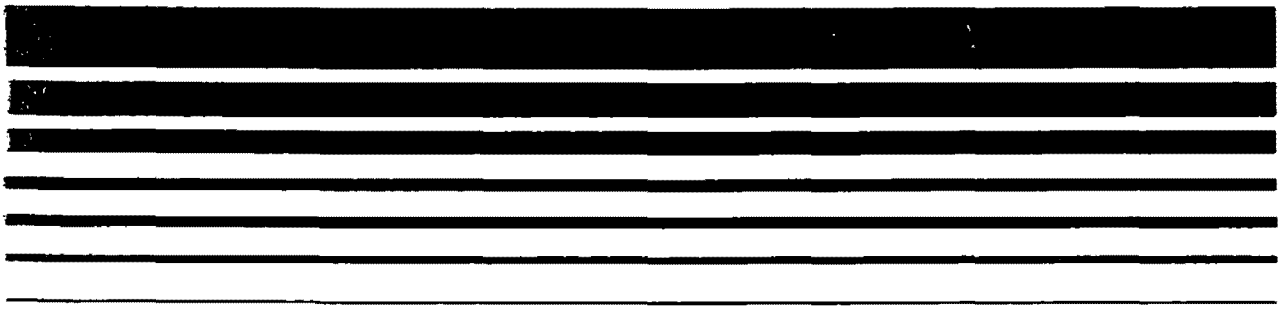
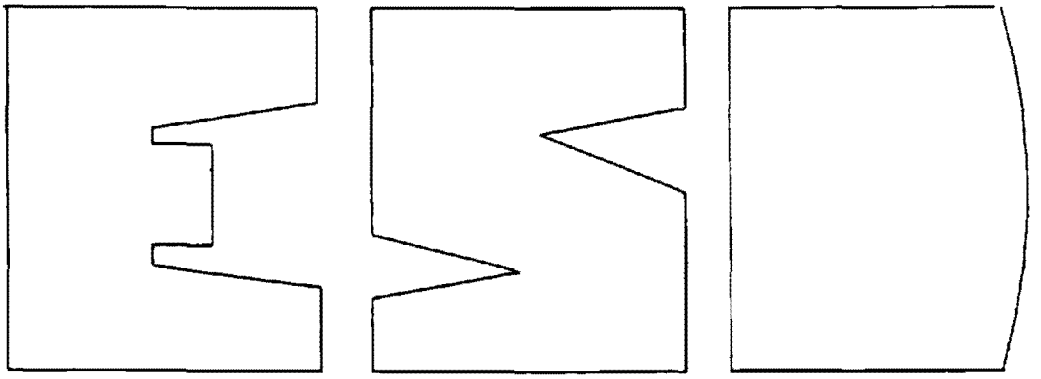
United States Environmental Protection Agency
Office of Air Quality Planning and Standards Research Triangle Park NC 27711
EPA-450/3-92-010 February 1994

EPA

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





United States
Environmental
Protection Agency

Office of Air Quality
Planning and Standards
Research Triangle Park NC 27711

EPA-450/3-92-010
February 1994

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

Emissions Standards Division

TECHNICAL REPORT DATA

(Please read Instructions on reverse before completing)

1. REPORT NO.	2.	
EPA-450/3-92-010		

4. TITLE AND SUBTITLE	5. REPORT DATE
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.	February 1994
	6. PERFORMING ORGANIZATION CODE

7. AUTHOR(S)	8. PERFORMING ORGANIZATION REPORT NO.
Dr. Jane Caldwell-Kenkel Dr. Cheryl Seigal Scott	

9. PERFORMING ORGANIZATION NAME AND ADDRESS	10. PROGRAM ELEMENT NO.
U.S. Environmental Protection Agency Office of Air Quality Planning and Standards Research Triangle Park, NC 27711	11 CONTRACT/GRANT NO.

12. SPONSORING AGENCY NAME AND ADDRESS	13. TYPE OF REPORT AND PERIOD COVERED
Director Office of Air Quality Planning and Standards Office of Air and Radiation U.S. Environmental Protection Agency Research Triangle Park, NC 27711	Final
	14. SPONSORING AGENCY CODE EPA/200/04

15. SUPPLEMENTARY NOTES

16. ABSTRACT

Section 112(g) of the Clean Air Act ("the ACT"), as amended in 1990, requires control technology determinations for "modifications" to plant sites that are major sources of hazardous air pollutants (HAP). Under 112(g) pollutants are designated as either "threshold" or "non-threshold" since emission increases in pollutants for which "no safety threshold for exposure can be determined" can only be offset by corresponding decreases in emissions of similiar pollutants.

17. KEY WORDS AND DOCUMENT ANALYSIS

hazard ranking, modifications, threshold

a. DESCRIPTORS	b. IDENTIFIERS/OPEN ENDED TERMS	c. COSATI Field/Group
MODIFICATIONS, HAZARD RANKING, THRESHOLD, EMISSION RATES	Air Pollution control	

18. DISTRIBUTION STATEMENT	19. SECURITY CLASS *(Report)*	21. NO. OF PAGES
Release Unlimited	Unclassified	
	20. SECURITY CLASS *(Page)* Unclassified	22. PRICE

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

Prepared by: Jane C. Caldwell-Kenkel
Program Integration and Health Section
Pollutant Assessment Branch
Office of Air Quality Planning and Standards

and

Cheryl Siegel Scott
Human Health Assessment Group
Office of Health and Environmental Assessment
Office of Research and Development

Acknowledgement:

The following people have contributed their time and expertise to the development of this document and its attendant data: Hal Zenick, HERL, ORD, RTP; Jim Cogliano, ECAO, ORD Washington D.C.; Chon Shoaf, ECAO, ORD, RTP; John Vandenberg, HERL, ORD, RTP; Bob Fegley, OSPR, ORD Washington D.C., and Mark Townsend, OPPTS, Washington D.C.

Table of Contents

SECTION 1: THE HAZARD RANKING

A. Purpose of the Hazard Ranking

1.0 INTRODUCTION

1.1 Background:

Title III of the 1990 Clean Air Act amendments establishes a control technology-based program to reduce stationary source emissions of hazardous air pollutants (HAP). In section 112(b) of the Act, 189 HAP or chemical groups are listed for the purposes of regulation. Section 112(g) establishes control technology requirements for new, modified, or reconstructed major sources of these pollutants. Modifications are defined as a physical change at a major source that increases emissions above a de minimis level. Increases in a HAP's emissions from existing sources are not considered a modification if those emissions can be offset by decreases in emissions of more hazardous pollutants. Furthermore, under section 112(g) pollutants are designated as either "threshold" or "non-threshold" since emission increases in pollutants for which "no safety threshold for exposure can be determined" can only be offset by corresponding decreases in emissions of similar pollutants.

Within 18 months of enactment (November 15, 1990), the EPA must issue guidance that assigns, to the extent practicable, the relative hazard to human health of each HAP listed in the section 112(b) of the Act. This report describes the methodology and supporting data for developing a hazard ranking and offsetting

provisions for pollutants under section 112(g) of the Clean Air Act Amendments of 1990.

1.2 Issues for Ranking Hazard:

Developing a relative hazard ranking is a large undertaking in which several issues need to be considered. A fundamental issue is the objective of the ranking. It can be envisioned that the ability to rank pollutants by hazard has application to several problems. However, no one single ranking can be designed to fit the many different purposes for which the idea of ranking for hazard or risk might be considered. For this reason, rankings need to be specific to their intended use. The use to which the hazard ranking of section 112(g) is designed for is the determination of relative hazard between pollutants in order to provide an offset (emissions decrease of some HAP) which will have a great probability of reducing hazard produced by the emission increase of another HAP. Thus, the structure of the ranking with its attendant offsetting guidance is designed to provide that outcome. Assumptions and policy decisions are incorporated into the ranking methodology for the purpose of making a relative comparison between pollutants and not for instance, as is the case for Reportable Quantities under CERCLA, to establish broad categories for reporting requirements. For the ranking of hazard used in CERCLA, the actual difference in hazard between pollutants is not a paramount consideration, but rather a general determination of hazard for assignment into broad bins.

Given the placement in the Clean Air Act, a ranking of inhalation hazards is of primary interest in the section 112(g) rulemaking. In certain cases, such as metals which can deposit in media other than air, the oral route also becomes important. The task, thus becomes more complicated since two exposure routes need to be considered. One approach would be to develop two rankings (a ranking for each exposure route). The demand for high quality exposure data and dose-response data is great with this approach. Alternatively, the ranking could be one based on hazard data from the most sensitive route or the integration of data from both the inhalation and oral routes. In the case of the hazard ranking for section 112(g), inhalation routes of exposure have been generally assumed to be most representative of hazard from HAP but oral data has been used when appropriate and in the absence of inhalation data.

Another question concerns which chemicals should be considered in the hazard ranking. Section 112(g) identifies 189 chemicals and chemicals classes. This list could be broken down into subclasses for chemicals with similar properties. For example, a metals or organic solvents subclass could be used for such purposes. However, several different rankings of chemical subclasses, would result in more restrictive offsetting requirements since equivalence determinations would be difficult.

The last issue concerns the ability to characterize true differences in hazard between pollutants. Uncertainties exist with any ranking. For evaluations of carcinogenicity, a broad variety

of data have been used by the EPA in the past. For example, data range from screening studies which were designed to quickly identify carcinogenic hazards to well-designed 2-year chronic bioassays and epidemiologic studies. For noncarcinogens the differences in quality of the available studies, as well as endpoint studied, varies widely. Based upon available data, determinations of hazard will be unequal due to varying quality. Other uncertainties exist such as measurement differences between the risk descriptors or surrogates which are used to rank pollutants. The task is made particularly difficult by the magnitude of the list (189 pollutants, 17 of which are multi pollutant groupings and the varying degrees of knowledge concerning the health effects caused by exposure to these HAP. The aggregate of uncertainties, differences in data, and scope of HAP to be ranked results in difficulty in making explicit distinctions between pollutants. Thus rankings such as the one developed for section 112(g), need to be robust and should be considered to portray relative differences and not absolute differences in hazard.

1.3 Methodology:

The requirement to identify the relative hazard of the 189 HAP and the requirement to provide offsetting guidance for determining whether an emission decrease is "more hazardous" present a formidable challenge to the EPA. In developing an approach to the "more hazardous" finding, legal, policy, scientific, and practical judgements must be made. From a legal standpoint, the approach

must be consistent with the statutory language. From a scientific standpoint, the approach should maximize its use of the currently available science and data and should be consistent with the EPA's overall goal of incorporating the best scientific information available for decision-making. From a policy standpoint, any approach must: (1) ensure that offsets are unlikely to increase the overall hazard to public health and (2) ensure consistency with the EPA's overall goal of providing the regulated community with flexibility and incentives to seek emission reductions that are environmentally beneficial and cost-effective. From a practical standpoint, the approach must be implementable by applicants and by the State and local permitting authorities, and thus not be overly complex. Therefore the overall goal of the hazard ranking and offsetting guidance for section 112(g) should strike an appropriate balance between the objectives described above.

The EPA consulted an independent panel of scientific experts for input into the considerations that should be made in identifying the "practicable" limitations in methodologies and data for the relative hazard ranking. This panel of the EPA's Science Advisory Board (SAB) was apprised of the EPA's draft outline for hazard ranking in a public meeting held on October 28 and 29, 1991. The consultation meeting provided members of the SAB an opportunity to provide verbal feedback on several approaches. One of the concerns the SAB expressed was comparing the hazard between carcinogens and pollutants which are of concern for chronic or acute exposures. The creation of the "high-concern" category in

the hazard ranking is an attempt to address this issue. Another concern for the SAB was that there be an appeal process for offsets since no system can be error free. Such a process is mentioned in the preamble of the proposed rule. Finally, the SAB suggested that possibly a "matrix" approach may be considered for the comparison of relative hazard which employed all aspects of a pollutants potential hazard (i.e. neurotoxicity, carcinogenicity, developmental toxicity, and general toxicity from chronic and acute exposures, etc.). Furthermore the SAB suggested that offsets only be allowed between pollutants whose matrices of information showed that hazard was decreased for all aspects of toxicity for the pollutants. The approach proposed by the EPA does not employ a "matrix approach" for the determination of relative hazard between pollutants for the following reasons: there is a lack of data to fill out the matrix of information needed for such a system; and the attending offsetting guidance would be too complex to implement.

Section 112(g) requires that the EPA distinguish between pollutants, for which "no safety threshold for exposure can be determined," and other listed pollutants for the purposes of offsetting. Consequently the pollutants must be at a minimum categorized as either "non-threshold" or "threshold." Under EPA's proposed approach, the first step in the relative ranking of the pollutants is to assign the pollutants to one of four categories and to establish the relative hazard between the categories. Pollutants which are not identified specifically as "non-threshold"

pollutants are categorized as "threshold" pollutants. As a second step the EPA separated out pollutants which are of "high-concern" for short term exposure and chronic toxicity. Such pollutants are assigned to the "high-concern" category. Finally pollutants with insufficient data to be placed in the "non-threshold," "threshold," or "high-concern" category are considered to be "unrankable".

1.4 Determination of "More Hazardous:"

The EPA reviewed several alternatives for determining the relative hazard between pollutants for the proposed rule. One such approach is to develop an ordinal ranking of potency estimates for cancer and non-cancer endpoints. Such a ranking would treat the potency estimate for each pollutant as a discrete value and would ignore the uncertainty of that estimate. For example, a potency value of 10 would indicate a greater hazard than a potency value of 9.5. The EPA believes that for the purposes of the ranking, such fine scale distinctions should not be made when the uncertainty in the hazard estimate is taken into account. Additionally, this approach could prompt frequent reordering of the ranking as new scientific data becomes available and potency estimates change.

Another approach the EPA considered would subdivide potency estimates into groupings or "bins." This approach increases the stability of the ranking, because for any given pollutant, small changes in the potency value would probably not cause a change in the bin assignment. This approach may also have advantages in the treatment of multiple-pollutant streams (it may be easier to evaluate and compare the hazard of pollutants by their bin

assignments). However, this approach does not adequately reflect the differences in hazard for pollutants especially those immediately adjacent to the borderline of the bins (the "borderline effect"). For example, using bins of 1-10, 11-100, and 101-1000, a pollutant with a value of 101 would be treated as more hazardous than a pollutant with a value of 99, while a pollutant with a value of 99 would be treated as equally hazardous as another pollutant with a value of 1.

The EPA's proposed approach separates the HAPS into four categories and then attempts to assign the relative hazard between the four categories. For individual pollutants in each category, if possible, a "range of equivalent hazard" is established for individual pollutants so that the relative hazard between pollutants can be established. Thus this hazard ranking methodology tries to appropriately take into account the uncertainty in the hazard estimates of each pollutant and minimize the "borderline effect."

1.5 Definitions:

Definitions used in construction of the proposed ranking are given below.

(1) **Hazardous air pollutant.** - The term "hazardous air pollutant" refers to any air pollutant listed in section 112(b) of the Clean Air Act Amendments of 1990.

(2) **Carcinogenic effect.** - Unless revised, the term "carcinogenic effect" shall have the meaning consistent with that of the EPA under the guidelines for Carcinogenic Risk Assessment (1) as of the

date of enactment for potential evidence for carcinogenicity.

(3) **"Non-threshold" pollutants.** - For the purposes of the proposed ranking, hazardous air pollutants with a weight of evidence classification pertaining to the potential human carcinogenicity of either Group A (known), B (probable), or C (possible) are considered to be "non-threshold" pollutants. In addition, the EPA identified several pollutants which have been classified by the International Agency for Research on Cancer (IARC), but which have not been formally reviewed by the EPA. These pollutants are categorized by the IARC as Group 1 (agents carcinogenic to humans), Group 2A (probable human carcinogen and Group 2B (possible human carcinogens). The EPA currently takes the position that unless there is adequate evidence to the contrary, the assumption should be made that carcinogens have "no safety threshold of exposure," i.e. any level of exposure carries with it some risk of cancer, albeit very small in many cases. The EPA recognizes that the definition of "non-threshold" effects is not straightforward and may include other endpoints besides cancer. Therefore non-carcinogens may be assigned to the category of "non-threshold" pollutant if adequate evidence exists consistent with current EPA guidelines (1-2).

(4) **"Threshold pollutants".** - For the purposes of proposed ranking, "threshold" pollutants are those pollutants which either have a weight of evidence pertaining to potential human carcinogenicity of Group D (not classified as to human carcinogenicity) or Group E (evidence of non-carcinogenicity for

humans) according to the Guidelines for Carcinogenic Risk Assessment (1) or which have not been evaluated for carcinogenicity by EPA or IARC. These pollutants are considered to have a "threshold of safety" unless there is adequate evidence available to the contrary consistent with current EPA guidelines (1).

(5) **Hazard.** - Section 112(g) requires that pollutants are to be ranked by hazard to human health. The EPA interprets this phrase to mean that only potential human health effects should be considered in the ranking and not an assessment which includes exposure, residence time, or ecotoxicology. These factors are considered elsewhere in the Act.

(6) **"High-concern" pollutant.** - The EPA is assigning pollutants to this category which are of high concern for toxicity from long- or short-term exposures at relatively low exposure concentrations.

(7) **De minimis level.** - The EPA is proposing to define a de minimis level for each pollutant to be an emission for which "the burdens of regulation yield a gain of trivial or no value"(3). Specifically, the EPA uses the guidance provided in sections 112(c) and 112 (f) of the Act to help define a <u>de minimis</u> level based on protection of human health. Therefore, a <u>de minimis</u> emission of a hazardous air pollutant is one which would likely result in: (a) less than a lifetime risk of cancer of one in a million to the maximum exposed individual or (b) a level below which public health is protected with "an ample margin of safety for a lifetime exposure" to a non-carcinogen.

1.6 Legislative Language:

Section 112(g) - The modifications provision for emission of hazardous air pollutants listed in section 112(b) is given below:

"(g) Modifications. -

"(1) Offsets. -

"(A) A physical change in, or change in the method of operation of, a major sources which results in a greater than de minimis increase in actual emissions of a hazardous air pollutant shall not be considered a modification, if such increase in the quantity of actual emissions of any hazardous air pollutant from such source will be offset by an equal or greater decrease in the quantity of emissions of another hazardous air pollutant (or pollutants) from such source which is deemed more hazardous, pursuant to guidance issued by the administrator under subparagraph (b). The owner or operator of such source shall submit a showing to the Administrator (or the State) that such increase has been offset under the preceding sentence.

"(B) The Administrator shall, after notice and opportunity for comment and not later than 18 months after the date of enactment of the Clean Air Act Amendments of 1990, publish guidance with respect to implementation of this subsection. Such guidance shall include an identification, to the extent practicable, of the relative hazard to human health resulting from emissions to the ambient air of each of the pollutants listed under subsection (b) sufficient to

facilitate the offset showing authorized by subparagraph (A).

Such guidance shall not authorize offsets between pollutants where the increased pollutant (or more than one pollutant in a stream of pollutants) causes adverse effects to human health for which no safety threshold for exposure can be determined unless there are corresponding decreases in such types of pollutant(s).

1.7 Interpretation of Legislative Language

Under section 112(g) (1) (A) the language contained in the first sentence is subject to two interpretations as it describes a "more hazardous decrease" in emissions. Therefore, two approaches may be used to construct guidance for the determination of "a more hazardous emissions decrease" for an acceptable offset. The EPA will propose one approach in the hazard ranking guidance and ask for public comment.

The EPA's proposed approach allows for an equal or greater quantity of "a more hazardous" pollutant or a set percentage of the emissions increase of a "more hazardous quantity" of an "equally hazardous" pollutant to be an acceptable offset. Under this approach an attempt is not made to determine the magnitude of difference in hazard between pollutants.

B. Methodology for Ranking "Non-threshold" Hazardous Air Pollutants Under Section 112(g), Clean Air Act Amendments of 1990

1. INTRODUCTION

1.1 BACKGROUND

Under section 112(g), pollutants are designated as either "non-threshold" or "threshold" since emission increases in pollutants "for which no safety threshold for exposure can be determined" can only be offset by corresponding decreases in emissions of similar pollutants.

For the purposes of section 112(g), a "non-threshold" pollutant is defined as one in which some hazard is presumed to exist with any level of exposure. However, sufficient data on which to base such mechanistic arguments are lacking for all HAP at the current time. Data currently being developed on dioxin appears most promising for making inferences regarding important elements associated with dioxin's observed toxicities.

The EPA presumes, in the absence of relevant biological information to the contrary, that some risk of cancer is associated with exposure to a carcinogenic agent. This assumption acknowledges that if the agent acts by adding to or accelerating the same carcinogenic process that leads to the background occurrence of cancer, there is an absence of a no-effect level (1). In addition, it is assumed that the added effect of the carcinogenic agent at low doses will be virtually linear (4).

The theory behind presuming cancer as a "non-threshold" process derives from the understanding that cancer may result, in part, from a single event such as a change in DNA resulting in

mutation or some other change resulting in a heritable event. Changes in the transformed cell may become amplified through replication resulting in a large colony of altered cells that may become cancerous as the final result. Although the body contains processes that repair damage, it can be hypothesized that some probability exists that these processes may fail and that the probabilities for failure add to that probability associated with "background". Under this framework, any level of exposure may be associated with an effect with the inference of an increasing dose-response function for neoplasia.

Alternatively, chemicals indicating effects other than cancer are considered "threshold" air pollutants since no-effect levels, in contrast, are generally presumed for systemic effects. Such toxicity can be thought to result from disruption of a collection of cells or a tissue. For example, damage to one cell is not thought to induce physiological aberrations to an organ system. However, damage to an aggregate of cells potentially leads to dysfunction and physiological change, e.g., a systemic effect. Thus theoretically, there is some threshold of exposure before such an aggregate of cells is affected.

For the hazard ranking of section 112(g) a weight-of-evidence classification of either Groups A, B, and C is used to identify, in the absence of other information concerning mechanism, hazardous air pollutants as "non-threshold." The EPA considers the data to be sufficient on carcinogenicity in humans and/or animals under these categories to provided adequate support for consideration of

a HAP as a likely human cancer hazard. Furthermore, although there is not specific direction in the statutory language of section 112(g) to identify such pollutants as "non-threshold", there is congressional testimony indicating that Congress at a minimum intended to include HAP with a weight-of-evidence of Group A, B, or C as "non-threshold" pollutants. Approximately 115 pollutants and pollutant classes, listed as hazardous air pollutants under the Act, are identified as "non-threshold" pollutants. Currently the designation of "non-threshold" is based on carcinogenicity for all cases.

The possibility of a "non-threshold" mechanism has been raised for the neurobehavioral effects associated with lead. These effects are seen with current environmental exposure levels (13). Thus the apparent absence of a "no-effect level" for lead indicates that current environmental exposures are above any "threshold" level, if such a level exists. In addition, a susceptible period during organogenesis is thought to exist and that any exposure to lead during this critical period will result in a developmental effect. However, the identification of the mechanism of toxicity as "non-threshold" for such noncarcinogenic effects has not yet been established.

Exceptions to these generalizations are expected. Some chemicals may be found to engender carcinogenic effects through "threshold" mechanisms and other chemicals may engender noncancer effects through "non-threshold" mechanisms. Thus, the designation of "non-threshold" will not necessarily be limited to agents with

toxicities other than carcinogenicity where sufficient evidence exists to make such a determination.

1.2 Approaches to Ranking the Hazard of Carcinogens

An evaluation of carcinogenic potential consists of an examination of many factors, one of which is the quantitative description of the relationship between does and response. Other important qualitative factors include the demonstration of tumorigenesis in multiple species and sexes, the ability to produce tumors at multiple sites, and whether tumors are rare or have a high background incidence. Of additional importance are factors such as physical-chemical properties, structural relationship to other chemicals rendering carcinogenic effects, and depth of understanding of the cellular and molecular interactions and processes in which a carcinogenic effect may be engendered. The weight-of-evidence evaluation approach currently employed by the EPA attempts to integrate many of the above factors into a classification system. Besides these risk surrogates, secondary criteria such as biodegradation, hydrolysis, and photolysis can, also, be factored into a ranking.

Several approaches may be used for ranking the hazard of pollutants which produce carcinogenic effects. One approach is to base a ranking on only one parameter of risk or hazard. Typically, the surrogate has been a measure of potency (or its inverse). The ranking scheme developed by Ames and colleagues (5-6) is one example of this approach. Ames and colleagues (5) propose the use of the Human Exposure Dose/Rodent Potency dose (HERP) as an index

of possible hazard from a specific exposure. Human exposure levels are compared to the dose associated with an increased tumor incidence of 50 percent (TD_{50}) in rodents.

For the hazard ranking of carcinogens under section 112(g) the EPA has chosen to use a related measure of potency, the ED_{10}, or estimated dose associated with an increased cancer incidence of 10 percent as the surrogate for carcinogenic potency. a hazard ranking based on such a system does not depend on any particular exposure scenario as it is based only on the inherent hazard of the HAP. A 10 percent increased incidence is chosen because environmental exposures are expected to be much lower than those associate with risks of 50 percent Wartenberg and Gallo (7) point out that the rank order of pollutants can change over a reasonable range of doses. Each pollutant has its own distinct dose-response function, thus, a comparison or relative ranking between pollutants at doses associated with a 50 percent increased tumor incidence may be different than a ranking using doses associated with say a 10 percent increased tumor incidence. Consequently, approaches which only capture one dimension of a pollutant's ability to elicit a carcinogenic potential cannot fully portray the multidimensional nature of carcinogenicity.

From the above discussion, an integration of qualitative and quantitative elements of carcinogenic potential into a relative ranking scheme is desirable. One such scheme is that developed by the EPA for Reportable Quantities provisions under the Comprehensive Environmental response, Compensation, and Liability

Act of 1980 (CERCLA), section 102 (8), and for the Clean Water Act (CWA), section 311. For the Reportable Quantity determinations, bins identified as "high", "medium", and "low: were defined for carcinogenic hazard (9). The following matrix was employed to determine bin assignment:

Weight-of-Evidence	$1/ED_{10}$ per (mg/kg-d) Range >100	$1/ED_{10}$ per (mg/kg-d) Range 1-100	$1/ED_{10}$ per (mg/kg-d) Range 1-100
A	HIGH	HIGH	MEDIUM
B	HIGH	MEDIUM	LOW
C	MEDIUM	LOW	LOW
D	NO RANKING	NO RANKING	NO RANKING
E	NO RANKING	NO RANKING	NO RANKING

A strength of this approach is that ranking of hazard is supported both by quantitative and qualitative descriptors of carcinogenicity. Such a scheme can be expanded to examine the hazard of effects other than cancer by developing criteria (again, judgement based) for how different effects may lead to rankings of similar concern.

A limitation for using such a scheme to rank HAP with carcinogenic properties for section 112(g) is that pollutants whose $1/ED_{10}$s approach the margins of discrete categories can have hazard determinations very different than chemicals with the same weight-

of-evidence classification and only a slightly different $1/ED_{10}$. This is discussed in a previous section as the "borderline" effect. Another limitation lies in the inherent feature using a quantitative adjustment for weight-of-evidence in the ranking which may not be appropriate for assigning differences in relative hazard between pollutants. Under CERCLA, for which this scheme was originally developed, the determination of hazard was used to assign carcinogens to broad-ranged bins of hazard for the assignment of a Reportable Quantity. The goal of that exercise was not to determine the relative hazard between pollutants (i.e., is one pollutant more hazardous than another..?), as it is in the hazard ranking developed in conjunction with section 112(g). Thus, while many of the concepts used to construct the ranking under CERCLA (a multidimensional approach using potency and weight of evidence to determine hazard, and use of the ED_{10}), are applicable to the ranking developed for section 112(g), the relative hazard between pollutants could be distorted by using broad based bins and incorporation of a quantitation of weight of evidence to determine hazard.

Yet another variation of the multidimensional approach is the scheme developed by Nesnow et al. (10) for the International Commission for Protection Against Environmental Mutagens and Carcinogens to describe carcinogenic activity. The scheme starts with a weighted value (in Log units) of the TD_{50}, in the case of a positive bioassay, or the highest average daily dose, in the case of a negative bioassay. Additional weights are assigned for

factors considered important for describing carcinogenic potential. These factors are: the ability of the chemical to induce tumors (benign or malignant) at more than one site, whether tumors are at sites for which the historical background incidence is over 10%, concordance between sexes within a single species, and concordance between species. Nesnow et al. (10) have applied this scheme to 142 chemicals tested via the oral route by the National Toxicology Program or National Cancer Institute.

The potential advantages of this scheme are its flexibility in regard to addition of other information (e.g., mechanistic) important to describe the carcinogenic process and the use of scores or weights as a way of characterizing the cumulative evidence of two pollutants' carcinogenic potential. Nesnow (10) states that weight values are based on scientific judgement and intuition. Consequently, weight values should not necessarily be interpreted as indices of carcinogenic activity (i.e., potency). For example, the carcinogenic activity of a chemical exposure causing increased incidence of a "low" background tumor, defined as a background incidence of less than 10 percent, is considered twice that of a chemical exposure causing increased incidence of a "high" background tumor. At the current time, an exact measure of the difference between such chemicals is not known. Therefore, weights assigned by Nesnow should be considered relative and not absolute.

Whether weight of evidence is used in a quantitative manner or other "weight factors" developed to describe carcinogenic hazard, the limitation exists as discussed by Frohlich and Hess (11) in

their description of the scoring system of Squire (12). They comment on the summation of individual scores (or weights) as an overall summary measure which proportedly describes the carcinogenic behavior of a chemical. Frohlich and Hess (11) believe the sum of the weights can not be considered an index of carcinogenic ability since the resultant value obscures individual difference. Since an important goal of the hazard ranking of section 112(g) is to compare the relative hazard between pollutants, distortion of hazard by a quantitative assignment of weight-of-evidence and other "weighting factors" should be minimized to insure that offsetting error is also minimized.

Frohlich and Hess' (11) comments signify that it is important to understand the factors contributing to an overall summary score for the overall placement in a ranking and to understand underlying differences between two chemicals which may be similarly ranked. However, judgements regarding the final placement in a ranking may still need to be made independently of any quantitative indicator. As with any ranking system the intended use of the ranking must always be a primary consideration in its development, which will help to determine the appropriate application of qualitative aspects of hazard.

Weight-of-evidence classification covers a range of conclusiveness about a likely human carcinogen and is a statement about the compound's ability to engender a carcinogenic hazard in humans regardless of the route of exposure. A greater human hazard concern may be inferred when an agent is believed to be a "known

human carcinogen" or when carcinogenicity demonstrated in animals satisfies more rather less of the weight-of-evidence factors identified in Appendix A. Consequently, greater confidence of a likely human cancer hazard can be inferred when sufficient evidence in humans' and/or animals exists. Conversely, a human cancer concern has much less confidence when cancer has only been demonstrated in animals and to a limited extent. Thus, for the purposes of the 112(g) hazard ranking, HAP identified as having a weight-of-evidence classification of Group A or B are determined to be more hazardous than those with weight-of-evidence classification of Group C.

Under the EPA's current practices, the route of exposure is not taken into consideration in weight-of-evidence evaluations. This may change as the EPA attempts to revise the guidelines for assessing carcinogenic hazards.

The International Agency for Research on Cancer (IARC) has evaluated the carcinogenicity evidence on several compounds that the EPA has not yet evaluated. For purposes of section 112(g), IARC classifications of Group 1 "carcinogenic to humans" and group 2 (2A) "probably carcinogenic to humans", and group 2B "possibly carcinogenic to humans" are considered to be "non-threshold" pollutants. For the present time, the EPA considers the IARC summaries are sufficient for distinguishing "non-threshold" versus

"threshold", however, the relative hazard of these chemicals and those with an EPA weight-of-evidence assignment cannot be determined as EPA evaluations do not as yet exist.

Weight-of-evidence classification should be considered qualitatively in the determination of relative hazard between HAP for several reasons. First, one cannot determine how much more hazardous a classification of Group A is that of a Group C. A full knowledge of a pollutant's ability to engender a carcinogenic hazard is not known for all HAP. Various levels of information exists on these pollutants.

Second, even though several pollutants may have the same overall weight-of-evidence classification, it is important to keep in mind the factors providing the greatest contribution for rendering the classification. This is the comment of Frohlich and Hess (11) as discussed previously.

Within each of the weight-of-evidence classifications categories (Groups A/B, and C) in the section 112(g) ranking, a second criteria upon which to base relative hazard determinations is used. This criteria is based on potency and utilizes the estimates of the $1/ED_{10}$ which is expressed in units of $(mg/kg\text{-}day)^{-1}$. The reciprocal of the ED10 is used as the potency factor for the relative ranking. The more potent the pollutant, the smaller the ED_{10} and the larger its inverse will be. Thus, more potent pollutants will be considered "more hazardous" based on $1/ED_{10}$'s. The potency value assignment to each HAP should be considered relative and for comparative purposes as the estimate of the $1/ED_{10}$

is not an absolute value. Uncertainties associated with making inferences about potential human risk by a particular route, data quality constraints, and the variation in dose-response curves of individual HAP all preclude its use as an absolute value.

2. INFORMATION SOURCES

A work group organized by the Office of Air Quality Planning and Standards and composed of representatives from the Offices of Research and Development (ORD); Pollution Prevention and Toxic Substances (OPPTS); Policy, Planning and Evaluation (OPPE), and Air, Noise and Radiation (OAR) developed criteria which serve as the basis for the data needs of the hazard ranking of HAP with carcinogenic effects. A hierarchal scheme of information sources is proposed to identify the toxicity of "non-threshold" HAP's: (1) the Integrated Risk Information System (IRIS), (2) ORD documents such as Reportable Quantity (Evaluations of the Potential Carcinogenicity of <<chemical name>>) or like documents such as Health Assessment Documents (HADs), their updates, any Science Advisory Board Comments; Health Effects and Environmental Profiles (HEEPs) and Health and Environmental Assessments (HEAs), and (3) IARC documents.

These documents are chosen as providing the background for identifying carcinogenic potential since they have undergone some sort of peer review. Some data in the HEEPs and HEAs, such as evaluations from the perspective of making risk inferences about

oral exposures, are outdated due to the age of the document, and newer information has been subsequently reported. When such data are incorporated into a more recent evaluation (one which resulted in a document other than those identified above), memorandums are considered sufficient documentation. Additionally, data in HEEPs and HEAs are considered less reliable since the documents either have not received an Agency-wide peer review, such as chemicals identified in IRIS, or, if discussed by the Carcinogen Risk Assessment Verification Endeavor group, issues were raised and have yet to be resolved.

IARC documents contain high quality information, but are listed last since their classification scheme for carcinogenicity does not always have a parallel under the EPA's weight-of-evidence scheme. The IARC summaries are used qualitatively for inferring potential hazard. Chemicals identified as having IARC Classifications of Group 1 (carcinogenic to humans) or Group 2 (including 2A, probably carcinogenic to humans; 2B, possibly carcinogenic to humans), which have not been evaluated by the EPA, are identified as "non-threshold" HAP based on the existence of limited or sufficient animal and/or human evidence of carcinogenicity (as specified in the IARC summary). The EPA is presently evaluating the data cited by IARC in order to make its own weight-of-evidence determinations and, possibly, to make quantitative inferences that may be used to place them appropriately in the hazard ranking.

SECTION 3. METHODOLOGY

As discussed previously for the ranking of "non-threshold" pollutants, a scheme which incorporates qualitative and quantitative elements is desirable since it attempts to capture the multidimensional aspects of carcinogenicity. As such, a reference point was the scheme developed for CERCLA Reportable Quantities which was based on weight-of-evidence classification and potency ($1/ED_{10}$). The use of weight-of-evidence and the $1/ED_{10}$ as components for supporting a hazard ranking is rational since these elements are readily at hand, are in common use, and are understood by the regulated community as well as by risk assessors and risk managers both inside and outside the EPA.

The approach recommended for ranking the "non-threshold" HAP which have evidence of carcinogenicity is to use both the weight-of-evidence classification and the inverse of the ED_{10}. Appendix A contains a description of the data supporting a weight-of-evidence evaluation and the methods and assumptions for estimating the ED_{10}.

Of the "non-threshold" pollutants, quantitative inferences may be made for 83 HAPs, thus, $1/ED_{10}$ estimates exist for these pollutants. Data sets supporting an estimate of the inhalation unit risk identified in the Integrated Risk Information System (IRIS) were also used to support and estimate of the $1/ED_{10}$. Thus, these $1/ED_{10}$'s can be considered relevant to inhalation exposures. It must be noted that for many of the pollutants for which quantitative estimate exist for the inhalation route, inferences

about inhalation hazards are based on data from chronic oral studies and route-to-route extrapolations, with their associated uncertainties. Additionally, estimates of the $1/ED_{10}$ have been made for chemicals not found on IRIS, In these cases, when inferences are made from studies via the inhalation route, resultant estimates of the $1/ED_{10}$ may be considered relevant to inhalation exposure.

In the absence of inhalation data or route-to-route extrapolation, estimates of the $1/ED_{10}$ have been supported using data from the oral exposure route. The use of oral data carries much greater uncertainty for making references about inhalation hazards. However, as mentioned previously, oral exposure may be an important secondary exposure concern.

The system developed by the EPA to relatively rank the carcinogens for the purposes of section 112(g) is a multidimensional approach which can best be described as a combination of criteria being used to determine the relative hazard between pollutants. Another way to describe it is as stratification of the weight of evidence with a substratification of the estimate of potency. For two "non-threshold" pollutants to be considered different in hazard, for the purposes of offsetting under section 112(g), they must be assigned weight of evidence classifications and potency estimates which meet the criteria set forth in the offsetting guidance of the rule. Therefore a determination of hazard is dependent on a combination of hazard determinants. This approach does not assign a weighting factor to

weight of evidence or use "fixed bins" of hazard (other than the four main categories, "non-threshold," "threshold," etc.) thus avoiding, as much as possible, distortion of the hazard determination for each HAP within each category.

Under the hazard ranking of section 112(g), two conditions must be satisfied for one "non-threshold" pollutant to be considered "more hazardous" than another. First, a more hazardous pollutant must have a weight of evidence which is not considered to be less hazardous. As stated above, Group C carcinogens are, as a group, considered to be less hazardous than Group A or B carcinogens.

Second, the more hazardous "non-threshold" pollutant must have a potency estimate (1/ED10) that exceeds that of the less hazardous "non-threshold" pollutant by a factor of 3. To attempt to account for uncertainty in the estimation of hazard, the EPA is making a policy decision to create a "range of equivalence" a half an order of magnitude (approximately 3 times) below or above the potency estimate. Therefore under the hazard ranking of section 112(g) for two pollutants differ significantly enough in potency for one to be designated as more hazardous, the potency estimate of the more potent pollutant must exceed the "range of equivalence" of the less potent pollutant. Consequently, if the potency estimates of two "non-threshold" pollutants fall within each other's "range of equivalence" (within a factor of three of each other) and the pollutant being decreased does not have a weight of evidence classification considered to be less hazardous than that of the

pollutant being increased, then the two "non-threshold" HAP are considered to be equally hazardous.

The application of "range of equivalence" does not have the same effect as incorporating weighting factors in the hazard assessment. The "range of equivalence" around each estimate of potency is designed to address the uncertainty in the estimates when relative comparisons of hazard are made. Used in this fashion, they do not distort the estimate as adding a quantitative weighting factor to the estimate itself would do. Thus, mistakes in offsets due to uncertainty in potency estimates is minimized with the "range of equivalence" approach rather than increased as is the case by direction application of weighting factor.

For the purposes of this rule, if a pollutant has no potency estimate but is categorized using EPA's Guidelines for Carcinogen Risk Assessment as either a known, probably, or possibly carcinogenic to human or is categorized by IARC as having sufficient animal or human studies, it is considered to be a "non-threshold" pollutant. However, due to the lack of a potency estimate, its relative hazard cannot be compared among the other "non-threshold" pollutants. Therefore it can not be relatively ranked with the other "non-threshold" pollutants and could not be offset or allowed to offset other "non-threshold" pollutants. The

weight-of-evidence and potency estimates (expressed in terms of 1/ED10) used for ranking the "non-threshold" pollutants are presented in Table 1.

One advantage of the proposed ranking approach is its simplicity for making determinations of "more" or "less" hazardous, which is considered very important to facilitate trades between pollutants. However, no insight can be obtained with respect to the validity of such determinations. A policy decision was made to consider "non-threshold" pollutants as being more hazardous than "threshold" pollutants. The relative hazard between "non-threshold" an "high-concern" pollutants was not considered to be determinable (see discussion in later sections).

There are a number of limitations however to the proposed approach. First, although carcinogens which are identified as causing severe non-cancer toxicity from short-term exposure have additional trading restrictions from their placement into the "high-concern" category, this approach does not consider, in depth, the non-cancer health effects associated with pollutants possessing some evidence of carcinogenicity. The EPA is currently assessing the database for the HAPs identified as carcinogens to determine if there are data to support a finding of a noncarcinogenic endpoint rather than cancer as the endpoint to be ranked for such HAPs. Second, the treatment of noncancer effects (which have no weight-of-evidence) which are engendered through "non-threshold" mechanisms is not clearly specified. With respect to these last two points, it is not advisable to infer from the ranking that the

effects of cancer are considered "more serious" than other health effects. However, language in the Clean Air Act implies that the increases of a "non-threshold" pollutant may not be offset by the decreases of a "threshold" pollutant.

The EPA recognizes that "non-threshold" pollutants may produce a variety of health effects in addition to cancer, including non-cancer toxicity from acute, sub-chronic, and chronic exposures. EPA's proposed approach ranks carcinogens primarily by their carcinogenic potency. Inclusion of additional offsetting restrictions on carcinogens because of concern for chronic toxicity is hampered by inadequate data on such effects and by the increased complexity of the current scheme, both which may make implementation of the program difficult.

4. UNCERTAINTIES IN THE DATA AND THEIR IMPACT ON A RANKING

Several uncertainties regarding the qualitative and quantitative aspects of a cancer hazard arise when using data from animals for making inferences regarding inhalation hazards for humans. These uncertainties are more pronounced when only oral data are available from which to make these inferences. In most cases, inhalation data are lacking so that oral data support the cancer hazard and dose-response inferences. Furthermore, the quality of data on any particular pollutant varies. In some cases a rich data base on the pharmacokinetics of the pollutant exists and consequently this information has been used to address

uncertainty associated with differences in metabolism over experimental doses, in animal-to-human extrapolations, and in route extrapolation. Unfortunately, more frequently inhalation data do not exist and only oral data are available for which to make qualitative inferences of hazard associated with inhalation exposure. A further complication arises in that dose-response relationships are inferred from administered doses in a dietary or gavage experiment. First-pass and dose-rate effects may be important considerations when making extrapolations from the gavage route to the inhalation route. Thus, uncertainty is greater when using oral rather than inhalation data resulting in the possibility that for some pollutants oral exposure may be a poor predictor of inhalation risk.

For the hazard ranking of section 112(g) EPA made several assumptions for making inferences of human health hazard from oral data. First , it is assumed that carcinogenicity is a property of the pollutant and not of the route or rate of exposure. Second, in the absence of human data, an assumption is made that human sensitivity may be as great as the most sensitive responding animals. That is neoplastic response at any site in animals is presumed to be a qualitative and quantitative predictor of a potential human carcinogenic response via any exposure route. However, site concordance is not presumed to hold across species resulting in an animal response that may differ from humans regarding the site of tumor development. While all chemicals identified as "human carcinogens" have also produced carcinogenic

response in animals, the specificity of rodent bioassays for predicting the human experience is not really known. As stated previously, a potential human concern contains more confidence when carcinogenicity has been demonstrated in two animal species.

A number of factors are important for determining the association between dose and the degree of toxic reaction engendered (14). Such factors influence uncertainty of the hazard estimate and include differences between exposure routes: (a) in tissue distribution; (b) in the rate of delivery which can lead to different concentration profiles; (c) in the degree of metabolism; and (d) across species and among target tissue concentration in the amount of toxic reaction caused by the agent at its site of action. These factors have both qualitative and quantitative influences with respect to extrapolating observed response in animals to a ranking of inhalation human health hazard.

Differences in the pharmacokinetics of a pollutant, i.e., the absorption, metabolism, distribution, and elimination, is expected between exposure routes and between species. Once a pollutant becomes absorbed, i.e. it becomes available systemically, then the proportionality between the exposure route and the target tissue becomes important. Differences across species and across exposure routes may exist. Additionally, the influence of route of exposure on quantitative inferences has only been accounted for in a limited way. When route extrapolations have been made, i.e. inhalation unit risks (in IRIS) are based on oral data, in almost all cases, lacking information, an assumption of 100 percent

absorption from both an inhalation and oral exposure route is made. Only for bromoform was a different assumption made; absorption via inhalation 50 percent that of gavage exposure.

Some information on pharmacokinetics differences between species is taken into account in the estimation of the $1/ED_{10}$ for four other HAP. Absorption differences between species (for perchloroethylene and trichloroethane) or between high and low exposure (for perchloroethylene, trichloroethane, and 1,3-butadiene) are included in the dose-response estimates. This approach is limited since absorption via inhalation exposure is not constant with time. A more rigorous accounting of disposition is included in the estimate ED_{10} for methylene chloride where a physiologic pharmacokinetics model was used to examine differences between high and low dose and between species.

Questions arise as to the inhalation hazard and the pollutant's placement in the ranking when the only available data indicate portal-of-entry and not systemic effects via oral exposure. This question needs further examination; it may be that an oral-related portal-of-entry effect may be qualitatively predictive of an (untested) inhalation portal-of-entry effect.

In addition, the rate of delivery of the compound may have an important influence on the observation of a neoplastic response. Inhalation exposure is expected to be chronic, exposure occurring over a protracted period of time. Much of the data supporting the ranking, however, is from gavage exposure which is episodic. Large peak blood concentrations are expected with gavage administration.

If toxicity depends on the on some critical concentration, this has significant bearing on both the qualitative and quantitative determination of a cancer hazard. For the "non-threshold" HAP, the relationship between exposure pattern and subsequent tumor development is not yet clearly known.

Species differences in the presumed mechanism of action will also introduce errors into a hazard ranking. Recent research shows that the development of kidney tumors through proximal tubule damage resulting from accumulation of $alpha_2$ micro-globulin in hyaline droplets appears specific to the male rat (15). In such a case, there should not be a human cancer concern based only on kidney cancer in male rats generated by this mechanism. Animal experiments on several hazardous air pollutants have demonstrated kidney cancer in male rats by this mechanism. The present ranking system does not consider this observation to be indicative of human cancer hazard. The demonstration of animal cancers as irrelevant for a human cancer concern may exist for other cases besides kidney cancer via an $alpha_2$ micro-globulin mechanism. These are not accounted for in the present ranking system.

How the above uncertainties bear on the hazard ranking is difficult to determine. Some limited information on the impact of using oral data, when systemic toxicity has been observed, to estimate the ED_{10} can be derived from the study of Pepelko (16). This study generally observed differences of less than an order of magnitude between oral and inhalation dose routes associated with either a 1% or 25% additional risk of cancer. This study was based

on 14 agents in rats and 9 agents in mice. Larger discrepancies between the two exposure routes could be partially explained by several factors: dosing at levels above saturation, the outcome of which is an overestimate of the does associated with increased tumor incidence; differences in strains of tested animals; and the longer retention time of solid particulate matter leading to greater dissolution compared to the relatively faster passage of the particle through the gastrointestinal tract. Based on this limited comparison, Pepelko (16) concluded that the carcinogenic potencies are not substantially influenced by dose route, and largely; that errors are unlikely if data are from adequately designed and conducted experiments; if the agent in question is not relatively insoluble particulate matter, and corrections are made for incomplete activation. It can be asserted from these observations that if a hazard is assumed from oral exposure, the absence of inhalation data may not lead to a large misclassification of HAP in the relative ranking.

5.0 DETERMINATION OF A "MORE HAZARDOUS EMISSIONS DECREASE"

One possible approach towards the determination of a "more hazardous emissions decrease" is to allow only a decrease in a "more hazardous pollutant" to satisfy the requirements for a "more hazardous emissions decrease" as an offset. Under this approach, if any pollutant is considered to be "more hazardous" than a "non-threshold pollutant" whose emissions have increased, then decreases

by an equal or greater amount of that "more hazardous" pollutant may be used as an offset. The carcinogenic potencies of two "non-threshold" pollutants are compared and if the differences in potency between them exceeds a half an order of magnitude then one may be considered to be more hazardous than another. If the potency estimates of two "non-threshold" pollutants are within a factor of 3 of each other, then they are considered to be equally hazardous. Pollutants which are equally or less hazardous cannot be used to offset such a pollutant.

The EPA's recommended approach for the section 112(g) offsetting guidance allows for a more hazardous quantity of a pollutant to be also used as an allowable offset. This approach is basically the same as that describing the use of a "more hazardous pollutant" except that not only is an equal or greater quantity of a "more hazardous" pollutant acceptable as an offset, but a fixed percentage of the increased emissions (125 percent) of an "equally hazardous" pollutant may also be used as an acceptable offset. The fixed percentage is a policy-based decision.

6. SUMMARY

Developing a ranking is a difficult task which intermixes risk assessment processes with risk management decisions. The present ranking is developed with application to the needs of section 112(g) in mind. That is, section 112(g) implies maintainance of a theoretical limit on hazard/risk by offsetting a less hazardous

increase in emissions for a decrease of a more hazardous one.

The approach for ranking "non-threshold" pollutants is based on the criteria of weight-of-evidence and the ED_{10}, and a hierarchal scheme for identifying support documentation which EPA scientists considered important. The use of qualitative (weight-of-evidence) and quantitative (ED_{10}) risk descriptors is attractive since they include information regarding the multidimensional nature of carcinogenic potential. Additionally, these risk descriptors are common to the regulated community and to risk assessors and managers both inside and outside the agency.

The present approach for ranking the hazard of "non-threshold" pollutants is dependent on the database at hand. Not all pollutants have been tested equally. The quality of the data vary and our ability to infer dose-response relationships with confidence varies. Additionally, data from oral exposures support the ranking and these data have additional uncertainty associated with them in determining hazards resulting from inhalation exposure. Consequently, it is difficult to verify the accuracy of any ranking, by whatever proposed methodology.

In sum, the present ranking of "non-threshold" pollutants that have evidence of carcinogenicity provides guidance for making general comparisons regarding "more" hazardous; the ranking should be considered comparative in that quantitative differences between pollutant cannot be determined.

C. Methodology for Ranking "Threshold" Hazardous Air Pollutants Under Section 112(g), Clean Air Act Amendments

1. INTRODUCTION

1.1 BACKGROUND

Consistent with EPA's technical support document for the development of Inhalation Reference Concentrations (IRIS), toxic endpoints other than cancer and gene mutation are referred to as "non-cancer toxicity." Most chemicals that produce non-cancer toxicity do not cause a similar degree of toxicity in all organs, but usually affect one or two organs adversely before others show signs of dysfunction. Hence the term "target organ" is used to describe the organ or system which is most sensitive to the effects of the toxicant. Based on the understanding of homeostatic and adaptive mechanisms, non-cancer toxicity is assumed to have a threshold of response both for the individual and the population (17). However there are difficulties in the identification of thresholds of exposure below which there are no observable effects (18). The assumption of a threshold of response distinguishes non-cancer endpoints from carcinogenic and mutagenic endpoints which are generally assumed to have no threshold of response.

For the hazard ranking of 112(g) all the pollutants listed in section 112(b) which are not described as either known, probable, or possible human carcinogens, or which have not been investigated for carcinogenic effects are considered for purposes of 112(g) to

have a "safety threshold for exposure" (see section B above). Many of the same issues described for the ranking of "non-threshold" HAP in part B are applicable to the "threshold" pollutants. These issues include discussions of uncertainty and appropriate application of ranking methodologies. "Threshold" pollutants are listed in Table II, III, and IV.

1.2 Methodology

One approach EPA considered in its ranking of "non-threshold" pollutants is to use Inhalation Reference Concentrations (RfC) as the measurement of potential hazard. The RfC is an approach which is based on the assumption that if the dose to the animal is below the critical toxic effect to the target organ, then all toxic effects are avoided (17). Therefore a health effects benchmark (RfC) can be developed by applying uncertainty factors to the critical toxic effect derived from the no adverse effect level of a pollutant. The RfC is 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 appreciable risk of deleterious effect during a lifetime (chronic exposure).

If RfCs were available for more "threshold" pollutants listed under section 112(b), it may be an appropriate determinant of relative hazard between such pollutants. However, as of the time of the proposed rule for section 112(g), RfCs were available for only a small number of the "threshold" pollutants to be ranked. Another disadvantage to using RfCs for relative ranking hazard is

that the method is limited in its consideration of severity of effect. Conceivably two pollutants with similar RfCs may cause effects which vary greatly in severity. Although there is an application of severity in the RfC methodology, it is more operational and less rote (no numerical application is made in the RfC process as is made in the Reportable Quantities process). The toxicologist makes a decision of severity when (s)he decides to use a lowest observable adverse effect level (LOAEL) or no observed adverse effect level (NOAEL) from a given study in order to develop an RfC. The EPA believes that severity of effect should be considered in the determination of hazard. The RfC was developed to serve as a health safety benchmark to set maximal concentration of a HAP in air that would pose no appreciable risk to those exposed. A similar concern for the application of uncertainty factors to the RfC exists for the assignment of weighting factors to carcinogen hazard estimates as discussed by Frolich and Hess (11) in section B. Therefore the application of such uncertainty factors in the development of RfCs may distort the relative hazard of HAPs when a comparison between HAPs is done. As preciously discussed in section B, a relative ranking system must be consistent with the primary goal for which it was developed. The RfCs were not designed for relative ranking but developed for purposes of dose-response assessments.

An alternative to using RfCs is basing the determination of hazard on Oral Reference Doses (RfDs). The RfD is similar to the RfC except that it is an estimate for oral exposures. An RfD may

not be an appropriate tool to determine the hazard of chemicals under a program for which inhalation exposures are the primary concern. Oral studies are limited as indicators of non-cancer inhalation toxicity because of factors such as portal of entry effects and (appropriate in the case of metals, irritants, and sensitizers) liver first-pass effects. Additionally, RfDs have the same limitations as RfC's in regard to severity of effect considerations and use of uncertainty factors.

The approach recommended by the EPA, for the ranking of hazardous air pollutants with "thresholds" under section 112(g), is a determination of hazard based on inhalation chronic toxicity data. The hazard potential of each pollutant for chronic toxicity is determined on the basis of its Composite Score. The Composite Score was originally developed by the EPA for the determination of relative hazard to human health of chronically toxic pollutants in the Reportable Quantities methodology under CERCLA or "Superfund." Therefore it's development as a tool for ranking relative hazard is applicable to the purposes of the section 112(g) hazard ranking.

The Composite Score reflects two primary attributes of each pollutant:

1. The minimum effective dose levels (MED) which are extrapolated for human exposure and which result in adverse effects from chronic exposures.
2. The severity of effect (e.g. mortality, rated as the most severe effect and given the highest score) resulting from the MED in animal or human studies.

For the derivation of a Composite Score, there is an inverse relationship between dose required to elicit an effect and the dose rating assigned to it. In effect, the 1/MED is a potency estimate. Procedurally, the dose of the pollutant given in animal studies is transformed to an equivalent human dose (MED) and then assigned a dose rating ranging from 1 to 10. The rating values for dose exhibit a quantitative logarithmic relationship to each other. Thus, those pollutants having an adverse effect at a relatively low dose receive a high rating for dose (RVd) (see Table V).

Similarly, a rating value is also assigned to the effect produced from exposure to the pollutant. Effects resulting from such doses are rated on a scale from 1 to 10 (see Table V). The severity rating value is a weight reflecting the severity of effect associated with the MED. These effects can range from subtle effects at a cellular level to mortality. Consequently, the rating values for effect are based on subjective categories of adverse effect and are therefore a qualitative measure. The more severe the effect the higher the effect rating or RVe. (Mortality receives the highest score of 10).

The function of the effect rating (RVe) is to convert a multitude of non-carcinogenic effects into a standardized measure which can be done for all observed non-carcinogenic effects. The RVe is not necessarily target organ specific. For example, the severity of effect rating system does not attempt to rate kidney effects as being more or less severe than those of the liver, but rates an effect (e.g., hyperplasia) regardless of where the effect

occurs. However a few specific target organs are named in the general guidance (reference 10 and Table II) for severe effects (nervous, reproductive, and developmental).

The qualitative nature of the severity rating system is easily demonstrated by the following example: an effect of death (RVe = 10) divided by 2 does not equal reversible cellular changes (RVe = 5). The derivation of the Composite Score which includes dose and severity of effect ratings for representative studies of each pollutant are given in Appendix B.

SECTION 2. INFORMATION SOURCES

2.1 Hierarchy of Data Source Selection:

The age of the RQ determinations was considered in acquisition of composite score summary tables. The hierarchy of data sources was as follows:

1. If available, data from recent (i.e., 1987 to 1991) RQ (Reportable Quantity) documents were used as first preference.
2. For substances with RQ documents dated prior to 1987, data were sought from EPA documents such as HEEDs (Health and Environmental Effects Document) and HEEPs (Health and Environmental Effects Profile)(11) - in that order, which were more recent than the RQ documents.
3. Finally, for substances with RQ documents dated prior to 1987, but for which no later HEEDs or HEEPs were

available, data from the older RQ documents were used.

4. When no composite scores were available for a "threshold" pollutant but an RfC had been developed or data collected for RfC development, a composite score was developed from the RfC data base. Pollutants with composite scores from less current literature sources also had Composite Scores developed from the RfC data base for consideration of the selection of the most appropriate Composite Score.

The most recent available RQ documents were obtained from various sources. In some cases older RQ documents were used as data sources because of the unavailability of more recent HEEPs or HEEDs. An attempt was made to update data from older Reportable Quantities documents so as to find newer and more appropriate studies. Studies which were rejected as not being adequate for determination of the reportable quantity in Reportable Quantities documents, HEEDs, or HEEPs were also rejected for use for the hazard ranking of section 112(g). Sources of the RQ values are noted in Appendix B.

2.2 Selection of Composite Score

There is more than one study available from which to assign a Composite Score for most of the hazardous pollutants listed in section 112(b) of the Clean Air Act. To select the highest Composite Score for each pollutant, as a policy decision, would not necessarily be health protective for the purposes of offsetting. The Composite Score assigned to each pollutant should most adequately reflect the hazard to human health from airborne

pollutants so as to minimize distortion of the hazard comparison between HAP.

Therefore, a protocol was developed to choose the most appropriate Composite Score for each of the hazardous air pollutants. Information on dose, duration and route of exposure, species, and effects of exposure was extracted from the studies for each pollutant in the Reportable Quantity documents and sources stated above. From this information the most appropriate composite score was chosen for each pollutant. Appendix B contains such information as well as the rationale for the composite score selection of each "threshold" pollutant. The selection criteria for assigning the most appropriate Composite Score for each pollutant is as follows:

1. If inhalation data existed, it was preferred over oral data.
2. Composite Scores derived from human data were preferred over that from other species. If human data were unavailable, primate data were preferred. If the Composite Scores were only available from rodent data (rat, guinea pig, and mouse), rat studies were generally preferred.
3. Studies were preferred in which a dose-response relationship was demonstrated within the study or between other available studies.

4. Composite Scores were preferred from studies with general agreement as to the nature of the toxicity, i.e., the target of toxicity was consistent with that of other studies.
5. Consideration was given to choose a Composite Score that reflected a consistent response between species and was consistent with other values reported for the pollutant.
6. Composite Scores derived from studies using very large doses, that resulted in severe effects (e.g., such as mortality), were not used if other studies were available which used lower doses and produced less severe effects. When such studies involving severe effects at large doses were the only ones available, then the resulting composite scores were identified accordingly.
7. The age of the data was considered in choosing the Composite Score. If there was more than one appropriate study, preference was given to the newest one.
8. The duration of the study was considered in choosing the Composite Score. Chronic studies were given preference over those which were sub-chronic.

2.3 Verification and Calculation of the Composite Score:

When Composite Scores were not available for some "threshold" pollutants but RfCs had been derived or information had been collected to support the development of RfCs, such studies were used to develop a Composite Score. In addition, RfC data were used to develop Composite Scores to provide support for or replace

existing Composite Scores for a few chemicals (e.g., when the existing Composite Score is based on an older study). Because the RfC validation is so complete with considerable attention paid to quality assurance and control, the EPA used this data source as the basis for Composite Score development. When a verified RfC existed, an attempt was made to take advantage of the extra rigor of the RfC review process and make the data source for Composite Score development consistent with that for the RfC. A step-by-step methodology described in Appendix B was used both to verify that the chosen Composite Score for each "threshold" pollutant was calculated consistently and to derive a Composite Score, based on information collected to support an RfC determination, for pollutants with no available Composite Score.

The methodology used in Appendix B is based on the general outlines given in the CERCLA technical background document as to methodology and guidelines for ranking chemicals based on chronic toxicity (18) and the Guidelines for Criteria Derivation; Water quality and the general quantitative risk assessment guidelines for non-cancer effects (20). This method produced composite scores that were identical to those listed in the RQ source documents for all but a few pollutants. Such differences in composite score were relatively minor and described in detail in Appendix B. Calculated Composite Scores were added as potential studies considered for

selection as most appropriate Composite Score for each pollutant and are described in Appendix B. A similar methodology was used when data used to support an RfC determination was used to construct a composite score.

In general, a study of less than or equal to 90 days duration was considered to be sub-chronic. However when a description of study duration (chronic vs. sub-chronic) was given in RQ documents or by the author'(s) of the primary publication, this description was used to determine the appropriate application of a correction factor for study duration.

The assumptions regarding species weights and inhalation rates for calculating MEDs are given in Table 2. For such MEDs, 100 percent absorption was assumed in the absence of specific information. Most of the MEDs reviewed from the Reportable Quantities documents had been based on 100 percent absorption even for systemic effects due to inhalation exposure. Therefore in order to maintain consistency, 100 percent absorption was assumed in deriving chronic human MEDs from data used to develop RfCs.

However for human occupational exposures, an absorption fraction of 0.5 (50 percent absorption) was used to derive the chronic human MEDs. Again, this was done to maintain consistency. A review of available composite scores revealed that MEDs based on human occupational exposure data had been calculated assuming 50 percent absorption.

3. METHODOLOGY

3.1 Introduction

The composite score assigned to rank each pollutant for chronic toxicity is the mathematical product of the RVd and RVe and therefore takes into account both dose and severity of effect information. The range of composite scores is 1 to 100. Using this method, pollutants which elicit severe effects at relatively low doses are assigned a high composite score and those which produce relatively minor effects at high doses are given a low composite score. The EPA does not consider the Composite Score assigned each pollutants to represent an absolute value but to be used to give an indication of the relative hazard between HAPs. However, the Composite Score is useful and appropriate as a relative ranking tool for the section 112(g) hazard ranking.

3.2 Determination of a "More Hazardous" Finding.

The relative hazard of "threshold" pollutants is determined primarily by qualitative information (Composite Score). Although based on observed toxicity data, the Composite Score system for relatively ranking chronic toxicity is not considered to be a health risk assessment (19). This ranking system has undergone a limited peer review and a public review and is currently in use by the EPA and the regulated community.

The EPA is making a policy decision for how one "threshold" pollutant is to be considered "more hazardous" than another. Similar to the range of equivalence" created for the "non-threshold" pollutants, a range of 4 Composite Score units is used to account for the uncertainty of the hazard estimate and to take

into account such factors as the intra-species variability, sensitivity of sub-populations, and relevance of extrapolating animal effects to humans. Therefore under EPA's approach, one chronically toxic pollutant is considered to be more hazardous than another when its Composite Score exceeds the other by at least 4 Composite Score units. Equally hazardous pollutants would be pollutants whose Composite Scores do not vary from each other by more than 3 Composite Score units.

The risk management factor for the "range of equivalence" for "threshold" pollutants is not directly a function of the average differences (variance) in Composite Scores, but is a function of judgement. A precise mathematical evaluation of the average differences in Composite Scores may not be applicable to the determination of the uncertainty factor for several reasons. The mean Composite Score was not used as the basis for Composite Score assignment for each pollutant. The study which best represented the toxicity of each pollutant was selected using the criteria described in section C(2.2). All available studies are not equally suitable to have a Composite Score derived and all composite scores were not equally representative of the toxicity of each pollutant. For example, Composite Scores from studies using large doses to elicit severe endpoints of effect were not as appropriate for use in the hazard ranking as those which used lower doses and elicited milder effects. Duration of study is an integral part of study selections and cannot be taken into account by merely using a mean Composite Score to represent the hazard to human health by chronic

toxicity. Thus although more than one composite score may be assigned to a pollutant through number of studies, Composite Scores were not considered to be of equal relevance.

