P/kg-day (221 mg H_3O_4P/kg-day) for this group of food additives (phosphoric acid and its salts), provided that the diet is adequate in calcium. The ADI included ingestion of phosphates from natural sources together with phosphates from food additives; WHO (1974) stated that it represented total dietary phosphorus load. Assuming 70 kg body weight, the WHO ADI of 0-70 mg P/kg-day corresponds to total intakes of 0-4900 mg P/day. By way of comparison, NAS-NRC (1989) has established RDAs (Recommended Dietary Allowances) for phosphorus of 800 mg P/day for children 1-10 years and adults >24 years and 1200 mg P/day for ages 11-24 years and for pregnancy and lactation.

U.S. EPA (1992) lists mineral acids (including phosphoric acid) as pesticides of the fungicide, herbicide, and antimicrobial type. Phosphoric acid is awaiting reregistration and has been placed in the reregistration group of lowest concern (List D), in terms of potential for exposure and other factors. Its status is further described as "Awaiting Data/Data in Review," defined as follows: "OPP awaits data from the pesticide's producer(s) regarding its human health and/or environmental effects, or OPP has received and is reviewing such data, in order to reach a decision about the pesticide's eligibility for reregistration."

Further calculations

In the absence of an IRIS RfD for phosphoric acid, the WHO (1974) ADI, 221 mg phosphoric acid/kg-day, is taken as an RfD estimate for the purposes of toxicity weight derivation for oral exposure to phosphoric acid. Following TRI Environmental Indicator methods, the RfD estimate corresponds to a chronic oral toxicity weight of 1. Confidence in the toxicity weight is medium due to the lack of chronic studies describing dose-response relationships for this chemical. Nevertheless, the widespread use of this substance as a food additive and the GRAS status of oral exposure to phosphoric acid suggest that a low toxicity weight is appropriate for chronic oral exposure to phosphoric acid.

Chronic Inhalation

Basis of toxicity weight

The Integrated Risk Information System (IRIS; U.S. EPA, 1996) reports a chronic inhalation RfC of 0.01 mg/m^3 for phosphoric acid based on two 13-week studies of rats exposed for 2.25 hours/day on 4 consecutive days/week to an aerosol of combustion products from burning 95% red phosphorus and 5% butyl rubber (Aranyi et al., 1988). In the first study, groups of 176 male Sprague-Dawley rats were exposed to 0, 300, 750 or 1200 mg/m^3 combustion products. In the second study, groups of 20 male Sprague-Dawley rats were exposed to 0, 50, 180 or 300 mg/m^3 of the same combustion products. Mass median aerodynamic diameters of the aerosols ranged from 0.40 to 0.65 µm with a σg of 1.56-1.83; the phosphoric acid content of the aerosol ranged from 71.4 to 79.5% (w/w). Increased incidence for terminal bronchiolar fibrosis was found in groups exposed to concentrations ≥ 180 mg/m^3.

The IRIS summary stipulates that the data for bronchiolar fibrosis were modeled with a no-threshold Weibull model to arrive at a maximum likelihood estimate of the concentration producing a 10% extra risk for bronchiolar fibrosis (EC10) of 150 mg/m^3 and a BMC10 (95% lower confidence limit of the EC10) of 100 mg/m^3, and that the BMC10 was used to derive the RfC for phosphoric acid of 0.01 mg/m^3 by: 1) adjusting the BMC10 to continuous exposure [(100 mg/m^3) (2.25 hours/24 hours × 4 days/7 days) = 5.4 mg/m^3 = BMC10(ADJ)]; 2) multiplying the BMC10(ADJ) by an RDDR (Regional Deposited Dose Ratio) of 0.64 for an effect in the tracheobronchial area to obtain a BMC10(HEC) of 3.4 mg/m^3; and 3) dividing the BMC10 (HEC) by an uncertainty factor of 300 (3 for interspecies extrapolation since dosimetric considerations were partially accounted for by calculation of an RDDR, 10 to protect sensitive individuals, and 10 for the use of data for subchronic exposure) (3.4 mg/m^3/300 = 0.01 mg/m^3).

The RDDR of 0.64 was calculated using a model for insoluble and nonhygroscopic particles (as described in U.S. EPA, 1990), information on the growth characteristics of phosphoric acid aerosols in human airways, and assumptions that aerosol growth and deposition processes are similar between rodents and humans and between sulfuric and phosphoric acids. The IRIS summary concluded that there was no concern for systemic toxicity at the RfC, because toxicity in the prinicpal studies was limited to the portal of entry and phosphorus acid anions are present in normal human tissues. The RfC was stated to be most appropriate for phosphoric acid aerosols in the range of 0.4 to 1.0 microns. Medium confidence was ascribed to the principal study. The database also was rated medium due to the lack of chronic data. Overall confidence in the RfC thus was given a medium rating.

Further calculations

Following TRI Environmental Indicator methods, the chronic RfC of 0.01 mg/m^3 is converted to 0.003 mg/kg-day by multiplying by a reference human inhalation rate of 20 m^3/day and dividing by a reference human body weight of 70 kg. An RfD equivalent of 0.003 mg/kg-day corresponds to a chronic inhalation toxicity weight of 1000. Confidence in this toxicity weight is medium reflecting medium confidence in the RfC for phosphoric acid.

Caveat

The combustion product from burning 95% red phosphorus and 5% butyl rubber is not purely phosphoric acid. Phosphoric acid is expected to be less toxic than the combustion product.

Cancer Oral and Inhalation

Basis of toxicity weight

No data were found to support the calculation of cancer toxicity weights for phosphoric acid.

A Superfund Health Risk Technical Support Center Risk Assessment Issue Paper (U.S. EPA ORD, n.d.) reports that no studies regarding the carcinogenic potential of phosphorus pentoxide, phosphoric acid, or white phosphorus smoke were located. Genotoxicity studies were limited to two studies of phosphoric acid and two of white phosphorus smoke or condensate, but no positive results were found. The risk assessment issue paper classified phosphorus pentoxide in EPA weight-of-evidence group D - not classifiable as to human carcinogenicity. No other data were found to support the derivation of a cancer toxicity weight.

Sources

Aranyi, C., M.C. Henry, S.C. Vana, R.D. Gibbons, W.O. Iverson. 1988. "Effects of multiple intermittent inhalation exposure to red phosphorus/butyl rubber obscurant smokes in Sprague-Dawley rats." *Inhalation Toxicol.* 1: 65-68.

FAO/WHO (Food and Agriculture Organization of the United Nations/World Health Organization). 1971. *Toxicological Evaluation of Some Extraction Solvents and Certain Other Substances. Phosphoric Acid, Phosphates and Polyphosphates*. Fourteenth Report of the Joint FAO/WHO Expert Committee on Food Additives. FAO Nutrition Meetings Report Series No. 48A. p. 62-73

FDA (Food and Drug Administration). 1989. *Food and Drugs. 21 CFR 182 - Substances Generally Recognized as Safe*. p. 388-391, 396-397.

FDA (Food and Drug Administration). 1991. PAFA (Priority-Based Assessment of Food Additives) DataBase. Selected fields provided to Syracuse Research Corporation by FDA.

Mazariegos-Ramos, E., F. Guerrer-Romero, M. Rodriguez-Moran, G. Lazcano-Burciaga, R. Paniagua, and D. Amato. 1995. "Consumption of soft drinks with phosphoric acid as a risk factor for the development of hypocalcemia in children: A case-control study." *J. Pediatrics* 126: 940-942.

B.2.16. Picric Acid (2,4,6-Trinitrophenol) (88-89-1)

Chronic Oral

Basis of toxicity weight

The Risk Assessment Issue Paper for: Review of Proposed Oral RfD for Picric Acid (U.S. EPA ORD Superfund Health Risk Technical Support Center, n.d.) contained an oral RfD of 6×10^{-5} mg/kg-d from a 1914-1915 study by Koizumi (described in Von Oettingen, 1941), who gave dogs "repeated" 1.8 mg/kg oral doses of picric acid, and observed "injury of the kidney." No other details of the study are given; it was assumed that the dose was administered daily. Because of the low quality of the data, the LOAEL was divided by an uncertainty factor of 30,000. The

authors stated that "the lack of experimental details makes the uncertainty in using this study as the basis of the RfD so great, that derivation cannot be recommended."

Further calculations

Despite the limitations of the study cited above, in the absence of other data the RfD of 6×10^{-5} mg/kg-d was used to derive an oral toxicity weight of 10,000. Confidence in the toxicity weight is very low due to the poor quality of the data and the lack of supporting studies.

Chronic Inhalation

Basis of toxicity weight

The toxicity weight for inhalation exposure to picric acid is based on an RfD of 3×10^{-4} mg/kg-d, reported in the Risk Assessment Issue Paper for: *Review of Proposed Oral RfD for Picric Acid* (U.S. EPA ORD Superfund Health Risk Technical Support Center, n.d.). The RfD is based on the American Conference of Governmental Industrial Hygienists (ACGIH) Threshold Limit Value-Time Weighted Average (TLV-TWA) of 0.1 mg/m^3, which was suggested in the absence of extensive inhalation data. The TLV-TWA was converted to daily dose units by multiplying by a reference human respiration rate of $20m^3/d$ and dividing by a reference human body weight of 70 kg. This dose was then divided by an uncertainty factor of 100; 10 for sensitive populations, and 10 "to adjust for the use of TWA exposure and the healthy worker effect" (U.S. EPA, 1993). No additional modifying factor was used.

Further calculations

Following TRI Environmental Indicator methods, the RfD of 3×10^{-4} mg/kg-d yielded an inhalation toxicity weight of 10,000. Because of the lack of supporting data, confidence in the toxicity weight is low.

Cancer Oral and Inhalation

No dose-response data were found from which to calculate a cancer toxicity weight for picric acid.

Sources

U.S. EPA. 1993. Hazardous Substances Data Bank. Accessed via TOXNET.

U.S. EPA ORD Superfund Health Risk Technical Support Center. n.d. *Risk Assessment Issue Paper for: Review of Proposed Oral RfD for Picric Acid*. Draft.

No other sources of information were used, though the existence of a 1993 HEAST entry and a 1984 HEEP were noted.

B.2.17. Propylene (115-07-1)

Chronic Oral

No data were found to support the calculation of an oral toxicity weight for propylene (propene). HSDB did report, however, that propylene is a gas under environmental conditions; therefore the most likely route of human exposure to propylene is via inhalation. Following TRI Environmental Indicator methods, the chronic inhalation toxicity weight of 1 was applied to both exposure pathways (see below).

Chronic Inhalation

Basis of toxicity weight

HSDB reported a study by Quest et al. (1984), who exposed 50/sex F344/N rats and 49 or 50 B6C3F1 mice/sex to 0, 5,000, and 10,000 ppm for six hours per day, five days per week for 103 weeks. Exposure to propylene increased incidence of non-neoplastic lesions in the nasal cavity, including epithelial hyperplasia (high dose females), and squamous metaplasia (low and high dose females, low dose males). In addition, inflammatory changes (lymphocyte, macrophage, and granulocyte influx into the submucosa, granulocytes into the lumen) occurred in low and high dose male rats.

Further calculations

The LOAEL of 5,000 ppm was converted to a constant dose of 615 mg/kg-d by multiplying by a molecular weight of 42.08 g/mol, a reference rat respiration rate of 0.2 m^3/d, 6/24 hrs/d, 5/7 d/wk, and dividing by 24.45 L/mol and a reference rat body weight of 0.5 kg. The constant dose of 615 mg/kg-d was then divided by an uncertainty factor of 1,000 (10 each for intra- and interspecific extrapolation and 10 for the use of a LOAEL) to obtain an inhalation RfD of 0.62 mg/kg-d. Following TRI Environmental Indicator methods, this RfD yielded a chronic inhalation toxicity weight of 1. Confidence in the toxicity weight is medium due to the high quality of the study but the lack of supporting data.

Cancer Oral and Inhalation

IARC assigned propylene a ranking of Group 3; not classifiable as to its carcinogenicity to humans. No cancer toxicity weight was calculated.

Sources

U.S. EPA. 1993. Hazardous Substances Data Bank. Accessed via TOXNET.

NTP. 1993. *Toxicology and Carcinogenesis Studies of Propylene (CAS No. 115-07-1) in F344/N Rats and B6C3F$_1$ Mice (Inhalation Studies).*

No other sources of information were found.

B.2.18. Propylenimine (75-55-8)

Chronic Oral and Inhalation

No data were found to support the calculation of chronic toxicity weights for propylenimine.

Cancer Oral and Inhalation

Basis of toxicity weight

In the *Evaluation of the Potential Carcinogenicity of 1,2-Propylenimine In Support of Reportable Quantity Adjustments Pursuant to CERCLA Section 102* (1988), U.S. EPA OHEA identified Ulland et al. (1971) as the critical study in the derivation of a cancer potency for the chemical. In this study, 26 Charles River CD female rats were administered 10 mg/kg 1,2-propylenimine by gavage twice weekly for 421 days, for a constant dose of 2.9 mg/kg-d. Twenty of the 26 rats developed adenomas and/or carcinomas of the mammaries. No tumors were observed in the 12 control rats. Based on this study, OHEA derived a cancer potency of 259 per mg/kg-d. In addition, OHEA ranked propylenimine a B2 carcinogen (probable human carcinogen).

The *Technical Background Document to Support Rulemaking Pursuant to the Clean Air Act Section 112(g): Ranking of Pollutants With Respect to Hazard to Human Health* (U.S. EPA OHEA, 1993), however, noted that OHEA had incorrectly assumed that the study duration was 730 days in calculating the above cancer potency of 259 per mg/kg-d when in fact the study lasted only 421 days. Using the shorter study duration, OHEA recalculated the cancer potency to be 150 per mg/kg-d.

Further calculations

Following TRI Environmental Indicator methods, the cancer potency of 150 per mg/kg-d calculated by OHEA and the weight of evidence (WOE) classification of B2 yielded a maximum cancer toxicity weight of 1,000,000. Confidence in the toxicity weight is low due to the small sample size and the incomplete database.

Sources

U.S. EPA OHEA. 1988. *Evaluation of the Potential Carcinogenicity of 1,2-Propylenimine In Support of Reportable Quantity Adjustments Pursuant to CERCLA Section 102*.

U.S. EPA OHEA. *Technical Background Document to Support Rulemaking Pursuant to the Clean Air Act Section 112(g): Ranking of Pollutants With Respect to Hazard to Human Health*.

U.S. EPA. 1993. Hazardous Substances Data Bank (HSDB). Accessed via TOXNET.

U.S. EPA. 1993. Integrated Risk Information System (IRIS). Accessed via TOXNET.

No other sources of information were used, though the presence of an RQTox database entry was noted.

B.2.19. Sulfuric Acid (7664-93-9)

Chronic Oral

Basis of toxicity weight

An RfD for sulfuric acid is not available from the Integrated Risk Information System (IRIS; U.S. EPA, 1996) or the Health Effects Assessment Summary Table (HEAST; U.S. EPA, 1995). No oral exposure studies which could be used to derive an RfD estimate for sulfuric acid were located. Sulfuric acid is very corrosive and probably causes severe pain or spasms which would prevent the consumption of large doses. If swallowed, sulfuric acid will induce rapid, full-thickness necrosis of the stomach wall with perforation within several days, and is often fatal (Gosselin et al., 1984). In the absence of adequate data for sulfuric acid, the oral toxicity database on sulfate may be used as a surrogate. In aquatic media of pH >7, sulfuric acid reacts with carbonate, bicarbonate, or hydroxides in the sediment or suspended particles to form sulfates (U.S. EPA, 1984).

Sulfate has a well-known acute, laxative effect in humans. The laxative effects are assumed to be transient based on the finding that residents with high-sulfate drinking water seem to have no adverse effects, but newcomers initially experience the laxative effects. Based on mucosal cell turnover rate in the intestine, U.S. EPA (1994) estimated that acclimation to the laxative properties of sulfate would occur in approximately 2 weeks. Infants are more susceptible to the dehydration which can result from the sulfate-induced diarrhea and consume greater volumes of water relative to body weight, suggesting that infants are a more sensitive population than adults.

In a survey conducted by the North Dakota Department of Health, residents were asked to submit a water sample and complete a survey on the color, taste, and laxative qualities of their water (Peterson, 1951). The laxative effects question was aimed at newcomers and visitors. By plotting sulfate concentrations of the water against the incidence of laxative effects for approximately 300 samples and questionnaires (approximately 12-15% of the samples and questionnaires collected), it was concluded that sulfate concentrations exceeding 750 ppm

resulted in laxative effects in most residents. Sulfate concentrations between 600 and 750 ppm may or may not be laxative, and drinking water with <600 ppm sulfate is not likely to have laxative properties. In a re-examination of these data, Moore (1952) found that the percentages of residents reporting laxative effects were 22, 24, 33, and 62% when the water contained <200 ppm, 200-500 ppm, 500-1000 ppm and 1000-1500 ppm sulfate, respectively (the percentages are based on the number of residents answering the questions regarding laxative effects). Laxative effects were also reported by residents consuming water with high concentrations of dissolved solids and high levels of magnesium and sulfate. However, the laxative effects observed in these residents may have been due to the concominant high concentrations of sulfate; sulfate was the primary dissolved solid in the well water. U.S. EPA (1994) proposed a maximum contaminant level goal (MCLG) of 500 mg/L for sulfate based on the results of the North Dakota Survey.

Chien et al. (1968) reported case histories of 3 infants developing diarrhea after they were given formula reconstituted with well water. The well water samples contained 630, 720, and 1150 ppm sulfate. In all three cases, the infants had just recently moved into a new house with well water. The diarrhea stopped when a municipal or bottled water was used and returned when the infant was given the well water. In the case of the infant exposed to 1150 ppm sulfate in the water, the child's parents and two siblings also developed intermittent diarrhea, and the grandfather of the infant exposed to 720 ppm developed diarrhea when he visited the family. Chien et al. (1968) also briefly reports on three other infants with diarrhea that stopped when use of well water containing sulfate concentrations of 475, 600, or 680 mg/L was discontinued. This study has been criticized for not considering the potential effects of osmolarity or viral gastroenteritis, and a recommendation was made that this study be used for hazard identification but not for dose-response assessment (U.S. EPA, 1994).

A subchronic rat study found no adverse effects after 90 days or 10 months of exposure to high levels of sulfate in drinking water (Würzner, 1979). Groups of 25 male and 25 female Sprague Dawley rats were given tap water (9-10 mg/L sulfate) or natural mineral water containing <10, 280, or 1595 mg/L sulfate for 90 days. The mineral waters differed with respect to other ions and minerals. Using calculated time-weighted-average water intakes and body weights, the waters containing 280 and 1595 mg/L sulfate were estimated to provide sulfate doses of 36 and 207 mg/kg-day for males and 40 and 223 mg/kg-day for females. At 90 days, 20 rats/sex/group were killed; the remaining 5 rats/sex/group were continued on the exposure regimen for another 7 months. Daily sulfate doses for rats exposed for 10 months were calculated using body weights and water intakes measured at 11 weeks; the calculated doses were 17 and 95 mg/kg-day for males in the 280 and 1595 mg/L groups, respectively and 21 and 118 mg/kg-day for the females. No evidence of soft feces or diarrhea were observed in the sulfate-exposed rats. The only adverse effect observed was a statistically significant decrease in BUN levels in rats exposed to 1595 mg/L for 10 months. The toxicological significance of the decreased BUN levels in the absence of evidence of overhydration or liver damage is not known. No adverse effects on appearance or behavior, body weight gain, food or water consumption, hematological parameters, other serum chemistry parameters, organ weights (liver, kidneys, adrenals, brain, and testis), or

histopathology (stomach, duodenum, ileum, cecum, colon, kidneys, liver, adrenals, gonads, heart, lung, thyroid, pancreas, thymus, spleen, bladder, and aorta examined) were observed.

In a reproductive/developmental toxicity study, groups of 10 female ICR mice were administered 0, 625, 1250, 2500, or 5000 ppm sulfate as sodium sulfate in the drinking water (Andres and Cline, 1989). Sulfate doses of 150, 300, 600, 1200 mg/kg-day, respectively, were calculated using a reference water intake of 0.0085 L/day and body weight of 0.0353 kg. The sodium concentration (2392 ppm) was the same in the four groups of sulfate-exposed mice and in one of the two control groups. All groups of mice had ad libitum access to drinking water. After one week of exposure, the mice were mated with unexposed males and sulfate exposure was continued throughout gestation and lactation. After the pups were weaned, the dams were rebred to unexposed males and exposure continued through gestation and lactation of the second litter. As compared to the tap water control group, water consumption was significantly higher in the sulfate groups and the sodium control group; no significant alterations in water consumption were observed when the sulfate exposure groups were compared to the sodium control group. No significant alterations in maternal weight gain during gestation and lactation, litter size, or litter weaning weights were observed.

In the absence of relevant data on the oral toxicity of sulfuric acid, the oral toxicity database for sulfate is being used as a surrogate. The available data on the toxicity of sulfate provide evidence that the most sensitive effect is acute, transient diarrhea seen in humans. In infants, such diarrhea may lead to dehydration. The data from the North Dakota survey [as analyzed by Peterson (1951) and Moore (1952)] suggest that exposure to <500 mg/L sulfate would not likely result in laxative effects in adults. The Würzner (1979) study did not find any adverse effects in rats exposed to sulfate in the drinking water at concentrations of 280 or 1595 mg/L for 90 days, and no reproductive/developmental effects were observed in mice exposed to 5000 mg/L sulfate in a two generation study (Andres and Cline, 1989).

