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NATIONAL AIR TOXICS PROGRAM: THE INTEGRATED URBAN STRATEGY
Report to Congress

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Office of Air and Radiation
Office of Air Quality Planning and Standards
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Acronym List

AEGL	acute exposure guidance level
AIHA	American Industrial Hygiene Association
AIRS	Aerometric Information Retrieval System
ARE	acute reference exposure
ASPEN	Assessment System for Population Exposure Nationwide
ATSDR	Agency for Toxic Substances and Disease Registry
BCF	bioconcentration factor
BMD	benchmark dose
CAA	Clean Air Act
CAS	Chemical Abstract Services
CASAC	Clean Air Scientific Advisory Committee
CEP	Cumulative Exposure Project
CERCLA	Comprehensive Environmental Response, Compensation, and Liability Act
CFR	Code of Federal Regulations
CHAD	Consolidated Human Activity Database
CMAQ	Community Multi-Scale Air Quality
C/MSA	consolidated metropolitan statistical area
CO	carbon monoxide
CWA	Clean Water Act
DNA	deoxyribonucleic acid
DOT	Department of Transportation
EMPACT	Environmental Monitoring for Public Access and Community Tracking
EPA	Environmental Protection Agency
EPCRA	Emergency Planning and Community Right-to-Know Act
ERPG	emergency response planning guideline
ES	Executive Summary
FIFRA	Federal Insecticide, Fungicide and Rodenticide Act
FR	Federal Register
GACT	generally available control technology
GIS	geographic information systems
GLC	ground-level concentration
HAP	hazardous air pollutant
HAPEM	Hazardous Air Pollutant Exposure Model
HASTE	Houston Area Source Toxic Emissions
HC	hydrocarbon
HEAST	Health Effects Assessment Summary Tables
HEC	human equivalent concentration
HI	hazard index
HQ	hazard quotient
IEM	Integrated Exposure Methodology

Acronym List (Continued)

I/M	inspection and maintenance
IRIS	Integrated Risk Information System
ISC3	Industrial Source Complex
km	kilometers
K_{ow}	octanol-water partition coefficient
LCA	Life Cycle Analysis
LOAEL	lowest-observed-adverse-effect level
LOC	level of concern
LIDAR	Light Detecting and Ranging
MACT	maximum achievable control technology
MEASURE	Mobile Emissions Assessment System for Urban and Regional Evaluation
MMT	methylcyclopentadienyl manganese tricarbonyl
MOU	memorandum of understanding
MPCA	Minnesota Pollution Control Agency
MPO	Metropolitan Planning Organizations
MRL	minimal risk level
MSA	metropolitan statistical area
MTBE	methyl tertiary butyl ether
MWC	municipal waste combustor
MWI	municipal waste incinerator
NAAQS	national ambient air quality standard
NAC	National Advisory Committee
NERL	National Exposure Research Laboratory
NESHAP	national emission standards for hazardous air pollutants
NHAPS	National Human Activity Pattern Survey
NHEXAS	National Human Exposure Assessment Survey
NOAEL	no-observed-adverse-effect level
NO_x	nitrogen oxide
NTI	National Toxics Inventory
PAH	polycyclic aromatic hydrocarbons
PAMS	Photochemical Assessment Monitoring Stations
PBPK	physiologically based pharmacokinetic (model)
PBT	persistent, bioaccumulative, and toxic
PCB	polychlorinated biphenyls
PCDD	polychlorinated dibenzo-p-dioxin
PCDF	polychlorinated dibenzofuran
PM	particulate matter
PM_x	particulate matter (x microns or smaller)
PNGV	Partnership for a New Generation of Vehicles
POM	polycyclic organic matter
PPA	Pollution Prevention Act

Acronym List (Continued)

PSI	pollutant standard index
QSTR	quantitative structure-toxicity relationship
RBC	risk-based concentration
RBD	risk-based dose
RCRA	Resource Conservation and Recovery Act
RDDR	regional deposited dose ratio
REL	reference exposure level
RfC	reference concentration
RfD	reference dose
RFG	reformulated gasoline
RMP	Risk Management Program
SAB	Science Advisory Board
SAR	structure-activity relationship
SARA	Superfund Amendments and Reauthorization Act
SIC	Standard Industrial Classification
TCDD	2,3,7,8-tetrachlorodibenzo-p-dioxin
TCDF	2,3,7,8-tetrachlorodibenzofuran
TEAM	Total Exposure Assessment Methodology
TEF	toxic equivalency factor
TMDL	total maximum daily load
TNRCC	Texas Natural Resources Conservation Commission
TRI	Toxics Release Inventory
TRIM	Total Risk Integrated Methodology
TSCA	Toxic Substance Control Act
TSD	treatment, storage, and disposal
UF	uncertainty factors
U.S.	United States
U.S.C.	United States Code
VMT	vehicle-miles of travel
VOC	volatile organic compounds
WMPT	Waste Minimization Prioritization Tool

Executive Summary

On July 19, 1999, we published a notice in the *Federal Register* entitled "National Air Toxics Program: The Integrated Urban Air Strategy" (Strategy) that outlined the U.S. Environmental Protection Agency's (EPA's) plans for addressing cumulative health risks in urban areas[1]. The Strategy presented our plan for future actions to reduce emissions of air toxics and improve our understanding of the health risks posed by toxics in urban areas.

Section 112(k) of the Clean Air Act (CAA) requires the EPA Administrator to submit two Reports to Congress on actions taken under the CAA that reduce the risk to public health posed by the release of hazardous air pollutants (HAP) from area sources. This Report to Congress (Report), originally due in 1998, was prepared to meet the first part of that requirement. In addition, it expands on much of the information provided in the Strategy, such as the methodology for developing the emissions inventory, identifying the 33 urban HAP and identifying the area source categories that will be subject to regulation. Furthermore, this Report summarizes existing information on risk assessments that have been conducted in various urban areas. These studies were performed by EPA and various States over the last several years. Taking into consideration the uncertainties and limitations of each study, these assessments provide useful information on the potential nature and magnitude of exposures and health risks in urban areas. Finally, this Report also provides a very detailed discussion of 13 research needs to address in achieving the goals of the Strategy. These needs were identified in the following areas: exposure assessment, health effects, dose-response assessment, risk assessment, risk characterization and risk management. In addition, Chapter 6 of this Report provides a summary of ongoing EPA activities to address those needs.

Section 112(k) also requires EPA to identify specific metropolitan areas that continue to experience high risks to public health as the result of emissions from area sources. Since we have only recently begun to work toward implementing the Strategy, we are unable to identify in this first Report the metropolitan areas that continue to experience high risks to public health as the result of emissions from areas sources. However, in the next few years, as we make progress toward the goals of the Strategy, we will be better able to identify those metropolitan areas with high risks due to air toxics.

The following sections provide an overview of the Strategy and describe the four components of the Strategy and explain their role in achieving its goals. The four components are: Standard Setting Activities, National and Local Initiatives, Air Toxics Assessments, and Education and Outreach. These components also form the framework of our National Air Toxics Program. Finally, Chapter 1 of this Report summarizes the contents of each chapter and their key points. Important health and other general information about each one of the 33 urban HAP is provided in the Appendix.

[1]64 FR 38705. National Air Toxics Program: The Integrated Urban Strategy (Notice). July 19, 1999.

Overview of the Strategy

The Strategy presents a framework for further reducing HAP emissions from all types of sources found in urban areas, including major industrial sources, smaller stationary sources, and cars and trucks. Air toxics can pose special threats in urban areas because of the large number of people and the variety of sources that emit HAP. Individually, some of these sources may not emit large amounts of toxic pollutants. However, all of these pollution sources combined can potentially pose significant health threats. We are also concerned about the impact of toxics emissions on minority and low income communities which are often located close to industrial and commercial urbanized areas. Accordingly, there are three goals for the Strategy:

1. Reduce, by 75 percent, the incidence of cancer associated with air toxics from both large and small industrial/commercial sources. This is relevant to all HAP from both major and area stationary sources in all urban areas nationwide. Reductions can be the result of actions by Federal, State, local and/or Tribal governments achieved by any regulations or voluntary actions.

2. Substantially reduce noncancer health risks (e.g., birth defects and reproductive effects) associated with air toxics from small industrial/commercial sources. This includes health effects other than cancer posed by all HAP. Reductions can be the result of actions by Federal, State, local and/or Tribal governments achieved by any regulations or voluntary actions.

3. Address disproportionate impacts of air toxics hazards across urban areas, such as those in areas known as "hot spots," and minority and low-income communities in urban areas. This will necessarily involve consideration of both stationary and mobile source emissions of all HAP, as well as sources of HAP in indoor air. We intend to characterize exposure and risk distributions both geographically and demographically. This will include particular emphasis on highly exposed individuals (such as those in geographic "hot spots") and specific population subgroups (e.g., children, the elderly, and low-income communities).

To accomplish these goals, the Strategy is comprised of four key components:

1. Standard setting activities addressing sources of air toxics at both the national and local level;

2. Initiatives at both the national and local level to address specific pollutants (e.g., mercury) and to identify and address specific community risks (e.g., through pilot projects);

3. Air toxics assessments (including expanded air toxics monitoring and modeling) to identify areas of concern, to prioritize efforts to reduce risks, and to track progress; and

4. Education and outreach efforts to inform stakeholders about the Strategy and to get input into designing programs to implement it.

Standard Setting Activities

This first component includes our regulatory tools and programmatic activities for source-specific and sector-based standard setting, as well as those of States, local agencies, and Tribes. These standards contribute to reductions in emissions of air toxics from major, area, and mobile sources. This component includes activities such as selecting urban HAP, setting emission standards, conducting studies, developing policies, and conducting enforcement and compliance assistance activities. These actions result in emission reductions, as well as associated reductions in risk.

The CAA includes certain specific requirements for the Strategy. First, we must identify at least 30 HAP, "which, as the result of emissions from area sources, present the greatest threat to public health in the largest number of urban areas" (CAA § 112(k)(3)(B)(i)). To select these HAP, we evaluated the health effects information available for 188 HAP, estimated emissions from all known sources using a variety of techniques, assessed available air quality monitoring data, reviewed existing studies, and produced a list of pollutants based on the relative hazards they pose in urban areas, considering toxicity, emissions, and related characteristics. From this effort, we established a list of 33 urban HAP which pose the greatest threats to public health in urban areas, considering emissions from major, area and mobile sources (see Exhibit ES-1). This list includes not only those that are emitted from area sources, but reflects the integrated nature of the Strategy by including those posing public health concerns in urban areas regardless of emissions source type. Included among the 33 urban HAP are the 30 HAP with greatest emissions contributions from area sources (i.e., the "area source HAP"). The remaining three urban HAP (i.e., coke oven emissions, 1,2-dibromoethane and carbon tetrachloride) have less significant emissions contributions from area sources. Under section 112(k), there are no specific regulatory implications of listing these three HAP, but we'll use all 33 HAP in prioritizing efforts to address risks.

Second, we're required to assure that sources accounting for 90 percent of the emissions of identified area source HAP are subject to standards (CAA § 112(c)(3) and (k)(3)(B)(ii)). We adopted a two-step process for selecting the source categories which will be subject to regulation under the Strategy. First, we identified those area source categories that emit one or more of the 30 area source HAP that are already listed for regulation under the CAA. For each of those source categories, we identified the percentage contribution to the total area source emissions for each of the 30 area source HAP.

In the second step, we added area source categories that, based on inventory data, contribute at least 15 percent of the national urban emissions of at least one of the 30 area source HAP. We adopted this criterion to account for the uncertainties in our current emissions inventory data. While we've been able to significantly improve our baseline emissions inventory

EXHIBIT ES-1
LIST OF URBAN HAP FOR THE INTEGRATED URBAN AIR TOXICS STRATEGY
("URBAN HAP LIST")

HAP	CAS No. +	HAP	CAS No. +
Acetaldehyde	75070	Formaldehyde	50000
Acrolein	107028	Hexachlorobenzene	118741
Acrylonitrile	107131	Hydrazine	302012
Arsenic compounds		Lead compounds	
Benzene	71432	Manganese compounds	
Beryllium compounds		Mercury compounds	
1,3-butadiene	106990	Methylene chloride (dichloromethane)	75092
Cadmium compounds		Nickel compounds	
Carbon tetrachloride*	56235	Polychlorinated biphenyls (PCBs)	1336363
Chloroform	67663	Polycyclic organic matter (POM)	
Chromium compounds		Quinoline	91225
Coke oven emissions*	8007452	2,3,7,8-tetrachlorodibenzo-p-dioxin (& congeners & TCDF congeners)	1746016
1,2-dibromoethane*	106934	1,1,2,2-tetrachloroethane	79345
1,2-dichloropropane (propylene dichloride)	78875	Tetrachloroethylene (perchloroethylene)	127184
1,3-dichloropropene	542756	Trichloroethylene	79016
Ethylene dichloride (1,2-dichloroethane)	107062	Vinyl chloride	75014
Ethylene oxide	75218		

+ Chemical Abstracts System number. *HAP with less significant contributions from area sources.

data, data gaps and uncertainty still remain. The list of source categories will be modified to reach the 90 percent requirement by 2003.

As a result of this two-step approach, the Strategy identified and listed 29 area source categories that emit significant amounts of one or more of the 30 area source HAP. Currently, we have regulations under development or completed for 16 of these area source categories. We

expect to develop regulations for the remaining 13 area source categories over the next five years. Exhibit ES-2 shows those area source categories, as listed in the Strategy, that contribute to emissions of the 30 area source HAP, and are either subject to existing standards, or will be subject to standards that are currently being developed. Exhibit ES-3 shows the area source categories listed in the Strategy for the first time, as required in section 112(c)(3). These are the area source categories that contribute at least 15 percent of the total area source emissions of at least one of the 30 area source HAP.

EXHIBIT ES-2
AREA SOURCE CATEGORIES ALREADY SUBJECT TO STANDARDS OR WHICH WILL BE SUBJECT TO STANDARDS

Chromic Acid Anodizing	Industrial Boilers
Commercial Sterilization Facilities	Institutional/Commercial Boilers
Other Solid Waste Incinerators (Human/Animal Cremation)	Medical Waste Incinerators
Decorative Chromium Electroplating	Municipal Waste Combustors
Dry Cleaning Facilities	Open Burning Scrap Tires
Halogenated Solvent Cleaners	Portland Cement
Hard Chromium Electroplating	Secondary Lead Smelting
Hazardous Waste Combustors	Stationary Internal Combustion Engines

EXHIBIT ES-3
NEW AREA SOURCE CATEGORIES BEING LISTED

Cyclic Crude and Intermediate Production	Municipal Landfills
Flexible Polyurethane Foam Fabrication Operations	Oil & Natural Gas Production
Hospital Sterilizers	Paint Stripping Operations
Industrial Inorganic Chemical Manufacturing	Plastic Materials and Resins Manufacturing
Industrial Organic Chemical Manufacturing	Publicly Owned Treatment Works
Mercury Cell Chlor-Alkali Plants	Synthetic Rubber Manufacturing
Gasoline Distribution Stage I	

With respect to mobile sources, title II of the CAA provides several mechanisms to achieve reductions in HAP. The most direct of these is section 202(l) which requires us to identify the need for and consider regulations for control of HAP from motor vehicles and their fuels. Those standards are to reflect the greatest degree of emissions reductions achievable through the application of technology which will be available, taking existing standards, availability and costs of the technology, noise, energy and safety factors into account. Section 202(l)(2) further specifies that, at a minimum, benzene and formaldehyde emissions must be addressed.

The section 202(l)(2) proposal will identify the HAP emitted by motor vehicles and their fuels, assess the reductions achieved by our current and recently proposed title II regulations, and evaluate the appropriateness of additional motor vehicle and fuel controls. With regard to control strategies, several of the existing emission control programs developed under section 202(a) (motor vehicle controls) and section 211 (fuel controls) of the CAA already limit many HAP emissions from motor vehicles and their fuels. In our assessment of whether additional action is appropriate under section 202(l)(2), we'll consider the impacts of these programs, our recent and ongoing regulatory activities (such as our recent final rulemaking for new light-duty "Tier 2" emission standards and gasoline sulfur controls[2] and our recent proposal for heavy-duty engine and vehicle standards and on-highway diesel fuel sulfur controls[3]), and such other mobile source programs as are relevant to mobile source air toxics controls.

As we review existing regulations for a number of motor vehicle and nonroad engine categories, the Strategy's goal of reducing disproportionate air toxics risks will be considered. In addition, we envision that work done in the early stages of implementing the Strategy, such as improving monitoring and inventories, will help us compare options related to the various emissions sources in urban areas and control authorities to provide the best relative reduction of risks to the urban public. To the extent possible, we will consider costs in the development of regulations aimed at reducing those risks. Capital costs, fuel costs and incremental labor costs to operate equipment are some but not all of the factors that may be considered in assessing the cost effectiveness of a particular control strategy.

Overall, in meeting the Strategy's goals, we'll consider reductions in HAP resulting from Federal actions both to address air toxics (e.g., maximum achievable control technology (MACT) standards under section 112(d), residual risk standards, mobile source emission controls) and attain the national ambient air quality standards (NAAQS) for particulate matter (PM) and ozone, as well as State, local and Tribal measures. We'll consider cumulative risks presented by exposures to emissions of all HAP from all sources in a given area. Further, consistent with the

[2] 65 FR 6698. Tier 2 Motor Vehicle Emission Standards and Gasoline Sulfur Control Requirements. February 10, 2000.

[3] 65 FR 35430. Proposed Heavy-Duty Engine and Vehicle Standards and Highway Diesel Fuel Sulfur Control Requirements. June 2, 2000.

direction of section 112(k)(4) to encourage and support areawide strategies developed by State or local air pollution control agencies, we'll work with State, local, and Tribal air pollution control programs for additional progress toward these goals.

National and Local Initiatives

The second component of the Strategy involves local and community-based initiatives to focus on multimedia and cumulative risks within urban areas. Developing the Strategy is a challenge at the national level because urban air toxics problems vary significantly across the country. Because of this variability, the Strategy is being approached as a partnership between EPA and State, local and Tribal governments. These governments (including municipal offices other than pollution control departments) have the most experience with local air pollution issues, and can lend their expertise and knowledge to address and resolve air toxics concerns that are unique to cities. Many of these governments also have existing air pollution control programs that currently address, and can effectively continue to address, some or all of these issues. In addition, these governments are often able to act much more quickly than we can to address local concerns, which leads to less overall pollution, particularly in the areas where pollution is of greatest concern.

At the Federal level, we can contribute Federal standards and requirements using our authorities to develop and implement a national regulatory program. We also have the knowledge base and expertise to evaluate, or to help other agencies evaluate, air pollution problems. By integrating our relative strengths, we can provide a stronger, more efficient, and more effective program to address toxic air pollution in urban areas. For example, as discussed in Chapter 5 of this Report, once we've completed the initial assessment, we'll have a better understanding of our status with regard to the risk reduction goals of the Strategy. This will inform us about additional Federal activities needed to meet those goals, and what additional State, local and Tribal activities are needed to complement these activities. Periodic assessments will continue to inform us about needed programs over time.

Concurrent with the initial assessments, we plan to meet with our State, local and Tribal partners. We'll be reviewing the goals and the various components of the Strategy and how they interrelate. In particular, we'll focus on the assessment tools and their role in defining Federal, State, local, and Tribal activities. These activities may include pilot projects to identify and address risk and may rely on some of the assessment activities and tools described below.

Air Toxics Assessments

The third component of the Strategy discussed in this Report is the urban component of national air toxics assessments (NATA). NATA will provide us with meaningful information and allow us to describe progress that we've made in meeting our overall program and strategy-specific goals. We'll identify the pollutants and sources that contribute to any failures in meeting our risk reduction goals and provide information to support regulatory and policy decisions needed to move us closer to meeting these goals. These activities rely on improving our base of

knowledge (e.g., concerning health effects and exposure characteristics) and tools (e.g., emissions inventories, monitoring networks, and computer models), along with our plans for their improvement and related research.

Historically, EPA's risk assessment and decisionmaking have focused on the likelihood of health effects associated with exposure to individual environmental contaminants. In recent years, our risk assessment emphasis has shifted increasingly to a greater consideration of multiple pollutants, endpoints, pathways, routes of exposure, and holistic reductions of risks. This complex analysis is often called "cumulative risk assessment." It describes who or what is at risk of adverse effects and identifies sources and stressors considering several different routes of exposure over varied timeframes. Assessing progress in reducing cumulative risks from HAP will require us to move away from a focus on assessing reductions in tons per year emitted toward a focus on estimating reductions in cancer and noncancer risks associated with lower emissions.

In general, the choice of appropriate risk assessment approaches will be influenced by both the availability of data to support exposure assessment, and the level of detail and resolution needed to support the purpose of the assessment. Possible approaches span a wide range, from simple weighting adjustments of emissions data or ambient concentrations, to detailed multipathway risk assessments. Our assessment approaches will be iterative in nature to take advantage of emerging science, new data, and improved tools that become available as future assessments are performed. Beginning in early 2000, we'll conduct an initial set of assessments that will be based on final, updated emissions data for the 1990-93 and 1996 time periods and the best available methods and tools.

We'll tailor each assessment to the purpose(s) it is to serve (e.g., measuring progress against the 75 percent estimated cancer incidence reduction goal). Accordingly, assessments will vary in scope, level of refinement, and, thus, data and resource requirements. The scope of each assessment will generally be defined by the following characteristics:

- The number of HAP to be evaluated (all 188 or some subset);
- Types of sources included (area, major, mobile);
- Spatial resolution (e.g., aggregation of results on the national, State, or urban scale); and
- Pathways and media to be evaluated (inhalation and air only or multipathway and multimedia).

Further, for each assessment, we will specify an appropriate approach for estimating progress toward our risk reduction goals since it will not be possible to directly measure reductions in cancer incidence or noncancer risks attributable to HAP emissions. Alternative approaches will range from rough approximations to more precise risk estimates, depending on data and resource requirements.

Our risk assessment science has been extensively peer-reviewed, is widely used and understood by the scientific community, and continues to expand and evolve as scientific knowledge advances. We intend to use the most current and appropriate risk estimation methods to track progress under the Strategy.

Education and Outreach

The fourth component of the Strategy, communicating about risks through education and outreach to the public, ensures that the activities we undertake are responsive to stakeholder concerns. Over the course of implementing the Strategy, we plan to work with State, local, and Tribal governments and other stakeholders on developing the national assessments of the risks from air toxics and the materials to communicate the findings with the public. We will include State, local and Tribal authorities, and in particular mayors, in planning activities to assess and address local air quality concerns and plan pilot project activities under the Strategy.

We will also explore the formation of groups such as roundtables and panels to involve communities, small businesses and other stakeholders, including representatives from universities and hospitals. These groups will explore issues related to rulemaking coordination, risk assessments, and the process of defining roles and responsibilities for Federal and State, local and Tribal agencies in implementing the Strategy. In addition, many of the activities identified in the Strategy will require public notice and comment, which will provide further opportunities for stakeholder input as the various activities are developed. We'll also continue to use the established Integrated Urban Air Toxics Strategy website on the Internet to update the public on ongoing activities and opportunities to participate in implementation of the Strategy. This will include updates on rule development, assessment activities, and progress toward meeting all of the Strategy goals.

As noted above, we're required by the CAA to provide two Reports to Congress on actions taken to reduce the risks to public health posed by the release of HAP from area sources. The CAA also requires that the reports identify specific metropolitan areas that continue to experience high risks to public health as the result of emissions from area sources. This document is our first Report to Congress. The second report is required to be submitted by 2002. We also expect to report to the public about air toxics emissions trends and air quality in urban and other areas in our annual Air Quality and Emissions Trends Reports.

Research Needs

The Strategy describes the process we'll use for identifying the various risks that may be present in an urban environment. Part of that process is to determine gaps in our scientific information and to identify the tools we'll need to assess urban risks and to implement the risk reduction elements of the Strategy. Chapter 6 of this Report describes the activities and research needed to assist in our assessment and management of risks in urban environments and to improve risk assessment and risk management of air toxics from all emission sources.

We're also developing an Air Toxics Research Strategy which will build on the research needs presented in this Report, as well as other research strategies that our Office of Research and Development has prepared that address specific air toxics research issues (e.g., the draft Mercury Research Strategy, the draft Human Health Risk Assessment Research Strategy, and the Ecological Research Strategy). The Air Toxics Research Strategy will identify the key scientific questions that need to be answered for risk assessment and management of air toxics from all emission sources and describe the research needed to answer them and, thereby, guide our research efforts.

1. Introduction

Since the enactment of the CAA Amendments of 1990, we have made considerable progress in reducing emissions of air toxics from major stationary sources through regulatory, voluntary and other programs. Our efforts to characterize, prioritize and address the impacts of HAP on the public health and the environment have resulted, or are projected to result, in large reductions in HAP emissions. However, the pollution sources addressed by our efforts so far account for only part of the air toxics problem.

Recently, EPA announced a Strategy that aims at reducing the health risks associated with air toxics exposures affecting populations in urban areas. In addition to addressing specific statutory requirements for area sources as outlined in section 112(k), the Strategy has the following goals:

- Attain a 75 percent reduction in incidences of cancer attributable to exposure to HAP emitted by stationary sources in urban areas nationwide;
- Attain a substantial reduction in public health risks posed by HAP emissions from area sources in urban areas nationwide;[1] and
- Address disproportionate impacts of air toxics hazards across urban areas.

By integrating activities and programs under different parts of the CAA, we expect to address more effectively the aggregate exposure to air toxics in areas where emissions and risks are most significant.

This Report responds to a requirement in section 112(k)(5) of the CAA that calls for EPA to submit a Report to Congress:

> *On actions taken under this subsection and other parts of this Act to reduce the risk to public health posed by the release of hazardous air pollutants from area sources. The reports shall also identify specific metropolitan areas that continue to experience high risks to public health as the result of emissions from area sources.*

Even though this Report is being released shortly after the publication of the Strategy, it provides further details on many of its key areas. For example, this Report contains a more detailed discussion of the research needs to be addressed as part of the Strategy. Also, the emissions inventory and methodology for the selection of the urban HAP are discussed more thoroughly here. Since the Strategy has not been implemented yet, we're unable, in this Report,

[1]Examples of area sources include hospital sterilizers, dry cleaners, and small publicly owned treatment works.

to identify specific metropolitan areas that continue to experience high risks to public health. Nevertheless, we are providing, in this Report, a summary of recent risk-based assessments in various urban areas. These assessments provide useful information on the potential nature and magnitude of exposures and health risks in urban areas.

The following sections will provide a glimpse of the main issues discussed in each chapter of this Report. Also, the Appendix gives key information about each of the urban HAP.

1.1 Characterization of Urban Air Pollution (Chapter 2)

The urban environment is very unique since the combination of high population densities and large concentrations of commercial activity provide the conditions conducive to high exposures and health risks as a result of the emissions of air toxics. Hazardous air pollutants are emitted from thousands of sources ranging from small commercial facilities to large industrial sources and also mobile sources. As the ambient concentrations of HAP in urban areas result from a combination of different sources (e.g., area, major[2], and mobile[3]) emitting many of the same pollutants, we need to consider contributions from all types of sources in order to achieve the reductions envisioned by Congress. The Strategy, described in detail in this Report, is that part of the overall air toxics program that specifically focuses on the urban environment. The Strategy will consider contributions from area, major, and mobile sources of HAP in addressing reductions in public health risks.

Chapter 2 provides general information on our current understanding of the urban environment and presents a summary of risk analyses that have been conducted over the past 10 years. Although it is not possible to draw any specific conclusions on current health risks, the data that are available today support our concern that potential problems exist in urban areas and suggest that we should continue our efforts to study the urban environment and to implement the Strategy this Report presents.

1.2 Emissions Inventory and Selection of the Urban Pollutants (Chapter 3)

Chapter 3 presents two very important components of the Strategy. The first is the baseline emissions inventory for 40 candidate HAP used to identify the final list of urban HAP. The baseline inventory quantifies the emissions of the candidate urban HAP and identifies the source categories that emit them. The second is the ranking methodology used to identify the final list of 33 priority urban HAP which are judged to present the greatest threats to public health in the largest number of urban areas.

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[2]Major stationary sources are sources that emit more than 10 tons per year of any one HAP or 25 tons per year of a combination of HAP. Examples include chemical plants, oil refineries, aerospace manufacturers and steel mills.

[3]Mobile sources include motor vehicles (e.g., cars and trucks), and off-road equipment (e.g., construction equipment and lawn mowers) and their fuels.

In developing the final HAP list, we estimated emissions from all known sources using a variety of techniques, evaluated available health effects information for the 188 HAP, assessed available air quality monitoring data, reviewed existing studies, and produced a list of pollutants based on the relative hazards they pose in urban areas, considering toxicity, emissions, and related characteristics. From this effort, we established a list of urban HAP which pose the greatest threats to public health in urban areas, considering emissions from major, area and mobile sources. Among these urban HAP are a subset of 30 HAP with the greatest emissions contributions from area sources (the "area source HAP"). The analyses leading up to the selection of these priority urban HAP are the focus of this chapter.