The details of the procedure used to determine the Composite Score for chronically toxic pollutants appears in the technical background document used to support rulemaking pursuant to CERCLA section 102 (19). The conversion of a human MED to an RVd is given in Figure 1 of that document (18) and also below. The derivation of the severity of effect rating is reproduced in Table V as stated in the CERCLA technical support document (19). Appendix B of this document contains information on the representative study used to assign Composite Score for each pollutant and the rationale for its selection.

3.3 Determination of a "More Hazardous Emissions Decrease"

Consistent with the " more hazardous pollutant" approach used for determining "a more hazardous emissions decrease" for "non-threshold" pollutants, an equal or greater amount of a "more hazardous" "threshold" pollutant may be used as an acceptable offset for increased emissions of a "less hazardous" "threshold" pollutant. "Less hazardous" "threshold" pollutants cannot be used as offsets for other "threshold" pollutants.

EPA's proposed approach to determine "more hazardous emissions decrease" is basically the same as for "threshold" and "non-threshold" pollutant. After a "more" or "equally hazardous"

pollutant is identified, an equal or greater quantity of a "more hazardous pollutant" or 125% of the emissions increase of an "equally hazardous" pollutant may be used as an acceptable offset.

D. Identification and Ranking of "High-Concern" Pollutants

1. INTRODUCTION

1.1 Background

The EPA also recognizes that some "threshold" pollutants may not necessarily be less of a hazard to human health than some "non-threshold" pollutants. At present the relative hazard between pollutants that elicit severe non-carcinogenic effects from a short term (acute) or continuous (chronic) exposure and "non-threshold" pollutants cannot be determined. The creation of a "high-concern" category is attempt to address overlap in hazard between the "threshold" and "non-threshold" categories of pollutants.

1.2 Methodology

The EPA proposes to create a third category for the hazard ranking which contains pollutants of "high-concern" for non-carcinogenic effects. The identification and categorization of pollutants with such diverse endpoints into a single grouping has several advantages. The hazard ranking already separates the pollutants into two distinct categories ("non-threshold" and "threshold") in accordance with requirements of the Act. However, A situation may exist where the relative hazard between specific

"threshold" and "non-threshold" pollutants cannot be made. Such a situation exists for pollutants which are of concern from short-term or long-term exposures. Pollutants whose toxicity from long-term or short-term exposure may outweigh the concern for carcinogenicity are placed in this category and are listed in Table III.

2.0 INFORMATION SOURCES

The Composite Score for the "high-concern" pollutants are derived by the same methodology and come from the same data sources as do the other "threshold" pollutants. The pollutants in the "high-concern" category which are identified by a Level of Concern for toxicity from short-term exposure taken from the technical support document for section 302 of CERCLA (21). Updated values were provided by Office of Solid Waste and Emergency Response/U.S. EPA.

3.0 METHODOLOGY

3.1 Selection of Pollutants for Assignment to the "High-Concern Category:

The selection criteria that the EPA proposes to use to assign chronically toxic pollutants to the "high-concern" category is based on the categorization and assignment of Reportable Quantities under CERCLA. Chronically toxic pollutants with a composite score

of 21 or above are considered to be especially hazardous by CERCLA and are accordingly assigned reportable quantities of 100 pounds or less (19). The 100 lb. Reportable Quantity also corresponds to the assignment of a Reportable Quantity to the lowest potency carcinogens under CERCLA. For purposes of the hazard ranking of section 112(g), a policy judgement based on the Reportable Quantities methodology is made so that a Composite Score of 21 or above also places a threshold pollutant into the "high-concern" pollutant category.

Pollutants of concern from short-term exposure are also placed in the "high-concern" category for the hazard ranking. In the technical background document used to support CERCLA (21), an analysis is provided comparing toxicity data from short-term exposure (LD50's) and maximum composite scores. For a varied series of chemicals, it was concluded that chronic toxicity cannot necessarily be predicted from that from short-term exposures. Therefore, support is given to the well established principle in the field of toxicology that expressions of chronic toxicity is not a redundant feature of arising from short-term exposures.

The selection criteria that the EPA proposes to use to assign pollutants of concern from short-term exposure to the "high-concern" category is an approach used in CERCLA section 302 to identify "Levels of Concern" or LOCs for such pollutants. LOCs are levels of airborne concentrations of chemicals below which no serious irreversible health effect or death may occur following a single short term exposure (30 minutes).

By definition, the LOC is intended to protect general and sensitive members of a population from toxicity from short-term exposure. LOCs are defined as 1/10 "Immediately Dangerous to Life and Health" levels (IDLHs) produced by National Institute for Occupational Safety and Health (NIOSH). The a factor of 10 was used to derive LOCs from IDLHs: (1) to insure protection of the general population, including sensitive individuals; (2) to protect against health effects from acute exposure which occur for more than 30 minutes; and (3) to protect against serious and irreversible health effects. IDLHs are approximately one to two orders of magnitude below the median lethal concentration (LD50). They are designed to protect workers from serious and irreversible health effects and are based on a 30-minute exposure. When no IDLH exists, animal toxicity data consisting of LC50 (lethal concentration for 50 percent of the experimental animals) or LD50 (lethal dose for 50 percent of the experimental animals) data from the NIOSH Registry of Toxic Effects of Chemical Substances were used to derive LOC values. The LC50 data were preferred when available. Estimated IDLH values derived from such data are equivalent to 1/10 or the LC50 of 1/100 of the LD50. The resulting LOC is equal to 1/10 of the IDLH.

For chemicals with no LD50 of LC50 data available, LDLO or LCLO (lowest lethal dose or concentration) were used to derive LOCs. When available, LCLOs were preferred over LDLOs to derive

and LOC. Estimated IDLHs are equal to LCLOs or 1/10 the LDLO. As stated above, the resulting estimate of the IDLH is divided by 10 to derive an LOC.

There are several advantages of using LOC values as selection criteria to identify pollutants of concern for short-term toxicity:

1. They are the only available values used by the EPA which are designed to protect from serious effects of short term or acute exposures.

2. They are intended to protect the general population including sensitive individuals.

3. LOC values exist for many pollutants of concern for acute toxicity on the 112(b) list.

4. LOC values apply to airborne pollutants.

5. LOCs have already been used by the EPA in conjunction to section 302 of CERCLA.

There are disadvantages for using the LOCs to set health protective exposure levels. The same rationale precludes the use of LOCs to determine the relative hazard between such pollutants. First, most of the LOC values are based upon animal LC50, LD50, LCLO, and LDLO data which may not protect against all health effects in humans. Second, the factor of 10 which is applied to IDLHs to protect sensitive individuals of the population and for protection against serious health effects may not be adequate. There are questions concerning the level of scientific peer review of the rationale for each LOC and supporting data. It is not known what the maximum duration of exposure at the LOC would be for

protection against adverse effects. Finally, the dependence of LOC's on multiple uncertainty factors limits its use in establishing relative hazard between HAPs.

However, by using LOCs as a screening tool to identify pollutants with respect to severe toxicity from short-term exposure, some of these problems may be avoided. The EPA proposes to use LOCs in the hazard ranking to identify acutely toxic pollutants (e.g. phosgene) that would not be rankable by the criteria of carcinogenicity or chronic toxicity.

Under section 112(g), pollutants with an LOC of less than 0.008 g/m^3 are included in the "high-concern" pollutant category. The selection of this level is a policy-based decision supported by an analysis of all LOCs (46 total) that are available for the CAS numbered pollutants listed in section 112(b). These levels are taken directly from the technical support document for section 302 of CERCLA (21). One-third of these LOCs are below the 0.008 g/m^3 level and are consequently considered to be the most toxic.

Under this scheme, 24 HAPs with only non-carcinogenic effects and 14 HAPs with carcinogenic effects are categorized as "high-concern" pollutants due to severe acute toxicity (see Table III). Of those pollutants identified as "high-concern" for severe toxicity from short-term exposure, more than half are members of chemical groups listed under section 112(b). Many of the carcinogens selected for toxicity from short-term exposure do not have carcinogenic potency estimates so that under the offsetting guidance of 112(g), whether they are categorized as "high-concern"

pollutants or as "non-threshold" pollutants with no potency estimate, similar offsetting restrictions would apply in each case.

3.2 Determination of a "More Hazardous" finding:

The relative hazard or determination of a "more hazardous emissions decrease" between two "high-concern" pollutants can be determined by the same criteria as the "threshold" pollutants if a Composite Score is available for both and neither is considered to be "non-threshold". The supporting data for listing "high-concern" pollutants based on chronic toxicity is listed in Appendix B.

The EPA believes that using Levels of Concern is a reasonable first step to identify pollutants for which toxicity from short-term exposure is a high concern. However the EPA believes that these values are inadequate for use in relatively ranking the hazard between such pollutants. The LOC values indicate the potential of a pollutant to cause lethality at a given dose and does not indicate other serious effects from short-term exposure such as neurological, developmental, or reproductive effects. What is needed for such a ranking may be a short-term RfC or dose response information. Currently the EPA has developed only one such benchmark for developmental toxicity from short-term exposure of ethylene oxide.

3.3 Determination of a "More Hazardous Emissions Decrease"

Pollutants of concern for chronic or long term exposure which appear in the "high-concern" category can be used to offset each

other if a Composite Score is given and they do not violate the offsetting criteria given for the "threshold" pollutants in Table II.

Because the relative hazard between pollutants of concern for short-term toxicity is not established in the hazard ranking, the EPA is proposing, for the purposes of this rule, the following offsetting limitations: pollutants of concern for short-term exposure cannot offset or be used as offsets for each other; such HAP which are also "non-threshold" pollutants are to have offsetting restrictions due to toxicity from short-term exposure and not allowed as offsets or to be offset by other "non-threshold" pollutants. "Non-threshold" pollutants which are also of concern for short-term exposure are identified among the "high-concern" pollutants listed in Table III as well as Appendix E.

E: Ranking of Pollutants with Insufficient Data

If a pollutant has not been assigned a Composite Score, is not categorized as a "high-concern" pollutant, or does not meet the criteria for a "non-threshold" pollutant given above, then the relative hazard of this pollutant and others listed in section 112(b) cannot be determined. The EPA considers this pollutant not "practicable" to rank at this time. "Unrankable" pollutants are listed in Table VI. Pollutant categories may also be considered not "practicable" to rank; for example asbestos, mineral fibers,

and radionuclides may require a risk assessment beyond the scope of the hazard ranking of 112(g) and therefore are considered "unrankable" (see Appendix C).

F. Treatment of Chemical Groups

There are 17 hazardous air pollutants listed in section 112(b) which are chemical groupings and have no CAS number assigned to them (e.g. chromium and compounds). Individual pollutants within these chemical groups having similar toxicological profiles will be ranked similarly. However, unless there is evidence of similarity, pollutants will be ranked on an individual basis. Of the pollutants belonging to the listed chemical groupings, only those which have met the data requirements for consideration as either a "non-threshold", "threshold", or "high-concern" pollutant are ranked. Pollutants from the listed chemical groups which the EPA currently considers having sufficient data to rank are presented in Tables I, II, and III. Any pollutant or class of pollutant (e.g mineral fibers), from the listed chemical groups, that is categorized as being "not practicable" to rank is listed in Table IV.

G. Relative Ranking of the Four Categories of Pollutants

While the language in section 112(g) specifically prohibits increases in emissions of "non-threshold" pollutants to be offset

by decreases from "threshold" pollutants, the converse is not true. Therefore, the relative hazard of both types of pollutants to each other must also be determined. The EPA recognizes the difficulty in comparing different types of effect (cancer and chronic non-cancer endpoints) and assigning their relative hazard. For purposes of offsetting the pollutants listed in section 112(b) of the Clean Air Act Amendments, a policy choice is made by the EPA that "non-threshold" pollutants listed in Table 1 are considered to be more hazardous than "threshold" pollutants listed in Table 2. As stated in section B, historically the EPA has treated potential carcinogenicity with more caution than chronic toxicity (9). The severity of effect (mortality), lack of a demonstrable threshold, cumulative nature of the risk, and latency of effect provide the rationale for such a position.

In EPA's proposed approach for determining a "more hazardous emissions reduction" for setting acceptable offsets, there are no allowable offsets between "high-concern" pollutants and "non-threshold" pollutants. The EPA considers it impracticable to determine the relative hazard between these two categories of HAP which results in a prohibitions of offsets between members of the two categories. However, for the purposes of the hazard ranking "high-concern" pollutants are considered to be more hazardous than the "threshold" pollutants listed in Table II. The relative hazard between "unrankable" pollutants and all of the other

pollutant categories in the ranking cannot be determined. Consequently "unrankable" pollutants can neither be offset or used as offsets for any HAPs.

H. Changes to the ranking

The hazard ranking guidance is subject to revision as either new data for the pollutants becomes available, pollutants are added or deleted from the list in section 112(b), or the EPA's current guidelines or methods for assessing the hazard potential of a particular type of pollutant are updated. New data concerning one of the listed pollutants would have to be reviewed by the EPA and determined to be of sufficient quality and applicability to the methods used in the ranking to merit a change in the status of that pollutant in the hazard ranking. Pollutants which have been deleted from the section 112(b) list of hazardous pollutants through the provisions of section 112(b)(2) will simultaneously be deleted from the hazard ranking. Pollutants which are added to the section 112(b) list of hazardous air pollutants will be ranked "if practicable" by the current ranking methodology.

If the EPA's guidance or methods for assessing the hazard of certain pollutants are modified, those modifications will be appropriately reflected in the ranking. For example, if the EPA's guidelines for cancer risk assessment were modified such that the weight of evidence scheme for carcinogens changed, then the ranking would be adjusted accordingly.

The ranking will be reviewed periodically after promulgation of the section 112(g) rulemaking for changes in the data supporting the ranking. The methodology and guidance used to construct the ranking may be revised as the need is determined by the EPA. Any person may submit data to support a changes in the ranking status of a particular pollutant prior to review of the ranking data. Within 12 months after receiving such a request and accompanying data, the EPA will review the data and make a determination as to whether to change the ranking at the next scheduled review period.

SECTION II: TABLES, FIGURES, REFERENCES, AND APPENDIXES.

TABLE I: "NONTHRESHOLD" POLLUTANTS

CAS #	Chemical Name	WOE CLASSIF	1/ED10 [per(mg/kg)/d]
92671	4-Aminobiphenyl	1, IARC	**
96093	Styrene oxide	2A, IARC	**
64675	Diethyl sulfate	2A, IARC	**
59892	N-Nitrosomorpholine	2B, IARC	**
68122	Dimethyl formamide	2B, IARC	**
680319	Hexamethylphosphoramide	2B, IARC	**
60355	Acetamide	2B, IARC	**
101779	4,4'-Methylenedianiline	2B, IARC	**
90040	o-Anisidine	2B, IARC	**
1746016	2,3,7,8-Tetrachlorodibenzo-p-dioxin	B	660000
-	Beryllium salts	B	18000
92875	Benzidine	A	2200
684935	N-Nitroso-N-methylurea	B	2100
542881	Bis(chloromethyl)ether	A	1400
79447	Dimethyl carbamoyl chloride	B	500
-	Chromium compounds (hexavalent)	A	390
75558	1,2-Propylenimine (2-Methyl aziridine)	B	150
99999904	Arsenic and inorganic arsenic compounds ***	A	140
302012	Hydrazine	B	110
57147	1,1-Dimethyl hydrazine	B	83
7440417	Beryllium compounds ****	B	80
96128	1,2-Dibromo-3-chloropropane	B	80
62759	N-Nitrosodimethylamine	B	61
-	Cadmium compounds	B	58
50328	Benzo (a) pyrene	B	54
1336363	Polychlorinated biphenyls (Aroclors)	B	50
76448	Heptachlor	B	42
119937	3,3'-Dimethyl benzidine	B	27
12035722	Nickel subsulfide	A	16
79061	Acrylamide	B	16
118741	Hexachlorobenzene	B	13
57749	Chlordane	B	11
1120714	1,3-Propane sultone	B	10
106990	1,3-Butadiene	B	8.4
-	Nickel refinery dust	A	8
53963	2-Acetylaminofluorine	B	7.7
91941	3,3'-Dichlorobenzidine	B	7.5
58899	Lindane (hexachlorcyclohexane, gamma)	B/C	7.4
95807	2,4-Toluene diamine	B	6.5
111444	Dichloroethyl ether (Bis(2-chloroethyl)ether)	B	6.4
122667	1,2 - Diphenylhydrazine	B	4.3
8001352	Toxaphene (chlorinated camphene)	B	4.3

TABLE I: "NONTHRESHOLD" POLLUTANTS

121142	2,4-Dinitrotoluene	B	3.8
119904	3,3'-Dimethoxybenzidine	B	3.1
50000	Formaldehyde	B	3
101144	4,4'-Methylene bis(2-chloroaniline)	B	2.4
107131	Acrylonitrile	B	2.3
106934	Ethylene dibromide(1,2-Dibromoethane)	B	2.1
72559	DDE (1,1-p-chlorophenyl 1-2 dichloroethylene)	B	1.9
510156	Chlorobenzilate	B	1.8
62737	Dichlorvos	B	1.7
75014	Vinyl chloride	A	1.6
99999908	Coke Oven Emissions	A	1.5
75218	Ethylene oxide	B	1.3
96457	Ethylene thiourea	B	0.98
593602	Vinyl bromide (bromoethene)	B	0.93
7488564	Selenium sulfide (mono and di)	B	0.93
67663	Chloroform	B	0.76
87865	Pentachlorophenol	B	0.67
51796	Ethyl carbamate (Urethane)	B	0.64
107062	Ethylene dichloride (1,2-Dichloroethane)	B	0.39
78875	Propylene dichloride (1,2-Dichloropropane)	B	0.36
56235	Carbon tetrachloride	B	0.34
71432	Benzene	A	0.27
140885	Ethyl acrylate	B	0.22
75569	Propylene oxide	B	0.16
62533	Aniline	B	0.13
106467	1,4-Dichlorobenzene(p)	B	0.13
95534	o-Toluidine	B	0.093
88062	2,4,6-Trichlorophenol	B	0.09
117817	Bis(2-ethylhexyl)phthalate (DEHP)	B	0.086
114261	Propoxur	B	0.053
79016	Trichloroethylene	B/C	0.035
123911	1,4-Dioxane (1,4-Diethyleneoxide)	B	0.034
75070	Acetaldehyde	B	0.033
75252	Bromoform	B	0.029
133062	Captan	B	0.026
106898	Epichlorohydrin	B	0.021
75092	Methylene chloride (Dichloromethane)	B	0.013
127184	Tetrachloroethylene (Perchloroethylene)	B/C	0.012
53703	Dibenz (ah) anthracene	B	-
218019	Chrysene	B	-
60117	Dimethyl aminoazobenzene	B	-
56553	Benzo (a) anthracene	B	-
205992	Benzo (b) fluoranthene	B	-
1309644	Antimony trioxide	B	-
79469	2-Nitropropane	B	-
542756	1,3-Dichloropropene	B	-
57976	7, 12-Dimethylbenz(a)anthracene	B	-

TABLE I: "NONTHRESHOLD" POLLUTANTS

193395	Indeno(1,2,3-cd)pyrene	B	-
189559	1,2:7,8-Dibenzopyrene	B	-
79345	1,1,2,2-Tetrachloroethane	C	1.7
91225	Quinoline	C	1.4
75354	Vinylidene chloride (1,1-Dichloroethylene)	C	1.2
87683	Hexachlorobutadiene	C	0.36
82688	Pentachloronitrobenzene (Quintobenzene)	C	0.25
78591	Isophorone	C	0.016
79005	1,1,2-Trichloroethane	C	0.21
74873	Methyl chloride (Chloromethane)	C	0.052
67721	Hexachloroethane	C	0.051
1582098	Trifluralin	C	0.037
-	Nickel compounds *****	@	-
1319773	Cresols/Cresylic acid (isomers and mixture)	C	-
108394	m-Cresol	C	-
75343	Ethylidene dichloride (1,1-Dichloroethane)	C	-
95487	o-Cresol	C	-
106445	p-Cresol	C	-
74884	Methyl iodide (Iodomethane)	C	-
100425	Styrene	@	-
107051	Allyl chloride	C	-
334883	Diazomethane	*	-
95954	2,4,5 - Trichlorophenol	*	-
133904	Chloramben	*	-
106887	1,2 - Epoxybutane	*	-
108054	Vinyl acetate	*	-
126998	Chloroprene	*	-
123319	Hydroquinone	*	-
92933	4-Nitrobiphenyl	*	-

1, 2A, or 2B IARC = IARC classification for carcinogenicity (sufficient human or animal evidence exists to be placed in the "non-threshold" category)
* = Currently an EPA weight of evidence classification is under review
** = An EPA weight of evidence classification and possible ED10 are under development
*** = except arsenic pentoxide, arsenous oxide, and arsine
**** = except beryllium salts
***** = except subsulfide, carbonyl, and refinery dust

A = Known human carcinogen
B = Probable human carcinogen
C = Possible human carcinogen
@= For the purposes of section 112(g) this pollutant or pollutant class is treated as if it were assigned an EPA weight-of-evidence of Group C (see data report forms of appendix A for comments on individual pollutants. There is not currently an official EPA weight-of-evidence classification for these pollutants.

TABLE II: "THRESHOLD" POLLUTANTS

CAS #	Chemical Name	Composite Score
75058	Acetonitrile	20
94757	2,4-D, salts and esters	18
156627	Calcium cyanamide	16
110805	2-Ethoxy ethanol	15
121448	Triethylamine	14
110543	Hexane	13
91203	Naphthalene	11
7647010	Hydrochloric acid	11
98828	Cumene	11
111762	Ethylene glycol monobutyl ether	11
79107	Acrylic acid	10
107211	Ethylene glycol	10
63252	Carbaryl	10
92524	Biphenyl	10
78933	Methyl ethyl ketone (2-Butanone)	10
84742	Dibutylphthalate	9
105602	Caprolactam	9
100414	Ethyl benzene	9
106423	p-Xylenes	8
95476	o-Xylenes	8
1330207	Xylenes (isomers and mixture)	8
72435	Methoxychlor	8
108383	m-Xylenes	8
67561	Methanol	7
131113	Dimethyl phthalate	7
108883	Toluene	7
1634044	Methyl tert-butyl ether	6
80626	Methyl methacrylate	5
108101	Methyl isobutyl ketone	4
120821	1,2,4-Trichlorobenzene	4
75003	Ethyl chloride	4
106503	p-Phenylenediamine	4
108907	Chlorobenzene	3
71556	Methyl chloroform (1,1,1-Trichloroethane)	2

TABLE III: "HIGH-CONCERN" POLLUTANTS

CAS #	Chemical Name	Composite score
-	Lead and lead compounds	C*
56382	Parathion	A*
13463393	Nickel Carbonyl	A*
60344	Methyl hydrazine	A*
75218	Ethylene oxide	A*
151564	Ethylene imine	A*
77781	Dimethyl sulfate	A*
107302	Chloromethyl methyl ether	A*
57578	beta-Propiolactone	A*
100447	Benzyl chloride	A*
98077	Benzotrichloride	A*
107028	Acrolein	A*
584849	2,4 - Toluene diisocyanate	A*
7784421	Arsine	A
7550450	Titanium tetrachloride	A
75741	Tetramethyl lead	A
78002	Tetraethyl lead	A
10102188	Sodium selenite	A
13410010	Sodium selenate	A
143339	Sodium Cyanide	A
151508	Potassium cyanide	A
7723140	Phosphorous	A
75445	Phosgene	A
12108133	Methylcyclopentadienyl manganese	A
624839	Methyl isocyanate	A
7783075	Hydrogen selenide	A
7664393	Hydrogen fluoride	A
77474	Hexachlorocyclopentadiene	A
62207765	Fluomine	A
10210681	Cobalt carbonyl	A
10025737	Chromic chloride	A
79118	Chloroacetic acid	A
7782505	Chlorine	A
1306190	Cadmium oxide	A
1327533	Arsenous oxide	A
1303282	Arsenic pentoxide	A
7783702	Antimony pentafluoride	A
534521	4,6-Dinitro-o-cresol, and salts	A
101688	Methylene diphenyl diisocyanate	46
7440484	Cobalt (and compounds)	46
1345046	Antimony trisulfide	46
108952	Phenol	44
[illegible]	Selenium and compounds [illegible]	42

TABLE III: "HIGH-CONCERN" POLLUTANTS

10045940	Mercuric nitrate	42
7439965	Manganese and compounds ***	41
748794	Mercuric chloride	40
28300745	Antimony potassium tartrate	38
62384	Mercury, (acetato-o) phenyl	37
98862	Acetophenone	37
108316	Maleic anhydride	35
532274	2-Chloroacetophenone	32
51285	2,4-Dinitrophenol	30
108864	2 Methoxy ethanol	24
98953	Nitrobenzene	23
74839	Methyl bromide (Bromomethane)	23
75150	Carbon disulfide	23
121697	N,N-Dimethylaniline	21

A = On the list because of severe acute toxicity
* = Also elicits carcinogenic effects
** = except hydrogen selenide, selenium sulfide, selenium disulfide, sodium selenate, and sodium selenite
*** = Except methylcyclopentadienyl manganese
C = Of concern for chronic noncarcinogenic effects which have been demonstrated at current exposure levels

TABLE IV: "UNRANKABLE" POLLUTANTS

CAS #	Chemical Name	IARC
106514	Quinone	III
123386	Propionaldehyde	
120809	Catechol	III
85449	Phthalic anhydride	
463581	Carbonyl sulfide	
132649	Dibenzofurans	
100027	4 - Nitrophenol	
540841	2,2,4 - Trimethylpentane	
11422	Diethanolamine	
822060	Hexamethylene,-1, 6 -diisocyanate	
1332214	Asbestos	
7803512	Phosphine	
	- Radionuclides	
	- Mineral fibers @	
	- Antimony compounds *	
	- Cyanide compounds **	
	- Glycol ethers ***	
	- Mercury compounds ****	
	- Polycyclic organic matter *****	
	- Trivalent chromium compounds ******	

* = Except for animony trioxide, antimony trisulfide, antimony tartrate, and antimony pentafluoride

** = Except for sodium cyanide and potassium cyanide

*** = Except for 2-ethoxy ethanol, ethylene glycol monobutyl ether and 2-methoxy ethanol

**** = Except for mercuric nitrate, mercuric chloride, mercury, (acetato-o) phenyl, and ethyl mercuric phosphate

***** = Except for benzo(b)fluoranthene, benzo(a)athracene, benzo (a) pyrene, 7,12-dimethylbenz(a)anthracene, benz(c)acridine, chrysene, dibenz(ah) anthracene, 1,2:7,8-dibenzopyrene, indeno(1,2,3-cd)pyrene, but including dioxins and furans

****** = Awaiting a determination by the Agency (except for chromic chloride)

@ = Including crystalline silica, erionite, talc containing asbestiform fibers, glass wool, rock wool, slag wool, and ceramic fibers

TABLE V.

Severity of effect rating values for NOAELs, LOAELs, and FELs used to derive the Composite Score.

RATING	EFFECT
1	Enzyme induction or other biochemical change with no pathologic changes and no change in organ weights.
2	Enzyme induction and subcellular proliferation or other changes in organelles but no other apparent effects.
3	Hyperplasia, hypertrophy, or atrophy but no change in organ weights.
4	Hyperplasia, hypertrophy, or atrophy with changes in organ weights.
5	Reversible cellular changes: cloudy swelling, hydropic change or fatty changes.
6	Necrosis, or metaplasia with no apparent decrement of organ function. Any neuropathy without apparent behavioral, sensory, or physiologic change.
7	Necrosis, atrophy, hypertrophy, or metaplasia with a detectable decrement of organ functions. Any neuropathy with a measurable change in behavioral, sensory, or physiologic activity.

8 Necrosis, atrophy, hypertrophy, or metaplasia with definitive organ dysfunction. Any neuropathy with gross changes in behavior, sensory, or motor performance. Any decrease in reproductive capacity. Any evidence of fetotoxicity.

9 Pronounced pathologic changes with severe organ dysfunction. Any neuropathy with loss of behavioral or motor control or loss of sensory ability. Reproductive dysfunction. Any teratogenic effect* with maternal toxicity.

10 Death or pronounced life shortening. Any teratogenic effect* without signs of maternal toxicity.

* EPA's Office of Research and Development recommends that the word teratogenic be replaced with developmental.

TABLE VI.

Default Species weights and inhalation rates used to calculate composite scores.

Species	Weight(kg)	Inhalation rates (cubic meters/day)
Rat	0.35	0.223
Rabbit	3.8	2.0
Monkey	5.0	1.31
Mouse	0.03	0.039

FIGURE 1: Rating Values for Doses used to Rank Chronic Toxicity

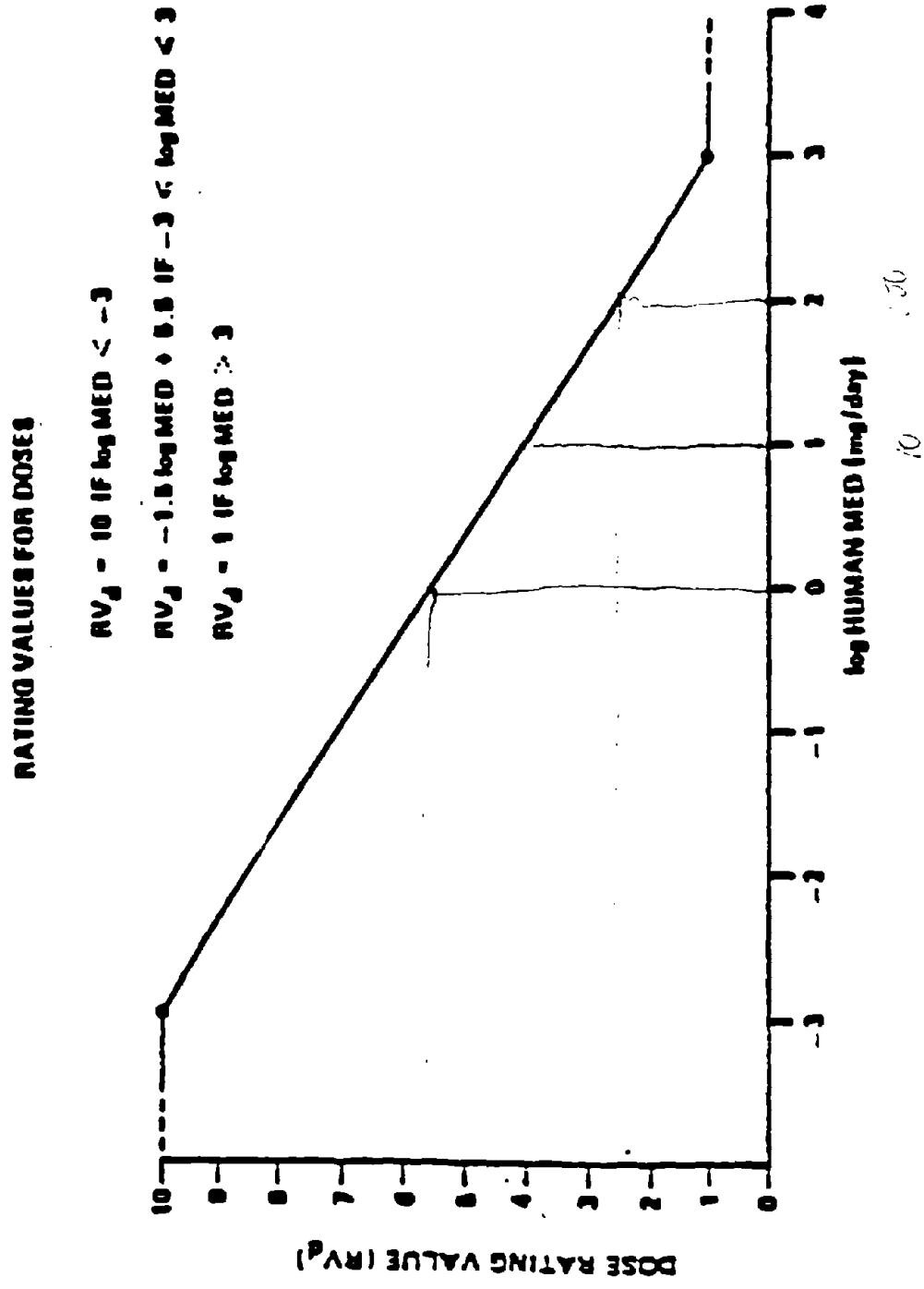
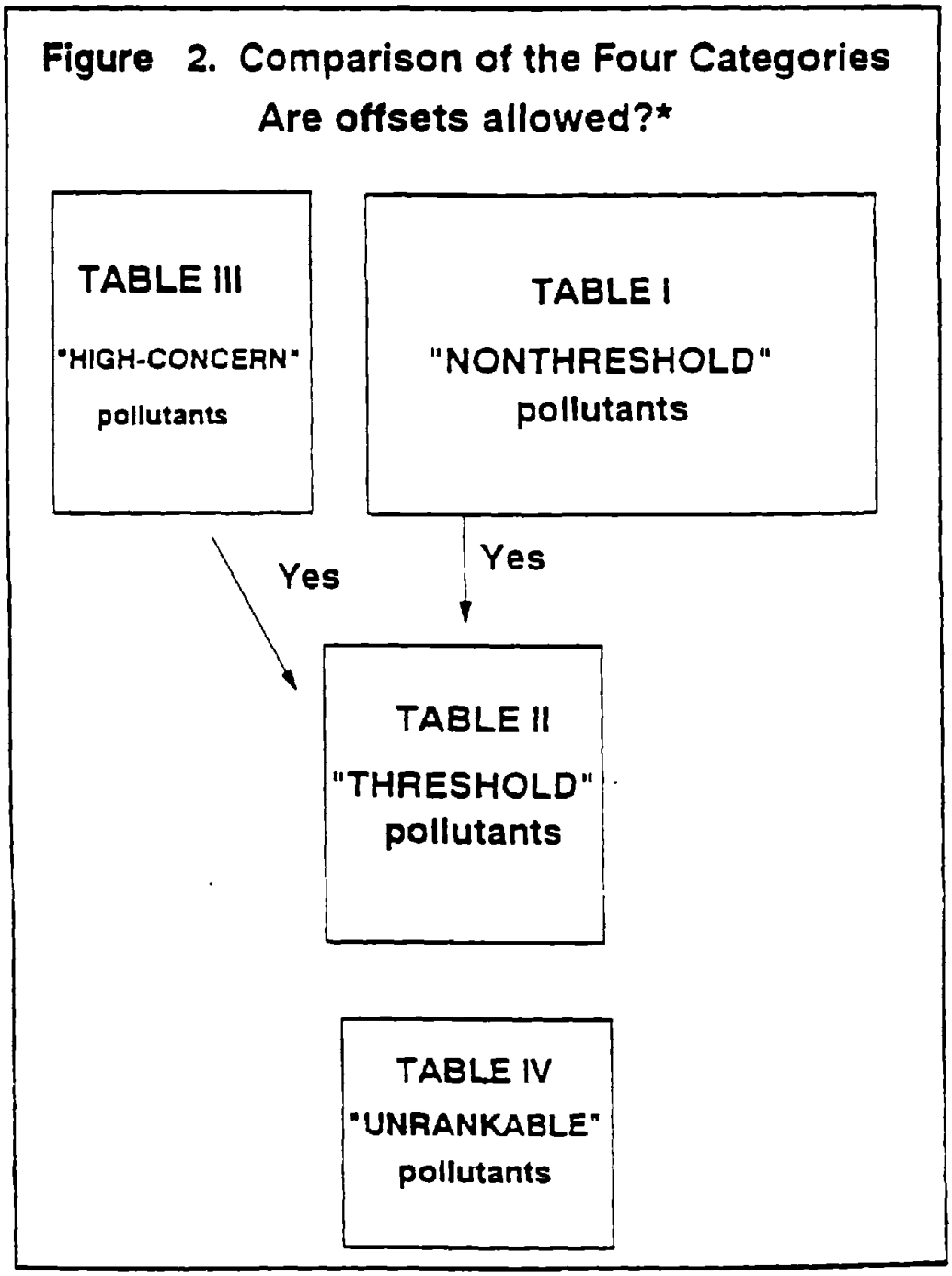


FIGURE 1

Rating Values for Doses used to Rank Chronic Toxicity



* This diagram illustrates pollutant comparisons BETWEEN categories. The proposed rule also includes an approach for comparisons WITHIN categories

References

1. U.S. Environmental Protection Agency (1986) Guidelines for carcinogen risk assessment Federal Register (September 24) 51:33992-35003.

2. Thyroid follicular cell carcinogenesis: mechanistic and science policy considerations U.S. EPA, ORD, Draft document December 1987 (edited 1988, EPA 265/3-88-014A).

3. De minimis definition. (Power v. Costle, 13 ERC 61225).

4. Crump, K.S.; Hoel, D.G.; Langley, D.H ; Peto R. (1976) Fundamental carcinogenic processes and their implications for low dose risk assessment. Cancer Res 36:2973-2979

5. Ames B.N; Magaw,R; Gold, L. (1987) Ranking possible carcinogenic hazards. Science 236:271-280.

6. Peto, R.; Pike, M.C.; Bernstein, L.S.; Ames, B.N. (1982) The TD_{50}: a proposed general convention for the numerical description of the carcinogenic potency of chemicals in chronic-exposure animal experiment. Environ Health Perspec 58: 1-8.

7. Wartenberg, D.; Gallo, M.A. (1990) The fallacy of ranking possible carcinogenic hazards using the TD_{50}. Risk Analysis 10: 609-613.

8. U.S. Environmental Protection Agency (1988) Methodology for evaluating potential carcinogenicity in support of reportable quantities adjustments pursuant to CERCLA section 102. Washington, D.C: Office of Health and Environmental Assessment, Human Health Assessment Group; EPA/600//8888-89 053.

9. Cogliano, V.J. (1986) The EPA's Methodology for Adjusting the Reportable Quantities of Potential Carcinogens, Proceedings from the 7th National Conference on Management of Uncontrolled Hazardous Waste Sites.

10. Nesnow, S. (1990) ICPEMC Working Paper 1/2. A multifactor ranking scheme for comparing the carcinogenic activity of chemicals. Mutation Research 239:83-115.

11. Frohlich, E.; Hess, R. (1983) Letter to editor: re ranking carcinogens for regulation. Science 219:238.

12. Squire, R.A. (1981) Ranking animal carcinogens: a proposed regulatory approach. Science 214: 877-880.

FIGURE 2: Comparison of the Four Categories: Are Offsets Allowed?

13. U.S. Environmental Protection Agency (1990) Air Quality Criteria for Lead: Supplement to the 1986 addendum.

14. Rhomberg, L. (in Press) What constitutes "dose" (definitions?) in: Dose-Response relationships in Carcinogen risk Assessment, ILSI press, Washington, DC.

15. Pepelko, W.E. (1991) Effect of exposure route on potency of carcinogens. Regulatory Toxicology and Pharmacology 13: 3-17.

16. U.S. Environmental Protection Agency. (1991) Risk Assessment Forum, Kidney Cancer Report.

17. U.S. Environmental Protection Agency (1990) Interim Methods for Development of Inhalation Reference Concentrations. ORD, Draft document August 1990 (EPA/600/8-90-066A).

18. Gaylor, D.W. (1985) The question of the existence of thresholds: extrapolation from high to low dose. In: Flamm, W.G.; Lorentzen, R. J., eds. Mechanisms in toxicity of chemical carcinogens and mutagens. Princeton, NJ: Princeton Scientific Publishing Co., Inc.; pp. 249-260. (advances in modern environmental toxicology:v12)

19. U.S. Environmental Protection Agency (1986) Technical background document to support rulemaking pursuant to CERCLA section 102 vol. II August 1986. Appendix: methodology and guidelines for ranking chemicals based on chronic Toxicity Data, ECAO-CIN-R213 Nov 1984.

20. U.S. Environmental Protection Agency (1980) Water quality and general quantitative risk assessment guidelines for noncancer effects (FR/vol.45#231/ November 28, 1980/ Notice).

21. U.S. Environmental Protection Agency (1987) Section 302 of Title II of SARA supplement NRT-1. Technical guidance for hazards analysis, emergency planning for extremely hazardous substance (FEMA, Dec 1987).

APPENDIX A

Supporting data for each ranked "non-threshold" pollutant

Section 1: Description of Inputs into a Weight-of-evidence Evaulation and Estimation of the $1/ED_{10}$

1.1 Qualitative Element: Weight-of-Evidence for Carcinogenicity

The EPA has long based the qualitative determination of carcinogenic hazard on data from human studies and/or from animal (rodent) bioassays. Information from short-term tests pharmacokinetic studies, comparative metabolism studies, structure-activity relationships, and other relevant toxicologic studies supplement the bioassay and epidemiologic data. These data are evaluated in the hazard identification component of risk assessment. The quality and findings of individual animal and human studies are characterized first. The consolidated data base of animal, human, and other supporting information is next assessed to draw inferences regarding the totality of the evidence for potential human carcinogenicity.

Human evidence of carcinogenicity comes from case reports and epidemiologic studies. An evaluation of these studies includes a determination of whether a causal inference can be made. Characteristics of the epidemiologic study such as its relevance, the assessment of exposure, the size of studied population, the selection of the comparison group, the adequacy of response rates for studied and comparison groups, the treatment of missing data, the collection of data, valid ascertainment of causes of morbidity and death, and analysis of data, including considerations of latency effects, confounders, convariates, effect modifiers, and more sensitive subpopulations, are critically analyzed so as to draw causal inferences.

In general, an established set of criteria for causality are employed. The foundations of these criteria were first proposed by sir Bradford Hill in the examination of the relationship between lung cancer and cigarette smoking and have been expanded over time. These criteria are that an inference of a causal association is aided when: (1) disease is known to occur a reasonable time after initial exposure, (2) several independent studies of similar exposure observe elevations in risk as the same site, (3) when the association (e.g., the elevated risk) is strong and precise, (4) a dose-response relationship is present, and (5) the association between exposure and disease makes sense in terms of biological knowledge and can be logically interpreted with what is known about the natural history and biology of the disease.

The EPA's cancer risk assessment guidelines (U.S. EPA 1986) are employed so as to classify the data as either "sufficient," "limited," "inadequate," "no data," or "no evidence." The classification of the human data is intended to reflect the reasonableness of the human data is intended to reflect the reasonableness of the hypothesized exposure-effect association and the conclusiveness of the data.

Evidence of carcinogenicity in animals is determined from bioassay or long-term exposure data in rodents which include doses at or near the maximum tolerated dose. Evidence for carcinogenicity is based on the observation of biologically and statistically significant tumor responses in specific organs or tissues. Chemicals which induce benign tumors frequently also

indicate malignant tumors, and it is thought that benign tumors will often progress into a malignancy (U.S. EPA 1986). Therefore, presence of benign and malignant tumors, when scientifically supported, will be considered indication of potential hazard.

The evidence in animals that an agent is potentially carcinogenic for humans increases: (1) with the increase in the number of tissue sites affected by the agent; (2) with the increase in number of animals species, strains, sexes, and number of experiments and doses showing a carcinogenic response; (3) with the occurrences of clear-cut dose-response relationships as well as a high level of statistical significance of the increase tumor incidence in treated compared to control groups; (4) when there is a dose-related shortening of the time to tumor occurrence or time to death with tumor (U.S. EPA 1986). As with the classifications for human data, the animal data are identified as whether "sufficient," "limited," "inadequate," "no data," or "no evidence" according to the EPA's cancer guidelines (U.S. EPA 1986).

The EPA's current scheme for categorizing the weight of evidence for carcinogenicity (U.S. EPA 1986) is grounded primarily on carcinogenic responses in animal bioassays and human studies, with support from secondary information, which may include structure-activity relationships, short-term assays, physiological, biochemical, toxicological, comparative metabolism, and kinetic studies.

The EPA is in the process of modifying the 1986 caner guidelines. It is proposed that experimental evidence other than bioassay data should have a greater contribution in identifying hazard that under the present scheme.

The current weight-of-evidence categories are arranged according to the perceived confidence in the inference of human carcinogenicity from different arrays of evidence. The categorization as a "human carcinogen" (Group A) is based on sufficient evidence from epidemiologic studies to support a causal association between exposure to the agent and cancer, or when sufficient human an animal evidence for a causal association exists. The category "probably carcinogenic to humans" (Group B) is supported by sufficient evidence of carcinogenicity in animals, e.g., increased tumor incidence in more than one bioassay, accompanied by human evidence that is either limited (Group B1) or inadequate (Group B2). The existence of only limited animal evidence in the presence of no or inadequate human data support the category "possibly carcinogenic to humans " (Group C). The category "not classifiable as to human carcinogenicity" (Group D) is generally employed when no data are found regarding carcinogenicity or when exposure-effect inferences cannot be made from such data. The last category "evidence of non-carcinogenicity for humans" (Group E) is defined by lack of no evidence of carcinogenicity in either well-conducted studies in two animal species or in animals and humans.

For the purposes of the section 112(g) hazard ranking, weight-of-evidence classifications of Groups A, B, and C are used to identify, in the absence of other information concerning mechanism, hazardous air pollutants as "non-threshold." It is felt that sufficient data on carcinogenicity in humans and/or animals provides support for a likely human cancer hazard. In addition, some evidence of carcinogenicity in animals is supportive of a presumption of a human cancer concern.

1.2 Quantitative Element: Estimation of Potency

The characterization of the dose-response relationship is useful for making inferences about response (cancer or some other endpoint engendered through a mechanism of additivity to background) association with a particular level of exposure and for making relative comparisons between chemicals based on potency. The data upon which quantitative estimate are derived are varied. The use of human data is preferred over animal data for quantitative estimation. Human data, however, are not always available, or if available, the quality may not be suitable for making quantitative risk inferences. In the absence of adequate human data, potency estimates are based on the animal experiences. Criteria for data selection are described in the cancer guidelines (U.S. EPA 1986).

For the hazard ranking of section 112(g). the dose associated with a 10 percent increase over background in cancer incidence (effective $dose_{10}$ or ED_{10}) has been chosen as the measure with which to compare relative potencies across "non-threshold" HAP.

The ED_{10} provides a sound measure with which to compare relative hazard for several reasons. First, the ED_{10} is considered to be within the observable range of the experimental data. Thus, issues related to the shape of the dose-response curve as extrapolated to low doses are not relevant. Second, the ED_{10} is a statistically stable estimate which is relatively insensitive to the choice of the dose-response model. The stability of the ED_{10} diminishes the need for using an upper bound used for taking the uncertainty of low dose extrapolation of the estimate into account. Thus, criticisms regarding the use of conservative estimates via the upper bound are not germane. The ED_{10} is expressed in units of mg/kg/day, under the assumption that a 70 kg human breathers $20m_3$/day or ingests 2 liters of water per day. The reciprocal of the ED_{10} is used as the potency factor for the relative ranking. The more potent the pollutant, the smaller the ED_{10} and he larger its inverse will be. Thus, higher potency pollutants will be placed higher in a ranking based on $1/ED_{10}$'s.

Several assumptions are inherent in using response in animals for making quantitative statements about expected human response. First, humans are presumed to have equal sensitivity to animals when doses are scaled as surface area. Second,if humans are going to respond, response sites in animals are used to make predictions of the magnitude of human response.

Section II describes the methods used to adjust experimental doses into human equivalent doses. The EPA assumes it is the average daily dose (averaged over a lifetime) not dose rate that

is predictive of neoplastic response. Additionally, the dose in humans that is considered "toxicologically equivalent," that is, the dose that engenders the same magnitude of response as seen in animals is assumed to scale with surface area. Therefore, for equal daily doses on a mg/kg basis, humans are expected to process the pollutant more slowly than animals which results in a larger internal dose. This assumption is supported by the slower metabolic rats and longer processing times in humans compared to rodent species. To account for these differences, EPA has historically scaled animal doses to a so-called "human equivalent doses" (HED). The HED is currently determined as the intake to mg that maintains the same ratio to body weights to be 2/3 power as does the animal dose. The EPA and other federal regulatory agencies have proposed 3/4 power as the basis for cross-species scaling (U.S. EPA 1992).

An estimation of potency may incorporate information about time to tumor, competing risks, and kinetic differences between high and low dose and between species. Such information, however, is often unavailable. In practice, estimates of potency are based on experimental exposures and observed response in control and several treatment groups. In some cases, the only available study for quantitative inferences is one conducted with a single treatment and control group. Generally, the ED_{10}s used in the hazard ranking are estimated from the same data set(s) as the estimate of the unit risk as identified in IRIS and EPA documents. Data supporting estimates inhalation risks as identified in IRIS

are preferred. However, unit risks are not always available for inhalation exposure for all "non-threshold" HAPS. In this case, data supporting oral hazard inferences are used. The chemical-specific summary sheets of section III of this Appendix identify the data set used for potency estimations and the source of the information. Additionally, the summary sheets identify whether a route extrapolation of oral data may be inferred for inhalation exposures.

Several methods exist for estimating potency and the method selected depends upon the type of data available. Three models have been applied to model epidemiologic data. These are the average relative risk, multiplicative relative risk, and excess additive risk models. For example, the average relative risk modes was used to estimate the unit risk associated with acrylonitrile. For nickel refinery workers and nickel subsulfate, all three models were used to estimate the unit risk. Duration of exposure and background risk are accounted for differently in each of these models. The description of model used for each "non-threshold" pollutant appears in section III of this Appendix.

In general, the multistage procedure is applied to the animal data for making inferences of human cancer risk. Since the ED_{10} is not highly dependent on the model employed, this default position of using the multistage model for such data, by the EPA seems reasonable. In addition, it provides a consistent approach for estimating the ED_{10} for the large number of HAP.

Using the multistage procedure, the lifetime probability of developing cancer under constant exposure d is:

Eq. 1 $P(d) = 1 - \exp [- (q^0 + q^1 d + q^2 d_2 + ... + q^k d_k)]$

where, p(d is the probability of response and the q's are fitted parameters.

In a limited number of cases, a time parameter has been incorporated into the equation which accounts for the differential risk of less than lifetime exposure, variable exposure, or non-tumor mortality. The chemical-specific summary sheet will identify these cases.

Section II: Transformation of Animal Dose Data

All exposure information is transformed to standard units of milligram (mg) per kilogram (kg)/animal weight per day, administered over the entire length of the study. If exposures are given in units other than mg/kg/day, or if animals are exposed in a non-continuous manner then the data is converted into a "transformed animal dose" (TAD). As a second set, animal's exposures are scaled to humans using the ratio of body weights to the 2/3 power. The resulting dose unit is called the "human equivalent dose" (HED). The following sections describe the methods for calculating TADs and HEDs for three exposure routes: diet, water, and air.

2.1 Dietary Exposures

Dietary dose (d) is calculated based upon body weight and food consumptions information. Such information is given by the study authors, or if absent, estimated by using standard food consumption values based on the fraction of body weight that is consumed each day (f) (U.S EPA 1988):

Species	f
mouse	0.13
rat	0.05
human	0.028

In order to obtain the dietary does (d), the daily experimental dose (ppm) is multiplied by f:

(2-1) d(mg/kg/d) - ppm (mg/kg food) x f kg food/kg body weight)

2.2 Drinking Water Exposures

Dietary dose (d) is based upon body weight and water consumption data which is either provided by the study author or estimated using standard consumption values based on the fraction of the body weight consumed as water per day (fw) (U.S. EPA 1988). The assumptions and procedure for making this estimate are the same as for dietary concentrations but the following rates for fw apply:

Species	fw
mouse	0.17
rat	0.078
human	0.029

The drinking water dose (d) in mg/kg/day is calculated by multiplying the daily dose in ppm by the species-specific values of fw:

(2-2) d (mg/kg/d) = ppm (mg/l water) x

FW (l water/kg body weight/day)

2.3 Atmospheric exposures

When exposure is via inhalation, two approaches are employed which take into consideration whether the HAP is (1) a highly water-soluble gas or aerosol or (2) a poorly water-soluble gas that reaches equilibrium between the air breathed in and body compartments.

For Case 1, it is reasonable to expect that absorption of particulate matter or virtually absorbed gases is proportionate to inhalation rate. The inhalation rate (I) for various species is

calculated from observation (FASEB, 1974, as cited in U.S. EPA 1988) that 25-g mice breathe 0.0345 m_3/day and 113-g rats breathe 0.103 m_3/day. For mice and rats of body weights (W) other than the above, surface-area proportionality is used for scaling breathing rates:

(2-4) mice, $I = 0.0345\ (W/0.025)^{2/3}\ m^3/d$; and

(2-5) rats, $I = 0.105\ (W/0.113)^{2/3}\ m^3/d$.

For humans, a value of $I = 20\ m^3/d$ is adopted as the "standard" breathing rate. This is based upon the observation (ICRP, 1977, as cited in U. S. EPA 1988) that average breathing rate is $10^7\ cm^3$ per 8-hour workday and $2 \times 10^7\ cm^3$ in 24 hours.

The empirical factors for air intake per kg/day, $i = I/W$, are tabulated as follows:

Species	W	i = I/W
mouse	0.03	1.3
rat	0.35	0.64
human	70	0.29

The inhalation dose (d) in mg/kg/day is calculated by multiplying the air concentration (v) in mg/m^3 by the intake factor (i) and absorption fraction (r):

(2-6) $d\ (mg/kg/d) = v\ (mg/m^3) \times i\ (m^e/kg\text{-}d) \times r$

Lacking information, r is assumed to be equivalent across species.

In the second case, proportionality between rate of absorption and rate of metabolism is expected. An assumption is also made that metabolic rate is proportional to 0_2 consumption (which is a function of surface area, $w^{2/3}$) (U. S. EPA 1988). In

addition, dose is proportional to the solubility of the gas in body fluids which can be expressed as an absorption coefficient (r).

When the absorption fraction (r) is assumed to be equivalent across species in the absence of data (as in Case 1), concentration in ppm or mg/m^3 is equivalent across species. This is supported by the observation that the minimum alveolar concentration necessary to produce give "stage" of anesthesia is similar in man and animals (Dripps et al. 1977, as cited in U.S. EPA 1988). The dose-response relationship is estimated in units of ppm or mg/m^3.

A reexpression of ppm or mg/m^3 into units of mg/kg/d is performed only for humans making the assumption that a 70kg human breathes 20 m^3/d (0_2 consumption).

(2 - 7) $\quad d\ (mg/kg/d) = v\ (mg/m^3/d \times (1/70\ kg)$

For either inhalation case, exposure given in terms of ppm (by volume) in air can be converted to units of mg/m^3:

(2 - 8) $\quad v = 0.041 \times MW\ (g/mole) \times ppm$

(Note that 1 mL in m^3 is 1 ppm (by volume) therefore, 0.041 x MW is the weight in mg of 1 mL of gas.)

2.4 Adjustment for Non-Continuous Exposure

The risk of cancer is assumed to be dependent on total exposure (as averaged over a lifetime). Oftentimes, exposure in experimental studies are for less than lifetime or are given on a discontinuous basis. To average discontinuous exposure over a lifetime, the exposure must be multiplied by the fraction of the

study over which the animal was actively exposed:

(2 - 9) transformed dose - d x (le/Le), where,

le is the duration of treatment and Le is duration of the study.

2.5 Cross-species Scaling

The primary objective of using animal data, in the absence of human data, is to make predictions of the probability of response to humans. Experimental exposures in animals, when expressed as a TAD, however is not "toxicologically equivalent" in humans due to the difference in scale between species (U. S. EPA 1992). A "toxicologically equivalent" dose is one which elicits a similar magnitude of response in both animals and humans. Humans, as a larger species (in terms of body weight), have slower rates of processing the pollutant compared to rodents. Thus, humans will need to experience the chronic exposure for a long period of time.

The exact identify of the dose unit or dosimetric important for eliciting the toxic effect is problematic. Much discussion has ensued on this topic (Rhomberg, 1992, ILSI talk; Andersen, 1987, NAS drinking Water document; Monro, 1992; toxicol. appl. Pharmacol. 112), the nature of which is briefly discussed insection I of this Appendix.

The EPA currently applies a factor based on the ratio of body weights to the 2/3 power for scaling animal doses to humans (HEDs). The ratio of body weight$^{2/3}$ is considered to approximate surface area. Thus,

(2 - 10) HE (mg/kg/d) = TAD (mg/kg/d) x $(W_a/W_h)^{2/3}$

The EPA has proposed a cross-species scaling of the ratio of body

study over which the animal was actively exposed:

(2 - 9) transformed dose - d x (le/Le), where,

le is the duration of treatment and Le is duration of the study.

2.5 Cross-species Scaling

The primary objective of using animal data, in the absence of human data, is to make predictions of the probability of response to humans. Experimental exposures in animals, when expressed as a TAD, however is not "toxicologically equivalent" in humans due to the difference in scale between species (U. S. EPA 1992). A "toxicologically equivalent" dose is one which elicits a similar magnitude of response in both animals and humans. Humans, as a larger species (in terms of body weight), have slower rates of processing the pollutant compared to rodents. Thus, humans will need to experience the chronic exposure for a long period of time.

The exact identify of the dose unit or dosimetric important for eliciting the toxic effect is problematic. Much discussion has ensued on this topic (Rhomberg, 1992, ILSI talk; Andersen, 1987, NAS drinking Water document; Monro, 1992; toxicol. appl. Pharmacol. 112), the nature of which is briefly discussed insection I of this Appendix.

The EPA currently applies a factor based on the ratio of body weights to the 2/3 power for scaling animal doses to humans (HEDs). The ratio of body weight$^{2/3}$ is considered to approximate surface area. Thus,

(2 - 10) HE (mg/kg/d) = TAD (mg/kg/d) x $(W_a/W_h)^{2/3}$

The EPA has proposed a cross-species scaling of the ratio of body

weights to the 3/4 based on allometry equivalent tissue AUCs scale across species by $W^{3/4}$ (Fed. Reg., June 5, 1992). The EPA is currently taking comments on this approach and has not yet adopted this a final. The impact of using a ratio of body weight to the 3/4, instead of the 2/3, power would imply that some misclassification would be expected between ED_{10} estimated based on data from different species. Only a handful of ED_{10} estimates are supported by human experiences (benzene, benzidine, BCME, cadmium, and acrylonitrile), thus, large misclassification in the present ranking is not expected.

2.6 Adjustment for Less Than Lifetime Follow-up

The current procedure for quantitative estimation is predicting human risk over a lifetime. Chronic bioassays in animals, usually conducted for 2 years in rats and mice, are considered lifetime bioassays. In some cases, however, the experiment was terminated before the animal's "lifetime" was achieved. In this case, the potency factor derived from the experimental data would represent only a fraction (Le/L) of the animals' lifespan.

Age-specific cancer rates for humans increase at least by the second power of age and often by a considerably higher power, as demonstrated by Doll (1971, as cited in U.S. EPA 1988). The EPA, thus, expects cumulative tumor rates to increase by at least the third power of age and animal-based estimate of potency are scaled by the length of observation in the experimental study (Le) and lifespan (L).

Section III: Supporting data for each ranked "non-threshold" pollutant: elements of hazard ranking

Elements of Hazard Ranking

Chemical Name: acetaldehyde

CAS Number: 75-07-0

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$):[b] 0.033 per (mg/kg)/d

Reference: Uloutersen, R; Van Garderan-Hoetner, A; Appelman, L.M., 1985. Lifespan (27 months) inhalation carcinogenicity study of acetaldehyde in rats. Final report Report No. V85/145/190172 - CIVO - Institutes TNO, The Netherlands.

Exposure route:	inhalation			
Species	rat			
Strain:	wistar			
Sex:	M			
Vehicle or physical state:	vapor			
Body weight:[b]	0.5 kg			
Duration of treatment (le):	121 weeks			
Duration of study (Le):	121 weeks			
Lifespan of animal (L):[c]	121 weeks			
Target organ:	nasal cavity			
Tumor type:	squamous cell carcinoma and adenocarcinoma			
Experimental doses/exposure:	3000 ppm	1500 ppm	750 ppm	0 ppm
Continuous exposure equivalent (ppm):[d]	279	257	130	0
Tumor incidence:	31/41	40/54	17/52	1/55

Comments: The high dose group experienced elevated early nontumor mortality. All animals dying during the first 52 weeks of exposure (before the first tumor appeared) were not included as these deaths did not have a sufficient latent period. The ED_{10} is based only on data from continuous exposure to acetaldehyde. These data, plus data from follow-up after discontinuous exposure (Woutersen and Appelman, 1984. Lifespan inhalation carcinogenicity study of acetaldehyde in rats. III. Recovery after 52 weeks of exposure. Final report. Report No. V84.288/1901X2. CIVO - Institutes TNO, The Netherlands) support the estimate of the unit risk, which was estimated using a multistage procedure with adjustment for variable exposure and nontumor differential mortality. An ED_{10} which accounts for these adjustments would not be significantly different than that estimated from the continuous exposure data.

Source: U.S. Environmental Protection Agency, 1992. IRIS, Integrated Risk Information System. Online. Cincinnati, OH: U.S. Environmental Protection Agency, Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office.

75-07-0 acetaldehyde (continued)

U.S. Environmental Protection Agency, 1981. Health assessment document for acetaldehyde. External review draft. EPA/600/8-86/015A. Research Triangle Park, N.C.: Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.
[b]It is assumed that ppm in air is equivalent from rats to humans. Units of ppm were expressed in units of (mg/kg)/d by multiplying (ED_{10}-ppm) x (molecular weight) x (0.041). It was assumed a 70 kg human had a breathing rate of 20 m^3/d.
[c]Estimated.
[d]Experimental dose (ppm) x (5 treatment days per week/7 days per week) x (6 hours exp/24 hour per day).

Elements of Hazard Ranking

Chemical Name: acetamide

CAS Number: 60-35-5

IARC Classification:[1] 2B

Comments: Increased incidences of malignant lymphoma in male mice and of benign and malignant liver tumors in rats following oral exposure was considered "sufficient evidence for carcinogenicity to animals". "No data" on humans was found.

Source: International Agency for Research on Cancer, 1987. IARC monographs on the evaluation of carcinogenic risks to humans. Overall evaluations of carcinogenicity: an updating of IARC monographs volumes 1 to 42. Supplement 7: 389-390.

---

[a]1-the agent is carcinogenic to humans, 2A-the agent is probably carcinogenic to humans (limited human evidence), 2B-the agent is probably carcinogenic to humans (limited evidence in humans in the absence of sufficient evidence in animals, or inadequate human evidence/non-existent human data and sufficient evidence in animals), 3-the agent is not classifiable as to its carcinogenicity to humans, 4-the agent is probably not carcinogenic to humans.

Elements of Hazard Ranking

Chemical Name: 2-acetylaminofluorine (AAF; acetamide, N-fluoren-2-yl)

CAS Number: 53-96-3

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): 7.7 per (mg/kg)/day

Reference: Farmer, H.J.; Kodell, R.L.; Greenman, D.L., 1980. Dose and time response models for the incidence of bladder and liver neoplasms in mice fed 2-acetylaminofluorene continuously. J. Enviom. Pathol. Tox. 3:55-68.

Exposure route:	oral							
Species:	mouse							
Strain:	BALB/cStCrlfC3Hf/NCTR							
Sex:	F							
Vehicle or physical state:	diet							
Body weight:[b]	0.03 kg							
Duration of treatment (le):	1000 days							
Duration of study (Le):	1000 days							
Lifespan of animal (L):[c]	1000 days							
Target organ:	liver							
Tumor type:	hepatoma and cholangiocarcinoma							
Experimental dose/exposure (ppm):	150	100	75	60	45	35	30	0
Transformed animal dose (mg/kg/day):[d]	19.5	13.0	9.8	7.8	5.9	4.6	3.9	0.0
Human equivalent dose (mg/kg/day):[e]	1.47	0.98	0.74	0.59	0.44	0.34	0.29	0.0
Overall tumor incidence at study's end:	44/ 1282	30/ 1276	45/ 1983	41/ 2846	47/ 2263	78/ 3366	22/ 5055	17/ 2379

Comments: The ED10 or megamouse study conducted by the National Center for Toxicological Research, as reported by Farmer et al. (1980), was considered more adequate for estimating an ED_{10} than the Miller et al. study (1956) cited in the U.S. EPA (1988). This study was specifically designed to examine dose-response relationships at low exposures. Thus, this study contains a larger number of treatment groups and animals on test than the study by Miller et al. (1956).