Further calculations

If the 500 mg/L sulfate identified from the North Dakota Health Survey (Peterson, 1951; Moore, 1952) is taken as a NOAEL, an RfD estimate for sulfuric acid can be derived. Because infants are a more sensitive population than adults, the RfD estimate is calculated using reference water intake and body weights for infants. The 500 mg/L concentration is converted to a daily dose by multiplying it by the infant water intake of 1 L/day and dividing by the infant body weight of 10 kg; the resultant dose is 50 mg/kg-day. This dose can be expressed in terms of sulfuric acid by multiplying the dose by the ratio of sulfuric acid and sulfate molecular weights:

$$50 \text{ mg } SO_4\text{/kg-day} \times (98.08/96.08) = 51 \text{ mg } H_2SO_4\text{/kg-day}$$

The 51 mg/kg-day sulfuric acid dose is divided by an uncertainty factor of 1 to derive an RfD estimate of 5×10^1 mg/kg-day. A larger uncertainty factor to account for human variability is not needed because the RfD estimate is based on a sensitive population.

Following the TRI Environmental Indicator methods, the RfD estimate of 5×10^{1} mg/kg-day for sulfuric acid corresponds to a chronic oral toxicity weight of 1. Confidence in this toxicity weight is low reflecting low confidence in the Peterson (1951) and Moore (1952) reports of the North Dakota survey and low confidence in the database which lacks oral toxicity studies for sulfuric acid.

Chronic Inhalation

Basis of toxicity weight

Because the vapor pressure of sulfuric acid is very low, it will exist in air as an aerosol. The site of deposition of an aerosol in the respiratory tract is important in assessing toxicity. Both the respiratory tract anatomy and patterns of airflow influence the site of deposition. Particles having an aerodynamic diameter of 5-10 µm are primarily deposited in the nasopharyngeal region; very fine particles (0.01 µm) are also efficiently trapped in the upper airways. The tracheobronchial region is the site of deposition of particles having an aerodynamic diameter of 1 to 5 µm. Smaller particles (<1 µm) are generally deposited in the alveolar region (U.S. EPA, 1989). In addition to particle size, several other factors can influence the site of deposition. Hygroscopic aerosols, such as sulfuric acid, take on water and can grow in size while in transit in the humid atmosphere of the upper respiratory tract. For example, a 1 µm particle of sulfuric acid can grow to 3 µm while in the nasal cavity. This increase in particle size would result in an alteration in the site and amount of particles deposited (approximately twice as many 3 µm particles would be deposited as compared to the 1 µm particles) (U.S. EPA, 1989). Factors that modify the diameter of the conducting airway, the pattern of breathing, and the breathing route (nasal versus oral inhalation) can also affect deposition. Irritants which produce bronchoconstriction tend to increase tracheobronchial deposition; exercise increases the amount of air inhaled and increases deposition in the conducting airways and alveoli; and oral breathing will result in a higher deposition of particles in the respiratory tract than nasal breathing.

Two important chemical defenses against inhaled acid are endogenous ammonia and airway surface liquid buffers (U.S. EPA, 1989). Expired ammonia can react with a significant portion of the inhaled acid to produce ammonium sulfate and ammonium bisulfate. The particle size of the acid aerosol, amount of ammonia in the airway, concentration of acid in the aerosol, and residence time of the aerosol in the airways can influence the amount of acid neutralized by ammonia. Smaller particles undergo a more rapid neutralization by ammonia than larger particles. Acid particles that are not neutralized by ammonia prior to deposition can be buffered by airway surface fluids. Reported mean values of airway pH in mammals range from 6.5 to 7.5. Acidification of the mucus layer by inhaled acids results in an increased mucus viscosity and increased clearance. However, if the pH of the mucus layer is sufficiently lowered, a reduction in ciliary motility will occur, resulting in a decrease in pulmonary clearance. The total capacity of the respiratory system to buffer or neutralize acid is substantial. However, there are regional differences in buffering capacity, and some regions of the respiratory tract have a fairly limited capacity. For example, in the non-ciliated airways and in the alveoli, the surface liquid buffering capacity is quite low and alveolar ammonia levels are lower than in the oral cavity. Thus,

accumulation of acid at a specific site can overwhelm the neutralization/buffering capacity of that region and result in toxic effects.

An RfC for sulfuric acid is not available on IRIS (U.S. EPA, 1996) or HEAST (U.S. EPA, 1995). A large amount of data has been collected on the acute toxicity of sulfuric acid in humans and animals. As reviewed by U.S. EPA (1989) and Costa and Amdur (1996), the primary target of sulfuric acid toxicity is the conducting airways resulting in bronchoconstriction, impaired pulmonary function and hyperresponsiveness, alterations in pulmonary clearance mechanisms, and symptoms of respiratory irritation. Some human studies have found very slight changes in indices of pulmonary function in healthy subjects exposed to approximately 1.0 mg/m^3 for 4 hours or less; however many studies did not find any alterations in pulmonary function at this concentration, and no studies found alterations at less than 0.5 mg/m^3 [mass median aerodynamic diameter (MMAD) 0.1-1.5 µm]. In contrast, alterations in pulmonary function have been observed in asthmatics exposed to 0.40 mg/m^3 (MMAD of 0.5-1.0 µm). Hyperresponsiveness (an alteration in the degree of reaction to exogenous bronchoactive agents resulting in increased airway resistance at levels which do not affect normal individuals) has been observed in guinea pigs exposed to concentrations at or above 19 mg/m^3 (MMAD 1.01 µm) for 1 hour and in rabbits exposed to 0.25 mg/m^3 (MMAD 0.3 µm) for 1 hour/day for 4-12 months. Increased airway reactivity to bronchoconstrictive drugs has also been observed in normal and asthmatic human subjects exposed to 1.0 mg/m^3. By constrast, exposure to 0.5 mg/m^3 may result in a delayed increase in reactivity, and no hyperresponsive effects have been observed at 0.1 mg/m^3. Symptoms of respiratory irritation have been reported by healthy and asthmatic subjects exposed to approximately 1 mg/m^3 or higher.

Sulfuric acid can interfere with the normal mechanisms of pulmonary clearance of particles. The response to sulfuric acid is dependent on the exposure concentration and exposure time. In rabbits, a brief single exposure to 0.25 mg/m^3 can result in an acceleration of pulmonary clearance, while reduction in pulmonary clearance was observed after exposure to 1.0 mg/m^3. In donkeys, a weekly 1 hour exposure to 0.2-1.0 mg/m^3 produced a transient depression of bronchial clearance. After 6 weeks of exposure, the depressed clearance persisted and lasted 2 months after sulfuric acid exposure was terminated. The pathological significance of transient alterations in pulmonary clearance in healthy individuals is not known. However, persistent impairment of clearance may lead to the inception or progression of acute or chronic respiratory illness.

A number of studies have investigated the long-term toxicity of sulfuric acid. In workers, long-term exposure to sulfuric acid can result in tooth surface loss (due to etching and erosion) (Tuominen et al., 1991; Petersen and Gormsen, 1991; Gamble et al., 1984). Although these studies measured current sulfuric acid levels (0.41 ->5 mg/m^3), it is not known if the current exposure levels accurately reflect past sulfuric acid concentration. In an occupational exposure study of lead acid battery workers exposed to sulfuric acid (mean length of employment was 10 years), Gamble et al. (1984) did not find a significant difference in the incidence of cough, phlegm, dyspnea, and wheezing, most measures of pulmonary function, or abnormal chest x-rays between workers with low cumulative exposure and workers with high cumulative exposure.

(The incidence of respiratory effects was not compared to a control group). At the time of the study, the average acid concentration was 0.18 mg/m^3 (concentrations ranged from non-detectable to 1.7 mg/m^3) (Jones and Gamble et al., 1984) and the range of particles sizes was 2.6-10 µm (MMAD). It is not known if this accurately reflected past exposure levels.

Subchronic and chronic animal studies have found impaired lung function and histological damage after long-term exposure to <1 mg/m^3 sulfuric acid (particle size of <5 µm). Alarie et al. (1973) exposed groups of 5 male and 4 female cynomolgus monkeys continuously to 0, 0.38 [mass median diameter (MMD) of 2.15 µm], 0.48 (0.54 µm), 2.43 (3.60 µm), or 4.79 (0.73 µm) mg/m^3 sulfuric acid for 78 weeks and groups of 50 male and 50 female Hartley guinea pigs to 0, 0.08 (MMD of 0.84 µm) or 0.10 (2.78 µm) mg/m^3 23 hours/day for 52 weeks. A number of alterations in pulmonary function were observed in the sulfuric acid-exposed monkeys, including increased respiratory rate at 2.43 mg/m^3, a transient increase in respiratory rate at 0.38 or 4.79 mg/m^3, lower decline in respiratory flow resistance during inspiration and expiration at 2.43 mg/m^3, and deterioration of distribution of ventilation at 0.48 mg/m^3. No alterations in hematological or serum clinical chemistry parameters or organ weights were observed. Histological alterations in the monkeys were limited to the lungs. Significant increases in bronchiolar epithelial hyperplasia were observed at 0.38, 2.43, or 4.79 mg/m^3; the severity of the hyperplasia was concentration related. Thickening of the walls of the respiratory bronchioles was also observed at 2.43 or 4.79 mg/m^3, and an increased thickness of alveolar walls was observed in the 2.43 mg/m^3 group. In the guinea pigs, no significant alterations in pulmonary function, growth, hematological or serum chemistry parameters, organ weights, or histological alterations were observed. Thus, this study identifies a LOAEL of 0.38 mg/m^3 for transient increases in respiratory rate and bronchiolar epithelial hyperplasia in monkeys.

Lewis et al. (1973) found significant alterations in pulmonary function (carbon monoxide diffusion capacity, residual volume, lung volume, and resistance) in 16 female beagle dogs exposed to 0.889 mg/m^3 sulfuric acid 21 hours/day for 620 days. The authors noted that 90% of the particles were smaller than 0.5 µm in diameter. No consistent alterations in hematological parameters, growth, or lung histology were observed.

Schlesinger et al. (1992) exposed groups of 20 male New Zealand white rabbits via nose-only exposure to 0 or 0.125 mg/m^3 sulfuric acid [MMAD 0.3 µm with a geometric standard deviation (σ_g) of 1.6] 2 hours/day, 5 days/week for 3-12 months. Exposure to sulfuric acid resulted in an acceleration of pulmonary clearance followed by a progressive slowing of clearance (as compared to pre-exposure baseline clearance rates). Statistically significant increases in pulmonary clearance rates were observed during months 1-4 and 5-8, and clearance after 9-12 months of exposure was not significantly different than pre-exposure values. However, in the rabbits exposed to sulfuric acid for 12 months and allowed to recover for 6 months, the pulmonary clearance rate was significantly slower in the recovery period than in the pre-exposure period. No significant alterations in airway diameter or histological alterations in the intrapulmonary conducting airways were observed. However, a statistically significant increase in the number of airway secretory cells was observed in the rabbits exposed for 12 months as

compared to the control group.

Murray et al. (1979) exposed groups of pregnant CF-1 mice (35/group) and New Zealand white rabbits (20/group) to 0, 5, or 20 mg/m^3 sulfuric acid [count median diameter of 0.4 (reflecting airborne dust in the chamber), 1.6, and 2.4 µm, respectively) for 7 hours/day on gestational days 6 through 15 (mice) or 6 through 18 (rabbits). Maternal effects in the mice were limited to a significant decrease in absolute and relative liver weight in the mice exposed to 20 mg/m^3. In the rabbits, no consistent alterations in maternal body weight gain or liver weights were observed. Dose-related increases in the incidence of subacute rhinitis and tracheitis were observed in the rabbit dams, but no alterations in the lungs were observed. No significant alterations in the number of implants/dam, live fetuses/litter, resorptions/litter, sex ratio (analyzed on a per litter basis), or fetal body weights or length (on a per litter basis) were observed in the mice or rabbits. The incidences of fetal malformations in the mice and rabbits exposed to sulfuric acid did not significantly differ from the incidences in the control groups.

The available human and animal studies provide evidence that the respiratory tract is the most sensitive target following acute or long-term exposure to sulfuric acid. A number of factors can influence the toxicity of inhaled sulfuric acid including the respiratory tract's ability to buffer/neutralize the acid, particle size, hygroscopic growth in the respiratory tract, pre-existing conditions (i.e., asthma), exposure concentration, and total deposited dose (concentration x exposure time). Not all of these factors will equally influence a given endpoint. There are limited data on the chronic toxicity of sulfuric acid in humans. Gamble et al. (1984) did not find any significant associations between sulfuric acid exposure and pulmonary function, symptoms of respiratory disease, or chest x-rays in lead acid battery workers, with an average employment length of 10 years, exposed to an average concentration of 0.18 mg/m^3. However, the lack of comparison to a control group limits the usefulness of this study. Chronic exposure to low concentrations of sulfuric acid has been shown to increase the amount of tooth surface loss from etching and erosion; however, lack of adequate exposure information (e.g., past exposure levels) precludes identifying a LOAEL for this effect. Respiratory irritation and impaired pulmonary function has been observed in healthy humans exposed to 1.0 mg/m^3 for < 4 hours (particle size of <1.5 µm). Adverse pulmonary function effects have been observed in asthmatics after a brief exposure to 0.40 mg/m^3 (as reviewed by U.S. EPA, 1989 and Costa and Amdur, 1996). Impaired pulmonary function, as well as altered pulmonary clearance and histological alterations in the lungs have also been observed in animals exposed to sulfuric acid for acute and long-term durations. Alarie et al. (1973) identified a LOAEL of 0.38 mg/m^3 for impaired pulmonary function and histological damage to the lungs in monkeys continuously exposed to sulfuric acid for 78 weeks. A LOAEL of 0.125 mg/m^3 for impaired pulmonary clearance was identified in rabbits exposed to sulfuric acid for 2 hours/day, 5 days/week for 12 months (Schlesinger et al., 1992).

The LOAEL of 0.38 mg/m^3 in monkeys identified in the Alarie et al. (1973) study can be used to derive an RfC-equivalent-estimate for sulfuric acid. Although the Schlesinger et al. (1992) rabbit study identified a lower LOAEL (0.125 mg/m^3 for impaired pulmonary clearance),

the Alarie et al. (1973) study was selected as the principal study because it utilized a longer duration of daily exposure (24 hours/day) than the Schlesinger et al. (1992) study (2 hours/day). An RfC-equivalent-estimate based on the Alarie et al. (1973) study would be protective against decreased pulmonary clearance and tooth surface loss and would also protect asthmatics from adverse effects.

Further calculations

Using the TRI Environmental Indicator methods, the LOAEL of 0.38 mg/m^3 identified in monkeys continuously exposed to sulfuric acid was divided by an uncertainty factor of 300 (10 for use of a LOAEL, 3 for interspecies extrapolation, and 10 for human variability) to yield an RfC-equivalent-estimate of 1.3×10^{-3} mg/m^3.

Following TRI Environmental Indicator methods, the RfC-equivalent-estimate of 1.3×10^{-3} mg/m^3 corresponds to a chronic inhalation toxicity weight of 10,000. Confidence in this inhalation toxicity weight is medium, reflecting medium confidence in the Alarie et al. (1973) study which was the basis of the RfC-equivalent-estimate and medium confidence in the database.

Cancer Oral and Inhalation

Basis of toxicity weight

A carcinogenicity assessment for sulfuric acid is not available on IRIS (U.S. EPA, 1996) or HEAST (U.S. EPA, 1995). IARC (1992) has determined that there is sufficient evidence to judge that occupational exposure to strong inorganic acid mists containing sulfuric acid is carcinogenic to humans. Several cohort mortality studies and case-control studies have examined workers predominantly exposed to sulfuric acid mists and found increases in the incidences of laryngeal cancer and/or lung cancer or significant associations of cancer with exposure (Beaumont et al., 1987; Soskolne et al., 1984, 1992). A common limitation of these studies is the lack of quantified contemporaneous exposure information. The Beaumont et al. (1987) cohort mortality study provides some information on exposure levels. This study examined a cohort of 1165 workers employed at 3 steel-manufacturing facilities between 1940 and 1964. Sulfuric acid and other acids were used to remove oxides from newly manufactured steel (pickling process). It was estimated that 722 of the workers were exposed only to sulfuric acid, of which 595 workers had daily exposure to sulfuric acid. The remaining workers were exposed to sulfuric acid and other acids (254 workers) or only other acids (189 workers). The only available exposure data were from 3 surveys taken at one of the facilities in 1975, 1977, and 1979. The average sulfuric acid concentration (as obtained by personal samplers) was 0.19 mg/m^3 (range of <0.03 to 0.48 mg/m^3). Most of the workers in the cohort worked at this facility, and the pickling processes were similar at all three facilities. The authors noted that it was likely that air concentrations in past years were similar to those measured in the late 1970s; however, it was possible that exposures were reduced in the 1970s due to increased worker awareness of the hazards of workplace exposures. Cause-specific mortality was compared to the 1978 U.S. population mortality rates. A statistically significantly increased standard mortality ratio (SMR) for lung cancer deaths (SMR=1.64; 95% confidence interval of 1.14-2.28) was found for the whole cohort; among workers with daily

exposure to only sulfuric acid, the SMR was 1.58 (95% confidence interval not reported, but authors noted that the confidence interval included 1). Duration of exposure did not influence lung cancer mortality; the SMR was 1.61 in workers with daily exposure for 0.5 to <5 years as compared to 1.40 in workers exposed daily for 10 to >15 years. But the time since first employment (latency period) did influence the lung cancer mortality. The SMR (1.93) was higher in workers with a latency period of 20 years or more as compared to less than 20 years (SMR=0.65). Individual smoking habits were not available for the cohort. The authors estimated the potential effect of differences in the number of ex-smokers and current smokers between the study cohort and the comparison U.S. population. If the assumption was made that the number of smokers in the study cohort was the same or 5, 10, 15, or 20% higher than the comparison population, then the mortality rate ratios attributed to smoking alone would have been 1.0, 1.06, 1.12, 1.18, and 1.24, respectively, suggesting that increased smoking habits alone would not explain the increased lung cancer mortality in the study cohort (SMR of 1.64). The authors found this supported by the finding of fewer than the expected number of deaths from non-malignant respiratory disease or cardiovascular disease in the study cohort.

Soskolne et al. (1992) examined the relationship between laryngeal cancer and exposure to sulfuric acid in a case-control study of male residents of four Canadian cities. The authors used self-reported information on work experience to estimate exposure concentration and frequency of exposure to sulfuric acid. Statistically significant associations between sulfuric acid exposure and the incidence of laryngeal cancer were found after controlling for smoking and alcohol consumption; the proportion of laryngeal cancer cases among residents with occupational exposure to sulfuric acid was compared to the proportion of case among residents with no occupational exposure to sulfuric acid. Higher proportions of cases of laryngeal cancer were observed in workers with high exposure to sulfuric acid for greater than10 years (odds ratio of 6.91; 95% confidence interval of 2.20-21.74) and in workers with low exposure to sulfuric acid for greater than 10 years (3.85; 95% confidence interval of 1.60-9.24). A statistically significant increase in the proportion of laryngeal cancer cases was also observed in workers with low exposure for a short duration ($\leq$10 years) (odds ratio of 2.66; 95% confidence interval of 1.09-6.49), but not in workers with high exposure for a short duration (odds ratio of 3.34, 95% confidence interval of 0.60-18.53).

Soskolne et al. (1984) also found a statistically significantly higher proportion of workers exposed to high concentrations of sulfuric acid among cases of laryngeal cancer at a large refinery and chemical plant in Baton Rouge, Louisiana than among age, race, employment duration, and hire-date matched controls, after controlling for tobacco use, alcoholism, and history of ear, nose, or throat disease.

No oral studies examining the carcinogenicity of sulfuric acid or sulfate were located.

Further calculations

There are limited human data and no animal data on the carcinogenicity of sulfuric acid; the available carcinogenicity data for sulfuric acid appear to correspond to a weight of evidence classification of B1 in the U.S. EPA classification scheme. The available human carcinogenicity studies do not provide accurate information which could be used to determine exposure concentrations. Although the Beaumont et al. (1987) study reported exposure levels during the late 1970s, most of the workers began working at the steel facilities in the 1940s and 1950s, and it is not known if the exposure concentrations in the 1940s and 1950s were similar to those measured in the 1970s. Thus, an inhalation cancer toxicity weight can not be determined.

There are no oral cancer studies on sulfuric acid or sulfate which could be used to derive an oral cancer toxicity weight.

Sources (*indicates key references)

*Alarie, Y., W.M. Busey, A.A. Krumm and C.E. Ulrich. 1973. Long-term continuous exposure to sulfuric acid mist in Cynomolgus monkeys and guinea pigs. Arch. Environ. Health. 27: 18-24.

Andres, C.J. and T.R. Cline. 1989. Influence of sulfate in drinking water on mouse reproduction during two parities. J. Anim. Sci. 67: 1313-1317.