1.3 Regulatory Programs and Activities to Reduce Air Toxics Emissions (Chapter 4)

Chapter 4 presents the list of area source categories that were identified in the Strategy and explains how we intend to ensure that, as required, we reach the goal of addressing the source categories that represent 90 percent of the emissions of each of the 30 area source HAP. Also, this chapter describes the regulatory options that will be considered in order to address air toxics from area sources. The role of mobile sources is also noted in this chapter, and the current and future programs are described. Finally, a very important component of the Strategy is described in this chapter – the role of State, local and Tribal programs in helping us address air toxics and achieve the desired goals.

Chapter 4 describes the regulatory approaches to enable the emission reductions necessary to achieve the goals of the Strategy. We plan to pursue a tiered approach that will consider three standard-setting processes. The specific process selected for a particular source category will depend on the criteria outlined below:

- Tier 1 – Maximum achievable control technology (MACT) standard process;
- Tier 2 – Source category-specific generally available control technology (GACT) standard process; and
- Tier 3 – Flexible GACT process.

The Strategy outlined a timeframe for the completion of area source standards, as shown in the time line below:

- 2004 – Promulgate the area source standards newly listed in the Strategy; we'll attempt to meet this demanding schedule as expeditiously as practicable;
- 2006 – Promulgate some additional area source standards to meet the 90 percent requirement;

- 2009 – Promulgate all remaining area source standards necessary to meet the 90 percent requirement; and

- 2012 – Expected compliance under all standards.

We'll prioritize the order in which we regulate source categories to address those posing the greatest risks first.

Mobile sources and their role in the air toxics problem are also discussed in Chapter 4. Several of our existing emission control programs limit HAP emissions from mobile sources, primarily through the regulation of hydrocarbon (HC), oxides of nitrogen (NO_x) and particulate matter (PM) emissions. We achieve mobile source controls through a range of programs under various sections of the CAA, including motor vehicles controls, emission standards for nonroad engines and vehicles and urban bus standards. In addition, section 202(l)(2) of the CAA directs us to set standards for air toxics emissions from motor vehicles or their fuels, or both. Some of the current and future regulations and programs aimed at reducing HAP emissions from mobile sources are highlighted in this chapter.

1.4 Assessment of Progress Toward the Goals (Chapter 5)

The discussion of our assessment activities in this chapter first focuses on how we generally intend to assess progress in meeting the goals of the Strategy. We then discuss in more detail our methods and tools for estimating health risks and describe more specifically how we intend to apply these risk assessment methods and tools in assessing progress and in supporting implementation of the Strategy.

As we move from a focus on emissions reductions to a focus on estimated risks reduction, we note that Agency risk assessment and decisionmaking have historically focused on the likelihood of health effects associated with exposure to individual environmental contaminants. In recent years, our risk assessment emphasis has shifted increasingly to a greater consideration of multiple pollutants, endpoints, pathways and routes of exposure, and integrated reduction of risks. This more complex assessment is often called "cumulative risk assessment," defined according to who or what is at risk of adverse effects, from identifiable sources and stressors, through several routes of exposure over varied timeframes. While various integrated approaches are now being used within the Agency, we realize that there are significant gaps in methods, models and data that limit our ability to assess cancer and noncancer risks associated with cumulative exposure to mixtures of pollutants having different endpoints. Progress toward more refined assessments of cumulative risks will depend upon the pace and evolution of our policy and guidance on cumulative risk and the underlying research.

We've identified four basic approaches that we plan to use for various assessments to evaluate the progress of the Strategy in reducing estimated risks. Each of these approaches uses the same dose-response information, but relies on different types of data to represent exposures. The four basic approaches that we intend to use are:

- Emissions or ambient concentration weighting;
- Comparisons between ambient concentrations and risk-based concentrations (RBCs);
- Comparisons between estimated exposures and RBCs; and
- Quantitative estimates of carcinogenic risks for individuals and populations.

Each of these approaches is discussed in Chapter 5.

1.5 Research Needed to Address Knowledge Gaps (Chapter 6)

The purpose of Chapter 6 is to describe the types of scientific information and related research needed to better inform future risk assessment and risk management judgments that will be made in carrying out the Strategy. The research needs presented in this chapter are categorized into both short-term (less than five years) and long-term (greater than five years). These needs are organized around the risk assessment/risk management paradigm, first promulgated by the National Academy of Sciences in 1983. The needs are listed below:

Exposure Assessment Information Needs

Need 1. Improved ambient monitoring methods, characterization, and network design to support a national ambient air toxics monitoring network.

Need 2. Improved area source emissions estimation methodologies and spatial allocation methods.

Need 3. Methodologies that allow for identification and speciation of important HAP and their combustion and transformation products.

Need 4. A more accurate nonroad mobile source emissions characterization.

Need 5. Improved characterization of air toxics from trucks and improvement of modal emissions modeling capabilities for all vehicle classes.

Need 6. Development of source-based urban-scale air quality models for the urban HAP.

Need 7. An understanding of the distribution of human exposures (including susceptible subpopulations) and the pathways by which HAP reach humans.

Health Effects Information Needs

Need 8. Use alternative sources of human health effects data (chronic and acute) for urban HAP to develop and update dose-response assessments.

Need 9. Development of statistical and mode of action methods for developing acute and chronic dose-response assessments.

Risk Assessment and Risk Characterization Information Needs

Need 10. Improved risk assessment methods for mixtures.

Need 11. Development of better information for more effective techniques for communicating the results of health risk assessments for urban HAP.

Risk Management Information Needs

Need 12. Identification of processes contributing to the HAP emissions from area source categories, and listing of control options and pollution prevention alternatives for these processes.

Need 13. Identification of pollution prevention alternatives for HAP emissions from mobile sources.

Each of these needs for further research are discussed in Chapter 6.

2. Characterization of Urban Air Pollution

2.1 Introduction

The urban environment is unique in many ways. In urban areas, you will find a mix of chemicals and their sources in close proximity to diverse populations, leading to large numbers of people being exposed to the emissions of many HAP from many sources. While urban exposures to some pollutants may be fairly similar across the country, studies in a number of urban areas indicate that exposures and associated risks may vary significantly from one urban area to the next. Recognizing this, Congress instructed us to develop a strategy for air toxics in urban areas that includes specific regulatory actions addressing the large number of smaller, stationary sources (i.e., area sources), and which also contains broader risk reduction goals encompassing all stationary sources. Specifically, section 112(k)(1) of the CAA states:

> *The Congress finds that emissions of hazardous air pollutants from area sources may individually, or in the aggregate, present significant risks to the public health in urban areas. Considering the large number of persons exposed and the risks of carcinogenic and other adverse health effects from hazardous air pollutants, ambient concentrations characteristic of large urban areas should be reduced to levels substantially below those currently experienced.*

As the ambient concentrations of HAP in urban areas result from a combination of different sources (i.e., area, major, and mobile) emitting many of the same pollutants, we need to consider contributions from all types of sources in order to achieve the reductions envisioned by section 112(k). The Strategy presented in the July 19, 1999 *Federal Register* (U.S. EPA, 1999a), and discussed in this Report, is a part of our overall national effort to reduce toxics but with a specific focus on the urban environment. The Strategy will consider contributions from area, major, and mobile sources of HAP in addressing reductions in public health risks.

This chapter is intended to provide general information on our current understanding of the air quality in the urban environment, to present a summary of risk analyses that have been conducted over the past 10 years, and to provide the basis for our continuing support for an urban program that will enhance our understanding of the urban environment and provide the strategy for protecting the health of the public.

2.2 What Do We Know About HAP?

Section 112(b) of the CAA identifies 188 chemicals as HAP[1]. They include pollutants like benzene, perchloroethylene, methylene chloride, heavy metals like mercury and lead, polychlorinated biphenyls (PCBs), dioxins, and some pesticides. More than half of the HAP are known or suspected to be human carcinogens. In addition, many are known to affect the

[1]Caprolactam was delisted on June 18, 1996 (61 FR 30816)

respiratory, neurologic, immune, reproductive, or developmental systems, particularly for more susceptible or sensitive populations, such as children. Hazardous air pollutants are also known to cause adverse effects in many species (e.g., toxicity in fish or reproductive decline in bird species), including endangered species. These environmental effects may impact individual species within a single level of the food chain or the entire ecosystem where multiple species are affected.

Health concerns result from both short- and long-term exposures. Some health problems occur very soon after a person inhales a toxic air pollutant (i.e., from a short-term exposure). These immediate effects may be serious, such as life-threatening lung damage, or they may be minor. Health problems which are usually associated with long-term exposures may develop slowly over time or may not appear until many months or years after a person's first exposure to the toxic air pollutants (e.g., cancer). Depending on their characteristics (e.g., vapor pressures and atmospheric transformation rate), HAP may disperse locally, regionally, nationally, or globally and may deposit in the environment and in some cases, bioaccumulate in the food chain.

2.3 What Do We Know About HAP Emissions?

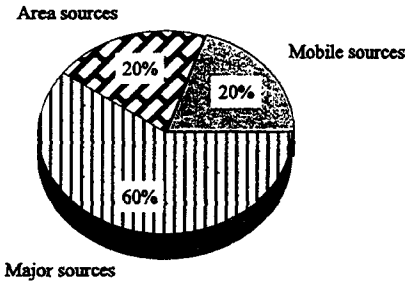
Hazardous air pollutants are emitted from a variety of stationary sources of varying sizes and from mobile sources. Emissions data, along with specific information about the emitting sources (e.g., the height and location of the emissions release points, size of emitting facility, local meteorology), may be used as inputs to computer models. These models generate estimates of ambient HAP concentrations in areas surrounding a source. Although these concentrations are not estimates of personal exposure and risk, an understanding of these emissions and their sources is necessary when preparing a strategy for dealing with associated risks to public health and the environment.

For this reason, we developed the National Toxics Inventory (NTI). The NTI contains emissions data for major, area and mobile sources. The data for the NTI have been gathered from EPA (i.e., MACT development data and the Toxic Release Inventory, or TRI[2]), State, and

[2]Section 313 of the Emergency Planning and Community Right-To-Know Act (EPCRA) and section 6607 of the Pollution Prevention Act (PPA) mandate a publicly accessible database containing information on the release and other waste management activities of toxic chemicals by facilities that manufacture, process, or otherwise use them. The EPCRA specifically requires manufacturers to report releases of more than 600 designated toxic chemicals to the environment. The reports are submitted to the EPA and State governments. The EPA compiles these data in an on-line, publicly accessible national computerized TRI. More information about the TRI database is available at the following website: http://www.epa.gov/opptintr/tri/.

local studies and databases. A baseline year NTI[3] has been developed and estimates emissions at the county level. According to this inventory, approximately 8.1 million tons of air toxics were released annually (during the 1990 to 1993 timeframe) to the air nationwide with approximately 6 million tons being released annually into urban areas[4]. Exhibit 2-1 provides a breakdown of the total, national emissions by source.

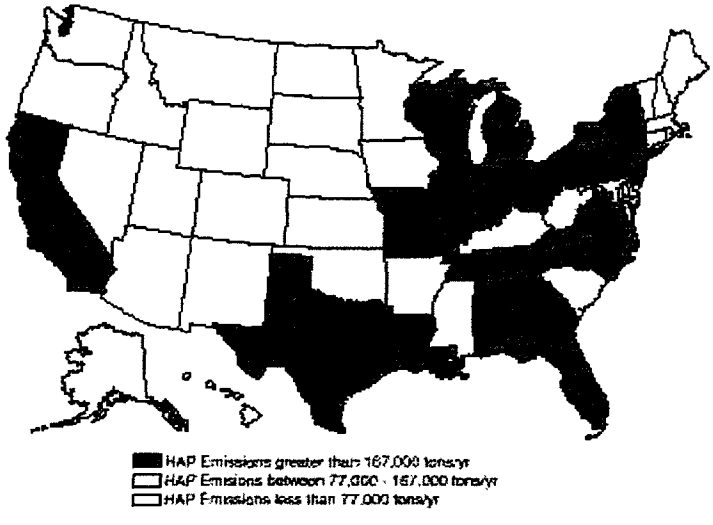
EXHIBIT 2-1
HAP BASELINE NTI
EMISSIONS BY SOURCE



Adapted from Trends Report (EPA, 1998)
Representative of 1990 - 1993 period

Although the level of specificity of this inventory is insufficient for drawing conclusions about population exposure levels in individual urban areas versus rural areas, these data show that the largest emissions are found in those States which are highly industrialized and contain some of the largest urban areas in the country. Exhibit 2-2 (taken from 1997 Trends Report (EPA, 1998)) illustrates the distribution of HAP baseline emissions by State. While these national-level emission estimates are useful for describing general trends, they do not necessarily reflect the specific situation that may exist in specific urban areas where a wider variety of HAP are emitted. This is particularly important because some pollutants which individually would not be expected to present harm, may work together as a mixture resulting in a potential for harm. Thus, depending on exposure levels

EXHIBIT 2-2
HAP EMISSIONS BY STATE BASED ON 1993 NTI



[3]The baseline NTI that we have compiled over the past few years is representative of the years 1990-93.

[4]In estimating the amount of emissions from urban areas, we have totaled emissions from all U.S. counties that include a metropolitan statistical area with a population greater than 250,000 or for which more than 50 percent of the population has been designated "urban" by the U.S. Census Bureau. For a more detailed description of emissions allocation among urban and rural areas, see the technical support document for the emissions inventory which is available through the public docket (Docket No. A-97-44).

and characteristics of the pollutants, multiple pollutant exposures which may be more prevalent in urban populations may pose increased public health risks.

An updated version of the NTI containing emission data from 1996 is currently being developed. This 1996 NTI will be our first effort to estimate HAP emissions from all sources on a national scale and to associate with them source-specific parameters necessary for modeling. Important modeling parameters include location and facility characteristics which describe the emission points (e.g., stack heights, stack exit velocities, emission temperatures). This new inventory will have greater utility for assessing trends in emissions, for providing data in sufficient detail to perform regional, urban, and local level air quality and exposure modeling assessments, and to monitor progress on risk reductions.

Emissions data such as the NTI provide useful estimates of emissions in outdoor air, but they do not reflect the levels of HAP that exist in many indoor air environments. It is estimated that most people spend as much as 80 to 90% of their time indoors[5]. This is of particular concern because over the past several decades, exposure to indoor air pollutants is believed to have increased due to a variety of factors, including the construction of more tightly sealed buildings, reduced building ventilation rates (to save energy), the increased use of synthetic building materials and furnishings, and the increased use of chemically formulated personal care products, pesticides, and household cleaners. Our current lack of understanding of the nature of indoor sources of HAP and our limited information on the movement of air between the outdoor and indoor environments leave a gap in our ability to more completely characterize human exposures, especially in urban areas[6].

2.4 What Do Monitoring Data Tell Us?

Monitoring data provide information about the ambient levels of HAP in specific areas and generally represent a snapshot of what HAP are present. These data, like modeled ambient concentration data, may provide information about the potential for exposure and risk. When monitoring data are used, however, the ability to identify the particular emitting source may be lost unless the placement of the monitor allows for the detection of HAP contributions from uniquely identifiable sources. Where the source or sources contributing to the monitored HAP levels are not known, the monitored HAP levels may be considered to be a background concentration[7]. In these cases, background concentration data may provide a comparison and/or

[5]An analysis of human activities published in 1996 reported that people spend as much as 69% of their time in personal residences with an additional 18% of time being spent in other indoor environments (EPA, 1996).

[6]More information on indoor air quality may be obtained at the following website: http://www.epa.gov/iaq.

[7]The concentration of HAP present in the ambient air that is not solely attributable to a specific or identifiable source being studied. For example, a monitor may detect HAP emissions from stationary, mobile, or nonanthropogenic sources while the source being modeled (i.e., the source of the emissions data being used) is a stationary source.

a context concentration for ambient HAP levels estimated by modeling. In other cases, background concentration data for a specific HAP may be added to the ambient HAP levels estimated by modeling to account for known HAP sources not considered in the modeling analysis. This may be done for HAP such as formaldehyde because of its ability to be formed by the direct chemical transformation[8] from other HAP in the air (see Section 2.6 of this Report for more detailed discussion of transformation).

Currently, there is no national ambient air quality monitoring network designed to measure the ambient levels of HAP in the environment. The data we have available nationally come from monitoring that is done under programs like the Photochemical Assessment Monitoring Stations (PAMS) program, the $PM_{2.5}$ monitoring network, and from the many voluntary State monitoring programs. The ambient air monitoring information collected by States in certain metropolitan areas provides us with a limited understanding of HAP ambient concentrations in urban areas. Data collected during the 1990's demonstrate elevated concentrations of several HAP in urban areas across the country. For example, a limited evaluation of the subset of HAP monitored indicate the presence of HAP in some cities which, when evaluated cumulatively, is suggestive of upper bound estimates of additional, lifetime cancer risks at or above 1 in 10,000[9]. Comparisons of estimated concentrations to RBCs can provide indicators of a potential public health problem but should not be considered a characterization of actual health risks.

2.5 What Do We Know About Urban Populations?

A unique feature of urban areas is the proximity of many stationary and mobile sources and their pollutants to each other and to the populations which live or work in these areas. According to a 1997 report on population (U.S. Department of Commerce, 1997), approximately 212 million people (including 57 million children) or 80% of the estimated 1996 U.S. population live in metropolitan areas. This estimate represented a gain of 13 million people in these areas since the 1990 census estimate. Given (as described earlier) that the largest levels of HAP emissions are found in those States which contain some of the largest urban areas, we seem to have mixtures of HAP and increasingly high density populations existing together in urban areas.

The issue becomes complex when other population factors such as age, socio-economic status, proximity to emitting sources, decreased health and nutrition status, and lifestyles are considered because it is known that these factors may lead to increased sensitivity and

[8]An air contaminant may undergo a chemical change in the atmosphere as it either breaks down or reacts with other chemicals. The pollutants that are formed as a result of this transformation process may be more or less toxic than the pollutants originally released.

[9]The technical support documentation for this assessment analysis is available from the public docket (Docket No. A-97-44) and includes a presentation of ambient monitoring data in 17 cities for a variety of HAP. Also presented are the upper bound estimates of excess cancer risks associated with continuous lifetime exposures at those concentrations.

susceptibility to the effects of HAP exposures. Within the general population, children, for example, are likely to have additional susceptibility and vulnerability to HAP exposures because of their daily activities, their immature or developing metabolic systems, or their developing organ systems. In addition, the poverty factor (over 20% of the urban population consists of children in poverty (U.S. Department of Commerce, 1997)) increases their vulnerability because they are more likely than other children to lack sufficient nutrition and access to health care.

In conducting an assessment that considers the population (i.e., an exposure assessment), models are used to characterize population exposures based on ambient concentration data (derived from modeling or monitoring). Specific population exposure factors such as the location of various populations, population demographics, and group activity patterns[10] when coupled with HAP toxicity information provide a clearer picture of how, when, and for how long people are exposed to HAP and what their potential risks may be. These are a few of the many aspects that are considered when evaluating public health risks from HAP in urban areas.

2.6 Characterization of Air Toxics in Urban Areas

As discussed above, different types of information may be useful for characterizing the urban environment. In this Report, we have focused on nine risk-based assessments performed by EPA and various States over the past ten years. Although some general similarities are evident across these assessments, the identity and concentration of air toxics may vary significantly from one city to the next depending on the particular sources present (or dominant), the substances emitted, the local meteorology, and other factors. It should be noted that most of these studies were based upon the situation that existed in urban environments up to ten years ago. Given our current, national information, the situation is likely to have improved. That notwithstanding, the summaries contribute to our understanding of the potential nature and magnitude of exposures and health risks in specific urban areas and to the pollutants and sources contributing to those exposures and risks.

To put these assessments in perspective, it is useful to first discuss some of the uncertainties that were inherent in these assessments because of the lack of information at the time or because of the way these assessments were designed. We can evaluate uncertainties from the perspective of what we don't know or what wasn't considered in the analysis. For example, most of these assessments did not consider risks from endpoints other than cancer, pathways other than inhalation, or exposures other than long-term. The potential exposure to HAP for which we have little or no health data was assumed to have resulted in no adverse health effects. These uncertainties are not quantifiable but are our reason to err on the side of conservatism when it comes to interpreting the different assessments. The other side of the uncertainty question (i.e., what we do know now that we didn't know then) may have quantifiable effects.

[10]The movement of people through different daily micro-environments as they participate in various activities. For example, being in an indoor or outdoor environment, or riding in a car are a few of micro-environments to consider in an exposure assessment.

One HAP, 1,3-butadiene, was identified as a very common urban HAP responsible for much of the estimated risk seen in these assessments. Currently, we are reevaluating the cancer potency value, and it is likely that the potency value will decrease (i.e., the potency will likely be lower than what was used in these assessments). This is important to keep in mind because many of the assessments highlighted this HAP as being a major contributor to risk levels[11].

Uncertainty is also present when various policy assumptions are used in deriving cancer risk estimates. In most of these assessments (as well as many current screening assessments), measurements and estimates of air concentrations are used, with the assumption of a lifetime exposure to these concentrations, to calculate upper-bound estimates of an individual's lifetime increased cancer risk from each pollutant. Upper-bound estimates are used in order to avoid underestimating the true value. The true value may, however, be lower than the estimate and may, in fact, be zero. The upper-bound estimates for each HAP are summed to obtain a worst-case estimate of individual lifetime increased cancer risk resulting from exposure to the mixture of HAP. For each of the studies described below, these worst-case estimates were on the order of a 1 in 10,000 chance of getting cancer for someone exposed continuously over a 70-year lifetime[12]. For substances that are not thought to cause cancer, air concentration estimates are compared to concentrations considered unlikely to be harmful. These rough worst-case estimates are used to identify those HAP posing the greatest likelihood of harm. For these nine assessments, it must be kept in mind that other HAP which may have been present in the urban air, and for which toxicity information was insufficient for the risk assessments, were excluded from these calculations.

Additionally, not all possible HAP were considered in these assessments because HAP selected usually met one or more of the following conditions: they were known or suspected to be present in urban air, they were suspected to be important contributors to health risk based on knowledge of their toxicity (most urban air studies to date have focused primarily on pollutants either known to cause cancer in humans or for which test data are less conclusive yet provide an indication of a potential to cause cancer), and/or there were available data on their emissions or ambient concentrations. Pollutants that have been commonly studied in urban areas include arsenic, benzene, 1,3-butadiene, cadmium, carbon tetrachloride, chromium, ethylene dichloride, formaldehyde, methylene chloride, perchloroethylene, polycyclic organic matter (POM) (which

[11]The review and revision of data (resulting in revised unit risk and reference values) for the HAP in these studies, (e.g., 1,3-butadiene) and for the other HAP not included in these studies is an ongoing process. It is likely that the results of the studies described here would be different had these results been reevaluated. Future assessments will have the benefit of the most current health effects data.

[12]As described in Chapter 5 of this Report, our assessment approach will be generally iterative in nature, so as to take advantage of emerging science, new data, and improved tools that become available at the time future assessments are performed, (e.g., with better emissions and exposure data, our exposure estimates will be more central tendency than upper bound). The resulting risk characterizations in these future assessments should reflect this shift in data quality.

include polycyclic aromatic hydrocarbons and certain other chemicals that have multiple benzene rings that are emitted as products of incomplete combustion), and trichloroethylene. Each of these pollutants has been evaluated in multiple major studies of urban air, including the nine assessments discussed below. Benzene and formaldehyde were evaluated in all nine of the studies.

These assessments relied on source inventories that were created much earlier than the assessments. Although a variety of sources were identified and assessed in different urban areas, no attempt was made to identify all of the possible, specific sources of emissions. The particular emission sources of concern can vary widely from one city to the next, and many of these assessments concentrated only on what were thought to be the largest sources or only on one type of source (e.g., area sources). Today's inventories have reduced the potential uncertainty in this area because more source data are available and have been included in the recent NTI (discussed previously). These data which include area, major, and mobile source data will be used in future urban risk assessments.

Emission estimates (i.e., inventories) do not consider that some HAP may disperse over great distances (mercury, for example, may disperse globally). This type of HAP dispersion or long-range transport would be of particular concern for HAP that have longer half-lives or which may persist in the environment for a longer time. In the case of persistent HAP, re-volatilization or resuspension of a deposited HAP may continue the transport of that HAP to more distant locations. When developing an emissions inventory (i.e., a list of sources emitting HAP of interest or concern), it is not always possible to consider sources that are too distant from the geographic areas of interest. This may lead to an underestimate of the ambient HAP concentrations predicted by modeling (dispersion models typically limit the ambient concentration estimates calculated to a 50 kilometer (approximately 30 mile) radius around an identified source). This is less of an issue when monitoring data are used as the basis for the ambient HAP concentrations because monitors detect HAP regardless of their sources or their distance from the monitor. The inventories developed for the urban assessments discussed below did not consider the long-range transport of the HAP of interest into the geographic areas of study.

The inventories developed for these assessments, also, did not consider the potential effects of atmospheric transformation. An air contaminant may undergo a chemical change in the atmosphere as it either breaks down or reacts with other chemicals. The pollutants that are formed as a result of this transformation process may be more or less toxic than the pollutants originally released. Just as some contaminants may degrade to less harmful chemicals, sometimes relatively innocuous airborne chemicals may combine with other chemicals in the atmosphere to form HAP (e.g., the formation of formaldehyde (a HAP) from the chemical reaction among the components of "smog" and isoprene, a less harmful chemical). Transformation in the atmosphere may occur as the chemicals are dispersed and transported from an emitting source. If the transformation process is not considered or only partially considered (by adding some "background value," as some of the urban assessments did), the significance of this

on the final result must be part of the evaluation process when considering the results of these assessments.

None of the urban assessments discussed below considered specific sub-populations (i.e., populations that may be more susceptible or vulnerable to HAP exposure) in their calculations of potential risks. In addition, these assessments, with the exception of the Mobile Vehicle Study, did not project changes in those aspects of daily lives that will continue to change the profile of emissions and exposures especially in urban areas. For example, the number of miles traveled by commercial and private vehicles nationally from 1990 to 1996 increased by approximately 310 billion miles (an average increase of 52 billion (2.5%) vehicle miles traveled (VMT) per year) (U.S. Department of Transportation, 1998). If the change in the U.S. population during this time is considered (248.7 to 265.3 million people, respectively (U.S. Department of Commerce, 1997)), the increase in VMT is not due solely to a population increase but to an increase in the number of miles "each person" traveled. This becomes an important factor when the overall results of many of the urban assessments point to mobile sources and their HAP as contributing to potential urban area risks.

In general, for each of the assessments discussed below, outdoor HAP concentrations (estimated using computer modeling projections or ambient air monitoring) were used to represent potential human exposures. When combined with simplifying assumptions that can lead to either under- or overestimates of risk, researchers were able to reach conclusions about the chemicals, and in some cases the air pollution sources, that seem to contribute the most to risks from urban air pollution. In these assessments (e.g., benzene, 1,3-butadiene, and formaldehyde were consistently shown to be most responsible for the higher risk estimates), the studies identified all three major source categories (area, major and mobile sources) as contributing emissions and potential risks in urban areas, and they presented estimates of increased individual lifetime cancer risks from air toxics from multiple sources across the studies that ranged from 3 in 1,000 to 2 in 1,000,000 (with a median of 1 in 10,000) (although the true risks could be higher or lower[13]). While providing useful information on the potential nature and magnitude of health risks in urban areas, these assessments are limited by the lack of exposure information and by the incompleteness of our knowledge regarding the range of health effects associated with any additional HAP that may be found in urban environments. The nine assessments listed in Exhibits 2-3 and 2-4 are summarized below.

[13]The design of each of the studies discussed included assumptions described as conservative or worst case. In these cases, the incidence values presented within the context of each study may overestimate the true incidence. Conversely, the limitations of the study designs and assumptions (i.e., these studies did not consider pathways of exposure other than inhalation, exposures other than long term, risks from other HAP present in these study areas or their potential synergistic interactions) leave open the possibility that the incidence values presented may underestimate the true risk.