A two stage Weibull model gave the lowest value of the q^{1*}. Data in Farmer et al. (1980) were insuficient for determining whether deaths were tumor related; deaths are treated as incidental tumors (for the purposes of the dose-response modeling). The ED_{10} is based on data for oral exposure; an estimate of potency for the inhalation route is not currently available.

Source: U.S. Environmental Protection Agency, 1988. Evaluation of the potential carcinogenicity of acetamide, N-fluoren-2-yl. OHEA-C-073-1. Washington, DC: Office of Health and Environmental Assessment.

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.
[b]Average mouses's weight.
[c]Estimated.
[d]Experimental dose (ppm)x0.13(fraction of mouses body weight consummed as food per day)x(le/Le)x(Le/L)^3.
[e]Transformed animal dose (mg/kg/day)/(human body weight/animal body weight)$^{1/3}$

Elements of Hazard Ranking

Chemical Name: acrolein

CAS Number: 10-72-8

Weight-of-Evidence Classification:[a] C

Estimate of Potency ($1/ED_{10}$): See comments.

Comments: The available data are inadequate for estimating an ED_{10}.

Source: U.S. Environmental Protection Agency, 1992. IRIS, Integrated Risk Information System.Online. Cincinnati, OH: U.S. Environmental Protection Agency, Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans,
D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.
[b]Estimated.
[c]Estimated.
[d]Experimental dose (mg/kg/d) x (no. treatment days per week/7 days per week) x (Ie/Le).
[e]Transformed animal dose (mg/kg/d)/(human body weight/animal body weight) $^{(1/3)}$.

Elements of Hazard Ranking

Chemical Name: acrylamide

CAS Number: 79-06-1

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): 16 per (mg/kg)/d

Reference: Johnson K, Gorzinski S, Bodner K, et al., 1986. Chronic toxicity and oncogenicity study on acrylamide incorporated in the drinking water of fisher 344 rats. Toxicol. Appl. Pharmacol. 85: 154-168.

Exposure route:	oral				
Species:	rat				
Strain:	F344				
Sex:	F				
Vehicle or physical state:	drinking water				
Body weight:[b]	0.2 kg.				
Duration of treatment (le):	104 weeks				
Duration of study (Le):	104 weeks				
Lifespan of animal:[c]	104 weeks				
Target organ:	CNS, mammary and thyroid glands, uterus, oral cavity				
Tumor type:	gliomas and astrocytomas (CNS), adenomas and adenocarcinomas (mammary, thyroid, uterus), papillomas (oral cavity)				
Experimental doses/exposure (mg/kg/day):	2.0	0.5	0.1	0.01	0
Human equivalent doses[d] (mg/kg/day):	0.305	0.076	0.015	0.001	0
Tumor incidence:	46/60	21/60	14/60	18/60	13/60

Comments: The ED10 is based on oral data and can be extrapolated to inhalation exposures using the default assumptions of 100% absorption by both routes and that a 70 kg human has a breathing rate of 20 m^3 day.

Source: U.S. Environmental Protection Agency, 1992. IRIS, Integrated Risk Information System. Online. Cincinnati, OH: U.S. Environmental Protection Agency, Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans,
D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

[b]Estimated.

[c]Estimated.

[d]Transformed animal dose /(human body weight/animal body weight)$^{(1/3)}$.

Elements of Hazard Ranking

Chemical Name: acrylonitrile

CAS Number: 107-13-1

Weight-of-Evidence Classification:[a] B1

Estimate of Potency ($1/ED_{10}$): 2.3 per (mg/kg)/day

Reference: O'Berg, M., 1980. Epidemiologic study of workers exposed to acrylonitrile. J. Occup. Med. 22: 245-252.

Exposure route:	inhalation
Species:	human
Sex:	M
Vehicle or physical state:	ambient air
Body weight:[b]	70 kg
Duration of treatment (le):[c]	10+ yr
Duration of study (Le):	20 yr
Lifespan (L):	70 yr
Target organ:	lung
Experimental dose/exposure:[d]	5 to 20 ppm
Tumor incidence:	8/1345

Comments: The ED_{10} is calculated by extrapolation of the unit risk [2.4E-1per(mg/kg)/day] to the dose causing 10 percent mortality.

Source: U.S. Environmental Protection Agency, 1988. Evaluation of the potential carcinogenicity of acrylonitrile. OHEA-C-073-2. Washington, DC: Office of Health and Environmental Assessment.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

[b]Assumed.

[c]Length of time from initiation of study.

[d]Monitoring data were not available.

Elements of Hazard Ranking

Chemical Name: allyl chloride

CAS Number: 107-05-1

Weight-of-Evidence Classification:[a] C

Estimate of Potency ($1/ED_{10}$): see comments

Comments: The available data are inadequate for estimating an ED_{10}.

Source: U.S. Environmental Protection Agency, 1992. IRIS, Integrated Risk Information System. Online. Cincinnati, OH: U.S. Environmental Protection Agency, Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

Elements of Hazard Ranking

Chemical Name: 4-aminobiphenyl

CAS Number: 92-67-1

IARC Classification:[1] 1

Comments: Observed bladder cancer in occupationally-exposed workers support "sufficient evidence of carcinogenicity to humans." Bladder papillomas and carcinomas in rabbits and dogs and dose-related increases in incidences of angiosarcomas, hepatocellular tumors, and bladder carcinomas in mice, following oral administration, and induced mammary gland and intestinal tumors following subcutaneous administraton to rats support "sufficient evidence for carcinogenicity to animals." 4-aminobiphenyl, in addition, is genotoxic both *in vivo* and *in vitro*.

Source: International Agency for Research on Cancer, 1987. IARC Monographs on the evaluation of carcinogenic risks to humans. Overall evaluations of carcinogenicity: an updating of IARC monographs volumes 1 to 42. Supplement 7: 91-92.

---

[a]1-the agent is carcinogenic to humans, 2A-the agent is probably carcinogenic to humans (limited human evidence), 2B-the agent is probably carcinogenic to humans (limited evidence in humans in the absence of sufficient evidence in animals, or inadequate human evidence/non-existent human data and sufficient evidence in animals), 3-the agent is not classifiable as to its carcinogenicity to humans, 4-the agent is probably not carcinogenic to humans.

Elements of Hazard Ranking

Chemical Name: aniline

CAS Number: 62-53-2

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): 0.13 per (mg/kg)/day

Reference: CIIT. 1982. 104-week chronic toxicity study in rats: aniline hydrochloride. Final report.

Exposure route:	oral			
Species:	rat			
Strain:	CD-F			
Sex:	M			
Vehicle or physical state:	diet			
Body weight:[b]	0.35 kg.			
Duration of treatment (le):	104 weeks			
Duration of study (Le):	104 weeks			
Lifespan of animal (L):[c]	104 weeks			
Target organ:	spleen			
Tumor type:	combined fibrosarcoma, stromal sarcoma, capsular sarcoma, and hemangiosarcoma			
Experimental doses/exposure (mg/kg/day):	2000	600	200	0
Transformed animal doses[d] (mg/kg/day):	100	30	10	0
Human equivalent doses[e] (mg/kg/day):	12.29	3.69	1.23	0
Tumor incidence:	31/90	1/90	0/90	0/64

Comments: The ED_{10} is based on data from oral exposure; an estimate of potency for the inhalation route is not currently available.

Source: U.S. Environmental Protection Agency, 1992. IRIS, Integrated risk information system. Online. Cincinnati, OH: U.S. Environmental Protection Agency, Office Health and Environmental Assessment, Environmental Criteria and Assessment Office.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for Humans.
[b]Estimated.
[c]Estimated.
[d]Experimental dose (ppm) x 0.05 (fraction of body weight consumed in food per day).
[e]Transformed animal dose /(human body weight/animal body weight) $^{(1/3)}$.

Elements of Hazard Ranking

Chemical Name: o-anisidine

CAS Number: 90-04-0

IARC Classification:[1] 2B

Comments: "Sufficient evidence for carcinogenicity to animals" and "no data" in humans.

Source: International Agency for Research on Cancer, 1987. IARC monographs on the evaluation of carcinogenic risks to humans. Overall evaluations of carcinogenicity: an updating of IARC monographs volumes 1 to 42. Supplement 7: 57.

---

[a]1-the agent is carcinogenic to humans, 2A-the agent is probably carcinogenic to humans (limited human evidence), 2B-the agent is probably carcinogenic to humans (limited evidence in humans in the absence of sufficient evidence in animals, or inadequate human evidence/non-existent human data and sufficient evidence in animals), 3-the agent is not classifiable as to its carcinogenicity to humans, 4-the agent is probably not carcinogenic to humans.

Elements of Hazard Ranking

Chemical Name: antimony trioxide

CAS Number: 130-96-44

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): see comments

Comments: The available data are inadequate for estimating an ED_{10}.

Source: U.S. Environmental Protection Agency, 1981. Health effects assessment for antimony compounds. EPA/600/8-88/018. Prepared by the Office of Health and Environmental Assessment, Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH.

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

Elements of Hazard Ranking

Chemical Name: arsenic and inorganic arsenic compounds

CAS Number: not applicable

Weight-of-Evidence Classification:[a] A

Estimate of Potency ($1/ED_{10}$): 140 per (mg/kg)/day

References: Brown, C.C.; Chu, K.C., 1983a. Approaches to epidemiologic analysis of prospective and retrospective studies: example of lung cancer and exposure to arsenic. In: Risk assessment: proceedings of the SIMS conference on environmental epidemiology; June 28-July 2, 1982. Alta, UT: SIAM Publication.

Brown, C.C.; Chu, K.C., 1983b. Implications of the multistage theory of carcinogenesis applied to occupational arsenic exposure. J. Natl. Cancer Inst. 70: 455-463.

Brown, C.C.; Chu, K.C., 1983c. A new method for the analysis of cohort studies: implications of the multistage theory of carcinogenesis applied to occupational arsenic exposure. Environ. Health Perspect. 50: 293-308.

Enterline, P.E.; Marsh, G.M., 1982. Mortality among workers exposed to arsenic and other substances in a copper smelter. Am. J. Epidemiol. 116: 895-910.

Higgins, I.; Welch, K.; Burchfiel, C., 1982. Mortality of anaconda smelter workers in relation to arsenic and other exposures. Ann Arbor, MI: University of Michigan, Department of Epidemiology.

Lee-Feldstein, A., 1983. Arsenic and respiratory cancer in man: followup of an occupational study. In: Lederer, W.; Fensterheim, R., eds. Arsenic: industrial, biomedical, and environmental perspectives. New York: Van Nostrand Reinhold.

Exposure route:	inhalation
Species:	human
Sex:	M
Vehicle or physical state:	ambient air
Body weight:	70 kg
Target organ:	lung

Comments: The data set used to determine the unit risk factor consisted of six studies: Brown and Chu, 1983a,b,c; Lee-Feldstein, 1983; Higgins et al., 1982; and Enterline and Marsh, 1982. The absolute-risk linear model was used to extrapolate from actual exposure levels to risk estimate levels, and the geometric mean of these values is the final estimate of unit risk. The ED_{10} is calculated by extrapolation of the unit risk (4.3E-3 per $\mu g/m^3$) to the dose that causes 10 percent lung cancer mortality.

Source: U.S. Environmental Protection Agency, 1988. Evaluation of the potential carcinogenicity of arsenic and inorganic arsenic compounds. OHEA-C-073-5. Washington, DC: Office of Health and Environmental Assessment.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

Elements of Hazard Ranking

Chemical Name: benz(c)acridine

CAS Number: 225-51-4

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): see comments

Comments: The available data are inadequate for estimating an ED_{10}.

Source: U.S. Environmental Protection Agency, 1988. Evaluation of the potential carcinogenicity of benz(c)acridine. OHEA-C-073-27. Washington, DC: Office of Health and Environmental Assessment.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans,
D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

Elements of Hazard Ranking

Chemical Name: benz(a)anthracene

CAS Number: 56-55-3

Weight-of-Evidence Classification[a]: B2

Estimate of Potency ($1/ED_{10}$): see comments

Comments: The available data are inadequate for estimating an ED_{10}.

Source: U.S. Environmental Protection Agency, 1992. IRIS, Integrated Risk Information System System. Online. Cincinnati, OH: U.S. Environmental Protection Agency. Office of Health and Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

Elements of Hazard Ranking

Chemical Name: benzo(a)pyrene

CAS Number: 50-32-8

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): 54 per (mg/kg)/1d

Reference: Neil, J.; Rigdon, H., 1987. Gastric tumors in mice fed benzo(a)hyrene: a quantitative study. Texas Reports on Biology and Medicine. 25(4):553-557.

Exposure route:	oral									
Species	mice									
Strain:	CFW									
Sex:	unknown									
Vehicle or physical state:	diet									
Body weight:[b]	0.034 kg									
Duration of treatment (le):	≤197 days									
Lifespan of animal (L):[c]	730 days									
Target organ:	forestomach									
Tumor type:	squamous cell papillomas and carcinomas									
Experimental doses/exposure (ppm):	250	100	50	45	40	30	20	10	1	0[d]
Tumor incidence:	66/73	19/23	24/34	4/40	1/40	0/37	1/23	0/24	0/25	0/289[d]

Reference: Brune, H.; Deutsch-Wenzep, R.P.; Habs, M.; Ivankovic, S.; Schmahe, D., 1981. Investigation of the tumorigenic response to benzo(a)pyrene in aquous caffeine solution applied orally to Sprague-Dawley rats. J. Cancer Res., Clin. Oncol. 102:153-157.

Exposure route:	oral		
Species	rat		
Strain:	Sprague-Dawley		
Sex:	M/F		
Vehicle or physical state:	diet		
Body weight:[b]	104 wks		
Duration of treatment (le):	104 wks		
Duration of study (Le):	104 wks		
Lifespan of animal (L):[c]	104 wks		
Target organ:	forestomach larynx, and esophagus		
Tumor type:	papillomas and carcinomas		
Experimental doses/exposure (mg/kg/yr):	39	6	0
Tumor incidence:	10/64	3/64	3/64

50-32-8 benzo(a)pyrene (continued)

Comments: The ED_{10} is based on oral data and is a geometric mean of three analyses. An estimate of potency for the inhalation route is not currently available. Estimates of the ED_{10} are based on Neil and Rigdon (1987) using a modified two-stage (Clement Associates, 1990) and Weibull-type modelling approaches and on Brune et al. (1981) using a linearized multistage procedure.

Source: U.S. Environmental Protection Agency, 1992. IRIS, Integrated Risk Information System. Online. Cincinnati, OH: Office of Health and Environmental Assessment, Environmental Criteria Assessment Office.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.
[b]Estimated.
[c]Estimated.
[d]Besides the control incidence of Neil and Rigdon, data of Rabstein et al. (1973) was used as additional controls. Rabstein et al. (1973) reports background incidence of forestomach tumors in males is 2/268 and females, 1/402.

Elements of Hazard Ranking

Chemical Name: benzene

CAS Number: 71-43-2

Weight-of-Evidence Classification:[a] A

Estimate of Potency ($1/ED_{10}$): 0.27 per (mg/kg)/day

References: Rinsky, R.A.; Young, R.J.; Smith, A.B., 1981. Leukemia in benzene workers. Am. J. Ind. Med. 2: 217-245.

Ott, M.G.; Townsend, J.C.; Fishbeck, W.A.; Langner, R.A., 1978. Mortality among individuals occupationally exposed to benzene. Arch. Environ. Health. 33: 3-9.

Wong, O.; Morgan, R.W.; Whorton, M.D., 1983. Comments on the NIOSH study of leukemia in benzene workers. Technical Report submitted to Gulf Canada, Ltd., by Environmental Health Associates.

Exposure route:	inhalation
Species:	human
Sex:	M
Vehicle or physical state:	ambient air
Body weight:	70 kg
Target organ:	blood
Tumor type:	acute non-lymphocytic leukemia

Comments: The epidemiologic database upon which the estimate of potency is based is derived from separate studies by Rinsky et al. (1981), Wong et al. (1983), and Ott et al. (1978). Equal weight is given to the cumulative dose and the weighted cumulative dose as well as relative and absolute maximum likelihood model point estimates. The ED_{10} is estimated through extrapolation of the unit risk [2.9E-2 per (mg/kg)/day] to the dose causing an increased cancer risk of 10 percent.

Source: U.S. Environmental Protection Agency, 1988. Evaluation of the potential carcinogenicity of benzene. OHEA-C-073-29. Washington, DC: Office of Health and Environmental Assessment.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

Elements of Hazard Ranking

Chemical Name: benzidine

CAS Number: 92-87-5

Weight-of-Evidence Classification:[a] A

Estimate of Potency ($1/ED_{10}$): 2200 per (mg/kg)/day

Reference: Zavon, M.R.; Hoegg, U.; Bingham, E.; 1973. Benzidine exposure as a cause of bladder tumors. Arch. Environ. Health 27: 1-7.

Exposure route:	inhalation
Species:	human
Sex:	M
Vehicle or physical state:	ambient air
Body weight:[b]	70 kg
Duration of treatment (le):	13 yr
Duration of study (Le):	13 yr
Lifespan (L):	71.3 yr
Target organ:	bladder
Experimental dose/exposure:[c]	0.005 to 17.6 mg/m^3 (mean total accumulated dose=130 mg/kg)
Human equivalent dose (mg/kg/day):[d]	0.0063
Tumor incidence:	13/25

Comments: The ED_{10} is estimated through extrapolation of the unit risk [2.3E+2 per (mg/kg/-day] to the dose causing an increased cancer risk of 10 percent. The unit risk estimate is based on a one-hit model which includes a parameter for time (less than lifetime follow-up of the studied cohort).

Source: U.S. Environmental Protection Agency, 1988. Evaluation of the potential carcinogenicity of benzidine and its salts. OHEA-C-073-30. Washington, DC: Office of Health and Environmental Assessment.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

[b]Average human body weight.

[c]Estimated from urinary benzidine levels.

[d]Daily lifetime exposure calculated from a mean urine benzidine level of 0.04 mg/l at the end of the workshift, 1.2 l/day average urine output, a 1.45 percent recovery factor in urine, 70 kg body weight, 240 workdays/yr, 11.46 yr average exposure duration, and 56.5 yr average cohort age at the end of the study.

Elements of Hazard Ranking

Chemical Name: benzo(b)fluoranthene

CAS Number: 205-99-2

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): see Comments

Comments: The available data are inadequate for estimating an ED_{10}.

Source: U.S. Environmental Protection Agency, 1992. IRIS, Integrated Risk Information System. Online. Cincinnati, OH: U.S. Environmental Protection Agency, Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

Elements of Hazard Ranking

Chemical Name: benzotrichloride

CAS Number: 98-07-7

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): 87 per (mg/kg)/day

Reference: Fukuda, K.; Matsushita, H.; Takemoto, K., 1978. Carcinogenicity of benzotrichloride by the oral route of administration (J-4774). In: Proceedings of the 52nd annual meeting of the Japanese Industrial Health Association. pp. 516-517. (Taken from International Agency for Research on Cancer, 1982. Benzotrichloride. IARC monographs evaluating the carcinogenic risk of chemicals to humans. Lyon, France: WHO, v. 29, pp. 73-82.)

Exposure route:	oral				
Species:	mouse				
Strain:	ICR				
Sex:	F				
Vehicle or physical state:	none reported				
Body weight:	0.03 kg				
Duration of treatment (le):	25 wk				
Duration of study (Le):	78 wk				
Lifespan of animal (L):[b]	104 wk				
Target organ:	forestomach				
Tumor type:	squamous cell carcinoma				
Experimental dose/exposure:	2.7 mg	0.7 mg	0.17 mg	0.043 mg	0.0 mg
Transformed animal dose (mg/kg/day):[c]	3.48	0.90	0.23	0.055	0.0
Human equivalent doses (mg/kg/day):[d]	0.262	0.068	0.017	0.004	0.0
Tumor incidence:	10/35	16/40	9/38	1/37	0/35

Comments: The ED_{10} is based on data for oral exposure; an estimate of potency for inhalation exposure is not currently available.

Source: U.S. Environmental Protection Agency, 1988. Evaluation of the potential carcinogenicity of benzotrichloride. OHEA-C-073-34. Washington, DC: Office of Health and Environmental Assessment.

U.S. Environmental Protection Agency, 1992. IRIS, Integrated Risk Information System. Online. Cincinnati, OH: U.S. Environmental Protection Agency, Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

[b]Estimated.

98-07-7 benzotrichloride (continued)

[c]Experimental dose (mg)/animal weight (0.030 kg)x2 (treatment days/wk)/7 (days/wk)x(le/Le)x(Le/L)^3.
[d]Transformed animal dose (mg/kg/day)/(human body weight/animal body weight)$^{(1/3)}$.

Elements of Hazard Ranking

Chemical Name: benzyl chloride

CAS Number: 100-44-7

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): 0.66 per (mg/kg)/day

Reference: Lijinsky, W., 1985. Chronic bioassay of benzyl chloride in F344 rats and (C57BL/6J x BALB/c)F1 mice. J. Natl. Cancer Inst. [vol., pp. UNK].

Exposure route:	gavage		
Species:	mouse		
Strain:	(C57BL/6J x BALB/c)F1		
Sex:	M		
Vehicle or physical state:	corn oil		
Body weight:[b]	0.03 kg		
Duration of treatment (le):	104 wk		
Duration of study (Le):	107 wk		
Lifespan of animal (L):[b]	107 wk		
Target organ:	forestomach		
Tumor type:	carcinoma/papilloma		
Experimental dose/exposure:[c]	100 mg/kg	50 mg/kg	0 mg/kg
Transformed animal dose (mg/kg/day):[d]	42	21	0
Human equivalent dose (mg/kg/day):[e]	3.166	1.583	0.0
Tumor incidence:	32/52	4/52	0/51

Comments: The ED_{10} is based on data for oral exposure; an estimate of potency for the inhalation route is not currently available.

Source: U.S. Environmental Protection Agency, 1988. Evaluation of the potential carcinogenicity of benzyl chloride. OHEA-C-073-35. Washington, DC: Office of Health and Environmental Assessment.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.
[b]Estimated.
[c]Given 3 times/wk.
[d]Experimental dose (mg/kg)x3 (treatment days/wk)/7 (days/wk)x(le/Le).
[e]Transformed animal dose (mg/kg/day)/(human body weight/animal body weight)$^{(1/3)}$.

Elements of Hazard Ranking

Chemical Name: beryllium compounds (except beryllium salts)

CAS Number: not applicable

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): 79.7 per (mg/kg)/day

Reference: Wagoner, J.K.; Infante, P.F.; Bayliss, D.L., 1980. Beryllium: an etiologic agent in the induction of lung cancer, non-neoplastic respiratory disease and heart disease among industrially exposed workers. Environ. Res. 21(1): 15-34.

Exposure route:	inhalation			
Species:	human			
Sex:	M			
Vehicle or physical state:	ambient air			
Body weight:	70 kg			
Fraction of lifetime:	1.00	0.25	1.00	0.25
Duration of study (Le):	35 years			
Target organ:	lung			
Beryllium concentration in workplace:	1000 $\mu g/m^3$	1000 $\mu g/m^3$	100 $\mu g/m^3$	100 $\mu g/m^3$
Effective dose:	219.18 $\mu g/m^3$	54.79 $\mu g/m^3$	21.92 $\mu g/m^3$	5.48 $\mu g/m^3$

Comments: The weight-of-evidence classification and estimate of potency are based on epidemiologic data (Wagoner et al., 1980), where exposure is to less soluble forms of beryllium, mostly beryllium oxides. The ED_{10} is estimated by extrapolation of the unit risk (2.4E-3 per $\mu g/m^3$) to the dose associated with a 10 percent mortality in lung cancer.

Source: U.S. Environmental Protection Agency, 1988. Evaluation of the potential carcinogenicity of beryllium. OHEA-C-073-36. Washington, DC: Office of Health and Environmental Assessment.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

Elements of Hazard Ranking

Chemical Name: beryllium salts

CAS Number: not applicable

Weight-of-Evidence Classification: Footnote "a"

Estimate of Potency ($1/ED_{10}$): 18,000 per (mg/kg)/d

Reference: Reeves AL and Deitch D, 1969. Influence of age on the carcinogenic response to beryllium inhalation. In: Harishima, S, ed. Proceedings of the 16th international congress on occupational health. Tokyo, Japan: Japan Industrial Safety Association; pp. 652-652.

Schepers GWH, 1971. Lung tumors of primates and rodents: Part II. Ind. Med. 40: 23-31.

Schepers GWH, 1961. Neoplasia experimentally induced by beryllium compounds. Prog. Exp. Tumor Res. 2: 203-244.

Schepers GWH, Durkan TM, Delahant AB, Creedon FT, 1957. The biological action of inhaled beryllium sulfate: A preliminary chronic toxicity study on rats. AMA Arch. Ind. Health 15: 32-58.

Vorwald AJ, 1968. Biologic manifestations of toxic inhalants in monkeys. In: Vagtborg, H, Ed. Use of nonhuman primates in drug evaluation. Austin, TX: University of Texas Press; pp. 222-228.

Vorwald AJ, Reeves AL, Urban ECJ, 1966. Experimental beryllium toxicology. In: Stokinger HE, ed. Beryllium: industrial hygiene aspects. New York, NY: Academic Press; pp.201-234.

Vorwald AJ, 1953. Adenocarcinoma in the lung of albin rats exposed to compounds of beryllium. In: Cancer of the lung: An evaluation of the problem: Proceedings of the scientific session, annual meeting; November; New York, NY: American Cancer Society, Inc.; pp. 103-109.

Comments: The ED10 was derived from a linear extrapolation of the individual unit risks to the dose associated with a 10 percent tumor incidence. The ED_{10} is a geometric mean of all studies.

Source: U.S. Environmental Protection Agency, 1987. Health assessment document for beryllium. EPA/600/8-84/026F. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office. Research Triangle Park, NC.

---

[a]Every soluble beryllium compound that has been tested, including beryllium sulfate, fluoride, oxide, phosphate, as well as beryl ore, zinc beryllium silicate, and beryllium metal has been shown to be carcinogenic. It is considered highly likely that all soluble forms of beryllium (i.e., the salts) are carcinogenic in animals.

BERYLLIUM SALTS

Investigator	Beryllium compound	Mean beryllium concentration exposure pattern	Standardized experimental concenration[a] (microg/m^3)	Pulmonary tumor incidence rate	Human equivalent concentration (microg Be/m^3)	Maximum likelihood estimate slope[b] (microg/m^3)$^{-1}$
Vorwald et al. (1966)	$BeSO_4$	2.8 microg/Be/m^3 35 hr/wk for 18 months	0.58	13/21	0.22	4.3×10^{0}
Reeves and Deitch (1969)	$BeSO_4$	35.7 microg/Be/m^3 35 hr/wk for varying durations				8.1×10^{1}
Reeves and Deitch (1969)	$BeSO_4$	35.7 microg/Be/m^3 35 hr/wk for 18 months	7.4	13/15	2.8	7.1×10^{-1}
Schepers et al. (1957)	$BeSO_4$	33.5 microg/Be/m^3 35 hr/wk for 7.5 months	2.9	58/136	1.1	5.0×10^{-1}
Vorwald (1953)	$BeSO_4$	33 microg/Be/m^3 35 hr/wk for 13 months	5.0	4/8	1.9	3.7×10^{-1}
Schepers (1961)	$Be F_4$	9 microg/Be/m^3 35 hr/wk for 10.5 months	1.0	11/200	0.42	1.4×10^{-1}
Schepers (1961)	$BeHPO_4$	227 microg/Be/m^3 35 hr/wk for 6.5 months	17.1	7/40	6.5	3.0×10^{-2}

GUINEA PIGS:

Investigator	Beryllium compound	Mean beryllium concentration exposure pattern	Standardized experimental concenration[a] (microg/m^3)	Pulmonary tumor incidence rate	Human equivalent concentration (microg Be/m^3)	Maximum likelihood estimate slope[b] (microg/m^3)$^{-1}$
Schepers (1971)	$BeSO_4$	36 microg/Be/m^3 35 hr/wk for 12 months	5.1	2/20	1.7	6.5×10^{-1}

RHESUS MONKEYS:

Vorwald	$BeSO_4$	3.8 microg/Be/m^3 15 hr/wk for 3 years	0.69	8/11[d]	0.36	3.6×10^{-0}

[a]Standardized experimental concentration is calculated by c x (h/168) x (L/18) where c is the mean experimental concentration, h is the number of hours exposed per week (168 hours), and L is the number of months exposed.
[b]Estimated by assuming that the control reponse is zero.
[c]A life span of 15 years is assumed.
[d]Response is among animals surviving more than 1 year.

Elements of Hazard Ranking

Chemical Name: bis(chloromethyl)ether (BCME)

CAS Number: 542-88-1

Weight-of-Evidence Classification:[a] A

Estimate of Potency ($1/ED_{10}$): 1,400 per (mg/kg)/day

Reference: Kuschner, M.; Laskin, S.; Drew, R.T.; Cappiello, V.; and Nelson, N., 1975. Inhalation carcinogenicity of alpha haloethers: III. lifetime and limited period inhalation studies with bis(chloromethyl)ether at 0.1 ppm. Arch. Environ. Health 30: 73-77.

Exposure route:	inhalation						
Species:	rat						
Strain:	Sprague-Dawley						
Sex:	M						
Vehicle/physical state:	air						
Body weight:[b]	0.5 kg						
Duration of study (Le) (days):[c]	350	301	427	497	483	483	462
Lifespan of animal (L):[b]	728 days						
Target organ:	lung, nasal						
Tumor type:	neuroepitheliomas, malignant olfactory tumors (unclassified), ganglioneuroepitheliomas, squamous cell carcinomas of turbinates and gingiva, poorly differentiated epithelial tumors of the nose, nasal cavity adenocarcinomas, and squamous cell carcinomas and adenocarcinomas of the lung.						
Experimental dose/ exposure:[d]	0.1ppm	0.1ppm	0.1ppm	0.1ppm	0.1ppm	0.1ppm	0.1ppm
No. of exposures:	100	80	60	40	20	10	0
Transformed animal dose (mg/kg/day):[e]	0.0194	0.0180	0.00955	0.00545	0.00281	0.00140	0.0
Human equivalent dose (mg/kg/day):[f]	3.73×10^{-3}	3.47×10^{-3}	1.84×10^{-3}	1.05×10^{-3}	5.41×10^{-4}	2.7×10^{-4}	0.0
Tumor incidence:	12/20	15/34	4/18	4/18	3/46	1/41	0/240

Comments: None.

Source: U.S. Environmental Protection Agency, 1988. Evaluation of the potential carcinogenicity of bis(chloromethyl)ether. OHEA-C-073-44. Washington, DC: Office of Health and Environmental Assessment.

U.S. Environmental Portection Agency, 1992. IRIS, Integrated Risk Information System Online. Cincinnati, OH: U.S. Environmental Protection Agency, Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office.

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.
[b]Estimated.
[c]Data are based on the median lifespan at each dosage level as given in the study report.
[d]For 6 hr per exposure.
[e]Experimental dose (mg/kg/day)x(no. exposure days/Le) x (6 hr/24 hr/day).
[f]Transformed animal dose (mg/kg/day)/(human body weight/animal body weight)$^{(1/3)}$.

Elements of Hazard Ranking

Chemical Name: bis(2-ethylhexyl)phthalate (DEHP)

CAS Number: 117-81-7

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): 0.086 per (mg/kg)/day

Reference: National Toxicology Program, 1982. Carcinogenesis bioassay of di(2-ethylhexyl)phthalate (CAS no. 117-81-7) in F344 rats and B6C3F1 mice (feed study). NTP-80-37, NIH Publication 82-1773. Research Triangle Park, NC: NTP.

Kluwe, W.M.; Haseman, J.K.; Douglas, J.F.; Huff, J.E., 1982. The carcinogenicity of dietary di(2-ethylhexyl)phthalate (DEHP) in Fischer 344 rats and B6C3F1 mice. J. Toxicol. Environ. Health. 10(4-5): 797-815.

Exposure route:	oral		
Species:	mouse		
Strain:	B6C3F1		
Sex:	M		
Vehicle or physical state:	diet		
Body weight:	0.035 kg		
Duration of treatment (le):	103 wk		
Duration of study (Le):	105 wk		
Lifespan of animal (L):	105 wk		
Target organ:	liver		
Tumor type:	hepatocellular carcinoma and adenoma		
Experimental dose/exposure:	6000 mg/kg diet	3000 mg/kg diet	0 mg/kg diet
Transformed animal dose (mg/kg/day):[b]	780	390	0
Human equivalent dose (mg/kg/day):[c]	62	31	0
Tumor incidence:	29/50	25/48	14/50

Comments: The ED_{10} is based on data for oral exposure; an estimate of potency for the inhalation route is not currently available.

Source: U.S. Environmental Protection Agency, 1992. IRIS, Integrated Risk Information System. Online. Cincinnati, OH: U.S. Environmental Protection Agency, Office of Health and Environmental Assessment, Environmental Criteria Assessment Office.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

[b]Experimental dose (mg/kg) x 0.13 (fraction of species' body weight consumed in food per day).

[c]Transformed animal dose (mg/kg/day)/(human body weight/animal body weight)$^{(1/3)}$.

Elements of Hazard Ranking

Chemical Name: bromoform

CAS Number: 75-25-2

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$):[b] 0.029 per (mg/kg)/d

Reference: National Toxicology Program, 1989. Toxicology and carcinogenicity studies of tribromomethane and bromoform in F344/N rats and B6C3F1 mice (Gavage Study). NTP-350.

Exposure route:	gavage		
Species:	rat		
Strain:	F344		
Sex:	F		
Vehicle or physical state:	corn oil		
Body weight:[c]	0.225 kg. (high dose); 0.25 kg. (low dose)		
Duration of treatment (le):	103 weeks		
Duration of study (Le):	103 weeks		
Lifespan of animal (L):[c]	104 weeks		
Target organ:	large intestine		
Tumor type:	adenomatous polyps or adenocarcinomas		
Experimental doses/exposure (mg/kg/d):	200	100	0
Transformed animal doses[d] (mg/kg/day):	142.9	71.4	0
Human equivalent doses[e] (mg/kg/day):	20.5	10.6	0
Tumor incidence:	8/50	1/50	0/50

Comments: Decreased body weight (high-dose females, 10-25%) suggested that the MTD was reached. Adenomatous polyps or adenocarcinomas of the large intestine were also observed in the large intestine of male rats; adenocarcinomas alone were not significantly increased compared with controls. An extrapolation was made from the oral to the inhalation exposure route by accounting for 50% respiratory absorption.

Source: U.S. Environmental Protection Agency, 1992. IRIS, Integrated Risk Information System. Online. Cincinnati, OH: U.S. Environmental Protection Agency, Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.
[b]The ED_{10} for an inhalation exposure is presented. ED_{10} (inhalation exposure)=ED_{10} (oral exposure route) x (1/0.5, the absorption factor).
[c]Actual.

75-25-2 bromoform (continued)

[d]Experimental dose (mg/kg/d) x (5 treatment days per week/7 days per week).
[e]Transformed animal dose /(human body weight/animal body weight)$^{(-1/3)}$.

Elements of Hazard Ranking

Chemical Name: 1,3-butadiene

CAS Number: 106-99-0

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$):[b] 8.4 per (mg/kg)/d

Reference: National Toxicology Program, 1984. Toxicology and carcinogenesis studies of 1,3-Butadiene (CAS 106-99-0) in B6C3F1 mice (inhalation studies). U.S. DHHS, PHS, NIH Tech. Rep. Series. No. 288.

Exposure route:	inhalation					
Species:	mice					
Strain:	B6C3F1					
Sex:	M/F					
Vehicle or physical state:	gas					
Body weight:[c]	0.03 kg.					
Duration of treatment (le):	60 weeks (males), 61 week (females)					
Duration of study (Le):	60 weeks (males), 61 week (females)					
Lifespan of animal:[c]	103 weeks					
Target organ:	heart, hematopoietic system, lung, forestomach, prepurtial gland, zymbal gland (males); heart, hemtopoetic system, lung, forestomach, ovary, mammary gland, liver, brain (females)					
Tumor type:	hemangiosarcoma, lymphoma, adenomas, carcinomas, gliomas, granulosa cell tumors					
Experimental doses/exposure	males			females		
(ppm):	1250	625	0	1250	625	0
Delivered animal doses (mg/kg/day):	5.4	3.5	0	5.6	3.7	0
Tumor incidence:	40/45	43/49	2/50	45/49	31/48	4/48

Comments: The ED_{10} is a geometric mean of males and females. Delivered animal doses derived from absorption data of NTP (1985; Quarterly report from Lovelace Research Institute, January 1 through March 31, 1985. Interagency agreement 22-Y01-ES-0091). The ED10 accounts for 54% percent absorption in humans at low exposure levels. New data (Bond et al., 1986; Toxicol. Appl. Pharmacol. 84:617-627) suggest absorption may be 20% at lower doses. The estimate of the $1/ED_{10}$ based on the more recent Bond et al. information would be 1.8 per (mg/kg/d).

Source: U.S. Environmental Protection Agency, 1992. IRIS, Integrated Risk Information System. Online. Cincinnati, OH: U.S. Environmental Protection Agency, Office of Health and Environmental Assessment, Environmental Protection Agency.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans,

D-not classifiable as to human carcinogenicity, evidence of noncarcinogenicity for humans.

[b]The ED_{01} is expressed in units of absorbed dose. The ED_{10} was expressed in absorbed dose units under the assumption that a 70 kg human has a breathing rate of 20 m^3/d.

$ED_{10human} = ED_{10\ absorbed\ dose\ in\ mice} \times [1\ ppm/1.5\ mg/kg/d]_{mouse} \times [0.35\ (mg/kg/d)/1\ ppm]_{human}$.

These conversion factors are based on a 54% absorption in both species at lower doses.

For mice, 1 ppm = molecular $weight_{1,3\text{-butadiene}}$ x (0.41) x (0.54, absorption fraction) x (4.3E-2 m^3/d, breathing rate mice) x (1/0.035 kg).

For humans, 1 ppm = molecular $weight_{1,3\text{-butadiene}}$ x (0.41) x (0.54, absorption fraction) x (20 m^3/d, breathing rate human) x (1/70 kg).

[c]Estimated.

Elements of Hazard Ranking

Chemical Name: cadmium compounds

CAS Number: not applicable

Weight-of-Evidence Classification:[a] B1

Estimate of Potency ($1/ED_{10}$):[b] 58 per (mg/kg)1d

Reference: Thun, M.J.; Schnorr, T.M; Smith, A.B.; Halperin, W.E., 1985. Mortality among a cohort of U.S. cadmium production workers: an update. J. Nat. Cancer Inst. 74(2):325-333.

Exposure route:	inhalation + dermal + oral		
Species:	humans		
Sex:	M		
Vehicle or physical state:	ambient air		
Body weight:[c]	70 kg		
Duration of study (Le):	59 yr		
Lifespan of animal (L):[c]	70 yr		
Target organ:	lung, trachea, bronchus		
Experimental doses/exposure[e] (ng/m^3):	2522	727	168
Observed no. deaths/expected no. deaths:	7/2.50	7/4.61	2/3.77

Comments: The ED_{10} is estimated by extrapolation of the unit risk (1.8E-3 per ug/m^3) to the dose causing 10 percent mortality (over background).

Source: U.S. Environmental Protection Agency, 1992. IRIS, Integrated Risk Information System. Online. Cincinnati, OH: U.S. Environmental Protection Agency, Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office.

---

[a] A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

[b] Units of ng/m^3 were expressed in (mg/kg)/d by assuming a 70 kg human has a breathing rate of 20 m^3/d.

[c] Estimated.

[d] Estimated.

[e] Median cumulative exposure, $mg/d/m^3$ (8 hours/24 hours per day) x (1 day/365 days per yr) x (240 days/365 days per yr).

Elements of Hazard Ranking

Chemical Name: captan

CAS Number: 133-06-2

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): 0.026 per (mg/kg)/d

Reference: Chevron, 1982. MRID. No. 00068076. Available from EPA. Submitted to U.S. EPA, Office of Pesticides Programs.

Exposure route:		oral			
Species		mice			
Strain:		CD-1			
Sex:		M, F			
Vehicle or physical state:		dietary			
Body weight:[b]		0.03 kg.			
Duration of treatment (le):		113 weeks			
Duration of study (Le):		113 weeks			
Lifespan of animal (L):[c]		113 weeks			
Target organ:		small intestine			
Tumor type:		combined adenomas and carcinomas			
Experimental doses/exposure (mg/kg/day):		16000	10000	6000	0
Transformed animal doses[d] (mg/kg/day):		2400	1500	900	0
Human equivalent doses[e] (mg/kg/day):		190	113.1	67.9	0
Tumor incidence:	male	39/80	22/80	19/80	3/80
	female	29/80	21/80	26/80	3/80

Comments: The ED_{10} is a geometric mean of the dose giving a 10% tumor response in males and females. The ED_{10} is based on data from oral exposure; an estimate of potency for inhalation exposure is not currently available.

Source: Memorandum from R. Engler to H. Jacoby, December 29, 1986, "Peer Review of Captan, Caswell No: 159." Memorandum from E. Rinde to R. Mountford, July 20, 1988, "Peer Review of Captan, Addendum."

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

[b]Estimated.

[c]Estimated.

[d]Experimental dose (ppm) x .15 (fraction of body weight consumed as food).

[e]Transformed animal dose /(human body weight/animal body weight) $^{(1/3)}$.

Elements of Hazard Ranking

Chemical Name: carbon tetrachloride

CAS Number: 56-23-5

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): 0.34 per (mg/kg)/day

Reference: Della Porta, G.; Terracini, B.; Chubik, P., 1961. Induction with carbon tetrachloride of liver cell carcinomas in hamsters. J. Natl. Cancer Inst. 26: 855-863.

Exposure route:	oral	
Species:	hamster	
Strain:	Syrian Golden	
Sex:	M, F	
Vehicle or physical state:	gavage	
Body weight:[b]	0.12 kg	
Duration of treatment (le):	30 wk	
Duration of study (Le):	55 wk	
Lifespan of animal (L):[b]	128 wk	
Target organ:	liver	
Tumor type:	hepatocellular carcinoma	
Experimental dose/exposure:[c]	0.95 mg/day	0.0 mg/day
Transformed animal dose (mg/kg/day):[d]	8.50	0.0
Human equivalent dose (mg/kg/day):[e]	1.02	0.0
Tumor incidence:	10/19	0/80

Reference: Edwards et al., 1942 [no further bibliographic information available].

Exposure route:	oral	
Species:	mouse	
Strain:	L	
Sex:	M, F	
Vehicle or physical state:	gavage	
Body weight:[b]	0.035 kg	
Duration of treatment (le):	4 mo	
Duration of study (Le):	7.5 mo	
Lifespan of animal (L):[b]	24 mo	
Target organ:	liver	
Tumor type:	hepatoma	
Experimental dose/exposure:	15 mg/day	0 mg/day
Transformed animal dose (mg/kg/day):[d]	29.0	0.0
Human equivalent dose (mg/kg/day):[e]	2.3	0.0
Tumor incidence:	34/73	2/152

56-23-5 carbon tetrachloride (continued)

Reference: National Cancer Institute, 1976. Report on carcinogenesis bioassay of carbon tetrachloride. NCI Carcinogenesis Program, Division of Cancer Cause and Prevention. Bethesda, MD.

Exposure route:	oral		
Species:	mouse		
Strain:	B6C3F1		
Sex:	M, F		
Vehicle or physical state:	gavage		
Body weight:[b]	0.035 kg		
Duration of treatment (le):	78 wk		
Duration of study (Le):	110 wk		
Lifespan of animal (L):[b]	110 wk		
Target organ:	liver		
Tumor type:	hepatocellular carcinoma		
Experimental dose/exposure:	42 mg/day	21 mg/day	0 mg/day
Transformed animal dose (mg/kg/day):[d]	1396.0	698.0	0.0
Human equivalent dose (mg/kg/day):[e]	110.8	55.4	0.0
Tumor incidence:	90/93	89/89	6/157

Reference: National Cancer Institute, 1976. Report on carcinogenesis bioassay of carbon tetrachloride. NCI Carcinogenesis Program, Division of Cancer Cause and Prevention. Bethesda, MD.

Exposure route:	oral				
Species:	rat				
Strain:	Osborne-Mendel				
Sex:	M, F				
Vehicle or physical state:	gavage				
Body weight:[b]	0.35 kg				
Duration of treatment (le):	78 wk				
Duration of study (Le):	110 wk				
Lifespan of animal (L):[b]	110 wk				
Target organ:	liver				
Tumor type:	hepatocellular carcinoma				
Experimental dose/exposure (mg/day):	36 (F)	21 (M)	18 (F)	11 (M)	0 (M, F)
Transformed animal dose (mg/kg/day):[d]	87.1	50.9	43.3	26.3	0.0
Human equivalent dose (mg/kg/day):[e]	14.9	8.7	7.4	4.5	0.0
Tumor incidence:	1/30	2/27	4/46	2/45	0/37

Comments: The ED_{10} is a geometric mean of the four data sets and is extrapolated from the oral to the inhalation exposure route.

Source: U. S. Environmental Protection Agency, 1992. IRIS, Integrated Risk Information System. Online. Cincinnati, OH: U.S. Environmental Protection Agency, Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office.

56-23-5 carbon tetrachloride (continued)

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.
[b]Assumed.
[c]For the first 7 weeks, 0.25 ml of 0.05% carbon tetrachloride in corn oil was administered; this dose was halved for the remainder of the exposure period.
[d]Experimental dose (mg/day)/body weight (kg)x(5 days/7days/wk)x(le/Le)x(Le/L)^3.
[e]Transformed animal dose (mg/kg/day)/(human body weight/animal body weight)$^{(1/3)}$.

Elements of Hazard Ranking

Chemical Name: chloramben

CAS Number: 133-90-4

Weight-of-Evidence Classification:[a] see comments

Estimate of Potency ($1/ED_{10}$): see comments

Comments: The Office of Research and Development/Office of Health and Environmental Assessment is currently evaluating the carcinogenic evidence on chloramben. A draft preliminary assessment indicates that the weight-of-evidence classification is such that this chemical may be considered a "nonthreshold" hazardous air pollutant. This evaluation is currently undergoing internal peer review, thus, the exact placement of this chemical with respect to other "nonthreshold" HAPs can not be determined at this time.

Source: U.S Environmental Protection Agency, 1992. Preliminary assessment evaluation of the potential carcinogenicity of chloramben. First draft. Prepared by the Chemical Hazard Evaluation Program, Health and Safety Research Division, ORNL, for the Office of Health and Environmental Assessment, Human Health Assessment Group.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

Elements of Hazard Ranking

Chemical Name: chlordane

CAS Number: 57-74-9

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): 11 per (mg/kg)/day

Reference: Epstein, S.S., 1976. Carcinogenicity of heptachlor and chlordane. Sci. Total. Environ. 6: 103-154.

Exposure route:		oral			
Species:		mouse			
Strain:		CD-1			
Sex:		M			
Vehicle or physical state:		diet			
Body weight:[b]		0.03 kg			
Duration of treatment (le):		550 days			
Duration of study (Le):		550 days			
Lifespan of animal (L):[b]		730 days			
Target organ:		liver			
Tumor type:		carcinoma			
Experimental dose/exposure:		50 ppm[c]	25 ppm	5 ppm	0 ppm
Transformed animal dose: (mg/kg/day):[d]		6.55[c]	3.25	0.65	0.0
Human equivalent dose (mg/kg/day):[e]		0.49[c]	0.25	0.05	0.0
Tumor incidence:	females	26/37	32/50	0/61	0/45
	males	32/39	41/52	5/55	3/33

Reference: NCI, 1977. Bioassay of chlordane for possible carcinogenicity. NCI Carcinogenesis Tech. Rep. Ser. No. 8. DHEW Publication No. (NIH) 77-808.

Exposure route:	oral		
Species:	mouse		
Strain:	B6C3F1		
Sex:	M		
Vehicle or physical state:	diet		
Body weight:[b]	0.035 kg		
Duration of treatment (le):	730 days		
Duration of study (Le):	730 days		
Lifespan of animal (L):[b]	730 days		
Target organ:	liver		
Tumor type:	carcinoma		
Experimental dose/exposure:	56.2 ppm[c]	29.9 ppm	0 ppm (males)
	63.8 ppm[c]	30.1 ppm	0 ppm (females)
Transformed animal dose: (mg/kg/day):[d]	7.31[c]	3.91	0.0 (males)
	8.32[c]	3.91	0.0 (females)

57-74-9 chlordane (continued)

Human equivalent dose (mg/kg/day):[e]	0.58[c]	0.31	0.0 (males)
	0.66[c]	0.31	0.0 (females)
Tumor incidence:	43/49	16/48	2/18 (males)
	34/49	3/47	0/19 (females)

Comments: The ED_{10} is a geometric mean of the four data sets. The ED_{10} was extrapolated from the oral exposure route to the inhalation route.

Source: U.S. Environmental Protection Agency, 1992. IRIS, Integrated Risk Information System. Online. Cincinnati, OH: U.S. Environmental Protection Agency, Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.
[b]Estimated.
[c]High-dose data were not used in estimate of potency because of the high incidence of mortality.
[d]Experimental dose (mg/kg/day)x(no. treatment days per wk/7 days per wk)x(le/Le).
[e]Transformed animal dose (mg/kg/day)/(human body weight/animal body weight)$^{(1/3)}$.

Elements of Hazard Ranking

Chemical Name: chloroform

CAS Number: 67-66-3

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): 0.76 per (mg/kg)/day

Reference: National Cancer Institute, 1976. Report on carcinogenesis bioassay of chloroform. Available from: NTIS, Springfield, VA. PB-264018.

Exposure route:	oral (gavage)			
Species:	mouse			
Strain:	B6C3F1			
Sex:	M, F			
Vehicle or physical state:	corn oil			
Body weight:[b]	0.03 kg			
Duration of treatment (Ie):	546 days			
Duration of study (Le):	644 to 651 days			
Lifespan of animal (L):[c]	730 days			
T2arget organ:	liver			
Tumor type:	hepatocellular carcinoma			
Experimental dose/exposure:[d]	477 mg/kg	238 mg/kg	0 mg/kg	(females)
	277 mg/kg	138 mg/kg	0 mg/kg	(males)
Transformed animal dose (mg/kg/day):[e]	250	124	0	(females)
	157	78	0	(males)
Human equivalent dose (mg/kg/day):[f]	19.9	9.9	0.0	(females)
	12.5	6.2	0.0	(males)
Tumor incidence:	39/41	36/45	0/20	(females)
	44/45	18/50	1/18	(males)

Comments: The ED_{10} is a geometric mean of males and females. An extrapolation from the oral to an inhalation exposure route was carried out.

Source: U.S. Environmental Protection Agency, 1988. Evaluation of the potential carcinogenicity of chloroform. OHEA-C-073-54. Washington, DC: Office of Health and Environmental Assessment.

U.S. Environmental Protection Agency, 1992. IRIS, Integrated Risk Information System. Online. Cincinnati, OH: U.S. Environmental Protection Agency, Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably (carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for

humans.
[b]Reported.
[c]Assumed.
[d]Exposures were 5 days/wk. Duration of the study was assumed to be 647 days.
[e]Experimental dose (mg/kg/day)x(no. treatment days per wk/7 days per wk)x(Ie/Le).
[f]Transformed animal dose (mg/kg/day)/(human body weight/animal body weight)$^{(1/3)}$.

Elements of Hazard Ranking

Chemical Name: chloromethyl methyl ether

CAS Number: 107-30-2

Weight-of-Evidence Classification:[a,b] A

Estimate of Potency ($1/ED_{10}$): See comments

Comments: The available data are inadequate for estimating an ED_{10}.

Source: U.S. Environmental Protection Agency, 1988. Evaluation of the potential carcinogenicity of chloromethyl methyl ether. OHEA-C-073-55. Washington, DC: Office of Health and Environmental Assessment.

U.S. Environmental Portection Agency, 1992. IRIS, Integrated Risk Information System Online. Cincinnati, OH: U.S. Environmental Protection Agency, Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

[b]Technical grade chloromethyl methyl ether is contaminated with 1%-8% bis(chloromethyl) ether, which is a known human carcinogen; hence, the human evidence for this compound and the hazard ranking are based on the evidence for bis(chloromethyl) ether.

Elements of Hazard Ranking

Chemical Name: chloroprene

CAS Number: 126-99-8

Weight-of-Evidence Classification:[a] see comments

Estimate of Potency ($1/ED_{10}$): see comments

Comments: The Office of Research and Development/Office of Health and Environmental Assessment is currently evaluating the carcinogenic evidence on chloroprene. A draft preliminary assessment indicates that the weight-of-evidence classification is such that this chemical may be considered a "nonthreshold" hazardous air pollutant. This evaluation is currently undergoing internal peer review, thus, the exact placement of this chemical with respect to other "nonthreshold" HAPs can not be determined at this time.

Source: U.S Environmental Protection Agency, 1992. Preliminary assessment evaluation of the potential carcinogenicity of chloroprene. First draft. Prepared by the Chemical Hazard Evaluation Program, Health and Safety Research Division, ORNL, for the Office of Health and Environmental Assessment, Human Health Assessment Group.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

Elements of Hazard Ranking

Chemical Name: chromium (total) (+3 and +6)

CAS Number: not applicable

Weight-of-Evidence Classification:[a] A

Estimate of Potency ($1/ED_{10}$): 390 per (mg/kg)/day

Reference: Mancuso, T.F., 1975. Consideration of chromium as an industrial carcinogen. International Conference on Heavy Metals in the Environment. Toronto, Ontario, Canada. Oct. 27-31. (Cited in Towill, L.E.; Shriner, L.R.; Drury, J.S.; Hammons, A.S.; Holleman, J.W., 1978. Reviews of the environmental effects of pollutants: III. chromium. Prepared for Health Effects Research Laboratory, Office of Research and Development. U.S. Environmental Protection Agency, Cincinnati, OH. Report no. ORNL/EIS-80, EPA 600/1-78-023.)

Exposure route:	dermal + inhalation + oral	
Species:	human	
Sex:	M	
Vehicle or physical state:	air/dust	
Body weight:[b]	70 kg	
Duration of exposure (le):[c]	< 45 yr	
Duration of study (Le):	43 yr	
Lifespan (L):[b]	70 yr	
Target organ:	respiratory tract (lung)	
Experimental dose/exposure:	from < 1.0 to > 8.0 mg/m^3	0.0 mg/m^3
Equivalent dose (mg/kg/day):	from < 0.041 to > 0.33	0.0
Mortality rate:	39/332	1.6/1000[c]

Comments: The ED_{10} is estimated by extrapolation of the unit risk (1.2E-2 per $\mu g/m^3$) to the dose causing 10 percent mortality from lung cancer. The dose-response data for lung cancer is for exposure to both trivalent and hexavalent chromium.

It is prudent to consider both trivalent and hexavalent states together. The Health Assessment Document (U.S. EPA, 1984; EPA-600/8-83-014F) identifies hexavalent chromium as a known human carcinogen (Group A) based on epidemiologic data of chromate workers exposed to both hexavalent and to trivalent chromium, and on positive toxicologic data from rats following subcutaneous injection or intrabronchial, intrapleural, intramuscular, or intratracheal implantation of hexavalent chromium compounds.

The testing of trivalent chromium compounds is more limited and is considered inconclusive for assessment at this time. Although available toxicological studies have not shown dose-related increases in carcinogenic response, there is reason for concern for trivalent compounds. Trivalent chromium compounds exhibit genotoxic potential. Trivalent chromium compounds, also, can enter living cells through active transport, although it is recognized that the passive transfer of hexavalent chromium preferentially leads to greater intracellular accumulation. The in vivo reduction of Cr+6 to Cr+3 is believed to be important in chromium's mechanism of carcinogenicity. Additional concern about trivalent chromium compounds from evidence of oxidation to the hexavalent state under certain

chromium (total) (+3 and +6) continued

environmental conditions (Barlett, 1991. Environment Health Perspectives 92:17-24).

Source: U.S. Environmental Protection Agency, 1988. Health assessment document for chromium. EPA-600/8-83-014F. Washington, DC: Office of Health and Environmental Assessment.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.
[b]Estimated.
[c]Based on estimate that exposure period=0.65 of lifetime.
[d]Estimated; based on 1964 U.S. Vital Statistics.

pages 149-150 is repeat

Elements of Hazard Ranking

Chemical Name: chrysene

CAS Number: 218-01-9

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): see comments

Comments: The available data inadequate for estimating an ED_{10}.

Source: U.S. Environmental Protection Agency, 1992. IRIS, Integrated Risk Information System. Online. Cincinnati, OH: U.S. Environmental Protection Agency, Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

Elements of Hazard Ranking

Chemical Name: coke oven emissons

CAS Number: 8007-45-2

Weight-of-Evidence Classification:[a] A

Estimate of Potency ($1/ED_{10}$): 1.5 (mg/kg)/day

Reference: Land, C.E., 1976. Presentation at OSHA hearing on coke oven standards. Mazumdar, S; Redmond, C: Sollecito, W.; Sussman, N., 1975. An epidemiologic study of exposure to coal-tar-pitch volatiles among coke oven workers. APCA J. 25(4): 382-389.

Exposure route:	inhalation
Species:	human
Sex:	M
Vehicle or physical state:	ambient air
Body weight:[b]	70 kg
Target organ:	respiratory system

Comments: The ED_{10} is derived using the multistage procedure which best fit the human data on lung cancer mortality in coke oven workers. This procedure was employed, rather than a linear extrapolation of the unit risk, for several reasons. First, the dose-response function has a much smaller slope at lower doses than at higher doses (e.g., at 10% incidence point). Second, the ED_{10} reflects a maximum-likelihood estimate rather than an estimate extrapolated from upper bound risk (as represented by the unit risk for coke oven emissions). The ED_{10} represents a geometric mean of estimates obtained for four latency periods (0, 5, 10, and 15 years).

Source: U.S. Environmental Protection Agency, 1988. Evaluation of the potential carcinogenicity of coke oven emissions. OHEA-C-073-69. Washington, DC: Office of Health and Environmental Assessment.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.
[b]Estimated.

Elements of Hazard Ranking

Chemical Name: cresols/cresylic acid (isomers and mixtures)

CAS Number: 131-97-73

Weight-of-Evidence Classification:[a] Footnote "b"

Estimate of Potency ($1/ED_{10}$): see comments

Comments: The available data for o-, m-, and p-cresol were inadequate for inferring an ED_{10} for cresols/cresylic acid compounds.

Source: U.S. Environmental Protection Agency, 1992. IRIS, Integrated Risk Information System. Online. Cincinnati, OH; U.S. Environmental Protection Agency, Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.
[b]The weight-of-evidence is inferred from the individual isomers o-, m-, p-cresol. EPA has classified these isomers as having a weight-of-evidence of "C, possibly carcinogenic to humans."

Elements of Hazard Ranking

Chemical Name: cresols (o-, m-, p-)

CAS Number: 95-48-7 (o-cresol), 108-39-4 m-cresol), 106-44-5 (p-cresol)

Weight-of-Evidence Classification:[a] C

Estimate of Potency ($1/ED_{10}$): see comment

Comments: The available data are inadequate for estimating an ED_{10}.

Source: U.S. Environmental Protection Agency, 1992. IRIS, Integrated Risk Information System. Cincinnati, OH: U.S. Environmental Protection Agency, Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

Elements of Hazard Ranking

Chemical Name: diazomethane

CAS Number: 334-88-3

Weight-of-Evidence Classification:[a] see comments

Estimate of Potency ($1/ED_{10}$): see comments

Comments: The Office of Research and Development/Office of Health and Environmental Assessment is currently evaluating the carcinogenic evidence on diazomethane. A draft preliminary assessment indicates that the weight-of-evidence classification is such that this chemical may be considered a "nonthreshold" hazardous air pollutant. This evaluation is currently undergoing internal peer review, thus, the exact placement of this chemical with respect to other "nonthreshold" HAPs can not be determined at this time.

Source: U.S Environmental Protection Agency, 1992. Preliminary assessment evaluation of the potential carcinogenicity of diazomethane. First draft. Prepared by the Chemical Hazard Evaluation Program, Health and Safety Research Division, ORNL, for the Office of Health and Environmental Assessment, Human Health Assessment Group.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

Elements of Hazard Ranking

Chemical Name: dibenz(ah)anthracene

CAS Number: 53-70-3

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): See comments

Comments: The available data are inadequate for estimating an ED_{10}.

Source: U.S. Environmental Protection Agency, 1992. IRIS, Integrated Risk Information System. Online. Cincinnati, OH: U.S. Environmental Protection Agency, Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

Elements of Hazard Ranking

Chemical Name: 1,2:7,8-dibenzopyrene

CAS Number: 189-55-9

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): see comments

Comments: The available data are inadequate for estimating an ED_{10}.

Source: U.S. Environmental Protection Agency, 1988. Evaluation of the potential carcinogenicity of 1,2:7,8-dibenzopyrene. OHEA-C-073-79. Washington, D.C.: Office of Health and Environmental Assessment.

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

Elements of Hazard Ranking

Chemical Name: 1,2-dibromo-3-chloropropane (DBCP)

CAS Number: 96-12-8

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): 79

Reference: National Toxicology Program, 1982. Carcinogenesis bioassay of 1,2-dibromo-3 -chloropropane (CAS No. 96-12-8) in F344 rats and B6C3F1 mice (inhalation study). NTP Technical Report No. 81-21. DHHS(NIH) 82-1762.

Exposure route:	inhalation		
Species:	rat		
Strain:	F344		
Sex:	M, F		
Vehicle or physical state:	vapor		
Body weight:[b]	0.32 (males)	0.22 (females)	
Duration of treatment (le):	84 wks (high dose)	104 wks (low dose)	107 wks (controls)
Duration of study (Le):	84 wks (high dose)	104 wks (low dose)	107 wks (controls)
Lifespan of animal (L):[c]	104 wks		
Target organ:	nasal cavity; tongue; pharynx		
Tumor type:	carcinoma, adenocarcinoma, papilloma, adenoma		
Experimental doses/exposure (ppm):	3.0 (30 mg/m^3)	0.6 (5.9 mg/m^3)	0.0
Transformed animal doses (mg/kg/day):[d]	1.81	0.72	0.0 (males)
	1.63	0.60	0.0 (females)
Human equivalent doses (mg/kg/day):[e]	0.30	0.12	0.0 (males)
	0.27	0.10	0.0 (females)
Tumor incidence:	40/48	42/50	0/50 (males)
	45/48	29/50	1/50 (females)

Comments: The high dose group experienced early mortality and doses are corrected accordingly.

Source: Memorandum from J. Jinot (OHEA) to D. Pagano (OAQPS), November 12, 1992.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

[b]Estimated.

[c]Estimated.

[d]First convert experimental dose in ppm to mg/m^3: 0.041 x molecular weight of 1,2-dibromo-3-chloropropane x concentration (ppm). Calculate preliminary transformed dose (mg/kg/day) based on breathing rate and animal weight: concentration (mg/m^3) x breathing rate ([0.105(W/0.113)$_{2/3}$ m^3/d] for rats)/animal weight (kg). Determine final transformed dose by adjusting for duration of study and discontinuous exposure: transformed dose (mg/kg/day) x duration of treatment (days)/duration of

study (days)x5 (treatment days/wk)/7 (days/wk)x6 (treatment hr/day)/24 (hr/day). The high dose was adjusted for less than lifetime followup, $(Le/L)^3$.

[e]Transformed animal dose (mg/kg/day)/(human body weight/animal body weight)$^{(1/3)}$.dExperimental dose

Elements of Hazard Ranking

Chemical Name: 1,4-dichlorobenzene (pDCB)

CAS Number: 10-64-67

Weight-of-Evidence Classification: B2

Estimate of Potency ($1/ED_{10}$): 0.13 per (mg/kg)/d

Reference: NTP, 1986. Toxicology and carcinogenesis studies of 1,4-Dichlorobenzene in F344/N rats and B6CF1, mice -- Galley draft. U.S. DHHS, PHS. NIH Tech. Rep. Ser. No 319.