*Beaumont, J.J., J. Leveton, K. Knox, et al. 1987. Lung cancer mortality in workers exposed to sulfuric acid mist and other acid mists. J. Natl. Cancer Institut. 79: 911-921.

Chien, L., H. Robertson, and J.W. Gerrard. 1968. Infantile gastroenteritis due to water with high sulfate content. Can. Med. Assoc. J. 99: 102-104.

Costa, D.L. and M.O. Amdur. 1996. Air Pollution. In: Klaassen, C.D. Casarett and Doull's Toxicology: The Basic Science of Poisons. Fifth edition. New York: McGraw-Hill. Pp. 868-870.

Gamble, J. W. Jones, J. Hancock and R.L. Meckstroth. 1984. Epidemiological-environmental study of lead acid battery workers. III. Chronic effects of sulfuric acid on the respiratory system and teeth. Environ. Res. 35: 30-52.

Gosselin, R.E., R.P. Smith and H.C. Hodge. 1984. Clinical Toxicology of Commercial Products, 5th ed., Section III, Therapeutics Index, Baltimore: Williams & Wilkins. pp. 8-12.

IARC (International Agency for Research on Cancer). 1992. Occupational Exposures to Mists and Vapours from Strong Inorganic Acids; and Other Industrial Chemicals. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, Volume 54. Lyons, France: IARC, World Health Organization. pp. 41-119.

Jones, W. And J. Gamble. 1984. Epidemiological-environmental study of lead acid battery workers. I. Environmental study of five lead acid battery plants. Environ. Res. 35: 1-10.

Lewis, T.R. W.J. Moorman, W.F. Ludmann and K.I. Campbell. 1973. Toxicity of long-term exposure to oxides of sulfur. Arch. Environ. Health. 26: 16-21.

*Moore, E.W. 1952. Physiological effects of the consumption of saline drinking water. A progress report to the Subcommittee on Water Supply of the Committee of Sanitary Engineering and Environment of the National Research Council. Bulletin, Water Supply, Appendix B: 1-7.

Murray, F.J., B.A. Schwetz, K.D. Nitschke, A.A. Crawford, J.F. Quast and R.E. Staples. 1979. Embryotoxicity of inhaled sulfuric acid aerosol in mice and rabbits. J. Environ. Sci. Health. C13: 251-266.

Petersen, P.E. and C. Gormsen. 1991. Oral conditions among German battery factory workers. Comm. Dent. Oral Epidemiol. 19: 104-106.

*Peterson, N.L. 1951. Sulfates in drinking water. Official Bulletin North Dakota Sewage Works. 18 (10/11): 11.

Schlesinger, R.B., J.E. Gorcyzinski, J. Dennison, L. Richards, P.L. Kinney and M.C. Bosland. 1992. Long-term intermittent exposure to sulfuric acid aerosol, ozone, and their combination: alterations in tracheobronchial mucociliary clearance and epithelial secretory cells. Exper. Lung Res. 18: 505-534.

Soskolne, C.L., E.A. Zeigham, N.M. Hanis, L.L. Kupper, N. Herrmann, J. Amsel, et al. (1984). Laryngeal cancer and occupational exposure to sulfuric acid. Am. J. Epidemiol. 120: 358-369.

Soskolne, C.L., G.S. Jhangri, J. Siemiatycki, R. Lakhani, R. Dewar, J.D. Burch, et al. 1992. Occupational exposure to sulfuric acid in southern Ontario, Canada, in association with laryngeal cancer. Scand. J. Work Environ. Health. 18: 225-232.

Tuominen, M.L., R.J. Tuominen, F. Fubusa and N. Mgalula. 1990. Tooth surface loss and exposure to organic and inorganic acid fumes in workplace air. Comm. Dent. Oral Epidemiol. 19: 217-220.

U.S. EPA. 1984. Health Effects Assessment for Sulfuric Acid. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Emergency and Remedial Response, Washington, DC. ECAO-CIN-H031.

U.S. EPA. 1988. Recommendations for and Documentation of Biological Values for Use in Risk Assessment. Prepared by the Office of Health and Environmental Assessment,

Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Emergency Response, Washington, DC.

U.S. EPA. 1989. An Acid Aerosols Issue Paper: Health Effects and Aerometrics. Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Research Triangle Park, NC. EPA-600/8-88-005F, NTIS PB91-125864.

U.S. EPA. 1994. Drinking Water; National Primary Drinking Water Regulations-Sulfate; National Primary Drinking Water Regulation Implementation. Fed. Reg. 59(243): 65578-65583.

U.S. EPA. 1995. Health Effects Assessment Summary Tables. FY-1995 Annual and FY-1995 Supplement. Office of Research and Development, Office of Emergency and Remedial Response, Washington DC. NTIS 95-921199 and PB95-921101.

U.S. EPA. 1996. Integrated Risk Information System. Online. Office of Research and Development, National Center for Environmental Assessment, Cincinnati, OH.

Würzner, H.P. 1979. Exposure of rats during 90 days to mineral water containing various amounts of sulphate. Z. Ernährungswiss. 18: 119-127.

B.2.20. Thiourea (62-56-6)

Chronic Oral and Inhalation

No dose-response data were available from which to calculate chronic toxicity weights for thiourea.

Cancer Oral and Inhalation

Basis of toxicity weight

Using the Crump linearized multistage polynomial (Crump et al., 1977), the California EPA Office of Environmental Health Hazard Assessment (OEHHA) derived a cancer potency of 0.072 per mg/kg-d for thiourea, based on a study of Hebrew University male rats administered 0.2 percent thiourea (approximately 100 mg/kg-d) in their drinking water for 14 to 23 months (Vasquez-Lopez, 1949). Thiourea-induced epidermoid carcinomas of the eyelid and auricular region occurred in 7/8 of the dosed rats. U.S. EPA OHEA (1992) calculated a cancer potency of 1.05 per mg/kg-d for use in deriving a Reportable Quantity ranking for thiourea. The *Public Docket for Reportable Quantity Adjustments on thiourea* (Docket Number 102 RQ-273C), however, contained no information on the critical study used by OHEA to calculate the potency factor. The *PMN Analogue Profile for thiourea* (EPA, 1990) listed six studies in which rats showed increased incidence of tumors following oral exposure to thiourea. One study (Fitzhugh and Nelson, 1948) reported in the *PMN Analogue Profile* showed increased incidence of hepatic

adenomas at doses of 2, 5, 10, and 20 mg/kg-d, but at non-dose related rates (3/5, 4/8, 2/8, and 5/8, respectively). Because of the small number of rats in each study, the authors of the *PMN Analogue Profile* commented that the studies provided only suggestive evidence for the carcinogenicity of thiourea.

The U.S. EPA OHEA cancer potency of 1.05 per mg/kg-d was chosen for use in developing a cancer toxicity weight because it is more protective than the OEHHA cancer potency factor.

The International Agency for Research on Cancer (IARC) ranks thiourea a Group 2B carcinogen (possible human carcinogen). Based on sufficient evidence of carcinogenicity in rats and no data on carcinogenicity in humans, the U.S. EPA OHEA gave thiourea a WOE classification of B2.

Further calculations

Based on a cancer potency of 1.05 per mg/kg-d and a WOE of B2, thiourea was assigned a cancer toxicity weight of 10,000 for both oral and inhalation exposure. Confidence in the toxicity weight is low, based on lack of knowledge of the critical study and the small sample sizes of the supporting studies.

Sources

California EPA OEHHA. 1992. *Expedited Cancer Potency Values and Proposed Regulatory Levels for Certain Proposition 65 Carcinogens*.

IARC. 1993. *Monographs on the Evaluation of Carcinogenic Risk to Humans*. Lyon, France.

U.S. EPA. 1990. *PMN Analogue Profile for Thiourea*. Working Draft.

U.S. EPA. 1993. Hazardous Substances Data Bank (HSDB). Accessed via TOXNET.

U.S. EPA OHEA. 1992. Reportable Quantity tables

U.S. EPA OSWER. 1989. *Technical Background Document to Support Rulemaking Pursuant to CERCLA Section 102*.

No other sources of information were found.

B.2.21. Thorium Dioxide (1314-20-1)

According to *Radiochemical Manual* (2nd Ed., 1966), all forms of thorium are radioactive and release ionizing radiation. Various isomers of thorium are part of the thorium

(4n), uranium (4n+2) and uranium/actinium (4n+3) decay series. Thorium occurs early in the decay schemes and its daughters release alpha, beta, and gamma emissions. All three types of emissions have been associated with cancer in numerous studies on humans and animals. In addition, short term exposure to these radioactive emissions cause cell disruption, particularly to cells with rapid turnover rates, such as red blood cells.

The subchronic or chronic reference dose and cancer potency of a radioisotope depends on both its concentration and specific activity. In addition, its potency is affected by its transport, deposition, and retention in the body. Consequently, it is difficult to address cancer potency for thorium dioxide using the same approach as was used for other TRI chemicals.

Chronic Oral

No dose-response data were available from which to calculate a chronic oral toxicity weight. Following TRI Environmental Indicator methods, the chronic inhalation toxicity weight of 10,000 was applied to both exposure pathways (see below).

Chronic Inhalation

Basis of toxicity weight

HSDB cited a study reported in Venugopal (*Metal Toxicity in Mammals 2*, 1978) in which dogs, rabbits, guinea pigs, and mice were exposed to 10 to 80 mg/m^3 thorium dioxide for 60 to 270 days. Increased leukocyte levels and abnormal bone marrow and lung lesions of uncertain etiology were observed. No other study specifics were reported.

Further calculations

Assuming that the lowest dose level produced these effects, 10 mg/m^3 was used as a LOAEL in order to calculate an RfD estimate and chronic inhalation toxicity weight for thorium dioxide. Dogs were assumed to be the most sensitive species since they experienced the lowest dose/kg body weight. The LOAEL of 10 mg/m^3 was converted to a constant dose of 3.6 mg/kg-d by multiplying by a reference dog respiration rate of 4.5 m^3/d and dividing by a reference dog body weight of 12.6 kg. The LOAEL of 3.6 mg/kg-d was divided by an uncertainty factor of 10,000 (10 each for intra- and interspecific extrapolation, 10 for the use of a LOAEL, and 10 for the use of a subchronic study) to derive an RfD estimate of 3.6×10^{-4} mg/kg-d. Following TRI Environmental Indicator methods, this RfD yielded a chronic inhalation toxicity weight of 10,000 for thorium dioxide. Because no information was given on the specific activity of the thorium dioxide used in the study, however, confidence in the toxicity weight is low.

Cancer Oral and Inhalation

Basis of toxicity weight

The *Drinking Water Criteria Document for Alpha Emitting Radionuclides* (U.S. EPA OGWDW, 1991) reports that the only available data regarding the effects of thorium in humans

are from Thorotrast studies. Thorium dioxide (Thorotrast) was given to tens of thousands of patients between the 1930s and the 1950s, primarily for radiological visualization of blood vessels and/or kidneys (HSDB). The primary effects of intravenously injected Thorotrast were liver tumors, bone tumors, splenic cirrhosis, and blood disorders, including aplastic anemia, myelofibrosis, and leukemia.

A number of clinical and epidemiological studies cited in HSDB and the *Drinking Water Criteria Document for Alpha Emitting Radionuclides* link intravenous administration of thorium dioxide to leukemia and liver, spleen, lung, cranial, and kidney cancer in humans, with latency periods up to 45 years.

Further calculations

The above data suggest a possible U.S. EPA weight of evidence classification of A (carcinogenic to humans). Due to data limitations described above, no quantitative cancer potency was calculated. Rather, the maximum cancer toxicity weight of 1,000,000 was assigned to thorium dioxide based on IV administration toxicity.

Sources

NIOSH. 1993. Registry of Toxic Effects of Chemical Substances (RTECS). Accessed via TOXNET.

Radiochemical Center. 1966. *Radiochemical Manual*. 2nd Edition. Amersham, England.

U.S. EPA. 1993. Hazardous Substances Data Bank. Accessed via TOXNET.

U.S. EPA OGWDW. 1991. *Drinking Water Criteria Document for Alpha Emitting Radionuclides*.

No other sources of information were found.

B.2.22. 1,1,1-Trichloroethane (71-55-6)

Chronic Oral

The ATSDR did not find adequate data to calculate a chronic Minimum Risk Level (MRL) for 1,1,1-trichloroethane (1,1,1-TCE) via the oral route (ATSDR, 1995). EPA has withdrawn the oral RfD value from the IRIS data base for further consideration (U.S. EPA, 1996).

Basis for toxicity weight

One chronic study reviewed by ATSDR (1995) reported a reduced body weight gain of 12% after 80 weeks of dosing in rats via oral gavage with 500 mg/kg/day of 1,1,1-TCE (Maltoni et al., 1986 as cited in ATSDR, 1995).

Further calculations

Taking 500 mg/kg/day as a LOAEL and applying an uncertainty factor of 1,000 (10 for the use of the LOAEL, 10 for extrapolation from animals to humans, and 10 for human variability) gives a provisional RfD of 0.5 mg/kg/day and a toxicity weight of 10. Confidence in the toxicity weight is low because the ATSDR found the Maltoni et al. (1986 as cited in ATSDR, 1995) study to be inadequate based on the use of a single dose, no detailed information and the lack of supporting data.

Chronic Inhalation

The ATSDR did not derive a chronic inhalation MRL for 1,1,1-TCE (ATSDR, 1995). Generation of an inhalation RfC by EPA is pending (U.S. EPA, 1996).

Basis for toxicity weight

The ATSDR did derive a subchronic inhalation MRL of 0.7 ppm based on a NOAEL of 70 ppm derived from a study by Rosengren, et al. (1985 as cited in ATSDR, 1996). The continuous-exposure NOAEL(HEC) of 382 mg/m^3 for increased GFA protein in the sensorimotor cerebral cortex in gerbils (Rosengren et al., 1985) was selected as the basis of a chronic RfC for 1,1,1-trichloroethane. This study was selected because:

1) it used the gerbil, a sensitive species to 1,1,1-trichloroethane toxicity;

2) it used a continuous exposure scenario (24 hours/day, 7 days per week: 0, 70, 210 or 1000 ppm or 382, 1147 or 5460 mg/m^3 (***please note that according to EPA (1994) guidelines, these gerbil exposure concentrations were, by default, assumed to be Human Equivalent Concentrations (HECs) due to the lack of data for a gerbil blood/gas partition coefficient for 1,1,1-trichloroethane***);

3) it measured brain levels of GFA protein, a sensitive and reliable marker for brain damage (astrogliosis);

4) other available studies did not measure brain levels of GFA protein following exposure; and

5) it found that, although the exposure was not of a chronic (i.e., lifetime) duration, the

effects occurred at the end of a 3-month exposure period and persisted for 4 months after exposure ended (when the experiment was terminated), suggesting that the effect was irreversible and probably would have been observed in a chronic study, if it were assayed.

The Quast et al. studies (1978; 1988) were well designed, conducted, and reported, (e.g., sufficient numbers of animals were included for statistical purposes, interim sacrifices were included, several exposure levels were included, and comprehensive histological examinations of tissues were conducted: see brief summaries below). Endpoints evaluated included hematology, serum chemistry, urinalysis, body weights, organ weights and comprehensive gross pathology and histopathology, but the study did not evaluate any neurological endpoints. Although the Quast studies used a longer duration of exposure (12 months and 2 years) than the Rosengren et al. (1985) study (3 months), the Rosengren study was selected for RfC derivation because the Quast studies did not evaluate any neurological endpoints.

Quast et al. (1978) exposed groups of male and female Sprague-Dawley rats (n = 189, 94 and 92 per sex) to 0, 875 or 1750 ppm (4778 and 9555 mg/m^3) for 6 hours/day, 5 days/week for 12 months; rats were observed for 19 months after the exposure period, when all survivors were sacrificed. The only significant exposure-related effect observed was an increased incidence of focal hepatocellular changes in female rats (at the end of the observation period) exposed to 1750 ppm compared with control rats. This effect was not observed in the small number (n = 3 per sex) of rats sacrificed at the end of the exposure period.

The 1988 study (Quast et al., 1988) exposed groups of male and female F344 rats and B6C3F1 mice (n = 80 per sex per species) to 0, 150, 500 or 1500 ppm (0, 819, 2730 or 8190 mg/m^3) 1,1,1-trichloroethane for 6 hours/day, 5 days per week for 2 years. No exposure-related effects were found in exposed mice of either sex compared with controls. In exposed rats, the only exposure-related effects found, compared with controls, were slightly decreased body weights ($\leq$ 7% less than controls) and mild histopathological changes in livers of rats exposed to 1500 ppm.

Using the NOAEL(HEC) of 382 mg/m^3 (Rosengren et al., 1985) and applying an uncertainty factor of 300 (10 for subchronic study, 3 for interspecies differences, 10 for intraspecies sensitivity), an RfC of 1 mg/m^3 was derived following U.S. EPA (1994) guidelines for derivation of inhalation reference concentrations. An additional uncertainty factor for incomplete data base was not applied because the only major deficiency, lack of a multigeneration study, was judged to be partially addressed by a rat developmental toxicity study that included a premating exposure schedule and postnatal observations. Confidence in the principal study was rated medium, because it was an adequately designed study that examined a sensitive neurologic endpoint (although brain histology and neurobehavioral performance were not evaluated). Confidence in the data base was rated to be medium, although CNS effects are well characterized in various species, corroborating data are lacking for 1) the endpoint used as the indicator of the critical effect (i.e., brain GFA protein) and 2)

non-neurologic effects in gerbils. Reflecting medium confidence in the key study and data base, confidence in the chronic RfC was rated medium.

To derive a toxicity weight for 1,1,1-trichloroethane, the chronic RfC, 1 mg/m^3, would be converted to 0.29 mg/kg-day by multiplying it by a reference inhalation rate for humans (20 m^3/day; U.S. EPA, 1987) and dividing by a reference body weight (70 kg; U.S. EPA, 1987). The value of 0.29 mg/kg-day corresponds to a toxicity weight of 10 (U.S. EPA, 1996).

Cancer Oral

The EPA has rated the weight-of-evidence for the carcinogenicity of 1,1,1-TCE as D: not classifiable as to human carcinogenicity. There are no reported human data; animal studies (one lifetime gavage) have not demonstrated carcinogenicity (U.S. EPA, 1996).

The NCI (1977, as cited in U.S. EPA, 1996) treated Osborne-Mendel rats (50/sex/dose) with 750 or 1500 mg/kg technical-grade 1,1,1-TCE 5 times/week for 78 weeks by gavage. The rats were observed for an additional 32 weeks. Twenty rats of each sex served as untreated controls. Low survival of both male and female treated rats (3%) may have precluded detection of a significant number of tumors late in life. Although a variety of neoplasms was observed in both treated and matched control rats, they were common to aged rats and were not dose-related. Similar results were obtained when the NCI (1977, as cited in U.S. EPA, 1996) treated B6C3F1 hybrid mice with time-weighted average doses of 2807 or 5615 mg/kg 1,1,1-TCE by gavage 5 days/week for 78 weeks. The mice were observed for an additional 12 weeks. The control and treated groups had 20 and 50 animals of each sex, respectively. Only 25 to 45% of those treated survived until the time of terminal sacrifice. A variety of neoplasms were observed in treated groups, but the incidence was not statistically different from matched controls (U.S. EPA, 1996).

Cancer Inhalation

The EPA has rated the weight-of-evidence for the carcinogenicity of 1,1,1-TCE as D: not classifiable as to human carcinogenicity. There are no reported human data; animal studies (one intermediate-term inhalation) have not demonstrated carcinogenicity (U.S. EPA, 1996).

Quast et al. (1978, as cited in U.S. EPA, 1996) exposed 96 Sprague-Dawley rats of both sexes to 875 or 1750 ppm 1,1,1-TCE vapor for 6 hours/day, 5 days/week for 12 months, followed by an additional 19-month observation period. The only significant sign of toxicity was an increased incidence of focal hepatocellular alterations in female rats at the highest dosage. It was not evident that a maximum tolerated dose (MTD) was used, nor was a range-finding study conducted. No significant dose-related neoplasms were reported, but these dose levels were below those used in the NCI study (U.S. EPA, 1996).

Sources

ATSDR (Agency for Toxic Substances and Disease Registry). 1995. *Toxicological Profile for 1,1,1-Trichloroethane (Update)*. Public Health Service, U.S. Department of Health and Human Services. TP-94/10.

Calhoun, L.L., F.J. Quast, A.M. Schumann et al. 1981. *Chloroethene VG: Preliminary studies to establish exposure concentrations for a chronic inhalation study with rats and mice*. Unpublished study. Toxicology Research Laboratory, Health and Environmental Sciences, The Dow Chemical Company, Midland, MI.

Quast, J.F., L.W. Rampy, M.F. Balmer, B.K.J. Leong and P.J. Gehring. 1978. *Toxicologic and carcinogenic evaluation of a 1,1,1-trichloroethane formulation by chronic inhalation in rats*. Unpublished study. Toxicology Research Laboratory, Health and Environmental Sciences, The Dow Chemical Company, Midland, MI.