EXHIBIT 2-3
RISK-BASED ASSESSMENTS COVERING URBAN AREAS

Risk-based Assessments	Abbreviated Name
U.S. EPA, 1989. *Analysis of Air Toxic Emissions, Exposures, Cancer Risks and Controllability in Five Urban Areas.* This study was designed to define the multisource, multipollutant nature of the urban air toxics problem and determine what control measures can best be employed to mitigate the problem.	*Five City Study*
Engineering-Science, 1990. *The Transboundary Air Toxics Study: Final Summary Report.* Risk assessment to evaluate the source types and pollutants which contribute to increased cancer risk from air pollution in the Southeast Michigan/Windsor-Sarnia area.	*Transboundary Study*
MPCA, 1992. *Estimation and Evaluation of Cancer Risks from Air Pollution in the Minneapolis/St. Paul Metropolitan Area.* Study by the Minnesota Pollution Control Agency to analyze sources of HAP suspected or known to cause cancer, and to estimate the health risk from exposure to these pollutants.	*Twin Cities Study*
U.S. EPA, 1993b. *Staten Island/New Jersey Urban Air Toxics Assessment Project: Summary of the Project Report.* Assesses risk to Staten Island residents from ambient air pollutants and generates an inventory of major, area and mobile sources to qualitatively examine sources of high risk and high observed concentrations.	*Staten Island Study*
U.S. EPA, 1993a. *Motor Vehicle-Related Air Toxics Study.* Summarizes what is known about motor vehicle-related air toxics.	*Motor Vehicle Study*
U.S. EPA, 1994. *A Screening Analysis of Ambient Monitoring Data for the Urban Area Source Program.* Summarizes currently available ambient monitoring data sets for HAP from various urban areas in the U.S. and estimates the risks associated with these HAP.	*Ambient Monitoring Study*
ENSR, 1995a, b, c. *Arizona Hazardous Air Pollution Research Program.* Risk assessment to determine which HAP and sources should be the focus of future research and control strategies in Arizona.	*Arizona Study*
TNRCC, 1996. *Houston Area Source Toxics Emissions Project.* Risk assessment to determine which HAP from area sources should be focused on for future research and control strategies in Houston.	*HASTE Study*
Woodruff et al., 1998. *Cumulative Exposure Project.* Assessment which compared modeled ambient air concentration estimates with health benchmarks for 148 HAP nationwide.	*CEP*

EXHIBIT 2-4
OVERVIEW OF ASSESSMENTS

Study	Approach		No. Air Contaminants Studied	Location	Health Effects Evaluated
	Hazard Assessment	Ambient Monitoring			
Five City Study	✔		23	5 unspecified cities	Cancer
Transboundary	✔		57	Southeast Michigan/Windsor-Sarnia area	Cancer
Twin Cities Study	✔		29	Minneapolis/St. Paul metropolitan area	Cancer
Staten Island Study	✔	✔	40	Counties in NJ and NY[a]	Cancer, Noncancer
Motor Vehicle Study	✔		4[b]	U.S. locations	Cancer
Ambient Monitoring Study	✔	✔	195[c]	40 U.S. locations	Cancer, Noncancer
Arizona Study	✔	✔	163[d]	Phoenix, Tucson, Casa Grande, and Payson, AZ	Cancer, Noncancer
HASTE Study	✔	✔	40	Harris County, TX	Cancer, Noncancer
CEP	✔		148	National assessment	Cancer, Noncancer

[a] Middlesex and Union Counties in New Jersey and Staten Island in New York for area and mobile sources, with the addition of Monmouth, Essex, and Hudson Counties in New Jersey and Brooklyn (Kings County) in New York for major sources.
[b] Study included four HAP and three mixtures (diesel and gasoline particulates and gasoline vapors).
[c] Monitoring data available for 195 air contaminants, but assessment focused on 93 HAP for which health effects data were available.
[d] Of the 163 possible contaminants, 25 chemicals of interest were selected for each of the four regions.

Five City Risk Assessment

This assessment, published in 1989, was done to help characterize the multisource, multipollutant nature of the urban environment (U.S. EPA, 1989). A base year emissions inventory was compiled for each of five, unspecified cities from a number of different data sources and included inventories representing point, area, and mobile source emissions. The base year nominally represents 1980 but selected source updates

Five City Study

Time Period Covered: 1980 – 1987

Top HAP Contributing to Predicted HAP-Related Cancer Risk: POM, 1,3-butadiene, formaldehyde, benzene, and chromium

Individual Lifetime Cancer Risk Estimates: Ranged from 2×10^{-4} to 7×10^{-4} (two to ten excess cancer cases per year across the five cities)

were included so that the inventory was actually more reflective of the 1980 to 1985 timeframe. Emissions and source data were modeled to estimate annual average ambient HAP concentrations for all 23 HAP included in this assessment. Monitoring data for formaldehyde were included in order to calculate estimates of formaldehyde ambient concentrations that were due to atmospheric transformation[14]. The ambient data for all HAP were then converted to estimates of individual, lifetime cancer risks and incidence by applying the cancer unit risk factors that were available at that time. The individual lifetime cancer risks ranged from 2×10^{-4} to 7×10^{-4} and provided an estimate of the multisource, multipollutant contribution to exposure for the entire study area. This assessment did not consider routes of exposure other than inhalation nor endpoints other than cancer.

Transboundary Study

Transboundary Study

Time Period Covered: 1980 – 1989

Top HAP Contributing to Predicted HAP-Related Cancer Risk: Formaldehyde, coke oven emissions, 1,3-butadiene, carbon tetrachloride, chromium, POM, dioxins

Individual Lifetime Cancer Risk Estimates: 9×10^{-5} or five cancer cases per year over total study area

This assessment was initiated to prepare an emissions inventory that through risk assessment would help define the relative contributions of various source types to the risk estimated in the urban transboundary area (Southwest Michigan/ Windsor-Sarnia area) (Engineering-Science, 1990). The pollutants chosen were "generally substances known to be atmospherically deposited in this region, substances known to pose carcinogenic risk or other substantial human health risk, or both." Of the 57 pollutants chosen, inventories for 42 were identified. These inventories were not designed to cover all possible sources but rather only the largest contributors to overall emissions for each of the pollutants. They did consider area, point, and mobile sources. Only data between the years 1980 and 1989 were considered with the target year being 1985. Background concentrations and local ambient concentrations due to long-range transport were assumed to be zero, with two exceptions. The background concentration levels for formaldehyde and carbon tetrachloride were assumed to be $2.2 \mu g/m^3$ and $0.8 \mu g/m^3$, respectively. These background concentration estimates were combined with modeled ambient concentration estimates for these HAP.

The individual, lifetime excess cancer risks in this study was 9×10^{-5}. This translates into an estimated total cancer incidence of approximately 373 cases over 70 years or five cases per year. Over 90% of these resulted from exposure to seven pollutants: formaldehyde, coke oven emissions, 1,3-butadiene, carbon tetrachloride, chromium, POMs, and dioxin; with more than 50% being attributed to formaldehyde and carbon tetrachloride alone. The contribution of the additional "background" concentrations to these latter results was not discussed, but the added

[14]Modeled ambient concentrations were subtracted from ambient values derived from monitoring to yield that portion of the ambient concentration due to the atmospheric transformation of other chemicals to formaldehyde.

background may have played a role in their higher contribution to overall incidence. No attempt was made to include other routes of exposure or effects other than cancer in this assessment.

Twin Cities Study

> ***Twin Cities Study***
>
> **Time Period Covered:** Completed in 1992
>
> **Top Air Contaminants Contributing to Cancer Risk:** Diesel, gasoline, and wood-stove particulate emissions, formaldehyde, benzene, 1,3-butadiene
>
> **Individual Lifetime Cancer Risk Estimates:** $2x10^{-4}$ (2 cancer cases per year per million over study area)

The purpose of this assessment was to analyze sources of HAP suspected or known to cause cancer and to estimate the cancer risks resulting from exposure to these HAP (MPCA, 1992). Emission inventories were developed for point, area, and mobile sources, and modeled to estimate the ambient concentrations of 29 pollutants and three different POM mixtures (diesel, wood-stove, and gasoline particulates). This assessment developed estimates of increased lifetime individual and population risks in the Minneapolis/St. Paul metropolitan area, but did not estimate maximum risks. The results yielded an estimated individual lifetime cancer risk of 2 x 10^{-4} over the entire study area. This may result in an estimated two excess cancer cases per year per million residents. Overall, 61% of the excess incidence may be attributed to road vehicles which contributed gasoline and diesel particulates (including POMs) as well as formaldehyde, benzene, and 1,3-butadiene. Wood stoves and fireplaces were also an important source is this area, accounting for 17% of the incidence. It was concluded that mobile sources and area sources were the dominant contributors to risk in this assessment, but it should be noted that the assessment area did not include some of the major point sources that are present near the study area. Noncancer endpoints, risks due to background concentrations, or risks due to routes of exposure other than inhalation were not considered in this study.

Staten Island Study

> ***Staten Island Study***
>
> **Time Period Covered:** October 1987 – September 1989 for ambient air (plus July 1990 – March 1991 for indoor air)
>
> **Top HAP Contributing to Risk:** Benzene, arsenic, chromium, nickel, cadmium, formaldehyde
>
> **Individual Lifetime Cancer Risk Estimates:** 1 x 10^{-4} (1 excess cancer case per year per million)
>
> **Noncancer Effects:** HI > 2 for both respiratory and hematopoietic effects

This ambient monitoring-based assessment estimated the increased risk of cancer and noncancer effects in Middlesex and Union Counties in New Jersey, and in Staten Island (Richmond County) in New York (U.S. EPA, 1993b). Monitoring data were collected from October 1987 to September 1989. A total of 40 pollutants were monitored but only 20 had adequate toxicological data to use for the risk assessment. The study found that lifetime cancer risk estimate was approximately 1 x 10^{-4} or one to two excess cancer cases per year per million population. As in other studies, only

inhalation risk was considered. This study did include an evaluation of noncancer effects as well. A hazard index (HI)[15] of two was estimated for the respiratory tract as the target (chromium and nickel) and also for the blood (hematopoietic) system (benzene).

Motor Vehicle Study

In 1993, EPA published the assessment of risks due to motor vehicles and their fuels beginning in 1990 and projecting out to 2010 (U.S. EPA, 1993a)[16]. The assessment focused on the emissions of benzene, formaldehyde, 1,3-butadiene, acetaldehyde, and a group of mixtures (diesel and gasoline particulates and gasoline vapors) and on the assessment of carcinogenic risk. It used exposure to carbon monoxide (CO) as a tracer for toxic exposures and used the relationship between CO emission factors and toxic emissions factors to estimate toxic emissions. Monitoring data were used to evaluate the modeling results, and modeled concentrations were adjusted to match the upper end of the monitored data. This assessment focused on eleven urban areas and two rural areas, but the results were extrapolated to the entire Nation using population data beginning in 1990. From 1990 to 2000 (projections), predicted cancer incidence or deaths decreased for all HAP. During the years 2000 to 2010, the projected estimates associated with 1,3-butadiene increased. Increases in the cancer incidence projected for those later years were attributed to projected increases in the number of VMT for those later years. It was also shown that for each HAP studied, the urban incidence accounted for over 80% of the total (i.e., 80% of the total number of cancer deaths was due to exposure levels in urban vs. rural areas).

Motor Vehicle Study

Time Period Covered: 1990 projected to 2010

HAP Studied: Benzene, 1,3-butadiene, formaldehyde, acetaldehyde, diesel particulates, gasoline particulates

Estimated Cancer Deaths Per Year or Incidence:

For year:	1990	2000	2010
Benzene	70	35	35
Formaldehyde	44	21	22
1,3-Butadiene	304	176	204
Acetaldehyde	5	3	3

[15]The sum of hazard quotients (HQs) for multiple chemicals where the HQ is the ratio of a level of exposure for a single substance to a reference level (e.g., a reference concentration) for that chemical derived from a single exposure. An HQ or HI greater than one usually suggests that additional, more refined, analysis may be warranted.

[16]It is important to note that since the completion of this study, EPA has promulgated or proposed a number of programs that are expected to significantly reduce air toxics emissions in the future, including our reformulated gasoline (RFG) program, the national low emission vehicle (NLEV) program, Tier 2 motor vehicle emissions standards and gasoline sulfur control requirements, and our recently proposed heavy-duty engine and vehicle standards and on-highway diesel fuel sulfur control requirements. As discussed in Chapter 4 of this Report, EPA is updating estimates of motor vehicle toxic emissions and exposure (EPA, 1999b).

Ambient Monitoring Study

> ***Ambient Monitoring Study***
>
> **Time Period Covered:** 1986 – 1993 (individual studies varied from a few months to multiple years)
>
> **Air Contaminants Studied:** 195 detected, 93 with health reference values: 1,3-butadiene, benzene, formaldehyde, acrolein, 1,2-dibromoethene, and manganese were more consistently ranked among the top with respect to health concerns
>
> **Individual Lifetime Cancer Risk Estimates:**
> 1,3-butadiene: 2×10^{-3} to 5×10^{-4}
> benzene: 2×10^{-4} to 1×10^{-5}
> formaldehyde: 1×10^{-4} to 2×10^{-5}
>
> **Noncancer Concern:** Acrolein, 1,2-dibromoethene, manganese

This assessment summarizes the analyses of ambient monitoring data obtained from 16 monitoring studies some of which were collecting data since 1987. They represented over 40 urban areas and 195 air contaminants (U.S. EPA, 1994). Risk was calculated for only 93 contaminants (most of which are listed as HAP in section 112(b) of the CAA) for which health effects data required for risk assessments were available. For each site, a long-term average concentration was calculated and then applied to health reference values to estimate lifetime excess cancer risks and potential noncancer health effects for each. Because the data were derived from monitoring studies rather than modeling, no discussion of potential sources was included in the report. No estimates of population risks were made nor were routes of exposure other than inhalation considered.

With respect to cancer risks, 1,3-butadiene possessed the highest estimated individual risk among all pollutants. Estimates for benzene and formaldehyde also ranked consistently near the top. Acrolein, 1,2-dibromoethene, and manganese exhibited exceedances of noncancer reference values more consistently than other contaminants. However, there were gaps in the data presented. For example, not every contaminant was detected in every area due to variations in the methodologies used in the different studies. The data, however, do provide a snapshot view of urban areas with respect to contaminant concentrations and their potential to pose health risks of concern.

Arizona Study

This assessment examined cancer and noncancer risks posed by air pollutants in four areas of Arizona (Phoenix, Tucson, Casa Grande, and Payson) and was designed to evaluate the existing risk to public health and to provide options and recommendations for programs to control releases (ENSR, 1995a, 1995b, 1995c). These regions were assumed to represent a large fraction of the State's population and were characteristic of many of the types of communities in the State. Monitoring of the selected HAP was done primarily in residential neighborhoods.

About 25 HAP of "greatest concern" were selected for each region. Half of the estimated cancer risks for air pollutants was caused by 1,3-butadiene. Other significant contributors included benzene and formaldehyde. Acrolein was identified in all four regions as the HAP most likely to pose health risks other than cancer. Smaller likelihoods of noncancer risks were attributed to acetaldehyde, benzene, and manganese. Motor vehicles were found to be the largest contributor to estimates of cancer risks from HAP in three of the four areas. Non-inhalation pathway risk was determined not to be of significance in any region studied.

Arizona Study

Time Period Covered: 1990 – 1995

Top HAP Contributing to Concern:
1,3-butadiene, benzene, formaldehyde, acrolein, acetaldehyde, manganese, arsenic

Lifetime Cancer Risk Estimates:
1 to 5 x 10^{-4} (two to seven excess cancer cases per year per million)

Noncancer HI: 6 to 15 for all endpoints

The urban centers, Phoenix, and to a lesser extent, Tucson, were found to have higher estimates of cancer risk from HAP than the two areas that are more rural. Although emission reduction mechanisms were expected to decrease the risk estimates in the near future, it was stated that increases in population growth along with increases in motor vehicle use in these urban areas would begin to erode any potential gains. The estimates of individual lifetime increased cancer risks from air pollutants in all study areas ranged from one to 5 x 10^{-4}. The total HI for noncancer risks, calculated for young children, was six to fifteen for all endpoints. The HI for respiratory effects was greater than one in all regions. Other HI greater than one were found for neurological and blood effects but not across all regions studied.

HASTE Study

This project was conducted in three phases: development of an emission inventory, modeling of the inventory, and a risk analysis (TNRCC, 1996). Only area sources of HAP were studied. Health reference concentrations (RfCs), when available, were used to compare against the ground-level concentrations (GLCs) estimated by modeling, for 87 air contaminants for cancer and noncancer effects. With the exception of acrylonitrile, benzene, 1,3-butadiene, ethylene dibromide, ethylene oxide, 2-nitropropane, and vinyl chloride, the estimated cancer risks for each of the remaining air contaminants was less than 1 x 10^{-6}. Individual lifetime cancer risks for the seven ranged from 2 x 10^{-6} to 2 x 10^{-5}. The acrolein GLC was the only one which exceeded its RfC (5 fold).

HASTE Study

Time Period Covered: 1995 – 1996

Contributors to Predicted Cancer Risk:
Acrylonitrile, benzene, 1,3-butadiene, ethylene dibromide, ethylene oxide, 2-nitropropane, vinyl chloride

Contributors to Noncancer Risk:
Acrolein (HQ = 5)

Individual Lifetime Cancer Risk Estimates:
2 x 10^{-6} to 2 x 10^{-5}

Cumulative Exposure Project (CEP)

CEP Analysis

Time Period Covered: 1990

Top HAP Contributing to Cancer Risk: Benzene, bis(2-ethylhexyl)phthalate, carbon tetrachloride, chloroform, ethylene dibromide, ethylene dichloride, formaldehyde, 1,3-butadiene

Top HAP Contributing to Noncancer Risk : Acrolein

The CEP is a recent effort by the EPA to model ambient HAP concentrations on a national scale (Woodruff et al., 1998). The CEP suggests that HAP exposures are prevalent nationwide, and that, in some locations, concentrations are significantly higher than the concentrations associated with a one-in-one million excess cancer risk (SAI, 1998; Woodruff et al., 1998)[17]. The estimated outdoor concentrations, based on 1990 emission estimates, for 119 of the 148 HAP modeled in more than 60,000 census tracts nationwide were compared to RBCs. The results suggest that HAP exposures are prevalent nationwide, particularly in urban areas. For 75% of the HAP modeled, the average estimated concentrations in urban areas were greater than the overall national average concentrations. The emissions of three HAP (benzene, formaldehyde and 1,3-butadiene) appear to contribute to concentrations above the associated one-in-one million excess cancer RBCs in at least 90% of the census tracts. Estimated concentrations are generally higher in urban areas, and concentrations of 28 HAP were greater than their RBCs in a larger proportion of urban areas as compared to rural areas. In a smaller number of locations (both urban and rural), concentrations of certain HAP were estimated to be more than a factor of 100 greater than the corresponding RBCs (Woodruff et al., 1998). Estimated exceedances seen in this assessment suggest potential public health problems especially in urban areas.

2.7 Why Is The Urban Strategy Needed?

The overall findings of these nine assessments may be summarized as follows:

- Benzene, 1,3-butadiene, and formaldehyde were consistently shown to be most responsible for the higher risk estimates;
- The studies identified all three major source categories (area, major and mobile sources) as contributing emissions and potential risks in urban areas; and
- Estimates of increased cancer risks for air toxics from multiple sources across the studies ranged from 3 in 1,000 to 2 in 1,000,000 with a median of 1 in 10,000.

[17]The estimated ambient concentrations were then compared to risk-based concentrations (termed benchmarks by the authors) intended to represent either continuous exposure levels associated with a one-in-a-million upper bound estimate of excess lifetime cancer risk, or continuous lifetime exposure levels associated with no significant risks of adverse noncancer effects (e.g., EPA's Inhalation RfC).

In addition, because many of these emission sources are area or mobile sources, their emissions are likely to be released at ground level where people are more likely to be exposed to them. The prevalence of minority and low income communities in urban industrial and commercial areas, where ambient concentrations of HAP may be greater, increases the likelihood of elevated HAP exposures among these subgroups. The potential for air toxics in urban areas, either directly or indirectly, to contribute to elevated health risks among these and other subgroups (especially children, the elderly and persons with existing illness or other potential vulnerabilities) demonstrates the need to assess risk distributions across urban populations in order to address disproportionate impacts of HAP.

As discussed earlier, each of these studies was limited in its scope and design (e.g., considered cancer effects from inhalation exposures only), and the results must be considered in the context of conditions which existed up to ten years ago. Thus, many were performed prior to the implementation of control strategies (including vehicle and fuel additive regulations, (e.g., HD2004 and Tier 2) and emission standards for numerous source categories) and do not reflect the progress made in reducing emissions from air toxics through regulatory, voluntary, and other programs at the State and Federal levels. For example, section 112(d), MACT standards (adopted to date) are projected to yield yearly emission reductions of approximately 1.5 million tons of HAP from stationary sources. Additional emission reductions are expected as the remaining MACT standards are promulgated. Additionally, automobile emissions which accounted for 20% of the total emissions of HAP in the baseline inventory mentioned earlier, decreased by approximately 258,000 tons per year between the years 1993 and 1996 (U.S. EPA, 1998), possibly as result of regulations requiring the use of reformulated fuels which may have contributed to the decreases seen in benzene emissions. Future assessments will be needed to determine the impact of these reduced emissions on potential air toxics-related health risks.

In the meantime, these assessments adequately support our concern that a potential problem exists in urban areas, and that we should continue with our efforts to study the urban environment and to implement the urban strategy described earlier in the *Federal Register* (U.S. EPA, 1999a) and presented again in this Report.

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3. Emissions Inventory and Selection of the Urban Pollutants

3.1 Introduction

Section 112(k)(3) of the CAA directs EPA to identify at least 30 HAP which, as the result of emissions from area sources, present the greatest threat to public health in the largest number of urban areas. In the Strategy, we identify 33 HAP ("urban HAP") to meet this requirement. The Appendix of this Report details the physical properties, sources of exposure, health hazards, and other pertinent information for each of the 33 urban HAP.

In developing the final HAP list, we estimated emissions from all known sources using a variety of techniques, evaluated available health effects information for the 188 HAP, assessed available air quality monitoring data, reviewed existing studies, and produced a list of pollutants based on the relative hazards they pose in urban areas, considering toxicity, emissions, and related characteristics. From these efforts, we established the list of urban HAP which pose the greatest threat to public health in urban areas, considering emissions from major, area and mobile sources. Among these urban HAP are a subset of 30 HAP with greatest emissions contributions from area sources (the "area source HAP").

The first step we took toward developing both an emissions inventory and a HAP ranking analysis was in 1997 when we conducted an initial screening analysis using a preliminary methodology. In addition to identifying HAP for which we separately conducted a public review of our emissions inventory information, this evaluation provided us with the opportunity for peer review of our preliminary methodology. In the peer review, outside experts reviewed the ranking methods and data used and offered suggestions on how the methodology could be used and improved to select the priority urban HAP. The draft emissions inventory for the HAP identified by the initial screening analysis was also made available for public comment. This was the first of two public comment opportunities for the emissions inventory.

In the sections below, the results of the final analyses are described in detail. The initial analyses are mentioned, as appropriate, primarily to give you a sense of how the final analyses were developed in response to public comment and improvements made to the methodologies.

In section 3.2 of this chapter, the methods and data sources used to develop the baseline emissions inventory are described. The baseline inventory quantifies the emissions of the candidate urban HAP and identifies the source categories that emit them. The limitations of the inventory are also discussed, and the final emissions estimates presented. In section 3.3, the ranking methodology is described; the final selection criteria and the list of urban HAP are presented in section 3.4. References are provided in section 3.5.

3.2 Baseline Emissions Inventory for the Integrated Urban Air Toxics Strategy

One of the building blocks of the Strategy is the baseline emissions inventory. The inventory is critical in order to evaluate our progress toward meeting the goals of the Strategy as described in Chapter 1. Specifically, the emissions inventory will help:

- Identify source categories that will be subject to regulations under the Strategy, as explained in more detail in Chapter 4;
- Evaluate progress toward the goal of assuring those source categories are subject to standards;
- Evaluate progress toward the goal of reducing by 75 percent the incidence of cancer associated with air toxics across all urban areas; and
- Evaluate progress toward the goal of substantially reducing noncancer health risks associated with air toxics across all urban areas.

To identify the required source categories and to measure our progress toward the other goals listed above, we developed a baseline emissions inventory of HAP emissions approximating emissions during the years 1990 to 1993. We believe the intention of the CAA is that reductions occur from 1990 levels because that was the year the CAA was amended to include these requirements. However, since there were very limited data for 1990, the inventory spans a longer period of time. We believe that this is an appropriate timeframe because these years represent HAP emissions prior to implementation of any MACT source category standards. The baseline inventory contains emissions estimates for major, area, and mobile sources of the 188 HAP and segregates according to whether the sources are located in urban or rural areas. A

Review of the Urban HAP Inventory

The *Draft 1990 Emission Inventory of Forty Section 112(k) Pollutants* was made available on EPA's World Wide Web site in 1997 for review by individuals within and external to the EPA (i.e., trade organizations, environmental advocacy groups, academic experts, and the general public). In addition, EPA contacted individuals representing trade organizations, industry, and environmental groups by letter to announce the availability of the inventory and to solicit review comments.

The technical comments related to development of the inventory were summarized in the EPA document *Public Comments Received About Technical Aspects of the 1990 Emission Inventory of Forty Pollutants in the Section 112(k)*. This document can be obtained from the EPA's website: http:// www.epa.gov/ttn/uatw/ urban/112kfac.html.

A few sections of the draft inventory were revised based on new data provided by the reviewers. The updated inventory was then made available for public review for the second time on September 14, 1998 as part of the draft integrated urban strategy. During this public review, a significant amount of new data were provided which greatly improved our facility-specific estimates for a number of important source categories. All of the changes made to the inventory subsequent to the September 14, 1998 release are reflected in the information presented in this document.

subset of the baseline inventory is information collected and publicly reviewed for 40 candidate HAP to support the analysis of the Strategy, and an additional two HAP developed to support the section 112(c)(6) efforts.

This section summarizes how the baseline emissions inventory was developed for each of the candidate urban HAP. The first inventory of 40 HAP, which was a product of the screening analysis described earlier, was the starting point for more intensive and refined inventory efforts. The final inventory estimates presented below in section 3.2.2 are the result of revisions made after two public comment opportunities as described in the accompanying sidebar.

3.2.1 Development of the Baseline Inventory

The national estimates of the HAP included in the NTI are calculated using existing information; no source testing or industry surveys were conducted specifically for the purposes of generating the inventory. Existing emissions inventory data are obtained from a variety of State and local databases and EPA programs (such as the TRI, standards development programs, and other studies required by the CAA). Sometimes, emissions information is available from direct measurement of emissions at a source. For logistical and financial reasons, direct measurement, or stack testing, is usually performed only at large point sources and is far less common than the use of emission factors.

Documentation of the Inventory

For complete documentation of the inventory, the reader is encouraged to refer to the *1990 Emissions Inventory of Forty Section 112(k) Pollutants, Supporting Data for EPA's Proposed 112(k) Regulatory Strategy, Final Report* (U.S. EPA, 1999a). The *Final Report* presents: emission estimates for each HAP by source category; estimates of total national emissions for each source category; separate urban and rural emission estimates; specific documentation for the subject pollutants of each source category; the input data used to calculate emissions; and the algorithms used to estimate national emissions. The *Final Report* can be obtained from the EPA's Internet Web site (www.epa.gov/ttn/uatw/urban/112kfac.html).

Many of the national emissions estimates in the inventory (primarily for area and mobile sources) were developed by applying an emission factor, or series of factors, to activity data which are representative of source categories nationally. Emission factors are one way to estimate emissions of various chemicals for a particular source category. To estimate emissions, these factors were combined with information about the activity levels of a source, such as the production capacity of the facility, the number of hours of operation, or the amount of fuel consumed. Emissions for each source category were then allocated according to whether they are emitted by major or area sources.

The baseline NTI that was used in developing the Strategy is the first one compiled. New NTI base year inventories will be compiled every three years (1996, 1999, 2001, etc.). Although the inventory development methodology described below applies in general to all emissions

inventories, the baseline and 1996 NTIs do differ in the level of detail they contain. Unlike the baseline NTI, which includes emissions estimates from all *counties* by source category and pollutant, the 1996 NTI will contain *facility*- and *location*-specific information that places individual facilities within those counties and makes the emissions data suitable as input to computer dispersion models that predict ambient air concentrations. The 1996 NTI data set was compiled in cooperation with State and local agencies which submitted data they have gathered during facility permitting and other regulatory activities.

Many estimates presented in the NTI (primarily for area and mobile sources) were developed by using an emission factor in combination with appropriate activity data. The emission factors were evaluated for age of the information, completeness and whether the data adequately represent current practices. The EPA made judgments about the overall quality of the information, and acceptable data were used to develop composite emission factors for use in the national estimates.

The availability and overall quality of the activity data vary by source category. Most of the activity data were obtained from published business/manufacturing sources, governmental statistics publications, and background information from EPA regulatory programs. Other sources of activity data were industrial trade associations, the Department of Transportation and the Department of Energy's Energy Information Administration.

For many source categories, multiple methods were available to develop emission estimates with some methods being preferable to others. The preferred approach was to use national emissions estimates from existing inventories previously prepared by EPA.

For pollutants where no EPA, State or local agency inventory was available, other sources of information were used. In general, other sources of information were prioritized in the following order.

1. National estimates available from other reference sources that were judged to be reasonable, complete, and well documented. These estimates were used directly in the inventories. Examples of these sources include air toxics inventories compiled by individual State or local agencies, various regulatory projects for different source categories, and Reports to Congress (e.g., the Utility Air Toxics Study). Estimates obtained from such programs were generally accepted as the best available data for the inventory. These estimates are based on recent test data, control information, representative modeling scenarios, and input from informed industry and government experts and are considered to be of higher quality than estimates derived through the use of an overall emission factor and associated activity data.

2. Inventory data from TRI. These data sources received lower priority based on the evaluation criteria. The TRI contains national inventory data only for sources that meet certain reporting criteria, and the emission calculation methods cannot be confirmed.

While considered a relatively low-priority reference source, TRI data provide a significant amount of emissions data for sources that might be missed completely by other inventory compilation methods.