Exposure route:	oral		
Species	mice		
Strain:	B6C3F1		
Sex:	M		
Vehicle or physical state:	gavage		
Body weight:[b]	0.042 kg		
Duration of treatment (le):	103 weeks		
Duration of study (Le):	104 weeks		
Lifespan of animal (L):[c]	104 weeks		
Target organ:	liver		
Tumor type:	adenoma and carcinoma		
Experimental doses/exposure (mg/kg/day):	600	300	0
Transformed animal doses[d] (mg/kg/day):	424.45	212.23	0
Human equivalent doses[e] (mg/kg/day):	35.89	17.94	0
Tumor incidence:	40/42	22/40	17/44

Comments: The ED_{10} is based on oral data; an estimate of potency from inhalation exposure is not currently available.

Source: U.S. Environmental Protection Agency, 1987. Health effects assessment for dichlorobenzenes. EPA/600/8-88/0.28. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

[b]Estimated.

[c]Estimated.

[c]Experimental dose (mg/kg/d) x (5 treatment days per week/7 days per week) x (le/Le).

[e]Transformed animal dose /(human body weight/animal body weight) $^{(1/3)}$.

Elements of Hazard Ranking

Chemical Name: 3,3'-dichlorobenzidine

CAS Number: 91-94-1

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): 7.5 per (mg/kg)/day

Reference: Stula, E.F.; Sherman, H.; Zapp, J.A., Jr.; Clayton, J.W., Jr., 1975. Experimental neoplasia in rats from oral administration of 3,3'-dichlorobenzidine, 4,4'-methylene-bis(2-chloroaniline), and 4,4'-methylene-bis-(2-methylaniline). Toxicol. Appl. Pharmacol. 31: 159-176.

Exposure route:	oral	
Species:	rat	
Strain:	Charles River-CD	
Sex:	F	
Vehicle or physical state:	diet	
Body weight:[b]	0.35 kg	
Duration of treatment (le):	349 days	
Duration of study (Le):[b]	349 days	628 days
Lifespan of animal (L):[b]	730 days	
Target organ:	mammary gland	
Tumor type:	adenocarcinoma	
Experimental dose/exposure:	1000 ppm	0 ppm
Transformed animal dose (mg/kg/day):[c]	50	0
Human equivalent dose (mg/kg/day):[d]	8.5	0.0
Tumor incidence:	26/44	3/44

Comments: The ED_{10} is based on data for oral exposure; an estimate of potency for inhalation exposure is not currently available.

Source: U.S. Environmental Protection Agency, 1988. Evaluation of the potential carcinogenicity of 3,3'-dichlorobenzidine. OHEA-C-073-81. Washington, DC: Office of Health and Environmental Assessment.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

[b]Estimated.

[c]Experimental dose (ppm)x0.05 (fraction of rat's body weight consumed in food/day).

[d]Transformed animal dose (mg/kg/day)/(human body weight/animal body weight)$^{(1/3)}$.

Elements of Hazard Ranking

Chemical Name: 1,1-dichloro-2,2-bis(p-chlorophenyl)ethylene (DDE)

CAS Number: 72-55-9

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): 1.9 per (mg/kg)/day

Reference: National Cancer Institute, 1978. Bioassays of DDT, TDE, and p,p'-DDE for possible carcinogenicity. U.S. Department of Heath, Education, and Welfare; Public Health Service; National Institutes of Health. Publication no. NCI-CG-TR-131, p.117.

Exposure route:		oral		
Species:		mouse		
Strain:		B6C3F1		
Sex:		F/M		
Vehicle or physical state:		diet		
Body weight:[a]		0.03 kg		
Duration of treatment (le):		546 days		
Duration of study (Le):		644 days		
Lifespan of animal (L):[b]		730 days		
Target organ:		liver		
Tumor type:		hepatocellular carcinoma		
Experimental dose/exposure:		261 ppm	148 ppm	0.0 ppm
Transformed animal dose (mg/kg/day):[c]		19.7	11.2	0.0
Human equivalent dose (mg/kg/day):[d]		1.5	0.8	0.0
Tumor incidence:	females	34/48	19/47	0/19
	males	17/47	7/41	0/19

Reference: Tomatis, L; Turusov, V.; Charles, R.T.; and Boiocchi, M., 1974. Effect of long-term exposure to 1,1-dichloro-2,2-bis(p-chlorophenyl)ethylene, to 1,1-dichloro-2,2-bis(p-chlorophenyl)ethane, and to the two chemicals combined on CF-1 mice. J. Natl. Cancer Inst. 52:883-891.

Exposure route:	oral
Species:	mouse
Strain:	CF-1
Sex:	F/M
Vehicle or physical state:	diet
Body weight:[b]	0.03 kg
Duration of treatment (le):	130 weeks
Duration of study (Le):	130 weeks
Lifespan of animal (L):[b]	130 weeks
Target organ:	liver
Tumor type:	hepatomas

72-55-9 1,1-dichloro-2,2-bis(p-chlorophenyl)ethylene (DDE) (continued)

Experimental dose/exposure:		250 ppm	0.0 ppm
Transformed animal dose (mg/kg/day):[c]		32.5	0.0
Human equivalent dose (mg/kg/day):[d]		2.45	0.0
Tumor incidence:	females	54/55	1/90
	males	39/53	33/98

Reference: Rossi, L.; Barbieri, O.; Sanguineti, M.; Cabral, J.R.P.; Bruzzi, P.; Santi, L., 1983. Carcinogenicity study with technical-grade DDT and DDE in hamsters. Cancer Res. 43:776-781.

Exposure route:		oral		
Species:		hamster		
Strain:		Syrian golden		
Sex:		F/M		
Vehicle or physical state:		diet		
Body weight:[b]		0.12 kg		
Duration of treatment (le):		128 weeks		
Duration of study (Le):		128 weeks		
Lifespan of animal (L):[b]		128 weeks		
Target organ:		liver		
Tumor type:		neoplastic nodules		
Experimental dose/exposure:		100 ppm	500 ppm	0.0 ppm
Transformed animal dose (mg/kg/day):[c]		80	40	0.0
Human equivalent dose (mg/kg/day):[d]		9.57	4.79	0.0
Tumor incidence:	females	5/24	4/26	0/31
	males	8/24	7/15	0/10

Comments: The ED_{10} is based on data for oral exposure; an estimate of potency fot the inhalation route in not currently available. The ED_{10} is based on a geometric mean of the six data sets.

Source: U.S. Environmental Protection Agency, 1988. Evaluation of the potential carcinogenicity of DDE. OHEA-C-073-74. Washington, DC: Office of Health and Environmental Assessment.

U.S. Environmental Protection Agency, 1992. IRIS, Integrated Risk Information System. Online. Cincinnati, OH: U.S. Environmental Protection Agency, Office of Health and Environmental Assessment, Environmental Assessment and Criteria Office.

U.S. Environmental Protection Agency, 1985. The Assessment of the Carcinogenicity of Dicofol (Kelthane), DDT, DDE, and DDD(TDE). PB87-110904. Washington, D.C.: U.S. Environmental Protection Agency, Office of Health and Environmental Assessment, Carcinogen Assessment Group.

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

[b]Estimated.

72-55-9 1,1-dichloro-2,2-bis(p-chlorophenyl)ethylene (DDE) (continued)

[c]Experimental dose (ppm) x an empirically derived food factor corresponding to the fraction of body weight that is consumed each day as food (0.13 in mice, 0.08 in hamsters).
[d]Transformed animal dose (mg/kg/day)/(human body weight/animal body weight)$^{(1/3)}$.

Elements of Hazard Ranking

Chemical Name: dichloroethyl ether [bis(2-chloroethyl)ether]

CAS Number: 111-44-4

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): 6.4 per (mg/kg)/day

Reference: Innes, J.R.M.; Ulland, B.M.; Valerio M.G.; et al., 1969. Bioassay of pesticides and industrial chemicals for tumorigenicity in mice: a preliminary report. J. Natl. Cancer Inst. 42: 1101-1114.

Exposure route:	oral	
Species:	mouse	
Strain:	(C57BL6 x C3H/Anf)F1	
Sex:	M	
Vehicle or physical state:	diet	
Body weight:[b]	0.03 kg	
Duration of treatment (le):	554 days	
Duration of study (Le):	560 days	567 days
Lifespan of animal (L):[b]	730 days	
Target organ:	liver	
Tumor type:	hepatoma	
Experimental dose/exposure:	300 ppm[c]	0 ppm
Transformed animal dose (mg/kg/day):[d]	18.6	0.0
Human equivalent dose (mg/kg/day):[e]	2.94	0.0
Tumor incidence:		14/16 8/79

Comments: An extrapolation was made from the oral to the inhalation route of exposure.

Source: U.S. Environmental Protection Agency, 1988. Evaluation of the potential carcinogenicity of bis(2-chloroethyl)ether. OHEA-C-073-43. Washington, DC: Office of Health and Environmental Assessment.

U.S. Environmental Protection Agency, 1992. IRIS, Integrated Risk Information System. Online. Cincinnati, OH: U.S. Environmental Protection Agency, Office of Health and Environmental Assessment, Environmental Assessment and Criteria Office.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.
[b]Estimated.
[c]Reported.

111-44-4 dichloroethyl ether (continued)

[d]100 mg/kg of bis(2-chloroethyl)ether was given in distilled water for 22 days, resulting in a total of 100 mg/kg x 22 days=2200 mg/kg. Subsequently, 300 ppm bis(2-chloroethyl)ether was provided in the food source for the next 538 days. The total dose during this period was 300 ppm x 0.13 (fraction of animal's body weight consumed in food per day)x538 days=20,982 mg/kg. Therefore, the total amount of bis(2-chloroethyl)ether administered was 2200 mg/kg+20,982 mg/kg=23,182 mg/kg. This represents a dose of 41.4mg/kg/day (23,182 mg/kg/560 days). Transformed animal doses were further adjusted for less than lifetime followup: $(560/730)^3$.

[e]Transformed animal dose (mg/kg/day)/(human body weight/animal body weight)$^{(1/3)}$.

Elements of Hazard Ranking

Chemical Name: 1,3-dichloropropene (Telone II)

CAS Number: 542-75-6

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): see comments

Comments: The available data are inadequate for estimating an ED_{10}.

Source: U.S Environmental Protection Agency, 1992. IRIS, Integrated Risk Information System. Online. Cincinnatii, OH: U.S. Environmnetal Protection Agency, Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

Elements of Hazard Ranking

Chemical Name: Dichlorovos (DDVP)

CAS Number: 62-73-7

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): 1.7 per (mg/kg)/d

Reference: National Toxicology Program, 1968a. Two-year mouse gavage study. Unpublished report prepared by Southern Research Institute, May 23. Study No. 05049.
National Toxicology Program (NTP), 1968b. Two-year gavage study in rats. Unpublished report prepared by Southern Research Institute, May 23. Study No. 05049.

Exposure route:	gavage						
Species:	mouse, rat						
Strain:	B6C3F1 (mouse), F344 (rat)						
Sex:	F (mouse), M (rat)						
Vehicle or physical state:	liquid						
Body weight:[b]	0.04 kg. (mouse), 0.35 kg. (rat)						
Duration of treatment (le):	104 weeks						
Duration of study (Le):	104 weeks						
Lifespan of animal:[c]	104 weeks						
Target organ:	forestomach (mouse); pancreas, blood system (rat)						
Tumor type:	papilloma, squamous and squamous cell carcinoma (mouse); acinar adenoma and leukemia (rat)						
Experimental doses/exposure (ppm):	mouse			rat			
	280	140	0	160	80	0	
Transformed animal doses (mg/kg/day):	20	10	0	8	4	0	
Human equivalent doses[d] (mg/kg/day):	3.15	1.58	0	43	0.72	0	
Tumor incidence:	19/50	6/49	5/49	30/50	24/49	16/50	(pancreas)
				21/50	20/50	11/50	(leukemia)

Comments: The ED10 is based on a geometric mean of the dose causing a 10 percent incidence of tumors of the forestomach (mouse), pancreas (rats), and leukemia (rat) individually. The ED_{10} is based on data for the oral route; an estimate of potency for the inhalation route is not currently available.

Source: U.S. Environmental Protection Agency, 1992. IRIS, Integrated Risk Information System. Online. Cincinnati, OH: U.S. Environmental Protection Agency, Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.
[b]Estimated.
[c]Estimated.

62-73-7 dichlorvos (cont.)

[d]Transformed animal dose /(human body weight/animal body weight)$^{(1/3)}$. Humans were assumed to weight 60 kg.

Elements of Hazard Ranking

Chemical Name: diethyl sulfate

CAS Number: 64-47-5

IARC Classification:[1] 2A

Comments: IARC has determined "sufficient evidence" exists that occupational exposure to strong-acid mists containing sulfuric acid is carcinogenic to humans (Group 1). Support for this conclusion is primarily based on epidemiologic studies where sulfuric acid was the most common exposure. Several reviewed studies assessed exposures in the manufacture and processing of isopropanol and ethanol. Sulfuric acid and dialkyl sulfate exposures are common in these studies. Excess upper respiratory (larynx) cancer risks have been noted in two cohort studies. It it difficult to separate exposure to diethyl sulfate from that of other exposures in these studies. One case-control study has examined the relationship between brain cancer and exposure to diethyl sulfate and reports a positive association.

With respect to diethyl sulfate, IARC classifies the human evidence on diethyl sulfate as "inadequate evidence for carcinogenicity to humans." A conclusion of "sufficient evidence for carcinogenicity to animals" is based on local (subcutaneous injection) and forestomach (gavage) tumors in rats. Prenatal exposure (oral) in rats has produced nervous sytem tumors among offspring. Diethyl sulfate is an alkylating agent causing genetic damage *in vitro*.

Source: International Agency for Research on Cancer, 1987. IARC monographs on the evaluation of carcinogenic risks to humans. Overall evaluations of carcinogenicity: an updating of IARC monographs volumes 1 to 42. Supplement 7: 198.

International Agency for Research on Cancer, 1992. IARC monographs on the evaluation of carcinogenic risks to humans. Occupational exposures to mists and vapours from strong inorganic acids; and other industrial chemicals. Vol. 54.

---

[a]1-the agent is carcinogenic to humans, 2A-the agent is probably carcinogenic to humans (limited human evidence), 2B-the agent is probably carcinogenic to humans (limited evidence in humans in the absence of sufficient evidence in animals, or inadequate human evidence/non-existent human data and sufficient evidence in animals), 3-the agent is not classifiable as to its carcinogenicity to humans, 4-the agent is probably not carcinogenic to humans.

Elements of Hazard Ranking

Chemical Name: 3,3'-dimethoxybenzidine

CAS Number: 119-90-4

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): 3.1 per (mg/kg)/day

Reference: Hadidian, Z.; Fredrickson, T.N.: Weisburger, E.K.; Weisburger, J.H.; Glass, R.M.; Mantel, N., 1986. Tests for chemical carcinogens: report on the activity of derivatives of aromatic amines, nitrosoamines, quinolines, nitroalkanes, amides, epoxides, aziridines and purine antimetabolites. J. Natl. Cancer Inst. 41:985-1039.

Exposure route:	oral						
Species:	rat						
Strain:	Fisher 344						
Sex:	M, F						
Vehicle or physical state:	steroid suspending vehicle (SSV) polysorbate 80 of NaCl, sodium carboxymethyl cellulose, polysorbate 80, benzyl alcohol, and water						
Body weight (kg):[b]	0.283	0.313	0.302	0.304	0.365	0.365	0.381
Duration of treatment (le):364 days							
Duration of study, (Le):	428	477	451	510	558	558	558
Lifespan of animal (L):[c]	730 days						
Target organ:	skin						
Tumor type:	squamous and basal cell carcinomas						
Experimental dose/exposure:	30.0	10.0	3.0	1.0	0.3	0.1	0.0
Transformed animal dose (mg/kg/day):[d]	64.4	17.4	5.73	1.68	0.38	0.13	0.0
Human equivalent dose (mg/kg/day):[e]	10.3	2.87	0.93	0.27	0.065	0.022	0.0
Tumor incidence:	3/6	8/29	1/6	1/6	0/6	0/6	2/653

Comments: The ED_{10} is based on oral data; an estimate of the ED_{10} for the inhalation route is not currently available. The Hadidian et al. study is limited by inadequate reporting of control group and small sample size. For example, tumor incidences of historical controls were used as the referents. Although limited, the Hadidian et al. study is considered a more adequate study in which to estimate the unit risk than Sullakumar et al. (as reported in U.S. EPA, 1987, Health and environmental effects profile for 3,3'-dimethoxybenzidine, EPA/600/x-87/101) due to larger number of treatment groups and the possibly greater sensitivity of rats to the effects of 3,3'-dimethoxybenzidine.

The estimate of the ED_{10} should be considered preliminary. National Toxicology Program (NTP) released results in 1990 of a drinking water study in male and female F344 rats with exposure to 3,3'-dimethoxybenzidine. This study needs evaluating in context of making quantitative inferences.

Source: U.S. Environmental Protection Agency, 1988. Evaluation of the potential carcinogenicity of 3,3'-dimethoxybenzidine. OHEA-C-073-89. Washington, DC: Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office.

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.
[b]Reported.
[c]Estimated.
[d]Experimental dose (mg/kg)/(weight of animal (kg)x5 (no. treatment days per wk/7 days per wk)x(le/Le)x(Le/L)^3. Average of 497 days for Le.
[e]Transformed animal dose (mg/kg/day)/(human body weight/animal body weight)$^{(1/3)}$. A body weight of 0.329 kg was used as an average in the calculations.

Elements of Hazard Ranking

Chemical Name: dimethyl aminoazobenzene

CAS Number: 60-11-7

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): see comments

Comments: The available data are inadequate for estimating an ED_{10}.

Source: U.S. Environmental Protection Agency, 1988. Evaluation of the potential carcinogenicity of dimethylaminoazobenzene. OHEA-C-073-91. Washington, DC: Office of Health and Environmental Assessment.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

Elements of Hazard Ranking

Chemical Name: 7,12-dimethylbenz(a)anthracene

CAS Number: 57-97-6

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): see comments

Comments: The available data are inadequate for estimating an ED_{10}.

Source: U.S. Environmental Protection Agency, 1988. Evaluation of the potential carcinogenicity of 7,12-dimethylbenz(a)anthracene. OHEA-C-073-92. Washington, DC: Office of Health and Environmental Assessment.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans,
D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

Elements of Hazard Ranking

Chemical Name: 3,3'-dimethylbenzidine

CAS Number: 119-93-7

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): 27 per (mg/kg)/day

Reference: Griswold, D.P, Jr.; Casey, A.E.; Weisburger, E.K.; Weisburger, J.H., 1968. The carcinogenicity of multiple intragastric doses of aromatic and heterocyclic nitro or amino derivatives in young female Sprague-Dawley rats. Cancer Res. 28: 924-933.

Exposure route:	gavage	
Species:	rat	
Strain:	Sprague-Dawley	
Sex:	F	
Vehicle or physical state:	oil	
Body weight:[b]	0.35 kg	
Duration of treatment (le):	30 days[c]	
Duration of study (Le):	314 days	
Lifespan of animal (L):	730 days	
Target organ:	mammary gland	
Tumor type:	carcinoma	
Experimental dose/exposure:	500 mg (total lifetime dose)	0
Transformed animal dose (mg/kg/day):[d]	4.5	0.0
Human equivalent dose (mg/kg/day):[e]	0.8	0.0
Tumor incidence:[f]	3/16	4/132

Comments: The ED_{10} is based on data for oral exposure; an estimate of potency for the inhalation route is not currently available.

Source: U.S. Environmental Protection Agency, 1988. Evaluation of the potential carcinogenicity of 3,3'-dimethylbenzidine. OHEA-C-073-93 Washington, DC: Office of Health and Environmental Assessment.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

[b]Estimated.

[c]Ten doses, 3 days apart.

[d]Experimental dose (mg/rat)/body weight (0.35 kg)/duration of study (days).

[e]Transformed animal dose (mg/kg/day)/(human body weight/animal body weight)$^{(1/3)}$.

[f]Tumor incidence data: Control incidence is based on the study report. Although distribution of tumor types was not specified for the treated rats, the more conservative approach is to assume four carcinomas were spread among the three rats with total mammary lesions.

Elements of Hazard Ranking

Chemical Name: dimethylcarbamoyl chloride

CAS Number: 79-44-7

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): 500 per (mg/kg)/day

Reference: Sellakumar, A.R.; Laskin, S; Kuschner, M.; Rusch, G.; Katz, G.V.; Snyder C.A.; Albert, R.E., 1980. Inhalation carcinogenesis of dimethylcarbamoyl chloride in Syrian Golden hamsters. J. Environ. Pathol. Toxicol. 4(1): 107-115.

Exposure route:	inhalation	
Species:	hamster	
Strain:	Syrian Golden	
Sex:	M	
Vehicle or physical state:	vapor	
Body weight:[b]	0.12 kg	
Duration of treatment (le):[b]	800 days	
Duration of study (Le):	812 days	
Lifespan of animal (L):	812 days	
Target organ:	nasal tract	
Tumor type:	squamous cell carcinoma	
Experimental dose/exposure:	1.0 ppm	0.0 ppm
Transformed animal dose (mg/kg/day):[c]	0.11	0.0
Human equivalent dose (mg/kg/day):[d]	0.013	0.0
Tumor incidence:	50/99	0/170[e]

Comments: The ED_{10} is estimated from inhalation data. Estimates of the transformed animal dose (TAD) are based on calculations presented in EPA (1988); a breathing rate of 0.017 m^3/d was estimated for a 0.12 kg hamster. This breathing rate is low; U.S. EPA (1987; Recommendations for and Documentation of Biological Values for Use in Risk Assessment, EPA/600/6-87/008) suggests a 0.12 kg hamster has a breathing rate of approximately 0.10 m^3/d. Estimates of a TAD of 0.66 mg/kg/d and a HED of 0.07 mg/kg/d would be calculated based upon a breathing rate of 0.10 m^3/d.

Source: U.S. Environmental Protection Agency, 1988. Evaluation of the potential carcinogenicity of dimethylcarbamoyl chloride. OHEA-C-073-94. Washington, DC: Office of Health and Environmental Assessment.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

[b]Estimated.

79-44-7 dimethylcarbamoyl chloride (continued)

[c]First, convert experimental dose in (ppm) to (mg/m^3): 0.041x107.5 g/mol (molecular weight of dimethylcarbamoyl chloride) x concentration (ppm). Calculate preliminary transformed dose (mg/kg/day) based on breathing rate and animal weight: concentration (mg/m^3) x breathing rate 0.017 m^3/day)/animal weight (0.12 kg). Determine final transformed dose by adjusting for duration of the study and discontinuous exposure: transformed dose (mg/kg/day)x(le/Le)x5 (treatment days/wk)/7 (days/wk)x6 (treatment hr/day)/24 (hr/day).

Elements of Hazard Ranking

Chemical Name: dimethylformamide

CAS Number: 68-12-2

IARC Classification:[1] 2B

Comments: "Limited evidence for carcinogenicity to humans" is support by excess risk from testicular germ-cell tumors among workers repairing aircraft who had exposure to a solvent mixture containing 80% dimethylformamide (DMF). In addition, excess risk for cancers of the buccal cavity or pharynx (statistically significant) and lung (not statistically significant) among workers exposed to DMF at a plant manufacturing acrylic fibers (DMF and acrylonitrile exposures). No excess in testicular cancer was seen in this study. "Inadequate data" in animals was noted. In addition, increased frequency of chromosomal aberrations was observed in lymphocytes of industrial workers exposed to DMF but no increases in DMF-induced DNA damage, mutation or sister chromiatid exchanges are observed *in vitro*.

Source: International Agency for Research on Cancer, 1989. IARC monographs on the evaluation of carcinogenic risks to humans. Some organic solvents, resin monomers and related compounds, pigments and occupational exposures in paint manufactur and painting. Volume 47:171-196.

---

[a]1-the agent is carcinogenic to humans, 2A-the agent is probably carcinogenic to humans (limited human evidence), 2B-the agent is probably carcinogenic to humans (limited evidence in humans in the absence of sufficient evidence in animals, or inadequate human evidence/non-existent human data and sufficient evidence in animals), 3-the agent is not classifiable as to its carcinogenicity to humans, 4-the agent is probably not carcinogenic to humans.

Elements of Hazard Ranking

Chemical Name: 1,1-dimethylhydrazine

CAS Number: 57-14-7

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): 83 per (mg/kg/)/day

Reference: Toth, B., 1972. Comparative studies with hydrazine derivatives. Carcinogenicity of 1,1-dimethylhydrazine, unsymmetrical (1,1-DMH) in the blood vessels, lung, kidneys and liver of Swiss mice. Proc. Am. Assoc. Cancer 13.34.

Toth, B., 1973. 1,1-Dimethylhydrazine (unsymmetrical) carcinogenesis in mice. Light microscopic and ultrastructural studies on noeplastic blood vessles. J. Natl. Cancer Inst. 50(1): 181-194.

Exposure route:	oral	
Species:	mouse	
Strain:	Swiss	
Sex:	M	
Vehicle or physical state:	drinking water	
Body weight:[b]	0.03 kg	
Duration of treatment (le):	455 days (treated), 840 days (controls)	
Duration of study (Le):	455 days (treated), 840 days (controls)	
Lifespan of animal (L):[c]	840 days	
Target organ:	vascular system	
Tumor type:	angiosarcoma	
Experimental doses/exposure:	0.7 mg/day	0 mg/day
Transformed animal dose (mg/kg/day):[d]	2.76	0.0
Human equivalent dose (mg/kg/day):[e]	0.28	0.0
Tumor incidence:	42/50	2/110

Comments: The ED_{10} is based on oral data; an estimate of potency for the inhalation route is not currently available. The inhalation data were judged as limited for estimating an ED_{10} due to unavailable pathology on individual animals and contamination of 1,1-DMH with <0.1% dimethylnitrosamine.

Source: U.S. Environmental Protection Agency, 1984. Health and environmental effects profile for 1,1-dimethylhydrazine. EPA/600/X-84/134. Prepared by the Office of Health and of Health and Environmental Assessment, Environmental Criteria Assessment Office, Cincinnati, OH.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.
[b]Estimated.
[c]Estimated.

[d]Experimental dose (mg/kg/d) x (no. treatment days per week/7 days per week) x (le/Le).
[e]Transformed animal dose (mg/kg/d)/(human body weight/animal body weight) $^{(1/3)}$.

Elements of Hazard Ranking

Chemical Name: dimethyl sulfate

CAS Number: 77-78-1

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): see comments

Comments: The available data are inadequate for estimating an ED_{10}.

Source: U.S. Environmental Protection Agency, 1988. Evaluation of the potential carcinogenicity of dimethyl sulfate. OHEA-C-073-90. Washington, DC: Office of Health and Environmental Assessment.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

Elements of Hazard Ranking

Chemical Name: 2,4-dinitrotoluene

CAS Number: 121-14-2

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): 3.8 per (mg/kg)/day

Reference: National Cancer Institute, 1978. Bioassay of 2,4-dinitrotoluene for possible Carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series No. 54.

Exposure route:	oral		
Species:	rat		
Strain:	Fischer 344		
Sex:	M		
Vehicle or physical state:	diet		
Body weight:[b]	0.095 kg		
Duration of treatment (le):	546 days		
Duration of study (Le):	728 days		
Lifespan of animal (L):[c]	730 days		
Target organ:	skin and subcutaneous tissue		
Tumor type:	fibroma		
Experimental dose/exposure:	0.02% (200 ppm)	0.008% (80 ppm)	0.0% (0 ppm)
Transformed animal dose (mg/kg/day):[d]	7.4	2.9	0.0
Human equivalent dose (mg/kg/day):[e]	0.8	0.3	0.0
Tumor incidence:	13/49	7/49	0/71

Comments: The ED_{10} was based on data for oral exposure; an estimate of potency for the inhalation route is not currently available.

Source: U.S. Environmental Protection Agency, 1988. Evaluation of the potential carcinogenicity of 2,4-dinitrotoluene. OHEA-C-073-98. Washington, DC: Office of Health and Environmental Assessment.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

[b]Reported.

[c]Estimated.

[d]Experimental dose (ppm)x0.05 (fraction of rat's body weight consumed as food per day)x(le/Le)x$(Le/L)^3$.

[e]Transformed animal dose (mg/kg/day)/(human body weight/animal body weight)$^{(1/3)}$.

Elements of Hazard Ranking

Chemical Name: 1,2-diphenylhydrazine

CAS Number: 122-66-7

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): 4.3 per (mg/kg)/day

Reference: National Cancer Institute, 1978. Bioassay of hydrazobenzene for possible carcinogenicity. NCI Carcinogenesis Technical Report Series No. 92. DHEW publication no. (NIH) 78-1342.

Exposure route:	oral		
Species:	rat		
Strain:	Fischer 344		
Sex:	M		
Vehicle or physical state:	diet		
Body weight:[b]	0.35 kg (high dose)	0.40 kg (low dose)	0.40 kg (control)
Duration of treatment (le):	546 days		
Duration of study (Le):	742 days (high dose)	749 days (low dose)	760 days (control)
Lifespan of animal (L):[c]	760 days		
Target organ:	liver		
Tumor type:	hepatocellular carcinomas and neoplastic nodules		
Experimental dose/exposure:	0.03%	0.008%	0.0%
Transformed animal dose (mg/kg/day):[d]	11.0	2.9	0.0
Human equivalent dose (mg/kg/day):[e]	1.9	0.52	0.0
Tumor incidence:	37/49	13/49	6/95[f]

Comments: The ED_{10} was extrapolated from the oral to the inhalation exposure route.

Source: U. S. Environmental Protection Agency, 1992. IRIS, Integrated Risk Information System. Online. Cincinnati, OH: U.S. Environmental Protection Agency, Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

[b]Reported.

[c]Assumed.

[d]First convert the experimental dose given as a percent value to ppm (1%=10,000 ppm), then calculate experimental dose (ppm)x.05 (fraction of rat's body weight consumed as diet per day)x(le/Le).
[e]Transformed animal dose (mg/kg/day)/(human body weight/animal body weight)$^{(1/3)}$.
[f]Mean of low-dose and high-dose controls.

Elements of Hazard Ranking

Chemical Name: 1,4-dioxane (1,4-diethylene dioxide)
CAS Number: 123-91-1

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): 0.034 per (mg/kg)/day

Reference: National Cancer Institute, 1978. Bioassay of 1,4-dioxane for possible carcinogenicity. NCI Carcinogenesis Technical Report Series No. 80. DHEW publication no. (NIH) PB-285-711.

Exposure route:	oral		
Species:	rat		
Strain:	Osborne-Mendel		
Sex:	F		
Vehicle or physical state:	drinking water		
Body weight:[b]	0.35 kg		
Duration of treatment (le):	770 days		
Duration of study (Le):	770 days	770 days	819 days
Lifespan of animal (L):[c]	777 days	777 days	819 days
Target organ:	nasal turbinates		
Tumor type:	squamous cell carcinoma		
Experimental dose/exposure:	1.0%	0.5%	0.0%
Transformed animal dose (mg/kg/day):[d]	640	350	0
Human equivalent dose (mg/kg/day):[e]	109.4	59.84	0.0
Tumor incidence:	8/35	10/35	0/34

Comments: The ED_{10} was based on data for oral exposure; an estimate of potency for inhalation exposure was not currently available.

Source: U.S. Environmental Protection Agency, 1988. Evaluation of the potential carcinogenicity of 1,4-dioxane. OHEA-C-073-100. Washington, DC: Office of Health and Environmental Assessment.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

[b]Estimated.

[c]Assumed.

[d]NCI (1978) determined average daily doses from the mean consumption of dioxane solution per week at intervals during the second year of treatment. All transformed doses are provided directly from the reference.

[e]Transformzed animal dose (mg/kg/day)/(human body weight/animal body weight)$^{(1/3)}$.

Elements of Hazard Ranking

Chemical Name: epichlorohydrin

CAS Number: 106-89-8

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): 0.021 per (mg/kg)/day

Reference: Laskin, S; Sellakumar, A.R.; Kuschner, M.; Nelson, N.; LaMendole, S.; Rusch, G.M.; Katz, G.V.; Dulak, N.C.; Albert, R.E. (1980). Inhalation carcinogenicity of epichlorohydrin in non inbred Sprague-Dawley rats. J. Natl. Cancer Inst. 65: 751-755.

Exposure route:	inhalation		
Species:	rat		
Strain:	Sprague-Dawley		
Sex:	M		
Vehicle or physical state:	gas		
Body weight:[b]	0.5 kg		
Duration of treatment (le):	730 days		
Duration of study (Le):	730 days		
Lifespan of animal (L):[b]	730 days		
Target organ:	nasal cavity		
Tumor type:	carcinomas		
Experimental dose/exposure:	30 ppm	10 ppm	0 ppm
Human equivalent dose (mg/kg/day):[c]	5.8	1.9	0.0
Tumor incidence:	1/100	0/100	0/150

Comments: None.

Source: U.S. Environmental Protection Agency, 1992. IRIS, Integrated Risk Information System. Online. Cincinnati, OH: U.S. Environmental Protection Agency, Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

[b]Estimated.

[c]Experimental dose (ppm) x (5/7 treatment days) x (6/24 treatment hours/day) x (20 m^3/day-human's breathing rate) x (1/70 kg body weight).

Elements of Hazard Ranking

Chemical Name: 1,2-epoxybutane

CAS Number: 106-88-7

Weight-of-Evidence Classification:[a] see comments

Estimate of Potency ($1/ED_{10}$): see comments

Comments: The Office of Research and Development/Office of Health and Environmental Assessment is currently evaluating the carcinogenic evidence on 1,2-epoxybutane. A draft preliminary assessment indicates that the weight-of-evidence classification is such that this chemical may be considered a "nonthreshold" hazardous air pollutant. This evaluation is currently undergoing internal peer review, thus, the exact placement of this chemical with respect to other "nonthreshold" HAPs can not be determined at this time.

Source: U.S Environmental Protection Agency, 1992. Preliminary assessment evaluation of the potential carcinogenicity of 1,2-epoxybutane. First draft. Prepared by the Chemical Hazard Evaluation Program, Health and Safety Research Division, ORNL, for the Office of Health and Environmental Assessment, Human Health Assessment Group.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

Elements of Hazard Ranking

Chemical Name: ethyl acrylate

CAS Number: 14-08-85

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): 0.22 per (mg/kg)/d

Reference: NTP, 1986. Carcinogenesis studies of ethyl acrylate in F344/N rats 2nd B6C3F1 mice (Gavage studies).

Exposure route:	oral		
Species:	rat		
Strain:	F344		
Sex:	M		
Vehicle or physical state:	gavage		
Body weight:[b]	0.44 kg.		
Duration of treatment (le):	103 weeks		
Duration of study (Le):	104 weeks		
Lifespan of animal (L):[c]	104 weeks		
Target organ:	forestomach		
Tumor type:	papillomas/carcinomas		
Experimental doses/exposure (mg/kg/day):	200	100	0
Transformed animal doses[d] (mg/kg/day):	141.5	70.7	0
Human equivalent doses[e] (mg/kg/day):	26.12	13.06	0
Tumor incidence:	36/50	18/50	1/50

Comments: Ethyl acrylate has produced tumors only with gavage exposure. An inhalation study of Miller et al. (1985; Chronic toxicity and oncongenicity bioassay of inhaled ethyl acrylate in Fischer 344 rats and B6C3F1 mice. Drug Chem. Toxicol. 8:1-42) found no evidence of carcinogenicity in B6C3F1 mice or F344 rats exposed to ethyl acrylate up to 75 ppm for 27 months or to 225 ppm for 6 months, then maintained for 21 months until terminal sacrifice. The ED_{10} represents oral exposure; an estimate of potency for inhalation exposure is not currently available.

The ED_{10} is described in EPA (1987; Health and environmental effects profile on ethyl acrylate EPA/600/X-87/162); this document has been presented before the Carcinogen Risk Assessment Verification Endeavor and is under review. Additionally, Fredrick et al. (1992; A physiologically based pharmacokinetic and pharmacodynamic model to describe the oral dosing of rats with ethyl acrylate and its implication for risk assessment, Toxicol. Appl. Pharmacol. 114: 256-260) have developed a physiologically-based pharmacokinetic model which describes delevered doses to the forestomach of rats. A non-linear relationship between dose delivered to the forestomach and experimental exposure is projected based upon this model. Thus an estimate of the ED_{10} supported by dosemetric considerations, is

14-08-85 ethyl acrylate (continued)

expected to be lower. An evaluation of this model is needed. Given the above considerations, the estimate of the ED_{10} should be considered tentative and needs to be reevaluated in light of purported non-linearities between delivered doses and experimental exposures.

Source: U.S. Environmental Protection Agency, 1987. Health and environmental effects profile for ethyl acrylate. EPA/600/X-87/162. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.
[b]Estimated.
[c]Estimated.
[d]Experimental dose (mg/kg/d) x (5 treatment days per week/7 days per week) x (Ie/Le).
[e]Transformed animal dose / (human body weight/animal body weight) $^{(1/3)}$.

Elements of Hazard Ranking

Chemical Name: ethyl carbamate (urethane)

CAS Number: 51-79-6

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): 0.64 per (mg/kg)/day

Reference: Toth, B.; Boreisha, I., 1969. Tumorigenesis with isonicotinic acid hydrazide and urethane in the Syrian Golden hamster. Europ. J. Cancer 5: 165-171.

Exposure route:	oral	
Species:	hamster	
Strain:	Syrian Golden	
Sex:	M	
Vehicle or physical state:	drinking water	
Body weight:[b,c]	0.105 kg	
Duration of treatment (le):[c]	95 wk	
Duration of study (Le):[c]	95 wk	
Lifespan of animal (L):[c]	95 wk	
Target organ:	forestomach	
Tumor type:	papillomas[d]	
Experimental dose/exposure:	15.1 mg/day[e]	0.0 mg/day
Transformed animal dose (mg/kg/day):[f]	143.8	0.0
Human equivalent dose (mg/kg/day):[g]	16.5	0.0
Tumor incidence:	36/52	6/100

Comments: The ED_{10} is based on the oral route of exposure; an adequate estimate of potency for the inhalation route is not currently available. The inhalation data were of limited quality for estimating an ED_{10}.

Source: U.S. Environmental Protection Agency, 1988. Evaluation of the potential carcinogenicity of ethyl carbamate (urethane). OHEA-C-073-103. Washington, DC: Office of Health and Environmental Assessment.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

[b]Reported.

[c]Treated animals.

[d]Forestomach carcinomas were also significantly increased. The incidence was 18/52 in the exposure group, compared to 0/100 in the control group. Some animals had both papillomas and carcinomas. If every animal with a carcinoma had a papilloma, the exposed-group incidence would be 36/52, as used in the potency calculation. On the other hand, if there was minimal overlapping of papillomas and carcinomas, the exposed group incidence could be as high as 100 percent.

51-79-6 ethyl carbamate (urethane) (continued)

Because the published report gives no information about the combined incidence of either papillomas or carcinomas, and because any estimate would be arbitrary, the incidence of papillomas alone is used for the potency calculation.

[e]Reported average daily urethane consumption (administered as 0.1 percent in the drinking water).

[f]Experimental dose (mg/day)/weight of animal (kg).

[g]Transformed animal dose (mg/kg/day)/(human body weight/animal body weight)$^{(1/3)}$.

Elements of Hazard Ranking

Chemical Name: ethyl 4,4'-dichlorobenzilate (chlorobenzilate)

CAS Number: 510-15-6

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): 1.8 per (mg/kg)/day

Reference: Bionetics Research Laboratories, 1968. Evaluation of carcinogenic, teratogenic and mutagenic activities of selected pesticides and industrial chemicals: I. carcinogenic study. Prepared for National Cancer Institute, report no. NCI-DCCP-CG-1973-1-1. Available from NTIS. PB-223-159.

Exposure route:[b]	oral	
Species:	mouse	
Strain:	(C57BL/6 x C3H/Anf)F1	
Sex:	M	
Vehicle or physical state:[b]	diet	
Body weight:[c]	0.038 kg	
Duration of treatment (le):	581 days	
Duration of study (Le):	581 days	
Lifespan of animal (L):[d]	730 days	
Target organ:	liver	
Tumor type:	hepatoma	
Experimental dose/exposure:	603 ppm	0 ppm
Transformed animal dose (mg/kg/day):[b,e]	42.0	0.0
Human equivalent dose (mg/kg/day):[f]	3.4	0.0
Tumor incidence:	9/17	8/79

Comments: The ED_{10} is based on data for oral exposure; an estimate of potency for the inhalation route of exposure is not currently available.

Source: U.S. Environmental Protection Agency, 1988. Evaluation of the potential carcinogenicity of ethyl 4,4'-dichlorobenzilate. OHEA-C-073-104. Washington, DC: Office of Health and Environmental Assessment.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

[b]Treatment was by gavage, at 215 mg chlorobenzilate/kg/day in 0.5 percent gelatin, from days 7 to 28 of animals' life. The compound was administered in the diet thereafter.

[c]Reported.

[d]Estimated.

510-15-6 chlorobenzilate (continued)

[e]For the first 21 days (28-7): experimental dose (215 mg/kg)x0.038 kg (animal's body weight) x duration of treatment (21 days)=172 mg (total). For the next 560 days (581-21): experimental dose (603 ppm)x0.038 kg (animal's body weight) x duration of the treatment (560 days)=1668 mg (total). Then, (172 mg+1668 mg)=1840 mg (total) chlorobenzilate administered during the entire study; 1840 mg/0.038 kg (animal's body weight) x duration of the study (581 days)=83.34 mg/kg/day. Transformed animal doses are adjusted for less than lifetime followup $(Le/L)^3$.

[f]Transformed animal dose (mg/kg/day)/(human body weight/animal body weight)$^{(1/3)}$.

Elements of Hazard Ranking

Chemical Name: ethylene dibromide

CAS Number: 106-93-4

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): 2.1 per (mg/kg)/day

Reference: National Toxicology Program, 1982. Carcinogenesis bioassay of 1,2-dibromoethane in F344 rats and B6C3F1 mice (inhalation study). NTP Technical Report Series No. 210. Also published as DHHS publication no. NIH (82)-1766.

Exposure route:	inhalation		
Species:	rat		
Strain:	Fischer 344		
Sex:	F		
Vehicle or physical state:	vapor		
Body weight:[b]	0.20 kg (high dose)	0.25 kg (low dose)	0.25 kg (control)
Duration of treatment (le):	91 wk (high dose)	103 wk (low dose)	106 wk (control)
Duration of study (Le):	92 wk (high dose)	104 wk (low dose)	106 wk (control)
Lifespan of animal (L):[c]	742 days		
Target organ:	nasal cavity		
Tumor type:	various[d]		
Experimental dose/exposure:[e]	40 ppm	10 ppm	0 ppm
Human equivalent dose:[f]	7.1 ppm	1.8 ppm	0.0 ppm
Tumor incidence:	41/50	39/50	1/50

Comments: For the estimate of ED_{10}, it was not possible to consider variable partial lifetime exposure patterns, as was done for estimating the unit risk associated with inhalation exposure (U.S. EPA, 1992). The estimte of the ED_{10} would decrease (i.e., the potency, $1/ED_{10}$, would increase) by less than a factor of two if this adjustment had been made.

Source: U.S. Environmental Protection Agency, 1988. Evaluation of the potential carcinogenicity of ethylene dibromide. OHEA-C-073-105. Washington, DC: Office of Health and Environmental Assessment.

U.S. Environmental Protection Agency, 1992. Integrated Risk Information System, IRIS. Online. Cincinnati, OH: U.S. Environmental Protection Agency. Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

[b]Reported.

[c]Assumed.

[d]Includes adenomas, adenocarcinomas, adematous polyps, squamous cell carcinomas, papillary adenomas, squamous cell papillomas, and carcinomas.

106-93-4 ethylene dibromide (continued)

[e]Exposures were 6 hr/day, 5 days/wk.
[f]Equivalent units of exposure for humans and rats in regard to carcinogenic response were assumed (ppm). Since rats were exposed 6 hr/day, 5 days/wk, continuous exposures were determined by (7/5 days/wk)x(24/6 hr/day).

Elements of Hazard Ranking

Chemical Name: ethylene dichloride (1,2-dichloroethane)

CAS Number: 107-06-2

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): 0.39 per (mg/kg)/day

Reference: National Cancer Institute, 1978. Bioassay of 1,2-dichloroethane for possible carcinogenicity. U.S. Department of Health, Education, and Welfare; Public Health Service; National Institutes of Health; NCI Carcinogenesis Testing Program. DHEW publication no. (NIH) 78-1305.

Exposure route:	oral (gavage)		
Species:	rat		
Strain:	Osborne-Mendel		
Sex:	M		
Vehicle or physical state:	corn oil		
Body weight:[b]	0.5 kg		
Duration of treatment (le):	78 wk		
Duration of study (Le):	104 wk		
Lifespan of animal (L):[c]	104 wk		
Target organ:	circulatory system		
Tumor type:	hemangiosarcoma		
Experimental dose/exposure (mg/kg/day):	95	47	0
Transformed animal metabolized dose (mg/kg/day):[d]	42.75	23.16	0.00
Human equivalent metabolized dose (mg/kg/day):[e]	8.23	4.46	0.00
Tumor incidence:	7/27	9/48	0/40

Comments: The ED_{10} was extrapolated from the oral to inhalation exposure route. Based on the data of Reitz et al. (1982; Toxicol. Appl. Pharmaco. 62:190-204), from an oral exposure, rats metabolize 92% of the low dose and 84% of the high dose. An assumption of 100% absorption via the inhalation route was made. A time-to-tumor model, as applied to these data for estimating the unit risk associated with inhalation exposure, was not used in the derivation of the ED_{10} estimate. The estimte of the ED_{10} would decrease (i.e., the potency, $1/ED_{10}$, would increase) by less than a factor of two using this procedure.

Source: U.S. Environmental Protection Agency, 1988. Evaluation of the potential carcinogenicity of 1,2-dichloroethane. OHEA-C-073-82. Washington, DC: Office of Health and Environmental Assessment.

U.S. Environmental Protection Agency, 1992. IRIS, Integrated Risk Information System. Online. Cincinnati, OH: U.S. Environmental Protection Agency, Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office.

107-06-2 ethylene dicholoride (continued)

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.
[b]Reported.
[c]Assumed.
[d]Reflects the fraction of a week when 1,2-dichloroethane was used (5/7), and adjustment by the ratio of duration of treatment/duration of the study. Transformed animal dose=metabolized dose (mg/kg/day) x 5/7 treatment days x duration of treatment (days)/duration of study (days) % metabolized.
[e]Transformed animal dose (mg/kg/day)/(human body weight/animal body weight)$^{(1/3)}$.

Elements of Hazard Ranking

Chemical Name: ethylene imine (aziridine)

CAS Number: 151-56-4

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): 340 per (mg/kg)/day

Reference: Innes, J.R.M.; Ulland, B.M.; Valerio, M.G.; Petrucelli, L.; Fishbein, L.; Hart, E.R.; Pallotta, A.J.; Bates, R.R.; Falk, H.L.; Gart, J.J.; Klein, M.; Mitchell, D.; and Peters, J., 1969. Bioassay of pesticides and industrial chemicals for tumorigenicity in mice: a preliminary note. J. Natl. Cancer Inst. 42: 1101-1114.

Exposure route:	initially gavage, followed by oral	
Species:	mouse	
Strain:[b]	(C57BL/6 x C3H/Anf)F1	
Sex:	M	
Vehicle or physical state:	initially in 0.5% gelatin, followed by incorporation into diet	
Body weight:[c]	0.03 kg	
Duration of treatment (le):	by gavage for 3 wk, followed by 17 mo of oral exposure	
Duration of study (Le):	18 mo (548 days)	
Lifespan of animal (L):[c]	730 days	
Target organ:	liver	
Tumor type:	hepatoma	
Experimental dose/exposure:	4.64 mg/kg/day (gavage) 13 ppm (diet)	0.0 mg/kg/day
Transformed animal dose (mg/kg/day):[c]	0.76	0.0
Human equivalent dose (mg/kg/day):[e]	0.057	0.0
Tumor incidence:	15/17	8/79

Comments: Only liver hepatoma responses in males were used to calculate the potency factor. Although an increase in lung adenomas was statistically significant, the grouping of hepatomas and lung adenomas was not possible from the data in this study. The ED_{10} is based on data for oral exposure; an estimate of potency for the inhalation route is not currently available.

Source: U.S. Environmental Protection Agency, 1988. Evaluation of the potential carcinogenicity of aziridine. OHEA-C-073-26. Washington, DC: Office of Health and Environmental Assessment.

151-56-4 ethylene imine (aziridine) (continued)

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

[b]Two strains of mice were tested; only the more susceptible strain is reported here.

[c]Estimated.

[d]4.64 mg/kg of aziridine were administered daily for 22 days, resulting in a total dose of 4.64 mg/kgx22 days=102.1 mg/kg. Subsequently, 13 ppm aziridine were provided in the food source for the next 520 days. The total dose during this period was 13 ppmx$3.9x10^{-3}$ kg (weight of food consumed daily by average mouse)x520 days/0.03 kg (animal weight)=8878.8 mg/kg. The total amount of aziridine administered was 102.1 mg/kg+878.8 mg/kg=980.9 mg/kg. Daily dose=0.76 mg/kg (980.9 mg/kg/548 days). Doses were adjusted for less than lifetime followup: $(Le/L)^3$ or $(548/730)^3$.

[e]Transformed animal dose (mg/kg/day)/(human body weight/animal body weight)$^{(1/3)}$.

Elements of Hazard Ranking

Chemical Name: ethylene oxide

CAS Number: 75-21-8

Weight-of-Evidence Classification:[a] B1

Estimate of Potency ($1/ED_{10}$): 1.3 per (mg/kg)/day

Reference: National Toxicology Program, 1986. Toxicology and carcinogenesis studies of ethylene oxide in B6C3F1 mice [final draft]. Research Triangle Park, NC: National Institutes of Health. NTP TR 326.

Exposure route:	inhalation		
Species:	mouse		
Strain:	B6C3F1		
Sex:	M		
Vehicle or physical state:	inhalation		
Body weight:	0.035 kg		
Duration of treatment (le):	730 days (6 hr/day, 5 days/wk)		
Duration of study (Le):	730 days		
Lifespan of animal (L):	730 days		
Target organ:	lung		
Tumor type:	adenomas and carcinomas		
Experimental dose/exposure:[b]	100 ppm	50 ppm	0 ppm
Transformed animal dose (mg/kg/day):[c]	39.9	20.0	0.0
Human equivalent dose (mg/kg/day):[d]	3.2	1.6	0.0
Tumor incidence:[e]	26/50[f]	19/50[g]	11/50

Comments: None.

Source: U.S. Environmental Protection Agency, 1988. Evaluation of the potential carcinogenicity of ethylene oxide. OHEA-C-073-106. Washington, DC: Office of Health and Environmental Assessment.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

[b]Exposure was via inhalation for 6 hr/day, 5 days/wk, for approximately 2 yr.

[c]Experimental dose (ppm)x0.041 x molecular weight of ethylene oxide (44.05 g/mol)x0.0432 mg/day (rat's breathing rate)/0.035 kg (animal weight)x5 (treatment days/wk)/7 (days/wk)x6 (treatment hr/day)/24 (hr/day).

[d]Transformed animal dose (mg/kg/day)/(human body weight/animal body weight)$^{(1/3)}$.

[e]Total tumor count ratios based on number of rats alive at 24 mo.

[f]One animal developed both an adenoma and a carcinoma.

[g]Two animals developed both an adenoma and a carcinoma.

Elements of Hazard Ranking

Chemical Name: ethylene thiourea

CAS Number: 96-45-7

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): 0.98 per (mg/kg)/d

Reference: National Toxicology Program, 1989. On the perinatal toxicity and carcinogenicity studies of ethylene thiourea in F/344 rats and B6C3F1 mice (feed studies). NTP Technical Report No. 388, NIH Publication 90-2843.

Exposure route:	diet			
Species:	mouse			
Strain:	B6C3F1			
Sex:	F			
Vehicle or physical state:	feed			
Body weight:[b]	0.048 kg.			
Duration of treatment (le):	prenatal exposure + 104 weeks			
Duration of study (Le):	prenatal exposure + 104 weeks			
Lifespan of animal:[c]	104 weeks			
Target organ:	liver			
Tumor type:	hepatocellular adenomas and carcinomas			
Experimental doses/exposure (ppm):	1000	330	100	0
Transformed animal doses[d] (mg/kg/day):	150.0	49.5	15.0	0
Human equivalent doses[e] (mg/kg/day):	14.2	4.7	1.4	0
Tumor incidence:	97/98	136/50	4/27	9/98

Comments: The ED_{10} is based on oral data; and estimate of potency for the inhalation route is not currently available.

Source: Memorandum to A. Kocialski from H.M. Pettigrew. Ethylene thiourea [ETU] - q_1^* calculation based on female mouse liver tumors (pooled data) from the NTP study. November 13, 1991.

Memorandum to K. Martin from A. B. Kocialski. Third peer review of ethylene thiourea. Selecting the q_1^* for ethylene thiourea [ETU]. September 26, 1991.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

[b]Actual.

[c]Actual.

[d]Experimental dose (ppm) x 0.15 (fraction of body weight consumed as food per day).

[e]Transformed animal dose (mg/kg/d)/(human body weight/animal body weight)$^{(1/3)}$. Humans were assumed to weight 60 kg.

Elements of Hazard Ranking

Chemical Name: ethylidene chloride (1,1-dichloroethane)

CAS Number: 75-34-3

Weight-of-Evidence Classification:[a] C

Estimate of Potency ($1/ED_{10}$): see comments

Comments: The available data are inadequate for estimating an ED_{10}.

Source: U.S. Environmental Protection Agency, 1992. IRIS, Integrated Risk Information System. Online. Cincinnati, OH: U.S. Environmental Protection Agency, Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

Elements of Hazard Ranking

Chemical Name: formaldehyde

CAS Number: 50-00-0

Weight-of-Evidence Classification:[a] B1

Estimate of Potency ($1/ED_{10}$):[b] 3.0 per (mg/kg)/day

Reference: Kerns, W.D.; Donofrio, D.J.; Pavkov, K.L., 1983. The chronic effects of formaldehyde inhalation in rats and mice: a preliminary report. Formaldehyde Toxicol. (Conf.): 111-131.

Exposure route:	inhalation			
Species:	rat			
Strain:	Fischer 344			
Sex:	M, F			
Vehicle or physical state:	air/vapor			
Body weight:[c]	0.30 kg			
Duration of treatment (le):	730 days			
Duration of study (Le):	912 days			
Lifespan of animal (L):	912 days			
Target organ:	nasal cavity			
Tumor type:	squamous cell carcinoma			
Experimental dose/exposure:[d]	14.3 ppm	5.6 ppm	2.0 ppm	0.0 ppm
Prorated dose (ppm):[e]	2.0 ppm	0.8 ppm	0.3 ppm	0.0 ppm
Tumor incidence:	94/140	2/153	0/159	0/156

Comments: None.

Source: U.S. Environmental Protection Agency, 1988. Evaluation of the potential carcinogenicity of formaldehyde. OHEA-C-073-109. Washington, DC: Office of Health and Environmental Assessment.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

[b]To express the potency in terms of $(mg/kg/day)^{-1}$ for humans, use the formula 1 ppm=0.041x30 (molecular weight of formaldehyde)x20 (m^3/day human inhalation rate)/70 (kg human weight) in mg/kg/day.

[c]Estimated.

[d]Equivalent units of exposure (ppm) for humans and rats was assumed regarding carcinogenic response.

[e]Experimental dose x (6 treatment hr/day)/(24 hr/day)x(5 treatment days/wk)(7 days/wk)x(730 days treatment duration)/(912 days study duration).

Elements of Hazard Ranking

Chemical Name: heptachlor

CAS Number: 76-44-8

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): 42 per (mg/kg)/day

Reference: Davis, H.J., 1965. Pathology report of mice fed aldrin, dieldrin, heptachlor or heptachlor epoxide for two years. Internal FDA memorandum to Dr. A.J. Lehman., as evaluated by Reuber, M.D., 1977. Histopathology of carcinomas of the liver in mice ingesting heptachlor or heptachlor epoxide. Exp. Cell Biol. 45: 147-157.

Exposure route:	oral	
Species:	mouse	
Strain:	C3H	
Sex:	M/F	
Vehicle or physical state:	diet	
Body weight:	0.04 kg	
Duration of treatment (le)	104 wk	
Duration of study (Le):	104 wk	
Lifespan of animal (L):[b]	104 wk	
Target organ:	liver	
Tumor type:	hepatocellular carcinoma	
Experimental dose/exposure:[c]	10 ppm	0 ppm
Transformed animal dose (mg/kg/day):[d]	1.30	0.0
Human equivalent dose (mg/kg/day):[e]	0.108	0.0
Tumor incidence:	57/78	2/53 (males)
	64/87	22/73 (females)

Reference: National Cancer Institue (NCI). 1977. Bioassay of heptachlor for possible carcinogenicity. NCI Carcinogenesis Tech. Rep. Ser. No. 9. [Also publ. as DHEW Publication Nol (NIH) 77-809].

Exposure route:	oral		
Species:	mouse		
Strain:	B6C3F1		
Sex:	M/F		
Vehicle or physical state:	diet		
Body weight:	0.035 kg		
Duration of treatment (le)	80 wk		
Duration of study (Le):	90 wk		
Lifespan of animal (L):[b]	104 wk		
Target organ:	liver		
Tumor type:	hepatocellular carcinoma		
Experimental dose/exposure:[c]	13.8 ppm	6.1 ppm	0 ppm (males)

76-44-8 heptachlor (continued)

	18.0 ppm	9.0 ppm	0 ppm	(females)
Transformed animal dose				
(mg/kg/day):[d]	1.79	0.79	0.0	(males)
(mg/kg/day):[d]	2.34	1.17	0.0	(females)
Human equivalent dose				
(mg/kg/day):[e]	0.140	0.063	0.0	(males)
(mg/kg/day):[e]	0.180	0.094	0.0	(females)
Tumor incidence:	34/47	11/46	5/19	(males)
	30/42	3/47	2/10	(females)

Comments: The ED_{10} is a geometric mean of the four data sets. The ED_{10} is extrapolated from the oral to inhalation exposure route.

Source: U.S. Environmental Protection Agency, 1986. Carcinogen assessment of chlordane and heptachlor/heptachlor epoxide. EPA-600/6-87/004. Washington, DC: U.S. Environmental Protection Agency, Office of Health and Environmental Assessment, Carcinogen Assessment Group.

U.S. Environmental Protection Agency, 1988. Evaluation of the potential carcinogenicity of heptachlor. OHEA-C-073-111. Washington, DC: Office of Health and Environmental Assessment.

U.S. Environmental Proetction Agency, 1992. IRIS, Integrated Risk Information System. Online. Cincinnati, OH: U.S. Environmental Protection Agency, Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

[b]Estimated.

[c]Dose is expressed as a time-weighted average.

[d]Experimental dose (mg/kg/day)x(no. treatment days per wk/7 days per wk)x(Ie/Le).

[e]Transformed animal dose (mg/kg/day)/(human body weight/animal body weight)$^{(1/3)}$.

Elements of Hazard Ranking

Chemical Name: hexachlorobenzene

CAS Number: 118-74-1

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): 13 per (mg/kg)/day

Reference: Erturk, E.; Lambrecht, R.W.; Peters, H.A.; Cripps, D.J.; Goceman, A.; Morris, C.R.; Bryan, G.T., 1986. Oncogenicity of hexachlorobenzene. In: Morris, C.R.; Cabral, J.R.P., eds. Hexachlorobenzene: proceedings of the international symposium; IARC Scientific Publication No. 77. Oxford, UK: Oxford University Press, pp. 417-423.

Exposure route:	oral		
Species:	rat		
Strain:	Sprague-Dawley		
Sex:	F		
Vehicle or physical state:	diet		
Body weight:[b]	0.5 kg		
Duration of treatment (le):	730 days		
Duration of study (Le):	730 days		
Lifespan of animal (L):[b]	730 days		
Target organ:	liver		
Tumor type:	hepatocellular carcinoma		
Experimental dose/exposure:	150 ppm	75 pp	0 ppm
Transformed animal dose (mg/kg/day):[c]	2.5	1.3	0.0
Human equivalent dose (mg/kg/day):[d]	1.46	0.73	0.0
Tumor incidence:	48/55	36/56	0/52

Comments: The ED_{10} was extrapolated from the oral to the inhalation route of exposure.

Source: U.S. Environmental Protection Agency, 1988. Evaluation of the potential carcinogenicity of hexachlorobenzene. OHEA-C-073-113. Washington, DC: Office of Health and Environmental Assessment.

U.S. Environmental Protection Agency, 1992. IRIS, Integrated Risk Information System. Online. Cincinnati, OH: U.S. Environmental Protection Agency, Office of Health and Environmental Assessment, Environmental Criteria Assessment Office.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

[b]Assumed.

[c]Experimental dose (ppm) x fraction of rat's body weight consumed as food each day.

[d]Transformed animal dose (mg/kg/day)/(human body weight/animal body weight)$^{(1/3)}$.

Elements of Hazard Ranking

Chemical Name: hexachlorobutadiene

CAS Number: 87-68-3

Weight-of-Evidence Classification:[a] C

Estimate of Potency ($1/ED_{10}$): 0.36 per (mg/kg)/day

Reference: Kociba, R.J.; Keyes, D.G.; Jersey, G.C.; et al, 1977. Results of a two-year chronic toxicity study with hexachlorobutadiene in rats. Am. Ind. Hyg. Assoc. J. 38: 589-602.

Exposure route:	oral			
Species:	rat			
Strain:	Sprague-Dawley			
Sex:	M			
Vehicle or physical state:	diet			
Body weight:[b]	0.61 kg			
Duration of treatment (le):	671 days			
Duration of study (Le):	730 days			
Lifespan of animal (L):[c]	730 days			
Target organ:	kidney			
Tumor type:	renal tubular adenomas and carcinomas			
Experimental dose/exposure (mg/kg/day):	20.0	2.0	0.2	0.0
Transformed animal dose (mg/kg/day):[d]	18.3	1.8	0.18	0.0
Human equivalent dose (mg/kg/day):[e]	3.8	0.38	0.038	0.0
Tumor incidence:	9/39	0/40	0/40	1/90

Comments: The ED_{10} is based on data for oral exposure and can be extrapolated to the inhalation exposure route.

Source: U.S. Environmental Protection Agency, 1988. Evaluation of the potential carcinogenicity of hexachlorobutadiene. OHEA-C-073-114. Washington, DC: Office of Health and Environmental Assessment.

U.S. Environmental Protection Agency, 1992. IRIS, Integrated Risk Information System. Online. Cincinnati, OH: U.S. Environmental Protection Agency, Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

[b]Reported.

[c]Estimated.

[d]Experimental dose (mg/kg/day)x(no. treatment days per wk/7 days per wk)x(le/Le).

[e]Transformed animal dose (mg/kg/day)/(human body weight/animal body weight)$^{(1/3)}$.

Elements of Hazard Ranking

Chemical Name: hexachloroethane

CAS Number: 67-72-1

Weight-of-Evidence Classification:[a] C

Estimate of Potency ($1/ED_{10}$): 0.051 per (mg/kg)/day

References: Weisburger, E.K., 1977. Carcinogenicity of halogenated hydrocarbons. Env. Health Perspect. 21: 7-16.

National Cancer Institute, 1978. Bioassay of hexachloroethane for possible carcinogenicity. Technical Report Series No. 68. DHEW publication no. (NIH) 78-1318. Washington, DC: U.S. Department of Health, Education, and Welfare.

Exposure route:	gavage		
Species:	mouse		
Strain:	B6C3F1		
Sex:	M		
Vehicle or physical state:	corn oil		
Body weight:[b]	0.032 kg		
Duration of treatment (le):	546 days		
Duration of study (Le):	637 days		
Lifespan of animal (L):[c]	730 days		
Target organ:	liver		
Tumor type:	hepatocellular carcinoma		
Experimental dose/exposure:	1179 mg/kg/day	590 mg/kg/day	0 mg/kg/day
Transformed animal dose (mg/kg/day):[d]	721.8	361.2	0.0
Human equivalent dose (mg/kg/day):[e]	55.5	27.8	0.0
Tumor incidence:	31/49	15/50	3/20

Comments: Inhalation data are absent. The oral data were extrapolated to the inhalation exposure route.