Quast, J.F., L.L. Calhoun and L.E. Frauson. 1988. "1,1,1-Trichloroethane formulation: A chronic inhalation toxicity and oncogenicity study in Fischer 344 rats and B6C3F1 mice." *Fund. Appl. Toxicol.* 11: 611-625.

Rosengren, L.E., A. Aurell, P. Kjellstrand et al. 1985. "Astrogliosis in the cerebral cortex of gerbils after long-term exposure to 1,1,1-trichloroethane." *Scand. J. Work Environ. Health* 11: 447-456.

U.S. EPA. 1996. IRIS Data Base Record for 1,1,1-Trichloroethane (CAS No. 71-55-6).

U.S. EPA. 1987. *Recommendations for and Documentation of Biological Values for Use in Risk Assessment*. Prepared by Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment, Cincinnati, OH. EPA No. 600/6-87-008.

U.S. EPA. 1994. *Methods for Derivation of Inhalation Reference Concentrations and Application of Inhalation Dosimetry*. Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment, Research Triangle Park, NC 27711. EPA/600/8-90/-66F.

U.S. EPA. 1996. *TRI Environmental Indicators Project: Toxicity Weighting Summary Document*. June 10, 1996 Draft. Economics, Exposure and Technology Division, Office of Pollution Prevention and Toxics, Washington, DC.

NAS-NRC (National Academy of Sciences - National Research Council). 1989. *Food and Nutrition Board: Recommended Dietary Allowances*. Tenth Revised Edition. Washington, DC: National Academy Press. p. 185-187.

Schrödter, K., Bettermann, G. Staffel, T. and Hofmann, T. 1991. "Phosphoric Acid and Phosphates: 4. Toxicology." In: *Ullmann's Encyclopedia of Industrial Chemistry*, Vol. A19., B. Elvers, S. Hawkins and G. Schulz, Ed. VCH Verlagsgesselschaft mbH, D-6940 Weinheim, Federal Republic of Germany. p. 465, 476, 501-503.

U.S. EPA. 1989. *Summary Review of Health Effects Associated with Elemental and Inorganic Phosphorus Compounds: Health Issue Assessment*. Prepared by the Office of Health and Environmental Assessment for the Office of Air Quality Planning and Standards, Washington, DC. EPA 600/8-89/072.

U.S. EPA. 1990. *Interim Methods for Development of Inhalation Reference Concentrations*. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Research Triangle Park, NC. EPA/600/8-90/066A, August, 1990. (Review Draft)

U.S. EPA. 1992. *Status of Pesticides in Reregistration and Special Review*. Special Review and Reregistration Division, Office of Pesticide Programs, Washington, DC.

U.S. EPA. 1996. Integrated Risk Information System (IRIS). Online. Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH.

U.S. EPA ORD. Superfund Health Risk Technical Support Center. n.d. *Risk Assessment Issue Paper for: Feasibility of RfD, RfC, Slope Factor, and Unit Risk Derivations for Phosphorus Pentoxide (CAS # 1314-56-3); Phosphoric Acid (CAS # 7664-38-2) as Potential Surrogate; White Phosphorus Smoke (CAS # not found) as Phosphorus Pentoxide-Containing Mixture*.

WHO (World Health Organization). 1974. *Toxicological Evaluation of Certain Food Additives with a Review of General Principles and of Specifications*. Seventeenth Report of the Joint FAO/WHO Expert Committee on Food Additives. WHO Technical Report Series. No. 539.

B.2.23. 1,2,4-Trimethylbenzene (95-63-6)

Chronic Oral

Basis of toxicity weight

In the draft *Risk Assessment Issue Paper for: Derivation of a Provisional Oral RfD for 1,2,4-Trimethylbenzene* (n.d.), written by the Superfund Health Risk Technical Support Center (U.S. EPA ORD), a provisional oral RfD was derived from an inhalation RfC of 6×10^{-3} mg/m^3, which was based on a human occupational LOAEL of 49 mg/m^3 (or a $LOAEL_{HEC}$ of 17.5 mg/m^3) (Battig et al., 1958). The LOAEL was converted to an inhaled dose of 5.0 mg/kg-day by multiplying by a reference adult human inhalation rate (20 m^3/d) and dividing by a reference adult human body weight (70 kg). An equivalent oral dose was estimated by multiplying the inhaled

dose by 0.80/0.88, the ratio of the absorption efficiencies by the inhalation and oral routes, respectively. This yielded an oral dose of 4.5 mg/kg-d. An uncertainty factor of 1,000 (10 for the use of a LOAEL, 10 for the use of subchronic data, 10 for intraspecific variability) and a modifying factor of 10 (to account for an inadequate database) was applied to the oral dose to yield an oral RfD of 5×10^{-4} mg/kg-d (rounded up from 4.5×10^{-4}). The authors of the Risk Assessment Issue Paper cited low confidence in the RfD because, "a small number of subjects were examined and the workers were also exposed to other chemicals in the solvent mixture," including 1,3,5-trimethylbenzene in the critical study.

Further calculations

Following TRI Environmental Indicator methods, the interim RfD yielded a chronic oral toxicity weight of 1,000 for 1,2,4-trimethylbenzene. Because of data limitations in the critical study, confidence in the toxicity weight is low.

Chronic Inhalation

Basis of toxicity weight

In the draft *Risk Assessment Issue Paper for: Derivation of a Provisional RfC for Trimethylbenzene (1,2,4 and 1,3,5)* (n.d.) written by the Superfund Health Risk Technical Support Center (U.S. EPA ORD), a provisional RfC was calculated using the 1958 occupational study by Battig et al. cited above. Workers were exposed to a solvent containing over 80 percent trimethylbenzenes. The LOAEL for the study (assuming the solvent to be 100 percent trimethylbenzenes was 10 ppm (49 mg/m^3). The RfC was calculated by adjusting the LOAEL to a constant exposure level (17.5 mg/m^3) and dividing by an uncertainty factor of 1,000 (10 for intraspecific variation, 10 for the use of a LOAEL, and 10 for the use of a subchronic study) and a modifying factor of 3 to account for an incomplete database. This yielded an RfC of 6×10^{-3} mg/m^3.

Further calculations

The provisional RfC of 6×10^{-3} mg/m^3 was converted to an RfD estimate of 1.7×10^{-3} mg/kg-d by multiplying by a reference human respiration rate of 20 m^3/d and dividing by a reference human body weight of 70 kg. Following TRI Environmental Indicator methods, this RfD estimate yielded a chronic inhalation toxicity weight of 1,000. Confidence in the toxicity weight is low due to data limitations in the critical study.

Cancer Oral and Inhalation

The Superfund Health Risk Technical Support Center also prepared a draft *Risk Assessment Issue Paper for: Evaluation of the Carcinogenicity of 1,2,4-Trimethylbenzene* (n.d.), which assigned 1,2,4-trimethylbenzene a weight of evidence classification of D: not classifiable as to human carcinogenicity, based on no human or animal data. No cancer toxicity weights were calculated due to a lack of data.

Sources

U.S. EPA. 1993. Hazardous Substances Data Bank. Accessed via TOXNET.

U.S. EPA ORD Superfund Health Risk Technical Support Center. n.d. *Risk Assessment Issue Paper for: Derivation of a Provisional Oral RfD for 1,2,4-Trimethylbenzene*. Draft.

U.S. EPA ORD Superfund Health Risk Technical Support Center. n.d. *Risk Assessment Issue Paper for: Derivation of a Provisional RfC for Trimethylbenzene (1,2,4 and 1,3,5)*. Draft.

U.S. EPA ORD Superfund Health Risk Technical Support Center. n.d. *Risk Assessment Issue Paper for: Evaluation of the Carcinogenicity of 1,2,4-Trimethylbenzene*. Draft.

Although no other sources of information were used, the Risk Assessment Issue Papers included reviews of the following: IRIS, MEDLINE, TOXLINE, RTECS, TSCATS, CARA, and HSDB databases, a 1987 HEA document, a 1987 U.S. EPA Health Advisory, the RfD/RfC Monthly Status Report (U.S. EPA, 1993), the Drinking Water Regulations and Health Advisories list (U.S. EPA, 1993), the HEAST and Supplement (U.S. EPA, 1993), and NTP Status Reports.

B.2.24. p-Xylene (106-42-3)

Basis for Toxicity Weight

The pharmacokinetics and metabolism of the three xylene isomers (ortho-, meta-, and para-) are expected to be the same. In our judgment, the toxicities of the three isomers may be reasonably expected to be similar. Based on this judgment, the use of the RfD estimate calculated by IRIS (U.S. EPA, 1996) for mixed xylenes can be used as a surrogate for individual isomers. Our assumption is that an RfD estimate calculated by IRIS is sufficient.

Further Calculations

IRIS (U.S. EPA, 1996) calculated the RfD estimate based on a two-year toxicity and carcinogenesis NTP study (1986) in rats and mice given mixed xylenes by gavage at doses of 0, 250 and 500 mg/kg/day for 103 weeks. Effects included decreases in body weight and dose-related increases in male mortality in rats and hyperactivity lasting 5-30 minutes in high-dose mice. Based on these observations, a LOAEL of 500 mg/kg/day and a NOAEL of 250 mg/kg/day were indicated. The NOAEL was adjusted for a gavage schedule of 5 days/week to give a NOAEL of 179 mg/kg/day which was divided by an uncertainty factor of 100 (10 for species to species extrapolation and 10 to protect sensitive individuals) and a modifying factor of 1 to yield a RfD estimate of 2 mg/kg/day. Confidence in the study was rated as medium by IRIS. Following the TRI Environmental Indicator methods, this RfD estimate was used to derive a chronic oral toxicity weight of 1.

Sources

U.S. EPA 1996. Integrated Risk Information System (IRIS) Data Base Record for Mixed Xylenes (CAS No.1330-20-7).

Appendix C.
Toxicity Information for TRI Chemicals and Chemical Categories with Interim Derived Toxicity Values

Appendix C. Toxicity Information for TRI Chemicals and Chemical Categories with Interim Derived Toxicity Values

C.1. Tables of Toxicity Weights for TRI Chemicals and Chemical Categories with Interim Derived Toxicity Values

Appendix C contains summary descriptions of the sources used and the additional calculations required to derive cancer and noncancer toxicity weights pertaining to chronic exposures to TRI chemicals and chemical categories that lack published noncancer RfDs or RfCs and cancer Oral Slope Factors and Inhalation Unit Risks and which have not been finalized by the Office of Pollution Prevention and Toxics (OPPT). Table C-1 lists these chemicals in alphabetical order. Table C-2 lists the same chemicals sorted by ascending CAS number. In Section C.2, summary discussions of the relevant toxicological information are ordered alphabetically by chemical name, with the CAS number of each chemical following the chemical name in each section heading. Note that each pathway-specific toxicity weight discussion for both chronic and cancer effects is divided into two subsections: *Basis of toxicity weight* and *Further calculations*. The *Basis of toxicity weight* subsections contain the relevant published dose-response data used to estimate toxicity weights for each chemical. The *Further calculations* subsections contain all the additional data manipulations used in deriving the calculated toxicity weights. The section entitled *Sources* for each discussion provides the relevant references.

All of the toxicity weights contained in Appendix C have been reviewed but not finalized by the OPPT Disposition Process. The methods used to calculate the toxicity weights given below are described in Chapter 5 of the TRI Relative Risk-Based Environmental Indicators: Interim Toxicity Weighting Summary Document.

Table C-1. Toxicity Weights for TRI Chemicals and Chemical Categories with Interim Derived Toxicity Values, in Alphabetical Order

CAS #	Chemical Name		Interim Toxicity Weight					Overall Toxicity Weight
			Cancer		Chronic			
			Basis of Weight	Toxicity Weight	Basis of Weight	Critical Effect	Toxicity Weight	
7429-90-5	Aluminum (fume or dust)	Oral	--	--	--	--	--	
		Inhalation	--	--	NOAEL of 0.05 mg/m^3	respiratory	100,000	100,000
90-04-0	Anisidine, o-	Oral	--	See App B	--	--	See App B	1,000
		Inhalation	--	--	LOAEL of 0.06 mg/kg-d	CNS, hematological	10,000	10,000
141-32-2	Butyl Acrylate	Oral	--	--	RfD of 0.5 mg/kg-d for acrylic acid	developmental	10,000	10,000
		Inhalation	--	--	RfD of 10^{-3} mg/m^3 for acrylic acid	respiratory	10	10
463-58-1	Carbonyl Sulfide	Oral	--	--	--	--	--	100*
		Inhalation	--	--	LOAEL of 50 ppm	cardiovascular	100	100

Table C-1. Toxicity Weights for TRI Chemicals and Chemical Categories with Interim Derived Toxicity Values, in Alphabetical Order

CAS #	Chemical Name		Interim Toxicity Weight					Overall Toxicity Weight
			Cancer		Chronic			
			Basis of Weight	Toxicity Weight	Basis of Weight	Critical Effect	Toxicity Weight	
120-80-9	Catechol (1,2-Dihydroxybenzene)	Oral	cancer potency estimate of 0.009 per mg/kg-d WOE estimate of B2	100	--	--	--	100
		Inhalation	--	--	--	--	--	100*
7440-48-4	Cobalt	Oral	--	--	--	--	--	100,000*
		Inhalation	--	--	RfC of 10^{-6} mg/m^3	respiratory	100,000	100,000
N096	Cobalt Compounds[a]	Oral	--	--	--	--	--	100,000*
		Inhalation	--	--	RfC of 10^{-6} mg/m^3	respiratory	100,000	100,000

Table C-1. Toxicity Weights for TRI Chemicals and Chemical Categories with Interim Derived Toxicity Values, in Alphabetical Order

CAS #	Chemical Name		Interim Toxicity Weight					Overall Toxicity Weight
			Cancer		Chronic			
			Basis of Weight	Toxicity Weight	Basis of Weight	Critical Effect	Toxicity Weight	
120-71-8	Cresidine, p-	Oral	cancer potency of 0.15 per mg/kg-d IARC Group 2B	1,000	--	--	--	1,000
		Inhalation	--	--	--	--	--	1,000*
110-82-7	Cyclohexane	Oral	--	--	--	--	--	1*
		Inhalation	--	--	NOAEL of 1,070 mg/kg-d	CNS	1	1
25376-45-8	Diaminotoluene (mixed isomers)	Oral	cancer potency of 23.2 per mg/kg-d WOE of B2	100,000	--	--	--	100,000
		Inhalation	--	--	--	--	--	100,000*

Table C-1. Toxicity Weights for TRI Chemicals and Chemical Categories with Interim Derived Toxicity Values, in Alphabetical Order

CAS #	Chemical Name		Interim Toxicity Weight					Overall Toxicity Weight
			Cancer		Chronic			
			Basis of Weight	Toxicity Weight	Basis of Weight	Critical Effect	Toxicity Weight	
25321-22-6	Dichlorobenzene (mixed isomers)	Oral	--	See App B	--	--	See App B	100
		Inhalation	--	--	RfC of 0.2 mg/m^3	HEAST value	10	10
541-73-1	Dichlorobenzene, 1,3-[b]	Oral	--	See App B	--	--	See App B	100
		Inhalation	--	--	RfC of 0.2 mg/m^3	HEAST value	10	10
111-42-2	Diethanolamine	Oral	--	--	NOAEL of 20 mg/kg-d	hepatological, renal	100	100
		Inhalation	--	--	--	--	--	100*
77-78-1	Dimethyl Sulfate	Oral	--	--	--	--	--	1,000,000 *
		Inhalation	cancer potency estimate of 11 WOE of B2	1,000,000	--	--	--	1,000,000

Table C-1. Toxicity Weights for TRI Chemicals and Chemical Categories with Interim Derived Toxicity Values, in Alphabetical Order

CAS #	Chemical Name		Interim Toxicity Weight					Overall Toxicity Weight
			Cancer		Chronic			
			Basis of Weight	Toxicity Weight	Basis of Weight	Critical Effect	Toxicity Weight	
534-52-1	Dinitro-o-cresol, 4,6-	Oral	--	--	ADI of 3.5×10^{-4} mg/kg-d	metabolic, ocular	10,000	10,000
		Inhalation	--	--	ADI of 10^{-4} mg/kg-d	"debilitating symptoms" in humans	10,000	10,000
78-84-2	Isobutyraldehyde	Oral	--	--	--	--	--	100,000*
		Inhalation	--	--	LOAEL of 50 mg/m^3	hematological	100,000	100,000
67-63-0	Isopropyl Alcohol	Oral	--	--	LOAEL of 1,400 mg/kg-d	developmental	1	1
		Inhalation	--	--	NOAEL of 0.66 mg/m^3	hematological	10,000	10,000

Table C-1. Toxicity Weights for TRI Chemicals and Chemical Categories with Interim Derived Toxicity Values, in Alphabetical Order

CAS #	Chemical Name		Interim Toxicity Weight					Overall Toxicity Weight
			Cancer		Chronic			
			Basis of Weight	Toxicity Weight	Basis of Weight	Critical Effect	Toxicity Weight	
7439-92-1	Lead	Oral	qualitative based on human studies	10,000	--	neurological	100,000	100,000
		Inhalation	qualitative based on human studies	10,000	--	neurological	100,000	100,000
N420	Lead Compounds[a]	Oral	qualitative based on human studies	10,000	--	neurological	100,000	100,000
		Inhalation	qualitative based on human studies	10,000	--	neurological	100,000	100,000
74-88-4	Methyl Iodide	Oral	cancer potency estimate of 2.9 per mg/kg-d WOE of C	1,000	--	--	--	1,000
		Inhalation	--	--	--	--	--	1,000*

Table C-1. Toxicity Weights for TRI Chemicals and Chemical Categories with Interim Derived Toxicity Values, in Alphabetical Order

CAS #	Chemical Name		Interim Toxicity Weight					Overall Toxicity Weight
			Cancer		Chronic			
			Basis of Weight	Toxicity Weight	Basis of Weight	Critical Effect	Toxicity Weight	
1313-27-5	Molybdenum Trioxide	Oral	--	--	LOAEL of 15 mg/L	developmental	1,000	1,000
		Inhalation	--	--	LOAEL of 1 mg/m^3	respiratory	10,000	10,000
139-13-9	Nitrilotriacetic Acid	Oral	cancer potency estimate of 0.02 per mg/kg-d IARC Group 2B	100	LOAEL of 0.73 mmol/kg-d	renal, urinary tract	100	100
		Inhalation	--	--	--	--	--	100*
55-63-0	Nitroglycerin	Oral	slope factor of 2.1 per mg/kg-d WOE of B2	10,000	RfD of 0.03 mg/kg-d	lower body weight	100	10,000
		Inhalation	--	--	--	--	--	10,000*

Table C-1. Toxicity Weights for TRI Chemicals and Chemical Categories with Interim Derived Toxicity Values, in Alphabetical Order

CAS #	Chemical Name		Interim Toxicity Weight					Overall Toxicity Weight
			Cancer		Chronic			
			Basis of Weight	Toxicity Weight	Basis of Weight	Critical Effect	Toxicity Weight	
79-21-0	Peracetic Acid	Oral	--	--	--	--	--	1,000*
		Inhalation	--	--	LOAEL of 186 mg/m^3	respiratory	1,000	1,000
7550-45-0	Titanium Tetrachloride	Oral	--	--	--	--	--	100,000*
		Inhalation	--	--	LOAEL of 0.1 mg/m^3	respiratory	100,000	100,000
26471-62-5	Toluene Diisocyanate (mixed isomers)	Oral	cancer potency of 0.039 per mg/kg-d IARC Group 2B	100	NOAEL of 23 mg/kg-d	respiratory	10	100
		Inhalation	--	--	Now IRIS		See App. A	
91-08-7	Toluene Diisocyanate, 2,6-[b]	Oral	cancer potency of 0.039 per mg/kg-d IARC Group 2B	100	NOAEL of 23 mg/kg-d	respiratory	10	100

Table C-1. Toxicity Weights for TRI Chemicals and Chemical Categories with Interim Derived Toxicity Values, in Alphabetical Order

CAS #	Chemical Name		Interim Toxicity Weight					Overall Toxicity Weight
			Cancer		Chronic			
			Basis of Weight	Toxicity Weight	Basis of Weight	Critical Effect	Toxicity Weight	
		Inhalation	--	--	LOAEL of 0.005 ppm	sensitization	100,000	100,000
584-84-9	Toluene Diisocyanate, 2,4-[b]	Oral	cancer potency of 0.039 per mg/kg-d IARC Group 2B	100	NOAEL of 23 mg/kg-d	respiratory	10	100
		Inhalation	--	--	LOAEL of 0.005 ppm	sensitization	100,000	100,000

*Toxicity weight is adopted from the other exposure pathway due to a lack of dose-response data.
[a]Data for metal compounds are the same as for the parent metal.
[b]Data gap exists for this chemical; data are taken from another isomer.