3. Calculated emission estimates. Emissions were calculated if national emissions estimates were not directly available from a preferred reference source, and emission factors and activity level data for a source category could be identified. The greatest influence on the quality of these calculated estimates is the validity of the emission factor(s) used (in terms of absolute accuracy), as well as representativeness for the processes to which they were applied. The activity data also affect the quality of an emissions estimate; however, many standardized and credible references for activity data preclude any large margin of error being associated with the activity level.

   Sometimes, data are available about the composition of emissions from a source category. This type of information, called a speciation profile, is a list of HAP on a percentage basis that are the constituents of the emission plume. Thus, if the total concentration of the plume is known, it can be multiplied by the speciation profile to determine the concentration of the various HAP which comprise the mixture. In this analysis, suitable speciation profiles were not available for most source categories in the inventory and were generally not used. Significant limitations were identified which limited the use of the speciation profiles, particularly the poor representation of source categories and the age of the data on which most profiles are based. However, there were some exceptions. For example, mobile source categories emissions were calculated by first estimating total HCs or particulates, then deriving the toxic components by using HAP profiles. In the case of these mobile source categories, this approach is deemed to provide high quality emissions estimates.

3.2.2 Baseline Inventory Results

Exhibit 3-1 summarizes the baseline inventory estimates developed for each candidate urban HAP. Total national emissions for each HAP are presented, and emissions are reported for major, area, and mobile sources. These data are also illustrated in Exhibits 3-2 and 3-3.

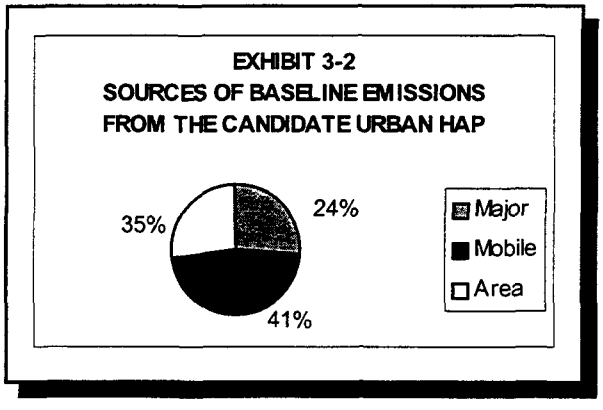
Because there are multiple programs investigating HAP emissions in the United States, emissions data and source activity data are continually changing and improving. The data presented in this section reflect emissions estimates that have been developed according to the input data and assumptions described above. The estimates are applicable for a specific time period and may not necessarily agree with the national estimates from other published estimates

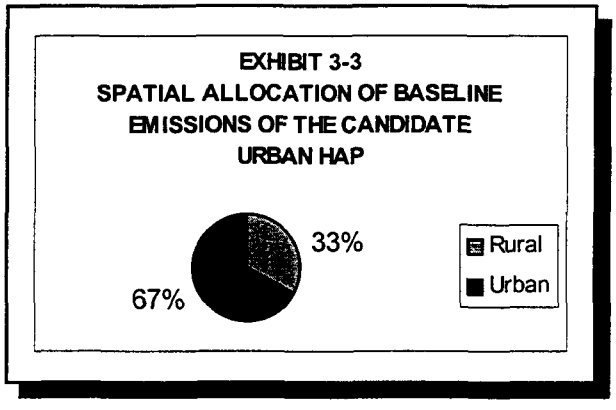
EXHIBIT 3-1
BASELINE EMISSIONS INVENTORY ESTIMATES FOR EACH OF THE 40 CANDIDATE URBAN HAP (1990 – 1993)

HAP	Baseline National Total (tons)	Baseline Major Sources (tons)	Baseline Area Sources (tons)	Baseline Mobile Sources (tons)
Benzene	390,000	36,000	74,000	280,000
Formaldehyde	350,000	32,000	140,000	180,000
Acetaldehyde	140,000	21,000	51,000	66,000
Tetrachloroethylene	130,000	22,000	100,000	0
Methylene Chloride	100,000	85,000	19,000	0
Trichloroethylene	75,000	61,000	14,000	0
1,3-Butadiene	72,000	4,000	20,000	48,000
Acrolein	68,000	750	55,000	12,000
Styrene	54,000	31,000	3,200	20,000
Chloroform	23,000	22,000	600	0
1,3-Dichloropropene	20,000	34	20,000	0
Methyl Chloride	6,400	6,300	89	0
Carbon Tetrachloride	5,500	5,400	110	0
1,4-Dichlorobenzene	5,100	735	4,400	0
Ethylene Dichloride	4,200	4,100	100	0
Lead Compounds	3,300	1,500	540	1,200
Manganese Compounds	2,800	2,100	650	52
Vinyl Chloride	2,700	2,100	570	0
Ethylene Oxide	2,600	1,200	1,300	0
Acrylonitrile	2,600	2,100	440	0
Coke Oven Emissions	1,800	1,800	0	0
Polycyclic Organic Matter as 7-PAH	1,300	250	1,000	48
Nickel Compounds	1,200	740	400	95
Chromium Compounds	930	490	390	54
bis(2-Ethylhexyl)phthalate	810	740	68	0
1,1,2-Trichloroethane	740	740	5	0
1,2-Dichloropropane	660	630	23	0
Arsenic Compounds	280	220	65	2.8
1,1,2,2-Tetrachloroethane	260	51	206	0
Methylene Diphenyl Diisocyanate	240	160	82	0
Vinylidene Chloride	220	170	48	0
Mercury Compounds	210	120	71	12
Cadmium Compounds	200	160	38	0.31
Ethyl Acrylate	160	140	20	0
Ethylene Dibromide	51	50	0.50	0
Acrylamide	35	32	3.3	0
Quinoline	26	24	1.6	0

EXHIBIT 3-1 (Continued)
BASELINE EMISSIONS INVENTORY ESTIMATES FOR EACH OF THE 40 CANDIDATE URBAN HAP (1990 – 1993)

HAP	Baseline National Total (tons)	Baseline Major Sources (tons)	Baseline Area Sources (tons)	Baseline Mobile Sources (tons)
Hydrazine	20	18	1.1	0
Beryllium Compounds	12	9.5	2.6	0.02
Dioxins/Furans as 2,3,7,8-TCDD TEQ	3.2e-03	2.2e-03	9e-04	1e-04
TOTAL	1,468,344	348,854	509,414	609,454





due to differences in base years, emission factors and activity data, and calculation assumptions. It should be recognized that some of the data presented here will likely change as more information and improved estimation approaches are developed.

3.2.3 Allocating Emissions Between Locations and Source Types

For purposes of selecting the priority urban HAP, the emission estimates were further refined in two ways. First, the emissions were allocated to either urban or rural areas so that it could be determined which pollutants were potentially the most significant in the largest number of urban areas. Second, the pollutants were allocated by source type including major sources, area sources and mobile sources. The statutory language of section 112(k) focuses on area sources, but as explained earlier, the Strategy will combine a number of statutory requirements for both stationary and mobile sources to address the urban air toxics problem in the most efficient and effective way. The subsections below describe these analyses.

Urban/Rural Source Allocations

Section 112(k) of the CAA specifically addresses HAP that "present the greatest threat to public health in the largest number of urban areas." However, the CAA does not provide a definition of "urban." In other sections of the CAA, urban areas with populations greater than

250,000 are singled out for air monitoring, although the possibility of monitoring other urban areas is also mentioned.

Statistical data from the Bureau of the Census were used to spatially allocate emissions on an urban and rural basis (U.S. Bureau of the Census, 1990). The Bureau of the Census has designated urban and rural areas within every county in the United States based on population density and total population. For this analysis, using population data and urban/rural designations for 1990, every county in the United States was classified as either urban or rural according to the following definitions:

- Urban counties are defined as those which include a metropolitan statistical area (MSA) with a population greater than 250,000, or those counties that do not have an MSA with a population greater than 250,000, but more than 50 percent of the county population has been designated by the Bureau of the Census as "urban." These counties include areas with one or more central places and adjacent, densely settled, surrounding urban fringe areas. The urban fringe consists of contiguous territory having a density of at least 1,000 persons per square mile.

- Rural counties do not have an MSA with a population greater than 250,000 and the Bureau of the Census designates more than 50 percent of the county population as "rural."

For the purpose of defining "urban" and "rural" for the Strategy, if more than 50 percent of the population was classified as rural, then that county was classified "rural." All remaining counties were classified as "urban."

Emissions were assigned to counties by various methods. In some cases, such as with TRI estimates and data obtained from regulatory programs studies, emissions could be assigned to the actual county. Where facility-specific data were not available, emissions were assigned to individual counties using surrogate approaches. Examples of these surrogate approaches include proportioning national level emissions to counties based on population, proportioning emissions from some industrial sectors to counties based on employment estimates, and assigning emissions from forest fires to counties based on forested acres.

Major/Area Source Allocation

The national emission estimates for stationary source categories were also allocated according to whether the emitting source category was classified as "major," "area," or could be classified partially as both. According to section 112(a) of the CAA, a "major source" is any stationary source (including all emission points and units located within a contiguous area and under common control) of air pollution that emits or has the potential to emit, considering controls, 10 tons or more per year of any single HAP or 25 tons or more per year of any combination of HAP. An "area source" is any stationary source of HAP that does not qualify as

a major source. The allocation of emissions for each source category on a major/area source basis will be helpful in evaluating the effects of existing and future regulatory programs on emissions reductions.

The major/area allocation proportions were derived in a variety of ways. The primary goal was to determine whether emissions from a category were predominantly emitted from major or area sources so that sources accounting for 90 percent of the aggregate area source emissions of each pollutant can be identified. The rationale used to make the major/area source determinations varied depending on available information. The EPA report *Documentation for Developing the Initial Source Category List*, which was used to identify major source categories for standards development purposes, was a key reference (U.S. EPA, 1992). In some cases, the accepted way that a source category is typically inventoried served as a guide for the classification (e.g., residential wood burning is always assessed as an area source). In other cases, technical analyses were conducted using actual and representative model plant data to determine typical facility sizes and emissions. With the above information, the percentage of facilities in a category likely to exceed the 10 or 25 ton-per-year HAP thresholds could be estimated. Engineering judgment was used to assign an allocation in cases where data were limited.

3.2.4 Limitations of the Emissions Inventory

In the development of emissions inventories, the quality of the final estimates varies considerably among the different source categories. The data for some source categories will have greater uncertainty and limited information especially if those categories have not been a priority for previous evaluations of emissions. Despite these uncertainties, we feel that the baseline inventory represents the best available data set for the 1990 to 1993 timeframe, and that it meets the inventory needs of the Strategy at this time, and the 1996 NTI will represent significant improvement because of its facility-level detail. Future NTI base year inventories are expected to continue to improve in quality as data collection and estimation methodologies improve. This section discusses some of the limitations of the data used to develop the inventory.

Consistency of Emissions Estimation Methods Within and Among Source Categories

Because the NTIs, regardless of base year, are compiled in part by the collection of data from other primary references (e.g., individual States, TRI, regulatory development programs, etc.), the methods for developing those estimates vary. For example, TRI emissions are self-reported by individual facilities. Those facilities may estimate their emissions via different technical approaches (e.g., mass balance versus stack testing) or report emissions on different bases in scope or time (actual versus potential, or daily versus annual emissions). In developing the NTI, we have made assumptions to allow us to standardize all of these reported emissions to develop emissions on an 'actual annual' emissions basis.

Emissions Inventories Continue to be Revised Over Time

Because there are multiple programs investigating HAP emissions in the U.S., emissions data and source activity data are continually changing and improving. To develop emission factors, extensive information about the different types of industrial processes is required. Research is always ongoing to update the emission factors so they reflect the most current knowledge about the industrial sources. Because estimating emissions requires making various assumptions, the estimates are applicable for a specific time period and may not necessarily agree with the national estimates from other published estimates due to differences in base years, emission factors and activity data, and calculation assumptions. It should be recognized that some of the data presented in the baseline inventory used in developing the Strategy are likely to change as more information and improved estimation approaches are developed.

Source Category Specific Limitations

In some cases, categories are known or suspected to emit candidate urban HAP, but it was not possible to develop emission estimates. At this time, the relative magnitude of these sources is unknown. The majority of this type of uncertainty is in emissions from chemical manufacturing facilities. In the baseline inventory, these emissions are reported in the baseline NTI as "unspeciated organic HAP." These emissions data were collected to develop the MACT standard for this industry and could not be speciated into the individual chemical compounds. Thus, the emissions estimates for benzene and the other HAP that may be included in the emissions from this source category may be underestimated.

Old or Limited Data

As described earlier, some of the emissions estimates in the NTI are based on calculations made using emissions factors and activity data. We consider some of these estimates to be of very high quality (e.g., mobile source estimates that are based on recently developed emissions factors, VMT, and criteria pollutant inventory data). However, for some source categories, primarily in the area source sector which has not been the focus of previous HAP studies, emissions are based on emission factors that are either old (i.e., from the 1980's) and/or very limited in terms of coverage. This means that for some source categories, a very limited number of data points were available to characterize an entire category.

Assumptions Required to Divide Emissions into Urban Versus Rural Counties and Major Versus Area Sources

As described in more detail below, for the sake of the Strategy, we had to allocate emissions by urban/rural and major/area splits. These distinctions required some technical assumptions. The major/area distinctions are generally a function of how the emissions estimates were derived. For example, a facility reporting emissions of one HAP in an amount greater than

10 tons would definitely be a 'major' source, but a similar facility that reports less than 10 tons may not be major unless other HAP are emitted as well.

For urban/rural designations, the distinction was simple if we knew the actual location of a facility within a county that has been designated as urban or rural using U.S. Census Bureau data. This was not so simple when no location was known, particularly for area sources. For example, if the area source category emissions were calculated for the entire Nation and then spatially allocated to urban and rural counties using a surrogate (e.g., population), an individual county's emissions may be skewed high or low, even though the national emissions estimate is accurate.

3.3 Ranking the Urban Hazardous Air Pollutants

This section describes the ranking analyses used to select the priority urban HAP. The analyses are described in more detail in an EPA technical support document (U.S. EPA, 1999b). As with the emissions inventory, the first step we took toward ranking the pollutants was the development of an initial screening methodology. While the final ranking used to identify the priority urban HAP is similar to that of the screening analysis, the methodology was revised to address the comments of the January 1998 peer review panel and public comments. The analysis was rerun using updated emissions, monitoring and toxicity information that became available in the interim. The accompanying text box describes the screening analysis and its peer review.

The purpose of these analyses was to identify which of the 188 HAP "present the greatest threat to public health" in urban areas. In order to use the available data in the most robust manner, we conducted three ranking analyses, each of which is described below. First, we ranked the HAP by combining indicators of toxicity and exposure into four risk-related ranking indices and then produced an overall ranking by combining each of the individual indices (i.e., the Exposure/Toxicity Indicators Ranking Analysis). Second, we reviewed a number of previously conducted risk or hazard assessments concerning HAP in urban areas and produced a list based on the results of these assessments (i.e., the Risk Assessment/Hazard Ranking Studies Analysis). Third, we used information provided by EPA's CEP which compares modeled ambient concentrations of HAP in urban areas with health-based benchmarks (i.e., the CEP Ranking Analysis). Each of these analyses have various limitations, but by assembling and assessing this variety of analyses and types of information, a weight of evidence approach was taken to provide a more sound identification of urban HAP than would be possible from a single

analysis. The three separate analyses and types of information are described below along with their strengths and limitations.

Limitations Shared By All Three Ranking Analyses

- The ranking analyses are uncertain because there are gaps and uncertainties associated with the health effects, monitoring and emissions data for the 188 HAP.

- Although all three ranking analyses used ambient concentration data in the same form, none considered personal exposure. Personal exposure, which includes physiological and behavioral factors that vary with individuals, may vary substantially from ambient concentrations.

- Only HAP having both toxicity data and emissions or ambient concentration data could be ranked. This could lead to overlooking potentially high-risk pollutants because of sparse data.

Initial Screening Analysis and Peer Review

The screening analysis for the initial HAP ranking used various types of information combined in five different rankings to assess the relative potential health risks posed by each of the 188 HAP. For each method, contributions from major, area, and mobile sources were considered. This approach accounted for risks from multiple sources and minimizes the impact of missing information for individual sources. The selection process for the candidate HAP as well as the methods and data used in the screening analysis are explained in detail in an EPA document, *"Prioritization of HAP for the Urban Air Toxics Study - Peer Review Draft"* (U.S. EPA, 1997a), which is available in the Urban Strategy Docket.

A technical review panel was convened on January 21, 1998 to review the preliminary methodology used to select the candidate list of HAP. Nine scientists from academia, government agencies and an EPA/industry-supported research institute participated as panel members. The panel was charged with reviewing the ranking methodology for scientific accuracy, objectivity, technical quality and validity. Reviewers were also asked to comment on the general approach taken, the individual ranking methods, the results of the ranking and other technical aspects of the ranking method such as uncertainties and data gaps, which were presented in the draft EPA report (U.S. EPA, 1997a).

In general, the reviewers agreed that the information available at the time of the review had been appropriately incorporated into the ranking approaches, and that the ranking results were systematically evaluated and integrated. The various ranking methods seemed to complement each other in that one method filled in data gaps that the other ranking methods may have missed. Overall, the ranking methodology appeared to result in the highest rankings for pollutants with the most potential to cause human health risks and lower rankings for those less likely to be priorities. However, the reviewers expressed concern that data gaps and the use of arbitrary cutoffs to select a predetermined number of pollutants could result in some priority pollutants being left off the list. The reviewers also suggested that EPA explain how missing or uncertain data could affect the ranking, that the analysis be updated periodically with new science as appropriate, and that the reasons for selecting each pollutant be illustrated more clearly. (The complete set of written comments by the peer reviewers may be obtained from the Urban Strategy Docket (A-97-44)).

3.3.1 Exposure/Toxicity Indicators Ranking Analysis

The first analysis ranked HAP by combining surrogates for toxicity and exposure into risk-related ranking indices. By considering short-term inhalation hazards and hazards posed by ingestion of HAP with a potential to accumulate in foods, this analysis complemented the other two ranking analyses described below, both of which considered only long-term inhalation hazards or risks.

The surrogates for toxicity were the RBC for inhalation and the risk-based dose (RBD) for ingestion. These are calculated by selecting a specified risk level (e.g., 1 in 1,000,000 excess cancer risk) and calculating exposure concentration or dose of the HAP which will cause the risk level to be exceeded, assuming the relevant acute or chronic exposure conditions. For effects other than cancer, the RBC or RBD is the chronic RfC (or similar value from another source). If available, the EPA's inhalation RfC was chosen as the chronic noncancer RBC. If an RfC was not available for a HAP, then a comparable value was obtained from another agency, such as the minimal risk level (MRL) developed by the Agency for Toxic Substances and Disease Registry, or the reference exposure level (REL) developed by the State of California Environmental Protection Agency. Similarly, the EPA's reference dose (RfD) was the first choice for the noncancer RBD. Acute RBCs were set equal to risk management exposure guideline levels (e.g., Acute Exposure Guideline Levels (U.S. EPA, 1997b)) for mild, transient or no effects from short exposure periods, when available.

For HAP categorized as "known," "probable," or "possible" human carcinogens, rankings were done separately for two risk levels. In the first case, the RBC or RBD was set at an exposure associated with a one in one million upper-bound predicted lifetime cancer risk, or the RfC/REL for noncancer effects (whichever was lower). In the second case, the RBC or RBD was set at an exposure associated with a one in ten thousand upper-bound predicted lifetime cancer risk, or the RfC/REL (whichever was lower). Two risk scenarios were selected because if the cancer risk level was preset at only one in one million upper bound lifetime cancer risk, the list of 30 substances selected likely would be dominated by carcinogens. This would in effect give cancer preference over noncancer effects because the amount of pollutant needed to trigger the one in one million cancer risk level would almost always be lower than the amount needed to trigger the risk level based on noncancer effects. Thus, the lower of the cancer or noncancer RBCs and RBDs is selected under two different risk scenarios to ensure that noncancer effects are given appropriate consideration in the ranking.

Surrogates for exposure included measured ambient concentrations and emission estimates from mobile, major and area sources. The Exposure/Toxicity Indicators ranking is necessarily based on databases which are not complete and contain information that varies in quality. While we believe that these databases contain the best available information, there is still substantial uncertainty in this analysis. The results should be considered estimates of the relative potential hazards of the various HAP and not a quantitative estimate of risks.

Four separate ranking indices – three of which had two separate risk scenarios (case 1 and case 2) as noted above – were prepared for each HAP. The pollutants were ranked on a normalized scale. To obtain the final ranking, the normalized scores from each index for each pollutant were averaged. The average normalized value for each pollutant was then ranked in order from highest to lowest. (If a score was not available for a pollutant in a given index, the value was treated as "missing," not zero, so as not to lower the average value.)

Normalized Scores

A normalized score is prepared by listing the score for each pollutant and dividing each score by the value of the highest score. By normalizing the scores, the magnitude of the differences between the scores of each pollutant is preserved. In addition, because each index is normalized in the same way, each is given equal weight, or importance, in the analysis.

Toxicity is inversely related to the value of the RBCs and RBDs. For example, the more toxic the HAP, the lower the concentration at which health effects would be realized. Consequently, the more toxic HAP would have lower RBCs and/or RBDs. In contrast, the relative concern for exposure increases with increasing ambient measures or emissions (i.e., surrogates for exposure). Therefore, higher emissions (or ambient concentrations) are of greater concern than lower emissions. In order to rank the HAP by toxicity and exposure, the exposure surrogate is divided by the RBC (or RBD), as illustrated by the following equation:

Exposure Surrogate/RBC = Ranking Index

The ranking indices are used to estimate the relative concern for public health. The four indices are:

- **Index 1: Ambient/Acute**. This index was intended to rank HAP by relative short-term inhalation hazard. The ambient acute index for each HAP was calculated by dividing the 95th percentile 24-hour concentration of the database of 24-hour urban area ambient concentrations by the RBC for acute inhalation exposure.

- **Index 2: Ambient/Chronic**. This index was intended to rank HAP by relative long-term inhalation hazard. The ambient chronic index for each HAP was calculated by dividing the average ambient long-term concentration for the urban areas monitored by the chronic RBC. This was done separately for case 1 (RBC set at 1 x 10^{-6} upper bound cancer risk or the RfC, whichever was lower) and case 2 (RBC set at 1 x 10^{-4} upper bound cancer risk or the RfC, whichever was lower).

- **Index 3: Emission/Chronic/Inhalation**. This index was intended to rank HAP by relative long-term inhalation hazard. The emissions-based chronic inhalation index for each HAP was calculated by dividing the national urban emissions estimate by the RBC for chronic inhalation exposure. The emissions estimates were obtained from the

baseline NTI (U.S. EPA, 1998a). As with the ambient chronic index, this was done separately for case 1 (RBC set at 1 x 10^{-6} upper bound cancer risk or the RfC, whichever was lower) and case 2 (RBC = 1 x 10^{-4} upper bound cancer risk or the RfC, whichever was lower).

- **Index 4: Emission/Chronic/Oral.** This index was intended to rank HAP by relative potential for oral toxicity and food-chain bioaccumulation. The emissions-based chronic oral index for each HAP was calculated by multiplying the national urban emissions estimate by the HAP's bioconcentration factor (BCF) and then dividing by the oral RBD for chronic oral exposure. As with the other chronic indices, this was done separately for case 1 (RBD set at 1 x 10^{-6} upper bound cancer risk or the RfD, whichever was lower) and case 2 (RBD = 1 x 10^{-4} upper bound cancer risk or the RfD, whichever was lower).

With the exception of radionuclides, each HAP was carried through the index calculations even if health benchmark, emission, or ambient data were not available. We believe that this presentation will allow readers to see data gaps more clearly and will serve as a guide for future efforts to prioritize data collection for the air toxics program. The results of the Exposure/Toxicity Indicators ranking are shown in Exhibit 3-4.

EXHIBIT 3-4
40 HIGHEST PRIORITY POLLUTANTS IDENTIFIED BY EXPOSURE/TOXICITY INDICATORS RANKING

Acetaldehyde	Chloroprene	Formaldehyde	2-Nitropropane
Acrolein	Coke oven emissions	Heptachlor	PCBs
Acrylonitrile	Chromium compounds	Hydrogen chloride	POM
Arsenic compounds	1,2-Dibromomethane	Hydrazine	Propylene dichloride
Benzene	1,4-Dichlorobenzene	Lead compounds	Quinoline
Bromomethane (methyl bromide)	1,3-Dichloroethane	Manganese compounds	1,1,2,2-Tetrachloro-ethane
1,3-Butadiene	1,1-Dichloroethylene	Mercury compounds	Tetrachloroethylene
Cadmium compounds	1,3-Dichloropropene	Methylene chloride	Trichloroethylene
Carbon tetrachloride	Dioxin (2,3,7,8-TCDD)	Napthalene	Vinyl chloride
Chloroform	Ethylene oxide	Nickel compounds	Xylene

Data Sources for the Exposure/Toxicity Indicators Ranking

In order to rank each of the HAP in the indices described above, data on health-based reference values, ambient air quality measurements, emissions, and bioconcentration factors were collected. Each of these are described below.

Health-Based Reference Values. Dose-response assessments for health effects of HAP were obtained from various sources, and prioritized according to: (1) applicability, (2) conceptual consistency with EPA risk assessment guidance, and (3) level of review received. The accompanying text box lists in priority order the health-based reference values which were used in this analysis. For dose response estimates that are currently under review or being revised, we reviewed current information to determine how potential changes to dose-response estimates might affect the outcome of the analysis[1]. The Technical Support Document contains additional details regarding these reference values (U.S. EPA, 1999b).

Estimates of Exposure. The second major part of the HAP ranking indices (the first part being the dose-response data described above) was information on exposure. Actual data describing human exposure to HAP are limited and lack the comprehensive geographic, temporal, and multicontaminant coverage that this ranking exercise required. Therefore, we chose to base the ranking on exposure surrogates – data related to, but not identical with, exposure. The two types of exposure surrogates chosen were long- and short-term ambient air quality measurements from urban areas, and estimated annual emissions of HAP from major, area, and mobile sources in urban areas.

The ambient air quality data set used in this analysis was created by combining all available monitoring data from EPA's Aerometric Information Retrieval System (AIRS) and Toxics Data Archive (12/31/97 version) databases for the 188 HAP. The analysis was restricted to data from 1990 through 1997, for 24-hour sampling intervals only from counties designated as "urban1" or "urban2." A minimum of 20 observations during a year were required for inclusion of that year's data, and for volatile and semi-volatile compounds it was further required that at least five observations were from the spring or summer and five from the fall or winter. Concentration data that were below the method detection limit were used as reported in the calculations, while data values designated only as "below detection limits" (i.e., without a reported concentration) were assumed to be present at one-half the detection limit (instead of

[1]For example, in the case of 1,3-butadiene, we determined that the EPA's Integrated Risk Information System (IRIS) risk estimate is no longer an appropriate basis from which to extrapolate human risk, and the updated assessment has progressed to the point where it is appropriate for use here. Use of this new assessment, however, does not affect the presence of 1,3-butadiene on the urban HAP list. In the case of vinyl chloride, we've chosen to use the Agency consensus assessment currently in IRIS rather than a draft assessment that may yet change significantly. However, we've confirmed that using the draft assessment for vinyl chloride wouldn't change its status on the final urban HAP list.

omitting the observation). For HAP having fewer than 10 percent of observations above the detection limit, the data were omitted altogether.

For input to the chronic exposure indices, selected ambient air quality data were first averaged arithmetically for each year, by HAP and monitoring site. The annual average concentrations from 1990 to 1997 for each site-pollutant combination were next averaged across years. Finally, the resulting multiyear average concentrations were averaged across monitoring sites into a single national long-term average concentration for each HAP for which data met the selection criteria.

To simulate acute exposure for each HAP, the 95th percentile concentration of the database of 24-hour ambient concentrations at all locations was selected. We judged that this concentration represented a reasonable maximum short-term exposure.

The second type of data used in this ranking analysis as a surrogate for exposure was the estimated emissions of HAP from major, area, and mobile sources in urban areas (U.S. EPA, 1998b).

Data Sources and Health-Based Reference Values Used in the Exposure/Toxicity Indicators Ranking Analysis

For chronic exposure (cancer and noncancer reference values, in order of preference):

1. EPA IRIS
2. Agency for Toxic Substances and Disease Registry (ATSDR) MRLs
3. EPA Health Effects Assessment Summary Tables (HEAST)
4. California EPA inhalation unit risks
5. EPA estimates of cancer risk from oral exposure converted to inhalation units (IRIS or HEAST)

For short-term exposure (noncancer effects):

1. National Advisory Committee (NAC) Guideline Level (1-hr Level I)
2. NAC Acute Exposure Guideline Level (1-hr Level II)
3. California EPA acute RELs
4. American Industrial Hygiene Association (AIHA) Emergency Response Planning Guidelines (ERPG) (1-hr Level I)
5. AIHA ERPG (1-hr Level II)
6. 10 percent of National Institute for Occupational Safety and Health Immediately Dangerous to Life or Health levels
7. ATSDR acute MRL

Bioconcentration Data. Measured and estimated BCFs for HAP were obtained from EPA's draft Waste Minimization Prioritization Tool (WMPT). The BCF provides an estimate of how much a pollutant will accumulate in tissues and be concentrated throughout the food web (U.S. EPA, 1998c).