Source: U.S. Environmental Protection Agency, 1988. Evaluation of the potential carcinogenicity of hexachloroethane. OHEA-C-073-115. Washington, DC: Office of Health and Environmental Assessment.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

[b]Reported.

[c]Estimated.

[d]Experimental dose (mg/kg)x(5 treatment days per wk/7 days per wk)x(le/Le).

[e]Transformed animal dose (mg/kg/day)/(human body weight/animal body weight)$^{(1/3)}$.

Elements of Hazard Ranking

Chemical Name: hexamethylphosphoramide

CAS Number: 680-31-9

IARC Classification:[1] 2B

Comments: "Sufficient evidence for carcinogenicity to aniamls" and "no data" in humans.

Source: International Agency for Research on Cancer, 1987. IARC monographs on the evaluation of carcinogenic risks to humans. Overall evaluations of carcinogenicity: an updating of IARC monographs volumes 1 to 42. Supplement 7: 64.

---

[1]1-the agent is carcinogenic to humans, 2A-the agent is probably carcinogenic to humans (limited human evidence), 2B-the agent is probably carcinogenic to humans (limited evidence in humans in the absence of sufficient evidence in animals, or inadequate human evidence/non-existent human data and sufficient evidence in animals), 3-the agent is not classifiable as to its carcinogenicity to humans, 4-the agent is probably not carcinogenic to humans.

Elements of Hazard Ranking

Chemical Name: hydrazine (hydrazine sulfate)

CAS Number: 302-01-2 (10034-93-2)

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): 107 (mg/kg)/day

Reference: MacEwen, J.D.; Vernot, E.H., 1980. A study of the oncogenic potential of inhaled hydrazine after chronic low level exposure. Toxic Hazards Research Unit Annual Report. Air Force Aerospace Medical Research Laboratory, August, pp. 16-32.

Exposure route:	inhalation		
Species:	rat		
Strain:	Fischer 344		
Sex:	M		
Vehicle or physical state:	air		
Body weight:[b]	0.35 kg		
Duration of treatment (le):	365 days		
Duration of study (Le):	910 days		
Lifespan of animal (L):	910 days		
Target organ:	nasal cavity		
Tumor type:	adenoma/adenocarcinoma		
Experimental dose/exposure:	5 ppm	1 ppm	0 ppm
Transformed animal dose (mg/kg/day):[c]	0.30	0.06	0.0
Human equivalent dose (mg/kg/day):[d]	0.05	0.01	0.0
Tumor incidence:	72/99	11/98	0/149

Comments: None.

Source: U.S. Environmental Protection Agency, 1988. Evaluation of the potential carcinogenicity of hydrazine. OHEA-C-073-116. Washington, DC: Office of Health and Environmental Assessment.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

[b]Estimated.

[c]First, convert experimental dose in (ppm) to (mg/m^3): 0.41 x molecular weight of hydrazine x concentration (ppm). Calculate preliminary transformed dose (mg/kg/day) based on breathing rate and animal weight: concentration (mg/m^3) x breathing rate for rats (0.22 m^3/day)/animal weight (0.35 kg). Determine final transformed animal dose by adjusting for duration of study and discontinuous exposure: transformed dose (mg/kg/day) x duration of treatment (days)/duration of study (days)x5 (treatment days/wk)/7(days/wk)x6 (treatment hr/day)/24 (hr/day).

[d]Transformed animal dose (mg/kg/day)/(human body weight/animal body weight)$^{1/3}$.

Elements of Hazard Ranking

Chemical Name: hydroquinone

CAS Number: 123-31-9

Weight-of-Evidence Classification:[a] see comments

Estimate of Potency ($1/ED_{10}$): see comments

Comments: The Office of Research and Development/Office of Health and Environmental Assessment is currently evaluating the carcinogenic evidence on hydroquinone. A draft preliminary assessment indicates that the weight-of-evidence classification is such that this chemical may be considered a "nonthreshold" hazardous air pollutant. This evaluation is currently undergoing internal peer review, thus, the exact placement of this chemical with respect to other "nonthreshold" HAPs can not be determined at this time.

Source: U.S Environmental Protection Agency, 1992. Preliminary assessment evaluation of the potential carcinogenicity of hydroquinone. First draft. Prepared by the Chemical Hazard Evaluation Program, Health and Safety Research Division, ORNL, for the Office of Health and Environmental Assessment, Human Health Assessment Group.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

Elements of Hazard Ranking

Chemical Name: indeno(1,2,3-cd)pyrene

CAS Number: 193-39-5

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): See comments.

Comments: The available data are inadequate for estimating an ED_{10}.

Source: U.S. Environmental Protection Agency, 1992. IRIS, Integrated Risk Information System. Online. Cincinnati, OH: U.S. Environmental Protection Agency, Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

Elements of Hazard Ranking

Chemical Name: isophorone

CAS Number: 78-59-1

Weight-of-Evidence Classification:[a] C

Estimate of Potency ($1/ED_{10}$): 0.016 per (mg/kg)/d

Reference: National Toxicology Program, 1986. Toxicology and carcinogenicity studies of isophorone (CAS No. 78-59-1) in F344/N rats and B6C3F1 mice (gavage). NTP Technical Report No. 291, NIH Publication 86-2547.

Exposure route:	gavage		
Species:	rat		
Strain:	F344/N		
Sex:	M		
Vehicle or physical state:	liquid		
Body weight:[b]	0.35 kg.		
Duration of treatment (le):	104 weeks		
Duration of study (Le):	104 weeks		
Lifespan of animal:[c]	104 weeks		
Target organ:	preputial gland; kidney		
Tumor type:	carcinomas		
Experimental doses/exposure (mg/kg/d):	500	250	0
Transformed animal doses[d] (mg/kg/day):	374	187	0
Human equivalent doses[e] (mg/kg/day):	64	32	0
Tumor incidence:	5/44	0/46	0/49

Comments: The ED_{10} is based on oral data; an estimate of potency for the inhalation route is not currently available.

Source: U.S. Environmental Protection Agency, 1992. IRIS, Integrated risk information system. Online. Cincinnati, OH: U.S. Environmental Protection Agency, Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

[b]Estimated.

[c]Estimated.

[d]Experimental dose (mg/kg/d) x no. treatment days (5) per week/7 days per week).

[e]Transformed animal dose (mg/kg/d) /(human body weight/animal body weight)$^{(1/3)}$.

Elements of Hazard Ranking

Chemical Name: lead and lead compounds

CAS Number: not applicable

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): see comments

Comments: The animal studies demonstrate carcinogenicity of soluble lead salts at relatively high dose levels. Statistically significant elevations in renal tumor incidence has been observed in one mouse and 10 rat bioassays with subsequent exposure to soluble lead salts. Supplementary information has shown several other forms of lead to be bioavailable, and therefore, highly likely to be carcinogenic at some dose. Considering that no lead compound can be called negative for either bioavailability and thus, carcinogenicity, there appears to be no evidence to rule out any form of lead as a potential carcinogen (U.S. EPA, 1988).

The available data are not sufficient for estimating an ED_{10}. A substantial body of accumulated information indicates that a variety of factors, some of which may be unique to lead, are involved in the mechanism of lead-induced cancer. The current data base is limited in its ability to shed insight on these important factors.

Source: U.S. Environmental Protection Agency, 1988. Evaluation of the potential carcinogenicity of lead and lead compounds. EPA/600/8-89/0454A. External Review Draft. Washington, D.C.: Office of Health and Environmental Assessment.

U.S. Environmental Protection Agency, 1989. Report of joint study group on lead. EPA-SAB-EHC-90-001. Washington, D.C.: Science Advisory Board.

---

[a] A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

Elements of Hazard Ranking

Chemical Name: lindane (hexachlorocyclohexane, gamma)

CAS Number: 58-89-9

Weight-of-Evidence Classification:[a] B2/C

Estimate of Potency ($1/ED_{10}$): 7.4 per (mg/kg)/day

Reference: Thorpe, E.; Walker, A.I.T., 1973. The toxicology of dieldrin (HEOD): II. comparative long-term oral toxicity studies in mice with dieldrin, DDT, phenobarbitone, beta-BHC and gamma-BHC. Food Cosmet. Toxicol. 11: 433-442.

Exposure route:	oral	
Species:	mouse	
Strain:	CF1	
Sex:	M	
Vehicle or physical state:	diet	
Body weight:[b]	0.03 kg	
Duration of treatment (le):	770 days	
Duration of study (Le):	770 days	
Lifespan of animal (L):[c]	770 days	
Target organ:	liver	
Tumor type:	hepatocellular carcinomas, hyperplastic nodules	
Experimental dose/exposure:	400 ppm	0 ppm
Transformed animal dose (mg/kg/day):[d]	52	0
Human equivalent dose (mg/kg/day):[e]	3.9	0.0
Tumor incidence:	27/28	11/45

Comments: The ED_{10} is based on data for oral exposure; an estimate of potency for the inhalation route is not currently available.

Source: U.S. Environmental Protection Agency, 1988. Evaluation of the potential carcinogenicity of gamma-hexachlorocyclohexane (lindane). OHEA-C-073-42. Washington, DC: Office of Health and Environmental Assessment.

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

[b]Estimated.

[c]Reported.

[d]Experimental dose (ppm)x0.13 (fraction of mouse's body weight consumed as food per day).

[e]Transformed animal dose (mg/kg/day)/(human body weight/animal body weight)$^{(1/3)}$.

Elements of Hazard Ranking

Chemical Name: methyl chloride

CAS Number: 74-87-3

Weight-of-Evidence Classification:[a] C

Estimate of Potency ($1/ED_{10}$): 0.052 per (mg/kg)/day

References: Pavkov, K.L.; Mitchell, R.I.; Persing, R.L., 1981. Final report on a chronic inhalation toxicology study in rats and mice exposed to methyl chloride. Prepared for the Chemical Industry Institute of Toxicology, Durham, NC, by Battelle Laboratories, Columbus, OH. TSCA 8d. OTS no. 878211741, microfiche no. 205861.

Chemical Industry Institute of Toxicology, 1983. Final report on 24-month inhalation study on methyl chloride. Prepared by Battelle-Columbus Laboratories, Columbus, OH.

Exposure route:	inhalation			
Species:	mouse			
Strain:	B6C3F1			
Sex:	M			
Vehicle or physical state:	air			
Body weight:[b]	0.03 kg			
Duration of treatment (le):	730 days			
Duration of study (Le):	730 days			
Lifespan of animal (L):	730 days			
Target organ:	kidney			
Tumor type:	cortical adenomas, adenocarcinomas, papillary cystadenomas, cystadenocarcinomas and tubular cystadenomas			
Experimental dose/exposure:	1000 ppm (2065 mg/m^3)	225 ppm (465 mg/m^3)	50 ppm (103 mg/m^3)	0 ppm (0 mg/m^3)
Transformed animal dose (mg/kg/day):[c]	481	111	25	0
Human equivalent dose: (mg/kg/day):[d]	36.2	8.2	1.8	0.0
Tumor incidence:[e]	22/82	2/57	0/61	0/67

Comments: High mortality was observed in the 1000 ppm group so that only two (2) animals survived until the end of the study.

Source: U.S. Environmental Protection Agency, 1986. Evaluation of the potential carcinogenicity of methyl chloride. OHEA-C-073-128. Washington, DC: Office of Health and Environmental Assessment.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

74-87-3 methyl chloride (continued)

[b]Measured.

[c]First, convert the experimental dose in ppm to mg/kg^3: 0.041 x molecular weight of methyl chloride (50.49 g/mol) x concentration (ppm). Calculate preliminary transformed dose (mg/kg/day) from breathing rate and animal weight: concentration (mg/m^3) x breathing rate (0.039 m^3/day for a 0.03 kg mouse)/animal weight (0.03 kg). Determine final transformed dose by adjusting for duration of study and discontinuous exposure: transformed dose (mg/kg/day)x(le/Le)x5 (treatment days/wk)/ 7(days/wk)x6 (treatment hr/day)/24 (hr/day).

[d]Transformed animal dose (mg/kg/day)/(human body weight/animal body weight)$^{(1/3)}$.

[e]To correct for intercurrent mortality, the method described by Peto et al. (1980, IARC Monograph, Supplement 2, p. 378) was used. The overall incidence of kidney tumors, excluding those that died or were killed before 12 months (when the first kidney tumor was observed) was 0/67 in the control group, 0/61 in the 50 ppm group, 2/57 in the 225 ppm gorup, and 18/22 in the 1000 ppm gorup.

Elements of Hazard Ranking

Chemical Name: 4,4'-methylene bis(2-chloroaniline)

CAS Number: 101-14-4

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): 2.4 per (mg/kg)/day

Reference: Komineni, C.; Groth, D.H.; Frockt, I.J.; Voelker R.W.; Stanovick, R.P., 1979. Determination of the tumorigenic potential of methylene-bis-ortho-chloroaniline. J. Environ. Pathol. Toxicol. 2: 149-172.

Exposure route:	oral			
Species:	rat			
Strain:	Sprague-Dawley			
Sex:	M			
Vehicle or physical state:	diet (protein adequate)			
Body weight:[b]	0.66 kg	0.79 kg	0.82 kg	0.77 kg
Duration of treatment (le):	504 days	504 days	504 days	504 days
Duration of study (Le):	672 days	728 days	728 days	728 days
Lifespan of animal (L):	672 days[b]	728 days[c]	728 days[c]	728 days[c]
Target organ:	lung			
Tumor type:	adenomas and adenocarcinomas[c]			
Experimental dose/exposure:	1000 ppm	500 ppm	250 ppm	0 ppm
Transformed animal dose (mg/kg/day):[e]	22	13	6	0
Human equivalent dose (mg/kg/day):[f]	4.75	1.94	0.95	0.0
Tumor incidence:	35/50	28/75	23/100	1/100

Comments: The ED_{10} is based on data from oral exposure; an estimate of potency for the inhalation route is not currently available.

Source: U.S. Environmental Protection Agency, 1988. Evaluation of the potential carcinogenicity of 4,4'-methylene bis(2-chloroaniline). OHEA-C-073-130. Washington, DC: Office of Health and Environmental Assessment.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

[b]Reported.

[c]Assumed; survival at 104 wk was 10 percent, 14 percent, and 20 percent in the middle, low, and control groups, respectively.

101-14-4 4,4'-methylene bis(2-chloraniline) (continued)

[d]Predominately adenocarcinomas.
[e]Transformation based on approximate reported food consumption and body weight data. The study reported a mean weekly food consumption of 138.5 g per rat (control group). Transformed animal dose=(mg toxicant consumed/wk)/(7 days/wk)/(animal weight in kg)x(le/Le).
[f]Transformed animal dose (mg/kg/day)/(human body weight/animal body weight)$^{(1/3)}$.

Elements of Hazard Ranking

Chemical Name: methylene chloride

CAS Number: 75-09-2

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): 0.013 per (mg/kg)/d

Reference: NTP, 1986 technical report on the toxicology and carcinogenesis studies of dichloromethane in F3441 rats and B6C3F1 mice (inhalation studies). U.S. DHHS, PHS. NIH Tech. Rep. Ser. No. 306.

Andersen M.E., Clewell H.J., Gargas M.L., Smith F.A., Reitz R.H., 1987. Physiologically based pharmacokinetics and the risk assessment process for methylene chloride. Toxicol. Appl. Pharmaco. 87: 185-205.

Exposure route:		inhalation		
Species		mouse		
Strain:		B6C3F1		
Sex:		F		
Vehicle or physical state:		vapor/air		
Body weight:[b]		0.0345 kg.		
Duration of treatment (le):		104 weeks		
Duration of study (Le):		104 weeks		
Lifespan of animal (L):[c]		104 weeks		
Target organ:		liver and lung		
Tumor type:		combined adenomas and carcinomas		
Experimental doses/exposure (mg/kg/day):		4000	2000	0
Delivered doses[d] (mg/L/day):	Liver	131.9	57.5	0
	Lung	19.25	8.80	0
Tumor incidence:	Liver	40/46	16/46	3/45
	Lung	41/46	30/46	3/45

Comments: The ED_{10} was obtained by applying human physiologic pharmacokinetic model (Andersen et al. 1984) to delivered dose (geo. mean of liver and lung) in mg/m^3 giving 10% tumor incidence. Equivalent units in (mg/kg)/d were derived assuming a breathing rate of 20 m^3/d and 70 Kg body weight.

Source: U.S. Environmental Protection Agency, 1992. IRIS, Integrated risk information system. Online. Cincinnati, OH: U.S. Environmental Protection Agency, Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

[b]Estimated.
[c]Estimated.
[d]Delivered dose to target organ obtained using physiologic pharmacokinetic model of Andersen et al. (1987) and scaled by (human body weight/animal body weight) $^{(1/3)}$.

Elements of Hazard Ranking

Chemical Name: 4,4'-methylenedianiline

CAS Number: 101-77-9

IARC Classification:[1] 2B

Comments: No case reports or epidemiologic data are available. 4,4'-MDA induces treatment-related increased incidences in thyroid and liver tumors in two species. Increased increases of thyroid follicular adenomas and hepatocellular neoplasms are observed in male and female mice, whereas, thyroid follicular cell carcinomas and hepatic nodules are seen in male rats and thyroid follicular cell adenomas in females rats. 4,4'-MDA is genotoxic *in vitro*.

Source: International Agency for Research on Cancer, 1986. IARC monographs on the evaluation of carcinogenic risks to humans. Some chemicals used in plastics and elastomers. 39: 347-365.

---

[1]1-the agent is carcinogenic to humans, 2A-the agent is probably carcinogenic to humans (limited human evidence), 2B-the agent is probably carcinogenic to humans (limited evidence in humans in the absence of sufficient evidence in animals, or inadequate human evidence/non-existent human data and sufficient evidence in animals), 3-the agent is not classifiable as to its carcinogenicity to humans, 4-the agent is probably not carcinogenic to humans.

Elements of Hazard Ranking

Chemical Name: methyl hydrazine

CAS Number: 60-34-4

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): 4.1 per (mg/kg)/d

Reference: Toth, B and Shimizu, H. 1973. Methyl hydrazine tumorigenesis in Syrian golden hamsters and the morphology of malignant histiocytomas. Cancer Res. 33:2744.

Exposure route:	oral	
Species	hamster	
Strain:	Syrian golden	
Sex:	M	
Vehicle or physical state:	drinking water	
Body weight:[b]	0.12 kg.	
Duration of treatment (le):	lifetime	
Duration of study (Le):	lifetime	
Lifespan of animal (L):[c]	128 weeks	
Target organ:	liver	
Tumor type:	histiocytoma	
Experimental doses/exposure:	0.01% (1.1 mg/day)	0
Transformed animal doses[d] (mg/kg/day):	9.2	0
Human equivalent doses[e] (mg/kg/day):	1.1	0
Tumor incidence:	27/50	0/50

Comments: Experiment contains only one treatment group leading to a linear dose-response curve. The ED_{10} is based on oral data; an estimate of potency for the inhalation route is not currently available.

Source: U.S. Environmental Protection Agency, 1984. Health and environmental effects profile for methyl hydrazine. Prepared by the Environmental Critieria and Assessment Office, Office of Health and Environmental Assessment, Cincinnati, OH.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

[b]Estimated.

[c]Estimated.

[d]Experimental dose (mg/kg) x (no. treatment days per week/7 days per week) x (le/Le).

[e]Transformed animal dose /(human body weight/animal body weight) $^{(1/3)}$.

Elements of Hazard Ranking

Chemical Name: methyl iodide (iodomethane)

CAS Number: 74-88-4

Weight-of-Evidence Classification:[a] C

Estimate of Potency ($1/ED_{10}$): see comments

Comments: The available data are inadequate for estimating an ED_{10}.

Source: U.S. Environmental Protection Agency, 1988. Evaluation of the potential carcinogenicity of methyl iodide. OHEA-C-073-131. Washington, DC: Office of Health and Environmental Assessment.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

Elements of Hazard Ranking

Chemical Name: nickel and other nickel (+2) compounds

CAS Number: not applicable

Weight-of-Evidence Classification:[a] See comment

Estimate of Potency ($1/ED_{10}$): see comments

Comments: Nickel, at least some forms, should be considered carcinogenic to humans when inhaled (U.S. EPA, 1986; Health Assessment Document). Evidence is strongest in the sulfide nickel matte refining industry where epidemiologic data support that nickel subsulfide and nickel refinery dust are considered to be carcinogenic to humans, "Group A" according to EPA's cancer guidelines (U.S. EPA, 1986). More recent analyses by the International Agency for Research on Cancer (IARC, 1990; based on the analysis of the International Committee on Nickel Carcinogenesis in Man, 1990, Scand. J. Work Environ. Health, 16:1-84) additionally concluded that "sufficient" evidence in humans also existed for the carcinogenenicity of nickel sulfate (a nickel salt) according to IARC's criteria.

Animal and *in vitro* studies on other nickel compounds support the concern that at least some forns of nickel should be considered carcinogenic. The animal studies employed mainly injection aw the route of exposure, with some studies using inhalation as the exposure route. While the majority of the compounds tested in the injection studies caused tumors at the injection site only, nickel acetate, when tested in Strain a mice, and nickel carbonyl, at toxic levels, have also caused distal site primary tumors. Three low-dose drinking water studies and one dietary study with soluble nickel compounds have not shown any increase in tumors of the dosed animals.

Nickel carbonyl is considered by EPA to have "sufficient animal evidence and no data in humans. This evidence is classified by EPA as Group B2, probably carcinogenic to humans.

In the presence of some cancer activity, the nickel and nickel salts (excluding nickel subsulfide and nickel carbonyl) were included in a hazard ranking of potential carcinogens under CERCLA. section 101, and treated like compounds having a weight of evidence classification of "Group C, possibly carcinogenic to humans". The exceptions were nickel subsulfide (classified by EPA as Group A, human carcinogen) and nickel carbonyl (classified by EPA as Group B2, probably carcinogenic to humans). IARC's (1990) recent overall evaluation was that nickel compounds (as a class) are carcinogenic to humans, Group 1.

For the purposes of ranking hazard for section 112(g) of the Clean Air Act Amendments of 1990, HHAG recommends treating nickel and nickel salts similarly as that done under CERCLA, section 101. The more recent evaluation by IARC raises questions as to whether this recommended treatment of nickel salts may not be conservative enough. It must be recognized that this is a temporary postition given the newer information from IARC and that this recommendation could change in the future.

nickel and other nickel (+2) compounds (continued)

The data are not suitable for estimating an ED_{10} for nickel compounds besides nickel refinery dust and nickel subsulfide.

Source: IARC, 1990. IARC mongraphs on the evaluation of carcinogenic risks to humans. Chromium, nickel, and welding. 49: 257-445.

U.S. Environmental Protection Agency, 1986. Health assessment document for nickel and nickel compounds. EPA/600/8-83/012FF. Washington, DC: Office of Health and Environmental Assessment.

U.S. Environmental Protection Agency, 1988. Evaluation of the potential carcinogenicity of nickel, nickel ammonium sulfate, nickel carbonyl, nickel chloride, nickel cyanide, nickel hydroxide, nickel nitrate, nickel sulfate. OHEA-C-073-137. Washington D.C.: Office of Health and Environmental Assessment.

U.S. Environmental Protection Agency, 1994. IRIS, Intergrated Risk Information System. Online. Cincinnati, OH: U.S. Environmental Protection Agency, Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

Elements of Hazard Ranking

Chemical Name: nickel refinery dust

CAS Number: none

Weight-of-Evidence Classification:[a] A

Estimate of Potency ($1/ED_{10}$): 8.0 per (mg/kg)day

Reference: Chovil, A.; Sutherland, R.B.; Halliday, M., 1981. Respiratory cancer in a cohort of nickel sinter plant workers. Br. J. Ind. Med. 38:327-333.

Enterline, P.E., Marsh, G.M., 1982. Mortality among workers in a nickel refinery and alloy manufacturing plant in West Virginia. J. Natl. Cancer Inst. 68:925-933.

Magnus, K.; Andersen, A.; Hogetveit, A.C., 1982. Cancer of the respiratory organs among workers at a nickel refinery in Norway. Int. J. Cancer 30:681-685.

Peto, J.; Cuckle, H.; Doll, R,; Hermon, C; Morgan, L.G., 1984. Respiratory cancer mortality of Welsh nickel refinery workers. In: Nickel in the human environment: proceedings of a joint symposium: March 1983; Lyon, France. Lyon, France: International Agency for Research on Cancer (IARC Scientific Publication No. 53).

Expsoure route:	inhalation
Species:	human
Sex:	M
Vehicle or physical state	ambient air
Body Weight:[b]	70 kg
Target organ	lung

Comments: The ED_{10} is estimated by linear extrapolation of the unit risk (2.4E-4 per ug/m^3) to the dose associated with 10% mortality.

Source: U.S. Environmantal Protection Agency, 1988. Evaluation of the potential carcinogenicity of nickel, nickel ammonium sulfate, nickel carbonly, nickel chloride, nickel cyanide, nickel hydroxide, nickel nitrate, nickel sulfate. OHEA-C-073-134. Washington D.C.: Ofice of Health and Envrionmental Assessment.

U.S. Environmental Protection Agency, 1992. IRIS, Integrated Risk Information System. Online. Cincinnati OH: U.S. environmental Protection Agency, Office of Health and Environmental Assessment, Environmental Criteria and Assessment.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

[b]Estimated.

Elements of Hazard Ranking

Chemical Name: nickel subsulfide

CAS Number: 12035-72-2

Weight-of-Evidence Classification:[a] A

Estimate of Potency ($1/ED_{10}$): 16.0 per (mg/kg)day

Reference: Chovil, A.; Sutherland, R.B.; Halliday, M., 1981. Respiratory cancer in a cohort of nickel sinter plant workers. Br. J. Ind. Med. 38:327-333.

Enterline, P.E., Marsh, G.M., 1982. Mortality among workers in a nickel refinery and alloy manufacturing plant in West Virginia. J. Natl. Cancer Inst. 68:925-933.

Magnus, K.; Andersen, A.; Hogetveit, A.C., 1982. Cancer of the respiratory organs among workers at a nickel refinery in Norway. Int. J. Cancer 30:681-685.

Peto, J.; Cuckle, H.; Doll, R,; Hermon, C; Morgan, L.G., 1984. Respiratory cancer mortality of Welsh nickel refinery workers. In: Nickel in the human environment: proceedings of a joint symposium: March 1983; Lyon, France. Lyon, France: International Agency for Research on Cancer (IARC Scientific Publication No. 53).

Expsoure route:	inhalation
Species:	human
Sex:	M
Vehicle or physical state	ambient air
Body Weight:[b]	70 kg
Target organ	lung

Comments: The ED_{10} is estimated by linear extrapolation of the unit risk (4.8E-4 per ug/m^3) to the dose associated with 10% mortality. The unit risk estimate for nickel subsulfide is twice the midpoint of estimates from four data sets of refinery workers (2.4e-4 per ug/m^3 and accounts for a nickel subsulfide compositions of roughly 50 percent.

Source: U.S. Environmantal Protection Agency, 1988. Evaluation of the potential carcinogenicity of nickel, nickel ammonium sulfate, nickel carbonly, nickel chloride, nickel cyanide, nickel hydroxide, nickel nitrate, nickel sulfate. OHEA-C-073-134. Washington D.C.: Ofice of Health and Envrionmental Assessment.

U.S. Environmental Protection Agency, 1992. IRIS, Integrated Risk Information System. Online. Cincinnati OH: U.S. environmental Protection Agency, Office of Health and Environmental Assessment, Environmental Criteria and Assessment.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

[b]Estimated.

Elements of Hazard Ranking

Chemical Name: 4-nitrobiphenyl

CAS Number: 92-93-3

Weight-of-Evidence Classification:[a] see comments

Estimate of Potency ($1/ED_{10}$): see comments

Comments: The Office of Research and Development/Office of Health and Environmental Assessment is currently evaluating the carcinogenic evidence on 4-nitrobiphenyl. A draft preliminary assessment indicates that the weight-of-evidence classification is such that this chemical may be considered a "nonthreshold" hazardous air pollutant. This evaluation is currently undergoing internal peer review, thus, the exact placement of this chemical with respect to other "nonthreshold" HAP can not be determined at this time.

Source: U.S Environmental Protection Agency, 1992. Preliminary assessment evaluation of the potential carcinogenicity of 4-nitrobiphenyl. First draft. Prepared by the Chemical Hazard Evaluation Program, Health and Safety Research Division, ORNL, for the Office of Health and Environmental Assessment, Human Health Assessment Group.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

Elements of Hazard Ranking

Chemical Name: 2-nitropropane

CAS Number: 79-46-9

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): see comments

References: Griffin, T.B.; Coulston, F.; Stein, A.A., 1980. Chronic inhalation exposure of rats to vapors of 2-nitropropane at 25 ppm. Ecotoxicol. Environ. Saf. 4: 267-281.

Griffin, T.B.; Stein, A.A.; Coulston, F., 1981. Histological study of tissues and organs from rats exposed to vapor of 2-nitropropane at 25 ppm. Ecotoxicol. Environ. Saf. 5: 194-201.

Lewis, T.R.; Ulrich, G.E.; Busey, W.M., 1979. Subchronic inhalation toxicity of nitromethane and 2-nitropropane. J. Environ. Pathol. Toxicol. 2: 233-249.

Comments: The results of two inhalation bioassays (Lewis et al., 1979; Griffin et al., 1980, 1981) provide a wide range of estimates of an ED_{10}. Shortcomings in these bioassays preclude the inference of an ED_{10}.

Source: U.S. Environmental Protection Agency, 1988. Evaluation of the potential carcinogenicity of 2-nitropropane. OHEA-C-073-145. Washington, DC: Office of Health and Environmental Assessment.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

Elements of Hazard Ranking

Chemical Name: N-nitrosodimethylamine

CAS Number: 62-75-9

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): 61 per (mg/kg)/day

Reference: Terracini, B.; Magee, P.N.; Barnes, J.M., 1967. Hepatic pathology in rats on low dietary levels of dimethylnitrosamine. Br. J. Cancer 21: 559-565.

Exposure route:	oral					
Species:	rat					
Strain:	Porton					
Sex:	M, F					
Vehicle or physical state:	arachis oil in diet					
Body weight:[b]	0.35 kg					
Duration of treatment (le):	421 days	421 days	421 days	728 days	728 days	728 days
Duration of study (Le):	421 days	421 days	421 days	728 days	728 days	728 days
Lifespan of animal (L):	728 days					
Target organ:	liver					
Tumor type:	hepatoma					
Experimental dose/ exposure:[c]	50 ppm	20 ppm	10 ppm	5 ppm	2 ppm	0 ppm
Transformed animal dose (mg/kg/day):[d]	1.0	0.4	0.2	0.1	0.04	0.0
Human equivalent dose (mg/kg/day):[e]	0.17	0.068	0.034	0.017	0.006	0.0
Tumor incidence:	10/12	15/23	2/5	5/68	1/37	0/41

Comments: The ED_{10} is based on oral data; an estimate of potency for the inhalation route is not currently available.

Source: U.S. Environmental Protection Agency, 1988. Evaluation of the potential carcinogenicity of N-nitrosodimethylamine. OHEA-C-073-149. Washington, DC: Office of Health and Environmental Assessment.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

62-75-9 N-nitrosodimethylamine (continued)

[b]Estimated.
[c]Reported.
[d]Experimental dose (ppm)x0.05 (fraction of rat's body weight consumed as food per day)x(544/728)^3. The average study duration for the five dosed groups was 544 days.
[e]Transformed animal dose (mg/kg/day)/(human body weight/animal body weight)$^{(1/3)}$.

Elements of Hazard Ranking

Chemical Name: N-nitroso-N-methylurea

CAS Number: 684-93-5

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): 2100

Reference: Reddy, J.K.; Rao, M.S., 1975. Pancreatic adenocarcinoma in inbred guinea pigs induced by N-methyl-N-nitrourea. Cancer Res. 35: 2269-2277.

Exposure route:	gavage	
Species:	guinea pig	
Strain:	Strain-13	
Sex:	M, F	
Vehicle or physical state:	1% in 0.015 M sodium citrate buffer	0.015 sodium citrate buffer control
Body weight:[b]	0.25 kg	
Duration of treatment (le):	308 days	
Duration of study (Le):	308 days	
Lifespan of animal (L):[c]	1584 days	
Target organ:	pancreas	
Tumor type:	adenocarcinoma	
Experimental dose/exposure:	10 mg/kg/week	0.0 mg/kg/day
Transformed animal dose (mg/kg/day):[d]	0.01	0.0
Human equivalent dose (mg/kg/day):[e]	0.001	0.0
Tumor incidence:	10/34	0/18

Comments: N-nitroso-N-methylurea is a direct-acting alkylating agent. The very short latent periods for tumor induction in many studies and tumorigenic response following single exposures suggest that NMU is active in the early stages of the carcinogenic process. The dose and duration adjustments usually performed for less-than-lifetime studies may not adequately characterize dosage for estimating the dose-response relationship.

The ED_{10} is based on data for oral exposure; an estimate of potency for the inhalation route is not currently available.

Source: U.S. Environmental Protection Agency, 1988. Evaluation of the potential carcinogenicity of N-nitroso-N-methylurea. OHEA-C-0-73-151. Washington, D.C: Office of Health and Environmental Assessment.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

684-93-5 N-nitroso-N-methylurea (continued)

[b]Reported.
[c]Value recommended by EPA (ECAO-CIN-477, September 1986)
[d]Experimental dose (mg/kg/wk)/7(days/wk)x(Ie/Le)x(Le/L)^3.
[e]Transformed animal dose (mg/kg/day)/(human body weight/animal body weight)$^{(1/3)}$.

Elements of Hazard Ranking

Chemical Name: N-nitrosomorpholine

CAS Number: 59-89-2

IARC Classification:[1] 2B

Comments: "Sufficient evidence for carcinogenicity to aniamls" and "no data" in humans.

Source: International Agency for Research on Cancer, 1987. IARC monographs on the evaluation of carcinogenic risks to humans. Overall evaluations of carcinogenicity: an updating of IARC monographs volumes 1 to 42. Supplement 7: 68.

---

[a]1-the agent is carcinogenic to humans, 2A-the agent is probably carcinogenic to humans (limited human evidence), 2B-the agent is probably carcinogenic to humans (limited evidence in humans in the absence of sufficient evidence in animals, or inadequate human evidence/non-existent human data and sufficient evidence in animals), 3-the agent is not classifiable as to its carcinogenicity to humans, 4-the agent is probably not carcinogenic to humans.

Elements of Hazard Ranking

Chemical Name: parathion

CAS Number: 56-38-2

Weight-of-Evidence Classification:[a] C

Estimate of Potency ($1/ED_{10}$): see comments

Comments: The available data are inadequate for estimating an ED_{10}.

Source: U.S. Environmental Protection Agency, 1992. IRIS, Integrated Risk Information System. Online Cincinnati, OH: U.S. Environmental Protection Agency, Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

Elements of Hazard Ranking

Chemical Name: pentachloronitrobenzene

CAS Number: 82-68-8

Weight-of-Evidence Classification:[a] C

Estimate of Potency ($1/ED_{10}$): 0.25 per (mg/kg)/day

Reference: Van der Heijden, C.A.; Till, M.P., 1974. Pentachloronitrobenzene (PCNB) carcinogenicity study in mice. Report No. R4365. Central Institute for Food and Nutrition, The Netherlands (as cited in U.S. EPA, 1977).

Exposure route:	oral			
Species:	mouse			
Strain:	Swiss albino			
Sex:	F			
Vehicle or physical state:	diet			
Body weight:[b]	0.3 kg			
Duration of treatment (le):	80 weeks			
Duration of study (Le):	80 weeks			
Lifespan of animal (L):[c]	104 weeks			
Target organ:	connective tissue			
Tumor type:	fibroma and fibrosarcomas			
Experimental dose/exposure:	1200 ppm	400 ppm	100 ppm	0
Transformed animal dose (mg/kg/day):[d]	71.0	23.7	5.9	0
Human equivalent dose (mg/kg/day):[e]	5.4	1.8	0.5	0.0
Tumor incidence:	12/09	3/91	3/95	0/90

Comments: The ED_{10} is based on data for oral exposure; an estimate of potency for the inhalation route is not currently available. PCNB was contaminated with 2.7% hexachlorobenzene; tumor response may be partially attributable to this contamination. A higher potency estimate ($1/ED_{10}$=1.42 per mg/kg/d) was obtained from the one-dose study of Innes et al. (1969, J. Natl. Cancer Inst., 42: 1101) in which pentachloronitrobenzene was contaminated with 11% hexachlorobenzene (U.S. EPA, 1988; Evaluation of the potential carcinogenicity of pentachloronitrobenzene. OHEA-C-073-159).

Source: U.S. Environmental Protection Agency, 1986. Health and environmental effects profile of pentachloronitrobenzene. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

[b]Reported.

[c]Assumed.
[d]Experimental dose (ppm) x 0.13 (fraction of mouse's body weight consumed as food per day) x $(Le/L)^3$.
[e]Transformed animal dose (mg/kg/day)/(human body weight/animal body weight)$^{(1/3)}$.

Elements of Hazard Ranking

Chemical Name: pentachlorophenol

CAS Number: 87-86-5

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): 0.67 per (mg/kg)/day

Reference: National Toxicology Program, 1989. Technical report on the toxicology and carcinogenesis studies of pentachlorophenol (CAS No. 87-86-5) in B6C3F1 mice (feed studies). NTP Technical Report No. 349. NIH publication no. 89-2804.

Exposure route:	oral						
Species:	mouse						
Strain:	B6C3F1						
Sex:	F						
Vehicle or physical state:	diet						
Body weight:[b]	0.03 kg						
Duration of treatment (le):	104 wk						
Duration of study (Le):	104 wk						
Lifespan of animal (L):[b]	104 wk						
Target organ:	liver, vascular system						
Tumor type:	hepatocellular adenoma/carcinoma, pheochromocytoma malignant/benign, hemangiosarcoma/hemangioma						
Experimental dose/exposure	technical grade			Dowicide EC-7			
(ppm):	200	100	0	600	200	100	0
Transformed animal dose (mg/kg/day):[c]	35	17	0	114	34	17	0
Human equivalent dose (mg/kg/day):[d]	2.7	1.4	0.0	8.7	2.7	1.3	0.0
Tumor incidence:	15/46	12/48	5/31	42/49	9/46	6/49	1/34

Comments: The ED_{10} is based on data for oral exposure in the absence of inhalation data.

Source: U.S. Environmental Protection Agency, 1992. IRIS, Integrated Risk Information System Online. Cincinnati, OH: U.S. Environmental Protection Agency, Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

[b]Assumed.

[c]Experimental dose (ppm)x0.135 (fraction of body weight consumed as food per day).

[d]Transformed animal dose (mg/kg/day)/(human body weight/animal body weight)$^{(1/3)}$.

Elements of Hazard Ranking

Chemical Name: polychlorinated biphenyls,(Aroclors)

CAS Number: 1336-36-3

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): 50 per (mg/kg)/day

Reference: Norback, D.H.; Weltman, R.H., 1985. Polychlorinated biphenyl induction of hepatocellular carcinoma in the Sprague-Dawley rat. Environ. Health Perspect. 60: 97-105.

Exposure route:	oral	
Species:	rat	
Strain:	Sprague-Dawley	
Sex:	F	
Vehicle or physical state:	diet	
Body weight:[b]	0.35 kg	
Duration of treatment (le):	24 mo	
Duration of study (Le):	29 mo	
Lifespan of animal (L):[b]	29 mo	
Target organ:	liver	
Tumor type:	trabecular carcinoma, adenocarcinoma, neoplastic nodule[c]	
Experimental dose/exposure:	100 ppm[d]	0.0 ppm
Transformed animal dose (mg/kg/day):[e]	3.45	0.0
Human equivalent dose (mg/kg/day):[f]	0.59	0.0
Tumor incidence:	45/47	1/49

Comments: The Aroclors are mixtures of polychlorinated biphenyls (PCBs). The manufacturing process for commercial PCB products yields mixtures of 20 to 60 different PCB compounds. Only Aroclors 1254 and 1260 have been tested for carcinogenic potential. For the purpose of ranking hazards under Sec. 112 (g) of the Clean Air Act, EPA uses the data from the study of Aroclor 1260 to derive a potency factor for all of the Aroclors. The $ED_{.c}$ is based on data for oral exposure; an estimate of potency for the inhalation route is not currently avaiable.

Source: U.S. Environmental Protection Agency, 1988. Evaluation of the potential carcinogenicity of polychlorinated biphenyls including specific Aroclors. OHEA-C-073-162. Washington, DC: Office of Health and Environmental Assessment.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

[b]Assumed.

[c]Because neoplastic nodules precede carcinomas, animals with neoplastic nodules were counted with those that developed carcinomas.

[d]100 ppm dosage administered for the first 16 mo, followed by 50 ppm for an additional 8 mo, and a control diet for the remaining 5 mo.
[e]100 ppm x 0.05 (fraction of rat's body weight consumed as food per day)x16 mo (1 mo=30.4 days)=2432 mg/kg total dose for the first 16 mo. Next, 50 ppm x 0.05 (fraction of rat's body weight consumed as food per day)x8 mo (1 mo=30.4 days)=608 mg/kg total dose for the subsequent 8 mo. Final transformed dose=(2432 mg/kg + 608 mg/kg)/29 mo (duration of study; 1 mo=30.4 days).
[f]Transformed animal dose (mg/kg/day)/(human body weight/animal body weight)$^{(1/3)}$.

Elements of Hazard Ranking

Chemical Name: 1,3-propane sultone

CAS Number: 1120-71-4

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): 10 per (mg/kg)/day

Reference: Ulland, B.; Finkelstein, M.; Weisburger, E.K.; Rice, J.M.; Weisburger, J.H., 1971. Carcinogenicity of the industrial chemicals propylene imine and propane sultone. Nature (London) 230: 460-461.

Exposure route:	gavage		
Species:	rat		
Strain:	Charles River CD		
Sex:	M		
Vehicle or physical state:	distilled water		
Body weight:[b]	0.35 kg		
Duration of treatment (le):	224 days	420 days	427 days
Duration of study (Le):	420 days	420 days	427 days
Lifespan of animal (L):[b]	728 days		
Target organ:	brain		
Tumor type:	glioma		
Experimental dose/exposure:	56 mg/kg twice/wk	28 mg/kg twice/wk	0 mg/kg twice/wk
Transformed animal dose (mg/kg/day):[c]	1.62	1.52	0.0
Human equivalent dose (mg/kg/day):[d]	0.27	0.26	0.0
Tumor incidence:	16/26	12/26	0/6[e]

Comments: The ED_{10} was based on data for oral exposure; an estimate of potency for the inhalation route is not currently available.

Source: U.S. Environmental Protection Agency, 1988. Evaluation of the potential carcinogenicity of 1,3-propane sultone. OHEA-C-073-170. Washington, DC: Office of Health and Environmental Assessment.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

[b]Estimated.

[c]Experimental dose (mg/kg/day)x(number treatment days per wk)/(7 days/wk)x(le/Le)x$(Le/L)^3$.

[d]Transformed animal dose (mg/kg/day)/(human body weight/animal body weight)$^{(1/3)}$.

[e]The paper states that 64 negative control animals served as controls for concurrent studies. Only 6 males and 6 females were killed at 61 wk. It is uncertain whether these animals had been treated with distilled water.

Elements of Hazard Ranking

Chemical Name: β-propiolactone

CAS Number: 57-57-8

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): see comments

Comments: The available studies are inadequate for estimating an ED_{10}.

Source: U.S. Environmental Protection Agency, 1992. Evaluation of the potential carcinogenicity of β-propriolactone. OHEA-C-073-202. Washington, DC: Office of Health and Environmental Assessment.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

Elements of Hazard Ranking

Chemical Name: propoxur (Baygon)

CAS Number: 114-26-1

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): 0.053 per (mg/kg)/d

Reference: Hazelton Laboratories, 1984. Report no. 12870, HLE no. 3563-262/32 and acc. 25517. Cited in memorandum from B. Fisher to B. Backus, April 21, 1992.

Exposure route:	oral			
Species:	rat			
Strain:	SPF (Bor:WISW)			
Sex:	M, F			
Vehicle or physical state:	diet			
Body weight:[b]	0.35 kg			
Duration of treatment (le):	107 wks			
Duration of study (Le):	107 wks			
Lifespan of animal (L):[c]	107 wks			
Target organ:	bladder			
Tumor type:	carcinoma and/or papilloma			
Experimental doses/exposure (ppm):	5000	1000	200	0
Transformed animal doses (mg/kg/day):[c]	250	50	10	0.0
Human equivalent doses (mg/kg/day):[e]	42.5	8.5	1.7	0.0
Tumor incidence: (males)	34/57	1/59	0/60	0.57
(females)	33/48	0/47	0/46	0/47

Comments: The ED_{10} is based on oral data; an estimate of potency for the inhalation route is not currently available and is a geometric mean of ED_{10} estimates of males and females.

Source: U.S. Environmental Protection Agency, 1992. Memorandum from B. Fisher to B. Backus, "Propoxur (Baygon) qualitative risk assessment, revised and quantitative risk assessment-two-year SPF rat dietary study. April 21, 1992.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

[b]Estimated.

[c]Estimated.

[d]Experimental dose (ppm) x (0.05, fraction of rat's body weight consumed as diet per day) x (le/Le).

[e]Transformed animal dose (mg/kg/d)/(human body weight/animal body weight) $^{(1/3)}$.

Elements of Hazard Ranking

Chemical Name: propylene dichloride (1,2-dichloropropane)

CAS Number: 78-87-5

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): 0.36 per (mg/kg)/d

Reference: National Toxicology Program, 1986. NTP technical report on the carcinogenesis studies of 1,2-dichloropropane (propylene dichloride). (CAS 78-87-5) in F3441N rats and B6C3F1 mice (gavage studies). NTP.82-092, NIH Publ. No. 84-2519, NTP TR 263. USDHHS, PHS, NIH. August 1986 draft.

Exposure route:	oral		
Species	mice		
Strain:	B6C3F1		
Sex:	M		
Vehicle or physical state:	corn oil		
Body weight:[b]	0.04 kg.		
Duration of treatment (le):	103 weeks		
Duration of study (Le):	105 - 107 weeks		
Lifespan of animal (L):[c]	105 - 107 weeks		
Target organ:	liver		
Tumor type:	adenoma and carcinoma		
Experimental doses/exposure (mg/kg/day):	250	125	0
Transformed animal doses[d] (mg/kg/day):	173.52	86.76	0
Human equivalent doses[e] (mg/kg/day):	14.43	7.22	0
Tumor incidence:	33/50	26/50	18/50

Comments: The ED_{10} is based on data from the oral route of exposure; an estimate of potency for the inhalation route is not currently available.

Source: U.S. Environmental Protection Agency, 1987. Health effects assessment 1,2-dichloropropane. EPA/600/8-88/029. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

[b]Estimated.

[c]Estimated.

[d]Experimental dose (mg/kg/d) x (5 treatment days per week/7 days per week) x (le/Le).

[e]Transformed animal dose /(human body weight/animal body weight) $^{(1/3)}$.

Elements of Hazard Ranking

Chemical Name: 1,2-propylenimine (2-methyl aziridine)

CAS Number: 75-55-8

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): 150 per (mg/kg)/day

Reference: Ulland, B.; Finkelstein, M.; Weisburger, E.K.; Rice, J.M.; Weisburger, J.H., 1971. Carcinogenicity of industrial chemicals propylene imine and propane sultone. Nature (London) 230: 460-461.

Exposure route:	gavage	
Species:	rat	
Strain:	Charles River-CD	
Sex:	F	
Vehicle or physical state:	distilled water	
Body weight:[b]	0.35 kg	
Duration of treatment (le):	421 days	
Duration of study (Le):	421 days	
Lifespan of animal (L):[b]	730 days	
Target organ:	mammary gland	
Tumor type:	adenoma and carcinoma	
Experimental dose/exposure:[c]	10 mg/kg (twice weekly)	0 mg/kg
Transformed animal dose (mg/kg/day):[c]	0.548	0.0
Human equivalent dose (mg/kg/day):[e]	0.094	0.0
Tumor incidence:[f]	20/26	0/12

Comments: The ED_{10} was based on data for oral exposure; an estimate of potency for the inhalation route is not currently available. EPA (1988) presented a potency ($1/ED_{10}$) of 260 per (mg/kg)/d. This estimate was based on an incorrect assumption of a 730 day duration of study (Le). The above estimate is based on a study duration of 60 weeks (421 days).

Source: U.S. Environmental Protection Agency, 1988. Evaluation of the potential carcinogenicity of 1,2-propylenimine. OHEA-C-073-171. Washington, DC: Office of Health and Environmental Assessment.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

[b]Estimated.

75-55-8 1,2-propylenimine (continued)

[c]The study also utilized a dose of 20 mg/kg, but those data were not used because at 20 mg/kg, the mortality was reported (by the author) to be "high." The actual number of deaths in the 26 high-dose animals exposed was not stated. However, since the incidence of mammary cancer was higher at 10 mg/kg, it was apparent that many of the high-dose animals died from paralysis before there was sufficient time for the development of mammary cancer.

[d]Experimental dose (mg/kg/day)x(le/Le)x2 (treatment days/wk)/7 (days/wk)x(Le/L)^3.

[e]Transformed animal dose (mg/kg/day/(human body weight/animal body weight)$^{(1/3)}$.

[f]Although both males and females exhibited significant increases in neoplasms, only the female mammary tumors were utilized for the potency estimate, since this results in the most conservative estimate.

Elements of Hazard Ranking

Chemical Name: propylene oxide

CAS Number: 75-56-9

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$):[b] 0.16 per (mg/kg)/d

Reference: National Toxicology Program, 1985. Toxicologic and carcinogenic studies of propylene oxide in F344/N rats and B6CF1 mice (inhalation studies). NTP Tech. Rep. Ser. No. 267, NTP Research Triangle Park, NC. NIH Publ. No. 85-2527.

Exposure route:	inhalation		
Species:	mice		
Strain:	B6CF1		
Sex:	M		
Vehicle or physical state:	vapor/air		
Body weight:[c]	0.03 kg.		
Duration of treatment (le):	103 weeks		
Duration of study (Le):	103 weeks		
Lifespan of animal (L):[c]	103 weeks		
Target organ:	nasal cavity		
Tumor type:	hemangioma or hemangiosarcoma		
Experimental doses/exposure (mg/kg/day):	400	200	0
Transformed animal absorbed doses[d] (mg/kg/day):	110	55	0
Human equivalent absorbed doses[e] (mg/kg/day):	8.30	4.15	0
Tumor incidence:	10/50	0/50	0/50

Comments: Transformed doses were calculated assuming 50% absorption via inhalation exposure.

Source: U.S. Environmental Protection Agency, 1992. IRIS, Integrated Risk Information System. Online. Cincinnati, OH: U.S. Environmental Protection Agency, Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

[b]The ED_{10} is expressed in units of absorbed dose; 50% absorption is assumed.

[c]Estimated.

[d]Experimental dose (ppm) x 0.041 x molecular weight 1/BW x breathing rate x (5 treatment days per week/7 days per week) x 6/24 hours per day x absorption fraction (0.05).

[e]Transformed animal dose /(human body weight/animal body weight) $^{(1/3)}$.

Elements of Hazard Ranking

Chemical Name: quinoline

CAS Number: 91-22-5

Weight-of-Evidence Classification:[a] C

Estimate of Potency ($1/ED_{10}$): 1.4 per (mg/kg)/d

Reference: Hirao KY, Shinohara H, Tsuda S, Fukushima M, et al., 1976. Carcinogenic activity of quinoline on rat liver. Cancer Res. 36(2, Pt. 1): 329-335.

Exposure route:	oral			
Species:	rat			
Strain:	Sprague-Dawley			
Sex:	M			
Vehicle or physical state:	diet			
Body weight:[b]	0.35 kg.			
Duration of treatment (le):	20 (high dose), 27.3 (mid dose), 36.5 (low dose) and 40 (controls) weeks			
Duration of study (Le):	20 (high dose), 27.3 (mid dose), 36.5 (low dose), and 40 (controls) weeks			
Lifespan of animal (L):[c]	104 weeks			
Target organ:	liver			
Tumor type:	hemangioendothelioma			
Experimental doses/exposure (ppm):	2500	1000	500	0
Transformed animal doses[d] (mg/kg/day):	125	50	25	0
Human equivalent doses[e] (mg/kg/day):	21.0	9.3	5.0	0
Tumor incidence:	17/60	9/60	5/60	5/60

Comments: Tumors could not be classified as to their degree of malignancy; it was assumed that not all non-neoplastic tumors would progress to malignancy. Human equivalent doses were not adjusted for less than lifetime follow-up in light of the uncertain pathology. Adjustment for less than lifetime follow-up would add additional conservatism to that already introduced by the uncertain pathology.

The ED_{10} is based on data for oral exposure; an estimate of potency for the inhalation route is not currently available.

Source: U.S. Environmental Protection Agency, 1985. Health and Environmental effects profile for Quinoline. Prepared by the Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment, Washington, D.C.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

[b]Estimated.
[c]Estimated.
[d]Experimental dose (ppm) x 0.05 (the amount of diet consumed daily by a rat).
[e]Transformed animal dose / (human body weight/animal body weight)$^{(1/3)}$.

Elements of Hazard Ranking

Chemical Name: selenium sulfide (mono-and di-)

CAS Number: 7446-34-6 (selenium monosulfide) 7488-56-4 (selenium disulfide)

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): 0.93 per (mg/kg)1d

Reference: NTP, 1980. Bioassay of selenium sulfide (gavage) for possible carcinogenicity. NCI-CG-TR-194, NTP-80-17; PB 82-164955.

Exposure route:	oral		
Species	rat		
Strain:	F344		
Sex:	F		
Vehicle or physical state:	0.5% aqueous carboxymethylcellulose		
Body weight:[b]	0.30 kg		
Duration of treatment (le):	721 days		
Duration of study (Le):	735 days		
Lifespan of animal (L):[c]	735 days		
Target organ:	liver		
Tumor type:	hepatocellular carcinoma		
Experimental doses/exposure (mg/kg/day):	15	3	0
Transformed animal doses (mg/kg/day):[d]	14.7	2.94	0.0
Human equivalent doses (mg/kg/day):[e]	2.39	0.48	0.0
Tumor incidence:	21/50	0/50	0/50

Comments: The ED_{10} is based is based on oral data; an estimate of potency for the inhalation route is not currently avaiable.

Source: U.S. Environmental Protection Agency, 1988. Evaluation of the potential carcinogenicity of selenium sulfide. OHEA-C-073-174. Washington, D.C.: Office of Health and Environmental Assessment.

U.S. Environmental Protection Agency, 1992. IRIS, Integrated Risk Information System. Online. Cincinnati, OH: Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

[b]Estimated.

[c]Estimated.

[d]Experimental dose (mg/kg/d) x (le/Le).

[e]Transformed animal dose (mg/kg/d)/(human body weight/animal body weight) $^{(1/3)}$.

Elements of Hazard Ranking

Chemical Name: styrene

CAS Number: 100-42-5

Weight-of-Evidence Classification[a]: see comments

Estimate of Potency ($1/ED_{10}$): see comments

Comments: The carcinogenicity evidence on styrene has been evaluated by the International Agency for Research on Cancer (IARC, 1987) and was classified, according to their guidelines, to be in Group 2B. IARC based their overall conclusions on "limited" evidence in animals, "inadequate" evidence in humans, and positive mutagenicity (for styrene and its metabolite styrene oxide, classified in Group 2A).

A draft Drinking Water Criteria Document for Styrene was presented to the Science Advisory Board (SAB) in 1988 for review. The SAB considered the evidence on styrene as classified into Group C (possible human carcinogen) and disagreed with the EPA conclusion of a classification of Group B2 (probable human carcinogen) (U.S. EPA, 1988). The issue under discussion was the classification of styrene into Group C or Group B2. No official position currently exists.

The Office of Science and Technology (formerly the Office of Drinking Water) has more recently promulgated a final maximum contaminant level goal for styrene (U.S. EPA, 1991). For the MCLG, styrene was treated like compounds who have classifications of Group C, that is, styrene was placed into Category II for the purposes of setting an MCLG (U.S. EPA, 1991)

The treatment of styrene for purposes for setting a MCLG provides a reasonable basis for the treatment of styrene under Section 112(g) of the Clean Air Act Amendments of 1990. In the absence of a classification for styrene, it is recommended that styrene be treated like hazardous air pollutants having a classification of Group C for the purposes of ranking hazard under Section 112(g).

Source: International Agency for Research on Cancer, 1987. Overall evaluations of carcinogenicity: an updating of Monograph Volumns 1 to 42, Supplement 7.

U.S. Environmental Protection Agency, 1991. Fed Register. January 30, 1991. pgs. 3540 -3541.

U.S. Environmental Protection Agency, 1988. Memorandum to Mr. William Reilley, Administrator, from Norton Nelson, Richard A. Griesemer, and Gary P. Carlson, Science Advisory Board. Science Advisory Board's review of styrene health criteria document. July 18, 1988.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

Elements of Hazard Ranking

Chemical Name: styrene oxide

CAS Number: 96-09-3

IARC Classification:[1] 2A

Comments: "Sufficient evidence for carcinogenicity to animals" and "no data" in humans. Additionally, IARC considered the positive genotoxicity data on styrene oxide to influence the making of the overall evaluation. Styrene oxide has induced genotoxic effects in a wide range of studies. *In vitro*, styrene oxide was mutagenic in bacteria, yeast, and insects tests, has induced chromosomal aberrations and micronuclei in plants, and has induced DNA damage, chromosomal aberrations, and sister chromatid exchanges in mammalian cells. *In vivo*, styrene oxide has induced DNA damage in mammalian cells and chromosomal aberrations in mice (in one study). No dominant lethal mutations, chromosomal aberrations, micronuclei, or sister chromatid exchanges were induced in mice or hamsters in other studies.

Source: International Agency for Research on Cancer, 1987. IARC monographs on the evaluation of carcinogenic risks to humans. Overall evaluations of carcinogenicity: an updating of IARC monographs volumes 1 to 42. Supplement 7:72.

International Agency for Research on Cancer, 1985. IARC monographs on the evaluation of carcinogenic risks to humans. Allyl compounds, aldehydes, epoxides and peroxides. Volume 35:245-263.

---

[a]1-the agent is carcinogenic to humans, 2A-the agent is probably carcinogenic to humans (limited human evidence), 2B-the agent is probably carcinogenic to humans (limited evidence in humans in the absence of sufficient evidence in animals, or inadequate human evidence/non-existent human data and sufficient evidence in animals), 3-the agent is not classifiable as to its carcinogenicity to humans, 4-the agent is probably not carcinogenic to humans.

Elements of Hazard Ranking

Chemical Name: 2,3,7,8-tetrachlorodibenzo-p-dioxin (2,3,7,8-TCDD)

CAS Number: 1746-01-6

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): 660,000 per (mg/kg)/day

Reference: Kociba, R.J.; Keyes, D.G.; Beyer, J.E.; et al., 1978. Results of a two-year chronic toxicity and oncogenicity study of 2,3,7,8-tetrachlorodibenzo-p-dioxin in rats. Toxicol. Appl. Pharmacol. 46(92): 279-303.

Exposure route:	oral			
Species:	rat			
Strain:	Sprague-Dawley			
Sex:	F			
Vehicle or physical state:	diet			
Body weight:[b]	0.45 kg			
Duration of treatment (le):	735 days			
Duration of study (Le):	735 days			
Lifespan of animal (L):	735 days			
Target organ:	liver			
Tumor type:	hepatocellular carcinoma, hepatocellular hyperplastic nodules			
Experimental dose/exposure:	0.1 µg/kg/day	0.011 µg/kg/day	0.001 µg/kg/day	0.0 µg/kg/day
Transformed animal dose (mg/kg/day):[c]	1×10^{-4}	1×10^{-5}	1×10^{-6}	0.0
Human equivalent dose (mg/kg/day):[d]	1.86×10^{-5}	1.86×10^{-6}	1.86×10^{-7}	0.0
Tumor incidence:[e]	34/48	8/50	3/50	9/86

Comments: The potency factor was calculated from the histopathological analyses by Squire (1980) of the Kociba et al. (1978) data. The ED_{10} was extrapolated from the oral to an inhalation exposure route.

Source: U.S. Environmental Protection Agency, 1988. Evaluation of the potential carcinogenicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin. OHEA-C-073-176. Washington, DC: Office of Health and Environmental Assessment.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

[b]Reported.

[c]Experimental dose (mg/kg/day)x(no. treatment days per wk/7 days per wk)x(le/Le); micrograms were converted to milligrams using a conversion factor of 1 $\mu g = 1 \times 10^{-3}$ mg.

1746-01-6 tetrachlorodibenzo-p-dioxin (continued)

[d]Transformed animal dose (mg/kg/day)/(human body weight/animal body weight)$^{(1/3)}$.
[e]Number of animals with one or more tumors/total number of animals; tumor incidence data reinterpreted by Squire (Squire, R.A., 1980. Pathologic evaluations of selected tissues from the Dow Chemical TCDD and 2,4,5,-T rat studies. Submitted to Carcinogen Assessment Group, U.S. Environmental Protection Agency, on August 15 under contract no. 68-01-5092.), who considered only those cases in which only one of the two types of hepatocellular changes was observed.

Elements of Hazard Ranking

Chemical Name: 1,1,2,2-tetrachloroethane

CAS Number: 79-34-5

Weight-of-Evidence Classification:[a] C

Estimate of Potency ($1/ED_{10}$): 1.7 per (mg/kg)/day

Reference: National Cancer Institute, 1978. Bioassay of 1,1,2,2-tetrachloroethane for possible carcinogenicity. NCI Carcinogenesis Technical Report Series No. 27. Also published as DHHS (NIH) PB-277-453.

Exposure route:	gavage		
Species:	mouse		
Strain:	B6C3F1		
Sex:	F		
Vehicle or physical state:	corn oil		
Body weight:[b]	0.03 kg		
Duration of treatment (le):	546 days		
Duration of study (Le):	637 days		
Lifespan of animal (L):[b]	730 days		
Target organ:	liver		
Tumor type:	hepatocellular carcinoma		
Experimental dose/exposure:	203 mg/kg/day	101 mg/kg/day	0 mg/kg/day
Transformed animal dose (mg/kg/day):[c]	115	58	0
Human equivalent dose (mg/kg/day):[d]	8.7	4.4	0.0
Tumor incidence:	43/47	30/48	0/20

Comments: The ED_{10} is based on data for oral exposure and can be extrapolated to the inhalation exposure route.

Source: U.S. Environmental Protection Agency, 1988. Evaluation of the potential carcinogenicity of 1,1,2,2-tetrachloroethane. OHEA-C-073-178. Washington, DC: Office of Health and Environmental Assessment.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

[b]Estimated.

[c]Experimental dose (mg/kg/day)x(no. treatment days per wk/7 days per wk)x(le/Le)x$(Le/L)^3$.

[d]Transformed animal dose (mg/kg/day)/(human body weight/animal body weight)$^{(1/3)}$.

Elements of Hazard Ranking

Chemical Name: tetrachloroethylene

CAS Number: 127-18-4

Weight-of-Evidence Classification:[a,b] B2/C

Estimate of Potency ($1/ED_{10}$):[c] 0.012 per (mg/kg)/day

Reference: National Toxciology Program, 1986. Toxicology and carcinogenesis of tetrachloroethylene (perchloroethylene) in F344/N rats and B6C3F1 mice (inhalation studies). NIH publication No. 86-2567. NTP TR 311.

Exposure route:	inhalation		
Species:	mouse		
Strain:	B6C3F1		
Sex:	M/F		
Vehicle or physical state:	vapor		
Body weight:[d]	0.035 kg		
Duration of treatment (le):	104 weeks		
Duration of study (Le):	104 weeks		
Lifespan of animal (L):[d]	104 weeks		
Target organ:	liver		
Tumor type:	carcinoma and carcinoma/adenoma		
Experimental dose/exposure:	200 ppm	100 ppm	0 ppm
Direct estimate of urinary metabolites (mg/kg):[e]	59.5	39.2	0.0 (m,f)
Human equivalent metabolized dose ($mg/W^{2/3}/day$):[f]	14.2	9.37	0.0 (males)
	13.5	8.92	0.0 (females)
Tumor incidence:[g] carcinoma	26/50	25/47	7/49 (males)
	36/47	13/42	1/47 (females)
carcinoma/ademona	40/50	31/47	16/49 (males)
	38/47	17/42	4/47 (females)

Reference: National Toxciology Program, 1986. Toxicology and carcinogenesis of tetrachloroethylene (perchloroethylene) in F344/N rats and B6C3F1 mice (inhalation studies). NIH publication No. 86-2567. NTP TR 311.