Table C-2. Interim Toxicity Weights For TRI Chemicals and Chemical Categories with Derived Toxicity Values, by CAS Number

CAS #	Chemical Name		Interim Toxicity Weight					Overall Toxicity Weight
			Cancer		Chronic			
			Basis of Weight	Toxicity Weight	Basis of Weight	Critical Effect	Toxicity Weight	
55-63-0	Nitroglycerin	Oral	slope factor of 2.1 per mg/kg-d WOE of B2	10,000	RfD of 0.03 mg/kg-d	lower body weight	100	10,000
		Inhalation	--	--	--	--	--	10,000*
67-63-0	Isopropyl Alcohol	Oral	--	--	LOAEL of 1,400 mg/kg-d	developmental	1	1
		Inhalation	--	--	NOAEL of 0.66 mg/m^3	hematological	10,000	10,000
74-88-4	Methyl Iodide	Oral	cancer potency estimate of 2.9 per mg/kg-d WOE of C	1,000	--	--	--	1,000
		Inhalation	--	--	--	--	--	1,000*

Table C-2. Interim Toxicity Weights For TRI Chemicals and Chemical Categories with Derived Toxicity Values, by CAS Number

CAS #	Chemical Name		Interim Toxicity Weight					Overall Toxicity Weight
			Cancer		Chronic			
			Basis of Weight	Toxicity Weight	Basis of Weight	Critical Effect	Toxicity Weight	
77-78-1	Dimethyl Sulfate	Oral	--	--	--	--	--	1,000,000 *
		Inhalation	cancer potency estimate of 11 WOE of B2	1,000,000	--	--	--	1,000,000
78-84-2	Isobutyraldehyde	Oral	--	--	--	--	--	100,000*
		Inhalation	--	--	LOAEL of 50 mg/m^3	hematological	100,000	100,000
79-21-0	Peracetic Acid	Oral	--	--	--	--	--	1,000*
		Inhalation	--	--	LOAEL of 186 mg/m^3	respiratory	1,000	1,000
90-04-0	Anisidine, o-	Oral	--	See App. B	--	--	See App. B	1,000
		Inhalation	--	--	LOAEL of 0.06 mg/kg-d	CNS, hematological	10,000	10,000

Table C-2. Interim Toxicity Weights For TRI Chemicals and Chemical Categories with Derived Toxicity Values, by CAS Number

CAS #	Chemical Name		Interim Toxicity Weight					Overall Toxicity Weight
			Cancer		Chronic			
			Basis of Weight	Toxicity Weight	Basis of Weight	Critical Effect	Toxicity Weight	
91-08-7	Toluene Diisocyanate, 2,6-[a]	Oral	cancer potency of 0.039 per mg/kg-d IARC Group 2B	100	NOAEL of 23 mg/kg-d	respiratory	10	100
		Inhalation	--	--	LOAEL of 0.005 ppm	sensitization	100,000	100,000
110-82-7	Cyclohexane	Oral	--	--	--	--	--	1*
		Inhalation	--	--	NOAEL of 1,070 mg/kg-d	CNS	1	1
111-42-2	Diethanolamine	Oral	--	--	NOAEL of 20 mg/kg-d	renal, hepatological	100	100
		Inhalation	--	--	--	--	--	100*

Table C-2. Interim Toxicity Weights For TRI Chemicals and Chemical Categories with Derived Toxicity Values, by CAS Number

CAS #	Chemical Name		Interim Toxicity Weight					Overall Toxicity Weight
			Cancer		Chronic			
			Basis of Weight	Toxicity Weight	Basis of Weight	Critical Effect	Toxicity Weight	
120-71-8	Cresidine, p-	Oral	cancer potency of 0.15 per mg/kg-d IARC Group 2B	1,000	--	--	--	1,000
		Inhalation	--	--	--	--	--	1,000*
120-80-9	Catechol (1,2-Dihydroxybenzene)	Oral	cancer potency estimate of 0.009 per mg/kg-d WOE estimate of B2	100	--	--	--	100
		Inhalation	--	--	--	--	--	100*

Table C-2. Interim Toxicity Weights For TRI Chemicals and Chemical Categories with Derived Toxicity Values, by CAS Number

CAS #	Chemical Name		Interim Toxicity Weight					Overall Toxicity Weight
			Cancer		Chronic			
			Basis of Weight	Toxicity Weight	Basis of Weight	Critical Effect	Toxicity Weight	
139-13-9	Nitrilotriacetic Acid	Oral	cancer potency estimate of 0.02 per mg/kg-d IARC Group 2B	100	LOAEL of 0.73 mmol/kg-d	renal, urinary tract	100	100
		Inhalation	--	--	--	--	--	100*
141-32-2	Butyl Acrylate	Oral	--	--	RfD of 0.5 mg/kg-d for acrylic acid	developmental	10,000	10,000
		Inhalation	--	--	RfD of 10^{-3} mg/m^3 for acrylic acid	respiratory	10	10
463-58-1	Carbonyl Sulfide	Oral	--	--	--	--	--	100*
		Inhalation	--	--	LOAEL of 50 ppm	cardiovascular	100	100

Table C-2. Interim Toxicity Weights For TRI Chemicals and Chemical Categories with Derived Toxicity Values, by CAS Number

CAS #	Chemical Name		Interim Toxicity Weight					Overall Toxicity Weight
			Cancer		Chronic			
			Basis of Weight	Toxicity Weight	Basis of Weight	Critical Effect	Toxicity Weight	
534-52-1	Dinitro-o-cresol, 4,6-	Oral	--	--	ADI of 3.5×10^{-4} mg/kg-d	metabolic, ocular	10,000	10,000
		Inhalation	--	--	ADI of 10^{-4} mg/kg-d	"debilitating symptoms" in humans	10,000	10,000
541-73-1	Dichlorobenzene, 1,3-[a]	Oral	--	See App. B	--	--	See App B	100
		Inhalation	--	--	RfC of 0.2 mg/m^3	HEAST value	10	10
584-84-9	Toluene Diisocyanate, 2,4-[a]	Oral	cancer potency of 0.039 per mg/kg-d IARC Group 2B	100	NOAEL of 23 mg/kg-d	respiratory	10	100
		Inhalation	--	--	LOAEL of 0.005 ppm	sensitization	100,000	100,000

Table C-2. Interim Toxicity Weights For TRI Chemicals and Chemical Categories with Derived Toxicity Values, by CAS Number

CAS #	Chemical Name		Interim Toxicity Weight					Overall Toxicity Weight
			Cancer		Chronic			
			Basis of Weight	Toxicity Weight	Basis of Weight	Critical Effect	Toxicity Weight	
1313-27-5	Molybdenum Trioxide	Oral	--	--	LOAEL of 15 mg/L	developmental	1,000	1,000
		Inhalation	--	--	LOAEL of 1 mg/m^3	respiratory	10,000	10,000
7429-90-5	Aluminum (fume or dust)	Oral	--	--	--	--	--	N/A[c]
		Inhalation	--	--	NOAEL of 0.05 mg/m^3	respiratory	100,000	100,000
7439-92-1	Lead	Oral	qualitative based on study averages	10,000	NOAEL of 3 ug/dL blood lead	neurological	100,000	100,000
		Inhalation	qualitative based on study averages	10,000	NOAEL of 3 ug/dL blood lead	neurological	100,000	100,000
7440-48-4	Cobalt	Oral	--	--	--	--	--	100,000*
		Inhalation	--	--	RfC of 10^{-6} mg/m^3	respiratory	100,000	100,-00-0

Table C-2. Interim Toxicity Weights For TRI Chemicals and Chemical Categories with Derived Toxicity Values, by CAS Number

CAS #	Chemical Name		Interim Toxicity Weight					Overall Toxicity Weight
			Cancer		Chronic			
			Basis of Weight	Toxicity Weight	Basis of Weight	Critical Effect	Toxicity Weight	
7550-45-0	Titanium Tetrachloride	Oral	--	--	--	--	--	100,000*
		Inhalation	--	--	LOAEL of 0.1 mg/m^3	respiratory	100,000	100,000
25321-22-6	Dichlorobenzene (mixed isomers)	Oral	--	See App B	--	--	See App B	100
		Inhalation	--	--	RfC of 0.2 mg/m^3	HEAST value	10	10
25376-45-8	Diaminotoluene (mixed isomers)	Oral	cancer potency of 23.2 per mg/kg-d WOE of B2	100,000	--	--	--	100,000
		Inhalation	--	--	--	--	--	100,000*

Table C-2. Interim Toxicity Weights For TRI Chemicals and Chemical Categories with Derived Toxicity Values, by CAS Number

CAS #	Chemical Name		Interim Toxicity Weight					Overall Toxicity Weight
			Cancer		Chronic			
			Basis of Weight	Toxicity Weight	Basis of Weight	Critical Effect	Toxicity Weight	
26471-62-5	Toluene Diisocyanate (mixed isomers)	Oral	cancer potency of 0.039 per mg/kg-d IARC Group 2B	100	NOAEL of 23 mg/kg-d	respiratory	10	100
		Inhalation	--	--			See App. A	
N096	Cobalt compounds[b]	Oral	--	--	--	--	--	100,000*
		Inhalation	--	--	RfC of 10^{-6} mg/m^3	respiratory	100,000	100,000
N420	Lead compounds[b]	Oral	qualitative based on study averages	10,000	NOAEL of 3 ug/dL blood lead	neurological	100,000	100,000
		Inhalation	qualitative based on study averages	10,000	NOAEL of 3 ug/dL blood lead	neurological	100,000	100,000

*Toxicity weight is adopted from the other exposure pathway due to a lack of dose-response data.
[a]Data gap exists for this chemical; data are taken from another isomer.
[b]Data for metal compounds are the same as for the parent metal.

C.2. Data Summaries Used as Bases for Interim Toxicity Values

C.2.1. Aluminum (fume or dust) (7429-90-5)

No studies were found that tested directly for aluminum toxicity; all studies tested for various aluminum compounds. Because of the lack of evidence relating the relative toxicity of aluminum to aluminum compounds, confidence in the toxicity weight calculated for aluminum is low.

Chronic Oral

Since TRI reporting requires reporting of aluminum only as fume or dust, oral toxicity weights were not derived.

Chronic Inhalation

Basis of toxicity weight

The ATSDR Toxicological Profile for Aluminum (1992) reports a study by Steinhagen et al. (1978) in which rats exposed to 0.5 mg/m^3 aluminum chlorhydrate for six hours per day, five days per week for six months developed lung nodules. The NOAEL for the study was 0.05 mg/m^3. This study reported the lowest LOAEL of the available studies examined.

Further calculations

The NOAEL of 0.05 mg/m^3 was multiplied by a reference rat respiration rate of 0.2 m^3/d and by 6/24 hrs/d and 5/7 days/week and divided by a reference rat body weight of 0.5 kg to yield a constant dose of 0.0036 mg/kg-d. This constant dose was divided by an uncertainty factor of 1000 (10 each for intra- and interspecific variation, and 10 for the use of a subchronic study) to yield an RfD estimate of 3.6×10^{-6} mg/kg-d. Following TRI Environmental Indicator methods, this RfD estimate results in a maximum chronic toxicity weight of 100,000. Confidence in the weight is low because the study is based on aluminum chlorhydrate, not aluminum.

Cancer Oral and Inhalation

ATSDR reports that aluminum is not known to cause cancer in humans. Animal studies designed to study potential noncarcinogenic effects of aluminum have not shown carcinogenic health effects. IARC rates aluminum a Group 3 carcinogen: not classifiable as to human carcinogenicity. No cancer toxicity weight was calculated.

Sources

Agency for Toxic Substances and Disease Registry. 1992. *Toxicological Profile for Aluminum*. TP-91/01.

NIOSH. 1993. Registry of Toxic Effects of Chemical Substances. Accessed via TOXNET.

U.S. EPA. 1993. Hazardous Substances Data Bank. Accessed via TOXNET.

U.S. EPA. 1993. Integrated Risk Information System. Accessed via TOXNET.

U.S. EPA OHEA. 1987. *Health Effects Assessment for Aluminum*. EPA/600/8-88/016. June.

No other sources were found.

C.2.2. o-Anisidine (90-04-0)

The Integrated Risk Information System (IRIS) reports that health effects data for chronic inhalation were reviewed by the EPA RfD/RfC Work Group and determined to be inadequate for the derivation of an inhalation RfD for ortho-anisidine. The Hazardous Substances Data Bank (HSDB), however, contained studies from which to calculate chronic toxicity weights for o-anisidine. The chronic oral and the cancer toxicity weights for o-anisidine have been finalized by EPA and appear in Appendix B. Only the interim chronic inhalation toxicity weight for o-anisidine is given below.

Chronic Oral

See Appendix B.

Chronic Inhalation

Basis of toxicity weight

A epidemiological study reported in HSDB by the American Congress of General Industrial Hygienists (1986) indicated that male workers exposed to air concentrations of 1.9 mg/m^3 3.5 hours per day for six months developed headaches, vertigo, increased sulfhemoglobin and methemoglobin, and increased occurrence of Heinz bodies.

Further calculations

A LOAEL of 0.06 mg/kg-d was calculated from this study by multiplying 1.9 mg/m^3 by a reference workday respiration volume of 20 m^3/day, 3.5 hrs exposure/24 hr day, and a 5 day/7 day work week, and dividing by a reference adult body weight of 70 kg. The LOAEL of 0.06 mg/kg-d was divided by an uncertainty factor of 1,000 (10 for intraspecific variability, 10 for the use of a LOAEL, and 10 for the use of a subchronic study) to derive a chronic inhalation RfD estimate of 0.00006 mg/kg-d. Following TRI Environmental Indicator methods, this RfD estimate was used to derive a chronic inhalation toxicity weight of 10,000. Confidence in the toxicity weight is low.

Cancer Oral and Inhalation

See Appendix B.

Sources

IARC. 1993. *Monographs on the Evaluation of Carcinogenic Risk to Humans*. Lyon, France.

NIOSH. 1993. *Registry of Toxic Effects of Chemical Substances*. Accessed via TOXNET.

U.S. EPA. 1993. Hazardous Substances Data Bank (HSDB). Accessed via TOXNET.

U.S. EPA. 1993. Integrated Risk Information System. Accessed via TOXNET.

No other sources were found.

C.2.3. Butyl Acrylate (141-32-2)

Although no data were found from which to calculate toxicity weights for butyl acrylate, it is known to hydrolyze to acrylic acid in its primary target tissues (lung, kidney, liver) (HSDB, 1993). Due to the lack of information on butyl acrylate, the toxicity weights of its metabolite acrylic acid were used to estimate its toxicity weights. Chronic RfDs for acrylic acid were obtained directly from the Integrated Risk Information System (IRIS).

Chronic Oral

Basis of toxicity weight

IRIS reports an oral RfD of 0.5 mg/kg-d for acrylic acid, based on a 1993 two-generation reproductive study by BASF in which acrylic acid was administered in drinking water at concentrations of 0, 500, 2500, and 5000 ppm to groups of 25 male and 25 female Wistar rats (35 days old at the beginning of treatment). The critical effect of the study was reduced pup weight, with a NOAEL of 53 mg/kg-d (500 ppm in water) and a LOAEL of 240 mg/kg-d (2500 ppm in water). The NOAEL was divided by an uncertainty factor of 100 (10 for interspecies and 10 to protect sensitive individuals) to obtain the RfD of 0.5 mg/kg-d. IRIS reports that confidence in the RfD is high, due to high confidence in the critical study and in the supporting database.

Further calculations

Following TRI Environmental Indicator methods, the RfD of 0.5 mg/kg-d corresponds to a chronic oral toxicity weight of 1. Confidence in the toxicity weight for use for acrylic acid is high, but confidence in the toxicity weight for use for butyl acrylate is low due to insufficient supporting data.

Chronic Inhalation

Basis of toxicity weight

IRIS reports an inhalation RfD of 1.0×10^{-3} mg/m^3 for acrylic acid, based on a 1981 study by Miller et al. in which 15/sex/dose Fischer 344 rats and 15/sex/dose B6C3F1 mice of each sex/group were exposed to 0, 5, 25, or 75 ppm acrylic acid (0, 14.9, 74.7, or 224 mg/cu.m) for 6 hours/day, 5 days/week for 13 weeks (duration-adjusted concentrations of 0, 2.66, 13.3, or 40.0 mg/cu.m). The critical effect was degeneration of the nasal olfactory epithelium, which occurred at the lowest dose level. The LOAEL of 14.94 mg/cu.m was converted to a constant human equivalent concentration ($LOAEL_{HEC}$) of 0.33 mg/m^3 and divided by an uncertainty factor of 300 (10 for sensitive human subpopulations, 3 for extrapolation from subchronic to chronic duration, and 10 for both interspecies extrapolation, because dosimetric adjustments were applied, and use of a LOAEL because the effect is considered mild) to yield an RfD of 1.0×10^{-3} mg/m^3. IRIS reports that confidence in the critical study and the supporting database are both medium, for a medium confidence in the RfD.

Further calculations

The RfD of 1.0×10^{-3} mg/m^3 was converted to an RfD estimate of 3×10^{-4} mg/kg-d by multiplying by a reference human respiration rate of 20 m^3/d and dividing by a reference human body weight of 70 kg. This RfD estimate yields a chronic inhalation toxicity weight of 10,000. Confidence in this chronic inhalation toxicity weight is medium for use for acrylic acid but low for use for butyl acrylate due to a lack of supporting data.

Cancer Oral and Inhalation

No data were found from which to calculate cancer toxicity weights for either acrylic acid or butyl acrylate.

Sources

U.S. EPA. 1993. Hazardous Substances Data Bank (HSDB). Accessed via TOXNET.

U.S. EPA. 1995. Integrated Risk Information System. Accessed via TOXNET.

No other sources were found.

C.2.4. Carbonyl Sulfide (463-58-1)

Chronic Oral

No data were found to support the calculation of a chronic oral toxicity weight. Following TRI Environmental Indicator methods, the chronic inhalation toxicity weight of 100 was used for both exposure pathways (see below).

Chronic Inhalation

Basis of toxicity weight

HSDB reported a NOAEL of 50 ppm carbonyl sulfide in rabbits exposed for one to seven weeks (Hugod et al., 1980) for histological effects in the coronary arteries or aorta. A second study in HSDB (Kamstrup et al., 1979) gave a LOAEL of 50 ppm in rabbits exposed to carbonyl sulfide for seven weeks for slightly elevated serum cholesterol.

Further calculations

The LOAEL of 50 ppm was converted to a LOAEL of 55 mg/kg-d by multiplying by the molecular weight of 60 g/mol and a reference rabbit respiration rate of 0.9 m^3/d, and dividing by a volume of 24.45 L/mol and a reference rabbit body weight of 2 kg. The LOAEL of 74 mg/kg-d was divided by an uncertainty factor of 10,000 (10 each for intra- and interspecific variation, 10 for the use of a subchronic study, and 10 for the use of a LOAEL) to derive a chronic inhalation RfD of 5.5×10^{-3} mg/kg-d. This RfD corresponds to a toxicity weight of 100. Confidence in the toxicity weight is low due to the poor quality of the database.

Cancer Oral and Inhalation

No data were found from which to calculate a cancer toxicity weight for carbonyl sulfide.

Sources

NIOSH. 1993. *Registry of Toxic Effects of Chemical Substances*. Accessed via TOXNET.

U.S. EPA. 1993. Hazardous Substances Data Bank (HSDB). Accessed via TOXNET.

No other sources of information were found.

C.2.5. Catechol (120-80-9)

Chronic Oral and Inhalation

No data were found to support the calculation of chronic toxicity weights for catechol.

Cancer Oral and Inhalation

Basis of toxicity weight

HSDB cited a study by Hirose et al. (1990) in which 30/sex F334 rats and B6C3F1 mice were fed diets containing 0.8 percent catechol for 104 weeks (rats) or 96 weeks (mice). Catechol induced glandular stomach adenocarcinomas in 15/30 ($P < 0.001$) male and 12/30 ($P < 0.001$) female rats. Controls showed no stomach adenocarcinomas or other histolopathological changes. Body weights of dosed animals were generally lower than in controls (17.1 to 41.1 percent reduction), though the relative liver and kidney weights were higher. Hirose et al. also reported that other studies showed catechol to induce hyperplasia in the forestomach and glandular stomach of hamsters, strongly enhanced forestomach and glandular stomach carcinogenesis of rats pretreated with N-methyl-N'-nitro-N-nitrosoguanidine, and induced adenomatous hyperplasia and adenocarcinomas in rats.

Further calculations

The dose rate of 0.8 percent catechol was converted to 304 mg/kg-d using a reference rat food intake rate of 19 g/d and a reference rat body weight of 0.42 kg (both are averages for males and females). Using combined male and female rat results and using a simplified method described in Chapter 1, a cancer potency estimate of 0.009 per mg/kg-d was derived.

No data on human carcinogenicity and sufficient data on animal carcinogenicity suggest a possible U.S. EPA weight of evidence (WOE) classification of B2 (probable human carcinogen) for catechol. Following TRI Environmental Indicator methods, a WOE estimate of B2 combined with a cancer potency estimate of 0.009 per mg/kg-d yields a cancer oral toxicity weight of 100. Confidence in the toxicity weight is low due to the lack of corroborating studies.

Sources

U.S. EPA. 1993. Hazardous Substances Data Bank (HSDB). Accessed via TOXNET.

Hirose, M., et al. 1990. "Stomach Carcinogenicity of Caffeic Acid, Sesamol, and Catechol in Rats and Mice." *Japanese Journal of Cancer Research*. 81: 207-212.

No other sources of information were found.