Limitations of the Exposure/Toxicity Indicators Ranking

In addition to the general limitations of all three ranking analyses, the Exposure/Toxicity Indicators ranking relied heavily on emissions data. Emissions-based indices do not consider dispersion or transformation of HAP and are, therefore, likely to be less reliable surrogates for exposure than are ambient concentrations. As a result, there are two limitations of this analysis:

(1) the ranking is relative rather than absolute, and (2) the results cannot be inferred as quantitative risk estimates.

3.3.2 Risk Assessment/Hazard Ranking Studies in Urban Areas

Much of the current information that has been collected to characterize urban air toxic exposures and potential risks comes from 14 major studies in urban areas. These studies were conducted by EPA and various State air pollution control agencies. All 14 included emissions inventory analyses, although seven studies also included air monitoring data. Eleven of the studies had a risk assessment component, while three studies were hazard rankings only and did not have a risk assessment component. The number of pollutants studied varied from 11 to 34. Most studies focused on carcinogens, but six of the 14 also assessed noncancer risks. Eleven of the 14 studies included major, area and mobile sources, and three evaluated area sources only.

These 14 studies were reviewed to determine which pollutants contributed the most to the total risk or hazard reported for the study area. For example, if the total excess cancer risk was estimated to be three cases per year and pollutant X contributed 0.3 cases per year, then pollutant X would receive a score of 0.10 because it accounted for 10 percent of the risk. This was done for each pollutant in each study. The scores for each pollutant were then added together, and the pollutants ranked from the highest aggregate score to the lowest. Two rankings (one for cancer as an endpoint and one for noncancer effects) were produced for the 11 studies that included major, area, and mobile sources. Similarly, two rankings were produced based on the three studies of area sources only. We used these four HAP rankings to select 27 HAP that appeared to contribute substantially more risk or hazard than the rest. The 27 HAP identified from this analysis are shown in Exhibit 3-5.

EXHIBIT 3-5
PRIORITY HAP IDENTIFIED BY STUDIES IN URBAN AREAS

Acrolein	Coke oven emissions	Methylene chloride
Acrylonitrile	Cyanide compounds	2-Nitropropane
Arsenic compounds	Ethylene dichloride	Nickel compounds
1,3-Butadiene	Ethylene oxide	POM
Benzene	Formaldehyde	Tetrachloroethyene
Cadmium compounds	Glycol ethers	Trichloroethylene
Carbon tetrachloride	Hexane	Toluene
Chloroform	Lead compounds	Vinyl chloride
Chromium compounds	Manganese compounds	Xylene

In addition to the general limitations shared by all three analyses, the urban studies summarized in this hazard ranking analysis studied only 11 to 34 HAP, substantially less than the 188 HAP listed in section 112 of the CAA. Thus, it is possible that high-risk HAP may have been overlooked. Despite these limitations, however, these studies represent high quality analyses which identified priority pollutants in a variety of urban areas in the United States. As a result, the analysis of these studies was a critical component of the overall ranking methodology and HAP selection process.

3.3.3 CEP Ranking Analysis

The third ranking analysis was based on EPA's CEP, initiated in 1994, with the objective of using existing data and methods to evaluate the combined exposures to multiple pollutants through three different routes of exposure – air, food and drinking water. In the air toxics component (the only component completed), long-term air concentrations of HAP (but not personal exposure) are estimated on a national scale (SAI, 1998).

In the CEP, the Assessment System of Population Exposure Nationwide (ASPEN) model was used with preliminary estimates of 1990 HAP emissions (see text box) to predict long-term average concentrations at the census tract level for 148 HAP. For some pollutants, modeled concentrations were augmented with estimates of background levels that were intended to represent contributions from natural sources as well as historic emissions of persistent pollutants. The estimated ambient concentrations were then compared to RBCs (termed benchmarks by the authors) intended to represent either continuous exposure levels associated with a one in one million upper bound estimate of excess lifetime cancer risk, or continuous lifetime exposure levels associated with no significant risk of adverse noncancer effects (e.g., EPA's inhalation RFC) (Caldwell et al., 1998). As stated earlier, estimated concentrations greater than RBCs should be viewed as indicators of a potential health problem and not as a characterization of health risks.

Sources of Emissions Data

In the CEP, emissions from manufacturing point sources are represented by data from the 1990 TRI. For the other five source categories, the CEP estimates HAP emissions by applying speciation profiles to inventories of VOC and PM. Speciation profiles were specific to industries or industrial processes. They provided estimates, on a percentage basis, of the amount of individual chemical constituents that comprise VOC or PM emissions.

As we wanted to focus the analysis on modeled concentrations resulting from controllable sources, and we are currently using updated RBCs which, in some cases, differ from those used in the CEP analysis, we took some additional steps. Prior to using this analysis as part of our final methodology, we repeated the analysis for the subset of HAP for which concentrations had been augmented with background concentrations or for which the health reference values needed to be updated. For this small re-analysis, we used the modeled concentrations resulting only

from current area, major and mobile sources (i.e., without addition of a background value) and an updated set of RCBs.

From these analyses, we identified those HAP for which the modeled concentrations exceeded RBCs in the greatest number of urban census tracts. There were 36 HAP for which modeled concentrations were greater than an RBC in at least 50 urban census tracts (see Exhibit 3-6). These 36 HAP are those of greatest potential concern based on our use of the CEP modeling analysis.

EXHIBIT 3-6
HAP WITH MODELED CONCENTRATIONS HIGHER THAN AN RBC IN AT LEAST 50 URBAN CENSUS TRACTS

Acetaldehyde	2,3,7,8-Tetrachlorodibenzo-p-dioxin (& congeners & TCDF congeners
Acrolein	Ethyl acrylate
Acrylamide	Ethylene oxide
Acrylonitrile	Formaldehyde
Arsenic and compounds	Heptachlor
Benzene	Hexachlorobenzene
Benzotrichloride	Hexachlorocyclopentadiene
Beryllium and compounds	Hydrazine
1,3-Butadiene	Lead and lead compounds
Cadmium and compounds	Manganese and compounds
Carbon tetrachloride	Methylene chloride (Dichloromethane)
Chloroform	Nickel and compounds
Chromium VI and compounds	PCBs
1,2-Dibromomethane	Quinoline
1,4-Dichlorobenzene	1,1,2-Trichloroethane
1,2-Dichloropropane (Propylene dichloride)	Tetrachloroethylene (Perchloroethylene)
Ethylene dichloride (1,2-dichloroethane)	Trichloroethylene
1,3-Dichloropropene	Vinyl chloride

Limitations of the CEP

In addition to the general limitations of all three ranking analyses, the modeling performed for this analysis was subject to the following uncertainties and limitations:

- The ASPEN model, as it had been run, may under- or over-estimate some HAP. Such a tendency could then lead to an under- or over-estimation of the number of census tracts with air concentrations higher than an RBC.

- This analysis prioritized HAP according to how frequently a modeled air concentration was higher than an RBC; how much higher was not examined. Thus, a HAP whose modeled concentration is slightly higher than the RBC in many census tracts would be listed as a higher priority than a HAP whose modeled concentration is higher than the RBC by a large margin in a smaller number of census tracts.

- A majority of the RBCs were for cancer effects, rather than noncancer effects. This reflects the fact that the cancer benchmarks set at a one in one million risk level are generally much lower concentrations that the noncancer benchmarks. Consequently, cancer as a health effect was emphasized over other health effects.

While we recognize certain limitations associated with this initial attempt at modeling HAP concentrations nationwide, and its inappropriateness for use in drawing conclusions at small geographic scales, this modeling effort is useful as a national screening tool.

3.4 Selection of the Urban Hazardous Air Pollutants

Exhibit 3-7 summarizes the three ranking methodologies and illustrates how the results of these analyses were considered to produce one listing of priority urban HAP. Results for all three ranking analyses are summarized in Exhibit 3-8.

For the final HAP list, we selected those HAP for which the baseline inventory data were publicly reviewed (through EPA's public request in September 1997 for additional information on 40 candidate compounds or during development of inventories for the specific HAP listed in section 112(c)(6) of the CAA) and which had been either:

- Identified by two of the ranking analyses (regardless of area source contribution), or

- Identified by at least one of the three analyses and had an area source contribution to total emissions of at least 25 percent.

Exhibit 3-9 summarizes the final integrated list. This list of 33 urban HAP includes not only those with emissions from area sources, but reflects the integrated nature of the Strategy by

EXHIBIT 3-7
HAP RANKING ANALYSIS FOR THE INTEGRATED URBAN STRATEGY

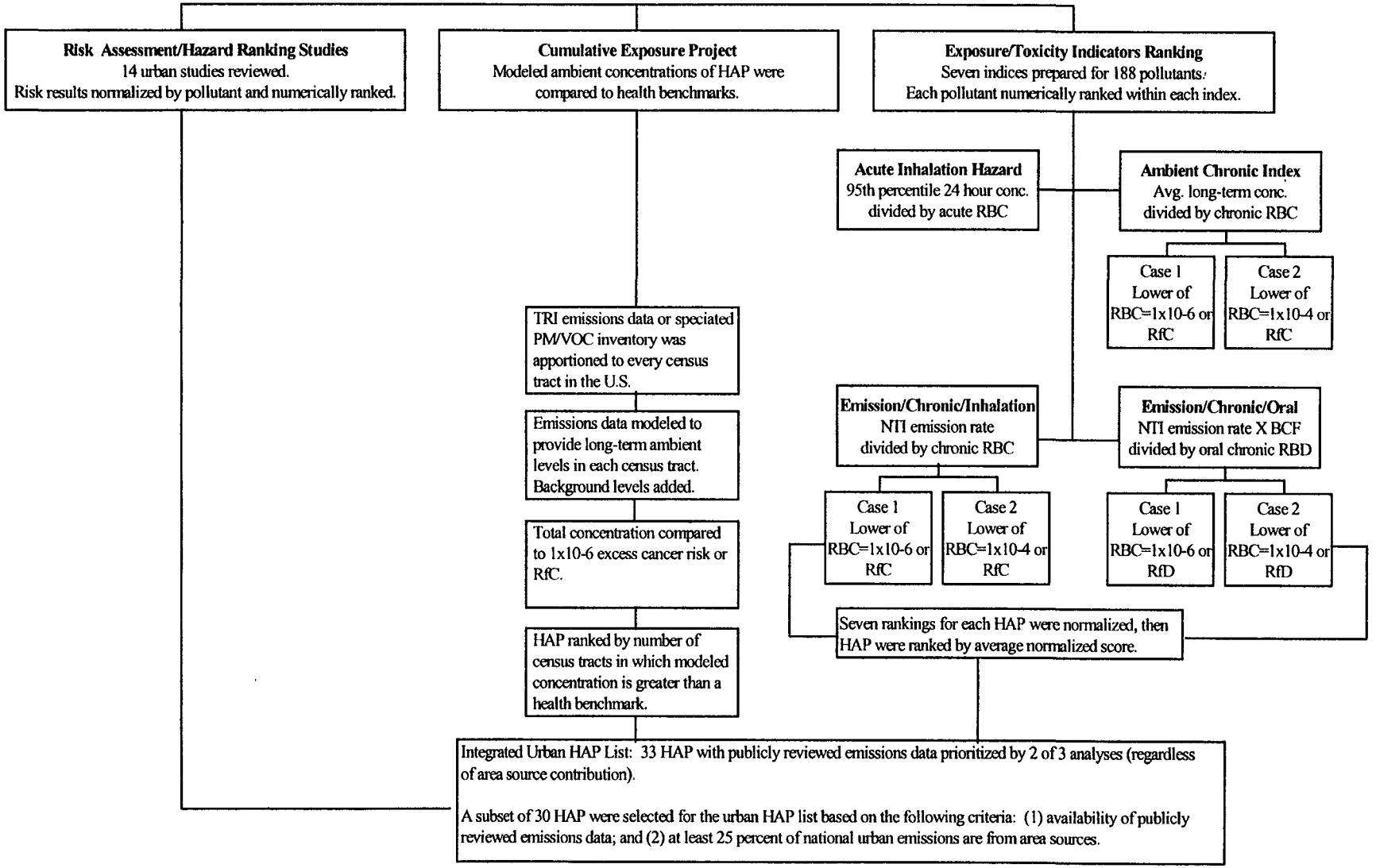


EXHIBIT 3-8
RESULTS OF THE THREE RANKING ANALYSES

Contaminant	Risk Assessment Hazard Ranking	CEP Urban Analysis (All Sources)	Exposure Toxicity Ranking System	Ratio of Area/Total Emissions	Urban Strategy List[a]
Tetrachloroethylene	X	X	X	81.4%	X
Acrolein	X	X	X	66.9%	X
Ethylene oxide	X	X	X	53.0%	X
Chromium VI and compounds	X	X	X	44.2%	X
Nickel and compounds	X	X	X	33.0%	X
Manganese and compounds	X	X	X	26.1%	X
Formaldehyde	X	X	X	23.7%	X
Vinyl chloride	X	X	X	20.2%	X
Trichloroethylene	X	X	X	19.3%	X
Cadmium and compounds	X	X	X	19.1%	X
Methylene chloride	X	X	X	17.7%	X
Acrylonitrile	X	X	X	16.8%	X
Arsenic and compounds	X	X	X	16.4%	X
1,3-Butadiene	X	X	X	13.3%	X
Benzene	X	X	X	11.2%	X
Chloroform	X	X	X	3.8%	X
1,2-Dichloroethane	X	X	X	2.9%	X
Carbon tetrachloride	X	X	X	2.7%	X
1,3-Dichloropropene		X	X	99.8%	X
Carcinogenic PAHs: 7-PAH	X		X	61.8%	X
2,3,7,8-TCDD (dioxin)		X	X	23.5%	X
Hexachlorobenzene		X	X	22.3%	X

EXHIBIT 3-8 (Continued)
RESULTS OF THE THREE RANKING ANALYSES

Contaminant	Risk Assessment Hazard Ranking	CEP Urban Analysis (All Sources)	Exposure Toxicity Ranking System	Ratio of Area/Total Emissions	Urban Strategy List[a]
PCBs		X	X	19.9%	X
Acetaldehyde		X	X	18.8%	X
Lead and lead compounds	X	X		16.7%	X
Hydrazine, hydrazine sulfate		X	X	8.0%	X
Quinoline		X	X	6.3%	X
1,2-Dichloropropane (propylene dichloride)		X	X	3.6%	O
1,2-Dibromoethane		X	X	1.5%	O
Coke Oven Emissions	X		X	0.0%	O
1,1,2,2-Tetrachloroethane			X	79.5%	X
Mercury and compounds			X	34.5%	X
Beryllium and compounds		X		27.7%	X
1,1-Dichloroethylene			X	19.3%	
Ethyl acrylate		X		12.5%	
Acrylamide		X		9.1%	
1,1,2-Trichloroethane		X		1.0%	

[a] HAP to be used in selecting area sources for regulation under the Strategy are marked with an "X." HAP selected for the Strategy, but not for area source selection, are marked with an "O."

EXHIBIT 3-9
LIST OF URBAN HAP FOR THE INTEGRATED URBAN AIR TOXICS STRATEGY

Acetaldehyde	Formaldehyde
Acrolein	Hexachlorobenzene
Acrylonitrile	Hydrazine
Arsenic compounds	Lead compounds
Benzene	Manganese compounds
Beryllium compounds	Mercury compounds
1,3-Butadiene	Methylene chloride (dichloromethane)
Cadmium compounds	Nickel compounds
Carbon tetrachloride*	PCBs
Chloroform	POM
Chromium compounds	Quinoline
Coke oven emissions*	2,3,7,8-tetrachlorodibenzo-p-dioxin (& congeners & TCDF congeners)
1,2-Dibromoethane*	1,1,2,2-Tetrachloroethane
1,2-Dichloropropane (propylene dichloride)	Tetrachloroethylene (perchloroethylene)
1,3-Dichloropropene	Trichloroethylene
Ethylene dichloride (1,2-dichloroethane)	Vinyl chloride
Ethylene oxide	

* These 3 HAP are identified mainly due to emissions from major sources, and therefore are not considered urban area source HAP at this time.

including those posing public health concerns in urban areas regardless of emissions source type. Included among the 33 urban HAP are the 30 HAP with greatest emissions contributions from area sources (i.e., the "area source HAP"). The 3 HAP noted with an asterisk are listed mainly due to major source emissions. Nonetheless, they are included in the Integrated Urban Air Toxics Strategy (which considers emissions in urban areas from all source types) based on the criteria presented in this chapter. Under section 112(k), there aren't any specific regulatory implications of listing the other three HAP, and we'll use all 33 HAP in prioritizing efforts to address risk.

It is important to note that the HAP list in Exhibit 3-9 was generated based on our best estimates representing national baseline air toxics emissions and ambient concentrations for

urban areas. For example, implementation of technology-based standards for coke ovens has reduced the benzene, coke oven gases, and POM from these sources by 80 percent (or 1,408 tons per year) since 1993. In addition, certain urban areas have reduced other benzene emissions by as much as 30 or 40 percent. Much of this reduction is attributable to the implementation of mobile source reformulated gasoline requirements. To ensure that we appropriately target reductions of urban air toxics to support the protection of public health, it will be important to reevaluate our priorities as we develop emissions estimates and obtain more comprehensive monitoring information covering more recent years.

3.5 References

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4. Regulatory Programs and Activities to Reduce Air Toxics Emissions

4.1 Introduction

The Strategy describes many of the programs and regulatory activities that will help achieve the goals of reducing cancer and noncancer risks. One of the key aspects described by the Strategy is that national regulatory programs are but one of the many tools that we will use to address emissions of air toxics. Other authorities and laws will, directly or indirectly, also allow us to address these pollutants. Furthermore, by working collaboratively with State, local, and Tribal governments, we will ensure that localized air toxics issues are addressed as well.

Section 4.2 presents the list of area source categories that were identified in the Strategy and explains how we intend to ensure that, as required, we reach the goal of addressing the source categories that represent 90 percent of the emissions of each of the 30 area source HAP. Section 4.3 describes the regulatory options that will be considered in order to address air toxics from area sources. The role of mobile sources is noted in section 4.4, and current and future programs are described. Other emission sources which may be affected by the Strategy are described in section 4.5, while other programs and authorities which may also account for emissions reductions are described in section 4.6. A very important component of the Strategy is described in section 4.7 – the role State, local, and Tribal programs will play in helping us address air toxics and achieve the Strategy goals. References are listed in section 4.8.

4.2 List of Area Source Categories

Our selection of the area source categories was a two-step process. First, we identified area sources that contribute to emissions of the area source HAP and that are subject to existing standards or will be subject to standards that are currently being developed. These area source categories have already been listed for regulation under the CAA. For each of these source categories, we identified the percent contribution to the total area source emissions for each of the 30 area source HAP. These source categories are provided in Exhibit 4-1. We have included hazardous waste combustors[1] on this list, despite the fact that information related to the percentage contribution of emissions from this area source category was not known at the time that the list was developed. Once we determine the percentage of urban area emissions from the area source categories affected by this rule, their emissions will be counted toward the 90 percent requirement for the appropriate HAP[2].

[1]The Hazardous Waste Combustor source category combines the following: hazardous waste incinerators, hazardous waste-burning cement kilns, and hazardous waste lightweight aggregate kilns.

[2]We have recently promulgated MACT standards for hazardous waste combustors (U.S. EPA, 1999a) and will be using the support information for that rule to update our information on this source category.

EXHIBIT 4-1
AREA SOURCE CATEGORIES ALREADY SUBJECT TO REGULATION OR WHICH WILL BE SUBJECT TO REGULATION

Chromic Acid Anodizing	Industrial Boilers
Commercial Sterilization Facilities	Institutional/Commercial Boilers
Other Solid Waste Incinerators (Human/Animal Cremation)	Medical Waste Incinerators
Decorative Chromium Electroplating	Municipal Waste Combustors
Dry Cleaning Facilities	Open Burning Scrap Tires
Halogenated Solvent Cleaners	Portland Cement
Hard Chromium Electroplating	Secondary Lead Smelting
Hazardous Waste Combustors	Stationary Internal Combustion Engines

In the second step, we added to the list those area source categories that contribute at least 15 percent of the total area source emissions of any of the individually-listed HAP. This criterion was adopted to account for uncertainties in our current inventory data. Although the baseline emissions inventory data have improved, data gaps and uncertainty still remain. By listing only those additional sources contributing 15 percent of the area source emissions of at least one of the area source HAP, we can be fairly certain that, despite the gaps in our inventory data, a listed source category genuinely contributes to emissions of that HAP. Once listed, we counted the percent contribution, even if less than 15 percent, to emissions of any other listed HAP because once the source is subject to regulation, its emissions of any of the 30 listed HAP can be counted toward the 90 percent goal for each of the listed HAP. Exhibit 4-2 includes those new area source categories listed under section 112(c)(3) for the first time.

The result of these criteria for the source selection process is that the current list of 29 source categories does not, at this time, contain area source categories representing 90 percent of the emissions of each individual HAP. The current list meets the 90 percent or greater requirement for 11 of the 30 area source HAP[3]. For 10 other HAP, the list accounts for at least 80 percent of the emissions[4], and for ethylene dichloride the list accounts for approximately 78 percent of the emissions. Improved inventory data may demonstrate that the current list of area sources already meets the 90 percent requirement for some of these HAP. For the remaining HAP on the list, less than 75 percent of their emissions are accounted for in the list of source

[3]1,1,2,2-tetrachloroethane, 1,2-dichloropropane, POM, acetaldehyde, acrolein, benzene, dioxins/furans, ethylene oxide, formaldehyde, quinoline, and tetrachlorethylene.

[4]1,3-butadiene, 1,3-dichloropropene, acrylonitrile, beryllium compounds, chloroform, hydrazine, mercury compounds, methylene chloride, trichloroethylene, and vinyl chloride.

EXHIBIT 4-2
NEW AREA SOURCE CATEGORIES AS LISTED

Cyclic Crude and Intermediate Production	Municipal Landfills
Flexible Polyurethane Foam Fabrication Operations	Oil & Natural Gas Production
Hospital Sterilizers	Paint Stripping Operations
Industrial Inorganic Chemical Manufacturing	Plastic Materials and Resins Manufacturing
Industrial Organic Chemical Manufacturing	Publicly Owned Treatment Works
Mercury Cell Chlor-Alkali Plants	Synthetic Rubber Manufacturing
Gasoline Distribution Stage I	

categories: arsenic compounds, cadmium compounds, chromium compounds, hexachlorobenzene, lead compounds, manganese compounds, nickel compounds and PCBs.

It's important to clarify that we still intend to meet our statutory obligation to list area sources accounting for 90 percent of the emissions of each of the 30 area source HAP. We have chosen to complete this list in stages by keeping the option to add or delete source categories from the list as we gather more and improved data. This first stage lists those area sources that we are reasonably confident add real contributions to the total area source emissions of a particular area source HAP. We anticipate to begin evaluating the source categories for the HAP for which we haven't reached a 90 percent emission reduction, including the six metal HAP, PCBs, and hexachlorobenzene, when we conduct an initial risk assessment by the end of 2000 (discussed in Chapter 5 of this Report). That initial assessment will use the updated 1996 NTI. We'll use this information as part of our process to reevaluate the source categories listed in the Strategy. Based on this updated information, we may decide to remove an area source category listed here if, for example, the reason for the listing was inaccurate (e.g., faulty reporting to the TRI) or if no urban area sources exist. We'll also use this assessment to evaluate area source categories to be added and will complete the list by 2003.

4.3 Regulatory Activities for Area Sources

We plan to pursue a tiered approach that will consider three standard-setting processes. The specific process selected for a particular source category will depend on the criteria outlined below. We intend to determine which one of these approaches is most appropriate when we conduct rulemaking. The three tiers of standard setting processes that will be considered are:

- Tier 1 – MACT standards;
- Tier 2 – Source category-specific GACT standards; and
- Tier 3 – Flexible GACT.

4.3.1 Tier 1 – MACT Standards

We'll develop MACT standards in accordance with section 112(d)(3) for those area sources whose emissions pose the greatest threat to human health and the environment, and for which the technology to achieve maximum reductions in HAP emissions is appropriate. Section 112(d)(3) requires the standards to reduce HAP emissions as much as is achievable, considering the cost of these reductions, effects on health or the environment (other than air), and energy requirements.

Section 112(d)(3) requires us to use a minimum statutory baseline ("floor") when setting MACT standards. For new sources, the MACT standards for a source category or subcategory must be at least as stringent as the emission control achieved in practice by the best controlled similar source. The standards for existing sources can be less stringent than standards for new sources, but they can't be less stringent than the average emission limitation achieved by the best-performing 12 percent of existing sources (excluding certain sources) for categories or subcategories with 30 or more sources, or by the best-performing five sources for categories or subcategories with fewer than 30 sources.

We've issued MACT standards for area sources in previous cases. For example, in the chromium electroplating national emission standards for hazardous air pollutants (NESHAP), we developed MACT standards for area sources because of the high toxicity of chromium. Similarly, in the Portland Cement NESHAP, we determined that MACT controls were appropriate because of the quantity and toxicity of the HAP being emitted from area sources. In addition, both of these source categories have numerous, widespread sources. We've also determined in a recent rulemaking that air toxic emissions from area source hazardous waste combustors present a threat of adverse effects to human health and, thus, will be required to meet MACT controls.

4.3.2 Tier 2 – Source Category-Specific GACT Standards

While we may develop MACT standards for some area sources, we expect most sources will be subject to GACT standards developed in accordance with section 112(d)(5). As with MACT standards, GACT standards would be developed for a specific source category, but they would be based on the use of GACT rather than MACT. This approach will be used to address source categories that present a human health risk or environmental concern, but where GACT is a more appropriate approach for reducing HAP emissions than MACT. To make these decisions, we'll consider economic feasibility and other factors that could lead us to GACT.

4.3.3 Tier 3 – Flexible GACT Process

Considering the large number and diversity of area sources and limitations in the data and information currently available for many of them, it may be appropriate to develop flexible requirements that would apply to several area source categories where more flexibility is appropriate (e.g., where there are very few area sources, they are confined to a limited geographic

area, or they contribute to localized public health or environmental risks). Under this option, we might develop general requirements, such as a process rule similar to the one developed under section 112(g) of the CAA, which would be applicable to area sources in several source categories. These general requirements could outline procedures for determining what constitutes "generally available control technology." In this context, by following these procedures, States, local governments, and Tribal agencies could elect to develop GACT for the area sources. We would review these resulting standards to ensure they were developed following the procedures contained within the general requirements and, if appropriate, we would adopt the standards as GACT for these area sources.

We believe this approach presents several advantages. It could be implemented in a manner that permits States, local and Tribal agencies to address cumulative risk posed by exposures to HAP emissions from many different source categories. It also permits greater flexibility in tailoring GACT to individual area sources or area source categories which may contribute to an undue public health risk in a particular area. For example, a State, local or Tribal agency could tailor GACT to a particular source by requiring potentially more stringent controls when the source contributes emissions that, when aggregated with emissions from other sources in the area, pose health risk concerns. They could also require less stringent controls when the source is in an area where exposures to aggregated emissions don't present significant concern.

To supplement our general requirements, we may choose to issue control technique guidelines or alternative control technology documents to provide information on generally available control technologies for controlling HAP emissions. The CAA gives us flexibility in deciding which level of control to apply to a given source category. As long as the result of the rulemaking is that sources use enforceable GACT or management practices, we have the flexibility in choosing between the adoption of numerical emission limits and the promulgation of other requirements that result in sources applying GACT.

4.3.4 Issues on the National Versus Local Scope of Area Source Standards

Section 112(k) requires that listed area source categories be subject to standards under section 112(d). Section 112(d) standards are national standards that generally apply everywhere in the country. Consistent with this approach, we expect, in general, to apply area source standards developed under section 112(k) nationally; however, for those area source categories where the standards only apply in urban areas, we'll look to the consolidated metropolitan statistical area (C/MSA) boundaries as a starting point to define the urban area. Although we used the "urban 1" and "urban 2" definitions[5] for the development of the inventory to support the HAP and the source category analysis, we believe the C/MSAs are more appropriate for defining

[5]"Urban 1" areas are those counties that have a population of more than 250,000. "Urban 2" areas are counties where at least 50 percent of the population is considered to be urban.

applicability of area source standards, because the C/MSAs better reflect the nature of population density, commercial development, area growth, and air emissions that represent urban areas.

Although we generally believe that urban areas are those C/MSAs with populations of more than 50,000, we recognize that the appropriate area in which standards should apply may vary among area source categories. Consequently, we believe the determination of the appropriate urban area size for where standards apply should be made separately for each category.

4.3.5 Schedule for Area Source Standards

The Strategy outlined a timeframe for the completion of area source standards, as shown in the time line below:

- 2004 – Promulgate the area source category standards listed in Exhibit 4-2; we expect to meet this demanding schedule as expeditiously as practicable;
- 2006 – Promulgate some additional area source standards to meet the 90 percent requirement;
- 2009 – Promulgate all remaining area source standards necessary to meet the 90 percent requirement; and
- 2012 – Expected compliance under all standards.