Exposure route:	inhalation
Species:	rat
Strain:	F344
Sex:	M/F
Vehicle or physical state:	vapor
Body weight:[d]	0.35 kg
Duration of treatment (le):	104 weeks
Duration of study (Le):	104 weeks
Lifespan of animal (L):[d]	104 weeks
Target organ:	circulatory system
Tumor type:	mononuclear cell luekemia

127-18-4 tetrachloroethylene (continued)

Experimental dose/exposure:	400 ppm	200 ppm	0 ppm	
Direct estimate of urinary metabolites (mg/kg):[e]	16.1	11.9	0.0	(m,f)
Human equivalent metabolized dose ($mg/W^{2/3}/day$):[f]	8.45	6.26	0.0	(males)
	7.84	5.81	0.0	(females)
Tumor incidence:	37/50	37/50	28/50	(males)
	29/50	30/50	18/50	(females)

Comments: The ED_{10} is based on a geometric mean of the six data sets.

Source: U.S. Environmental Protection Agency, 1986. Addendum to the health assessment document for tetrachloroethylene (perchloroethylene). External review draft. EPA/600/8-82/005FA. Washington, DC: Office of Health and Environmental Assessment.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

[b]The weight of evidence lies on a continuum between B2 and C. The EPA proposed a classification of "B2, probably carcinogenic to humans". The Science Advisory Board (as relayed in letters from N. Nelson, R. Greisemer, and J. Doull to L. Thomas, U.S. Environmental Protection Agency, March 9, 1988, and from R. Loehr and B. Weiss to W. Reilly, U.S. Environmental Protection Agency, August 16, 1991) believed the evidence was between "B2" and "C".

[c]The ED_{10} is expressed in units of administered dose. The human equivalent metabolized dose associated with a 10% tumor incidence [1 $ug/m^3/(7.83E\text{-}6\ mg/W^{2/3}/d)$] = ED_{10} in inhalation units. To express this is mg/kg/d, it was assumed a 70 kg human had a breathing rate of 20 m^3/d.

[d]Estimated.

[e]As inferred using the data of Pegg et al. (1979; Toxic. Appl. Pharmacol. 51: 465-474) and Schumann et al., 1980; Toxicol. Appl. Pharmacol. 55:207-219).

[f]Human equivalent metabolized dose=concentration of urinary metabolites (mg/kg/d)x(5 treatment days/7 days per week)x$W^{1/3}$, where W=0.0374 kg for male mice, 0.0322 kg for female mice, 0.40 kg for male rats, and 0.32 kg for female rats.

[g]Denominators are the number of animals surviving beyond 60 weeks, the time of occurance of the fiirst liver tumor death.

Elements of Hazard Ranking

Chemical Name: 2,4-toluene diamine

CAS Number: 95-80-7

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): 6.5 per (mg/kg)/d

Reference: National Cancer Institute, 1979. Bioassay of 2,4-diaminotoluene for possible carcinogenicity. NCI Carcinogenesis Tech. Rep. Ser. No. 162.

Exposure route:	oral		
Species:	rat		
Strain:	F344		
Sex:	F		
Vehicle or physical state:	dietary		
Body weight:[b]	0.275 kg. (controls); 0.220 kg. (low dose); 0.175 kg. (high dose)		
Duration of treatment (le):	103 weeks (low dose); 84 weeks (high dose)		
Duration of study (Le):	103 weeks (low dose); 84 weeks (high dose)		
Lifespan of animal (L):[c]	104 weeks		
Target organ:	mammary gland		
Tumor type:	adenoma and carcinoma		
Experimental doses/exposure (mg/kg/day):	171 ppm	79 ppm	0
Transformed animal doses[d] (mg/kg/day):	4.5	3.82	0
Human equivalent doses[e] (mg/kg/day):	0.56	0.61	0
Tumor incidence:	41/50	38/50	1/20

Comments: A dose-related trend ($p<0.01$) for increased mortality was observed. Study terminated (high dose group) at 84 weeks; transformed animal dose adjusted accordingly $(Le/L)^3$. The ED_{10} is based on oral data; an estimate of potency for the inhalation route is not currently available.

Source: U.S. Environmental Protection Agency, 1986. Health and environmental effects profile for 2,4-toluene diamine. EPA 600/X-86/144. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.
[b]Estimated.
[c]Estimated.
[d]Experimental dose (ppm) x fraction of body weight consumed as food (.05) x $(Le/L)^3$.
[e]Transformed animal dose /(human body weight/animal body weight) $^{(1/3)}$.

Elements of Hazard Ranking

Chemical Name: toluene 2,4-diisocyanate

CAS Number: 584-84-9

IARC Classification:[1] 2B

Comments: "Sufficient evidence for carcinogenicity to animals" and "no data" in humans.

Source: International Agency for Research on Cancer, 1987. IARC monographs on the evaluation of carcinogenic risks to humans. Overall evaluations of carcinogenicity: an updating of IARC monographs volumes 1 to 42. Supplement 7:72.

---

[a]1-the agent is carcinogenic to humans, 2A-the agent is probably carcinogenic to humans (limited human evidence), 2B-the agent is probably carcinogenic to humans (limited evidence in humans in the absence of sufficient evidence in animals, or inadequate human evidence/non-existent human data and sufficient evidence in animals), 3-the agent is not classifiable as to its carcinogenicity to humans, 4-the agent is probably not carcinogenic to humans.

Elements of Hazard Ranking

Chemical Name: o-toluidine

CAS Number: 95-53-4

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): 0.093 per (mg/kg)/day

Reference: National Cancer Institute, 1979. Bioassay of o-toluidine-hydrochloride for possible carcinogenicity. Available from: NTIS, Springfield, VA. PB-290908, NCI-CG-TR-153.

Exposure route:	oral		
Species:	rat		
Strain:	Fischer 344		
Sex:	M		
Vehicle or physical state:	diet		
Body weight:[b]	0.375 kg	0.400 kg	0.450 kg
Duration of treatment (le):	100 wk	104 wk	104 wk
Duration of study (Le):	100 wk	104 wk	104 wk
Lifespan of animal (L):	100 wk	104 wk	104 wk
Target organ:	unspecified multiple organs		
Tumor type:	sarcoma		
Experimental dose/exposure:	6000 ppm	3000 ppm	0 ppm
Transformed animal dose (mg/kg/day):[c]	300	150	0
Human equivalent dose (mg/kg/day):[d]	52.5	26.8	0.0
Tumor incidence:	37/49	15/50	0/20

Comments: The estimate of the ED_{10} for o-toluidine is based on studies of o-toluidine HCL. In contrast to U.S. EPA (1988), the above estimate takes into account molecular weight differences between o-toluidine and its salt. The ED_{10} is based on data for oral exposure; an estimate of potency for the inhalation route is not currently available. Due to the multiple dose levels, the NCI study is considered a more adequate study for ranking hazard under the Clean Air Act, Section 112(g), than the one-dose, single sex, study of Hecht et al. (1982) (as cited in the Health and Environmental Effects Profile for Toluidines, EPA/600/x-84/151, 1984) from which an estimate of an $1/ED_{10}$ was 1.6 per (mg/kg/d).

Source: U.S. Environmental Protection Agency, 1988. Evaluation of the potential carcinogenicity of o-toluidine. OHEA-C-073-182. Washington, DC: Office of Health and Environmental Assessment.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

95-53-4 o-toluidine (continued)

[b]Reported; animal weight of 0.408 kg was used for potency calculation.
[c]Experimental dose (ppm)x0.05 (fraction of species body weight consumed as food per day).
[d]Transformed animal dose (mg/kg/day)/(human body weight/animal body weight)$^{(1/3)}$.

Elements of Hazard Ranking

Chemical Name: toxaphene

CAS Number: 8001-35-2

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): 4.3 per (mg/kg)/day

Reference: Litton Bionetics, 1978. Carcinogenic evaluation in mice: Toxaphene. Prepared by Litton Bionetics, Inc., Kensington, MD for Hercules, Inc., Wilmington, DE.

Exposure route:	oral			
Species:	mouse			
Strain:	B6C3F1			
Sex:	M			
Vehicle or physical state:	diet			
Body weight:[b]	0.03 kg			
Duration of treatment (le):	735 days			
Duration of study (Le):	735 days			
Lifespan of animal (L):[c]	735 days			
Target organ:	liver			
Tumor type:	hepatocellular carcinoma			
Experimental dose/exposure:	50 ppm	20 ppm	7 ppm	0 ppm
Transformed animal dose (mg/kg/day):[d]	6.5	2.6	0.91	0.0
Human equivalent dose (mg/kg/day):[e]	0.361	0.144	0.051	0.0
Tumor incidence:	18/51	12/53	10/54	10/53

Comments: The ED_{10} was extrapolated from the oral to the inhalation exposure route.

Source: U.S. Environmental Protection Agency, 1992. IRIS, Integrated Risk Information System. Online. Cincinnati, OH: U.S. Environmental Protection Agency, Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

[b]Assumed.

[c]Estimated.

[d]Experimental dose (ppm)x0.13 (fraction of species body weight consumed as food per day) x duration of treatment (days)/duration of study (days)$x(Le/L)^3$.

[e]Transformed animal dose (mg/kg/day)/(human body weight/animal body weight)$^{(1/3)}$.

Elements of Hazard Ranking

Chemical Name: 1,1,2-trichloroethane

CAS Number: 79-00-5

Weight-of-Evidence Classification:[a] C

Estimate of Potency ($1/ED_{10}$): 0.21 per (mg/kg)/day

Reference: National Cancer Institute, 1978. Bioassay of 1,1,2-trichloroethane for possible carcinogenicity. Technical Report Series No. 74. DHEW Publication No. (NIH) 78-1324. Washington, DC: U.S. Department of Health, Education, and Welfare.

Exposure route:	gavage		
Species:	mouse		
Strain:	B6C3F1		
Sex:	M		
Vehicle or physical state:	corn oil		
Body weight:[b]	0.03 kg		
Duration of treatment (le):	78 weeks		
Duration of study (Le):	91 weeks		
Lifespan of animal (L):	104 weeks		
Target organ:	liver		
Tumor type:	hepatocellular carcinoma		
Experimental dose/exposure (on treatment days):[c]	390 mg/kg/day	195 mg/kg/day	0 mg/kg/day
Transformed animal dose (mg/kg/day):[d]	239.1	119.4	0.0
Human equivalent dose (mg/kg/day):[e]	18.6	9.3	0.0
Tumor incidence:	37/49	18/49	2/20

Comments: The ED_{10} can be extrapolated to the inhalation exposure route from an oral route.

Source: U.S. Environmental Protection Agency, 1988. Evaluation of the potential carcinogenicity of 1,1,2-trichloroethane. OHEA-C-073-186. Washington, DC: Office of Health and Environmental Assessment.

U.S. Environmental Protection Agency, 1992. IRIS, Integrated Risk Information System. Online. Cincinnati, OH: U.S. Environmental Protection Agency, Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

[b]Estimated.
[c]Time-weighted-average.
[d]Experimental dose (mg/kg/day)x5 (treatment days/wk)/7 (days/wk)x78 weeks (duration of treatment)/91 weeks (duration of study).
[e]Transformed animal dose (mg/kg/day)/(human body weight/animal body weight)$^{(1/3)}$.

Elements of Hazard Ranking

Chemical Name: trichloroethylene

CAS Number: 79-01-06

Weight-of-Evidence Classification:[a,b] B2/C

Estimate of Potency ($1/ED_{10}$):[c] 0.035 per (mg/kg)/day

Reference: Maltoni, C.; G. Lefemine; and Cotti, G.,1986. Experimental research on trichloroethylene carcinogenesis. In: Archives of research on industrial carcinogensis, Vol. 5, Maltoni, C. and Mehlman, M.A., Ed. Princeton Scientific Publishing Co., Princeton, NJ.

Exposure route:		inhalation			
Species:		mouse			
Strain:		Swiss, B6C3F1			
Sex:		M/F			
Vehicle or physical state:		vapor			
Body weight:[d]		0.047 kg (Swiss, M), 0.040 kg (Swiss, F), 0.035 (B6C3F1, F)			
Duration of treatment (le):		78 weeks			
Duration of study (Le):		104 weeks			
Lifespan of animal (L):[d]		104 weeks			
Target organ:		lung			
Tumor type:		adenocarcinoma, adenoma, and early adenoma			
Experimental dose/exposure (mg/kg/day):[e]		600	300	100	0.0
Total trichloroethylene metabolized (mg/day):[f]	(Swiss, M)	16.1	8.59	2.74	0.0
	(Swiss, F)	14.4	7.71	2.46	0.0
	(B6C3F1, F)	12.4	6.64	2.12	0.0
Human equivalent metabolized dose ($mg/W^{2/3}/day$):[g]	(Swiss, M)	66.3	35.3	11.3	0.0
	(Swiss, F)	66.0	35.3	11.3	0.0
	(B6C3F1, F)	65.9	35.3	11.3	0.0
Tumor incidence:	(Swiss, M)	27/90	23/89	11/89	10/88
	(Swiss, F)	29/89	13/90	15/89	15/90
	(B6C3F1, F)	14/87	7/89	6/90	2/90

Reference: Fukuda, K.; Takemoto, K.; and Tsuruta, H., 1983. Inhalation carcinogenicity of trichloroethylene in mice and rats. Ind. Health. 21: 243-254.

Exposure route:	inhalation
Species:	mouse
Strain:	ICR
Sex:	F
Vehicle or physical state:	vapor
Body weight:[d]	0.04 kg
Duration of treatment (le):	103 weeks
Duration of study (Le):	103 weeks
Lifespan of animal (L):[d]	103 weeks

79-01-06 trichloroethylene (continued)

Target organ:	lung					
Tumor type:	carcinoma and adenoma					
Experimental dose/exposure (mg/kg/day):[e]	450	150	50	0.0		
Total trichloroethylene metabolized (mg/kg/day):[f]	11.1	4.12		1.53	0.0	
Human equivalent metabolized dose ($mg/W^{2/3}$/day):[g]		67.8	25.2		9.34	0.0
Tumor incidence:		11/46	13/50		5/50	6/49

Comments: The ED_{10} is a geometric mean of the four data sets.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

[b]The weight-of-evidece lies on a continuum between B2 and C. The EPA has proposed a classification of "B2, probably carcinogenic to humans" for trichloroethylene. The Science Advisory Board, however, (as relayed in a leter from N. Nelson, R. Greisemer, and J. Doull to L. Thomas, U.S.Environmental Protection Agency, March 9, 1988) believed the data lies on a continuum between "B2" and "C".

[c]The ED_{10} is expressed in units of administered dose. A 70 kg human breathing 1 ug/m^3 was estimated to metabolize 4.18E-3 $mg/W^{2/3}$/day of trichloroethylene (as inferred from the data of Monster et al., 1976; Int. Arch. Occup. Environ. Health 38:87-102). This relationship was used to derive an estimate of the ED_{10} in units of ug/m^3. This ED_{10} was expressed in mg/kg/d under the assumption that a 70 kg human breathes 20 m^3/d.

[d]Estimated.

[e]Time-weighted average given in reference study.

[f]Estimated total trichloroethylene metabolized based on data of Stott et al. (1982; Toxicol. Appl. Pharmacol. 62:137-151) and Prout et al. (1985; Toxicol. Appl. Pharmacol. 79:389-400).

[g][Total trichloroethylene metabolized x (5 treatment days per week/7 days per weeks) x (Ie/Le)]/($W^{2/3}$), where W is the body weight in kg.

Elements of Hazard Ranking

Chemical Name: 2,4,5-trichlorophenol

CAS Number: 95-59-4

Weight-of-Evidence Classification:[a] see comments

Estimate of Potency ($1/ED_{10}$): see comments

Comments: The Office of Research and Development/Office of Health and Environmental Assessment is currently evaluating the carcinogenic evidence on 2,4,5-trichlorophenol. A draft preliminary assessment indicates that the weight-of-evidence classification is such that this chemical may be considered a "nonthreshold" hazardous air pollutant. This evaluation is currently undergoing internal peer review, thus, the exact placement of this chemical with respect to other "nonthreshold" HAPs can not be determined at this time.

Source: U.S Environmental Protection Agency, 1992. Preliminary assessment evaluation of the potential carcinogenicity of 2,4,5-trichlorophenol. First draft. Prepared by the Chemical Hazard Evaluation Program, Health and Safety Research Division, ORNL, for the Office of Health and Environmental Assessment, Human Health Assessment Group.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

Elements of Hazard Ranking

Chemical Name: 2,4,6-trichlorophenol

CAS Number: 88-06-2

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$): 0.09 per (mg/kg)/day

Reference: National Cancer Institute, 1979. Bioassay of 2,4,6-trichlorophenol for possible carcinogenicity. NCI Carcinogenesis Technical Report Series No. 155. Also published as DHHS (NIH) 79-1711.

Exposure route:	oral		
Species:	rat		
Strain:	Fischer 344		
Sex:	M		
Vehicle or physical state:	diet		
Body weight:[b]	0.35 kg (high dose)	0.38 kg (low dose)	0.42 kg (control)
Duration of treatment (le):	742 days (high dose)	742 days (low dose)	749 days (control)
Duration of study (Le):[c]	742 days (high dose)	742 days (low dose)	749 days (control)
Lifespan of animal (L):	749 days		
Target organ:	hematopoietic system		
Tumor type:	leukemia		
Experimental dose/exposure:	10,000 ppm	5,000 ppm	0 ppm
Transformed animal dose (mg/kg/day):[d]	500	250	0
Human equivalent dose (mg/kg/day):[e]	94.4	44.6	0
Tumor incidence:	29/45	23/50	4/20

Comments: The ED_{10} was extrapolated from the oral to the inhalation exposure route.

Source: U.S. Environmental Protection Agency, 1992. IRIS, Integrated Risk Information System. Online. Cincinnati, OH: U.S. Environmental Protection Agency, Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

[b]Reported.

[c]Assumed.

[d]Experimental dose (ppm)x.05 (fraction of rat's body weight consumed as food per day)x(le/Le).

[e]Transformed animal dose (mg/kg/day)/(human body weight/animal body weight)$^{(1/3)}$.

Elements of Hazard Ranking

Chemical Name: trifluralin

CAS Number: 1582-09-8

Weight-of-Evidence Classification:[a] C

Estimate of Potency ($1/ED_{10}$): 0.037 per (mg/kg)/d

Reference: Emmerson JI, Pierce EC, McGrath JP, et al., 1980. The chronic toxicity of compound 36352 (trifluralin) given as a compound of the diet to the fisher 344 rat for two years. Studies R-87 and R-97 (unpublished study received September 18, 1980 by Office of Pesticide Programs under 1471-35; submitted by Elanco Products Co., Division of Eli Lilly and Co., Indianapolis, IN).

Exposure route:	oral			
Species:	rat			
Strain:	F344			
Sex:	M			
Vehicle or physical state:	diet			
Body weight:[b]	0.35 kg			
Duration of treatment (le):	104 weeks			
Duration of study (Le):	104 weeks			
Lifespan of animal (L):[c]	104 weeks			
Target organ:	kidney; bladder; and/or thyroid			
Tumor type:	renal carcinomas; bladder papillomas; thyroid adenomas and carcinomas			
Experimental doses/exposure (mg/kg/day):	6500	3250	813	0
Transformed animal doses (mg/kg/day):[d]	272	128	30	0
Human equivalent doses (mg/kg/day):[e]	46.5	21.9	5.1	0
Tumor incidence:	17/60	9/60	5/60	5/60

Comments: The ED_{10} is based on oral data: an estimate of potency for the inhalation route is not currently available.

Source: U.S. Environmental Protection Agency, 1992. IRIS, Integrated Risk Information System. Online. Cincinnati, OH: U.S. Environmental Protection Aency, Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

1582-09-8 trifluralin (continued)

[b]Estimated.
[c]Estimated.
[d]Experimental dose x fraction of body weight consumed as food per day. Differences in food consumption were observed between dose group: 4.2% for the high group, 3.9% for the mid group, and 3.7% for the lowest treatment group.
[e]Transformed animal dose/(human body weight/animal body weight)$^{(1/3)}$.

Elements of Hazard Ranking

Chemical Name: vinyl bromide

CAS Number: 59-36-02

Weight-of-Evidence Classification:[a] B2

Estimate of Potency ($1/ED_{10}$):[b] 0.93 per (mg/kg)/d

Reference: Benya, T.J., Busey, WM., Dorato, M.A., Berteau P.E., 1982. Inhalation carcinogenicity bioassay of vinyl bromide in rats. Toxic. Appl. Pharmacol. 64(3):367-379.

Exposure route:	inhalation			
Species:	rat			
Strain:	Sprague-Dawley			
Sex:	F			
Vehicle or physical state:	vapor/air			
Body weight:[c]	0.39 kg.			
Duration of treatment (le):	104 weeks			
Duration of study (Le):	104 weeks			
Lifespan of animal (L):[c]	104 weeks			
Target organ:	liver			
Tumor type:	angiosarcoma			
Experimental doses/exposure (ppm):	250	50	10	0
Transformed animal absorbed doses (mg/kg/day):[d]	60.0	12.0	2.4	0
Human equivalent absorbed doses (mg/kg/day):[e]	10.65	2.13	0.43	0
Tumor incidence:	61/120	50/120		10/120
0/144				

Comments: The highest experimental exposure level, 1250 ppm, caused early mortality (terminated dosing at 78 weeks). This exposure level was omitted from the estimation of the ED_{10}. Transformed doses account for 50% absorption via inhalation exposure.

Source: U.S. Environmental Protection Agency, 1984. Health and environmental effects profile for bromoethane (vinyl bromide). EPA/600/X-84/143. Prepared by the Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment, Cincinnati, OH.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

[b]The ED_{10} is expressed in units of absorbed dose.

[c]Estimated.

[d]Experimental dose (ppm) x .041 x molecular weight x 1/BW x inhalation rate (0.24 m^3/d) x 0.5 (the assumed absorption factor) x (5 treatment days per week/7 days per week) x 6 hours/24 hours per day.

[e]Transformed animal dose / (human body weight/animal body weight) $^{(1/3)}$.

Elements of Hazard Ranking

Chemical Name: vinyl acetate

CAS Number: 108-05-4

Weight-of-Evidence Classification:[a] C[b]

Estimate of Potency ($1/ED_{10}$): see comments

Comments: The available data are equivocal for estimating an ED_{10}.

Source: U.S Environmental Protection Agency, 1989. Health and environmental effects document. EPA/600/8-90/008. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

[b]The Office of Research and Development/Office of Health and Environmental Assessment is currently aware of a more recent inhalation exposure chronic toxicity study and studies examining proposed mechanism of action. Results from these studies are in the process of being submitted for publication (presentation by the Society of the Plastics Industry to the U.S. Environmental Protection Agency, April 21, 1993).

Elements of Hazard Ranking

Chemical Name: vinyl chloride

CAS Number: 75-01-4

Weight-of-Evidence Classification:[a] A

Estimate of Potency ($1/ED_{10}$): 1.6 per (mg/kg)/day

Reference: Maltoni, C.; Lefemine, G.; Ciliberti A.; Cotti, G.; Carreti, D., 1980. Vinyl chloride carcinogenicity bioassays (BT project) as an experimental model for risk identification and assessment in environmental and occupational carcinogenesis. Epidemiol. Anim. Epidemiolo. Hum.: Cas Chlorure Vinyle Monomere, (Reun. Club Cancerog. Chim.), 20th, Meeting Date 1979, 11-112. Publ. Essent., Paris, France.

Maltoni, C.; Lefemine, G.; Ciliberti, A.; Cotti, G.; Carreti, D., 1981. Carcinogenicity bioassays vinyl chloride monomer: A model of risk assessment on an experimental basis. Environ. Health Perspect. 41: 3-29.

Exposure route:	inhalation							
Species:	rat							
Strain:	Sprague-Dawley							
Sex:	M, F							
Vehicle or physical state:	vapor							
Body weight:[b]	0.35 kg							
Duration of treatment (le)	365 days							
Duration of study (Le):	up to 1029 days							
Lifespan of animal (L):	1029 days							
Target organ:	liver							
Tumor type:	angosarcoma							
Experimental dose/exposure:	250 ppm	200 ppm	150 ppm	100 ppm	50 ppm	25 ppm	10 ppm	0.0 ppm
Transformed animal dose (mg/kg/day):[c]	8.596	6.878	5.158	3.438	1.719	0.860	0.344	0.0
Human equivalent dose (mg/kg/day):[d]	1.468	1.175	0.881	0.587	0.294	0.147	0.0587	0.0
Tumor incidence:	3/59	12/120	6/119	1/120	1/60	5/120	1/119	0/363

Comments: Experimental exposures above 50 ppm were not used to estimate the ED_{10}. Saturable metabolism appears to occur at exposure levels above 200 - 250 ppm.

Source: U.S. Environmental Protection Agency, 1985. Health and environmental effects profile for chloroethene. EPA/600/X-85/374. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria Assessment Office, Cincinnati, OH, for the Office of Emergency and Remedial Response, Washington, DC.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

75-01-4 vinyl chloride (continued)

[b]Assumed.
[c]Experimental dose (ppm)x 0.041xmole.wt.x0.223 m^3/d (breating rate of rats)x5 (treatment days/wk)/ 7(days/wk)x4 (treatment hr/day)x24 (hr/day)x(le/Le).
[d]Transformed animal dose (mg/kg/day)/(human body weight/animal body weight)$^{(1/3)}$.

Elements of Hazard Ranking

Chemical Name: vinylidine chloride (1,1-dichloroethylene)

CAS Number: 75-35-4

Weight-of-Evidence Classification:[a] C

Estimate of Potency ($1/ED_{10}$):[b] 1.2 per (mg/kg)/day

Reference: Maltoni, C.; Lefemine, G.; Chieco, P.; Citti, G.; Patella, V.; 1985. Experimental research on vinylidine chloride carcinogenesis. In: Maltoni, C.; Mehlmen, M., eds. Archives of research on industrial carcinogens, vol. 3. Princeton, NJ: Princeton Scientific Publications.

Exposure route:	inhalation		
Species:	mouse		
Strain:	Swiss		
Sex:	M		
Vehicle or physical state:	vapor/air		
Body weight:[c]	0.03 kg		
Duration of treatment (le):	52 weeks		
Duration of study (Le):	121 weeks		
Lifespan of animal (L):[c]	121 weeks		
Target organ:	kidney		
Tumor type:	adenocarcinoma		
Experimental dose/exposure:[d]	25 ppm	10 ppm	0 ppm
Human equivalent body burden (mg/kg/day):[d]	0.195	0.078	0.0
Tumor incidence:[e]	28/119[f]	0/25	0/156[g]

Comments: The ED_{10} is based on body burden as inferred by the amout of radiolabelled vinylidene chloride remaining in the body after a 6 hour exposure. An assumption is made that metabolism is linear over the exposure levels of interest (i.e., below the level of saturation).

Source: U.S. Environmental Protection Agency, 1992. IRIS, Integrated Risk Information System. Online. Cincinnati, OH: U.S. Environmental Protection Agency, Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office.

---

[a]A-human carcinogen, B1-probably carcinogenic to humans (limited human evidence), B2-probably carcinogenic to humans (inadequate human evidence/no human data), C-possibly carcinogenic to humans, D-not classifiable as to human carcinogenicity, E-evidence of non-carcinogenicity for humans.

[b]The ED_{10} is in units of applied dose (mg/kg/day) under the assumption that 0.17 mg/kg/d body burden is equivalent to a continuous atmospheric exposure to 1 ppm for a lifetime and that a 70 kg human breathes 20 m_3/day.

[c]Given 4 hr daily, 4 to 5 days/wk for 52 wk.

75-35-4 vinylidine chloride (1,1-dichlooethylene) (continued)

[d]Lifetime average daily exposure for mice: body burden (mg metabolized/d) x Ie/Le x 4.5 (average treatment days/wk)/7 (days/wk). Body burden levels are based on data of McKenna et al. (1978, Toxicol. Appl. Pharmacol., 45(2): 599-610). The data are adjusted by 4/6 to account for exposure period differences between Maltoni et al. (1985) and McKenna et al. (1978). It is assumed that body burden in mice scales to humans by surface area (BW_H/BW_A), and is expressed in humans on a mg/kg/day basis.

[e]The number of animals surviving to the appearence of the first kidney adenocarcinoma are the denominator for tumor incidence.

[f]Results are pooled from two separate groups: 3/21 in one group and 25/98 in second group.

[g]Results are pooled from two separate groups: 0/56 in one group and 0/70 in second group.

APPENDIX B

Supporting data for each ranked "threshold" pollutant

SECTION I: Glossary of Terms and Reference Values for "Threshold" Pollutants

Glossary:

Source	The source from which the reference toxicity study and data were obtained. EPA sources may include a Reportable Quantity (RQ) report, a Health and Environmental Effects Document (HEED), a Health and Environ-mental Effects Profile (HEEP), and on-line data reported in the Integrated Risk Information System (IRIS). "Data collected for development of RfC" indicates that the reference study is from published journal articles collected by EPA for derivation of an inhalation reference concentration (RfC).
Reference Study	The primary author and year of the toxicity study containing the data from which the MED and CS are calculated. Study data were obtained from the document listed under "Source."
Exp. Route	The route by which the test species was exposed to the substance. "Inhalation" indicates air exposure and "oral" indicates ingestion of the substance in the diet or in drinking water, or by gavage (usually in developmental studies).
Test Species	The human, mammal (e.g., dog, monkey), or rodent (e.g., rat, mouse) receiving the exposure in the toxicity study.
Chronic Hum. MED	The human minimum effective dose (MED) derived from the lowest observed effect level (a concentration or dose) reported in the toxicity study. Deriving the MED may require dividing a the lowest dose level giving an effect by a correction factor for duration of exposure, converting intermittent exposure to continuous exposure, and converting from animal to human exposure.
RVd	The dose rating value (RVd), ranging from 1 to 10, based on the log of the MED value. Substances producing adverse effects at a low dose (i.e., those that are more toxic) will have a high RVd, while substances producing adverse effects only at high doses (less toxic) will have a low RVd.
RVe	The effect rating value (RVe), ranging from 1 to 10, based on the severity of the effect observed at the LOAEL.
CS	The composite score (CS), calculated by multiplying the RVd by the RVe. The range of CSs is from 1 to 100. Only those compounds eliciting the most severe effects at low doses receive a high CS; compounds eliciting minimal effects at high doses receive a low CS.
Correction Factor	A factor of 10 applied to subchronic exposure to estimate chronic exposure. For example, a subchronic LOAEL is divided by 10 to estimate a chronic LOAEL.

Chronic/subchronic The duration of exposure (either chronic or subchronic) to the substance during the toxicity study, as defined in the reference study. Subchronic duration is usually up to about 120 days for rodents, and up to a year for other mammals. Chronic exposure also includes occupational exposure (generally 8 hrs/day, 5 days/week for at least one year).

Effect The effect observed at the lowest dose producing and effect, and on which the RVe is based.

Exp. Conc. The concentration of the substance to which the test species is exposed. The concentration may be in ppm, indicating exposure in the diet or by inhalation; in mg/m^3 for inhalation exposure; or in mg/L for ingestion of drinking water. Exposure concentrations reported by the reference study as ppm are entered as "Exp. Conc. Val. 1." Concentrations in any other unit (e.g., mg/m^3 or mg/L) are entered as "Exp. Conc. Val. 2" with the units specified in "Conc. 2 Unit."

Exp. Time The number of hours of exposure per day.

Exp. Frequency The number of days of exposure per week.

Exp. Duration The total number of days, weeks, or months of exposure (determines whether the toxicity study is chronic or subchronic).

Transf. Anim. Transformed animal dose, the test species's estimated daily exposure to the **Dose** substance, based on kg of body weight (i.e., the dose). The transformed animal dose (mg/kg-day) is calculated by multiplying the exposure concentration, adjusted for continuous exposure, by a species-specific food factor, inhalation rate, or ingestion rate (depending on the route of exposure), and dividing by the species body weight, if necessary.

Inhal. Rate The inhalation rate, in m^3/day, for the test species.

Ingest. Rate The ingestion rate for the test species, which indicates either water consumption in mg/L or the fraction (i.e., a food factor) or percent of body weight that is consumed per day as food.

Absorption Coef. The assumption, based on pharmacokinetic data, regarding the percent of the substance that is actually absorbed from exposure (i.e., usually 100% or 1).

Species Weight The body weight of the test species.

Section II: Composite Score Derivation for "Threshold" Pollutants

Methodology for the derivation of Composite Scores:

1. Obtain the lowest observable adverse effect levels of exposure (LOAEL), frank effect levels (FEL), or no observable adverse effect levels (NOAEL) for the chemical from the data set used to develop the inhalation RfC. Identify whether the exposure level is chronic (> 90 day study in the rat) or sub-chronic (< 90 day study in the rat), continuous or intermittent exposure (i.e., note the exposure/dosing regimen). Furthermore, determine the test species and note the critical effects associated with the NOAEL, LOAEL, or FEL.

2. Correct for sub-chronic and intermittent exposure (e.g., if exposure is 5 days per week, multiply the exposure level by 5/7). Divide sub-chronic LOAEL (NOAEL or FEL) by 10 to obtain chronic value. There is no adjustment made for duration of study in developmental toxicity studies.

Adjusted LOAEL = chronic LOAEL x exposure/dosing regimen

(mg/m^3) = ___ (mg/m^3) x ___ hrs/24 hrs x ___ days/7 days

3. Derive the animal MED (in mg/kg-day) by converting the effect level (e.g., adjusted LOAEL) from animal exposure data (in units of mg/cubic meter) to units of mg/kg-day by adjusting for absorption fraction, species weight, and inhalation rate (see Table VI for default species weight and inhalation rates):

animal MED = LOAEL x animal inhalation rate/ weight x absorption fraction

(mg/kg/day) = (mg/m³) x (m³/day) / (kg) x (unit-less)

4. Convert the animal MED to a chronic human MED by assuming surface area equivalence (as approximated by the cubed root of the body weight ratio), which can be calculated as shown below:

human MED = animal MED x [animal weight/human weight]$^{1/3}$ x 70 kg

(mg/day) (mg/kg-day) (kg) (kg)

5. Use the log of the chronic human MED (mg/day) to assign an RVd to the exposure level as described in Figure 1.

6. Assign an RVe to the effect associated with the chronic human MED as described above in Table 1. If multiple effects were reported for a single study, the RVe assigned to the study was based on the effect which resulted in the highest RVe. By choosing the most severe effect elicited by a pollutant at any given dose, the Composite Score of a pollutant reflects the endpoint of concern shown in the study.

7. Calculate the Composite Score:

CS = RVd x RVe

This methodology is based on the general outlines given in the CERCLA technical background document as to methodology and guidelines for ranking chemicals based on chronic toxicity (10) and the Guidelines for Criteria Derivation; Water quality and the general quantitative risk assessment guidelines for non-cancer effects (Federal Registration/vol 45 # 231/Nov 28 1980/ Notices) and General Quantitative Risk Assessment Guidelines for Noncancer Health Effects (ECAO-CIN-538 May 1989). This method produced composite scores that were identical to those listed in the RQ

source documents for all but a few pollutants. Such differences in composite score were relatively minor and described in detail in section III of this Appendix.

Calculated Composite Scores were added as potential studies considered for selection as most appropriate Composite Score for each pollutant and are described in Appendix B. A similar methodology was used when data used to support an RfC determination was used to construct a composite score.

In general, a study of less than or equal to 90 days duration was considered to be sub-chronic. However when a description of study duration (chronic vs. sub-chronic) was given in Reportable Quantities documents or by the author'(s) of the primary publication, this description was used to determine the appropriate application of a correction factor for study duration.

The assumptions regarding species weights and inhalation rates for calculating MEDs are given in Table 2. For such MEDs, 100 % absorption was assumed in the absence of specific information. Although 50% absorption has been recommended to use for deriving a Composite Score for systemic effects due to inhalation exposure and may be incorporated into future guidance (11), most of the MEDs reviewed from the Reportable Quantities documents had been based on 100% absorption even for systemic effects due to inhalation exposure. Therefore in order to maintain consistency, 100% absorption was assumed in deriving chronic human MEDs from data used to develop RfCs.

However for human occupational exposures, an absorption fraction of 0.5 (50% absorption) was used to derive the chronic human MEDs. Again, this was done to maintain consistency. A review of available composite scores revealed that MEDs based on human occupational exposure data had been calculated assuming 50 % absorption to compensate for the nature of the exposure during the work week.

Reference Values:

The values for the species's body weight, inhalation rate, water consumption, and ingestion rate (or food factor), if not reported in the study, were taken from EPA (1986) "Reference Values For Risk Assessment" (Environmental Criteria and Assessment Office, ECAO-CIN-477, September 1986). These values are as follows:

Species	Body Weight (kg)	Inhalation Rate (m^3/day)	Water Consumption (L/day)	Food Factor
Rat	0.35	0.223	0.049	0.05
Mouse	0.03	0.039	0.0057	0.13
Dog	12.7	4.3	0.61	0.025
Monkey	8	5.4	0.53	0.04
Human	70	20	2.0	0.028

Section III: Bibliography

References for "Threshold" Pollutants

ACETONITRILE	Pozzani, U.C., M.A. Weil and C.P. Carpenter. 1959. The Toxicological Basis of Threshold Limit Values. 5. The Experimental Inhalation of Vapor Mixtures by Rats, with Notes upon the Relationship Between Single Dose Inhalation and Single Dose Oral Data. J. Ind. Hyg. (Oct. 1959): 364-369.
ACETOPHENONE	Imasheva, N.B. 1966. Threshold Concentrations of Acetophenone During Short- and Long-term Inhalation. Cited in: Nuttonson, M.Y. AICE Survey of USSR Air Pollution Literature, VIII. 1971. A Compilation of Technical Reports of the Biological Effect and the Public Health Aspects of Atmospheric Pollutants. pp 79-93.
ACRYLIC ACID	Miller, R.R., J.A. Ayers, G.C. Jersey, and M.J. McKenna. 1981. Inhalation Toxicity of Acrylic Acid. Fund. Appl. Toxicol 1:271-277.
ANTIMONY POTASSIUM TARTRATE	Schroeder, H.A., M. Mitchener and A.P. Nason. 1970. Zirconium, Niobium, Antimony, Vanadium and Lead in Rats: Life-term Studies. J. Nurt. 100: 59-69.
ANTIMONY TRISULFIDE	Brieger, H., C.W. Semisch III, J. Stasney and D.A. Piatnik. 1954. Industrial Antimony Poisoning. Ind. Med. Surg. 23: 521-523. Cited in: NIOSH, 1978.
BIPHENYL	Ambrose, A.M., A.N. Booth, F. DeEds and A.J. Cox. 1960. A Toxicological Study of Biphenyl, a Citrus Fungistat. Food Res. 25: 328-336.
CALCIUM CYANAMIDE	Kramer, A.W., Jr., G. Dambach and W.A. Pridgen. 1967. The Effects of Calcium Carbimide and Thyroid Powder on Thyroid Morphology and Feed Efficiency in Rats. Toxicol. Appl. Pharmacol. 11(3): 432-441.
CAPROLACTAM	NTP (National Toxicology Program). 1982. Carcinogenesis Bioassay of Caprolactam (CAS No. 105-60-2) in F344 Rats and B6C3F1 Mice (feed study). NTP Tech. Rep. Ser. No. 214 [Also published as NIH Publication NIH-81-1770].
CARBARYL	Carpenter, C.P., C.S. Weil, P.E. Palm, M.W. Woodside, J.H. Nair, III and J.F. Smyth, Jr. 1961. Mammalian Toxicity of 1-Naphthyl-N-methylcarbamate (Sevin Insecticide). J. Agric. Food Chem. 9: 30-39.

CARBON DISULFIDE	Kashin, L.M. 1965. Overall Immunological Reactivity and Morbidity of Workers Exposed to Carbon Disulfide. Hyg. Sanit. 30: 331-335.
	Vasilyeva, I.A. 1973. Effect of Small Concentrations of Carbon Disulfide and Hydrogen Sulfide on the Menstrual Function of Women and the Estrual Cycle Experimental Animals. Gig. Sanit. 7: 24-27. (Rus.)
2-CHLOROACETOPHENONE	NTP (National Toxicology Program). 1990. Toxicology and Carcinogenesis Studies of 2-Chloroacetophenone (CAS No. 532-27-4) in F344/N Rats and B6C3F1 Mice (inhalation studies). NTP Technical Report 379.
CHLOROBENZENE	Skinner, W.A., G.W. Newell and J.V. Dilley. 1977. Toxic Evaluation of Inhaled Chlorobenzene. Final Report Prepared for the Division of Biomedical and Behavioral Science, Natl. Inst. Occup. Safety and Health, Cincinnati, OH. June 15. Cited in: Deichmann, 1981.
COBALT AND COMPOUNDS	Kerfoot, E.J., W.G. Frederick, and E. Domeier. 1975. Cobalt metal inhalation on miniature swine. Am. Ind. Hyg. Assoc. J. 36: 17-25
	Kerfoot, E.J. 1973. Chronic animal inhalation toxicity to cobalt. NIOSH-TR-203-74, NTIS PB-232-247. National Technical Information Service, Springfield, VA. 42p.
CUMENE	Jenkins, L.J., Jr., R.A. Jones and J. Siegel. 1970. Long-term Inhalation Screening Studies of Benzene, Toluene, o-Xylene and Cumene on Experimental Animals. Toxicol. Appl. Pharmacol. 16(3): 818-823.
DIBUTYLPHTHALATE	Nikonorow, M., H. Mazur and H. Piekacz. 1973. Effect of Orally Administered Plasticizers and Polyvinyl Chloride Stabilizers in the Rat. Toxicol. Appl. Pharmacol. 26: 253.
2,4-D, SALTS AND ESTERS	Schwetz, B.A., G.L. Sparschu and P.J. Gehring. 1971. The Effect of 2,4-D and Esters of 2,4-D on Rat Embryonal, Fetal, and Neonatal Growth and Development. Food Cosmet. Toxicol. 9: 801-817.
N,N-DIMETHYLANILINE	SIB (Springborn Institute for Bioresearch, Inc.). 1980. Final Report on Sub-chronic Toxicity Test of N,N-Dimethylaniline in Rats and Mice. Submitted to Traco Jitco, Inc., Rockville, MD.
DIMETHYL PHTHALATE	Lehman, A.J. 1955. Insect Repellants. Assoc. Food Drug Office, U.S. Quart. Bull. 19: 87.

2,4-DINITROPHENOL	U.S. EPA. 1980. Ambient Water Quality Criteria for Nitrophenols. Environmental Criteria and Assessment Office, Cincinatti, OH. EPA 440/5-80-063. NTIS PB 81-117749.
	Horner, W.D. 1942. Dinitrophenol and its Relation to Formation of Cataracts. Arch. Opthalmol. 27: 1097-1121.
	Tainter, M.L., A.B. Stockton and W.C. Cutting. 1935. Dinitrophenol in the Treatment of Obesity: Final Report. J. Am. Med. Assoc. 105: 332-337.
ETHYL BENZENE	NTP (National Toxicology Program). 1988. Subchronic and Chronic Toxicity Study of Ethylbenzene. Principal investigator: Catherine Aranyi. Performing ORG: IIT Research Institute, Chicago, IL.
ETHYL CHLORIDE	NTP (National Toxicology Program). 1990. Toxicology and Carcinogenesis of Chloroethane (ethyl chloride) (CAS No. 75-00-3) in F344/N Rats and B6C3F1 Mice (Inhalation Studies). NTP Technical Report 346.
ETHYLENE GLYCOL	Developmental Toxicity Evaluation of Ethylene Glycol Administered by Gavage to CD-1 Mice: Determination of a No Observable Effect level. U.S. EPA, Office of Toxic Substances, Washington D.C.
ETHYLENE GLYCOL MONOBUTYL ETHER	Dodd, D.E., W.M. Snellings, R.R. Maronpot and B. Ballantyne. 1983. Ethylene Glycol Monobutyl Ether: Acute, 9-day, and 90-day Vapor Inhalation Studies in Fischer 344 Rats. Toxicol. and Appl. Pharmacol. 68: 405-414.
2-ETHOXYETHANOL	Barbee, S.J., J.B. Terrill, D.J. DeSousa and C.C. Conaway. 1984. Subchronic Inhalation Toxicology of Ethylene Glycol Monoethyl Ether in the Rat and Rabbit. Environ. Health Perspect. 57: 157-163.
Fluomine	Kinkead. E.R., C.C. Haun, R.S. Bowers, EH. Vernot, J.D. MacEwen and R.L. Amaster. 1982. Six month Inhalation Toxicity of Fluomine Dust. Am. Ind. Hyg. Assoc. J. 43:66-71.
HEXANE	Ono, Y., Y. Takeuchi, N. Hisanaga, M. Iwata, J. Kitoh and Y. Sugiura. 1982. Neurotoxicity of Petroleum Benzine Compared with n-Hexane. Int. Arch. Occup. Environ. Health. 50(3): 219-229.
HYDROCHLORIC ACID	Sellakumar, A.R., C.A. Snyder, J.L. Solomon and R.E. Albert. 1985. Carcinogenicity of Formaldehyde and Hydrogen Chloride in Rats. Toxicol. Appl. Pharmacol. 81: 401-406.

HYDROGEN SULFIDE	CIIT (Chemical Industry Institute of Toxicology). 1983 90-Day Vapor inhalation Toxicity Study of Hydrogen Sulfide in Fischer-344 Rats. U.S. EPA, Office of Toxic Substances Public Files. Fische Number 0000255-0. document Number FYI- OTS-0883-0255.
	CIIT (Chemical Industry Institute of Toxicology). 1983 90-Day Vapor inhalation Toxicity Study of Hydrogen Sulfide in Sprague-Dawley Rats. U.S. EPA, Office of Toxic Substances Public Files. Fische Number 0000255-0. document Number FYI- OTS-0883-0255.
MALEIC ANHYDRIDE	Ulrich, C.E., M. Blair and D.A. Rop. 1981. Six-month Multispecies Inhalation Toxicity Study (IRD-77-109). International Research and Development Corporation for Monsanto Co., St. Louis, MO. Unpublished 8DS submission. Microfiche No. OTS 0206655. Document ID 878214772.
MANGANESE	Wennberg, A. M. Hagman, and L Johansson. 1992. Preclinical Neurophysiological Signs of Parkinsonisn in occupational manganese Exposure. Neurotoxicology. 13(1):271-274
MERCURIC CHLORIDE	Knoflach, P., B. Albini and M.M. Wiser. 1986. Autoimmune Disease Induced by Oral Administration of Mercuric Chloride in Brown-Norway Rats. Toxicol. Pathol. 14: 188-193.
MERCURIC NITRATE	Neal, P., R.R. Jones, J.J. Bloomfield, J.M. Dalla Valle and T.I. Edwards. 1937. A Study of Chronic Mercurialism in the Hatters Furcutting Industry. Publ. Health Bull. 234. PHS, U.S. Treasury Dept. Cited in: Browning, E. 1969. Mercury. Toxicity of Industrial Metals. 2nd ed. Butterworth and Co., Ltd.
	Neal, P., R.H. Flinn, T.I. Edwards and W.H. Reinhart. 1941. Mercurialism and its Control in the Felt Hat Industry. PHS, Publ. Health Bull. 263. Cited in: Browning, E. 1969. Mercury. Toxicity of Industrial Metals. 2nd ed. Butterworth and Co., Ltd.
MERCURY, (ACETATO-O) PHENYL	Fitzhugh, D.G., A.A. Nelson, E.P. Laug and F.M. King. 1950. Chronic Oral Toxicities of Mercuri-phenyl and Mercuric Salts. Arch. Ind. Hyg. Occup. Med. 2: 433-442.
METHANOL	New Energy Development Organization (NEDO). 1987. Toxicological Research of Methanol as a Fuel for Power Station. Summary Report on Tests with Monkeys, Rats and Mice. p. 36, 20-31.

METHOXYCHLOR	NCI (National Cancer Institute). 1978. Bioassay of Methoxychlor for Possible Carcinogenicity. NCI-CG-TR-35. Carcinogenesis Program. p. 91.
2-METHOXYETHANOL	Miller, R.R., J.A. Ayres, J.T. Young and M.J. McKenna. 1983. Ethylene Glycol Monomethyl Ether. I. Subchronic Vapor Inhalation Study with Rats and Rabbits. Fund. Appl. Toxicol. 3(1): 49-54.
METHYL BROMIDE	Kato, N., S. Morinobu, and S. Ishizu. 1986. Subacute Inhalation Experiment for Methyl Bromide in Rats. Industrial Health. 24: 87-103.
METHYL CHLOROFORM TRICHLOROETHANE)	Quast, J.F. B.K.J. Leeng, L.W. Rampy and P.J. Gehring. (1,1,1- 1978. Toxicologic and Carcinogenic Evaluation of a Methylchloroform (1,1,1-Trichloroethane) Formulation by Chronic Inhalation in Rats — Interim Report after 24 Months. Dow Chemical Co., Midland, MI. 14 p. Cited in: U.S. EPA. 1981. Methyl Chloroform. Prepared for the U.S. Environmental Criteria and Assessment Office, U.S. EPA, Research Triangle Park, NC (draft).
METHYLENE DIPHENYL ISOCYANATE	Johnson, A., C.Y. Moira, L. MacLean, E. Atkins, A. Dybuncio, F. Cheng, and D. Enarson. 1985. Respiratory Abnormalities Among Workers in an Iron and Steel Foundry. Br. J. Ind. Med. Feb.; 42(2):94-100.
METHYL ETHYL KETONE	LaBelle, C.W. and H. Brieger. 1955. Vapor Toxicity of a Composite Solvent and its Principal Components. Arch. Ind. Health. 12: 623-627.
METHYL ISOBUTYL KETONE	Phillips R.D., E.J. Moran, D.E. Dodd, E.H. Fowler, C.D. Kary, and J. O'Donoghue. 1987. A 14-week Vapor Inhalation Toxicity Study of Methyl Isobutyl Ketone. Fund. Appl. Toxicol. 9: 380-388.
METHYL METHACRYLATE	Hazelton Laboratories America, Inc. 1979. A Two-year Vapor Inhalation Safety Evaluation Study in Rats. Methylmethacrylate Final Report. p. 1-127. Cited in: TSCA-ITC, 1980; Rohm and Haas Co.
METHYL TERT-BUTYL ETHER	Greenough, R.J., P. McDonald, P. Robinson, et al. 1980. Methyl Tertiary-butyl Ether (Driveron) Three-month Inhalation Toxicity in Rats (unpublished study). By Inveresk Research International for Chemische Werke Huls AG, West Germany. TSCATS/303353. EPA/OTS #86-870000172.

NAPHTHALENE	NTP (National Toxicology Program). 1980. Unpublished Subchronic Toxicity Study: Naphthalane (C52904), Fischer 344 Rats. Prepared by Battelle's Columbus Laboratories under Subcontract No. 76-34-106002. March 4, 1980.
NITROBENZENE	CIIT (Chemical Industry Institute of Toxicology). 1984. Ninety-day Inhalaion Study of Nitrobenzene in F-344 Rats, CD Rats, and B6C3F1 Mice with cover letter dated 6/24/84 and EPA response dated 8/06/84. Unpublished study. FYI-OTS-0784-0333 and computer print-out of pathology finding.
PHENOL	Deichmann, W.B., K.V. Kitzmiller, and S. Witherup. 1944. Phenol Studies VII. Chronic Phenol Poisoning, with Special Reference to the Effects upon Experimental Animals of the Inhalation of Phenol Vapor.
P-PHENYLENEDIAMINE	NCI (National Cancer Institute). 1979. Bioassay of p-Phenylenediamine Dihydrochloride for Possible Carcinogenicity. NCI Carcinogenesis Tech. Rep. Ser. No. 174. 46 p.
SELENIUM COMPOUNDS	Yang, G., S. Wang, R. Zhou and S. Sun. 1983. Endemic AND Selenium Intoxication of Humans in China. Am. J. Clin. Nutr. 37: 872-881.
TOLUENE	CIIT (Chemical Industry Institute of Toxicology). 1980. A Twenty-four Month Inhalation Toxicology Study in Fischer-344 Rats Exposed to Atmospheric Toluene. Executive Summary and Data Tables, October 15.
1,2,4-TRICHLOROBENZENE	Watanabe, P.G., R.J. Kociba, R.E. Hefner, Jr., H.O. Yakel and B.K.J. Leong. 1978. Subchronic Toxicity Studies of 1,2,4-Trichlorobenzene in Experimental Animals. Toxicol. App. Pharmacol. 45: 332-333.
TRIETHYLAMINE	Brieger, H. and W.A. Hodes. 1951. Toxic Effects of Exposure to Vapors of Aliphatic Amines. A.M.A. Arch. Ind. Hyg. Occup. Med. 3(3): 287-291.
XYLENES (MIXED)	Ungvary, G., E. Tatrai, A. Hudak, G. Barcza and M. Lorincz. 1980. The Embryotoxic Effects of o, m- and p-Xylene. Toxicol. 18(1): 61-74.

Section IV: Data Report Forms for "Threshold" Pollutants

DATA REPORT FORM

Chemical Name:	ACETONITRILE		
CAS Number:	000075-05-8		
Source:	EPA/600/X-85/357, Sept 1985		
Reference Study:	Pozzani et al., 1959		
Exp. Route:	Inhalation	Exp. Time:	7 hours/day
Test Species:	Monkey	Exp. Frequency:	5 days/week
Chron. Hum. MED:	105.400 mg/day	Exp. Duration:	90 days
RVd:	2.50	Transf. Anim. Dose:	40.700
RVe:	8	Dose Unit:	mg/kg-day
CS:	20	Inhal. Rate:	1.240 m^3/day
Corr. Factor:	10	Ingest. Rate:	N/A
Chronic/subchronic:	Subchronic	Ingest. Unit:	N/A
Exp. Conc. Val 1:	330.000 ppm	Absorption. Coef.:	1.0
Exp. Conc. Val 2:	554.000	Species Weight:	3.500 kg
Conc. 2 Unit:	mg/m^3		

Effect: Focal dural and subchronic dural hemorrhages or mild to moderate hemorrhage in sagittal sinuses of brain, neurological disorders; pulmonary changes as in dogs but with small caseous nodules in lungs of 2 of 4; renal cloudy swelling.

Note: N/A denotes either data not applicable or data not available.

Consistency with the Reportable Quantity Methodology:

Calculations are consistent with the Reportable Quantity methodology. A correction factor of 10 is used to estimate chronic MED from this subchronic study.

Reason for CS Selection:

From the available studies, a CS was selected for the hazard ranking from the study suitable for Reportable Quantity development that used the monkey (closest test-species to man), and that used the lowest inhalation doses. All the available subchronic inhalation studies are relatively old for this pollutant.

DATA REPORT FORM

Chemical Name:	ACETOPHENONE		
CAS Number:	000098-86-2		
Doc. Number:	ECAO-CIN-G001 (EPA/600/8-89/104), May 1987		
Reference Study:	Imasheva, 1966		
Exp. Route:	Inhalation	Exp. Time:	24 hours/day
Test Species:	Rat	Exp. Frequency:	7 days/week
Chron. Hum. MED:	0.056 mg/day	Exp. Duration:	70 days
RVd:	7.40	Transf. Anim. Dose:	0.045
RVe:	5	Dose Unit:	mg/kg-day
CS:	37	Inhal. Rate:	0.223 m^3/day
Corr. Factor:	10	Ingest. Rate:	N/A
Chronic/subchronic:	Subchronic	Ingest. Unit:	N/A
Exp. Conc. Val 1:	N/A	Absorption Coef.:	1.0
Exp. Conc. Val 2:	0.070	Species Weight:	0.350 kg
Conc. 2 Unit:	mg/m^3		

Effect: Liver dystrophy, congestion of cardiac vessels, decrease in albumin/globulin ratio.

Note: N/A denotes either data not applicable or data not available.

Consistency with the Reportable Quantity Methodology:

Calculations are consistent with the Reportable Quantity methodology. A correction factor of 10 is used to estimate chronic MED from this subchronic study.

Reason for CS Selection:

A CS was selected for the hazard ranking from the only inhalation study presented in the available HEED document. The Reportable Quantity and the Inhalation Reference Concentration were also derived from this study.

DATA REPORT FORM

Chemical Name:	ANTIMONY POTASSIUM TARTRATE		
CAS Number:	028300-74-5		
Source:	ECAO-CIN-R013, May 1983		
Reference Study:	Schroeder et al., 1970		
Exp. Route:	Oral-drinking water	Exp. Time:	24 hours/day
Test Species:	Rat	Exp. Frequency:	7 days/week
Chron. Hum. MED:	12.800 mg/day	Exp. Duration:	2 years
RVd:	3.80	Transf. Anim. Dose:	1.070
RVe:	10	Dose Unit:	mg/kg-day
CS:	38	Inhal. Rate:	N/A
Corr. Factor:	N/A	Ingest. Rate:	7.80
Chronic/subchronic:	Chronic	Ingest. Unit:	% weight/day
Exp. Conc. Val 1:	5.000 ppm	Absorption Coef.:	1.0
Exp. Conc. Val 2:	13.700	Species Weight:	0.350 kg
Conc. 2 Unit:	mg/L		

Effect: Reduced longevity.

Note: N/A denotes either data not applicable or data not available.

Consistency with the Reportable Quantity Methodology:

Calculations are consistent with the Reportable Quantity methodology. The document reports that the exposure concentration of 5 ppm antimony corresponds to 13.7 mg/L of antimony potassium tartrate, and if a rat drinks water corresponding to 7.8 percent of its body weight/day then the transformed animal dose is 1.07 mg/kg-day. No correction factor is used in this chronic study.

Reason for CS Selection:

A CS was selected for the hazard ranking from the only available study suitable for CS derivation. This study was also used to derive the Reportable Quantity for this pollutant.

DATA REPORT FORM

Chemical Name:	ANTIMONY TRISULFIDE		
CAS Number:	001345-04-6		
Source:	ECAO-CIN-R012, May 1983		
Reference Study:	Breiger et al., 1954		
Exp. Route:	Inhalation	Exp. Time:	8 hours/day
Test Species:	Human	Exp. Frequency:	5 days/week
Chron. Hum. MED:	0.714 mg/day	Exp. Duration:	2 years
RVd:	5.70	Transf. Anim. Dose:	N/A
RVe:	8	Dose Unit:	N/A
CS:	46	Inhal. Rate:	10.000 m^3/day
Corr. Factor:	N/A	Ingest. Rate:	N/A
Chronic/subchronic:	Chronic	Ingest. Unit:	N/A
Exp. Conc. Val 1:	N/A	Absorption Coef.:	0.5
Exp. Conc. Val 2:	0.200	Species Weight:	70.000 kg
Conc. 2 Unit:	mg/m^3		

Effect: Altered ECG patterns.

Note: N/A denotes either not applicable or data not available.

Consistency with the Reportable Quantity Methodology:

Calculations are consistent with the Reportable Quantity methodology. The chronic human MED for this study is calculated from the exposure concentration of 0.2 mg/m^3 by expanding the exposure from 5 to 7 days/week and by assuming that a man breathes 10 m^3 contaminated air during an 8-hour workday, and applying an absorption coefficient of 0.5. No correction factor is used in this chronic study.

Reason for CS Selection:

A CS was selected for the hazard ranking from the only available study of this compound that was suitable for Reportable Quantity derivation. This study was also chosen to derive the Reportable Quantity for this compound.

DATA REPORT FORM

Chemical Name:	ACRYLIC ACID		
CAS Number:	000079-10-7		
Source:	ECAO-CIN-R367, May 1987		
Reference Study:	Miller et al., 1981		
Exp. Route:	Inhalation	Exp. Time:	6 hours/day
Test Species:	Rat	Exp. Frequency:	5 days/week
Chron. Hum. MED:	29.9 mg/day	Exp. Duration:	13 weeks
RVd:	3.30	Transf. Anim. Dose:	25.100
RVe:	3	Dose Unit:	mg/kg-d
CS:	10.0	Inhal. Rate:	0.223 m^3/day
Corr. Factor:	10	Ingest. Rate:	N/A
Chronic/subchronic:	Sub	Ingest. Unit:	N/A
Exp. Conc. Val 1:	75.0 ppm	Absorption Coef.:	1.0
Exp. Conc. Val 2:	221.0	Species Weight:	0.350 kg
Conc. 2 Unit:	mg/m^3		

Effect: Focal degeneration of the olfactory epithelium.

Note: N/A denotes either not applicable or data not available.

Consistency with the Reportable Quantity Methodology:

Calculations are consistent with the Reportable Quantity methodology. A correction factor of 10 is used to estimate chronic MED from this subchronic.

Reason for CS Selection:

From the available studies, a CS was selected for the hazard ranking from a rat study using the lowest dose. All studies gave consistent effects and CSs. Exposure to this pollutant causes denudation of the nasal lining of rodents. The composite score used to derive the Reportable Quantity is from the mouse study by Miller et al. 1981, which gives a similar value (2 units apart) to that chosen for the hazard ranking.

DATA REPORT FORM

Chemical Name:	BIPHENYL		
CAS Number:	000092-52-4		
Doc. Number:	ECAO-CIN-R311, March 1985		
Reference Study:	Ambrose et al., 1960		
Exp. Route:	Oral-diet	Exp. Time:	24 hours/day
Test Species:	Rat	Exp. Frequency:	7 days/week
Chron. Hum. MED:	3,591.000 mg/day	Exp. Duration:	2 years
RVd:	1.00	Transf. Anim. Dose:	315.000
RVe:	10	Dose Unit:	mg/kg-day
CS:	10	Inhal. Rate:	N/A
Corr. Factor:	N/A	Ingest. Rate:	N/A
Chronic/subchronic:	Chronic	Ingest. Unit:	N/A
Exp. Conc. Val 1:	5,000.000 ppm	Absorption Coef.:	1.0
Exp. Conc. Val 2:	N/A	Species Weight:	0.302 kg
Conc. 2 Unit:			

Effect: Reduced survival in males, growth retardation, reduced blood hemoglobin levels, decreased food intake, kidney damage including irregular scarring, lymphocytic infiltration, tubular atrophy and patchy tubular dilation in all rats.

Note: N/A denotes either data not applicable or data not available.

Consistency with the Reportable Quantity Methodology:

Calculations from the transformed animal dose to the MED are consistent with the Reportable Quantity methodology. The animal dose could not be verified because of the lack of the necessary information; the Reportable Quantity document states only that "from the food intake and body weight data provided by the investigators, it is determined that the dietary level of 5000 ppm corresponded to a biphenyl intake of 315 mg/kg-day." No correction factor is used in this chronic study.

Reason for CS Selection:

A CS was selected for the hazard ranking from the only study in the Reportable Quantity document suitable to derive a CS. A very high dose was given to produce a severe effect. This was the only available study suitable to derive the Reportable Quantity.

DATA REPORT FORM

Chemical Name:	CALCIUM CYANAMIDE		
CAS Number:	000156-62-7		
Source:	ECAO-CIN-R631, July 1989		
Reference Study:	Kramer et al., 1967		
Exp. Route:	Oral-diet	Exp. Time:	24 hours/day
Test Species:	Rat	Exp. Frequency:	7 days/week
Chron. Hum. MED:	11.970 mg/day	Exp. Duration:	3 months
RVd:	3.88	Transf. Anim. Dose:	10.000
RVe:	4	Dose Unit:	mg/kg-day
CS:	16	Inhal. Rate:	N/A
Corr. Factor:	10	Ingest. Rate:	N/A
Chronic/subchronic:	Subchronic	Ingest. Unit:	N/A
Exp. Conc. Val 1:	N/A	Absorption Coef.:	1.0
Exp. Conc. Val 2:	N/A	Species Weight:	0.350 kg
Conc. 2 Unit:	N/A		

Effect: Increase in relative and absolute thyroid weights.

Note: N/A denotes either data not applicable or data not available.

Consistency with the Reportable Quantity Methodology:

Calculations from the transformed animal dose to the MED are consistent with the Reportable Quantity methodology. No correction factor is used in this chronic study.