C.2.6. Cobalt (7440-48-4) and Cobalt Compounds (N096)

The toxicity weights derived here represent both cobalt and cobalt compounds. IRIS reports that an oral RfD assessment for cobalt is pending, but that EPA has determined that insufficient health data exist to calculate an inhalation RfC. ATSDR has calculated a subchronic inhalation MRL. The Superfund Health Risk Technical Support Center (U.S. EPA ORD), after reviewing available studies on cobalt, also declined to establish an oral RfD, though they developed a provisional inhalation RfC. This provisional inhalation RfC was used to develop a chronic inhalation toxicity weight.

Chronic Oral

No adequate data from which to derive a chronic oral toxicity weight were found. Following TRI Environmental Indicator methods, the chronic inhalation toxicity weight of 100,000 was applied to both exposure pathways.

Chronic Inhalation

Basis of toxicity weight

The Superfund Health Risk Technical Support Center (U.S. EPA ORD) has derived a provisional inhalation RfC based on an occupational study by Sprince et al. (1988) which found a LOAEL of 0.003 mg/m^3 for respiratory effects in workers exposed to cobalt (no NOAEL was reported in Sprince et al.). The LOAEL was adjusted for intermittent exposure by multiplying by 10 m^3/20 m^3 (reference inhalation rate for 8 hrs over 24 hours) and by 5 days/7 days (average work week) to yield a $LOAEL_{HEC}$ of 0.001 mg/m^3. This $LOAEL_{HEC}$ was divided by an uncertainty factor of 1000 (10 each for intraspecific variability, the use of a LOAEL, and the use of a less-than-lifetime study) to derive an interim inhalation RfC of 10^{-6} mg/m^3. The Superfund Health Risk Technical Support Center (U.S. EPA ORD) judged confidence in the interim inhalation RfC to be low because of the lack of an identified NOAEL for respiratory effects or sensitization in humans.

Further calculations

An RfD of 2.9×10^{-7} mg/kg-d was derived from the RfC by multiplying the RfC of 10^{-6} mg/m^3 by a reference human respiration rate of 20 m^3/d and dividing by a reference human body weight of 70 kg. Following TRI Environmental Indicator methods, a maximum toxicity weight of 100,000 was calculated from this RfD. Because confidence in the RfC is low, confidence in the toxicity weight is also low.

Cancer Oral and Inhalation

ATSDR reported an IARC ranking of Group 2B (possible human carcinogen) for cobalt. The Health Effects Assessment document on cobalt (OHEA, 1991), however, assigned it to EPA group D (not classifiable as to human carcinogenicity). No cancer toxicity weight was calculated due to insufficient data.

Sources

ATSDR. 1992. *Toxicological Profile for Cobalt.* TP-91/10.

U.S. EPA ORD Superfund Health Risk Technical Support Center. n.d. *Draft Risk Assessment Issue Papers for: Evaluation of Carcinogenicity of Cobalt, Provisional RfD for Cobalt, and Provisional Inhalation RfC for Cobalt.*

U.S. EPA. 1987. TSCA Docket #400009 (Petition to Delist Nickel and Compounds, Manganese and Compounds, and Cobalt and Compounds)

U.S. EPA. 1993. Hazardous Substances Data Bank. Accessed via TOXNET.

U.S. EPA. 1993. Integrated Risk Information System. Accessed via TOXNET.

No other sources of information were used, although the existence of a Health Effects Assessment (U.S. EPA OHEA, 1991) and a RQTox document (U.S. EPA, 1989) were noted.

C.2.7. p-Cresidine (120-71-8)

Chronic Oral and Inhalation

No data were found to support the calculation of chronic toxicity weights for p-cresidine.

Cancer Oral and Inhalation

Basis of toxicity weight

The Office of Environmental Health Hazard Assessment (OEHHA) of the California EPA has derived a cancer potency of 0.15 per mg/kg-d for p-cresidine based on a 1979 National Cancer Institute feeding study in which 50/sex Fischer 344 rats were given 0, 0.5, and 1.0 percent p-cresidine, 50 male B6C3F1 mice were given 0, 0.22, and 0.46 percent, and 50 female B6C3F1 mice were given 0, 0.22, and 0.44 percent. Tumors were observed in mice and rats of both sexes in statistically-significant numbers, most frequently in the bladder. Olfactory neuroblastomas were found in low- and high-dose rats (1/50 and 21/47, respectively). Urinary bladder carcinomas and papillomas were found in low- and high-dose male rats (30/48 and 44/47, respectively), female

rats (31/49 and 43/46, respectively), male mice (40/42 and 31/31, respectively), and female mice (42/46 and 45/46, respectively). Liver tumors were also found in male mice at unreported rates. OEHHA used the results for benign and malignant urinary bladder tumors in female mice (0/45, 42/46, and 45/46 in the control, low-, and high-dose groups, respectively) to calculate the potency factor, and noted that "because survival was poor for the study in female mice, the potency was derived using a time-to-tumor analysis" (Crump et al., 1991).

The International Agency for Research on Cancer ranked p-cresidine a Group 2B carcinogen (possible human carcinogen), based on sufficient animal data and no human data.

Further calculations

The data used by IARC to rank p-cresidine a Group 2B carcinogen (sufficient animal data and no human data) suggest a possible U.S. EPA weight of evidence (WOE) classification of B2 (probable human carcinogen). Following TRI Environmental Indicator methods, the potency factor of 0.15 per mg/kg-d and the WOE estimate of B2 yield a cancer oral toxicity weight of 1,000. Confidence in the toxicity weight is medium due to the high quality of the study but the lack of supporting data.

Following TRI Environmental Indicator methods, the cancer oral toxicity weight of 1,000 was applied to both exposure pathways due to a lack of inhalation data.

Sources

California EPA OEHHA. *1992. Expedited Cancer Potency Values and Proposed Regulatory Level for Certain Proposition 65 Carcinogens*. April.

NCI. 1978. *Bioassay of p-Cresidine for Possible Carcinogenicity*.

NTP. 1993. *Environmental Health Perspectives Supplements*. Vol. 101. Suppl. 1. April.

U.S. EPA. 1990. *PMN Analogue Profile for p-Cresidine*. Working Draft.

U.S. EPA. 1993. Hazardous Substances Data Bank (HSDB). Accessed via TOXNET.

U.S. EPA OPTS. 1987. *A Review of the Carcinogenic Bioassays for p-Cresidine Using Individual Animal Pathology Data*.

No other sources of information were found.

C.2.8. Cyclohexane (110-82-7)

Chronic Oral

No data were found to support the derivation of a chronic oral toxicity weight for cyclohexane. Following TRI Environmental Indicator methods, the toxicity weight of 1 calculated for chronic inhalation exposure was assigned to both chronic exposure pathways (see below).

Chronic Inhalation

Basis of toxicity weight

HSDB cited a study by Frontali et al. (1981), which exposed rats to 2500 ppm (2676 mg/m^3 or 1070 mg/kg-d, constant dose) cyclohexane for 9 to 10 hours per day, 5 to 6 days per week, for between 7 and 30 weeks. Rats were then perfused with glutaraldehyde and their nerve samples examined under light microscopes. No alterations were found. It should be noted, however, that HSDB reported acute and subchronic adverse effects in other studies at exposures lower than these. In a subchronic study, rabbits exposed to 786 ppm (661 mg/m^3 constant dose) cyclohexane fifty times for six hours each time showed microscopic liver and kidney changes; no effect was shown after exposure for the same time period to 434 ppm (365 mg/m^3 constant dose) (ACGIH, 1980). Exposure to 300 ppm was found to be somewhat irritating to the eyes and mucous membranes in humans (ACGIH, 1980). Rats given intermittent daily inhalation exposure to 300, 1000, or 2000 ppm showed reduction in enzyme activity, especially of brain azoreductase (Savolainen et al., 1980). At 2000 ppm, cyclohexane caused significant increase in the liver biotransformation enzyme UDP-glucuronosyl transferase in rats (Jaervisalo et al., 1982).

Further calculations

The NOAEL of 1070 mg/kg-d was divided by an uncertainty factor of 1,000 (10 each for intra- and interspecific variability, and 10 for the use of a subchronic study) to yield an RfD estimate of 1.1 mg/kg-d. This RfD estimate yields a chronic inhalation toxicity weight of 1. Confidence in the toxicity weight for cyclohexane is low due to the acute adverse effects observed at lower dose levels.

Cancer Oral and Inhalation

No information on cyclohexane was located from which to derive a cancer toxicity weight.

Sources

U.S. EPA. 1993. Hazardous Substances Data Bank (HSDB). Accessed via TOXNET.

No other sources of information were found.

C.2.9. Diaminotoluene (mixed isomers) (25376-45-8)

Diaminotoluene comprises six isomers, the 2,4- isomer being the most important industrially (OHEA, 1988). The toxicity weight derived here represents both individual and mixed isomers of diaminotoluene.

Chronic Oral and Inhalation

No data were found to support the calculation of chronic toxicity weights for individual or mixed isomers of diaminotoluene.

Cancer Oral and Inhalation

Basis of toxicity weight

In the *Evaluation of the Potential Carcinogenicity of Diaminotoluene (Mixed)* (OHEA, 1988), the U.S. EPA Office of Health and Environmental Assessment (OHEA) used 2,4-diaminotoluene in deriving a reportable quantity for mixed isomers of diaminotoluene, due to its importance in industry. OHEA derived a cancer potency of 23.2 per mg/kg-d for mixed isomers of diaminotoluene based on a 1979 NCI study in which 50/group female F344 rats were fed 0 ppm, 79 ppm (3.95 mg/kg-d), or 171 ppm (8.55 mg/kg-d) 2,4-diaminotoluene for 721, 721, or 588 days, respectively. The rats developed mammary gland adenomas at an incidence rate of 1/20, 38/50, and 42/50, respectively. OHEA gave diaminotoluene a weight of evidence classification of B2 (probable human carcinogen) based on sufficient data in animals and no data in humans (OHEA, 1988).

Further calculations

Following TRI Environmental Indicator methods, the potency factor of 23.2 per mg/kg-d and the WOE of B2 yielded a toxicity weight of 100,000 for diaminotoluene. Confidence in the toxicity weight is medium due to the high quality of the study, but the lack of toxicity data on other isomers of diaminotoluene.

Sources

U.S. EPA. 1993. Hazardous Substances Data Bank. Accessed via TOXNET.

U.S. EPA OHEA. 1988. *Evaluation of the Potential Carcinogenicity of Diaminotoluene (mixed)*.

IARC. 1978. *IARC Monographs on the Evaluation of the Carcinogenicity of Chemicals to Man*. Vol. 16. Lyon, France.

No other sources of information were found.

C.2.10. Dichlorobenzene (mixed isomers and 1,3-) (25321-22-6 and 541-73-1)

The toxicity weights derived here represent all mixed isomers (1,2-, 1,3- and 1,4-) of dichlorobenzene (DCB), and the individual isomer 1,3-DCB (541-73-1). IRIS or HEAST values exist for the individual isomers 1,2-DCB and 1,4-DCB, and are given in Appendix A. The chronic inhalation toxicity weight described below is based on 1,2-DCB because available data shows it to be the most toxic of the three isomers (1,2-, 1,3-, and 1,4-) for chronic health endpoints. The chronic oral and cancer toxicity weights have been finalized by EPA and are shown in Appendix B. The interim chronic inhalation weight for dichlorobenzene is given below.

Chronic Oral

See Appendix B.

Chronic Inhalation

Basis of toxicity weight

The Superfund Health Risk Technical Support Center (U.S. EPA ORD) reports that the 1993 Health Effects Assessment Summary Tables (HEAST; EPA ORD, 1993) list an RfC of 0.2 mg/m^3 for 1,2-dichlorobenzene, based on an inhalation study on rats by Hollingsworth et al. (1958).

Further calculations

The RfC of 0.2 mg/m^3 listed in HEAST was converted to an RfD of 0.057 mg/kg-d by multiplying by a reference human respiration rate of 20 m^3/d and dividing by a reference human body weight of 70 kg. Following TRI Environmental Indicator methods, this RfD estimate yields a chronic inhalation toxicity weight of 10 for 1,2-dichlorobenzene, and therefore also for the mixed isomers of dichlorobenzene, and, due to the absence of data from which to calculate a chronic inhalation toxicity weight, 1,3-DCB. Confidence in the toxicity weight is low based on low confidence for the RfD.

Cancer Oral and Inhalation

See Appendix B.

Sources

IARC. 1978. *IARC Monographs on the Evaluation of the Carcinogenicity of Chemicals to Man*. Vol. 7. Lyon, France.

IARC. 1978. *IARC Monographs on the Evaluation of the Carcinogenicity of Chemicals to Man*. Vol. 29. Lyon, France.

U.S. EPA. 1993. Hazardous Substances Data Bank (HSDB). Accessed via TOXNET.

U.S. EPA. 1995. Integrated Risk Information System. Accessed via TOXNET.

U.S. EPA OHEA. 1989. *Ambient Water Quality Criteria Document Addendum for Dichlorobenzenes*.

U.S. EPA OHEA. 1987. *Health Effects Assessment for Dichlorobenzenes*.

U.S. EPA ORD. 1993. *Health Effects Assessment Summary Tables*. March.

U.S. EPA ORD Superfund Health Risk Technical Support Center. n.d. *Risk Assessment Issue Papers for: Evaluation of the Carcinogenicity of 1,4-Dichlorobenzene (106-46-7)*.

U.S. EPA ORD Superfund Health Risk Technical Support Center. n.d. *Risk Assessment Issue Papers for: Evaluation of the Inhalation Concentration for 1,2-Dichlorobenzene (95-50-1)*.

U.S. EPA ORD Superfund Health Risk Technical Support Center. n.d. *Risk Assessment Issue Papers for: Derivation of Provisional Oral RfD for 1,3-Dichlorobenzene (541-73-1)*.

No additional sources of information were found.

C.2.11. Diethanolamine (11-42-2)

Chronic Oral

Basis of toxicity weight

HSDB cited a study reported by PATTY (1981-82) which exposed rats to 0.02, 0.09, and 0.17 g/kg-d for 90 days. The 0.02 g/kg-d dose level showed no adverse effect, 0.09 g/kg-d caused changes in liver and kidney weights, and 0.17 g/kg-d caused microscopic pathology and deaths.

Further calculations

The NOAEL of 0.02 g/kg-d (20 mg/kg-d) was divided by an uncertainty factor of 1,000 (10 each for intra- and interspecific extrapolation, and 10 for the use of a subchronic study) to yield an RfD estimate of 0.02 mg/kg-d. Following TRI Environmental Indicator methods, this RfD yielded a chronic oral toxicity weight of 100 for diethanolamine. Because of the absence of other subchronic or chronic mammalian studies for diethanolamine, confidence in the toxicity weight is low.

Chronic Inhalation

No dose-response data were found to support the derivation of a chronic inhalation toxicity weight. Following TRI Environmental Indicator methods, the toxicity weight of 100 calculated for chronic oral exposure to diethanolamine was applied to both exposure pathways.

Cancer Oral and Inhalation

No data were found to support the calculation of a cancer toxicity weight for oral or inhalation exposure to diethanolamine.

Sources

U.S. EPA. 1993. Hazardous Substances Data Bank. Accessed via TOXNET.

No other sources of information were found.

C.2.12. Dimethyl sulfate (77-78-1)

Chronic Oral and Inhalation

No dose-response data were found to support the calculation of chronic toxicity weights for dimethyl sulfate.

Cancer Oral and Inhalation

Basis of toxicity weight

IRIS reports that the weight of evidence (WOE) classification for dimethyl sulfate is B2 (probable human carcinogen), based on sufficient data in animals and insufficient data in humans.

The authors of the Health and Environmental Effects Profile for Dimethyl Sulfate (EPA OHEA, 1985) did not attempt to calculate a cancer potency for dimethyl sulfate because of the low quality of the available animal studies (e.g., controls were incompletely reported and/or exposure routes were irrelevant to humans).

Two of the animal studies listed in HSDB have significant limitations, but may be used to calculate a cancer potency for inhalation exposure. The first, by Druckrey et al. (1970), exposed 20 rats to 3 ppm (17 mg/m^3), and 27 rats to 10 ppm (56.7 mg/m^3) dimethyl sulfate for one hour per day, five times per week, for 130 days. Three of the rats exposed to 3 ppm died with tumors: one with neurocytoma, one with ethesioneuroepithelioma of the olfactory nerve, and one with squamous carcinoma of the nasal cavity. Of the 15 that survived, five developed malignant tumors, including three squamous carcinomas of the nasal cavity, one mixed tumor of the cerebellum, and one lymphosarcoma of the thorax with multiple metastases to the lung. No information on controls was reported, nor is it certain that all of the tumor data were reported.

The second study, by Schlogel and Bannasch (1970), also has limitations for use as a basis for a toxicity weight. The study is reported in the HEEP as taken from an abstract with "the tumor occurrence...not associated with species or dose, and control data...incompletely reported." HSDB, however, appears to report the same results in a study by Schlogel (1972), with more detail. Rats, hamsters, and mice of both sexes were exposed to 3 mg/m^3 dimethyl sulfate for six hours per day, twice a week, for 15 months, or 8.7 mg/m^3 for six hours per day, once per 14 days for 15 months. Malignant tumors of the nasal cavity and lung were observed in 10 out of 74 animals in the high group (rats: 6/27 nasal carcinomas, 0/36 in controls, mice: 3/25 lung carcinomas, 0/19 in controls, hamsters: 1/22 lung carcinomas, 0/15 in controls) and four out of 97 animals in the low dose group (rats: 3/37 nasal and lung carcinomas, 0/36 in controls, mice: 1/32 lung carcinoma and sarcoma of the thorax, and hamsters, 0/28).

Further calculations

Using a simplified method to derive a cancer potency estimate described in Chapter 1, the results from the rats exposed to 3 ppm in Druckrey et al. (1970) were used to calculate a cancer potency estimate of 11 per mg/kg-d, assuming that controls showed no tumors. Combined with the WOE classification of B2 reported in IRIS, this cancer potency estimate yielded an inhalation cancer toxicity weight of 100,000. Confidence in the toxicity weight is low due to the poor quality of the study.

Following the same methods described in Chapter 1, results from Schlogel and Bannasch (1970) for low dose rats were used to derive a cancer potency estimate of 34 per mg/kg-d. Combining the cancer potency estimate with the WOE classification of B2 reported in IRIS, also yielded a toxicity weight of 100,000 for dimethyl sulfate. Confidence in the toxicity weight is low due to the poor quality of the study. A more thorough review of the primary literature is required to calculate a better supported potency factor.

Because of the severity of effects shown in Druckrey et al., and because of the uncertainty caused by the poor quality of the supporting studies, during review the EPA dispo group increased the cancer toxicity weight to a maximum weight of 1,000,000. Following TRI Environmental Indicator methods, due to a lack of data on oral exposure to dimethyl sulfate, the cancer inhalation toxicity weight of 1,000,000 was assigned to both exposure pathways.

Sources

U.S. EPA. 1993. Hazardous Substances Data Bank. Accessed via TOXNET.

U.S. EPA. 1993. Integrated Risk Information System. Accessed via TOXNET.

U.S. EPA OHEA. 1985. *Health and Environmental Effects Profile for Dimethyl Sulfate*. EPA/600/X-85/392. June.

No other sources of information were found.

C.2.13. 4,6-Dinitro-o-cresol (534-52-1)

Chronic Oral

Basis of toxicity weight

Of the studies examined for use in deriving a toxicity weight for 4,6-dinitro-o-cresol (DNOC), a study by Plotz (1936) listed in the *Health and Environmental Effects Profile for Dinitrocresols* (U.S. EPA OHEA, 1986) reported the lowest observed adverse effect level (LOAEL) in humans. Plotz reported that three people were treated for obesity with 0.35 to 1.5 mg/kg-d 4,6-dinitrocresol for up to 9 weeks. Patients experienced excessive sweating, thirst, fatigue, decreased appetite, elevated basal metabolic rate, and greenish-yellow conjunctivae. This study was also used as the basis of the 1982 reportable quantity (RQ) for 4,6-dinitrocresol (U.S. EPA OHEA, 1986). Three other studies cited in the HEEP document (Dodds and Robertson, 1933; Quick, 1937; and Horner, 1942) report similar toxic effects from treatment of obesity with 4,6-dinitrocresol at similar doses. The authors of the HEEP document divided the LOAEL of 0.35 mg/kg-d from Plotz (1936) by an uncertainty factor of 1000 (to account for intraspecific variation, the use of a LOAEL, and the use of a subchronic study) to calculate an acceptable daily intake (ADI; analogous to an RfD) of 3.5×10^{-4} mg/kg-d.

Further calculations

Following TRI Environmental Indicator methods, the ADI of 3.5×10^{-4} mg/kg-d reported in the HEEP document yielded a chronic oral toxicity weight of 10,000. Confidence in the toxicity weight is low due to the absence of chronic data and the age of the critical study.