We'll prioritize the order in which we regulate source categories to address those posing the greatest risks first. This will be a part of our initial assessments which will be done in the spring of 2000. We'll be developing standards between now and 2009. Compliance with these standards is required within 3 years of promulgation. Therefore, compliance with all standards is anticipated by no later than 2012.

4.4 Regulatory Activities for Mobile Sources

4.4.1 Urban HAP Emitted from Mobile Sources

There are hundreds of different compounds and elements that are known to be emitted from passenger cars, on-highway trucks, and various nonroad equipment. Using emission speciation data from several sources, we have determined that 15 of the compounds included in the list of 33 urban HAP may be emitted from mobile sources[6]. These are listed in Exhibit 4-3,

[6]As part of the air toxics rulemaking currently under development pursuant to the requirements of section 202(l) of the CAA, described below, we will be preparing a more comprehensive list of air toxics emitted by motor vehicles and their fuels.

along with their absolute and relative contributions as determined by our baseline emissions inventory.

The inventory estimates presented in Exhibit 4-3 are 1990 estimates. As we continue to improve our inventories for urban HAP from mobile sources, these values may change. For example, the 1996 NTI is incorporating new information based on improved data and methods.

Based on information in EPA's Integrated Risk Information System (IRIS) database, four of the urban HAP listed in Exhibit 4-3 are VOCs considered to be known or probable human carcinogens (acetaldehyde, benzene, 1,3-butadiene, and formaldehyde), and a fifth VOC, acrolein, is considered to be a possible human carcinogen (U.S. EPA, 1999b). POM includes a number of carcinogenic compounds such as benzo(a)pyrene. While 2,3,7,8-TCDD (& congeners & TCDF congeners) has a very high potency, it is emitted in only trace amounts by mobile sources (Truex et al., 1998; Gertler et al., 1997; U.S. EPA, 1998a). The eight remaining HAP listed in Exhibit 4-3 are metals that may be contained in very small quantities in particulate emissions from gasoline and/or diesel engines[7].

4.4.2 Diesel Exhaust

Diesel exhaust is one of the pollutants under consideration for inclusion on a comprehensive list of air toxics emitted by motor vehicles and their fuels in the section 202(l) rulemaking, described below. Diesel exhaust was not included by Congress on the list of 188 HAP under section 112(b) of the CAA and consequently was not included in the group of pollutants that were considered for inclusion on the urban HAP list. Because diesel exhaust emissions come almost exclusively from mobile sources, we are investigating the health risks associated with diesel exhaust and assessing its role in the urban air toxics problem as part of the section 202(l) rulemaking process.

Diesel exhaust includes components in the gas and particle phases. Gaseous components of diesel exhaust include at least one organic compound known to cause cancer in humans (e.g., benzene) while possible or probable human carcinogens and compounds causing noncancer effects are also present in the gas-phase (e.g., formaldehyde, acetaldehyde, 1,3-butadiene,

[7]These metals are arsenic compounds, beryllium compounds, cadmium compounds, chromium compounds, lead compounds, manganese compounds, mercury compounds, and nickel compounds. It is worth noting that: (1) hexavalent chromium, a known human carcinogen, is the carcinogenic compound of interest among chromium compounds; (2) nickel has been classified as a known human carcinogen; (3) while lead in gasoline has been phased-out for use in cars, it is still used in aircraft and in racing fuel; (4) recent studies have not been able to detect mercury compounds in measurable amounts in light-duty gasoline or heavy-duty diesel mobile source emissions (Ball, 1997; Truex et al., 1998); however, we are presently undertaking further study of mercury emissions from vehicles, and the Ball (1997) and Truex et al. (1998) studies should not be viewed as conclusive; and (5) we are investigating the potential health impact of manganese in fuels under our section 211 testing programs, described below; and (6) while mobile source emissions of beryllium compounds and cadmium compounds are reported in our baseline inventory, these emission estimates are derived from data that are more than 10 years old and thus may not be representative of current emissions.

EXHIBIT 4-3
1990 NATIONAL EMISSION ESTIMATES
FOR URBAN HAP EMITTED FROM MOBILE SOURCES†

HAP	Mobile Source Tons/year	Total Emissions Tons/year	Percent Mobile Source Contribution
Acetaldehyde	65,535	137,476	47
Acrolein	12,315	67,901	18
Arsenic compounds	3	284	1
Benzene	281,170	390,615	72
Beryllium compounds	0.02	12.15	0.16
1,3-butadiene	47,822	71,870	66
Cadmium compounds	0.31	203.34	0.15
Chromium compounds	54	927	6
Formaldehyde	177,031	350,617	50
Lead compounds	1,199	3,270	37
Manganese compounds	52	2,846	2
Mercury compounds	12	208	6
Nickel compounds	95	1,245	8
POM ‡	48	1,318	4
2,3,7,8-TCDD (& congeners & TCDF congeners)	0.0001	0.0032	2.9844

†Emissions and percentages for most of these compounds are rounded to the nearest whole unit. However, due to the small amount of emissions of beryllium and compounds and cadmium and compounds, these emissions and percentages are reported to 2 decimal places. Similarly, values for 2,3,7,8-TCDD (& congeners & TCDF congeners) emissions and percentages are reported to four decimal places.

‡ POM represents the 7-polycyclic aromatic hydrocarbons (7-PAH) group from the baseline emissions inventory.

acrolein). Because diesel exhaust is a mixture of particles and gases, the choice of a measure of exposure (i.e., dosimeter) is important. The EPA believes that exposure to whole diesel exhaust is best described, as many researchers have done over the years, by diesel particulate concentrations expressed in units of mass concentration (e.g., $\mu g/m^3$). This does not imply that mass is the only toxicologically important aspect of PM since other parameters such as particle

number, particle size, surface area, and chemical composition can influence toxicity. The choice of this dosimeter implies that the contribution of the gaseous components and diesel particulate constituents to toxicity are related by diesel particulate mass. This assumption is consistent with historic practice, but can only be validated when there is a better understanding of the toxicological mode of action for diesel exhaust.

While some gaseous components of diesel exhaust may play a role in the cancer hazard attributed to diesel exhaust exposure, studies suggest that the particulate component plays a substantial role in carcinogenicity and other noncancer effects. Diesel PM typically consists of a solid core, composed mainly of elemental carbon, which has a coating of various organic and inorganic compounds. The characteristically small particle size (on average 0.2 microns in diameter) increases the likelihood that the particles and the attached compounds will reach and lodge in the deepest and more sensitive areas of the human lung. Diesel PM may be influential in contributing to potential human health hazards from long term exposure.

Our draft health assessment for diesel emissions identifies lung cancer and several other adverse respiratory health effects (including respiratory tract irritation, immunological changes, and changes in lung function) as possible concerns for long term exposure to diesel exhaust (U.S. EPA, 1999c). The evidence for these health effects comes from occupational exposures and high exposure animal studies. The draft health assessment finds that diesel exhaust is a likely human carcinogen in the lung at environmental levels of exposure, and that exposure to diesel exhaust can pose a noncancer health risk. The draft health assessment document is currently being revised to address comments from a peer review panel of the Clean Air Scientific Advisory Committee (CASAC) (U.S. EPA, 2000a) and will be reviewed by CASAC again in late 2000.

4.4.3 Mobile Source Emission Control Programs

We regulate mobile sources emissions through a wide range of programs under the authority contained in several sections of the CAA. These include the motor vehicles provisions contained in section 202(a), the fuel requirements contained in section 211, the nonroad engine and vehicle provisions contained in section 213, and the urban bus standards contained in section 219. While many of our programs are designed primarily for control of criteria pollutants, especially ozone and PM, they also achieve important reductions in air toxics through VOC and HC controls. For example, vehicle- and engine-based control programs reduce benzene, 1,3-butadiene, formaldehyde, and acetaldehyde that are produced during the combustion process when there is incomplete combustion. Overall, vehicle- and engine-based HC controls have dramatically reduced exhaust emissions of gaseous air toxics emitted by mobile sources. Similarly, we have several programs that reduce diesel exhaust emissions from diesel engines and equipment. Finally, our evaporative control programs are designed to further reduce emissions of volatile air toxics due to engine design or faulty components that allow fuel vapors to escape into the atmosphere.

We also address mobile sources air toxics through fuel requirements. Our fuel control programs have resulted in significant reductions in the emissions of toxic substances from motor

vehicles. The phase-out of lead in gasoline has essentially eliminated mobile sources emissions of this highly toxic substance. More recently, the reformulated gasoline (RFG) program has assisted areas of the country with the worst ozone problems to help improve their air quality. By controlling fuel benzene content and vehicle emissions of air toxics, ozone-forming HC and NO_x, Phase I of the RFG program has removed thousands of tons of air pollutants for the 17 States and the District of Columbia currently participating in the program. Phase II of the RFG program began on January 1, 2000 and contains even more stringent emissions reductions requirements than Phase I.

In addition to vehicle and fuel control programs, we have established several programs to make sure vehicle emission controls are functioning properly in actual use. At the national level, vehicle manufacturers are required to install computerized diagnostic systems that alert drivers and mechanics to malfunctioning emission controls. We also follow up with manufacturers by performing selective engine testing as engines leave the assembly line to make sure they are manufactured as designed and meet the mandatory exhaust emission limits. At the State level, we have developed programs that States can adopt to require vehicle owners to have their vehicles periodically inspected. In addition, we follow up on in-use performance by testing or requiring that manufacturers test vehicles that have been in service.

In continuing our progress in controlling emissions from mobile sources, there are four major recent and ongoing mobile source rulemaking activities that have the potential to achieve additional reductions of health risks from air toxics. First, in October of 1999, we proposed to reconfirm heavy-duty diesel engine emission standards for the 2004 model year and proposed heavy-duty gasoline vehicle emission standards for the 2004 model year (U.S. EPA, 1999d). Second, we recently promulgated stringent new "Tier 2" emission standards and gasoline sulfur controls that will reduce NO_x and HC emissions from light-duty vehicles and light-duty trucks[8] (U.S. EPA, 2000b). The Tier 2 program also contains new PM limits that will reduce PM emissions from the diesel versions of these vehicles. Third, we recently proposed heavy-duty engine and vehicle standards for the 2007 model year and highway diesel fuel sulfur controls beginning in 2006 (U.S. EPA, 2000c). The proposed diesel fuel sulfur controls would enable the use of a new generation of emission control technologies for diesel engines to decrease diesel PM and other emissions. Fourth, we are conducting a technology review, to be concluded in 2001, for land-based compression ignition nonroad engines (U.S. EPA, 1998b).

4.4.4 Mobile Source Air Toxics Assessments and Controls

In addition to the general emission control provisions mentioned above, title II of the CAA contains provisions that call more directly for reductions in HAP from motor vehicles and their fuels. These provisions are contained in section 202(l) of the CAA. The first of these requirements, outlined in section 202(l)(1), requires us to study the need for and feasibility of

[8]Chapter 3 of the Regulatory Impact Analysis for this rule assesses the impacts of the Tier 2 program on air toxics (U.S. EPA, 1999e).

controlling emissions of toxic air pollutants associated with motor vehicles and their fuels that are otherwise unregulated under the CAA.

Pursuant to section 202(l)(1), in 1993 we released the *Motor Vehicle-Related Air Toxics Study* (U.S. EPA, 1993). The study summarized information on emissions of toxic air pollutants associated with motor vehicles and motor vehicle fuels, as well as estimated exposures and potential risks. The study also provided predictions of cancer risks associated with continuous lifetime exposure to motor vehicle emissions of several air toxics in the years 1990, 1995, 2000, and 2010 under various control scenarios. We have recently updated the emissions and exposure analyses done for the study to account for new information (U.S. EPA, 1999f). These analyses include base scenarios for the years 1990, 1996, 2007, and 2020, and control scenarios in 2007 and 2020. We modeled toxics emissions and exposure for 10 urban areas (Atlanta, Chicago, Denver, Houston, Minneapolis, New York, Philadelphia, Phoenix, Spokane, and St. Louis), and nationwide. In addition, we developed emission estimates for 16 geographic regions. We assessed emissions and exposure from benzene, formaldehyde, acetaldehyde, 1,3-butadiene, methyl tertiary butyl ether (MTBE), and diesel PM. As part of our section 202(l)(2) proposal (see below), we will outline the additional research and technical analysis we plan to conduct to improve these analyses.

We have several activities already under way to improve our understanding of the risks associated with exposure to mobile source air toxics. We are developing and updating information on health effects for some pollutants on the urban HAP list with contributions from mobile sources including, for example, our recent benzene cancer risk assessment (U.S. EPA, 1998c; U.S. EPA, 1985) and our draft 1,3-butadiene risk assessment (U.S. EPA, 1998d)[9]. We are also continuing our research on health effects of diesel exhaust through the development of our diesel health assessment document, and through the support of research efforts by organizations such as the Health Effects Institute. We are developing models of mobile source emissions as inputs for emissions inventory and dispersion modeling efforts such as the NTI and ASPEN (see discussion in Chapter 6 of this Report). In addition, we seek to better characterize emissions and exposures to HAPutants through research and testing efforts at EPA facilities such as the National Exposure Research Laboratory, as well as the National Vehicle Fuel and Emissions Laboratory. We also have programs requiring manufacturer-run fuel and fuel additive health effects testing programs under section 211(b) of the CAA, including testing of various fuels containing oxygenates, such as MTBE or ethanol, as well as research focused on the gasoline additive, methylcyclopentadienyl manganese tricarbonyl (MMT), and tailpipe emissions of manganese particulates[10].

[9]This assessment is currently being revised based on comments from the EPA Science Advisory Board (SAB) and others.

[10]The test requirements for fuels containing oxygenates include short and long term animal health effects testing, as well as human microenvironmental exposure measurement studies to determine how much of certain compounds we breathe in our everyday lives. The list of compounds includes, but is not limited to, air toxics such as benzene, 1,3-butadiene, formaldehyde, and acetaldehyde. The MMT testing program includes pharmacokinetic

Section 202(l)(2) of the CAA instructs us to set standards for HAP from motor vehicles or their fuels, or both. Those standards are to reflect the greatest degree of emissions reductions achievable through the application of technology which will be available, taking into consideration existing standards, availability and costs of the technology, noise, energy, and safety factors, and leadtime. The CAA also specifies that, at a minimum, benzene and formaldehyde emissions must be addressed. We are currently working on a proposal in compliance with section 202(l)(2). As indicated above, we are not limiting our examination of toxic emissions from motor vehicles and their fuels to benzene and formaldehyde; rather, we are preparing a more comprehensive list of air toxics emitted by motor vehicles and their fuels for consideration in the rulemaking.

4.5 Other Hazardous Air Pollutant Emission Sources

As discussed previously, section 112(k)(3)(B) of the CAA requires that we ensure that area sources accounting for 90 percent of the aggregate emissions of each of the 30 area source HAP are subject to standards. However, in achieving required reductions in cancer incidences, section 112(k)(3)(C) permits us to consider reductions in public health risks resulting from actions to reduce emissions from "all stationary sources and resulting from measures implemented by the Administrator or by the States under this or other laws." Therefore, we'll consider emission reductions from a combination of major and area sources in conducting risk assessments to address this requirement.

These assessments will support regulatory efforts under the CAA and other authorities, as necessary, to address the identified risk. For example, any reductions resulting from MACT, the NAAQS, and other programs that achieve reductions in HAP can be included in the assessment of reductions in risks. Therefore, if we determine that a source category or an individual source is presenting a significant health risk, then we'll address it using the appropriate regulatory authority. For example, if needed to provide an ample margin of safety to protect human health, section 112(f) residual risk standards will be developed for source categories currently subject to MACT. Additionally, if our analyses reveal a major source category that is currently unregulated or unlisted but poses a public health risk, we'll list that source category under the authority of section 112(c) and develop the necessary regulations under section 112(d), or we may address it through other activities like pollution prevention or voluntary programs. Similarly, if a specific source is contributing to a local risk problem, then the State, local or Tribal program may be more appropriate for addressing that risk.

We also intend to coordinate our authorities in addressing cumulative risks posed by exposures to aggregate emissions from multiple source types. For example, during the development of the Strategy, many commenters raised concerns about the risks from airports to the communities that surround them. Airports can be viewed as "mini-cities," which produce

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testing of manganese compounds and characterization of manganese emissions from vehicles utilizing fuels containing MMT.

numerous pollutants from multiple sources and are governed by many different authorities. We'll need to have an integrated plan to reduce air emissions and the many other environmental impacts associated with aviation activities.

Although airports don't meet the definition of "area" or "major" source under section 112 of the CAA, we're involved with numerous efforts to better understand and reduce the environmental impacts of aviation-related activities and their associated human health risks. For example, we co-chair the EPA/Federal Aviation Administration Voluntary Aircraft Emissions Reduction Initiative, a multistakeholder process designed to identify and evaluate technically feasible and cost-effective voluntary measures to reduce aviation emissions. We're actively involved in the International Civil Aviation Organization, which is the forum for evaluating and establishing international aircraft engine standards. We're also participating with other stakeholders in the development of the South Coast Ground Service Equipment memorandum of understanding (MOU) in California to identify ways to achieve additional emissions reductions from the commercial aviation community. Implementation of the MOU should yield emissions reductions through increased use of cleaner engines, electrification, and alternative fuels. In addition, we're developing a Green Airport Initiative to demonstrate innovative strategies for reducing the environmental impacts of aviation-related activities at an airport undergoing expansion. In April 1999, we released a report that assesses the current and potential impact of aircraft emissions on local air quality at ten selected airports (U.S. EPA, 1999g). The regulatory and voluntary actions under way for aviation will produce data that can inform the Strategy and begin to address the environmental impacts of aviation-related activities and their associated risks to the communities that surround them.

4.6 Other Programs and Authorities

We've already made progress in addressing air toxics emissions using existing programs. To put the problem in perspective, we estimate that approximately 8.1 million tons of 188 HAP were released in the United States in 1993 (U.S. EPA, 1998c). We've already issued at least 43 MACT and GACT standards and two section 129 standards with post-1993 compliance dates, which will address many sources of these emissions. Exhibit 4-4 lists the MACT standards that we have finalized as of June 2000. Emission controls for the Nation's cars, trucks and off-road equipment, and standards for fuels add even more to these reductions. In this section, we'll discuss the utility of these programs and others to achieve additional air toxics emissions reductions.

EXHIBIT 4-4
COMPLETED RULES from SECTION 112 of the CAA (MACT STANDARDS)[a]

Source Category	Final Rule Publication Date (Citation)[b]	Source Category	Final Rule Publication Date (Citation)[b]
Dry Cleaning	09/22/93 (58 FR 49354)	Hazardous Organic NESHAP (HON)	04/22/94 (59 FR 19402)
Aerospace Industry	09/01/95 (60 FR 45956)	Asbestos	11/30/95 (60 FR 61550)
Chronium Electroplating	01/25/95 (60 FR 4948)	Coke Ovens	10/27/93 (58 FR 57898)
Commercial Sterilizers	12/06/94 (59 FR 62585)	Degrease Organic Cleaners	12/02/94 (59 FR 61801)
Gasoline Distribution	12/14/94 (59 FR 64303)	Industrial Cooling Towers	09/08/94 (59 FR 46339)
Magnetic Tape	12/15/94 (59 FR 64580)	Marine Vessel Loading Operations	09/19/95 (60 FR 48399)
Off-site Waste and Recovery Operations	07/01/96 (61 FR 34140)	Petroleum Refineries	08/18/95 (60 FR 43244)
Polymers & Resins I	09/05/96 (61 FR 46906)	Polymers & Resins II	03/08/95 (60 FR 12670)
Polymers & Resins IV	09/12/96 (61 FR 48208)	Printing/Publishing	05/30/96 (61 FR 27132)
Secondary Lead Smelters	06/23/95 (60 FR 32587)	Shipbuilding & Ship Repair	12/15/95 (60 FR 64330)
Wood Furniture	12/07/95 (60 FR 62930)	Chromium Chemicals Manufacturing	06/04/96 (61 FR 28197)
Electric Arc Furnace: Stainless & Non-stainless Steel	06/04/96 (61 FR 28197)	Ferralloys Production	05/20/99 (64 FR 27450)
Flexible Polyurethane Foam Production	10/07/98 (64 FR 34853)	Generic MACT	06/30/99 (64 FR 34853)
Mineral Wool Production	06/01/99 (64 FR 29490)	Nylon 6 Production	02/12/98 (63 FR 7155)

EXHIBIT 4-4 (Continued)
COMPLETED RULES from SECTION 112 of the CAA (MACT STANDARDS)[a]

Source Category	Final Rule Publication Date (Citation)[b]	Source Category	Final Rule Publication Date (Citation)[b]
Oil & Natural Gas Production, Transmission & Storage	06/17/99 (64 FR 32610)	Pesticide Active Ingredient Production	06/23/99 (64 FR 33549)
Pharmaceuticals Production	09/21/98 (63 FR 50280)	Phosphoric Acid/ Phospate Fertilizers	06/10/99 (64 FR 31358)
Polyether Polyols Productions	06/01/99 (64 FR 29420)	Portland Cement Manufacturing	06/14/99 (64 FR 31897)
Primary Aluminum Production	10/07/97 (62 FR 52383)	Primary Lead Smelting	06/04/99 (64 FR 30194)
Pulp & Paper (Non-combust) MACT I	04/15/98 (63 FR 18504)	Pulp & Paper Cluster Rule (Non-chem) MACT III	03/08/96 (61 FR 9383)
Steel Pickling - HCL Process Facilities & Hydrochloric Acid Regeneration Plants	06/22/99 (64 FR 33202)	Tetrahydrobenzaldehyde Manufacture	05/12/98 (63 FR 26078)
Wood Treatment MACT	06/04/96 (61 FR 28197)	Wood Fiberglass Manufacturing	06/14/99 (64 FR 31695)
Cyanuric Chloride Production	02/12/98 (63 FR 7155)	Lead Acid Battery Manufacturing	06/04/96 (61 FR 28197)
Secondary Aluminum	03/23/2000 (65 FR 15689)	Publicly Owned Treatment Works (POTW)	10/26/99 (64 FR 57572)
Polymers & Resins III	01/20/2000 (65 FR 3275)	Antimony Oxides Manufacturing	11/18/99 (64 FR 63025)
Aerosol Can-Filling Facilities	11/18/99 (64 FR 63025)		

[a] Current as of June, 2000.
[b] Citation identifies the *Federal Register* (FR) volume and page number (e.g., 58 FR 49354 can be found in FR volume 58, page 49354).

4.6.1 Federal Regulatory Activities – CAA Section 112 Authorities

Section 112 of the CAA provides several authorities for us to use in meeting our air toxics goals. We've promulgated section 112(d) MACT and GACT standards that are projected to reduce air toxics emissions by approximately one million tons per year once fully implemented. Within the next ten years, as we complete more MACT and GACT standards, the air toxics program is projected to reduce emissions of toxic air pollutants by well over 1.5 million tons per year. These nationwide emissions reductions will contribute significantly to reductions needed in urban areas.

The need for section 112(f) standards, or "residual risk" standards, is under consideration for some of the early source categories covered by MACT standards. Where justified, these standards will address remaining public health and environmental impacts of HAP to ensure an ample margin of safety to protect public health and, in consideration of other factors, to prevent adverse environmental effects. Consistent with the requirements of the CAA, we'll consider such evaluation for those area source categories for which GACT standards have been promulgated.

The chemical accident prevention regulations ("Risk Management Program requirements," or "RMP rule") were promulgated under section 112(r). These regulations require owners and operators handling more than a threshold quantity of any substance on the list of regulated toxic substances and threshold quantities for accidental release prevention (40 CFR 68.130) to develop risk management plans to prevent and address accidental releases. Eighteen of these listed substances are HAP.

We've already received several requests for permits under the section 112(g) construction and reconstruction rule. This rule applies to new or reconstructed major sources and requires them to install MACT to reduce HAP emissions. In addition, the section 112(i)(5) rule (early reductions) provides incentives for sources to reduce emissions by up to 95 percent from 1990 levels prior to proposal of MACT for that source category. Approximately 27 title V permit applications have been received, representing HAP reductions of over 6,800 tons.

Section 112 (n)(1)(A) requires us to conduct a study of the hazards to public health reasonably anticipated to occur as a result of HAP emissions from fossil fuel-fired electric utility steam generating units (i.e., utilities) and on the alternative control strategies for HAP emissions which may warrant regulation. In addition, section 112 (n)(1)(A) requires us to regulate HAP emissions from utilities if we find such regulation is appropriate and necessary after considering the results of study. In February 1998, we published a report describing the results of the study described above (U.S. EPA, 1998h). The primary components of the report are: (1) a description of the industry, (2) an analysis of emissions data, (3) an assessment of hazards and risks due to inhalation exposures to 67 HAP, (4) assessments of risks due to multipathway (inhalation plus non-inhalation) exposures to 4 HAP (radionuclides, mercury, arsenic, and dioxins), and (5) a discussion of alternative control strategies. The overall conclusion of the 1998 Utility Study is as follows:

Based on available information and current analyses, the EPA believes that mercury from coal-fired utilities is the HAP of greatest potential concern and merits additional research and monitoring. There are uncertainties regarding the extent of risks due to mercury exposures, including those from utility emissions. Further research and evaluation are needed to gain a better understanding of the risks and impacts of utility mercury emissions. In addition, further research and evaluation of potential control technologies and strategies for mercury are needed.

For a few other HAP, there are still some remaining potential concerns and uncertainties that may need further study. First, the screening multipathway assessments for dioxins and arsenic suggest that these two HAP are of potential concern (primarily from coal-fired plants); however, further evaluations and review are needed to better characterize the impacts of dioxins and arsenic emissions from utilities. Second, nickel emissions from oil-fired utilities are of potential concern, but significant uncertainties still exist with regard to the nickel forms emitted from utilities and the health effects of. those various forms. The impacts due to HAP emissions from gas-fired utilities are negligible based on the results of this study; therefore, the EPA feels that there is no need for further evaluation of the risks of HAP emissions from natural gas-fires utilities (U.S. EPA, 1998h).

We plan to make the regulatory determination in December 2000. In the interim, we are collecting additional information on mercury emissions and potential control technologies as well as conducting various analyses to increase our understanding of the impact of HAP emissions (especially mercury) from utilities and the feasibility of reducing those emissions.

4.6.2 Other CAA Authorities

Other programs under the CAA also contribute to the reductions of HAP in urban areas. For example, section 109 requires States to develop State implementation plans to attain compliance with the NAAQS. Many of the activities that are designed to address criteria pollutants (e.g., ozone, PM, and lead) and attain the NAAQS also achieve reductions in air toxics. For example, many of the VOCs that form ozone are also air toxics, such as benzene and 1,3-butadiene. In addition, some VOCs can react in the atmosphere to form HAP, such as formaldehyde. Thus, controlling VOCs leads to reductions in air toxics. Similarly, compliance with the PM standards will provide incidental, but potentially significant, reductions in HAP that are either emitted in the form of PM or condense to form particles in the atmosphere. These include POM, chromium, mercury, and other metals. In addition, lead is a criteria pollutant and lead compounds are listed as a HAP, so reducing lead emissions through the lead NAAQS also reduces HAP.

With regard to mobile sources, in addition to authority under section 202(l) to address hazardous air toxics, other sections of title II that address mobile sources, including other parts of section 202 (motor vehicles), section 211 (fuel requirements), section 213 (emission standards

for nonroad engines and vehicles), and section 219 (urban bus standards), are resulting in reductions in urban air toxics by limiting VOCs, oxides of nitrogen, and PM.

We've established section 129 performance standards for two source categories for combustion sources. These are expected to result in over 50,000 tons per year in HAP reductions, much of which may be in urban areas. Finally, Title IV, The Acid Rain Program, and Title VI, Stratospheric Ozone Protection, also reduce or eliminate urban air toxics emissions.

4.6.3 Other Authorities, Laws, Rules, and Programs to Help Reduce HAP Emissions

There are a number of other authorities, laws, rules, and programs that will help reduce emissions of HAP and consequent exposures and risks. Some of these are discussed below. We're currently evaluating the appropriateness of these statutes for controlling emissions of HAP as described under section 112(k)(3) and intend to take further actions under these statutes as appropriate.

As discussed previously, the Strategy involves collaboration between offices within the air program to assess the risks from exposures to air toxics indoors and to assimilate non-regulatory, voluntary programs developed to address those risks. Title IV of the Superfund Amendments and Reauthorization Act.(SARA) provides EPA with the authority to perform research and provide information to the public on the health problems associated with air pollutants in the indoor environment.

Under the Toxic Substances Control Act (TSCA), chemicals produced or imported into the United States are evaluated as to toxicity to human health and the environment. To prevent adverse consequences of the many chemicals developed each year, TSCA requires that any chemical that will reach the consumer marketplace be tested for possible toxic effects prior to commercial manufacture. Any existing chemical that is determined to pose health and environmental hazards is tracked and reported under TSCA. Procedures are also authorized for corrective action under TSCA in cases of cleanup of toxic materials contamination. The TSCA is a complementary authority to the CAA and has contributed to decreased emissions of several HAP. For example, concern over the toxicity and persistence in the environment of PCB compounds led Congress to include, in TSCA, prohibitions on the manufacture, processing, and distribution in commerce of PCBs (TSCA section 6(e), 15 U.S.C. 2605(e)). In 1990, TSCA authority was relied upon to eliminate chromium use in, and emissions from, comfort cooling towers (i.e., industrial process cooling towers used exclusively for cooling, heating, ventilation, and air conditioning systems).