Reason for CS Selection:

From the available studies, a CS was selected for the hazard ranking from the study suitable for Reportable Quantities development which used the smallest dose to get a discernible effect. Composite Scores are consistent between available studies, but there is no consistent target of toxicity. The study chosen for the Reportable Quantity was of longer duration than the one chosen for the hazard ranking, but used mortality as the endpoint, used a much larger dose, and was performed in mice. The CS for the study chosen for the hazard ranking is identical to that chosen for the Reportable Quantity determination.

DATA REPORT FORM

Chemical Name:	CAPROLACTAM		
CAS Number:	000105-60-2		
Source:	ECAO-CIN-GO18, Jan 1988		
Reference Study:	NTP, 1982		
Exp. Route:	Oral-diet	Exp. Time:	24 hours/day
Test Species:	Rat (F344)	Exp. Frequency:	7 days/week
Chron. Hum. MED:	150.000 mg/day	Exp. Duration:	13 weeks
RVd:	2.20	Transf. Animal Dose:	125.000
RVe:	4	Dose Unit:	mg/kg-day
CS:	9	Inhal. Rate:	N/A
Corr. Factor:	10	Ingest. Rate:	5.00
Chronic/subchronic:	Subchronic	Ingest. Unit:	% weight/day
Exp. Conc. Val 1:	2,500.000 ppm	Absorption Coef.:	1.0
Exp. Conc. Val 2:	N/A	Species Weight:	0.350 kg
Conc. 2 Unit:	N/A		

Effect: Decreased body weight gain, decreased food consumption.

Note: N/A denotes either data not applicable or data not available.

Consistency with the Reportable Quantity Methodology:

Calculations are consistent with the Reportable Quantity methodology. The dose is calculated by assuming that a rat consumes 5 percent of its body weight in food per day. A correction factor of 10 is used to estimate chronic MED from this subchronic study.

Reason for CS Selection:

From the available studies, a CS was selected for the hazard ranking a suitable study for Reportable Quantities development in rat using the lowest dose. All the available studies used high doses. The effects are nonspecific: weight changes and, at very high doses, changes in fetal and maternal body weight. The study chosen to represent chronic toxicity for caprolactam for the hazard ranking was the same as that chosen for the Reportable Quantity.

DATA REPORT FORM

Chemical Name:	CARBARYL		
CAS Number:	000063-25-2		
Doc. Number:	ECAO-CIN-R317, March 1985		
Reference Study:	Carpenter et al., 1961		
Exp. Route:	Oral-diet	Exp. Time:	24 hours/day
Test Species:	Rat	Exp. Frequency:	7 days/week
Chron. Hum. MED:	238.000 mg/day	Exp. Duration:	2 years
RVd:	1.90	Transf. Anim. Dose:	20.000
RVe:	5	Dose Unit:	mg/kg-day
CS:	10	Inhal. Rate:	N/A
Corr. Factor:	N/A	Ingest. Rate:	5.00
Chronic/subchronic:	Chronic	Ingest. Unit:	% weight/day
Exp. Conc. Val 1:	400.000 ppm	Absorption Coef.:	1.0
Exp. Conc. Val 2:	N/A	Species Weight:	0.035 kg
Conc. 2 Unit:	N/A		

Effect: Cloudy swelling in liver and kidney.

Note: N/A denotes either data not applicable or data not available..

Consistency with the Reportable Quantity Methodology:

Calculations are consistent with the Reportable Quantity methodology. The dose is calculated from the exposure concentration by assuming that a rat consumes 5 percent of its body weight in food per day. No correction factor is used in this chronic study.

Reason for CS Selection:

From the availanle studies, a CS was selected for the hazard ranking from the study suitable for Reportable Quantity development with the lowest dose. Other studies cited teratogenic effects, but at very large doses. Composite scores from all the studies were consistent. This was also the study selected for the derivation of the Reportable Quantity.

DATA REPORT FORM

Chemical Name:	CARBON DISULFIDE		
CAS Number:	000075-15-0		
Source:	ECAO-CIN-R066, May 1983		
Reference Study:	Kashin, 1965; Vasilyeva, 1973		
Exp. Route:	Inhalation	Exp. Time:	8 hours/day
Test Species:	Human	Exp. Frequency:	5 days/week
Chron. Hum. MED:	33.000 mg/day	Exp. Duration:	occupational
RVd:	3.23	Transf. Anim. Dose:	N/A
RVe:	7	Dose Unit:	N/A
CS:	23	Inhal. Rate:	10.000 m^3/day
Corr. Factor:	N/A	Ingest. Rate:	N/A
Chronic/subchronic:	Chronic	Ingest. Unit:	N/A
Exp. Conc. Val 1:	3.000 ppm	Absorption Coef.:	0.5
Exp. Conc. Val 2:	9.300	Species Weight:	70.000 kg
Conc. 2 Unit:	mg/m^3		

Effect: Decreased immunoreactivity, altered menstrual cycle in humans.

Note: N/A denotes either data not applicable or data not available.

Consistency with the Reportable Quantity Methodology:

Calculations are consistent with the Reportable Quantity methodology. The chronic human MED for this occupational study is calculated from the exposure level of 9.3 mg/m^3 by expanding the exposure from 5-7 days/week for continuous exposure, and by assuming that a man breathes 10 m^3 of contaminated air during an 8-hour workday with an absorption coefficient of 0.5. The authors do not expand the 8 hour workday to a 24 hour continuous exposure. The complete definition of occupational exposure is not given.

Reason for CS Selection:

From the available studies, a CS was selected for the hazard ranking from the study suitable for Reportable Quantity development using the lowest dose in humans. This pollutant gave varied but severe effects even at fairly low concentrations. Data were old but consistent and extensive. This was also the study selected for the derivation of the Reportable Quantity.

DATA REPORT FORM

Chemical Name:	2-CHLOROACETOPHENONE		
CAS Number:	532-27-4		
Source:	Reference Concentration for Chronic Inhalation Exposure (RfC) from IRIS, reviewed 10/01/91		
Reference Study:	NTP, 1990		
Exp. Route:	Inhalation	Exp. Time:	6 hours/day
Test Species:	Rat	Exp. Frequency:	5 days/week
Chron. Hum. MED:	1.360 mg/day	Exp. Duration:	2 years
RVd:	5.30	Transf. Anim. Dose:	0.114
RVe:	6	Dose Unit:	mg/kg-day
CS:	32	Inhal. Rate:	0.223 m^3/day
Corr. Factor:	N/A	Ingest. Rate:	N/A
Chronic/subchronic:	Chronic	Ingest. Unit:	N/A
Exp. Conc. Val 1:	N/A	Absorption Coef.:	1.0
Exp. Conc. Val 2:	1.000	Species Weight:	0.350 kg
Conc. 2 Unit:	mg/m^3		

Effect: Dose-related increase in focal squamous hyperplasia and metaplasia of nasal respiratory epithelium in both sexes. Inflammation, ulcers, and squamous hyperlasia of the forestomach was observed in exposed females as a result of ingestion during grooming.

Note: N/A denotes either data not applicable or data not available.

Consistency with the Reportable Quantity Methodology:

The CS for this chemical was derived according to the Reportable Quantity methodology using Inhalation Reference Concentration data.

Reason for CS Selection:

From the available studies, a CS was selected for the hazard ranking from the suitable study for Reportable Quantity development which used the longest duration of exposure. Other available studies were of shorter duration or listed effects unrelated to exposure. This study was also chosen for derivation of an Inhalation Reference Concentration. An RVe of 6 is assigned to squamous metaplasia of the nasal respiratory epithelium. The Inhalation Reference Concentration for the compound is 3E-05 mg/m^3. The compound is extremely irritating from acute exposures and is used extensively as a tear gas agent.

DATA REPORT FORM

Chemical Name:	CHLOROBENZENE		
CAS Number:	000108-90-7		
Source:	ECAO-CIN-R157, May 1983		
Reference Study:	Skinner et al., 1977		
Exp. Route:	Inhalation	Exp. Time:	7 hours/day
Test Species:	Rat/rabbit	Exp. Frequency:	5 days/week
Chron. Hum. MED:	54.700* mg/day	Exp. Duration:	168 days
RVd:	2.90*	Transf. Anim. Dose:	45.700*
RVe:	1	Dose Unit:	mg/kg-day
CS:	3*	Inhal. Rate:	0.223 m^3/day
Corr. Factor:	10	Ingest. Rate:	N/A
Chronic/subchronic:	Subchronic	Ingest. Unit:	N/A
Exp. Conc. Val 1:	75.000 ppm	Absorption Coef.:	1.0
Exp. Conc. Val 2:	345.000	Species Weight:	0.350 kg
Conc. 2 Unit:	mg/m^3		

Effect: Changes in reticulocyte number.

* These values are not from the reference document, but instead relate to the chronic human MED as calculated by the Reportable Quantity methodology; see below.

Note: N/A denotes either data not applicable or data not available.

Consistency with the Reportable Quantity Methodology:

Calculations in the reference study are not consistent with the Reportable Quantity methodology. The document states, "If...345 mg/m^3 is considered the MED, the MED for humans can be estimated as 71.8 mg/day...using a safety factor of 10 for a subchronic study, assuming that a human breathes 20 m^3/day, and an absorption coefficient of 0.5." The Skinner et al. (1977) study discussed in this document is actually described in another referenced study (Deichmann, 1981) that does not include any information on animal inhalation rates and weights.

MED Recalculated According to the RQ Methodology:

Using standard default values (i.e., an inhalation rate of 0.223 m^3/day for a 0.35 kg rat and an absorption coefficient of 1), we obtained a transformed animal dose of 45.7 mg/kg-day and a subchronic MED of 547 mg/day. Dividing by a correction factor of 10 gives a chronic human MED of 54.7 mg/day, corresponding to an RVd of 2.9 and a CS of 2.9. In short:

Calculated Chronic MED:	54.7 mg/day
Calculated CS:	2.9

Reason for CS Selection:

From th available data, a CS was selected for the hazard ranking from the suitable inhalation study for Reportable Quantity development which used rats. The Reportable Quantity document stated that data were limited for inhalation exposures, and that caution should be exercised in using this data. The Reportable Quantity for this compound was derived from an oral study in dogs, in which death was the endpoint. The recalculated CS will be used for the hazard ranking because it was calculated in a fashion consistent with the Reportable Quantity methodology.

DATA REPORT FORM

Chemical Name:	COBALT and compounds		
CAS Number:	007440-48-4		
Source:	ECAO-CIN-R633, July 1989		
Reference Study:	Kerfoot et al., 1975 Kerfoot, 1973		
Exp. Route:	Inhalation	Exp. Time:	6 hours/day
Test Species:	Minature swine	Exp. Frequency:	5 days/week
Chron. Hum. MED:	0.180 mg/day	Exp. Duration:	90 days
RVd:	6.63	Transf. Anim. Dose:	0.035
RVe:	7	Dose Unit:	mg/kg-day
CS:	46	Inhal. Rate:	10.500 m^3/day
Corr. Factor:	10	Ingest. Rate:	N/A
Chronic/subchronic:	Subchronic	Ingest. Unit:	N/A
Exp. Conc. Val 1:	N/A	Absorption Coef.:	0.5
Exp. Conc. Val 2:	1.000	Species Weight:	27 kg
Conc. 2 Unit:	mg/m^3		

Effect: Loss of lung compliance, collagenization of lung, EKG changes.

Note: N/A denotes either data not applicable or data not available.

Consistency with the Reportable Quantity Methodology:

Calculations are consistent with the Reportable Quantity methodology. An absorption coefficient of 0.5 appears to have been used. A correction factor of 10 is used to estimate chronic MED from this subchronic study. This Reportable Quantity document recommends a Composite Score of 22.8 and an RVe of 6 derived from the Wehner et al. (1977) chronic inhalation study with hamsters, which reported pulmonary changes similar to those in this 1975 Kerfoot study.

Reason for CS Selection:

A Composite Score was selected for the hazard ranking from the available studies which used a species most like man (minature swine). In general, subchronic and chronic inhalation of cobalt resulted in lung dysfunction and cardiac lesions. Subchronic studies with swine, rats, and hamsters at low concentrations indicated relatively severe effects. The only truly chronic study used golden syrian hamsters at a much higher exposure concentration to get severe effects. The swine study was selected even though it was shorter in duration because of the severity of effects that were elicited at much lower exposure concentrations than the hamster study. The Composite Score from the swine study

was similar to that reported in NTP studies with rats and mice. The Reportable Quantity document for cobalt stated that the OSHA permissible Exposure Limit (PEL) for cobalt was lowered by half in 1989 to levels below which the Kerfoot study caused effects. The Reportable Quantities document for cobalt is inconsistent in its "derivation of RQ" section. It selected the chronic hamster study for RQ derivation but misstates the Composite Score for that study. The Reportable Quantities document states that there was not enough information in the available studies to address differences in the toxicity or irritant properties among the different compounds and metallic preparation of cobalt administered. Therefore, the Composite Score for cobalt is also assigned to cobalt compounds, metals, fumes, and dust.

DATA REPORT FORM

Chemical Name:	CUMENE		
CAS Number:	000098-82-8		
Source:	ECAO-CIN-G009, Aug 1987		
Reference Study:	Jenkins et al., 1970		
Exp. Route:	Inhalation	Exp. Time:	24 hours/day
Test Species:	Rat	Exp. Frequency:	7 days/week
Chron. Hum. MED:	14.000 mg/day	Exp. Duration:	90 days
RVd:	3.80	Transf. Anim. Dose:	11.500
RVe:	3	Dose Unit:	mg/kg-day
CS:	11	Inhal. Rate:	0.223 m^3/day
Corr. Factor:	10	Ingest. Rate:	N/A
Chronic/subchronic:	Subchronic	Ingest. Unit:	N/A
Exp. Conc. Val 1:	3.700 ppm	Absorption Coef.:	1.0
Exp. Conc. Val 2:	18.000	Species Weight:	0.350 kg
Conc. 2 Unit:	mg/m^3		

Effect: Leukocytosis.

Note: N/A denotes either data not applicable or data not available.

Consistency with the Reportable Quantity Methodology:

Calculations are consistent with the Reportable Quantity methodology. A correction factor of 10 is used to estimate chronic MED from this subchronic study.

Reason for CS Selection:

From the available studies, a CS was selected for the hazard ranking from the only inhalation study suitable for Reportable Quantity determination. This was also the study chosen for Reportable Quantity derivation.

DATA REPORT FORM

Chemical Name:	DIBUTYLPHTHALATE		
CAS Number:	000084-74-2		
Source:	ECAO-CIN-RO39, May 1983		
Reference Study:	Nikonorow et al., 1973		
Exp. Route:	Oral-gavage	Exp. Time:	N/A
Test Species:	Rat	Exp. Frequency:	N/A
Chron. Hum. MED:	147.000 mg/day	Exp. Duration:	90 days
RVd:	2.20	Transf. Anim. Dose:	120.000
RVe:	4	Dose Unit:	mg/kg-day
CS:	9	Inhal. Rate:	N/A
Corr. Factor:	10	Ingest. Rate:	N/A
Chronic/subchronic:	Subchronic	Ingest. Unit:	N/A
Exp. Conc. Val 1:	N/A	Absorption Coef.:	1.0
Exp. Conc. Val 2:	N/A	Species Weight:	0.350 kg
Conc. 2 Unit:	N/A		

Effect: Increased relative liver weight.

Note: N/A denotes either data not applicable or data not available.

Consistency with the Reportable Quantity Methodology:

Calculations from the transformed animal dose to the MED are consistent with the Reportable Quantity methodology. No exposure concentration, exposure regimen, or ingestion rates are available from the data sources we reviewed to verify the transformed animal dose. A correction factor of 10 is used to estimate chronic MED from this subchronic study.

Reason for CS Selection:

A CS was selected for the hazard ranking from one of two studies reported in the Reportable Quantity document that were suitable for Reportable Quantity determination. Two studies were cited that gave similar CSs. Data seem to be limited. The CS was chosen from a subchronic study rather than the teratogenic evaluation that was also reported in the Reportable Quantity document. The teratogenic study showed evidence of delayed ossification at a relatively high dose level (420 mg/day equivalent human dose).

DATA REPORT FORM

Chemical Name:	2,4-D, SALTS AND ESTERS (2,4-DICHLOROPHENOXY ACETIC ACID)		
CAS Number:	000094-75-7		
Source:	ECAO-CIN-R096, May 1983		
Reference Study:	Schwetz et al., 1971		
Exp. Route:	Oral-gavage	Exp. Time:	N/A
Test Species:	Rat	Exp. Frequency:	N/A
Chron. Hum. MED:	129.000 mg/day	Exp. Duration:	N/A
RVd:	2.30	Transf. Anim. Dose:	12.500
RVe:	8	Dose Unit:	mg/kg-day
CS:	18	Inhal. Rate:	N/A
Corr. Factor:	N/A	Ingest. Rate:	N/A
Chronic/subchronic:	Developmental	Ingest. Unit:	N/A
Exp. Conc. Val 1:	N/A	Absorption Coef.:	1.0
Exp. Conc. Val 2:	N/A	Species Weight:	0.225 kg
Conc. 2 Unit:	N/A		

Effect: Minor fetotoxic effects with no effect on maternal body weight in teratogenicity study.

Note: N/A denotes either data not applicable or data not available.

Consistency with the Reportable Quantity Methodology:

Calculations from the transformed animal dose to the MED are consistent with the Reportable Quantity methodology. No exposure concentration, exposure regimen, or ingestion rates are available in the data sources we reviewed to verify the transformed animal dose. No correction factor is applied for this developmental study.

Reason for CS Selection:

From the available studies, a CS was selected for the hazard ranking from a suitable study for Reportable Quantities which used the lowest dose; doses in other studies were very large. The effect, teratogenicity, was consistent among all the studies. There were many toxicity studies for this compound. Only four were considered for derivation of the Reportable Quantity. The study chosen to derive the Reportable Quantity was also that chosen for the hazard ranking. Most chronic studies showed no effects at levels (NOAELs) many times that which produced teratogenicity.

DATA REPORT FORM

Chemical Name:	N,N-DIMETHYLANILINE		
CAS Number:	000121-69-7		
Source:	EPA/600/X-87/052, Dec 1986		
Reference Study:	SIB, Inc., 1980		
Exp. Route:	Oral-gavage	Exp. Time:	24 hours/day
Test Species:	Rat	Exp. Frequency:	5 days/week
Chron. Hum. MED:	21.000 mg/day	Exp. Duration:	91 days
RVd:	3.50	Transf. Anim. Dose:	22.320
RVe:	6	Dose Unit:	mg/kg-day
CS:	21	Inhal. Rate:	N/A
Corr. Factor:	10	Ingest. Rate:	N/A
Chronic/subchronic:	Subchronic	Ingest. Unit:	N/A
Exp. Conc. Val 1:	N/A	Absorption Coef.:	1.0
Exp. Conc. Val 2:	31.200	Species Weight:	0.170 kg
Conc. 2 Unit:	mg/kg-day		

Effect: Splenomegaly and increased splenic hemosiderosis and hematopoiesis in the female rat.

Note: N/A denotes either data not applicable or data not available.

Consistency with the Reportable Quantity Methodology:

Calculations are consistent with the Reportable Quantity methodology. This study reports the oral gavage dose directly as 31.2 mg/kg-day, i.e., exposure concentration is not provided. This dose, however, can be converted to a transformed animal dose of 22.32 mg/kg-day by accounting for the 5 day/week exposure. A correction factor of 10 is used to estimate chronic MED from this subchronic study.

Reason for CS Selection:

A CS was selected for the hazard ranking from a rat study presented in the Health and Environmental Effects Profile (HEEP) for the pollutant. Only two studies were presented as suitable for derivation of a Reportable Quantity, both with similar results. The study selected for the hazard ranking was the same as that used for derivation of the Reportable Quantity.

DATA REPORT FORM

Chemical Name:	DIMETHYL PHTHALATE		
CAS Number:	000131-11-3		
Source:	ECAO-CIN-R404, July 1987		
Reference Study:	Lehman, 1955		
Exp. Route:	Oral-diet	Exp. Time:	24 hours/day
Test Species:	Rat	Exp. Frequency:	7 days/week
Chron. Hum. MED:	23,940.000 mg/day	Exp. Duration:	2 years
RVd:	1.00	Transf. Anim. Dose:	2000.000
RVe:	7	Dose Unit:	mg/kg-day
CS:	7	Inhal. Rate:	N/A
Corr. Factor:	N/A	Ingest. Rate:	5.00
Chronic/subchronic:	Chronic	Ingest. Unit:	% weight/day
Exp. Conc. Val 1:	N/A	Absorption Coef.:	1.0
Exp. Conc. Val 2:	4.000	Species Weight:	0.350 kg
Conc. 2 Unit:	percent dimethyl phthalate		

Effect: chronic nephritis.

Note: N/A denotes either data not applicable or data not available.

Consistency with the Reportable Quantity Methodology:

Calculations are consistent with the Reportable Quantity methodology. The dose is calculated by assuming that a rat consumes 5 percent of its body weight in food per day, so that 4 percent dimethyl phthalate in the diet is equivalent to 2000 mg/kg-day. No correction factor is used in this chronic study.

Reason for CS Selection:

A CS was selected for the hazard ranking from the available studies which used the lowest dose. Only two studies were suitable for Reportable Quantity derivation, both used very large doses. The study selected for the Reportable Quantity derivation was the same as that selected for the hazard ranking.

DATA REPORT FORM

Chemical Name:	2,4-DINITROPHENOL		
CAS Number:	000051-28-5		
Source:	ECAO-CIN-R119, May 1983		
Reference Study:	USEPA 1980; Horner 1942; Tainter et al., 1935		
Exp. Route:	Oral-diet	Exp. Time:	N/A
Test Species:	Human	Exp. Frequency:	2 times/day
Chron. Hum. MED:	14.000 mg/day	Exp. Duration:	90 days
RVd:	3.80	Transf. Anim. Dose:	N/A
RVe:	8	Dose Unit:	N/A
CS:	30	Inhal. Rate:	N/A
Corr. Factor:	10	Ingest. Rate:	N/A
Chronic/subchronic:	Subchronic	Ingest. Unit:	N/A
Exp. Conc. Val 1:	N/A	Absorption Coef.:	1.0
Exp. Conc. Val 2:	100.000	Species Weight:	70.000 kg
Conc. 2 Unit:	mg		

Effect: Bilateral cataracts, peripheral neuritis, elevated basal metabolic rate, skin rashes.

Note: N/A denotes either data not applicable or data not available.

Consistency with the Reportable Quantity Methodology:

Calculations are consistent with the Reportable Quantity methodology. Humans ingested 2-5 mg 2,4-dinitrophenol/kg body weight/day to aid in weight loss. The MED is calculated by taking the low end of the dose range for weight reduction, 2 mg/kg-day, multiplying by a body weight of 70 kg, and dividing by 10 to convert to a chronic value.

Reason for CS Selection:

A CS was selected for the hazard ranking from the available human study suitable for Reportable Quantity development. This study had a wide range of effects associated with exposure to the pollutant.

DATA REPORT FORM

Chemical Name:	ETHYL CHLORIDE		
CAS Number:	75-00-3		
Source:	Reference Concentration for Chronic Inhalation Exposure (RfC) from IRIS, reviewed 04/01/91		
Reference Study:	NTP, 1989		
Exp. Route:	Inhalation	Exp. Time:	6 hours/day
Test Species:	Rat	Exp. Frequency:	5 days/week
Chron. Hum. MED:	53,865.000 mg/day	Exp. Duration:	102 weeks
RVd:	1.00	Transf. Anim. Dose:	4,500.000
RVe:	4	Dose Unit:	mg/kg-day
CS:	4	Inhal. Rate:	0.223 m^3/day
Corr. Factor:	N/A	Ingest. Rate:	N/A
Chronic/subchronic:	Chronic	Ingest. Unit:	N/A
Exp. Conc. Val 1:	15,000.000 ppm	Absorption Coef.:	1.0
Exp. Conc. Val 2:	39,571.000	Species Weight:	0.350 kg
Conc. 2 Unit:	mg/m^3		

Effect: Decreased mean body weight gain in males and females.

Note: N/A denotes either data not applicable or data not available.

Consistency with the Reportable Quantity Methodology:

The CS for this chemical was derived according to the Reportable Quantity methodology using Inhalation Reference Concentration data.

Reason for CS Selection:

From the available studies, a CS was selected for the hazard ranking from a rat study suitable for Reportable Quantities development which was of longest duration. This study used a very high dose but effects were not severe. This was the only truly chronic study available. Gestational effects were noted in another study at high exposure concentation. The chronic human MED in mg/day was larger (89,519 mg/day) for that study than that of the study chosen for the hazard ranking (53,865 mg/day). Both studies produced relatively low CSs. An RVe of 4 is assigned to decreased mean body weight gain. The RfC for this compound is 1E+01 mg/m^3 and based on the gestational study.

DATA REPORT FORM

Chemical Name:	2-ETHOXYETHANOL		
CAS Number:	110-80-5		
Source:	Reference Concentration for Chronic Inhalation Exposure (RfC) from IRIS, reviewed 05/01/91		
Reference Study:	Barbee et al., 1984		
Exp. Route:	Inhalation	Exp. Time:	6 hours/day
Test Species:	Rabbit	Exp. Frequency:	5 days/week
Chron. Hum. MED:	368.000 mg/day	Exp. Duration:	13 weeks
RVd:	1.7	Transf. Anim. Dose:	139.00
RVe:	9	Dose Unit:	mg/kg-day
CS:	15	Inhal. Rate:	2.000 m^3/day
Corr. Factor:	10	Ingest. Rate:	N/A
Chronic/subchronic:	Subchronic	Ingest. Unit:	N/A
Exp. Conc. Val 1:	403.000 ppm	Absorption Coef.:	1.0
Exp. Conc. Val 2:	1,485.000	Species Weight:	3.800 kg
Conc. 2 Unit:	mg/m^3		

Effect: Decreased body weight and testes weight, focal degeneration of seminiferous tubules, and decreased hemoglobin, hematocrit and erythrocyte count.

Note: N/A denotes either data not applicable or data not available.

Consistency with the Reportable Quantity Methodology:

The CS for this chemical was derived according to the Reportable Quantity methodology using Inhalation Reference Concentration data.

Reason for CS Selection:

A CS was selected for the hazard ranking from the available study of longest duration suitable for Reportable Quantities development. This study was also chosen as the basis for the Reference Concentration determination. A correction factor for duration was used. This pollutant also causes fetotoxicity but requires massively high doses. Therefore, for this pollutant, the fetotoxic effects are severe but the doses required to elicit them are huge. For the study chosen for the hazard ranking, an RVe of 9 is assigned to decreased testis weight and seminiferous tubule degeneration based on the definition of an RVe of 9. In that definition, reproductive dysfunction is given as a criterion for the classification. The Reference Concentration for this pollutant is 2E-01 mg/m^3.

DATA REPORT FORM

Chemical Name:	ETHYL BENZENE		
CAS Number:	100-41-4		
Source:	Data collected for development of RfC		
Reference Study:	NTP, 1988		
Exp. Route:	Inhalation	Exp. Time:	7 hours/day
Test Species:	Rat	Exp. Frequency:	5 days/week
Chron. Hum. MED:	148.00 mg/day	Exp. Duration:	214 days
RVd:	2.2	Transf. Anim. Dose:	230.00*
RVe:	4	Dose Unit:	mg/kg-day
CS:	9	Inhal. Rate:	0.223 m^3/day
Corr. Factor:	10	Ingest. Rate:	N/A
Chronic/subchronic:	Subchronic	Ingest. Unit:	N/A
Exp. Conc. Val 1:	250,000 ppm	Absorption Coef.:	1.0
Exp. Conc. Val 2:	1,086.000	Species Weight:	0.350 kg
Conc. 2 Unit:	mg/m^3		

Effect: Significant dose-related increase in relative liver weight.

Note: N/A denotes either data not applicable or data not available.

Consistency with the Reportable Quantity Methodology:

The CS for this chemical was derived according to the Reportable Quantity methodology using inhalation data collected for the development of an RfC.

Reason for CS Selection:

From the available studies, a CS was selected for the hazard ranking from a study which was a well conducted subchronic inhalation study suitable for Reportable Quantity development. This study showed a dose-response in the effect elicited by ethyl benzene. The CS calculated for it was similar to the CS from a relatively older study (1956, Wolf et al.) without proper controls that also reported similar effects. The NTP study uses a shorter duration of exposure than the older study by Wolf et al., but also used a smaller dose to elicit similar effects. An RVe of 4 is assigned to increased relative liver weight.

DATA REPORT FORM

Chemical Name:	ETHYLENE GLYCOL		
CAS Number:	107-21-1		
Source:	ECAO-CIN-R637, May 1991		
Reference Study:	Union Carbide, 1989		
Exp. Route:	Oral-gavage	Exp. Time:	N/A
Test Species:	Mouse	Exp. Frequency:	N/A
Chron. Hum. MED:	2,640 mg/day	Exp. Duration:	gestation day (6-15)
RVd:	1.0	Transf. Anim. Dose:	500
RVe:	10	Dose Unit:	mg/kg-day
CS:	10	Inhal. Rate:	N/A
Corr. Factor:	N/A	Ingest. Rate:	N/A
Chronic/subchronic:	Developmental	Ingest. Unit:	N/A
Exp. Conc. Val 1:	N/A	Absorption Coef.:	1.0
Exp. Conc. Val 2:	500	Species Weight:	0.030 kg
Conc. 2 Unit:	mg/kg-day		

Effect: Increased skeletal and total fetal malformations, no maternal toxicity.

Note: N/A denotes either data not applicable or data not available.

Consistency with the Reportable Quantity Methodology:

Calculations in the source document are consistent with the Reportable Quantity methodology. This study reports the oral gavage dose directly as 500 mg/kg-day. No correction factor is used to derive the chronic human MED from the developmental (gestational) study.

Reason for CS Selection:

From the available studies, a CS was selected for the hazard ranking from a gestaional study used to determine the Reportable Quantity. There is one group of inhalation studies currently available to determine an RQ (Coon et al., 1970). The RQ document does not choose them for RQ determination because "these subchronic exposure experiments were.. of small sample size and short duration of exposure". Furthermore the RQ document states that no levels of significance were reported for the endpoints reported by Coon et al., (1970). Therefore although inhalation studies are preferred over oral studies for the ranking, the better study design, population size, and the consideration of the oral

study being chosen for CS for Reportable Quantities purposes, an oral study is chosen to represent the hazard of this chemical. The chosen study uses the lowest does for developmental effects.

However, given the nature of the currently available data, the use of the oral over inhalation data is not strongly supported. The inhaltion studies were performed in multiple species and although nonspecific, the reported effects were consistent with systemic effects seen in some of the oral studies.

DATA REPORT FORM

Chemical Name:	ETHYLENE GLYCOL MONOBUTYL ETHER		
CAS Number:	111-76-2		
Source:	RfC, verified by U.S. EPA RfD/RfC workgroup. Not yet on IRIS as of 2-22-94)		
Reference Study:	Dodd et al., 1983		
Exp. Route:	Inhalation	Exp. Time:	6 hours/day
Test Species:	Rat	Exp. Frequency:	5 days/week
Chron. Hum. MED:	58.600 mg/day	Exp. Duration:	13 weeks
RVd:	2.80	Transf. Anim. Dose:	49.0
RVe:	4	Dose Unit:	mg/kg-day
CS:	11	Inhal. Rate:	0.260 m^3/day
Corr. Factor:	10	Ingest. Rate:	N/A
Chronic/subchronic:	Subchronic	Ingest. Unit:	N/A
Exp. Conc. Val 1:	77.000 ppm	Absorption Coef.:	1.0
Exp. Conc. Val 2:	372.000	Species Weight:	0.350 kg
Conc. 2 Unit:	mg/m^3		

Effect: Transient decrease in body weight gain in females.

Note: N/A denotes either data not applicable or data not available.

Consistency with the Reportable Quantity Methodology:

The CS for this chemical was derived according to the Reportable Quantity methodology using inhalation data collected for Reference Concentration development.

Reason for CS Selection:

A CS was selected for the hazard ranking from the available study of longest duration suitable for Reportable Quantities development. Both a rat study and a dog study have similar durations and CSs (2 units apart). The dog study is old, reports results for only one dose, and uses a larger dose than the rat study. Hematological effects with some organ weight changes seem to predominate. The rat study was selected for Inhalation Reference Concentration determination. Although dog studies are considered more relevant to man, the rat study was chosen as most appropriate for the hazard ranking. Composite scores for all available studies were similar except for one using mortality as an endpoint at the largest reported dose. An RVe of 4 is assigned to a transient decrease in body weight gain in females.

DATA REPORT FORM

Chemical Name:	HEXANE		
CAS Number:	000110-54-3		
Source:	ECAO-CIN-G076, Sept 1989		
Reference Study:	Ono et al., 1982		
Exp. Route:	Inhalation	Exp. Time:	12 hours/day
Test Species:	Rat	Exp. Frequency:	7 days/week
Chron. Hum. MED:	270.000 mg/day	Exp. Duration:	24 weeks
RVd:	1.85	Transf. Anim. Dose:	200.000
RVe:	7	Dose Unit:	mg/kg-day
CS:	13	Inhal. Rate:	0.283 m^3/day
Corr. Factor:	10	Ingest. Rate:	N/A
Chronic/subchronic:	Subchronic	Ingest. Unit:	N/A
Exp. Conc. Val 1:	200.000 ppm	Absorption Coef.:	1.0
Exp. Conc. Val 2:	705.000	Species Weight:	0.500 kg
Conc. 2 Unit:	mg/m^3		

Effect: Axonopathy, nerve conduction alterations.

Note: N/A denotes either data not applicable or data not available.

Consistency with the Reportable Quantity Methodology:

Calculations are consistent with the Reportable Quantity methodology. A correction factor of 10 is used to estimate chronic MED from this subchronic study.

Reason for CS Selection:

From the available studies, a CS was selected for the hazard ranking from the study suitable for Reportable Quantity development using the smallest dose and with the most consistent endpoint of toxicity. There was a dose-response relationship for neurologic symptoms in 3 out of 4 studies. This was also the study used to derive the Reportable Quantity for this compound.

DATA REPORT FORM

Chemical Name:	HYDROCHLORIC ACID (HYDROGEN CHLORIDE GAS ONLY)		
CAS Number:	7647-01-0		
Source:	Reference Concentration for Chronic Inhalation Exposure (RfC) from IRIS, reviewed 01/01/91		
Reference Study:	Sellakumar et al., 1985		
Exp. Route:	Inhalation	Exp. Time:	6 hours/day
Test Species:	Rat	Exp. Frequency:	5 days/week
Chron. Hum. MED:	20.3 mg/day	Exp. Duration:	lifetime
RVd:	3.5	Transf. Anim. Dose:	1.7
RVe:	3	Dose Unit:	mg/kg-day
CS:	11	Inhal. Rate:	0.223 m^3/day
Corr. Factor:	N/A	Ingest. Rate:	N/A
Chronic/subchronic:	Chronic	Ingest. Unit:	N/A
Exp. Conc. Val 1:	10.000 ppm	Absorption Coef.:	1.0
Exp. Conc. Val 2:	15.000	Species Weight:	0.350 kg
Conc. 2 Unit:	mg/m^3		

Effect: Hyperplasia of nasal mucosa, larynx, and trachea.

Note: N/A denotes either data not applicable or data not available.

Consistency with the Reportable Quantity Methodology:

The CS for this chemical was derived according to the Reportable Quantity methodology using Inhalation Reference Concentration data.

Reason for CS Selection:

A CS was selected for the hazard ranking from the study chosen for the derivation of the Reference Concentration. This study was the longest in duration, and gave similar results to the only other suitable study available which used mice. An RVe of 3 is assigned for hyperplasia based on the description of an RVe of 3 given in Table 2-1 of the technical background document supporting rulemaking pursuant to CERCLA Section 102. The Reference Concentration for the compound is 7E-03 mg/m^3.

DATA REPORT FORM

Chemical Name:	MALEIC ANHYDRIDE		
CAS Number:	000108-31-6		
Source:	EPA/600/X-86/196, July 1986		
Reference Study:	Ulrich et al., 1981		
Exp. Route:	Inhalation	Exp. Time:	6 hours/day
Test Species:	Monkey	Exp. Frequency:	5 days/week
Chron. Hum. MED:	2.000* mg/day	Exp. Duration:	6 months
RVd:	5.0*	Transf. Anim. Dose:	0.82
RVe:	7	Dose Unit:	mg/kg-day
CS:	35	Inhal. Rate:	N/A
Corr. Factor:	10	Ingest. Rate:	N/A
Chronic/subchronic:	Subchronic	Ingest. Unit:	N/A
Exp. Conc. Val 1:	N/A	Absorption Coef.:	1.0
Exp. Conc. Val 2:	0.010	Species Weight:	3.000 kg
Conc. 2 Unit:	mg/L		

Effect: Dose-related increased severity of nasal and ocular irritation, coughing, dyspnea.

* These values are not from the reference document, but instead relate to the chronic human MED as calculated by the Reportable Quantity methodology; see below.

Note: N/A denotes either data not applicable or data not available.

Consistency with the Reportable Quantity Methodology:

Calculations in the reference study are not consistent with the Reportable Quantity methodology. Although the monkey study is for an exposure duration of 6 months, the authors do not use a correction factor to estimate the chronic human MED. The transformed animal dose could not be verified because the inhalation rate for the monkey was not reported in the data sources that we reviewed.

MED Recalculated According to the RQ Methodology:

A subchronic human MED of 20 mg/day was derived by multiplying the transformed animal dose of 0.82 mg/kg-day (females) by the ratio of body weights for monkeys and humans, raised to the one-third power, and then by multiplying by 70 kg. Tthis subchronic MED was divided by a correction factor of 10 to estimate chronic human MED. This MED corresponds to an RVd of 5. In short:

Calculated Chronic MED:	2.0 mg/day
RVd:	5

Reason for CS Selection:

From the available studues, a CS was selected for the hazard ranking from a monkey study (Urich et al., 1981) suitable for Reportable Quantity development that reports respiratory and ocular irritation, coughing, and dyspnea from subchronic exposure to 0.010 mg/L maleic anhydride vapor. No explanation was given in the Reportable Quantity document as to why a CS was not derived for this study. Only rat studies had CSs derived. The Reportable Quantity was derived from rat the study giving the highest CS.

DATA REPORT FORM

Chemical Name:	MANGANESE AND COMPOUNDS		
CAS Number:	007439-96-5		
Source:	Neurotoxicology 13(1): 271-274, 1992		
Reference Study:	Wennberg et al., 1992		
Exp. Route:	Inhalation	Exp. Time:	8 hours/day
Test Species:	Human	Exp. Frequency:	5 days/week
Chron. Hum. MED:	0.64 mg/day	Exp. Duration:	9.4 years (avg)
RVd:	5.8	Transf. Anim. Dose:	N/A
RVe:	7	Dose Unit:	N/A
CS:	41	Inhal. Rate:	10 m^3/day
Corr. Factor:	N/A	Ingest. Rate:	N/A
Chronic/subchronic:	Occupational	Ingest. Unit:	
Exp. Conc. Val 1:	0.18 mg/m^3 (avg.)	Absorption Coef.:	0.0
Exp. Conc. Val 2:	N/A	Species Weight:	70 kg
Conc. 2 Unit:	N/A		
Effect:	Impairment in the ability to perform rapidly alternating movements (diadochokinesis).		

Note: N/A denotes either not applicable or data not available.

Consistency with the Reportable Quantity Methodology:

The CS for this chemical was derived according to the Reportable Quantity methodology using Inhalation Reference Concentration data. The chronic human MED for this occupational study is calculated from the exposure concentration of 0.18 mg/m^3 total manganese dust by expanding the exposure from 5 to 7 days/week for continous exposure, and by assuming that a man breathes 10 m^3 of contaminated air during an 8-hour workday with an absorption coefficient of 0.5.

Reason for CS Selection:

From the available studies, a CS was selected for the hazard ranking from an inhalation study in humans which was identified to serve as a basis for determination of an Inhaltion Reference Concentration. There are 4 studies available which are for workers. They all give identical composite scores and report similar effects. The study chosen to represetn the hazard of inhaled manganese reported the lowest dose for the longest duration of exposure.

DATA REPORT FORM

Chemical Name:	MERCURY, (ACETATO-O)PHENYL		
CAS Number:	000062-38-4		
Source:	ECAO-CIN-R153, May 1983		
Reference Study:	Fitzhugh et al., 1950		
Exp. Route:	Oral-diet	Exp. Time:	24 hours/day
Test Species:	Rat	Exp. Frequency:	7 days/week
Chron. Hum. MED:	1.260 mg/day	Exp. Duration:	2 years
RVd:	5.30	Transf. Anim. Dose:	0.105
RVe:	7	Dose Unit:	mg/kg-day
CS:	37	Inhal. Rate:	N/A
Corr. Factor:	N/A	Ingest. Rate:	5.00
Chronic/subchronic:	Chronic	Ingest. Unit:	% weight/day
Exp. Conc. Val 1:	N/A	Absorption Coef.:	1.0
Exp. Conc. Val 2:	0.500	Species Weight:	0.350 kg
Conc. 2 Unit:	ppm mercury		

Effect: Moderate renal damage in females.

Note: N/A denotes either data not applicable or data not available.

Consistency with the Reportable Quantity Methodology:

Calculations from the transformed animal dose to the chronic human MED are consistent with the Reportable Quantity methodology. The document reports that the transformed animal dose is derived from the exposure concentration as follows: "Assuming that a rat consumes the equivalent of 0.05 of its body weight/day as food, 0.5 ppm dietary levels of mercury from phenylmercuric acetate correspond to doses for rats of...0.105 mg phenylmercuric acetate/kg bw/day." No correction factor is used in this chronic study.

Reason for CS Selection:

A CS was selected for the hazard ranking from the single study that was available and suitable for CS derivation. The dose chosen for CS derivation was the lowest dose which produced detectable effects. Females appeared to be more sensitive to the effects of the pollutant. There was a consistent target and dose-response between the doses reported. This study was also used to derive the Reportable Quantity for this pollutant.

DATA REPORT FORM

Chemical Name:	MERCURIC CHLORIDE		
CAS Number:	000748-79-4		
Source:	ECAO-CIN-R503, November 1987		
Reference Study:	Knoflach et al., 1986		
Exp. Route:	Oral-gavage	Exp. Time:	24 hours/day
Test Species:	Rat	Exp. Frequency:	3 days/week
Chron. Hum. MED:	0.766 mg/day	Exp. Duration:	39 weeks
RVd:	5.70	Transf. Anim. Dose:	0.640
RVe:	7	Dose Unit:	mg/kg-day
CS:	40	Inhal. Rate:	N/A
Corr. Factor:	10	Ingest. Rate:	N/A
Chronic/subchronic:	Subchronic	Ingest. Unit:	N/A
Exp. Conc. Val 1:	N/A	Absorption Coef.:	1.0
Exp. Conc. Val 2:	1.500	Species Weight:	0.350 kg
Conc. 2 Unit:	mg/kg		

Effect: Proteinuria, immunopathologic kidney response.

Note: N/A denotes either data not applicable or data not available.

Consistency with the Reportable Quantity Methodology:

Calculations are consistent with the Reportable Quantity methodology. The transformed animal dose is calculated by expanding the exposure concentration of 1.5 mg/kg from 3 to 7 days/week. A correction factor of 10 is used to estimate chronic human MED from this subchronic study.

Reason for CS Selection:

From the available studies, a CS was selected for the hazard ranking from the study suitable for Reportable Quantity development which used the lowest dose, was the most recent, and was one of the longest in duration. The kidney seemed to be the consistent target of the pollutant. This was also the study selected for the Reportable Quantity derivation for this pollutant.

DATA REPORT FORM

Chemical Name:	MERCURIC NITRATE		
CAS Number:	010045-94-0		
Source:	ECAO-CIN-R149, May 1983		
Reference Study:	Neal et al., 1937, 1941		
Exp. Route:	Inhalation	Exp. Time:	8 hours/day
Test Species:	Human	Exp. Frequency:	5 days/week
Chron. Hum. MED:	1.390 mg/day	Exp. Duration:	20 years
RVd:	5.30	Transf. Anim. Dose:	N/A
RVe:	8	Dose Unit:	N/A
CS:	42	Inhal. Rate:	10.000 m^3/day
Corr. Factor:	N/A	Ingest. Rate:	N/A
Chronic/subchronic:	Chronic	Ingest. Unit:	N/A
Exp. Conc. Val 1:	N/A	Absorption Coef.:	0.5
Exp. Conc. Val 2:	0.390	Species Weight:	70.000 kg
Conc. 2 Unit:	mg/m^3		

Effect: Tremor.

Note: N/A denotes either data not applicable or data not available.

Consistency with the Reportable Quantity Methodology:

Calculations are consistent with the Reportable Quantity methodology. The Reportable Quantity document reports that the exposure concentration of 0.24 mg mercury/m^3 is converted to 0.39 mg mercuric nitrate/m^3 by multiplying by the ratio of the formula weights (334.6 mg mercuric nitrate to 200.6 mg mercury). The human MED of 1.39 mg/day is calculated from the mercuric nitrate exposure concentration of 0.39 mg/m^3 by assuming that workers were in the factory 5 days/week and that they breathed 10 m^3 contaminated air/day, with an absorption coefficient of 0.5. No correction factor is used in this chronic study.

Reason for CS Selection:

A CS was selected for the hazard ranking from the only available study suitable for CS derivation. This study was also used to derive the Reportable Quantity for this pollutant.

DATA REPORT FORM

Chemical Name:	METHANOL		
CAS Number:	67-56-1		
Source:	Data collected for development of RfC		
Reference Study:	NEDO, 1986		
Exp. Route:	Inhalation	Exp. Time:	21 hours/day
Test Species:	Monkey	Exp. Frequency:	N/A
Chron. Hum. MED:	2,636 mg/day	Exp. Duration:	7 months
RVd:	1.0	Transf. Anim. Dose:	78.00
RVe:	7	Dose Unit:	mg/kg-day
CS:	7	Inhal. Rate:	5.400 m^3/day
Corr. Factor:	N/A	Ingest. Rate:	N/A
Chronic/subchronic:	Chronic	Ingest. Unit:	N/A
Exp. Conc. Val 1:	100.000 ppm	Absorption Coef.:	1.0
Exp. Conc. Val 2:	131.000	Species Weight:	8.000 kg
Conc. 2 Unit:	mg/m^3		

Effect: Abnormal cellular changes in the inside nucleus of the thalamus and cerebral white substance (increased number of responsive stellate cells).

Note: N/A denotes either data not applicable or data not available.

Consistency with the Reportable Quantity Methodology:

The CS for this chemical was derived according to the Reportable Quantity methodology using Inhalation Reference Concentration data.

Reason for CS Selection:

From the available data, a CS was selected for the hazard ranking from a study using monkeys, the most appropriate model for man. This was the study of longest duration available from those collected for RfC development. Studies in rats provided CSs that were similar for this pollutant, but used very large doses or short exposure times. An RVe of 7 is assigned to degeneration of the thalamic nucleus and the cerebral white substance.

DATA REPORT FORM

Chemical Name:	METHOXYCHLOR		
CAS Number:	000072-43-5		
Source:	ECAO-CIN-R345, March 1985		
Reference Study:	NCI, 1978		
Exp. Route:	Oral-diet	Exp. Time:	24 hours/day
Test Species:	Rat	Exp. Frequency:	7 days/week
Chron. Hum. MED:	269.000 mg/day	Exp. Duration:	78 weeks
RVd:	1.90	Transf. Anim. Dose:	22.500
RVe:	4	Dose Unit:	mg/kg-day
CS:	8	Inhal. Rate:	N/A
Corr. Factor:	N/A	Ingest. Rate:	5.00
Chronic/subchronic:	Chronic	Ingest. Unit:	% weight/day
Exp. Conc. Val 1:	N/A	Absorption Coef.:	1.0
Exp. Conc. Val 2:	449.000	Species Weight:	0.350 kg
Conc. 2 Unit:	mg/kg Time Weighted Average (TWA)		
Effect:	Reduced rate of body weight gain.		
Note:	N/A denotes either data not applicable or data not available.		

Consistency with the Reportable Quantity Methodology:

Calculations are consistent with the Reportable Quantity methodology. The exposure concentration of 449 mg/kg, time weighted average (TWA), is calculated by taking the TWA of a 360 mg/kg dose for 29 weeks and a 500 mg/kg dose for 49 weeks. Multiplying the TWA concentration of 449 mg/kg by a rat's food consumption of 5 percent of its body weight/day results in a transformed animal dose of 22.5 mg/kg-day. No correction factor is used in this chronic study.

Reason for CS Selection:

From the available studies, a CS was selected for the hazard ranking from the study suitable for Reportable Quantity development with the longest duration and the lowest dose. A wide variety of effects, with no consistent target, were reported for this pollutant. The Reportable Quantity was derived from the study producing the largest CS. Many of the studies used such large doses that an RVe of 1 was reported for a wide range of doses. Dog and swine would usually be the preferred species, but studies with each used such massive doses (e.g., 78,837 and 12,281 mg/day) that the lower dose rat study was chosen for the hazard ranking. Most CSs were similar among those studies suitable for derivation of the Reportable Quantity.

DATA REPORT FORM

Chemical Name:	2-METHOXY ETHANOL		
CAS Number:	109-86-4		
Source:	Reference Concentration for Chronic Inhalation Exposure (RfC) from IRIS, reviewed 05/01/91		
Reference Study:	Miller et al., 1983		
Exp. Route:	Inhalation	Exp. Time:	6 hours/day
Test Species:	Rabbit	Exp. Frequency:	5 days/week
Chron. Hum. MED:	77.300 mg/day	Exp. Duration:	13 weeks
RVd:	2.70	Transf. Anim. Dose:	29.2000
RVe:	9	Dose Unit:	mg/kg-day
CS:	24	Inhal. Rate:	2.000 m^3/day
Corr. Factor:	10	Ingest. Rate:	N/A
Chronic/subchronic:	Subchronic	Ingest. Unit:	N/A
Exp. Conc. Val 1:	100.000 ppm	Absorption Coef.:	1.0
Exp. Conc. Val 2:	311.000	Species Weight:	3.800 kg
Conc. 2 Unit:	mg/m^3		

Effect: Slight to moderate decrease in testes size and weight.

Note: N/A denotes either data not applicable or data not available.

Consistency with the Reportable Quantity Methodology:

The CS for this chemical was derived according to the Reportable Quantity methodology using Inhalation Reference Concentration data.

Reason for CS Selection:

There are two suitable inhalation studies available in two species (rabbit and rat), and both have a correction factor for dose duration. Study duration times and effects are the same in both studies. The rabbit study uses a smaller dose than the rat study. The Inhalation Reference Concentration is derived from the lower dose used in the rabbit study. Both studies give almost identical CSs (3 units apart). The rabbit study is chosen because it used the smaller of the two doses to give similar effects. An RVe of 9 is assigned to testicular damage based on the definition of an RVe of 9. In that definition, reproductive dysfunction is given as a criterion for the classification. The Reference Concentration for this pollutant is 2E-02 mg/m^3.

DATA REPORT FORM

Chemical Name:	METHYL BROMIDE		
CAS Number:	74-83-9		
Source:	Data collected for development of RfC		
Reference Study:	Kato et al., 1986		
Exp. Route:	Inhalation	Exp. Time:	4 hours/day
Test Species:	Rat	Exp. Frequency:	5 days/week
Chron. Hum. MED:	52.6 mg/day	Exp. Duration:	11 weeks
RVd:	2.9	Transf. Anim. Dose:	44.00
RVe:	8	Dose Unit:	mg/kg-day
CS:	23	Inhal. Rate:	0.223 m^3/day
Corr. Factor:	10	Ingest. Rate:	N/A
Chronic/subchronic:	Subchronic	Ingest. Unit:	N/A
Exp. Conc. Val 1:	150.000 ppm	Absorption Coef.:	1.0
Exp. Conc. Val 2:	582.000	Species Weight:	0.350 kg
Conc. 2 Unit:	mg/m^3		

Effect: Small focal necrosis of heart tissue, slight suppression of body weight, fibrosis of heart tissue.

Note: N/A denotes either data not applicable or data not available.

Consistency with the Reportable Quantity Methodology:

The CS for this chemical was derived according to the Reportable Quantity methodology using Inhalation Reference Concentration data.

Reason for CS Selection:

A CS was selected for the hazard ranking from the relatively recent study by Kato et al. (1986). This study uses a slightly lower dose than the other available inhalation studies suitable for Reportable Quantities development. The selected study gives heart necrosis as the effect from treatment while the others give severe neurotoxic symptoms. Kato et al. also reports neurotoxic effects from methyl bromide but at higher doses. A correction factor for duration is used. All studies reported very severe effects which could be a function of a steep dose-response curve for this pollutant. An RVe of 8 is assigned to necrosis of heart tissue.

DATA REPORT FORM

Chemical Name:	METHYL CHLOROFORM (1,1,1-TRICHLOROETHANE)		
CAS Number:	000071-55-6		
Source:	ECAO-CIN-R210, May 1983		
Reference Study:	Quast et al., 1978		
Exp. Route:	Inhalation	Exp. Time:	6 hours/day
Test Species:	Rat	Exp. Frequency:	5 days/week
Chron. Hum. MED:	12,999.00* mg/day	Exp. Duration:	1 year
RVd:	1.00	Transf. Anim. Dose:	1,087.00*
RVe:	2	Dose Unit:	mg/kg-day
CS:	2	Inhal. Rate:	0.223 m^3/day
Corr. Factor:	N/A	Ingest. Rate:	N/A
Chronic/subchronic:	Chronic	Ingest. Unit:	N/A
Exp. Conc. Val 1:	1,750.000 ppm	Absorption Coef.:	1.0
Exp. Conc. Val 2:	9,554.000	Species Weight:	0.350 kg
Conc. 2 Unit:	mg/m^3		

Effect: Focal hepatocellular changes in females.

* These values are not from the reference document, but instead relate to the chronic human MED as calculated by the Reportable Quantity methodology; see below.

Note: N/A denotes either data not applicable or data not available.

Consistency with the Reportable Quantity Methodology:

Calculations in the reference document are not consistent with the Reportable Quantity methodology. To adjust for intermittent exposure, the authors multiply the exposure concentration of 9,554 mg/m^3 by 6/24 and 5/7 to obtain an adjusted exposure concentration of 1,705 mg/m^3. They then multiply this adjusted exposure concentration by a human breathing rate of 20 m^3/day and an absorption coefficient of 0.5 to obtain a chronic human MED of 17,060 mg/day. No correction factor is used.

MED Recalculated According to the RQ Methodology:

The adjusted exposure concentration of 1,705 mg/m^3 was multiplied by the ratio of the inhalation rate (0.223 m^3/day) to the animal weight (0.35 kg) to obtain a transformed animal dose of 1,087 mg/kg-day. The transformed animal dose was then multiplied by the ratio of the body weights to the one-

third power, and by a human body weight of 70 kg, to obtain a chronic human MED of 12,999 mg/day, corresponding to an RVd of 1. In short:

Calculated Chronic MED:	12,999 mg/day
Calculated CS:	2

Reason for CS Selection:

From the available studies, a CS was selected for the hazard ranking from a rat inhalation study suitable for Reportable Quantity development. Two appropriate inhalation studies were cited in the Reportable Quantity document. Both used massive doses, produced minimal effects, and gave identical CSs.

DATA REPORT FORM

Chemical Name:	METHYLENE DIPHENYL DIISOCYANATE		
CAS Number:	101-68-8		
Source:	Reference Dose for Chronic Inhalation (RfC) for Methylene Diphenyl Iisocyanate, from IRIS, reviewed 5/14/90		
Reference Study:	Johnson et al., 1985		
Exp. Route:	Inhalation	Exp. Time:	8 hours/day
Test Species:	Human	Exp. Frequency:	5 days/week
Chron. Hum. MED:	0.180 mg/day	Exp. Duration:	12 years
RVd:	6.60	Transf. Anim. Dose:	N/A
RVe:	7	Dose Unit:	N/A
CS:	46	Inhal. Rate:	10.000 m^3/day
Corr. Factor:	N/A	Ingest. Rate:	N/A
Chronic/subchronic:	Chronic	Ingest. Unit:	N/A
Exp. Conc. Val 1:	0.005 ppm	Absorption Coef.:	0.5
Exp. Conc. Val 2:	0.051	Species Weight:	70.000 kg
Conc. 2 Unit:	mg/m^3		

Effect: Decrease in pulmonary function.

Note: N/A denotes either data not applicable or data not available.

Consistency with the Reportable Quantity Methodology:

The CS for this chemical was derived according to the Reportable Quantity methodology using Inhalation Reference Concentration data. The chronic human MED is obtained by adjusting the exposure concentration of 0.051 mg/m^3 for 5 days/week exposure and multiplying by a breathing rate of 10 m^3/day and an absorption coefficient of 0.5.

Reason for CS Selection:

From the available studies, a CS was selected for the hazard ranking from the most appropriate study suitable for Reportable Quantity development, which was an inhalation study in humans. Two recent studies in humans had identical CSs, so the study using the lowest dose was selected. An RVe of 7 is assigned to pulmonary dysfunction. The effect of pulmonary dysfunction was cited in several other human studies; however, this study showed the lowest-effect level and did not have concurrent exposure to toluene diisocyanate.

DATA REPORT FORM

Chemical Name:	METHYL ETHYL KETONE (2-BUTANONE)		
CAS Number:	000078-93-3		
Source:	EPA/600/X-85/363, Sept 1985		
Reference Study:	LaBelle and Brieger, 1955		
Exp. Route:	Inhalation	Exp. Time:	7 hours/day
Test Species:	Rat	Exp. Frequency:	5 days/week
Chron. Hum. MED:	110.400 mg/day	Exp. Duration:	12 weeks
RVd:	2.40	Transf. Anim. Dose:	92.000
RVe:	4	Dose Unit:	mg/kg-day
CS:	10	Inhal. Rate:	0.223 m^3/day
Corr. Factor:	10	Ingest. Rate:	N/A
Chronic/subchronic:	Subchronic	Ingest. Unit:	N/A
Exp. Conc. Val 1:	235.000 ppm	Absorption Coef.:	1.0
Exp. Conc. Val 2:	693.000	Species Weight:	0.350 kg
Conc. 2 Unit:	mg/m^3		

Effect: Decreased body weight gain.

Note: N/A denotes either data not applicable or data not available.

Consistency with the Reportable Quantity Methodology:

Calculations are consistent with the Reportable Quantity methodology. A correction factor of 10 is used to estimate chronic MED from this subchronic study.

Reason for CS Selection:

From the available studies, a CS was selected for the hazard ranking from the study suitable for Reportable Quantity development that used the lowest dose. However, all studies used very large doses to produce an effect. Two studies listed fetotoxicity as an effect, but gave chronic human MEDs of 19,734 and 6,566 mg/day. All CSs were similar. The study chosen to derive the Reportable Quantity was also chosen for the hazard screening.

DATA REPORT FORM

Chemical Name:	METHYL ISOBUTYL KETONE		
CAS Number:	108-10-1		
Source:	Data collected for development of RfC		
Reference Study:	Phillips et al., 1987		
Exp. Route:	Inhalation	Exp. Time:	6 hours/day
Test Species:	Rat	Exp. Frequency:	5 days/week
Chron. Hum. MED:	5,578.000 mg/day	Exp. Duration:	14 weeks
RVd:	1.00	Transf. Anim. Dose:	466.000
RVe:	4	Dose Unit:	mg/kg-day
CS:	4	Inhal. Rate:	0.223 m^3/day
Corr. Factor:	N/A	Ingest. Rate:	N/A
Chronic/subchronic:	Chronic	Ingest. Unit:	N/A
Exp. Conc. Val 1:	1,000.000 ppm	Absorption Coef.:	1.0
Exp. Conc. Val 2:	4,100.000	Species Weight:	0.350 kg
Conc. 2 Unit:	mg/m^3		

Effect: Increased liver weight and liver weight/body weight ratio. Increased incidence and extent of hyalin droplets in kidneys in males.

Note: N/A denotes either data not applicable or data not available.

Consistency with the Reportable Quantity Methodology:

The CS for this chemical was derived according to the Reportable Quantity methodology using inhalation data collected for a Reference Concentration determination.

Reason for CS Selection:

From available studies, a CS was selected for the hazard ranking from the available rat study of longest duration suitable for Reportable Quantity development. There is no correction factor used for study duration. All studies were conducted using high doses, and effects were consistent among studies. The study selected is one of the more recent studies. An RVe of 4 is given for the increase in liver weight. The hyalin droplet increase in the kidney is thought to be a rat-specific protein found predominantly in male rats, and may not be an appropriate effect to assess toxicity in man.

DATA REPORT FORM

Chemical Name:	METHYL METHACRYLATE		
CAS Number:	000080-62-6		
Source:	EPA/600/X-85/364, Sept 1985		
Reference Study:	Hazleton Laboratories America, Inc., 1979		
Exp. Route:	Inhalation	Exp. Time:	6 hours/day
Test Species:	Rat	Exp. Frequency:	5 days/week
Chron. Hum. MED:	139.000 mg/day	Exp. Duration:	2 years
RVd:	2.30	Transf. Anim. Dose:	11.600
RVe:	2	Dose Unit:	mg/kg-day
CS:	5	Inhal. Rate:	0.223 m^3/day
Corr. Factor:	N/A	Ingest. Rate:	N/A
Chronic/subchronic:	Chronic	Ingest. Unit:	N/A
Exp. Conc. Val 1:	N/A	Absorption Coef.:	1.0
Exp. Conc. Val 2:	102.000	Species Weight:	0.350 kg
Conc. 2 Unit:	mg/m^3		

Effect: Mild rhinitis.

Note: N/A denotes either data not applicable or data not available.

Consistency with the Reportable Quantity Methodology:

Calculations are consistent with the Reportable Quantity methodology. No correction factor is used in this chronic study.

Reason for CS Selection:

From the available studies, A CS was selected for the hazard ranking from the chronic inhalation study suitable for Reportable Quantity development that used the lowest exposure concentration. Most studies used massive doses. There was generally a good dose-response relationship between the studies, and similar CSs, except for one which apparently used a correction factor for duration of study (that study was not chosen). The study chosen for the hazard ranking used the lowest exposure concentration for the longest duration of exposure. The study chosen for the Reportable Quantity derivation yielded the highest CS.

DATA REPORT FORM

Chemical Name:	METHYL TERT-BUTYL ETHER		
CAS Number:	1634-04-4		
Source:	Draft Inhalation Reference Concentration for Methyl Tert-butyl Ether, Clement Assoc., Inc. 01/10/91		
Reference Study:	Greenough et al., 1980		
Exp. Route:	Inhalation	Exp. Time:	6 hours/day
Test Species:	Rat	Exp. Frequency:	5 days/week
Chron. Hum. MED:	491.000 mg/day	Exp. Duration:	13 weeks
RVd:	1.50	Transf. Anim. Dose:	409.00
RVe:	4	Dose Unit:	mg/kg-day
CS:	6	Inhal. Rate:	0.223 m^3/day
Corr. Factor:	10	Ingest. Rate:	N/A
Chronic/subchronic:	Subchronic	Ingest. Unit:	N/A
Exp. Conc. Val 1:	1,000.000 ppm	Absorption Coef.:	1.0
Exp. Conc. Val 2:	3,599.000	Species Weight:	0.350 kg
Conc. 2 Unit:	mg/m^3		

Effect: Decreased relative lung weights.

Note: N/A denotes either data not applicable or data not available.

Consistency with the Reportable Quantity Methodology:

The CS for this chemical was derived according to the Reportable Quantity methodology using Inhalation Reference Concentration data.

Reason for CS Selection:

A CS was selected for the hazard ranking from a subchronic rat study suitable for Reportable Quantity development that used the lowest dose in the available literature. All available subchronic studies used the same study duration and were conducted at very high exposure levels. The CS from the Greenough study was consistent with those of the other studies. This study used a correction factor for duration. Available developmental studies were conducted at extremely high exposure levels. In some of those studies maternal toxicity was reported while in others that data were incomplete regarding maternal effects. An RVe of 4 is assigned to decreased relative lung weights as stated in the definition of an RVe of 4.