Chronic Inhalation

Basis of toxicity weight

The authors of the *Health and Environmental Effects Profile for Dinitrocresols* (U.S. EPA OHEA, 1986) also calculated an interim ADI based on a TWA-TLV (time weighted average-threshold limit value) of 0.2 mg/m^3 for DNOC adopted by the American Conference of Governmental Industrial Hygienists (ACGIH) (1985). ACGIH notes that this TLV takes into account significant exposure occurring via the dermal pathway as well as through inhalation, and that the TLV is considered to be below the threshold for "debilitating symptoms." The authors of the HEEP document multiplied the TWA-TLV by a reference breathing volume of 10 m^3/8 hour work day and an absorption factor of 0.5, divided by a human body weight of 70 kg and assumed a 5-day work week to obtain a constant dose of 0.01 mg/kg-d. They then divided this constant dose by an uncertainty factor of 100 (to account for variability in humans and less-than-lifetime exposure) to obtain the interim ADI of 10^{-4} mg/kg-d.

Further calculations

Following TRI Environmental Indicator methods, this interim ADI of 10^{-4} mg/kg-d was used to derive a chronic inhalation toxicity weight of 10,000 for 4,6-dinitrocresol. Because the

ADI is based on a TWA-TLV, confidence in the toxicity weight is low.

Cancer Oral and Inhalation

The International Agency for Research on Cancer (IARC) ranked 4,6-dinitrocresol a Group 3 (not classifiable as to human carcinogenicity) carcinogen. The HEEP document also reported that no data regarding the carcinogenicity of DNOC were found. No cancer toxicity weights for 4,6-dinitrocresol were calculated.

Sources

ATSDR. 1992. *Toxicological Profile for Cresols: o-Cresol, p-Cresol, m-Cresol*. TP-91/11.

IARC. 1993. *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans*.

U.S. EPA. 1993. Hazardous Substances Data Bank. Accessed via TOXNET.

U.S. EPA ECAO. 1982. *4,6-Dinitro-o-cresol: Reportable Quantity (RQ) Ranking Based on Chronic Toxicity*. July.

U.S. EPA OHEA. 1986. *Health and Environmental Effects Profile for Dinitrocresol*. PB88-220769. July.

U.S. EPA ORD Superfund Health Risk Technical Support Center. n.d. Risk Assessment Issue Paper for: Derivation of a Provisional RfD for 4,6-Dinitrocresol.

No other sources of information were found.

C.2.14. Isobutyraldehyde (78-84-7)

Chronic Oral

No data were found to support the calculation of a chronic oral toxicity weight for isobutyraldehyde. Following TRI Environmental Indicator methods, the toxicity weight of 100,000 derived for chronic inhalation exposure was applied to both exposure pathways (see below).

Chronic Inhalation

Basis of toxicity weight

Over a 4-month period, Svintukhovskii (1972) exposed rats to 50 mg/m^3 (20 mg/kg-d) isobutyraldehyde for 4 hours per day. This exposure produced four effects: decreased hemoglobin and leukocytes, increased cholinesterase activity, and decreased gas exchange [sic].

Further calculations

The LOAEL of 50 mg/m^3 was converted to a constant dose of 3.3 mg/kg-d by multiplying by a reference rat inhalation rate of 0.2 m^3/d and 4/24 hrs/d and dividing by a reference rat body weight of 0.5 kg. The LOAEL of 3.3 mg/kg-d was then divided by an uncertainty factor of 10,000 (10 each for intra- and interspecific extrapolation, 10 for the use of a subchronic study, and 10 for the use of a LOAEL) to derive an inhalation RfD of 3.3×10^{-4} mg/kg-d. Following TRI Environmental Indicator methods, this RfD yielded a chronic inhalation toxicity weight of 10,000 for isobutyraldehyde. An additional data quality factor of 10 (to account for the incomplete database) was added to yield an inhalation RfD of 3.3×10^{-5} mg/kg-d and a chronic inhalation toxicity weight of 100,000. Because confidence in the critical study and in the supporting database is low, confidence in the toxicity weight is low.

Cancer Oral and Inhalation

No data were found to support the calculation of a cancer toxicity weight for isobutyraldehyde.

Sources

U.S. EPA. 1993. Hazardous Substances Data Bank. Accessed via TOXNET.

No other sources of information were found.

C.2.15. Isopropyl Alcohol (67-63-0)

Chronic Oral

Basis of toxicity weight

HSDB cites a study reported in the IARC Monographs (IARC, 1977) in which three generations of rats were given 1.5, 1.4, and 1.3 g/kg-d isopropanol, respectively, in drinking water. No effect on growth, reproductive function, or embryonic or postnatal development was observed, though first generation rats showed some growth retardation early in life.

Further calculations

The LOAEL of 1.4 g/kg/d (1,400 mg/kg-d) was divided by an uncertainty factor of 1,000

(10 each for intra- and interspecific variation, and 10 for the use of a LOAEL) to result in a chronic oral RfD estimate of 1.4 mg/kg-d. Following TRI Environmental Indicator methods, this RfD estimate yields a chronic oral toxicity weight of 1 for isopropanol. Confidence in the toxicity weights is medium due to the high quality of the critical study but the lack of supporting data.

Chronic Inhalation

Basis of toxicity weight

An unpublished EPA document entitled *Printing Industry Cluster Chemicals: Isopropanol (CAS No. 67-63-0)* (1993) cites a subchronic study by Baikov et al (1974, in Rowe and McCollister, 1982) in which rats were exposed to 0, 0.66, 2.6, or 20.5 mg/m^3 continuously for 3 months. Rats at the lowest dose level showed no adverse effects. At 2.6 mg/m^3 rats showed alterations in total nucleic acids, redox enzymes in their blood, and coproporphyrins in their urine. At 20.5 mg/m^3, rats showed changes in reflexes, enzyme activity, leukocyte fluorescence, BSP retention, total nucleic acids, coproporphyrins in urine, and lung, liver, spleen, and central nervous system morphology.

Further calculations

The NOAEL of 0.66 mg/m^3 was converted to a dose of 0.26 mg/kg-d by multiplying by a reference rat inhalation rate of 0.2 m^3/d and dividing by a reference rat body weight of 0.5 kg. The NOAEL of 0.26 mg/kg-d was then divided by an uncertainty factor of 1,000 (10 each for intra- and interspecific variation, and 10 for the use of a subchronic study) to derive an RfD estimate of 2.6×10^{-4} mg/kg-d. Following TRI Environmental Indicator methods, this RfD estimate yields a toxicity weight of 10,000. Confidence in the toxicity weight is low due to the incomplete database.

Cancer Oral and Inhalation

The International Agency for Research on Cancer (IARC) has ranked isopropanol a Group 3 carcinogen: not classifiable as to human carcinogenicity. Conversely, IARC listed isopropanol manufacture (a strong-acid process) as a Group 1 carcinogen: the exposure circumstance is known to be carcinogenic to humans. HSDB reports that workers at factories where isopropyl alcohol was manufactured experienced increased incidences of paranasal sinus cancer and possibly laryngeal cancer. Workers were simultaneously exposed to diisopropyl sulfate, isopropyl oils, and sulfuric acid. No cancer toxicity weight for isopropanol was derived due to a lack of dose-response data.

Sources

IARC. 1993. *Monographs on the Evaluation of Carcinogenic Risk to Humans*. Lyon, France.

NIOSH. 1993. *Registry of Toxic Effects of Chemical Substances*. Accessed via TOXNET.

U.S. EPA. 1993. Hazardous Substances Data Bank (HSDB). Accessed via TOXNET.

U.S. EPA. 1993. *Printing Industry Cluster Chemicals: Isopropanol (CAS No. 67-63-0).* Unpublished. October 18.

No other sources of information were found. Isopropanol is currently under review by EPA as to whether or not it should be removed from the TRI list. During the time period in which the toxicity weights for isopropanol acid were being developed, however, no additional data were available from this action.

C.2.16. Lead (7439-92-1) and Lead Compounds (N420)

The toxicity weights derived here represent both lead and lead compounds. Lead exposure is generally recognized as one of the most significant environmental health problems in the U.S. Exposure to lead is widespread in the United States, via multiple exposure pathways and sources including inhalation of lead particles or ingestion of lead-contaminated drinking water, food, soil, lead-based paint chips, and dust (ATSDR, 1993). Extensive study of lead exposure has revealed significant effects on adults and children at levels currently encountered in the environment and a threshold for effects has yet to be identified. Because lead is hypothesized to have a non-threshold dose-response relationship for chronic systemic effects, and because of widespread exposure, the standard methods used to evaluate other noncarcinogens in this exercise cannot be applied to lead. This analysis therefore used a combination of qualitative and quantitative information to assign a toxicity weight to lead for noncarcinogenic effects.

Chronic Oral and Inhalation

Basis of toxicity weight

The ATSDR *Toxicological Profile for Lead* (1993) reports that the human population most susceptible to adverse responses to lead exposure is preschool-age children (under six years). Young children absorb lead via the gastrointestinal tract more efficiently than adults (50 versus 15 percent relative absorption). They tend toward behaviors that increase potential lead exposure (e.g., thumb sucking and pica) and have immature detoxification enzyme systems, resulting in increased body burdens of lead. Children also have been shown to have lower blood thresholds for and more severe reactions to the hematological and neurological effects induced by lead exposure (ATSDR, 1993).

In 1991, the Centers for Disease Control issued the fourth revision of their publication *Preventing Poisoning in Young Children*. The CDC revised its 1985 statement based on "overwhelming and compelling" evidence showing adverse effects of lead in young children at increasingly lower blood lead levels. Because some adverse health effects have been clearly documented at blood lead levels at least as low as 10 µg/dL, the recommended intervention level was lowered to 10 µg/dL (from 25 µg/dL in 1985). Some studies report harmful effects at even

lower levels, but CDC concluded that such evidence is insufficient at this time to be evaluated definitively (CDC, 1991).

Lower levels of blood lead in children have been associated with neurological impairment. For example, Bellinger et al. (1991) found that the mean General Cognitive Index (GCI) score for children with blood lead levels below 3 µg/dL was 6.4 points higher than the GCI score for children with blood lead levels equal to or greater than 10 µg/dL. At higher blood lead levels, children show symptoms of encephalopathy (at approximately 90 µg/dL), other neurological symptoms of acute lead poisoning (from 60 to 450 µg/dL, with a mean of 178 µg/dL), death (with a mean of 327 µg/dL), childhood plumbism, and anemia (at or below 70 µg/dL) (NRC, 1972).

Further calculations

Because 1) no NOAEL has been established for the neurological effects of lead, 2) lead exposure is widespread and occurs through multiple exposure pathways, and 3) methods are not available to develop an RfD for lead, the maximum chronic toxicity weight of 100,000 was assigned to both the oral and inhalation exposure pathways for the purposes of calculating a toxicity weight for chronic exposure to lead. This toxicity weight reflects the conclusion that any additional exposure to lead may cause adverse neurological effects in children. Due to the substantial data on the chronic toxic effects of lead, confidence in the toxicity weight is high.

Cancer Oral and Inhalation

Basis of toxicity weight

The Evaluation of the Potential Carcinogenicity of Lead and Lead Compounds: In Support of Reportable Quantity Adjustments Pursuant to CERCLA Section 102 (EPA, 1989) noted that, across a number of bioassays, a total ingested lead dose of 1 to 10 g (4 to 40 mg/kg-d) appears to be associated with an increased cancer incidence of 10 percent in rats. For mice, the dose at which 10 percent of the study animals developed cancer appeared to be between 9 and 90 mg/kg-d. Despite this finding, the authors declined to make a quantitative cancer potency estimate based on these data, due to the lack of information on the potential differences in pharmacokinetics between animals and humans. They did, however, qualitatively characterize the cancer potency of lead as low (Group 3). In addition, the authors assigned lead a weight of evidence classification of B2 (probable human carcinogen). Based on a WOE classification of B2 and a Group 3 (low) potency group, the authors assigned lead and lead compounds a low hazard ranking among potential carcinogens.

Further calculations

Despite a lack of a quantitative cancer potency estimate, during the review process the EPA dispo group assigned lead and lead compounds a cancer toxicity weight of 10,000 based on the available data. Due to a lack of consensus on a cancer potency for lead, confidence in the toxicity weight is low.

Sources

ATSDR. 1993. *Toxicological Profile for Lead*.

Bellinger, D., J. Sloman, A. Leviton, M. Rabinowitz, H. L. Needleman, and C. Waternaux. 1991. "Low-level lead exposure and children's cognitive function in the preschool years." *Pediatrics*. 87(2): 219-227

CDC. 1991. *Preventing Poisoning in Young Children*.

National Research Council. 1993. *Measuring lead exposure in infants, children, and other sensitive populations*.

Piomelli et al. 1984. "Management of childhood lead poisoning." *Pediatrics*. 4: 105.

Silbergeld, E.K., Schwartz, J., and K. Mahaffey. 1988. "Lead and osteoporosis: mobilization of lead from bone in postmenopausal women." *Environmental Research*. 47: 79-94

U.S. EPA. 1986. *Quality Criteria For Lead*. Volume III.

U.S. EPA. 1989. *Evaluation of the Potential Carcinogenicity of Lead and Lead Compounds: In Support of Reportable Quantity Adjustments Pursuant to CERCLA Section 102*.

U.S. EPA. 1990. *Review of the National Ambient Air Quality Standards for Lead: Assessment of Scientific and Technical Information*.

U.S. EPA. 1993. *Modeling the Benefits of Reduced Exposure to Lead Leached from Solder into Drinking Water*.

C.2.17. Methyl Iodide (77-88-4)

Chronic Oral and Inhalation

No data were found from which to calculate chronic toxicity weights for methyl iodide (idomethane).

Cancer Oral and Inhalation

Basis of toxicity weight

The Hazardous Substances Data Bank reports a study cited in the IARC Monographs (IARC, 1977) in which 16 and 8 rats were given weekly subcutaneous injections of 10 and 20 mg/kg methyl iodide, respectively. Local tumors occurred in 9/16 low dose rats and in 6/8 high

dose rats after 500 to 700 days. Pulmonary metastases were also observed. No tumors were observed in the control rats.

IARC used the above study to rank methyl iodide as a Group 3 (not classifiable as to human carcinogenicity) carcinogen, based on limited evidence in animals and no data in humans. The U.S. EPA Office of Health and Environmental Assessment (OHEA), however, in developing a Reportable Quantity ranking for methyl iodide, ranked it as a weight-of-evidence Group C carcinogen (a possible human carcinogen), based on limited animal evidence and no human data. OHEA's weight of evidence assessment was based on Druckrey et al. (1970) and Preussmann (1968), in which rats given single (50 mg/kg methyl iodide) or repeated (10 or 20 mg/kg-dose methyl iodide) subcutaneous injections developed local sarcomas and, at the 50 mg/kg dose, pulmonary metastases. A Strain A mouse lung tumor assay (Poirer et al., 1975), however, showed equivocal results. OHEA concluded that the results of these studies "should only be interpreted as suggestive of a carcinogenic effect in animals." OHEA found these data inadequate for calculating a potency factor for methyl iodide.

Further calculations

Using a simplified method described in Chapter 1, a cancer potency estimate of 2.9 per mg/kg-d was derived from the low dose (1.4 mg/kg-d) from the study cited by IARC, discussed above. Following TRI Environmental Indicator methods, the cancer potency estimate of 2.9 per mg/kg-d was combined with the WOE of C reported by OHEA to obtain a cancer toxicity weight of 1,000 for methyl iodide. Confidence in the toxicity weight is low due to the poor quality of the data. It is suspected that further research would yield a higher cancer potency and/or WOE classification, leading to a higher toxicity weight for methyl iodide.

Sources

NIOSH. 1993. *Registry of Toxic Effects of Chemical Substances*. Accessed via TOXNET.

U.S. EPA. 1993. Hazardous Substances Data Bank (HSDB). Accessed via TOXNET.

U.S. EPA OHEA. 1988. *Evaluation of the Potential Carcinogenicity of Methyl Iodide (74-88-4) In Support of Reportable Quantity Adjustments Pursuant to CERCLA Section 102*.

U.S. EPA OERR and OSWER. 1993. Reportable Quantity (RQ) files.

No other sources of information were found.

C.2.18. Molybdenum Trioxide (67-63-0)

Chronic Oral

Basis of toxicity weight

HSDB cites a study by Schroeder et al. (1971) in which two generations of Charles River CD mice were given 10 mg/l molybdenum as the molybdate ion (equivalent to 15 mg/l molybdenum trioxide) in drinking water from the time of weaning. The first generation had an increased number of early deaths in their offspring. The surviving second generation offspring showed an increased number of maternal deaths, dead litters, and runts in the F3 generation.

Further calculations

The LOAEL of 15 mg/l molybdenum trioxide was converted to a LOAEL of 2.6 mg/kg-d by multiplying by a reference mouse daily water intake of 0.005 l/d and dividing by a reference mouse body weight of 0.03 kg. The LOAEL of 2.6 mg/kg-d was divided by an uncertainty factor of 1,000 (10 each for intra- and interspecific variability, and 10 for the use of a LOAEL) to yield an RfD estimate of 2.6×10^{-3} mg/kg-d and a toxicity weight of 1,000. Confidence in the toxicity weights is low due to the lack of supporting data.

Chronic Inhalation

Basis of toxicity weight

HSDB cites a 1963 occupational study reported in the *Handbook on the Toxicology of Metals* (1986) in which 3 out of 19 workers exposed to between 1 and 19 mg/m^3 metallic molybdenum and molybdenum trioxide for four to seven years developed pneumoconiosis. No other symptoms were reported.

Further calculations

The LOAEL of 1 mg/m^3 was converted to a constant dose of 0.07 mg/kg-d by multiplying by a reference human respiration rate of 20 m^3/d, a work day of 8/24 hrs/d, and 5/7 d/wk work week and dividing by a reference human body weight of 70 kg. The LOAEL of 0.07 mg/kg-d was divided by an uncertainty factor of 1,000 (10 each for intraspecific variation, the use of a LOAEL, and the use of a less-than-lifetime study) to result in an RfD estimate of 7.0×10^{-5} mg/kg-d. Following TRI Environmental Indicator methods, this RfD yielded a chronic inhalation toxicity weight of 10,000. Confidence in the toxicity weights is low due to poor quality of the study and the lack of supporting data.

Cancer Oral and Inhalation

No toxicity weights for the carcinogenic effects of molybdenum trioxide were calculated due to a lack of available quantitative dose-response data.

Sources

Friberg et al. 1979. *The Handbook on the Toxicology of Metals*.

Merck and Co., Inc. 1989. *The Merck Index*. Rahway, NJ: Merck and Co.

NIOSH. 1993. Registry of Toxic Effects of Chemical Substances (RTECS). Accessed via TOXNET.

U.S. EPA. 1993. Hazardous Substances Data Bank. Accessed via TOXNET.

Venugopal et al. 1978. *Metal Toxicity in Mammals*.

No other sources of information were found.

C.2.19. Nitrilotriacetic Acid (139-13-9)

Chronic Oral

Basis of toxicity weight

Merski (1982, in: HSDB, 1993) administered 0, 0.73, or 7.3 mmol/kg-d nitrilotriacetic acid (NTA) by gavage to male Sprague-Dawley rats for up to 30 days. Two animals from each dose group were killed 24 hours after dosing on day 9, 13, 16, 20, 23, 27, or 30. Rats from both dose groups showed cytoplasmic vacuolation and hyperplasia of the proximal convoluted tubules, with greater number and severity in the higher dose group. In addition, in the higher dose group, erosion and hyperplasia of the pelvic transitional epithelium were observed. The author noted that the results suggest that NTA-associated urinary tract lesions develop in a sequential manner and are dose-related.

Further calculations

The LOAEL of 0.73 mmol/kg-d was converted to a LOAEL of 139.5 mg/kg-d by multiplying by the molecular weight of NTA of 191 mg/mmol. The LOAEL of 139.5 mg/kg-d was divided by an uncertainty factor of 10,000 (10 each for intra- and interspecific extrapolation, 10 for the use of a LOAEL, and 10 for the use of a subchronic study) to obtain an RfD estimate of 0.014 mg/kg-d. Following TRI Environmental Indicator methods, this RfD estimate was used to derive a chronic oral toxicity weight of 100 for NTA. Confidence in this toxicity weight is low due to low confidence in the study and in the supporting database.

Chronic Inhalation

No data were found to support the derivation of a chronic inhalation toxicity weight for NTA. Following TRI Environmental Indicator methods, the chronic oral toxicity weight of 100 was applied to both exposure pathways.

Cancer Oral and Inhalation

Basis of toxicity weight

IARC assigned NTA a ranking of Group 2B based on sufficient evidence in animals and inadequate or no evidence in humans.

The CRC Critical Reviews in Toxicology (Anderson, et al., 1985) reported seven chronic dietary or drinking water bioassays with NTA in which tumorigenicity in rats and mice was examined. Ingestion of more than 0.4 mmol/kg-d NTA increased renal cortical tubular cell tumor incidence in rats and mice; and transitional epithelial cell tumors in the renal pelvis, ureter, and bladder of rats, but not mice. The review used reference consumption rates of 50 g food/kg-d for mice, 150 g food/kg-d for rats, and 145 ml water/kg-d for rats.

Based on this review, the authors determined that rats were the more sensitive species studied. The study that showed a significant increase in tumorigenicity at the lowest dose level was a 704-day study in which 0.52 mmol/kg-d (99 mg/kg-d) $Na_3NTA \bullet H_2O$ was administered to rats in their drinking water. Twenty-nine of the 183 rats studied developed renal cortical tubular cell tumors. No information on the controls was given in the CRC review; controls were assumed to have not developed tumors.