There are several provisions of the Resource Conservation and Recovery Act (RCRA) and its amendments which may yield reductions of urban air toxics. One impact evidenced in the 1990's was increased recycling and recovery of hazardous waste, including solvents which through volatilization contribute to HAP emissions. Section 3004(n) of RCRA has been the basis of a three-phased regulatory program to control air emissions from hazardous waste

treatment, storage and disposal facilities. The third phase would address any risks remaining after implementation of the control regulations issued in 1990 and 1994, which were estimated to reduce organic emissions by more than one million tons per year. Any resulting reductions in emissions and risk can be considered in assessing progress toward the 75 percent reduction in cancer incidence from the baseline.

Under the Comprehensive Environmental Response, Compensation and Liability Act (CERCLA), commonly known as Superfund, the clean-up of abandoned hazardous waste sites may also reduce emissions of HAP. Where significant health risks from chemical releases to the air have been identified at Superfund sites in urban areas, clean-up will reduce risks from urban air toxics.

Under the Clean Water Act (CWA), controls on the discharge of pollutants to surface water can also reduce the amount of HAP entering the environment. These controls may take the form of national technology-based standards under the effluent guidelines program or site-specific water quality-based controls to achieve State water quality standards. In addition to providing control by establishing discharge limitations on pollutants (including HAP) in the wastewater, process changes made in order to comply with these limitations may also reduce fugitive emission sources.

As part of the effluent guidelines program under the CWA, we've issued effluent limitations for the pharmaceuticals industry. Human health benefits from these guidelines include reductions in excess cancer risk through inhalation. The regulatory impact assessment prepared for these guidelines estimates that the number of excess cancer cases avoided per year nationwide ranges from 0.02 to 0.35. These reductions are due to reductions in VOC emissions, including 10 carcinogens (principally chloroform and methylene chloride). We can also point to air toxics benefits from the effluent guidelines for the pulp, paper, and particle board industry. These guidelines, coupled with the associated NESHAP, are expected to decrease background emission of HAP by 139,000 megagrams (152,900 tons) annually[11].

If a water body isn't meeting water quality standards even after all technology-based controls under the effluent guidelines program are in place, the State, local agency, or Tribe must list the water as "water quality limited" and prepare a total maximum daily load (TMDL) calculation that allocates the maximum amount of pollution, with a margin of safety, that the water body can absorb from point and nonpoint (including air deposited) sources. A plan must then be developed to implement the TMDL, which might include provisions to address air sources under Federal or State (or local or Tribal) programs. We're conducting a pilot project in two waterbodies to study models which can be used to identify the relative contributions of air pollutants deposited from various air pollution sources. This project will also examine how

[11]63 FR 18504. National Emission Standards for Hazardous Air Pollutants for Source Category: Pulp and Paper Production; Effluent Limitations Guidelines, Pretreatment Standards, and New Source Performance Standards: Pulp, Paper, and Paperboard Category. April 15, 1998.

Federal and State water programs can work together to reduce contamination of water due to air deposition.

The Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) provides Federal control of pesticide distribution, sale, and use. Several HAP listed in CAA section 112(b) have been used as pesticides. An EPA registration is required of all pesticides sold in the United States and is intended to ensure that pesticide use, when in accordance with label specifications, doesn't cause unreasonable harm to people or the environment. It's a violation of FIFRA to use a pesticide in a manner inconsistent with its label. Registered pesticides classified as "restricted use" may only be used by registered applicators who have passed a certification exam. This restricted use requirement minimizes the number of persons having access to certain pesticides. The FIFRA regulations may also reduce emissions and exposures by banning (canceling or denying registration) or severely restricting pesticide use. Seven individual HAP and members of three HAP compound groups have been banned or severely restricted in their use as pesticides.

Two other Federal laws discussed earlier in Chapter 2 of this Report, EPCRA and PPA, while not directly regulating air emissions of HAP, may influence decisions regarding chemical usage and storage and yield significant reductions in air toxics risks in urban areas. The goal of EPCRA is to reduce risks to communities through informing communities and citizens of chemical hazards in their areas. Sections 311 and 312 of EPCRA require certain facilities to report the locations and quantities of chemicals stored at their facilities to State and local governments. This information is used by State and local agencies in preparing for, and responding to, chemical spills and similar emergencies.

Through EPCRA, Congress mandated that TRIs be made public. The TRI provides citizens with information about potentially hazardous chemicals stored, manufactured and used in their community. Section 313 of EPCRA specifically requires certain manufacturers and all Federal facilities to report to EPA and State governments all releases of any of more than 600 designated toxic chemicals to the environment (including most of the 188 HAP). Each year, more than 20,000 manufacturing facilities and 200 Federal facilities submit information to us on the releases of chemicals to the environment. We compile these data in an on-line, publicly accessible national database, which is a significant source of information regarding HAP emissions. Reporting requirements for TRI became more comprehensive in 1991, highlighting the importance of pollution prevention. In 1997, we added seven industry groups (i.e., metal mining, coal mining, RCRA subtitle C treatment, storage, and disposal (TSD) and solvent recovery, petroleum distribution, electricity generating, and chemical distribution). We believe that for the manufacturing sector, this public spotlight on releases and other waste management of toxic chemicals has led to reductions in their environmental release.

The passage of the PPA established an environmental hierarchy that establishes pollution prevention as the first choice among waste management practices. Traditionally, much environmental protection has involved controlling, treating or cleaning up pollution. Pollution prevention, which eliminates or minimizes pollution at the source, is most effective in reducing health and environmental risks because it: (1) eliminates any pollutant associated risks; (2)

avoids shifts of pollutants from one medium (air, water or land) to another, which can result from certain waste treatments; and (3) reduces the waste of natural resources. For waste that cannot be avoided at the source, recycling is considered the next best option. A waste generator should turn to treatment or disposal only after source reduction and recycling have been considered. Pollution prevention strategies include redesigning products, changing processes, substituting raw materials for less toxic substances, increasing efficiency in the use of raw materials, energy, water, land, and other techniques. The EPA implements the PPA by promoting voluntary pollution reduction programs, engaging in partnerships, providing technical assistance, funding demonstration projects and incorporating cost-effective pollution prevention alternatives into regulations and other initiatives.

In addition, we've developed the "Waste Minimization National Plan," a voluntary, long term effort to reduce the quantity and toxicity of hazardous waste through waste minimization. The plan was built on extensive stakeholder involvement and was released in 1994. The plan focused on the following key objectives:

- Prioritize pollution prevention efforts based on risk;
- Promote source reduction over recycling;
- Adopt a multimedia approach and prevent cross media transfers;
- Provide flexibility in implementing pollution prevention activities;
- Provide accountability and measure progress; and
- Involve the public.

The plan calls for a 50 percent reduction in the presence of the most harmful persistent, bioaccumulative, and toxic (PBT) chemicals in hazardous waste by 2005.

The starting point for selecting chemicals for the national waste minimization list is EPA's Waste Minimization Prioritization Tool (WMPT), which is a software program that provides a screening-level assessment of the potential chronic risks that chemicals pose to human health and the environment based on their persistence, bioaccumulative potential, and human and ecological toxicity. This software program contains full or partial PBT data for approximately 4,200 chemicals. The draft WMPT was released for public comment on June 23, 1997 (U.S. EPA, 1997). We made significant changes in response to public comment and published a revised version on November 9, 1998 (U.S. EPA, 1998i). The revised software, in conjunction with a publicly reviewed methodology, was used to generate a draft list of 53 PBT chemicals, which is now in the process of being finalized.

4.7 State, Local, and Tribal Activities

This section describes the role of State, local and Tribal authorities in developing and implementing the Strategy.

4.7.1 Why are State, Local, and Tribal Programs Integral to the Strategy?

The CAA requires that the Strategy achieve the risk reduction goals considering control of emissions of HAP from all stationary sources, using measures implemented by EPA under the CAA, or by the States under the CAA, or other laws. By providing for State reductions in achieving the goals, Congress acknowledged that there are many State programs achieving HAP emissions reductions and, therefore, reducing the chances for exposure and health risks, including cancer. For example, before the CAA was amended in 1990, many State, local and Tribal governments developed their own programs for the control of air toxics from stationary sources. Some of these programs have now been in place for many years and, for some of the source categories, they may have succeeded in reducing air toxics emissions to levels at or below those required by the Federal standards. It's clear that Congress intended State and local governments to be important partners in carrying out the mandates of the Federal air toxics program, and the Strategy provides a mechanism to recognize the reductions made by them.

Because of the varied nature of the emissions sources, legislative structures, and other factors, the State, local and Tribal government programs address air toxics in a number of ways. For example, some programs have enacted technology standards for source categories that require controls for specific HAP, much like the MACT program. Other programs apply a risk standard that prohibits emissions that result in exceedances of a certain level of risk, or they use an ambient air standard for air toxics that is based on threshold or exposure levels. Still others may rely on reductions achieved through VOC, PM, or lead regulations developed under section 110 or subpart D of the CAA to meet NAAQS. Regardless of the approaches used to address air toxics, State, local and Tribal governments have accomplished and continue to accomplish reductions in HAP. As we proceed to implement the Strategy, we'll work with these governments to better characterize these reductions in emissions and the resulting reductions of public health risks, including risks of cancer.

Developing the Strategy at the national level is a challenge because urban air toxics problems vary significantly across the country. Because of this variability, the Strategy works best if approached as a partnership between EPA and State, local and Tribal governments. These governments (including municipal offices other than pollution control departments) have the most experience with local air pollution issues and can lend their expertise and knowledge to address and resolve air toxics concerns that are unique to cities. Many of these governments also have existing air pollution control programs that currently address, and can effectively continue to address, some or all of these issues. In addition, these governments are often able to act much more quickly than we can to address local concerns, which leads to less overall pollution.

At the Federal level, we can contribute Federal standards and requirements using our authorities to develop and implement a national regulatory program. We also have the expertise to evaluate, or to help other agencies evaluate, toxic pollution problems. By integrating our relative strengths, we can provide a stronger, more efficient, and more effective program to address air pollution in urban areas.

4.7.2 What are the Objectives of State, Local, and Tribal Activities?

As indicated before, the Strategy will be a partnership between EPA and State, local and Tribal governments to address the risks from air toxics in urban areas. Listed below are the objectives that we've identified to guide the CAA taken by us and our governmental partners so that those actions will be effective and efficient in achieving the goals of the Strategy:

- **Establish appropriate national measures, through guidance, policies and rulemaking, which enable State, local and Tribal agencies to be full partners.** Many of the State, local and Tribal agencies may be unable to do more than the Federal laws and rules require. These agencies could benefit from Federal rulemaking guidance in addressing local issues. As the same time, we recognize the need for flexibility for these agencies to identify and address the local issues. We need State, local and Tribal agencies' help to reach the CAA's goals for healthy air, and they'll benefit by being able to tailor the Strategy to their specific needs.

- **Provide flexibility for strong State, local and Tribal programs.** Many of these governments have developed their own air programs. In fact, during the development of the Strategy, we received many comments requesting that the Strategy acknowledge programs that are already in place. Those governments that have been proactive in controlling air toxics can benefit by tailoring the Strategy to their own needs, or by being able to implement a program earlier than we can.

- **Provide incentives for State, local and Tribal action.** Since enabling through standards, policies and guidance and providing flexibility can result in more effective and earlier controls of urban HAP, it will be beneficial to State, local, and Tribal governments, to EPA, and to the public to facilitate State, local and Tribal actions.

- **Set priorities among urban areas and source categories.** Given the broad scope of the Strategy and the time it may take to implement, it may be most effective to first identify and address those areas and sources with the highest air toxics emissions or exposure levels (including consideration of multipathway exposure where appropriate).

- **Provide information to the public on HAP and potential risk in urban areas.** The public benefits by having a sound basis to use in setting their pollution control priorities and communicating their priorities to us. Providing information to the public is also our responsibility, and an informed public will be better equipped to help us set priorities for appropriate State, local and Tribal HAP control actions. This public outreach will include not only information on exposure to air toxics, but also information on the link between water quality and the deposition of air toxics.

- **Facilitate a focus on areas with disproportionate impacts and greatest risks.** The Strategy is intended to recognize the potential for disproportionate impacts of air toxics hazards across urban areas. State, local and Tribal governments can be particularly

effective in identifying and addressing disproportionate impacts of HAP. We'll work with our regulatory partners to provide technical and policy guidance to help identify and address disproportionate impacts from HAP, including consideration of multipathway exposure as appropriate.

4.7.3 How Can State, Local or Tribal Agencies Participate in the Strategy?

The Strategy needs to be a partnership between EPA and State, local and Tribal agencies in order to focus on local urban air toxics concerns. But our relative roles may vary according to the needs of particular urban areas and any limitations faced by State, local and Tribal governments. With our regulatory partners, we'll discuss and explore options for how the State, local and Tribal agencies should participate in developing and implementing the Strategy to address public and other environmental issues related to air toxics.

We see a broad range of possibilities for State, local and Tribal agency participation. For example, as indicated above, many regulatory agency programs are designed to implement delegated Federal requirements. However, to provide additional flexibility, we may be able to provide a Federal program that allows the agencies to either develop and substitute their own requirements for an existing Federal program, or, if they wish, to simply adopt and implement a risk reduction program designed by EPA. For example, we could promulgate a Federal rule describing how we'd develop and implement a local risk reduction program. State, local or Tribal agencies could then either develop and implement a program modeled on ours, or submit an alternative program for our approval.

Alternatively, instead of promulgating a Federal rule setting out the details of an acceptable risk reduction program, we could promulgate a set of minimum elements that any local risk reduction program – whether implemented by EPA or a State, local or Tribal agency – must contain. This would provide agencies with more flexibility to design and implement their own risk reduction programs that we could approve.

The Federal role in developing additional risk reduction strategies for urban areas could be smaller still. It may not be necessary for us to directly guide development of State, local and Tribal programs. It may be enough for us to encourage them to meet the goals of the Strategy and to provide necessary guidance. In the end, we (or the State, local or Tribal agency) would still need to measure progress against the mandatory goals of the CAA. We might then need to determine whether additional Federal action is warranted to meet the goals.

In evaluating and comparing the options we develop together, we and our regulatory partners and other stakeholders will need to consider how well each option addresses our objectives. We'll also need to consider such other issues as practicality of implementation, resource burden at each governmental level, and possible adverse impacts on other Federal, State, local or Tribal programs.

4.7.4 What Elements Should a State, Local or Tribal Program Contain?

No matter who develops and implements State, local or Tribal programs, they should contain certain basic elements in order to meet the risk reduction goals of the Strategy. The following list of elements should be considered:

- Locally-focused assessments using existing information and sufficiently refined tools capable of identifying significant contributors to urban risk, problem chemicals and sources, and toxic "hot spots" within an urban area, and characteristics of at-risk populations;
- A process, regulatory or otherwise, to develop strategies aimed at reducing risks from those sources;
- Opportunity for public review of both the baseline assessment and the proposed risk reduction strategies;
- A process and schedule for implementing the risk reduction strategies;
- Evaluation of whether the goals of the Strategy have been met;
- Provisions to implement additional risk reduction strategies if the goals have not been met; and
- A process to encourage public participation.

At this point, this list is fairly general because we don't have enough information to more fully develop this program structure. However, over the next couple of years, we'll be working to further develop this aspect of the Strategy, to develop and use information from assessments and other tools to guide our thinking, and to get input from our stakeholders. Also, we've started to develop the framework for a number of pilot projects in several urban areas. These pilot projects will help us initiate and facilitate a broad partnership effort to get a better understanding of the local urban health risks from air toxics and to identify actions that can be taken to improve local air quality.

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5. Assessment of Progress Toward Goals

This discussion of our assessment activities first focuses on how we generally intend to assess progress in meeting the goals of the Strategy. We then discuss in more detail our methods and tools for estimating health risks and describe more specifically how we intend to apply these risk assessment methods and tools to assess progress and support implementation of the Strategy.

As we move from a focus on emissions reductions toward a focus on estimated risk reduction, we note that Agency risk assessment and decisionmaking have historically focused on the likelihood of health effects associated with exposure to individual environmental contaminants. In recent years, our risk assessment emphasis has shifted increasingly to a greater consideration of multiple pollutants, endpoints, pathways and routes of exposure, and integrated reduction of risks. This more complex assessment is often called "cumulative risk assessment," defined according to who or what is at risk of adverse effects, from identifiable sources and stressors, through several routes of exposure over varied timeframes. While various integrated approaches are now being used within the Agency, we realize that there are significant gaps in methods, models, and data that limit our ability to assess cancer and noncancer risks associated with cumulative exposure to mixtures of pollutants having different endpoints. We've identified both short-term and long-term research needs to fill these gaps, as highlighted in Chapter 6 of this Report. Progress toward more refined assessments of cumulative risks will depend upon the pace and evolution of our policy and guidance on cumulative risks and the underlying research.

5.1 Overview of Health Risks

Assessing progress in reducing cumulative risks from HAP will require us to move away from a focus on assessing reductions in tons per year emitted, toward a focus on estimating reductions in cancer and noncancer risks associated with lower emissions.

"Cancer" describes a group of related diseases that affect a variety of organs and tissues. Cancer results from a combination of genetic damage and non-genetic factors that favor the growth of damaged cells. Cancer currently causes approximately one fourth of all deaths in the U.S. (American Cancer Society, http://www.cancer.org/statistics/index.html). Cancer is associated with a wide range of factors, of which exposure to HAP is only one. Other causes of cancer, including genetic susceptibility, background radiation, diet, smoking, and other lifestyle factors, are thought to be the dominant factors determining total cancer incidence. Against the very high total cancer mortality rate of about one in four from all risk factors, the rate of cancer incidence associated with HAP alone cannot be observed directly. Attributing cancer to HAP is also complicated by the fact that many cancers do not appear for years or decades after exposure and, therefore, may have been caused by exposures long past and in different locations. In order to distinguish cancer risks associated with HAP from cancer risks due to other factors, we'll need to rely on modeled estimates of cancer risk rather than on direct measurements for assessing the Strategy's progress toward the goal of 75 percent reduction in cancer incidence associated with HAP.

Adverse health effects other than cancer ("noncancer risks") include a wide range of health endpoints in all organ systems (e.g., cardiovascular, immune, liver, or kidney)[1]. As with cancer, other factors such as genetics, diet, lifestyle, and other exposures (e.g., smoking) may exert a dominant influence over incidence of adverse noncancer health effects. Therefore, as with carcinogens, we expect to rely primarily on risk estimates to assess progress, rather than on direct measurements of changes in the incidence of adverse noncancer health impacts due to reductions in emissions.

The CAA sets a clear numerical goal for reductions in cancer incidence, but specifies only a "substantial" reduction in public health risks for effects other than cancer. We see a need to define and clarify this goal more fully as we work to implement this Strategy, but we haven't yet developed a specific numerical goal for risk reductions for various noncancer effects. One major purpose of our noncancer risk assessments will be to provide a sound technical basis for developing and defining noncancer goals that are quantifiable, attainable, and consistent with the CAA.

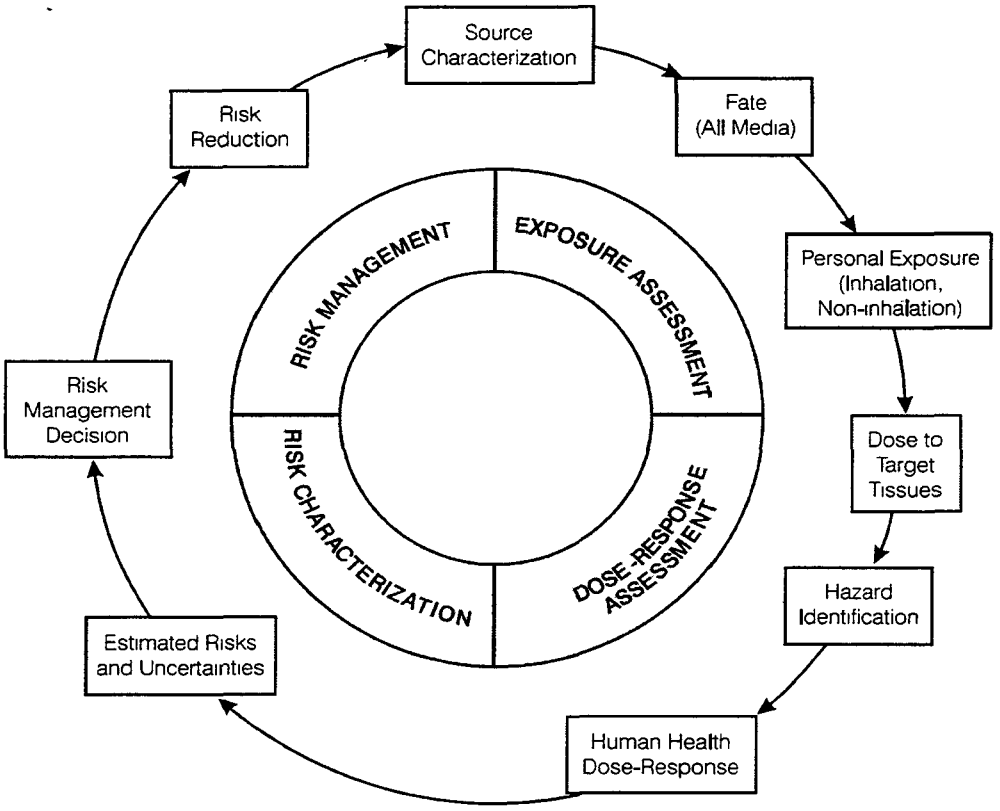
5.2 The EPA Risk Assessment Paradigm

Because cancer and noncancer health impacts can't be directly isolated and measured, we and others have spent more than two decades developing an extensive set of risk assessment methods, tools, and data that serve the purpose of estimating health risks for many of our programs. Our risk assessment science has been extensively peer-reviewed, is widely used and understood by the scientific community, and continues to expand and evolve as scientific knowledge advances. We intend to use the most current and appropriate risk estimation methods in tracking progress under the Strategy.

Our framework for assessing and managing risks reflects the risk assessment and risk management paradigm set forth by the National Academy of Sciences in 1983, shown in diagram form in Exhibit 5-1. The inner circle of the figure divides the risk assessment and management process into four general phases. The first three phases (exposure assessment, dose-response assessment, and risk characterization) comprise risk assessment. The fourth phase (risk management, shown shaded) involves evaluation of information provided by the risk assessment by the environmental manager who makes a risk management decision. The outer circle of the figure depicts a cycle of specific milestones or information produced during each phase of the process. This figure is intended to present a generalized model of our framework, but readers should realize that the framework is always applied in a flexible way to fit unique factors of specific environmental problems.

[1]Some HAP that cause cancer may also cause adverse noncancer health effects at environmentally relevant doses. Thus, when we discuss "noncarcinogens," we mean substances that may potentially cause noncancer effects in humans. Some of the same substances may also be evaluated as carcinogens.

EXHIBIT 5-1
EPA PARADIGM FOR RISK ASSESSMENT AND RISK MANAGEMENT



5.2.1 Exposure Assessment

Our 1992 guidelines for exposure assessment (U.S. EPA, 1992) establish a broad framework for exposure assessments by describing the general concepts of exposure assessment, including definitions and associated measurement units, and by providing broad guidance on the planning and conduct of an exposure assessment. The guidelines also provide information on presenting the results of the exposure assessment and characterizing uncertainty. Although the guidelines focus on exposure of humans to chemical substances, much of the guidance also pertains to assessing ecological exposure to chemicals, or to human exposures to biological, radiological, or other agents.

The guidelines define human exposure as contact with a chemical or agent at the visible external boundary of a person, including skin and openings into the body such as mouth and nostrils (but not necessarily contact with exchange boundaries where absorption may take place, such as skin, lung, and gastrointestinal tract). Therefore, an exposure assessment is the quantitative or qualitative evaluation of contact and includes such characteristics as intensity,

frequency, and duration of contact. Often, an assessment will also evaluate the rate and route at which a chemical crosses the external boundary (dose) and the amount absorbed (internal dose). The numerical output of an exposure assessment may be either exposure or dose, depending on the purpose of the evaluation and available data.

An exposure assessment has three major components: source characterization, environmental fate and transport characterization, and characterization of personal exposure. These components are discussed individually below.

Source Characterization

In the first step of exposure assessment for air toxics, the specific HAP emitted and the sources of their airborne emissions are determined. Data are collected on the emission rates of the pollutants and parameters of the sources. Knowledge of the emission rate and release characteristics enables the pollutant fate and transport to be estimated.

Ideally, the emission estimates are from direct measurements of source emissions. Although direct measurement is likely to provide the most accurate data for an emission source, these data are typically not available, as such sampling is often time- and resource-intensive. When specific emission measurements are not feasible or available, other emission estimation methods, including material balances and emission factors, are sometimes used as alternate methods. Emission factors indicate the quantity of a pollutant typically released to the atmosphere for a particular source operation and are usually considered to be representative of an industry or emission type as a whole. Each approach to estimating emissions, including use of direct measurement data, has an inherent level of uncertainty, which adds to the overall uncertainty of a risk analysis.

Depending on the analysis, source and emissions data can be derived from broad-scale emission inventories, specific data collection efforts with particular industries, or information from Regional, State, or local air toxics agencies. Other information, such as the geographic location of release points, the temporal pattern of emissions (e.g., periodic "puffs" vs. constant emission rates), and the release height may be necessary depending on the level of detail needed or types of exposure examined in the assessment.

Environmental Fate and Transport Characterization

After the pollutants of interest and their sources and emission rates are defined, the exposure assessment process continues with estimation of pollutant fate and transport. This step describes how the pollutant is transported, dispersed, and transformed over the area of interest. Initially, the fate of the emitted pollutants is largely determined by the source release characteristics. After pollutants are released to the atmosphere, their transport, dispersion, and transformation are governed by meteorological principles, terrain characteristics, wet and dry deposition rates, and certain chemical properties of the HAP (e.g., aqueous solubility, vapor pressure, molecular diffusivity, melting point, and adsorptivity). For a limited subset of HAP, it

is important to consider deposition from air to soil, vegetation, or waterbodies. For others, such deposition is not important.

A variety of mathematical models, each with specific data needs, has been developed or are under development to describe the transport and fate of pollutants released to the atmosphere. The model chosen must be appropriate for the intended application and may vary among estimates of short-term peak concentrations immediately adjacent to a facility, long-term concentrations over a city-wide area, or deposition over hundreds or even thousands of miles. The HAP's reactivity and persistence will influence its fate as well and can be important factors in estimating exposure for certain pollutants. Additionally, secondary transformation products of some HAP may need to be identified for consideration in risk assessment. High quality, representative meteorological information is crucial to a valid exposure assessment for air toxics, as well as information on local topography. Any available HAP monitoring data can be used either to check the validity of modeled concentration estimates or as a primary or supplemental source of information for the exposure assessment itself.

For a limited subset of HAP, greater human and ecological exposures to the HAP occur through non-inhalation exposures than through inhalation exposures. These HAP typically are persistent in the environment, have a strong tendency to bioaccumulate, and exhibit moderate to high toxicity. Exposure assessments can consider exposures that occur through routes other than inhalation by using multipathway models. The simplest multipathway exposure assessments require chemical-specific data (e.g., octanol-water partition coefficient (K_{ow})) to model the partitioning of the chemical in the environment and uptake rates (e.g., 2 liters water/day) to predict intakes. Combining this information yields general predictions of non-inhalation exposure.

Characterization of Personal Exposure

After ambient concentrations have been derived, human exposures to these concentrations are determined. In this component, the study population is defined in terms of geographic distribution and other characteristics relevant to the exposure pathways of concern.

For the more frequently performed human inhalation exposure analyses, the locations of resources, homes, workplaces, schools, and other receptor points will partially determine the extent of actual exposure. Factors such as age, sex, and activity patterns affect the amount of pollutant actually inhaled by an individual, while mobility of the subject affects the concentration levels to which an individual is exposed over time. Depending on the focus of the analysis, 5 to 10 percent output of the exposure assessment may vary. In some cases, the most highly exposed five to ten percent of the population may need to be well-characterized, while for others, the distribution of exposures across a wider area is needed. Information on specific sensitive populations, such as children or the elderly, is another layer of detail that may often be needed in refined analyses.

As with inhalation, assessing non-inhalation exposure to human populations involves combining pollutant concentration information with relevant information concerning the study population. After identification of the relevant exposure pathways, information such as soil, drinking water, and food ingestion rates (often including specific foods, such as fish, beef, pork, eggs, root vegetables, grains, and fruit), generally for both adults and children, as well as contact frequencies with soil and surface water, may be needed. Some activities of particular interest for non-inhalation modeling are subsistence farming and subsistence fishing because of the unique dietary habits of these two groups (i.e., eating much more garden vegetables and fish, respectively). Also, as with inhalation exposure, the extent to which these factors are included in the risk assessment depends on the purpose of the assessment, available resources, uncertainties in the assessment, and data quality and quantity. Not only are the data requirements often extensive, particularly when many different pathways are being assessed, but the computational demands also can be quite large in a multimedia, multipathway assessment.