DATA REPORT FORM

Chemical Name:	NAPHTHALENE		
CAS Number:	000091-20-3		
Source:	EPA/600/X-86/241, Aug 1986		
Reference Study:	NTP, 1980		
Exp. Route:	Oral-gavage	Exp. Time:	24 hours/day
Test Species:	Rat	Exp. Frequency:	5 days/week
Chron. Hum. MED:	68.100 mg/day	Exp. Duration:	13 weeks
RVd:	2.80	Transf. Anim. Dose:	71.000
RVe:	4	Dose Unit:	mg/kg-day
CS:	11	Inhal. Rate:	N/A
Corr. Factor:	10	Ingest. Rate:	N/A
Chronic/subchronic:	Subchronic	Ingest. Unit:	N/A
Exp. Conc. Val 1:	N/A	Absorption Coef.:	N/A
Exp. Conc. Val 2:	100.000	Species Weight:	0.180 kg
Conc. 2 Unit:	mg/kg-day		

Effect: Dose-related decrease in body weight of females.

Note: N/A denotes either data not applicable or data not available.

Consistency with the Reportable Quantity Methodology:

Calculations are consistent with the Reportable Quantity methodology. The authors expand the daily dosage of 100 mg/kg-day for a seven day week to obtain a transformed animal dose of 71 mg/kg-day. A correction factor of 10 is used to estimate chronic exposure from this subchronic study.

Reason for CS Selection:

From the available studies, a CS was selected for the hazard ranking from the study suitable for Reportable Quantity development that used the lowest dose. Both studies presented in the RQ document as being adequate for derivation of a CS have similar CSs. The study with the higher dose was chosen for Reportable Quantity derivation because it produced the largest CS.

DATA REPORT FORM

Chemical Name:	NITROBENZENE		
CAS Number:	000098-95-3		
Source:	EPA/600/X-85/365, Sept 1985		
Reference Study:	CIIT, 1984		
Exp. Route:	Inhalation	Exp. Time:	6 hours/day
Test Species:	Rat	Exp. Frequency:	5 days/week
Chron. Hum. MED:	11.000 mg/day	Exp. Duration:	90 days
RVd:	3.90	Transf. Anim. Dose:	9.200
RVe:	6	Dose Unit:	mg/kg-day
CS:	23	Inhal. Rate:	0.223 m^3/day
Corr. Factor:	10	Ingest. Rate:	N/A
Chronic/subchronic:	Subchronic	Ingest. Unit:	N/A
Exp. Conc. Val 1:	N/A	Absorption Coef.:	1.0
Exp. Conc. Val 2:	81.000	Species Weight:	0.350 kg
Conc. 2 Unit:	mg/m^3		

Effect: Nephrosis and liver necrosis.

Note: N/A denotes either data not applicable or data not available.

Consistency with the Reportable Quantity Methodology:

Calculations are consistent with the Reportable Quantity methodology. A correction factor of 10 is used to estimate chronic MED from this subchronic study.

Reason for CS Selection:

From the available studies, a CS was selected for the hazard ranking from the rat study suitable for Reportable Quantity development that used the lowest dose. Although the CSs were consistent across all the available studies, the effects were not. The Reportable Quantity was derived from the study using the largest dose because it produced the largest CS.

DATA REPORT FORM

Chemical Name:	PHENOL		
CAS Number:	108-95-2		
Source:	EPA/600/x-87/121, Feb. 1987		
Reference Study:	Deichmann et al., 1944		
Exp. Route:	Inhalation	Exp. Time:	7 hours/day
Test Species:	Guinea pig	Exp. Frequency:	5 days/week
Chron. Hum. MED:	5.6000 mg/day	Exp. Duration:	29 days
RVd:	4.4	Transf. Anim. Dose:	4.4
RVe:	10	Dose Unit:	mg/kg-day
CS:	44	Inhal. Rate:	0.090 m^3/day
Corr. Factor:	10	Ingest. Rate:	N/A
Chronic/subchronic:	Subchronic	Ingest. Unit:	N/A
Exp. Conc. Val 1:	N/A	Absorption Coef.:	1.0
Exp. Conc. Val 2:	100.000	Species Weight:	0.430 kg
Conc. 2 Unit:	mg/m^3		

Effect: Death in 5/12 exposed guinea pigs by 29th exposure; internal and external signs of toxicity.

Note: N/A denotes either data not applicable or data not available.

Consistency with the Reportable Quantity Methodology:

The CS for this chemical was derived according to the Reportable Quantity methodology.

Reason for CS Selection:

Data used for Reference Concentration development include an inhalation human study that is inappropriate to rank this pollutant because it has concurrent formaldehyde exposure, which confounds the results. There is a Reportable Quantity document for this pollutant currently available, and the most appropriate study from that document was a 1944 inhalation study using guinea pigs. Other available inhalation studies (Russian) involving rats were consistent with the guinea pig study, indicating that this pollutant is quite toxic at relatively low doses.

DATA REPORT FORM

Chemical Name:	P-PHENYLENEDIAMINE		
CAS Number:	000106-50-3		
Source:	EPA/600/X-85/113, April 1985		
Reference Study:	NCI, 1979		
Exp. Route:	Oral-diet	Exp. Time:	24 hours/day
Test Species:	Rat	Exp. Frequency:	7 days/week
Chron. Hum. MED:	224.000 mg/day	Exp. Duration:	18 months
RVd:	2.00	Transf. Anim. Dose:	18.700
RVe:	2	Dose Unit:	mg/kg-day
CS:	4	Inhal. Rate:	N/A
Corr. Factor:	N/A	Ingest. Rate:	N/A
Chronic/subchronic:	Chronic	Ingest. Unit:	N/A
Exp. Conc. Val 1:	625.000 ppm	Absorption Coef.:	1.0
Exp. Conc. Val 2:	N/A	Species Weight:	0.350 kg
Conc. 2 Unit:	N/A		

Effect: Decreased body weight gain.

Note: N/A denotes either data not applicable or data not available.

Consistency with the Reportable Quantity Methodology:

Calculations are consistent with the Reportable Quantity methodology. The ingestion rate is not given in the document; however, the concentration can be converted to the dose if the rat is assumed to consume 3 percent of its body weight in food per day, although this is less than the standard 5 percent value used in most studies. No correction factor is used in this chronic study.

Reason for CS Selection:

From the available studies, a CS was selected for the hazard ranking from the study suitable for Reportable Quantity development that used the lowest dose. The range of doses was limited. Effects (changes in body weight) were consistent among studies. The study chosen to derive the Reportable Quantity was also chosen for the hazard ranking.

DATA REPORT FORM

Chemical Name:	SELENIUM AND COMPOUNDS		
CAS Number:	007782-49-2		
Source:	ECAO-CIN-GO58, September 1989		
Reference Study:	Yang et al., 1983		
Exp. Route:	Oral-diet	Exp. Time:	24 hours/day
Test Species:	Human	Exp. Frequency:	7 days/week
Chron. Hum. MED:	3.210 mg/day	Exp. Duration:	Chronic
RVd:	4.70	Transf. Anim. Dose:	N/A
RVe:	9	Dose Unit:	N/A
CS:	42	Inhal. Rate:	N/A
Corr. Factor:	N/A	Ingest. Rate:	N/A
Chronic/subchronic:	Chronic	Ingest. Unit:	N/A
Exp. Conc. Val 1:	N/A	Absorption Coef.:	1.0
Exp. Conc. Val 2:	N/A	Species Weight:	70.000 kg
Conc. 2 Unit:	N/A		

Effect: Severe nervous symptoms, convulsions, paralysis, nail brittleness, dermatitis.

Note: N/A denotes either data not applicable or data not available.

Consistency with the Reportable Quantity Methodology:

Calculations are consistent with the Reportable Quantity methodology. This epidemiology study notes that selenosis (severe nervous symptoms, convulsions, and paralysis) was observed in persons consuming diets that provided doses of 3.2-6.7 mg selenium/day, but did not specify the duration of exposure.

Reason for CS Selection:

From the available studies, a CS was selected for the hazard ranking from the study suitable for Reportable Quantity development which involved exposure to humans. This was also the study chosen to derive the Reportable Quantity for this compound. This CS was consistent with those from rat and mouse studies that were suitable for CS derivation. This CS will be used to rank selenium compounds including sodium selenite, sodium selenate, selenium dioxide, and selenious acid.

DATA REPORT FORM

Chemical Name:	TOLUENE		
CAS Number:	000108-88-3		
Source:	ECAO-CIN-R206, May 1983		
Reference Study:	CIIT, 1980		
Exp. Route:	Inhalation	Exp. Time:	8 hours/day
Test Species:	Human	Exp. Frequency:	5 days/week
Chron. Hum. MED:	4,036.000 mg/day	Exp. Duration:	2 years
RVd:	1.00	Transf. Anim. Dose:	57.600
RVe:	7	Dose Unit:	mg/kg-day
CS:	7	Inhal. Rate:	10.000 m^3/day
Corr. Factor:	N/A	Ingest. Rate:	N/A
Chronic/subchronic:	Chronic	Ingest. Unit:	N/A
Exp. Conc. Val 1:	300.000 ppm	Absorption Coef.:	0.5
Exp. Conc. Val 2:	1,130.000	Species Weight:	70.000 kg
Conc. 2 Unit:	mg/m^3		

Effect: Reversible CNS dysfunction.

Note: N/A denotes either data not applicable or data not available.

Consistency with the Reportable Quantity Methodology:

Calculations are consistent with the Reportable Quantity methodology. The origin of the data and the calculation of the human MED are described in the document as follows: "The CIIT (1980) study is a comprehensive, chronic 24-month inhalation study with rats. Although it is the only chronic study in laboratory animals, there are 'deficiencies...which might becloud interpretation' (SRC, 1981). Other intermittent chronic and subchronic inhalation studies on humans are well documented and supported by acute animal experimental studies, but are not considered suitable for derivation of a Reportable Quantity if taken individually. In combination, however, they constitute a considerable body of human experience and provide a relatively consistent pattern of dose-response relationships. Based on all the available data and the effect level of 300 ppm defined in the chronic inhalation study with rats (CIIT, 1980), 300 ppm can be regarded as the unequivocal effect level in humans. Since this effect level is applicable to intermittent occupational exposures that are assumed to occur 5 days/week, a human MED can be calculated by expanding the exposure from 5 to 7 days/week and assuming that a human breathes 10 m^3 of contaminated air per workday with an absorption efficiency of 50 percent for toluene (SRC, 1981). This calculation gives a MED of 4036 mg/d for a 70 kg man".

Reason for CS Selection:

A CS was selected for the hazard ranking from the recommendation in the Reportable Quantity document. This CS was not based on a particular study, but was derived from a large body of human and animal data.

DATA REPORT FORM

Chemical Name:	1,2,4-TRICHLOROBENZENE		
CAS Number:	000120-82-1		
Source:	ECAO-CIN-R209, May 1983		
Reference Study:	Watanabe et al., 1978		
Exp. Route:	Inhalation	Exp. Time:	6 hours/day
Test Species:	Rat	Exp. Frequency:	5 days/week
Chron. Hum. MED:	10.100* mg/day	Exp. Duration:	90 days
RVd:	4.00*	Transf. Anim. Dose:	8.400*
RVe:	1	Dose Unit:	mg/kg-day
CS:	4*	Inhal. Rate:	0.223 m^3/day
Corr. Factor:	10*	Ingest. Rate:	N/A
Chronic/subchronic:	Subchronic	Ingest. Unit:	N/A
Exp. Conc. Val 1:	10.000 ppm	Absorption Coef.:	1.0
Exp. Conc. Val 2:	74.000	Species Weight:	0.350 kg
Conc. 2 Unit:	mg/m^3		

Effect: Increased uroporphryn.

* These values are not from the reference document, but instead relate to the chronic human MED as calculated by the Reportable Quantity methodology; see below.

Note: N/A denotes either data not applicable or data not available.

Consistency with the Reportable Quantity Methodology:

Calculations in the reference study are not consistent with the Reportable Quantity methodology. The authors convert the exposure concentration of 74 mg/m^3 to a human MED of 13.2 mg/day by expanding the exposure concentration from 6 to 24 hours/day, 5 to 7 days/week, and multiplying by a human inhalation rate of 20 m^3/day and an absorption coefficient of 0.5. A correction factor of 10 is used to estimate the chronic MED from this subchronic study.

MED Recalculated According to the RQ Methodology:

Using standard default values (i.e., an inhalation rate of 0.223 m^3/day for a 0.35 kg rat and an absorption coefficient of 1.0), a transformed animal dose is calculated to be 8.4 mg/kg-day and a subchronic MED of 100.5 mg/day. Dividing by a correction factor of 10 gives a chronic human MED of 10.1 mg/day, corresponding to an RVd of 4 and a CS of 4. In short:

Calculated Chronic MED:	10.1 mg/day
Calculated CS:	4

Reason for CS Selection:

From the available studies, a CS was selected for the hazard ranking from the inhalation study suitable for Reportable Quantity development which used the lowest exposure concentration. The recalculated CS rather than the CS in the document was used to maintain consistency between studies. The document stated that limited data were available. The study chosen to derive the Reportable Quantity had a higher dose and was selected because it produced a higher CS.

DATA REPORT FORM

Chemical Name:	TRIETHYLAMINE		
CAS Number:	121-44-8		
Source:	Reference Concentration for Chronic Inhalation Exposure (RfC) from IRIS, reviewed 04/01/91		
Reference Study:	Brieger and Hodes, 1951		
Exp. Route:	Inhalation	Exp. Time:	7 hours/day
Test Species:	Rabbit	Exp. Frequency:	5 days/week
Chron. Hum. MED:	58.00 mg/day	Exp. Duration:	6 weeks
RVd:	2.80	Transf. Anim. Dose:	22.00
RVe:	5	Dose Unit:	mg/kg-day
CS:	14	Inhal. Rate:	2.000 m^3/day
Corr. Factor:	10	Ingest. Rate:	N/A
Chronic/subchronic:	Subchronic	Ingest. Unit:	N/A
Exp. Conc. Val 1:	48.000 ppm	Absorption Coef.:	1.0
Exp. Conc. Val 2:	199.000	Species Weight:	3.800 kg
Conc. 2 Unit:	mg/m^3		

Effect: Corneal edema and punctate erosions of corneal epithelium, focal lymphocytic infiltration, and slight thickening of lung vascular walls.

Note: N/A denotes either data not applicable or data not available.

Consistency with the Reportable Quantity Methodology:

The CS for this chemical was calculated according to the Reportable Quantity methodology using Inhalation Reference Concentration data.

Reason for CS Selection:

From the available studies, a CS was selected for the hazard ranking from a supporting study for Reference Concentration development, which reports adverse effects. The study chosen for Reference Concentration determination produced no adverse effects precluding its use for Reportable Quantity development. The study chosen for the hazard ranking does not report whether changes are reversible. The RVe of 5 is assigned to the reported effects, and inflammatory changes are assumed to be reversible as they are in humans exposed to high concentrations at short durations. The Inhalation Reference Concentration for this compound is 7E-03 mg/m^3.

DATA REPORT FORM

Chemical Name:	XYLENES (mixed)		
CAS Number:	001330-20-7		
Source:	EPA/600/X-86/216, Aug 1986		
Reference Study:	Ungvary et al., 1980		
Exp. Route:	Inhalation	Exp. Time:	24 hours/day
Test Species:	Rat	Exp. Frequency:	7 days/week
Chron. Hum. MED:	1,120.000 mg/day	Exp. Duration:	7 gestational days
RVd:	1.00	Transf. Anim. Dose:	96.000
RVe:	8	Dose Unit:	mg/kg-day
CS:	8	Inhal. Rate:	0.223 m^3/day
Corr. Factor:	N/A	Ingest. Rate:	N/A
Chronic/subchronic:	Developmental	Ingest. Unit:	N/A
Exp. Conc. Val 1:	N/A	Absorption Coef.:	1.0
Exp. Conc. Val 2:	150.000	Species Weight:	0.350 kg
Conc. 2 Unit:	mg/m^3		

Effect: Delayed skeletal development.

Note: N/A denotes either data not applicable or data not available.

Consistency with the Reportable Quantity Methodology:

Calculations are consistent with the Reportable Quantity methodology. No correction factor is used to derive the chronic MED from the developmental (gestational) study.
[Note: The CS for mixed xylenes is based on toxicity data for the para-isomer.]

Reason for CS Selection:

From the available studies, a CS was selected for the hazard ranking from an inhalation study in rats. There were only two inhalation studies suitable for Reportable Quantity derivation. They produced similar CSs (8 vs. 9). The exposure concentrations were approximately the same. The Reportable Quantity was derived from an oral study. However, the CS for the oral study was similar to that of the two inhalation studies. No distinction was made in the toxicity between the different isomers for CS derivation in the reference document. Therefore, the CS chosen for the hazard ranking for mixed xylenes is appropriate for all isomeric forms (o-, m-, and p-).

APPENDIX C

Supporting data for ranking of pollutants within chemical groupings.

Section I: Overveiw of Ranking of Chemical Groups:

For the purposes of the Section 112(g) hazard ranking, the EPA is using the recommendations provided by the EPA's Human Health Assessment Group (HHAG) at OHEA for determining which pollutants within the chemical groups are to be ranked as "non-threshold" pollutants (4). Similarly, when pollutants within chemical groups, have available composite scores and are not ranked as "carcinogens" (have a weight of evidence of A, B or C), they are inserted into the ranking as either "high-concern" or "threshold" pollutants. Generally, pollutants belonging to chemical groups listed in section 112(b) of the Clean Air Act are ranked individually. When appropriate, pollutants with similar toxicological profiles are ranked as one homogeneous group.

The same methodology used to rank the pollutants listed in 112(b), in alphabetical order including CAS #, is also used to rank pollutants belonging to the chemical groups. Accordingly, the carcinogenic potential (ED10 and Weight of evidence), chronic toxicity (composite score from CERCLA), or acute toxicity (Levels of Concerns from CERCLA) of each pollutant are employed for ranking pollutants. Only pollutants with adequate data as mentioned above are included in the ranking.

Chemical groupings with members ranked as "non-threshold" pollutants (known, probable, or possible human carcinogens):

1. Antimony compounds
2. Arsenic compounds
3. Beryllium compounds

4. Cadmium compounds
5. Chromium compounds
6. Coke oven emissions
7. Lead compounds
8. Nickel compounds
9. Polycyclic organic matter
10. Selenium compounds

Chemical groupings with members ranked as "high-concern" pollutants:

1. Arsenic compounds
2. Antimony compounds
3. Cadmium Compounds
4. Chromium Compounds
5. Cobalt compounds
6. Cyanide compounds
7. Glycol ethers
8. Lead compounds
9. Manganese compounds
10. Mercury compounds
11. Nickel compounds
12. Selenium compounds

Chemical groupings with members ranked as "threshold" pollutants:

1. Glycol ethers

Chemical groupings with members considered "Unrankable":

1. Antimony compounds
2. Chromium compounds (trivalent)
3. Cyanide compounds
4. Fine mineral fiber compounds
5. Glycol ethers
6. Mercury compounds
7. Polycyclic organic matter
8. Radionuclides

Section II: Ranking of Individual Groups

Antimony Compounds

In a Health Effects Assessment document for antimony and compounds (EPA/600/8-88/018, June, 1987) the authors stated that "antimony is most appropriately classified in group B, possible human carcinogen based on sufficient animal data". They go on to state that the B classification only applies to inhalation and that orally administered antimony receives a D classification for carcinogenicity. The antimony compound cited in the study was antimony trioxide. Currently there are no specific antimony compounds considered to be carcinogens on IRIS, IARC or under CERCLA. EPA's Human Health and Assessment group recommends that, for the purposes of the hazard ranking guidance of section 112(g), Antimony trioxide is assigned a weight of evidence of B without a concurrent estimation of potency. The status of this group of compounds continues to be under review by the EPA.

Chronic toxicity data were evaluated and resulted in a composite score for three antimony compounds (antimony trioxide, antimony potassium tartrate, and antimony trisulfide). For the purposes of ranking the pollutants listed in 112(b), antimony trioxide will is defined as a "non-threshold" pollutant with a weight of evidence of B but no potency estimate. Antimony potassium tartrate, antimony pentafluoride, and antimony trisulfide will be inserted into the "high-concern threshold" pollutant ranking based on their respective composite scores for chronic toxicity or Levels of Concern for acute toxicity.

"High-concern" pollutants

Pollutant	CAS #	Level of Concern	Composite Score
Antimony potassium tartrate	28300745	-	38
Antimony trisulfide	1345046	-	46
Antimony pentafluoride	7783702	2.70 mg/cu m	-

"Non-threshold" Pollutants

Pollutant	CAS#	WOE	Inhalation unit risk	1/ED10 per (mg/kg)/d
Antimony trioxide	1309644	B	_	_

Arsenic Compounds

Under CERCLA (U.S. EPA, 1988), all inorganic arsenic compounds are of concern for carcinogenicity in humans via inhalation and are given a weight of evidence classification of A. The exact species of inorganic arsenic which causes cancer in humans is not known; however it is assumed arsenic is chemically convertible among the different chemical species in vivo . The potency factor is assumed to be the same for the inorganic Arsenic compounds as for "Arsenic" (U.S. EPA, 1988). The inhalation unit risk assigned the inorganic Arsenic compounds is 4.3 x 10-3 /micrograms/cubic meter (1/ED10 = 140).

Organic arsenic compounds such as arsine "are considered to be chemically different from the inorganic arsenic compounds such that they are assessed for carcinogenicity separately from the inorganic arsenic compounds"(U.S. EPA, 1988). Currently the only organic arsenic compound which is ranked is arsine. The following pollutants are examples of inorganic arsenic compounds which are ranked as "non-threshold" pollutants:

"Non-threshold" arsenic compounds:

Pollutant	CAS #	WOE	1/ED10 per (mg/kg)/d
Arsenic	7440382	A	140
Arsenic acid	1327522	"	"
Arsenic disulfide	1303328	"	"
Arsenic pentoxide	1303282	"	"
Arsenic trichloride	7784341	"	"
Arsenic trioxide	1327533	"	"
Arsenic trisulfide	130339	"	"
Calcium arsenate	7778441	"	"
Calcium arsenite	52740166	"	"
Cupric acetoarsenite	12002038	"	"

Lead arsenate	7784409	"	"
Potassium arsenate	7784410	"	"
Potassium arsenite	10124502	"	"
Sodium arsenate	7631892	"	"
Sodium arsenite	7784465	"	"

"High-concern" arsenic compounds:

Pollutant	CAS #	Level of concern	Composite score
Arsenic pentoxide	1303282	8.00 mg/cu m	-
Arsenous oxide	1327533	1.40 mg/cu m	-
Arsine	7784421	1.90 mg/cu m	-

Beryllium Compounds

Under CERCLA (U.S. EPA, 1988), all soluble forms of beryllium compounds that have been tested have been shown to be carcinogenic. It is therefore highly likely that all forms of beryllium are carcinogenic in animals. The potency factor for beryllium compounds with the exception of beryllium salts is based on human occupational exposure to less soluble forms of beryllium mostly beryllium oxides. The metal/oxide is assigned a weight of evidence classification of B and a inhalation unit risk determination of 2.4 x 10-3 /micrograms/cubic meter (1/ED10 = 80). Soluble beryllium salts are assigned a potency factor, expressed in terms of an

1/ED10 of 18000. The following compounds are examples of beryllium compounds and their ranking information:

"Non-threshold" beryllium compounds:

Pollutant	CAS #	WOE	1/ED10 per (mg/kg)/d
Beryllium	7440417	B	80
Beryllium oxide	1304569	B	"
Beryllium fluoride	7787497	B	14000
Beryllium chloride	7787475	"	"
Beryllium nitrate	13597994	"	"
Beryllium phosphate	3598900	"	"
Beryl ore	1302529	"	"
Zinc beryllium silicate	39413473	"	"
Beryllium sulfate	13510491	"	"

Cadmium Compounds

Under CERCLA (U.S. EPA, 1988), cadmium compounds are considered to be probable human carcinogens with a weight of evidence classification of B and potency estimate of 1.8 x 10-3 /cubic/meter inhalation unit risk (1/ED10 - 58). The potency

estimates are based on epidemiology data for cadmium workers exposed to cadmium oxide and/or cadmium fume. Human data are lacking for cadmium salts. However, soluble cadmium compounds produce a carcinogenic response in animals. cadmium chloride is especially potent in animal assays. Therefore, the potency for cadmium compounds, as a group, is assumed to be represented by the human data. The following compounds are examples of soluble cadmium compounds and are inserted into the "non-threshold" pollutant ranking accordingly:

"Non-threshold" cadmium compounds:

Pollutant	CAS #	WOE	Inhalation unit risk	1/ED10 per (mg/kg)/d
Cadmium	7740439	B	1.8e-3	58
Cadmium chloride	10108642	"	"	"
Cadmium acetate	543908	"	"	"
Cadmium bromide	7709426	"	"	"
Cadmium oxide/ cadmium fume	1306190	"	"	"

Cadmium oxide is also ranked as a "high-concern" pollutant by virtue of a Level of Concern of 4 mg/cu m.

Chromium Compounds

The hazard of chromium (both trivalent and hexavalent) is supported by epidemiologic evidence of chromate workers exposed to both hexavalent and trivalent chromium compounds. The Health Assessment Document on chromium (EPA 1984) identifies hexavalent chromium as a known human carcinogen (Group A) based on human data and the evidence of carcinogenicity in rats following subcutaneous injection or intrabrachial, intrapleural, intramuscular, or intratracheal implantation. Trivalent chromium has not shown carcinogenic potential in animals, with testing being inconclusive for assessment of cancer at this time. Trivalent chromium, however, exhibits genotoxic potential. In addition, trivalent chromium can oxidize to hexavalent chromium under certain conditions (Bartlett, 1990; Environmental Health Perspectives, Vol. 32). It is on this basis that the EPA believes it is appropriate to rank hexavalent chromium as a known human carcinogen and to use the data for chromate workers as a basis for its potency estimate of 390 as the 1/ED10. However, for the purposes of Section 112(g), trivalent chromium compounds are unranked and are awaiting a determination by the Agency as to a weight of evidence determination and potency estimate (with the exception of chromic chloride which is ranked as a high-concern pollutant by virtue of a Level of Concern of 0.0500 mg/cu m).

Chromium metal is considered to be biologically inert and has not been reported to produce toxic effects or other harmful effects in man. Examples of hexavalent chromium compounds are listed below and are ranked as non-threshold pollutants.

"Non-threshold" chromium compounds:

Pollutant	CAS #	WOE	1/ED10 per (mg/kg)/d
Ammonium bichromate	7789095	A	390
Ammonium chromate	7788989	"	"
Calcium chromate	13765190	"	"
Chromic acid	10025737	"	"
Lithium chromate	14307358	"	"
Potassium bichromate	7778509	"	"
Potassium chromate	7789006	"	"
Sodium bichromate	10588019	"	"
Sodium chromate	7775113	"	"
Strontium chromate	7789062	"	"

Cobalt Compounds

There are no adequate data available to rank cobalt compounds as carcinogens (U.S. EPA, 1988). The following cobalt compounds are ranked by chronic and acute toxicity and inserted appropriately into the "high-concern" pollutant ranking.

"High-concern" cobalt compounds:

Pollutant	CAS #	Level of Concern	Composite Score
Cobalt metal and compounds	7440484	-	46
Cobalt carbonyl	10210681	0.270 mg/cu m	-
Fluomine	62207765	3.00 mg/cu m	35

Coke Oven Emissions

For the purposes of 112(g) coke ovens emissions are treated as one entity for which potency and weight of evidence determinations are derived (U.S. EPA, 1988). Coke oven emissions are classified as known human carcinogens and with a 1/ED10 of 1.5 based on human epidemiologic data.

Cyanide Compounds

Currently, there are no cyanide compounds with adequate data available to rank as carcinogens (U.S. EPA, 1988). The following cyanide compounds are ranked by acute toxicity and inserted appropriately into the "high-concern" pollutant ranking:

"High-concern" cyanide compounds

Pollutant	CAS #	Level of Concern	Composite Score
Potassium cyanide	151508	5.00 mg/cu m	-
Sodium cyanide	143339	5.00 mg/cu m	-

Glycol Ethers

Currently there is inadequate evidence to rank any of the glycol ethers as carcinogens (U.S. EPA, 1988). Pollutants in this chemical grouping will be ranked by composite scores for chronic toxicity and placed appropriately in either the "threshold" or "high-concern" pollutant category. Currently there are only three pollutants with enough information to rank and they are listed below:

"Threshold" glycol ethers"

Pollutant	CAS #	Level of Concern	Composite Score
2-Ethoxy ethanol	110805	-	15

Ethylene glycol monomethyl ether	111762	-	11

"High-concern" glycol ethers:

Pollutant	CAS #	Level of Concern	Composite Score
2-Methoxy ethanol	108864	-	24

Lead Compounds

The basis for the Agency's determination that lead compounds are potential carcinogens is listed on IRIS and has undergone review by EPA's Science Advisory Board. This chemical group may be ranked as a "non-threshold" pollutant on the basis of a weight of evidence classification of B with no potency estimate (U.S. EPA, 1988). Documents within the Agency have suggested that at current exposure levels neurobehavioral effects are being elicited and are therefore of special concern. Consequently, consideration of non-cancer effects may also place them on the "high-concern" pollutant list (U.S. EPA 1989). Furthermore some organolead compounds are categorized by their acute effects and are also listed in the "high-concern" pollutant group. Because inorganic lead compounds may not have a safety threshold for exposure for either carcinogenic or non-carcinogenic effects, this group of compounds will be placed on the "high-concern" list for non-carcinogenic

effects and designated as also being a carcinogen. Examples of inorganic lead compounds are listed below as well as specific organolead compounds ranked by their acute effects and categorized as "high-concern" pollutants.

"High-concern" lead compounds (chronic effects):

Pollutant	CAS #	WOE	1/ED10 per (mg/kg)/d
Lead	7439921	B	-
Lead nitrate	10099748	"	"
Lead arsenate	7645252	"	"
Lead chloride	7758954	"	"
Lead fluoride	7783462	"	"
Lead fluoborate	13814965	"	"
Lead iodide	10101630	"	"
Lead phosphate	7446277	"	"
Lead sulfate	7446142	"	"
Lead sulfide	1314870	"	"
Lead thiocyanate	592870	"	"

"High-concern" lead compounds (acute effects):

Pollutant	CAS #	Level of Concern	Composite Score
Tetraethyllead	78002	4.00 mg/cu m	-
Tetramethyllead	75741	4.00 mg/cu m	-

Manganese Compounds

Based on currently available evidence (U.S. EPA, 1988), no manganese compounds are considered to be carcinogenic. There is chronic toxicity information on manganese compounds based on their metal content. Therefore manganese compounds are inserted into the "high-concern" pollutant ranking category as a group based on severe effects from chronic exposures identified by an RfC. Methylcyclopentadienyl manganese which is ranked by virtue of it's acute toxicity as a "high-concern" pollutant.

"High-concern" manganese compounds:

Pollutant	CAS #	Level of Concern	Composite Score
Manganese and compounds	7439965	-	41
Methylcyclopenta-dienyl manganese	12108133	0.600 mg/cu m	-

Mercury Compounds

Based on currently available evidence, there are no mercury compounds which are considered to be carcinogenic (U.S. EPA, 1988). There is information on the chronic and acute toxicity on a limited number of compounds. Consequently, these compounds are inserted into the "high-concern" pollutant ranking by virtue of their acute and chronic toxicity. The pollutants to be ranked are given below:

"High-concern" mercury compounds:

Pollutant	CAS #	Level of Concern	Composite Score
Mercuric chloride	748794	-	40
Mercuric nitrate	10045940	-	42
Mercury, (acetato-o) phenyl	62384	-	37

Fine Mineral Fibers

Under section 112(b) there is a footnote that defines mineral fibers to "include mineral fiber emissions from facilities manufacturing or processing glass, rock, or slag fibers (or other mineral derived fibers) of average diameter 1 micrometer or less". Currently there are seven members of the chemical grouping (mineral fibers) that are considered to have carcinogenic potential. They are erionite which is a known human carcinogen (IARC group 1), silica (IARC group 2A), talc (containing asbestiform fibers), which

is a known human carcinogen, (IARC group 1), glass wool (IARC 2B), rock wool (IARC 2B), slag wool (IARC 2B), and ceramic fibers (IARC 2 B). All of these compounds do not have a comparable potency estimate as no direct relationship exists between air concentration and mass; the relationship depends on the type of environmental sample, the type of mineral fiber in the air, and the size and shape of the fibers. Consequently, all members of this grouping as well as Asbestos (listed specifically) are considered "not practicable" to rank.

Nickel Compounds

Nickel compounds are considered to be carcinogenic by varying degrees under CERCLA (U.S. EPA, 1988). The latest Health Assessment Document which refers to Nickel, states that the nickel ion (+2) could be the ultimate carcinogenic form of nickel. Although this is not yet proven, nickel salts show some carcinogenic activity (testing is inconclusive for assessment of cancer potency at this time). The EPA considers it prudent to assume nickel ion is the ultimate carcinogenic form of covalent nickel and nickel salts. The EPA has previously determined that nickel refinery dust and nickel sub-sulfide are to be classified as Group A carcinogens while nickel carbonyl is classified as a Group B (probable) carcinogen. The potency estimate for all three is given below. No ED10 or unit risk is available for these nickel compounds. Nickel Salts and the metal also show some carcinogenic activity and are classified under IARC's (1990) most recent overall evaluation for nickel as a class to be Group I carcinogensic to

humans. Listed below are examples of nickel salts and the compounds mentioned above. Nickel carbonyl is also an acutely toxic pollutant and is inserted into the ranking as a"high-concern" pollutant. The rest of the nickel compounds cited above are inserted into the "non-threshold" ranking:

"Non-threshold" nickel compounds:

Pollutant	CAS #	WOE	1/ED10 per (mg/kg)/d
Nickel refinery dust	-	A	8
Nickel subsulfide	12035722	A	16
Nickel	7440020	IARC-Group I	-
Nickel ammonium sulfate	15699180	"	"
Nickel chloride	77188549	"	"
Nickel cyanide	557197	"	"
Nickel hydroxide	12854487	"	"
Nickel nitrate	14216752	"	"
Nickel sulfate	7786814	"	"

"High-concern" nickel compounds:

Pollutant	CAS #	WOE	1/ED10	Level of Concern
Nickel carbonyl	13463393	B	-	0.350 mg/cu m

Polycyclic Organic Matter

Currently EPA considers a subset of this chemical class to be rankable (U.S. EPA, 1988). The following compounds are inserted in the hazard ranking as "non-threshold" pollutants. Other members of this chemical group are considered to be "not practicable" to rank unless listed specifically on the 112(b) list.

"Non-threshold" polycyclic organic matter:

Pollutant	CAS #	WOE	1/ED10 per (mg/kg)d
Benz(a)anthracene	56553	B	-
Benzo(b)fluoranthene	205992	"	"
7,12-Dimethylbenz(a)-anthracene	57976	"	"
Benz(c)acridine	225514	"	"
Chrysene	218019	"	"

Dibenz(ah)anthracene	53703	"	"
1,2:7,8-Dibenzopyrene	189559	"	"
Indeno(1,2,3-cd)pyrene	193395	"	"
Benzo(a)pyrene	50328	B	54

Radionuclides

For the purposes of 112(g), it is not practicable to rank the hazard of radionuclides, either individually or as classes, since their carcinogenic potentials are expressed in either units of activity or emitted energy (pCuries, pCi, or Working-Level-Months, WLM), or in absorbed dose (millirad, mrad). Equal masses of different radionuclides will not produce equally adverse effects, thus limiting any comparison of hazard with chemicals characterized in units of mass. The dose of radiation to cells in the target tissue depends on the activity, decay particle and its energy, breathing patterns, and on biological characteristics of the target tissue. Thus, there is no way to adequately compare the carcinogenic potential of radionuclides and other carcinogens. Therefore this chemical grouping is considered to be "not practicable" to rank.

Selenium Compounds

The only selenium compound with adequate evidence to be considered a carcinogen is selenium sulfide, -mono, and -di (U.S. EPA 1988). Accordingly, selenium sulfide is appropriately ranked among the "non-threshold" pollutants. "High-concern" selenium compounds include selenium metal and compounds ranked together by chronic toxicity and sodium selenite, sodium selenate, and hydrogen selenide which are ranked by virtue of their acute toxicity.

"Non-threshold" selenium compounds:

Pollutant	CAS #	WOE	1/ED10 per (mg/kg)d
Selenium sulfide	7446346	B	0.93
Selenium disulfide	7488564	B	0.93

"High-concern" selenium compounds:

Pollutant	CAS #	Level of Concern	Composite Score
Selenium and compounds	7782492	-	42
Sodium selenate	13410010	2.30 mg/cu m	-
Sodium selenite	10102188	1.60 mg/cu m	-
Hydrogen selenide	7783075	0.660 mg/cu m	-

APPENDIX D

Examples of offsets which satisfy the conditions for the determination of a "more hazardous" decrease in emissions for the proposed offsetting guidance.

Section I: Offsets Between "Non-threshold" Pollutants

Given the following:

CAS #	Pollutant	Potency (1/ED10)	Weight of evidence
118741	Hexachlorobenzene	13	B
75558	1,2-Propylenimine	150	B
91941	3,3-Dichlorobenzidene	7.5	B
75354	Vinylidene chloride	1.2	C
95534	o-Toluidine	0.093	B
75014	Vinyl chloride	1.6	A
79469	2-Nitropropane	-	B

Summary tables of offsets which fulfill the requirements of a "more hazardous emissions" decrease under the EPA's proposed approach:

1. Increased emissions of 0.5 tns/yr hexachlorobenzene:

Offsetting Pollutant	tns/yr needed as offset under EPA's proposed approach
hexachlorobenzene	0.625 tns/yr
1,2-propylenimine	0.5 tns/yr
3,3-dichlorobenzidene	0.625 tns/yr
vinylidene chloride	-
o-toluidine	-
vinyl chloride	-
2-nitropropane	-

2. Increased emissions of 0.5 tns/yr 1,2-propylenimine:

Offsetting Pollutant	tns/yr needed as offset under EPA's proposed approach
hexachlorobenzene	-
1,2-propylenimine	0.625 tns/yr
3,3-dichlorobenzidene	-
vinylidene chloride	-
o-toluidine	-
vinyl chloride	-
2-nitropropane	-

3. Increased emissions of 0.5 tns/yr 3,3-dichlorobenzidene:

Offsetting Pollutant	tns/yr needed as offset under EPA's proposed approach
hexachlorobenzene	0.625 tns/yr
1,2-propylenimine	0.5 tns/yr
3,3-dichlorobenzidene	0.625 tns/yr
vinylidene chloride	-
o-toluidine	-
vinyl chloride	-
2-nitropropane	-

4. Increased emissions of 0.5 tns/yr vinylidene chloride:

Offsetting Pollutant	tns/yr needed as offset under EPA's proposed approach
hexachlorobenzene	0.5 tns/yr
1,2-propylenimine	0.5 tns/yr
3,3-dichlorobenzidene	0.5 tns/yr
vinylidene chloride	0.625 tns/yr
o-toluidine	-
vinyl chloride	-
2-nitropropane	-

5. Increased emissions of 0.5 tns/yr 0-toluidine:

Offsetting Pollutant	tns/yr needed as offset under EPA's proposed approach
hexachlorobenzene	0.5 tns/yr
1,2-propylenimine	0.5 tns/yr
3,3-dichlorobenzidene	0.5 tns/yr
vinylidene chloride	-
o-toluidine	0.625 tns/yr
vinyl chloride	0.5 tns/yr
2-nitropropane	-

6. Increased emissions of 0.5 tns/yr vinyl chloride:

Offsetting Pollutant	tns/yr needed as offset under EPA's proposed approach
hexachlorobenzene	0.5 tns/yr
1,2-propylenimine	0.5 tns/yr
3,3-dichlorobenzidene	0.5 tns/yr
vinylidene chloride	-
o-toluidine	-
vinyl chloride	0.625 tns/yr
2-nitropropane	-

7. increased emissions of 0.5 tns/yr 2-nitropropane:

- no allowable offsets of the other pollutants under any approach. May offset 0.625 tns/yr of same pollutant.

Section II: Offsets Between "Threshold" Pollutants.

Given the following:

CAS #	Pollutant	Composite Score
156627	Calcium cyanamide	16
105602	Caprolactam	9
1330207	Xylene	8
108883	Toluene	7
75003	Ethyl chloride	4

Summary tables of offsets which fulfill the requirements of a "more hazardous emissions" decrease under the EPA's proposed approach.

1. Increased emissions of 0.5 tns/yr calcium cyanamide:

Offsetting Pollutant	tns/yr needed as offset under EPA's proposed approach
Calcium cyanamide	0.625 tns/yr
Caprolactam	-
Xylenes (mixture and isomers)	-
Toluene	-
Ethyl chloride	-

2. Increased emissions of 0.5 tns/yr caprolactam:

Offsetting Pollutant	tns/yr needed as offset under EPA's proposed approach
Calcium cyanamide	0.5 tns/yr
Caprolactam	0.625 tns/yr
Xylenes (mixture and isomers)	0.625 tns/yr
Toluene	0.625 tns/yr
Ethyl chloride	-

3. Increased emissions of 0.5 tns/yr xylene (mixture and isomers):

Offsetting Pollutant	tns/yr needed as offset under EPA's proposed approach
Calcium cyanamide	0.5 tns/yr
Caprolactam	0.625 tns/yr
Xylenes (mixture and isomers)	0.625 tns/yr
Toluene	0.625 tns/yr
Ethyl chloride	-

4. Increased emissions of 0.5 tns/yr toluene:

Offsetting Pollutant	tns/yr needed as offset under EPA's proposed approach
Calcium cyanamide	0.5 tns/yr
Caprolactam	0.625 tns/yr
Xylenes (mixture and isomers)	0.625 tns/yr
Toluene	0.625 tns/yr
Ethyl chloride	0.625 tns/yr

5. Increased emissions of 0.5 tns/yr ethyl chloride:

Offsetting Pollutant	tns/yr needed as offset under EPA's proposed approach
Calcium cyanamide	0.5 tns/yr
Caprolactam	0.5 tns/yr
Xylenes (mixture and isomers)	0.5 tns/yr
Toluene	0.625 tns/yr
Ethyl chloride	0.625 tns/yr

Section III: Offsets Between Categories of Pollutants.

Given the following:

CAS #	Pollutant	Category	1/ED10	WOE	Composite score
91941	3,3-Dichloro-benzidine	NT	7.5	B	-
75014	Vinyl chloride	NT	1.6	A	-
748794	Mercuric chloride	HC	-	-	40
126998	Toluene	T	-	-	7
85449	Phthalic anhydride	NR	-	-	-

NT - "Non-threshold" pollutant
HC - "High-concern" pollutant
T - "Threshold" pollutant
NR - "Not ranked" pollutant

EPA's proposed approach:

Amount needed to offset 0.5 tns/yr increase of each pollutant

Pollutant with increased emissions of 0.5 tns/yr	3,3-Di-chloro-benzidine	Vinyl chloride	Mercuric chloride	Toluene	Pthalic anhydride
3,3-Dichloro-benzidine	0.625 tns/yr	-	-	-	-
Vinyl chloride	0.5 tns/yr	0.625 tns/yr	-	-	-
Mercuric chloride	-	-	0.625 tns/yr	-	-
Toluene	0.5 tns/yr	0.5 tns/yr	0.5 tns/yr	0.625 tns/yr	-
Pthalic anhydride	-	-	-	-	0.625 tns/yr

APPENDIX E

Identification of pollutants of concern for severe toxicity from short-term exposure.

Section 1: Overview

Under section 112(g), some pollutants are identified as being of concern for severe toxicity from short-term exposures and categorized as "high-concern" pollutants. These pollutants are identified by Levels of Concern (LOC) which are short-term exposure limits for chemicals on the Superfund Amendments and Reauthorization Act (SARA) Title III Section 302 list of Extremely Hazardous Substances. The LOC is an airborne concentration at which no serious, irreversible health effects, or death may occur following a single, short-term exposure.

Notes:

Physical state under ambient conditions is from the "Green Book" (Technical Guidance for Hazard Analysis; Emergency Planning for Extremely Hazardous Substances U.S. EPA, FEMA, and U.S. Dept. of Transportation 1987) and based on standard references.

Vapor pressure data for the chemicals at 20 to 25 degrees C are from the Green book. The Green Book values are the EPA Chemical Profiles (based on standard references such as the Merck Index), if available; in cases where no data were found, vapor pressure values were estimated by the EPA.

Data for acute toxicity are from the National Institute for Occupational Safety and Health (NIOSH) Registry of Toxic Effects of Chemical Substances (RTECs). "Updated" values are from the 1990 RTECs and include inhalation toxicity data, not oral or dermal data. Where no updated inhaltion values were used the appendix

includes toxicity values used as the basis for listing the chemicals as Extremely Hazardous Substances in 1986. OSHA thresholds are from OSHA's Process Safety Management Standard.

Abbreviations:

MUS - Mammalian unknown species

LC50 - Lethal concentration for 50% of treated subjects (inhalation exposure)

LD50 - Lethal dose for 50% of treated subjects (oral exposure)

LC1o - Lowest lethal concentration

LD1o - Lowest lethal dose

RfC - Inhalation reference concentration

Section 2: Data Report forms

Data Report Form

Chemical Name:	Acrolein
CAS Number:	107028
Ambient Physical State:	Liquid
Vapor Pressure:	220 mm Hg
Level of Concern:	1.15 mg/cu m
Basis for LOC:	IDLH (LC50, MUS)
RfC (chronic):	2.0 x 10-5 mg/cu m
RfC (acute):	None

Description of Acute Toxicity on IRIS:

Acrolein is extremely toxic. The probable oral human lethal dose is 5-50 mg/kg, between 7 drops and one teaspoon for a 70 kg (150 lb.) person (Gosselin, 1984). Inhalation of air containing 10 ppm of acrolein may be fatal in a few minutes (NRC,1981). Death from cardiac failure accompanied by hypothermia and hemorrhage of the lungs and degeneration of the bronchial epithelium is possible. Acrolein causes acute respiratory and eye irritation; severe gastrointestinal distress with slowly developing pulmonary edema (lungs fill up with fluid); and skin irritation (Gosselin, 1984, p. II-186).

Data Report Form

Chemical Name:	Antimony pentafluoride
CAS Number:	7783702
Ambient Physical State:	Liquid
Vapor Pressure:	7.00 mm Hg
Level of Concern:	2.700 mg/cu m
Basis for LOC:	Tox (LC50, Mouse)
RfC (chronic):	None
RfC (acute):	None

Description of Acute Toxicity on IRIS:

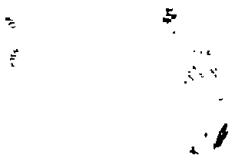
none

Data Report Form

Chemical Name:	Arsenic pentoxide
CAS Number:	1303282
Ambient Physical State:	Solid
Vapor Pressure:	1.00e-5 mm Hg
Level of Concern:	8.00 mg/cu m
Basis for LOC:	Tox (LD50, Rat)
RfC (chronic):	None
RfC (acute):	None

Description of Acute Toxicity on IRIS:

none



Data Report Form

Chemical Name:	Arsenous oxide
CAS Number:	1327533
Ambient Physical State:	Solid
Vapor Pressure:	1.00e-7 mm Hg
Level of Concern:	1.40 mg/cu m
Basis for LOC:	Tox (LD50, Rabbit)
RfC (chronic):	None
RfC (acute):	None

Description of Acute Toxicity on IRIS:

none

Data Report Form

Chemical Name:	Arsine
CAS Number:	7784421
Ambient Physical State:	Gas
Vapor Pressure:	Gas
Level of Concern:	1.90 mg/cu m
Basis for LOC:	IDLH (LC50, Monkey)
RfC (chronic):	None
RfC (acute):	None

Description of Acute Toxicity on IRIS:

none

Data Report Form

Chemical Name:	Benzotrichloride
CAS Number:	98077
Ambient Physical State:	Liquid
Vapor Pressure:	1.00 mm Hg
Level of Concern:	0.700 mg/cu m
Basis for LOC:	Tox (LC50, mouse)
RfC (chronic):	None
RfC (acute):	None

Description of Acute Toxicity on IRIS:

Benzotrichloride is toxic by inhalation; fumes are highly irritating to skin and mucous membranes (Merck 1983, Hawley 1981, p.119). Benzotrichloride may cause death or permanent injury after very short exposure to small quantities (Sax 1975).

Data Report Form

Chemical Name:	Benzyl chloride
CAS Number:	100447
Ambient Physical State:	Liquid
Vapor Pressure:	1.00 mm Hg
Level of Concern:	5.18 mg/cu m
Basis for LOC:	IDLH
RfC (chronic):	Inadq Data
RfC (acute):	None

Description of Acute Toxicity on IRIS:

Benzyl chloride is intensely irritating to skin, eyes, and mucous membranes (Merck, 1983). Benzyl chloride is highly toxic; may cause death or permanent injury after short exposure to small quantities (Sax, 1975). This substance has been listed as a direct-acting carcinogen or primary carcinogen (Doull, 1980). Largest doses cause central nervous system depression (Merck, 1983).

Data Report Form

Chemical Name:	beta-Propriolactone
CAS Number:	57578
Ambient Physical State:	Liquid
Vapor Pressure:	3.40 mm Hg
Level of Concern:	1.50 mg/cu m
Basis for LOC:	TLV (LC50, rat)
RfC (chronic):	Inadq Data
RfC (acute):	None

Description of Acute Toxicity on IRIS:

The toxicity potential of beta-propriolactone via inhalation or ingestion is high; may cause death or permanent injury after very short exposures to small quantities (Sax, 1968). Beta-propriolactone is a carcinogen (Weiss, 1980;p. 776).

Data Report Form

Chemical Name:	Cadmium oxide
CAS Number:	1306190
Ambient Physical State:	Solid
Vapor Pressure:	1.00e-5 mm Hg
Level of Concern:	4.00 mg/cu m
Basis for LOC:	IDLH (LC50, rat)
RfC (chronic):	None
RfC (acute):	None

Description of Acute Toxicity on IRIS:

none

Data Report Form

Chemical Name:	Chlorine
CAS Number:	7782505
Ambient Physical State:	Gas
Vapor Pressure:	Gas
Level of Concern:	7.25 mg/cu m
Basis for LOC:	IDLH (LC50, MUS)
RfC (chronic):	Under Rev
RfC (acute):	None

Description of Acute Toxicity on IRIS:

None

Data Report Form

Chemical Name:	Chloroacetic acid
CAS Number:	79118
Ambient Physical State:	Solid
Vapor Pressure:	0.500 mm Hg
Level of Concern:	1.80 mg/cu m
Basis for LOC:	Tox (LC50, Rat)
RfC (chronic):	None
RfC (acute):	None

Description of Acute Toxicity on IRIS:

None

Data Report Form

Chemical Name:	Chloromethyl methyl ether
CAS Number:	107302
Ambient Physical State:	Liquid
Vapor Pressure:	224 mm Hg
Level of Concern:	1.82 mg/cu m
Basis for LOC:	Tox (LC50, rat)
RfC (chronic):	Under Rev
RfC (acute):	None

Description of Acute Toxicity on IRIS:

The principle effect of chloromethyl methyl ether is irritation. The liquid causes severe irritation of eyes and skin; and vapor exposure of 100 ppm is severely irritating to eyes and nose. "this level is dangerous to life in 4 hours. Pulmonary edema or pneumonia may cause death (Encyc. Occupat. Health and safety, 1971). There was increased death rate from respiratory cancer among exposed victims (IARC, 1972-1985) and it is a regulated carcinogen (Aldrich, 1984).

Data Report Form

Chemical Name:	Chromic Chloride
CAS Number:	10025737
Ambient Physical State:	Solid
Vapor Pressure:	1.00e-5 mm Hg
Level of Concern:	0.0500 mg/cu m
Basis for LOC:	IDLH (LC50, Mouse)
RfC (chronic):	None
RfC (acute):	None

Description of Acute Toxicity on IRIS:

none

Data Report Form

Chemical Name:	Cobalt carbonyl
CAS Number:	10210681
Ambient Physical State:	Solid
Vapor Pressure:	0.1 mm Hg
Level of Concern:	0.270 mg/cu m
Basis for LOC:	Tox (LClow, Mouse)
RfC (chronic):	None
RfC (acute):	None

Description of Acute Toxicity on IRIS:

None

Data Report Form

Chemical Name:	Dimethyl sulfate
CAS Number:	77781
Ambient Physical State:	Liquid
Vapor Pressure:	0.1 mm Hg
Level of Concern:	5.00 mg/cu m
Basis for LOC:	IDLH (LC50, Rat)
RfC (chronic):	Inadeq Data
RfC (acute):	None

Description of Acute Toxicity on IRIS:

Acute: extremely toxic vapors and liquid -- a few whiffs or contact on skin could be fatal (NFPA, 1978). Dimethyl sulfate is also acutely toxic if ingested. Delayed effects which are ultimately fatal may also occur (Merck, 1983). Lethal concentrations as low as 97 ppm for 10 minutes have been reported in humans. Delayed appearance of symptoms may permit unnoticed exposure to lethal quantities (Merck, 1983, p.475).

Data Report Form

Chemical Name:	4,6-Dinitro-o-cresol, and salts
CAS Number:	534521
Ambient Physical State:	Solid
Vapor Pressure:	5.00e-5 mm Hg
Level of Concern:	0.500 mg/cu m
Basis for LOC:	IDLH (LD50, Rat)
RfC (chronic):	None
RfC (acute):	None

Description of Acute Toxicity on IRIS:

None

Data Report Form

Chemical Name:	Ethyleneimine
CAS Number:	151564
Ambient Physical State:	Liquid
Vapor Pressure:	207 mm Hg
Level of Concern:	4.00 mg/cu m
Basis for LOC:	Tox (LC50, Mouse)
RfC (chronic):	Inadeq Data
RfC (acute):	None

Description of Acute Toxicity on IRIS:

Ethyleneimine is classified as extremely toxic with a probable oral lethal dose of 5 - 50 mg/kg which is approximately 7 drops to 1 teaspoonful for a 70 kg (150 lb.) person (Gosselin, 1976). Ethyleneimine gives inadequate warning when over-exposure is by inhalation or skin absorption. It is a severe blistering agent, causing third degree chemical burns of the skin. Ethyleneimine also has a corrosive effect on mucous membranes and may cause scarring of the esophagus. It is corrosive to eye tissue and may cause permanent corneal opacity and conjunctival scarring (Weiss, 1980; p. 443). Severe exposure to ethyleneimine may result in overwhelming pulmonary edema. Renal damage has been described (Gosselin, 1984: p. II-207). Hemorrhagic congestion of all internal organs has been observed (Clayton and Clayton, 1981-82, p.2674).

Data Report Form

Chemical Name:	Ethylene oxide
CAS Number:	75218
Ambient Physical State:	Gas
Vapor Pressure:	Gas
Level of Concern:	144 mg/cu m
Basis for LOC:	IDLH (LC50, Rat)
RfC (chronic):	?
RfC (acute):	0.3 ppm (for developmental effects)

Description of Acute Toxicity on IRIS:

None

Data Report Form

Chemical Name:	Fluomine
CAS Number:	62207765
Ambient Physical State:	Solid
Vapor Pressure:	1.00e-5 mm Hg
Level of Concern:	3.00 mg/cu m
Basis for LOC:	Tox (LClo, Guinea pig)
RfC (chronic):	None
RfC (acute):	None

Description of Acute Toxicity on IRIS:

none

Data Report Form

Chemical Name:	Hexachlorocyclopentadiene
CAS Number:	77474
Ambient Physical State:	Liquid
Vapor Pressure:	8.00e-2 mm Hg
Level of Concern:	0.0195 mg/cu m
Basis for LOC:	Tox (LC50, rat)
RfC (chronic):	None
RfC (acute):	None

Description of Acute Toxicity on IRIS:

Hexachlorocyclopentadiene is very toxic and may be fatal if inhaled, swallowed, or absorbed through the skin. The probable human lethal dose is 50 - 500 mg/kg, or between 1 teaspoon and 1 ounce for a 150-lb. (70-kg) person. Severe exposure induces pulmonary hyperemia and edema, degenerative and necrotic changes in brain, heart and adrenal glands, and necrosis of liver and kidney tubules (DOT, 1984: Gosselin et al., 1984, p. II-169).

Data Report Form

Chemical Name:	Hydrogen fluoride
CAS Number:	7664393
Ambient Physical State:	Gas
Vapor Pressure:	Gas
Level of Concern:	1.64 mg/cu m
Basis for LOC:	IDLH (LC50, Mouse)
RfC (chronic):	Under Rev
RfC (acute):	None

Description of Acute Toxicity on IRIS:

None

Data Report Form

Chemical Name:	Hydrogen selenide
CAS Number:	7783075
Ambient Physical State:	Gas
Vapor Pressure:	Gas
Level of Concern:	0.660 mg/cu m
Basis for LOC:	IDLH (LC50, Guinea pig)
RfC (chronic):	None
RfC (acute):	None

Description of Acute Toxicity on IRIS:

none

Data Report Form

Chemical Name:	Methylcyclopentadienyl manganese
CAS Number:	12108133
Ambient Physical State:	Liquid
Vapor Pressure:	0.100 mm Hg
Level of Concern:	0.600 mg/cu m
Basis for LOC:	Tox (LC50, Mouse)
RfC (chronic):	None
RfC (acute):	None

Description of Acute Toxicity on IRIS:

None

Data Report Form

Chemical Name:	Methyl hydrazine
CAS Number:	60344
Ambient Physical State:	Liquid
Vapor Pressure:	49.6 mm Hg
Level of Concern:	0.940 mg/cu m
Basis for LOC:	IDLH (LC50, MUS)
RfC (chronic):	None
RfC (acute):	None

Description of Acute Toxicity on IRIS:

None

Data Report Form

Chemical Name:	Methyl isocyanate
CAS Number:	624839
Ambient Physical State:	Liquid
Vapor Pressure:	348 mm Hg
Level of Concern:	4.70 mg/cu m
Basis for LOC:	IDLH (LC50, Rat)
RfC (chronic):	Inadeq Data
RfC (acute):	None

Description of Acute Toxicity on IRIS:

Methyl isocyanate is a skin irritant and can cause permanent eye damage (ACGIH, 1980). A concentration of 2 ppm has been reported toxic in humans (NIOSH/RTECS, 1985). Methyl isocyanate attacks the respiratory system, eyes and skin. It can injure the lungs and bronchial airways, cause permanent eye damage and death. Death has been attributed to various forms of respiratory distress (Dagani, 1985, p. 38).

Data Report Form

Chemical Name:	Nickel carbonyl
CAS Number:	13463393
Ambient Physical State:	Liquid
Vapor Pressure:	400 mm Hg
Level of Concern:	0.350 mg/cu m
Basis for LOC:	TLV (LC50, MUS)
RfC (chronic):	None
RfC (acute):	None

Description of Acute Toxicity on IRIS:

The probable oral lethal dose of nickel carbonyl for a human is between 50 and 500 mg/kg, between 1 teaspoon and 1 ounce/150 lb. person (Gosselin et al., 1976). Nickel carbonyl has also been estimated to be lethal in humans at atmospheric exposures of 30 ppm for 20 minutes (Doull et al. 1980). Autopsies show congestion, collapse, and tissue destruction, as well as hemorrhage in the brain (Hamilton and Hardy, 1974). Dermatitis, recurrent asthmatic attacks, and increased number of white blood cells are acute health hazards (DOT, 1984). Nickel carbonyl is poisonous. It can be fatal if inhaled, swallowed, or absorbed through skin. Vapors may cause irritation, congestion, and edema of lungs (Merck, 1983).

Data Report Form

Chemical Name:	Parathion
CAS Number:	56382
Ambient Physical State:	Liquid
Vapor Pressure:	3.8e-5 mm Hg
Level of Concern:	2.00 mg/cu m
Basis for LOC:	IDLH (LC50, Rat)
RfC (chronic):	None
RfC (acute):	None

Description of Acute Toxicity on IRIS:

Parathion is extremely toxic; the probable oral lethal dose for parathion is 5 - 50 mg/kg, or between 7 drops and 1 teaspoonful for a 150-lb. person. As little as 1 drop of parathion can endanger life if splashed in the eye. Toxicity of parathion is highest by inhalation (Gosselin, 1976).

Data Report Form

Chemical Name:	Phosgene
CAS Number:	75445
Ambient Physical State:	Gas
Vapor Pressure:	Gas
Level of Concern:	0.800 mg/cu m
Basis for LOC:	IDLH (LC50, Rat)
RfC (chronic):	Inadeq Data
RfC (acute):	None

Description of Acute Toxicity on IRIS:

None

Data Report Form

Chemical Name:	Phosphorous
CAS Number:	7723140
Ambient Physical State:	Solid
Vapor Pressure:	5.00e-2 mm Hg
Level of Concern:	3.00 mg/cu m
Basis for LOC:	Tox (LDlo, Human)
RfC (chronic):	None
RfC (acute):	None

Description of Acute Toxicity on IRIS:

None

Data Report Form

Chemical Name:	Potassium cyanide
CAS Number:	151508
Ambient Physical State:	Solid
Vapor Pressure:	1.00e-5 mm Hg
Level of Concern:	5.00 mg/cu m
Basis for LOC:	IDLH (LD50, Rabbit)
RfC (chronic):	None
RfC (acute):	None

Description of Acute Toxicity on IRIS:

none

Data Report Form

Chemical Name:	Sodium cyanide
CAS Number:	143339
Ambient Physical State:	Solid
Vapor Pressure:	1.00e-5 mm Hg
Level of Concern:	5.00 mg/cu m
Basis for LOC:	IDLH (LD50, Domestic animal)
RfC (chronic):	None
RfC (acute):	None

Description of Acute Toxicity on IRIS:

none

Data Report Form

Chemical Name:	Sodium selenate
CAS Number:	13410010
Ambient Physical State:	Solid
Vapor Pressure:	1.00e-5 mm Hg
Level of Concern:	1.60 mg/cu m
Basis for LOC:	Tox (LD50, rat)
RfC (chronic):	None
RfC (acute):	None

Description of Acute Toxicity on IRIS:

none

Data Report Form

Chemical Name:	Sodium selenite
CAS Number:	10102188
Ambient Physical State:	Solid
Vapor Pressure:	1.00e-5 mm Hg
Level of Concern:	2.30 mg/cu m
Basis for LOC:	Tox (LD50, Domestic animal)
RfC (chronic):	None
RfC (acute):	None

Description of Acute Toxicity on IRIS:

none

Data Report Form

Chemical Name:	Tetraethyl lead
CAS Number:	78002
Ambient Physical State:	Liquid
Vapor Pressure:	0.200 mm Hg
Level of Concern:	4.00 mg/cu m
Basis for LOC:	IDLH (LC50, Rat)
RfC (chronic):	None
RfC (acute):	None

Description of Acute Toxicity on IRIS:

Tetraethyl lead is extremely poisonous; it may be fatal if inhaled, swallowed, or absorbed from the skin. Contact may cause burns to skin and eyes (DOT, 1984). Most symptoms of poisoning are due to the effects of tetraethyl lead on the nervous system (Gilman et al., 1980).

Data Report Form

Chemical Name:	Tetramethyl lead
CAS Number:	75741
Ambient Physical State:	Liquid
Vapor Pressure:	22.0 mm Hg
Level of Concern:	4.00 mg/cu m
Basis for LOC:	IDLH (LC50 Mouse)
RfC (chronic):	None
RfC (acute):	None

Description of Acute Toxicity on IRIS:

None

Data Report Form

Chemical Name:	2,4-Toluene diisocyanate
CAS Number:	584849
Ambient Physical State:	Liquid
Vapor Pressure:	1.00 mm Hg
Level of Concern:	7.00 mg/cu m
Basis for LOC:	IDLH (LC50, Rabbit)
RfC (chronic):	Under rev
RfC (acute):	None

Description of Acute Toxicity on IRIS:

None

Data Report Form

Chemical Name:	Titanium tetrachloride
CAS Number:	7550450
Ambient Physical State:	Liquid
Vapor Pressure:	10.0 mm Hg
Level of Concern:	1.00 mg/cu m
Basis for LOC:	Tox (LC50, Mouse)
RfC (chronic):	None
RfC (acute):	None

Description of Acute Toxicity on IRIS:

None