Further calculations

The data used by IARC to rank NTA a Group 2B carcinogen suggest a possible EPA weight of evidence (WOE) ranking of B2. In addition, following simplified methods described in Chapter 1, a cancer potency estimate of 0.02 per mg/kg-d was derived from the results of the 704-day study reported in Anderson et al. (1985), above.

The cancer potency estimate of 0.02 per mg/kg-d was combined with the WOE estimate of B2 to obtain a cancer oral toxicity weight of 100 for NTA. Confidence in the toxicity weight is medium because although this study reflects the critical effect (urinary tract tumorigenesis) found at statistically significant incidence rates in other chronic bioassays with mice and rats (Anderson et al., 1985), data on controls were not available for the study.

No data were found to support the calculation of a cancer toxicity weight for inhalation exposure to NTA. Following TRI Environmental Indicator methods, the cancer oral toxicity weight of 100 was applied to both exposure pathways.

Sources

Anderson et al. 1985. "Review of the Environmental and Mammalian Toxicology of Nitrilotriacetic Acid." In: *CRC Critical Reviews in Toxicology*. CRC Press. Vol. 15(1).

NTP. 1993. *Environmental Health Perspectives Supplements: Compendium of Abstracts from Long-Term Cancer Studies Reported by the National Toxicity Program from 1976 to 1992. Vol.*

101. Supplement 1. April.

U.S. EPA. 1993. Hazardous Substances Data Bank (HSDB). Accessed via TOXNET.

No other sources of information were found.

C.2.20. Nitroglycerin (55-63-0)

Chronic Oral

Basis of toxicity weight

In the Risk Assessment Issue Paper For: *Toxicity Information and Provisional Oral Slope Factor for Nitroglycerin (CAS# 55-63-0),* the Superfund Health Risk Technical Support Center (U.S. EPA ORD, n.d.), derived a provisional chronic oral RfD based on a study by Ellis et al. (1984). Ellis et al. (1984) conducted a chronic toxicity study with nitroglycerin (NTG) in dogs, rats, and mice. Six/sex/group beagle dogs were administered 0, 1, 5, or 25 mg NTG/kg-d in capsules daily for 12 months. Thirty-eight/sex CD rats and 58/sex CD-1 mice were fed diets containing 0, 0.01, 0.1, or 1 percent NTG for up to 24 months. The estimated dose levels for rats were 0, 3.04, 31.5, and 363 mg/kg-d for males, and 0, 3.99, 38.1, and 434 mg/kg-d for females. The dose levels (estimated by the authors) for mice were 0, 11.1, 114.6, and 1022 mg/kg-d for males, and 0, 9.72, 96.4, and 1058 mg/kg-d for females.

The only effect observed in dogs was occasional dose-related methemoglobinemia. The dose of 25 mg/kg-d was considered by the Superfund Health Risk Technical Support Center to be a NOAEL for dogs in a long-term oral study. In mice, body weight in the high dose groups was reduced throughout the study. After 12 months, high dose mice had a compensated anemia. Hyperpigmentation in the liver, spleen, and kidney of most high-dose mice and some mid-dose mice was also observed. Despite these observed effects, the study reviewers reported that they considered the high dose of 1022 mg/kg-d to be a NOAEL for mice.

Rats were observed to be the most sensitive species in the study. Body weight gain and final body weight were reduced in the high dose rats due to reduced food consumption. Unscheduled deaths occurred in all groups, due to pituitary adenomas, ulcerated subcutaneous tumors, and other, unspecified causes. Methemoglobinemia and compensatory reticulocytosis were shown in the high dose groups. High dose males showed signs of hepatocellular damage and cholestasis. High dose rats showed increased absolute and relative liver weight, cholangiofibrosis, proliferation of the bile ducts, and increased pigmentation of the spleen and kidney epithelium at 12 months. Foci of hepatocellular alterations were observed in some rats of all dosed groups. Lesions observed in rats after 24 months were similar, but more frequent and severe, than those seen at 12 months. The LOAEL in this study for hematological and hepatic effects was considered to be 363 mg/kg-d, and the NOAEL 31.5 mg/kg-d.

The Superfund Health Risk Technical Support Center derived a provisional chronic oral RfD of 0.03 mg/kg-d from the rat NOAEL of 31.5 mg/kg-d, applying an uncertainty factor of 100 (10 each for intra- and interspecific extrapolation) and a modifying factor of 10 to account for an incomplete database. They noted, however, that this RfD would not protect humans from acute adverse affects such as neurobehavioral and cardiovascular endpoints observed in epidemiological studies at similar or lower exposure.

Further calculations

Following TRI Environmental Indicator methods, the provisional RfD of 0.03 mg/kg-d was used to derive a toxicity weight of 100 for chronic oral exposure to NTG. Because this RfD is not expected to be protective for acute adverse effects in humans, confidence in this toxicity weight is low.

Chronic Inhalation

No data adequate for calculating a chronic inhalation toxicity weight were found. Following TRI Environmental Indicator methods, the chronic oral toxicity weight of 100 was applied to both exposure pathways.

Cancer Oral and Inhalation

Basis of toxicity weight

Human data on NTG carcinogenicity are limited to a study by Craig et al. (1985) examining mortality in workers in a Scottish explosives factory. The researchers found that the high exposure group of blasting workers experienced an excess of lung cancer deaths. The workers were simultaneously exposed to NTG and ethylene glycol dinitrate, however, which confounds the results of the study. The study by Ellis (1984) discussed above found statistically significant increased incidence of hepatocellular carcinomas in male and female rats and testicular interstitial cell tumors in male rats exposed to NTG. Suzuki et al. (1975) also showed limited evidence of carcinogenicity in mice. On the basis of these studies, the Superfund Health Risk Technical Support Center (U.S. EPA ORD, n.d.) assigned a weight of evidence (WOE) classification of B2 (probable human carcinogen), based on inadequate evidence for carcinogenicity in humans and sufficient evidence for carcinogenicity in animals.

The Superfund Health Risk Technical Support Center calculated a provisional oral slope factor of 2.1 per mg/kg-d using the same study by Ellis discussed above. Male rats developed hepatocellular carcinomas or neoplastic nodules at a rate of 1/24, 0/28, 4/26, and 15/21 for dose rates of 0, 0.01, 0.1, and 1 percent NTG in food, respectively. Female rats developed hepatocellular carcinomas or neoplastic nodules at a rate of 1/29, 1/32, 3/28, and 16/25 for dose rates of 0, 0.01, 0.1, and 1 percent NTG in food, respectively. Finally, male rats developed testicular interstitial cell tumors at a rate of 2/24, 1/28, 3/26, and 11/21 for dose rates of 0, 0.01, 0.1, and 1 percent NTG in food, respectively.

Incidence of hepatocellular carcinomas/neoplastic nodules in male and female rats combined were used do calculate a cancer potency for NTG. Only the combined dose rate of the highest dose group showed significantly increased incidence of tumorigenesis over the controls. The combined rates were 1/53 in controls, 1/60 (not significant) at dose levels of 3.04 (males) and 3.99 (females) mg/kg-d, 7/54 (not significant) at dose levels of 31.5 (males) and 38.1 (females) mg/kg-d, and 31/46 at dose levels of 363 (males) and 434 (females) mg/kg-d. The rat body weights for the low, medium, and high dose groups respectively were 0.69, 0.65, and 0.52 kg for the males, and 0.41, 0.40, and 0.27 kg for the females. The animal doses were scaled to human equivalent doses and used in a multistage model to obtain the provisional oral slope factor of 2.1 per mg/kg-d.

Further calculations

The provisional oral slope factor of 2.1 per mg/kg-d was combined with the WOE classification of B2 to obtain a cancer oral toxicity weight of 10,000 for NTG. Confidence in the toxicity weight is medium, since the critical study is adequate but the database is incomplete.

No data were found to support the calculation of a cancer toxicity weight for inhalation exposure to NTG; following TRI Environmental Indicator methods the cancer oral toxicity weight of 10,000 was applied to both exposure pathways.

Sources

U.S. EPA. 1993. Hazardous Substances Data Bank (HSDB). Accessed via TOXNET.

U.S. EPA ORD Superfund Health Risk Technical Support Center. n.d. *Risk Assessment Issue Paper for: Toxicity Information and Provisional Oral Slope Factor for Nitroglycerin*.

No other sources of information were found.

C.2.21. Peracetic Acid (79-21-0)

Chronic Oral

No dose-response data were found to support the calculation of a chronic oral toxicity weight for peracetic acid. Following TRI Environmental Indicator methods, the chronic inhalation toxicity weight of 1,000 was assigned to both exposure pathways (see below).

Chronic Inhalation

Basis of toxicity weight

HSDB reported a subchronic inhalation study by Heinze et al. (1984), which exposed mice

and guinea pigs to 186 or 280 mg/m^3 peracetic acid aerosol twice daily for thirty minutes for ninety days. Most of the animals showed bronchopneumonia and liver granuloma; mice also showed increased incidence of lung tumors and decreased leukocyte counts. No other information on the study was reported.

Further calculations

The lower dose rate of 186 mg/m^3 was used as a LOAEL in mice (the more sensitive species) to calculate a chronic inhalation toxicity weight. The LOAEL was converted to a constant dose of 10.3 mg/kg-d by multiplying by reference mouse respiration rate of 0.04 m^3/d and 1/24 hrs/d, and dividing by a reference mouse body weight of 0.03 kg. The LOAEL of 10.3 mg/kg-d was divided by an uncertainty factor of 10,000 (10 each for intra- and interspecific variability, 10 for the use of a LOAEL, and 10 for the use of a subchronic study) to yield an RfD estimate of 1.03×10^{-3} mg/kg-d. Following TRI Environmental Indicator methods, this RfD estimate yields a chronic inhalation toxicity weight of 1,000. Confidence in the toxicity weight is low due to the incomplete database.

Cancer Oral and Inhalation

Although the study by Heinze et al. (1984) cited in HSDB indicated increased incidence of lung tumors and decreased leukocyte counts in mice, it lacked information on dose-response rates in controls and test subjects, so could not be used to calculate a cancer potency. No other data were found to support the derivation of a cancer toxicity weight.

Sources

U.S. EPA. 1993. Hazardous Substances Data Bank (HSDB). Accessed via TOXNET.

No other sources of information were found.

C.2.22. Titanium Tetrachloride (7550-45-0)

Chronic Oral

No dose-response data were found on the effects of chronic oral exposure to titanium tetrachloride. Following TRI Environmental Indicator methods, the chronic inhalation toxicity weight of 100,000 was assigned to both exposure pathways (see below).

Chronic Inhalation

Basis of toxicity weight

The Dupont company submitted to the U.S. EPA an epidemiological study of workers exposed to titanium dioxide and titanium tetrachloride in which they found a slight elevation in

lung cancer incidence in employees exposed to titanium tetrachloride, though commented that "the association is most likely a spurious one" (Chen and Fayerweather, 1987). In a memo entitled "Review of Dupont's Epidemiological Analyses of Titanium Dioxide and Titanium Tetrachloride Workers," however, the EPA reviewer remarked that she found the Dupont submission to be poorly documented and of little use and that both chemicals have been associated with reduced ventilatory capacity and pleural disease in exposed workers, citing Garabrant et al. (1987). Neither Garabrant (1987), nor Chen and Fayerweather (1987), nor Fayerweather, Chen, Karus and Gilby, (1990) (a follow-up analysis on Chen and Fayerweather (1987)) contained human dose-response data from which to calculate a toxicity weight for titanium tetrachloride.

The *Reportable Quantity Document for Titanium Tetrachloride* (U.S. EPA OHEA, 1988) reports that, "titanium tetrachloride hydrolyzes rapidly in the presence of water...therefore it is assumed that the most probable inhalation exposure to titanium tetrachloride would be to its hydrolysis products." Both HSDB and the *Reportable Quantity Document for Titanium Tetrachloride* (1988) cite a study done by Lee et al. (1986), which exposed rats to 0, 0.1, 1.0, and 10 mg/m^3 titanium tetrachloride hydrolysis products for six hours per day, five days per week for two years. A mild rhinitis was observed at 0.1 mg/m^3. At 1.0 mg/m^3 incidence of mild rhinitis and tracheitis was increased, with slight Type II pneumocyte hyperplasia in alveoli adjacent to the alveolar ducts (corresponding to a "nuisance dust"). At 10 mg/m^3, extrapulmonary particle deposition occurred in the tracheobronchial lymph nodes, liver, and spleen without tissue response, and increased incidence of rhinitis, tracheitis, and dust cell response with Type II pneumocyte hyperplasia, alveolar bronchiolarization, foamy dust cell accumulation, alveolar proteinosis, cholesterol granuloma, and focal pleurisy were observed. In addition, a few well-differentiated cystic keratinizing squamous carcinomas were found in the lungs. These lung tumors were thought to be experimentally-induced and have not been observed in humans.

Further calculations

The LOAEL of 0.1 mg/m^3 was converted to a constant dose of 0.007 mg/kg-d by multiplying by a reference rat respiration rate of 0.2 m^3/d, 6/24 hrs/d, and 5/7 d/wk, and dividing by a reference rat body weight of 0.5 kg. The LOAEL of 0.007 mg/kg-d was divided by an uncertainty factor of 1,000 (10 each for intra- and interspecific variation, and 10 for the use of a LOAEL) to obtain an RfD equivalent of 7×10^{-6} mg/kg-d. Following TRI Environmental Indicator methods, this RfD yielded a maximum chronic toxicity weight of 100,000 for titanium tetrachloride. Confidence in the toxicity weight is medium due to the high quality of the study but the lack of supporting data.

Cancer Oral and Inhalation

No dose-response data were found from which to calculate cancer toxicity weights for titanium tetrachloride.

Sources

NIOSH. 1993. Registry of Toxic Effects of Chemical Substances (RTECS). Accessed via TOXNET.

U.S. EPA. 1993. Hazardous Substances Data Bank. Accessed via TOXNET.

Chen, J.L., and Fayerweather, W.E. 1987. *Epidemiologic Study of Lung Cancer, Chronic Respiratory Disease, and Pulmonary X-Ray Abnormalities in Workers Exposed to Titanium Dioxide and Titanium Tetrachloride*. DuPont.

Subsequent EPA reviews of Chen and Fayerweather (1987).

U.S. EPA OHEA. 1988. *Reportable Quantity Document for Titanium Tetrachloride*.

No other sources of information were found.

C.2.23. Toluene Diisocyanate (mixed isomers and 2,4-, 2,6-) (26471-62-5; 584-84-9; 91-08-7)

Toluene diisocyanate (TDI) is comprised primarily of two isomers, 2,4-TDI (584-84-9) and 2,6-TDI (91-08-7). Most available toxicological information is based on an 80:20 ratio of the two isomers. The toxicity weights for TDI represent the two isomers 2,4-TDI and 2,6-TDI individually and in mixtures.

It is also important to note that TDI is converted to diaminotoluene on contact with water. Diaminotoluenes have been assigned a ranking of Group 2B (possible human carcinogen) by IARC and have been assigned a TRI Environmental Indicator cancer oral toxicity weight of 100,000 (see Appendix B).

Chronic Oral

Basis of toxicity weight

The Generic Health Hazard Assessment of the Chemical Class Diisocyanates (EPA, 1987) reported a LOAEL of 49 mg/kg-d and a NOAEL of 23 mg/kg-d in rats for irritation of the lower respiratory tract, based on a 106-week study by NTP (1986). Mice were also tested at slightly higher rates and showed no adverse effects. Fifty/sex F344/N rats were administered doses of commercial grade TDI in corn oil by gavage five d/wk at a rate of 0, 23, and 49 mg/kg-d (males) and 0, 49, and 108 (females). Dose-related increased incidence of acute bronchopneumonia were observed.

Further calculations

The NOAEL of 23 mg/kg-d was divided by an uncertainty factor of 100 (10 each for intra- and interspecific variation) to yield an RfD estimate of 0.23 mg/kg-d. Following TRI

Environmental Indicator methods, this RfD estimate yields a chronic oral toxicity weight of 10. Confidence in the toxicity weight is medium, since the study is of high quality but the database is incomplete.

Chronic Inhalation

Basis of toxicity weight

The chronic inhalation toxicity weight for TDI is based on an occupational study cited in the *Chemical Hazard Information Profile* (Draft Report; EPA, 1984) in which approximately 10 percent of previously exposed workers developed an asthma-like sensitization response to levels of less than 5 ppb (0.005 ppm) TDI (Bernstein, 1982). This evidence led the ACGIH in 1982 to recommend lowering the TLV-TWA (threshold limit value-time weighted average) from 0.02 ppm to 0.005 ppm, with a STEL (short term exposure limit) of 0.02 ppm.

Further calculations

The LOAEL of 0.005 ppm was converted to a LOAEL of 0.036 mg/m^3 by multiplying by the molecular weight of 174.14 g/mol and dividing by the molecular volume of 24.45 l/mol. The LOAEL of 0.036 mg/m^3 was converted to a constant dose of 0.0024 mg/kg-d by multiplying by a reference human respiration rate of 20 m^3/d and an 8/24 hr/d, 5/7 d/wk workweek, and dividing by a reference human body weight of 70 kg. Finally, the LOAEL of 0.0024 mg/kg-d was divided by an uncertainty factor of 1,000 (10 to account for intraspecific variability, 10 for the use of a LOAEL, and 10 for the use of subchronic data) to yield an RfD estimate of 2.4×10^{-6} mg/kg-d. Following TRI Environmental Indicator methods, this RfD estimate results in a maximum chronic inhalation toxicity weight of 100,000. Confidence in the toxicity weight is medium due to the sensitive endpoint but the use of an occupational study.

Cancer Oral

The California EPA Office of Environmental Health Hazard Assessment (1992) derived a cancer potency of 0.039 per mg/kg-d for TDI, based on the same 106-week 1983 National Toxicology Program study cited above. Fifty male F344 rats were administered 0, 30, or 60 mg/kg TDI by gavage and fifty female F344 rats were administered 0, 60, or 120 mg/kg TDI by gavage. Groups of 50/sex B6C3F1 mice were administered by gavage 120 mg or 240 mg TDI and 60 mg or 120 mg TDI respectively. The cancer potency was based on the dose-response data for fibromas and fibrosarcomas of the subcutaneous tissue in male rats (3/50, 6/50, and 12/50, for controls, low, and high-dose groups, respectively), the most sensitive target site in the most sensitive group tested.

The International Agency for Research on Cancer ranked TDI a Group 2B carcinogen (possible human carcinogen) based on sufficient animal data and limited or insufficient evidence in humans. This classification is further supported by several positive mutagenicity studies reported in the Registry of Toxic Effects of Chemical Substances (RTECS) database. Recent studies have found positive mutagenicity in *Salmonella typhimurium* exposed to 100 ug/plate TDI, in mouse

lymphocytes exposed to 75 mg/L TDI, and in hamster ovaries (sister chromatid exchange) exposed to 300 mg/L TDI.

Further calculations

The data used by IARC in classifying TDI a Group 2B carcinogen suggest a possible EPA weight of evidence (WOE) classification of B1 or B2 (probable human carcinogen). The cancer potency of 0.039 per mg/kg-d calculated by OEHHA and the WOE estimate of B1 or B2 yields a cancer oral toxicity weight of 100 for TDI. Confidence in the toxicity weight is medium, due to the high quality of the study and the incomplete database.

Cancer Inhalation

The IARC Monographs (IARC, 1985) and the *Chemical Hazard Information Profile* (U.S. EPA, 1984) cited a study by Loeser (1983) with three to four week-old male and female CD-1 mice and Sprague-Dawley rats. One hundred twenty male and female mice were administered either 0, 0.36, or 1.07 mg/m^3 (0.05 or 0.15 ppm) 80:20 TDI for six hours per day, five days per week for 104 weeks. One hundred twenty six male and female rats were exposed to the same doses for 108 weeks (females) or 110 weeks (males). No dose-related carcinogenic responses were noted, and tumor incidences in animals of either species exposed to TDI corresponded to those seen in the controls. There was, however, a statistically-significant increase in mortality in the low- and high-dose female groups. Based on these results, no cancer inhalation toxicity weight for TDI was derived.

Sources

California EPA. 1992. *Expedited Cancer Potency Values and Proposed Regulatory Levels for Certain Proposition 65 Carcinogens.*

IARC. 1979. *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Volume 19*. Lyon, France.

IARC. 1985. *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Volume 39*. Lyon, France.

National Institute of Environmental Health Sciences. 1991. *Sixth Annual Report on Carcinogens Summary*.

U.S. EPA. TSCA Docket 400021. Incomplete reference.

U.S. EPA. 1984. *Chemical Hazard Information Profile for Toluene Diisocyanate*. Draft Report.

U.S. EPA. 1987. Final Report for Task 2-19: *Estimation of Carcinogenic Risk for Di-isocyanates*.

U.S. EPA. 1987. *Generic Health Hazard Assessment of the Chemical Class Diisocyanates*.

U.S. EPA. 1993. Hazardous Substances Data Bank (HSDB). Accessed via TOXNET.

No other information sources were found.