5.2.2 Dose-Response Assessment

The dose-response assessment phase of the risk assessment produces two sequential analyses (Exhibit 5-1, outer circle). The first analysis is the hazard identification, which identifies contaminants that may pose health hazards at environmentally relevant concentrations and qualitatively describes the effects that may occur in humans. The second analysis is the human health dose-response, which generally describes the relationship between exposure received and likelihood of effects in quantitative terms.

Hazard Identification

The dose-response assessment phase begins with hazard identification, in which we identify contaminants that are suspected to pose health hazards, describe the specific forms of toxicity (neurotoxicity, carcinogenicity, etc.) that they may cause, and evaluate the conditions under which these forms of toxicity might be expressed in exposed humans. The types of effects that are relevant to a particular chemical (e.g., cancer, noncancer) are determined as part of the hazard identification. The current approaches for dose-response assessment and risk characterization can differ for various types of effect. Factors such as the route of exposure, the type and quality of the effects, the biological plausibility of findings, the consistency of findings across studies, and the potential for bioaccumulation all contribute to the strength of the hazard identification statement.

There are many sources of information that can be brought to bear in the hazard identification. Exhibit 5-2 summarizes important sources of information for hazard identification.

EXHIBIT 5-2
SOURCES OF INFORMATION FOR HAZARD IDENTIFICATION

- **Epidemiologic Data.** Epidemiologic studies of human populations exposed to HAP in occupational settings or in the general environment can provide valuable information on the effects of HAP. These studies have advantages over other sources of information in that they directly assess the effects of exposure to humans and, in the case of studies of the general population, address exposures that actually occur in the environment. In addition, recent work with biomarkers (chemicals in the body which allow for better quantification of exposure) promises to boost the utility of epidemiology in the future. Shortcomings include concerns about the relevance of high exposure levels often seen in occupational studies to lower levels of environmental contamination, concerns over the control of confounding variables (such as tobacco use) that may obscure true causal relationships (or imply false ones), difficulties in adequately characterizing exposure, and the difficulty most epidemiologic studies have in discerning subtle effects.

- **Human Data from Case Reports or Controlled Exposure Studies.** Where available, human health effects data from case reports or controlled exposure studies can be extremely valuable, although such data generally have shortcomings. Case reports often involve one or a small number of people, limiting the ability to generalize from them, and they may involve exposures very different than typical environmental exposures. For most HAP and effect types of interest, controlled human exposure studies are unlikely to be available.

- **Animal Toxicology Data.** High quality studies of human populations exposed to HAP are rare, due to both expense and the inherent limitations of epidemiology. As a result, EPA and others commonly rely on animal studies to infer potential risk to humans. Animal toxicologic data are typically much easier to obtain than good epidemiologic data, and effects can be explicitly linked with exposure to the HAP(s) being tested with little fear of confounding. However, issues of high-to-low dose relevance are compounded by the need to extrapolate the effects seen in animals to those anticipated in humans. Although there have been considerable advances in understanding the relevance of specific results in animal studies to human biology, such extrapolations remain a considerable source of uncertainty. The EPA has operated under the conservative public health policy that assumes that adverse effects seen in animal studies indicate potential effects in humans.

- **Short-term *in Vitro* Assays.** *In vitro* ("test tube") tests can be carried out quickly and at relatively low cost, and they can provide valuable information on specific aspects of a pollutant's toxicity, such as a particular mechanism of mutagenicity that may be an initiating event for cancer. However, such tests typically provide only supporting information about a pollutant's effects, as few tests have been developed that are specific to a particular effect or disease.

- **Structure-activity Relationships (SARs).** By comparing the molecular structure of a pollutant with that of others of known toxicity, toxic effects can sometimes be inferred, particularly if there is knowledge about the mechanism of action. This approach is often useful when examining the hazards associated with individual compounds within a class of related compounds (e.g., dioxins) or when identifying compounds for future study. Although structure-activity analyses are rarely a substitute for existing experimental or epidemiologic data, and represent a relatively uncertain basis for hazard identification, they are useful when experimental data are absent.

Noncancer Effects – Chronic and Acute. Due to the wide variety of endpoints, hazard identification procedures for noncancer effects are less formally described in EPA guidance than are procedures for the identification of carcinogens. The EPA has published guidelines for assessing several specific types of noncancer effects, including mutagenicity (U.S. EPA, 1986a); developmental toxicity (U.S. EPA, 1991); neurotoxicity (U.S. EPA, 1998a); and reproductive toxicity (U.S. EPA, 1996a).

For identification of long-term (chronic) hazards other than cancer, we review the health effects literature and characterize its strengths and weaknesses, using a narrative approach rather than a formal classification scheme. Available data on different endpoints are arrayed and discussed, and the effects (and their attendant dose/exposure levels) are described. Particular attention is given to effects that occur at relatively low doses or that may have particular relevance to human populations. Information is presented in a narrative description that discusses factors such as the methodological strengths and weaknesses of individual studies (as well as the overall database), the length of time over which the studies were conducted, routes of exposure, and possible biological mechanisms. We consider the severity of effects, which may range from severe frank effects that can cause incapacitation or death to subtle effects that may occur at the cellular level but are early indicators of toxic effects. Not all effects observed in laboratory studies are judged to be adverse. The distinction between adverse and non-adverse effects is not always clear-cut, and considerable professional judgment is required in applying criteria to identify adverse effects. All of these observations are integrated into a presentation that gives a concise profile of the toxicological properties of the pollutant.

In addition to toxicity related to chronic exposures, many HAP also can cause toxic effects after acute (short-term) exposures lasting from minutes to several hours. Indeed, for some pollutants, acute exposures are of greater concern than chronic exposures. The hazard identification step for acute effects is comparable to that for chronic effects, with the primary difference being the duration of exposure. As with chronic exposures, the severity of effects from acute exposures may vary widely. While several EPA offices have addressed acute exposures across a variety of regulatory programs, we have only recently drafted Agencywide guidance on how to assess toxic effects from short-term exposures. This guidance for acute reference exposure (ARE) levels, when completed, will assist Agency acute risk assessment activities (U.S. EPA, 1998b).

Cancer. The EPA's 1986 *Guidelines for Carcinogen Risk Assessment* (U.S. EPA, 1986b) provide guidance on hazard identification for carcinogens. The approach recognizes three broad categories of data: (1) human data (primarily epidemiological); (2) results of long-term experimental animal bioassays; and (3) supporting data, including a variety of short-term tests for genotoxicity and other relevant properties, pharmacokinetic and metabolic studies, physio-chemical properties, and SARs. In hazard identification of carcinogens under the 1986 guidelines, the human data, animal data, and "other" evidence are combined to characterize the weight of evidence regarding the agent's potential as a human carcinogen into one of several hierarchic categories:

- **Group A - Carcinogenic to Humans:** Applies when there are adequate human data to demonstrate the causal association of the agent with human cancer (typically epidemiologic data).

- **Group B - Probably Carcinogenic to Humans:** Agents with sufficient evidence (i.e., indicative of a causal relationship) from animal bioassay data, but either limited (i.e., indicative of a possible causal relationship, but not exclusive of alternative explanations) human evidence (Group B1), or with little or no human data (Group B2).

- **Group C - Possibly Carcinogenic to Humans:** Agents with limited animal evidence and little or no human data.

- **Group D - Not Classifiable as to Human Carcinogenicity:** Agents without adequate data either to suggest or refute the suggestion of the human carcinogenicity.

- **Group E - Evidence of Noncarcinogenicity for Humans:** Agents that show no evidence for carcinogenicity in at least two adequate animal tests in different species or in both adequate epidemiologic and animal studies (U.S. EPA, 1986b).

In 1996, we proposed major revisions of the carcinogen hazard identification scheme. The proposed revision to the cancer risk assessment guidelines (U.S. EPA, 1996b), currently under public review prior to finalization, focuses on narrative statements describing the main lines of evidence and their interpretation, replacing the current pre-defined hierarchical categories with alphabetic designations. The proposed guidelines also replace the system of stepwise consideration of different types of data with a single comprehensive evaluation process that stresses the coherence of various data elements. The result is a single scientific interpretation that evaluates, to the extent possible, how well the commonality of mode of carcinogenic action between human beings and the various test systems has been established. Emphasis is also placed on defining the qualitative conditions under which carcinogenic hazards might be expected. If warranted, limitations to the finding of carcinogenic hazard can be drawn based on route of exposure, existence of other factors needed for tumorigenesis, and doses below which elevation of cancer risk is not expected.

Human Health Dose-Response

Human health dose-response assessment is the characterization of the relationship between the concentration, exposure, or dose of a pollutant and the resultant health effects. The nature of quantitative dose-response assessment varies among pollutants. Sufficient data often exist for criteria air pollutants, such as ozone or carbon monoxide, so that relatively complete dose-response relationships can be characterized. In such cases, there is no need for extrapolation to lower doses because adequate health effects data are available, often in humans, at environmental levels. However, such is not the case for most air toxics. Most epidemiologic and toxicologic data on HAP typically result from exposure levels that are high relative to environmental levels.

In summary, dose-response assessment methods for HAP generally consist of two parts. First is the evaluation of data in the observable range, and second is the extrapolation from the observable range to low doses/risks. Recent terminology refers to the result of analysis in the observable range as the "point of departure" from which extrapolation begins. The approaches used for evaluation in the observable range are similar for all types of effects, while the Agency's current extrapolation methods differ considerably for cancer and noncancer effects. The 1996 draft cancer guidelines bring a greater degree of consistency to the extrapolations.

Noncancer Effects – Chronic. The inhalation RfC and oral RfD are the primary Agency consensus quantitative toxicity values for use in noncancer risk assessment. The RfC or RfD is defined as an estimate, with uncertainty spanning perhaps an order of magnitude, of an inhalation exposure/oral dose to the human population (including sensitive subgroups) that is likely to be without appreciable risks of deleterious effects during a lifetime. The RfC or RfD is derived after a thorough review of the health effects database for an individual chemical and identification of the most sensitive and relevant endpoint and the principal study(ies) demonstrating that endpoint. Inhalation RfCs are derived according to the Agency's *Methods for Derivation of Inhalation Reference Concentrations and Application of Inhalation Dosimetry* (U.S. EPA, 1994a). The RfC or RfD should represent a synthesis of the entire data array. The evaluation of and choice of data on which to base the RfC or RfD derivation are critical aspects of the assessment and require scientific judgment.

Derivation of the RfC or RfD begins with identification of the critical adverse effect from the available valid human and animal study data, followed by identification of a lowest-observed-adverse-effect level (LOAEL) or, preferably, a no-observed-adverse-effect level (NOAEL). The LOAELs or NOAELs from animal studies are converted to human equivalent concentrations (HECs) using dosimetric methods (described in U.S. EPA, 1994a). The NOAEL[HEC] or LOAEL[HEC] from one or a few studies that is representative of the threshold region of observable effects is the key value gleaned from evaluation of the dose-response data. The RfC or RfD is then derived by consistent application of uncertainty factors (UFs) to account for recognized uncertainties in the extrapolation from the experimental data and exposure conditions to an estimate (the RfC or RfD) appropriate to the assumed human lifetime exposure scenario (U.S. EPA, 1994a).

The standard UFs are applied as appropriate for the following extrapolations or areas of uncertainty:

- Laboratory animal data to humans;
- Average healthy humans to sensitive humans;
- Subchronic to chronic exposure duration;
- LOAEL to NOAEL; and
- Incomplete database.

The composite UF will depend on the number of extrapolations required. The RfCs have been derived using composite UFs that range from 10 to 3,000, with most RfCs using factors of

100 to 1,000. The use of order-of-magnitude uncertainty factors for RfCs and RfDs and the definition of the RfC or RfD as having "uncertainty spanning perhaps an order of magnitude" are indications of the general lack of precision in the estimates.

It should be noted that exposures above an RfD or RfC do not necessarily imply unacceptable risk or that adverse health effects are expected. Because of the inherent conservatism of the RfC/RfD methodology, the significance of exceedances must be evaluated on a case-by-case basis, considering such factors as the confidence level of the assessment, the size of UFs used, the slope of the dose-response curve, the magnitude of the exceedance, and the number or types of people exposed at various levels above the RfD or RfC.

Typically, screening assessments will identify HAP for which exposures may exceed the RfC or RfD, and therefore have some potential to cause adverse effects. Because risk for noncarcinogens is dependent on total exposure to a particular pollutant (as opposed to incremental exposures as for carcinogens), it will be important for assessments to consider all sources of exposure. These screening assessments may identify for further study sources that exceed a default percentage (e.g., 20%) of a HAP exposure above an RfD or RfC. Sources that appear to contribute to RfD or RfC exceedances for HAP at the screening level may be prioritized for further analysis using more refined and localized assessment methods. In contrast to screening assessments, refined assessments developed in support of regulatory standards may include consideration of total uncertainty in the RfC or RfD, evidence of nonadditive interactions with other HAP, and actual percentage of contribution to total exposures.

The EPA is currently developing a risk management framework for the residual risk program. This framework is being developed to facilitate decisionmaking to protect public health with an "ample margin of safety." As part of the ample margin of safety framework, one must first determine the "acceptability" of risks based on health considerations alone. The framework will also include guidelines for appropriate consideration of factors other than risk in regulatory decisionmaking, e.g., cost, economic impacts and feasibility. The framework, which will be completed in time for the first residual risk standard, will address evaluating the significance of exposures above the RfC or RfD on a case-by-case basis considering the factors identified above.

Noncancer Effects - Acute. Methods for dose-response assessment of acute exposures are substantially similar to the approach for chronic exposure. Risk assessment for acute inhalation exposure is complicated by the steep concentration-response curves that are often observed, and because small differences in exposure duration (in some cases, a few minutes) need to be taken into account. Because increased exposure duration increases the incidence and severity of response, acute toxicity criteria or exposure guideline values are developed for a specified duration (e.g., one hour). Although many acute toxicity studies only report incidence of death, it is preferred to base criteria on studies that evaluate additional endpoints, including clinical signs, clinical chemistry, and histopathology. For an inhalation criterion, the exposure duration of the study should ideally be the same as the one of interest (e.g., one hour). If significant interpolation across exposure durations is required, multiple studies are preferred to

improve the quality of the interpolation. We are currently developing a new Agency method for acute dose-response assessment, the resultant value of which is an ARE (U.S. EPA, 1998b).

Cancer. Our cancer risk assessment guidelines of 1986 adopted a default assumption that chemical carcinogens would exhibit risks at any dose (U.S. EPA, 1986b). Extrapolation of cancer risk using the linearized multistage model, which results in a linear extrapolation of risk in the low dose region, was proposed as a reasonable upper-bound on risk, and this approach has been used for most chemicals with adequate data since then. However, as stressed in the *Proposed Guidelines for Carcinogen Risk Assessment* (U.S. EPA, 1996b), when there are adequate mechanistic data to suggest that other models would be more appropriate to estimate low exposure risk, they may be used on a case-by-case basis. In the absence of such data, the assumption of response linearity is maintained although the modeling scheme has been simplified.

In cancer dose-response assessments relying on ingestion animal studies for which chemical-specific data are not available to guide the scaling of results to human equivalents, a default scaling factor based on the body mass raised to the 3/4 power of the test animals relative to humans is generally used to calculate a human equivalent dose. For inhalation exposure studies, dosimetric methods such as those used in developing RfCs are generally used to calculate a HEC from animal data. Dose-response models such as the multistage model have historically been used to calculate upper-bound unit risk estimates. Typically, EPA has relied on the unit risk estimate as a quantitative measure of potential cancer hazard. A unit risk estimate represents an estimate of the increased cancer risk from a lifetime (assumed 70 year) exposure to a concentration of one unit of exposure. The unit risk estimate for inhalation exposures is typically expressed as risk per microgram per cubic meter for air contaminants. The unit risk estimate is a plausible upper-bound estimate of the risk (i.e., the risk is not likely to be higher but may be lower and may be zero).

Since the publication of the our original cancer guidelines (U.S. EPA, 1986b), considerable new knowledge has been developed regarding the processes of chemical carcinogenesis and the evaluation of human cancer risk. Currently, a revision of the cancer guidelines is in process (U.S. EPA, 1996b) that represents a considerable departure from the original guidelines (see Exhibit 5-3 for key differences in the dose-response assessment step between the two sets of guidelines). As mentioned above, a fundamental and important advance in the proposed revision is the distinction between linear and nonlinear modes of action. The cancer data in the observable range are analyzed using a dose-response model similar to the models used for noncancer effects. The method of extrapolation to lower doses from the point of departure differs depending on whether the assessment of the available data on the mode of action of the chemical indicates a linear or nonlinear mode of action.

EXHIBIT 5-3
SUMMARY OF MAJOR DIFFERENCES BETWEEN EPA'S 1986 GUIDELINES (U.S. EPA, 1986b) AND 1996 PROPOSED GUIDELINES FOR CARCINOGEN RISK ASSESSMENT (U.S. EPA, 1996b)

1986 Guidelines	1996 Proposed Guidelines
Default model used for linear dose-response relationships is the "linearized multistage" procedure.	Biologically based dose-response models are used whenever data are sufficient. Recommended default approaches include the margin of exposure approach (comparison of exposure level and point of departure) and linear extrapolation to zero dose, zero response.
Dose-response evaluation is limited to carcinogenicity data.	If appropriate, data on noncarcinogens effects may be used to help characterize the carcinogenicity dose-response relationship.

A linear extrapolation is generally appropriate when the evidence supports a mode of action of gene mutation due to direct deoxyribonucleic acid (DNA) reactivity or another mode of action that is thought to be linear in the low dose region. For linear extrapolation, a straight line is drawn from the point of departure to the origin, and the risk at any concentration is determined by interpolation along that line. A linear mode of action also will serve as a default when available evidence is not sufficient to support a nonlinear extrapolation procedure, even if there is no evidence for DNA reactivity.

Nonlinear methods are used when there is sufficient evidence to support a nonlinear mode of action. A nonlinear mode of action could involve a dose-response pattern in which the response falls much more quickly than linearly with dose, but still indicating risk at low doses. Alternatively, the mode of action may theoretically have a threshold if, for example, the cancer response is a secondary effect of toxicity or an induced physiological change which is a threshold phenomenon. In most cases, we will not try to distinguish between modes of action with a "true threshold" and those that are nonlinear through the origin, because data are rarely sufficient to make this determination. As a default science policy, nonlinear extrapolation to low doses will not be performed because there is no current basis to choose a model or determine the shape of the dose-response function. However, as more specific information on a HAP's mechanism of action becomes available and where the data are sufficient to support the use of alternative models, we will use them.

5.2.3 Risk Characterization

The final product in the risk assessment process is the risk characterization, in which the information from the previous steps is integrated and an overall conclusion about risk is synthesized that is complete, informative, and useful for decisionmakers. The nature of the risk characterization will depend on the information available, the regulatory application of the risk

information, and the resources (including time) available. In all cases, however, major issues associated with determining the nature and extent of the risk should be identified and discussed. Further, the EPA Administrator's March 1995 *Policy for Risk Characterization* (U.S. EPA, 1995a) specifies that a risk characterization "be prepared in a manner that is clear, transparent, reasonable, and consistent with other risk characterizations of similar scope prepared across programs in the Agency." The 1995 *Guidance for Risk Characterization* (U.S. EPA, 1995b) lists several guiding principles for defining risk characterization in the context of risk assessment. The three principles with respect to the information content and uncertainty aspects of risk characterization are as follows:

(1) The risk characterization integrates the information from the exposure and dose-response assessments, using a combination of qualitative information, quantitative information, and information regarding uncertainties. A good characterization should include different kinds of information from all portions of the foregoing assessment, carefully selected for reliability and relevance.

(2) The risk characterization includes a discussion of uncertainty and variability. The risk assessor must distinguish between variability (arising from true heterogeneity) and uncertainty (resulting from a lack of knowledge).

(3) Well-balanced risk characterizations present risk conclusions and information regarding the strengths and limitations of the assessment for other risk assessors, EPA decisionmakers, and the public. "Truth in advertising" is an integral part of the characterization, discussing all noteworthy limitations while taking care not to become mired in analyzing factors that are not significant.

The 1995 *Guidance for Risk Characterization* (U.S. EPA, 1995b) identifies several guiding principles, shown in Exhibit 5-4, with respect to descriptions of risk.

Risk assessments are intended to address or provide descriptions of risk to: (1) individuals exposed at average levels and those in the high-end portions of the risk distribution; (2) the exposed population as a whole; and (3) important subgroups of the population such as highly susceptible groups or individuals (e.g., children), if known. Because cancer and noncancer dose-response assessment methods are currently quite different, risk characterizations also differ and are discussed separately.

Noncancer Effects. Unlike cancer risk characterization, noncancer risks typically are not expressed as a probability of an individual suffering an adverse effect. Instead, "risk" for noncancer effects typically is quantified by comparing the exposure to the reference level as a ratio. The resultant HQ can be expressed as an equation, where HQ equals the exposure/ reference level. Exposures or doses below the reference level (HQ<1) are not likely to be associated with adverse health effects. With exposures increasingly greater than the reference level (i.e., HQs increasingly greater than 1), the potential for adverse effects increases. The HQ, however, should not be interpreted as a probability of adverse effects.

EXHIBIT 5-4
GUIDING PRINCIPLES WITH RESPECT TO RISK DESCRIPTORS

- **Information about the distribution of individual exposures is important to communicating the results of a risk assessment.** Both high-end and central tendency descriptors are used to convey the variability in risk levels experienced throughout the population.
- **Information about population exposure leads to another important way to describe risk.** Both a probabilistic number of cases (or environmental impacts) and an expected percentage of the exposed population (or ecological resource) with risk greater than a certain level are valuable ways to present information.
- **Information about the distribution of exposure and risk for different subgroups of the population are important components of a risk assessment.** Highly susceptible individuals or areas should be identified as well as those highly exposed, when possible.
- **Situation-specific information adds perspective on possible future events or regulatory options.** Consideration of alternative scenarios when conducting risk assessment can aid in risk management decisions.
- **An evaluation of the uncertainty in the risk descriptors is an important component of the uncertainty discussion in the assessment.** Both quantitative and qualitative evaluations of uncertainty can be useful to users of the assessment.

While some potential environmental hazards may involve significant exposure to only a single compound, exposure to a mixture of compounds that may produce similar or dissimilar noncancer health effects is more common. In a few cases, reference levels may be available for a chemical mixture of concern or for a similar mixture. In such cases, risk characterization can be conducted on the mixture using the same procedures used for a single compound. However, noncancer health effects data are usually available only for individual compounds within a mixture. In screening-level assessments for such cases, a conservative HI approach, in which all the HQs for individual contaminants are summed, is sometimes used. This approach is based on the assumption that even when individual pollutant levels are lower than the corresponding reference levels, some pollutants may work together such that their potential for harm is additive and the combined exposure to the group of chemicals poses greater likelihood of harm. This assumption of dose additivity is most appropriate to compounds that induce the same effect by similar modes of action (U.S. EPA, 1986c). As with the HQ, the HI should not be interpreted as a probability of adverse effects, nor as strict delineation of "safe" and "unsafe" levels (U.S. EPA, 1986c; U.S. EPA, 1989). Rather the HI is a rough measure of potential for risk and needs to be interpreted carefully.

Although the HI approach encompassing all chemicals in a mixture may be appropriate for a screening-level study (U.S. EPA, 1989), it is important to note that application of the HI equation to compounds that may produce different effects, or that act by different mechanisms,

could overestimate the potential for effects. Consequently, in a refined assessment, it is more appropriate to calculate a separate HI for each noncancer endpoint of concern when only mechanisms of action are known to be similar (U.S. EPA, 1986c).

Cancer. Risks for cancer are generally expressed as either individual risks or population risks. The distribution of exposures and individual risks within a given population can also be presented, providing an estimate of the number of people exposed to various predicted levels of risk. The Agency's risk characterization guidelines recommend that risk assessments describe individual risk, population risk, and risk to important subgroups of the population such as highly exposed or highly susceptible groups (U.S. EPA, 1995b). For air toxics emissions, cancer risks can be estimated by multiplying the corresponding exposure by the unit risk estimate. Our dose-response assessments for carcinogens are based on mathematical models and assumptions that support extrapolation from high to low doses and from nonhuman test species to humans. As a matter of science policy, many of these assumptions are protective to avoid underestimating cancer risks where data are incomplete. The most important of these assumptions for most carcinogenic chemicals is that risk is proportional to dose, with no threshold dose below which there is no risk. Our dose-response assessments for inhalation of carcinogens are expressed as a "unit risk," that is, risk per microgram per cubic meter of daily exposure during a lifetime. The unit risk is defined as a conservative estimate of an individual's excess probability of contracting cancer at the end of 70 years exposure to a continuous level of one microgram per cubic meter. Risks from exposures to concentrations other than one microgram per cubic meter are modeled as proportional, with half the concentration producing half the estimated risk, and so on.

Each word in the above definition of unit risk carries significant meaning. First, the unit risk is a conservative rather than a "best" estimate. This means that the actual unit risk is unknown and is very likely to be lower than estimated and very unlikely to be higher. Second, as already described, risks are estimated rather than measured. Third, the unit risk applies to an individual, although cancer incidence in a population can be estimated across a group by aggregating the risk of each person. Fourth, unit risk estimates focus only on the route of exposure being analyzed. Fifth, unit risks are expressed in terms of probability. For example, we may determine the unit risk of a particular HAP to be one in ten thousand per microgram per cubic meter. This means that, of ten thousand people who continuously inhale an average of one microgram per cubic meter of this particular HAP for 70 years, no more than one would be expected to contract cancer from the exposure. Sixth, risks are generally expressed in terms of contracting cancer, not dying from it. Finally, exposures are averaged over a 70-year lifetime to account for long-term exposures to low levels of carcinogens.

Cancer risk is defined as the upper-bound probability of contracting cancer following exposure to a pollutant at the estimated concentration over a 70-year period (assumed human lifespan). This predicted risk focuses on the additional risk of cancer predicted from the exposure being analyzed, beyond that due to any other factors. Estimates of risk are usually expressed as a probability represented in scientific notation as a negative exponent of 10. For example, an additional risk of contracting cancer of 1 chance in 10,000 (or one additional person

in 10,000) is written as $1x10^{-4}$. Because unit risk estimates are typically upper-bound estimates, actual risks may be lower than predicted.

Population risk is an aggregated estimate of individual risks, integrated across the entire population within the given area of analysis. The estimated level of individual risk for each population group (separated geographically, demographically, or both) is multiplied by the number of people in that group, producing an estimate of the incidence of cancer cases in the group during a lifetime of exposure. As with individual risk estimates, EPA has typically calculated these cancer incidence estimates based on upper-bound unit risk values. Therefore, they provide a high-end estimate of future cancer risk. The population risk estimates for each population group are then summed to provide a prediction of excess cancer incidence in the entire exposed population. These lifetime incidence estimates are sometimes divided by 70 to obtain an upper-bound prediction of the number of cancer cases per year.

People are often exposed to multiple chemicals rather than a single chemical. In those few cases where weight of evidence classifications and unit risk estimates are available for the chemical mixture of concern or for a similar mixture, risk characterization can be conducted on the mixture using the same procedures used for a single compound. However, cancer dose-response assessments and unit risk estimates are usually available only for individual compounds within a mixture. Consequently, in screening-level assessments of carcinogens for which there is an assumption of a linear dose-response, the cancer risks predicted for individual chemicals may be added to estimate total risk.

For carcinogens being assessed based on the assumption of nonlinear dose-response, the margin-of-exposure approach (MOE, analogous to the HQ approach for noncarcinogens) may be considered, consistent with the proposed revision of EPA's cancer guidelines (U.S. EPA, 1996b). The MOE approach leaves the decision about the appropriate reduction in exposure compared to the point of departure (i.e., the observable toxicity data) up to the risk manager.

In the risk characterization step of final assessments, estimates of health risk will be presented in the context of uncertainties and limitations in the data and methodology. Uncertainties and limitations related to the hazard identification and dose-response assessment may also be discussed. The degree to which all types of uncertainty need to be quantified and the amount of uncertainty that is acceptable varies. For a screening-level analysis, a high degree of uncertainty is often acceptable, provided that conservative assumptions are used to bias potential error toward protecting human health. Similarly, a regionwide or nationwide study will be more uncertain than a site-specific one. In general, the more detailed or accurate the risk characterization, the more carefully uncertainty needs to be considered.

5.3 Methods, Tools, and Data to Estimate Risk

5.3.1 Assessing Exposures and Characterizing Risks

In general, the choice of appropriate risk characterization approaches will be influenced by both the availability of data to support exposure assessment, and the level of detail and resolution needed to support the purpose of the assessment. Possible approaches range from simple weighting adjustments of emissions data or ambient concentrations to detailed multipathway risk assessments. We've identified four basic approaches that we plan to use for various assessments to evaluate the progress of the Strategy in reducing estimated risk. Each of these approaches uses the same dose-response information described above, but relies on different types of data to represent exposures. The four basic approaches we intend to use are: (1) emissions or ambient concentration weighting, (2) comparisons between ambient concentrations and RBCs[2], (3) comparisons between estimated exposures and RBCs that may yield quantitative estimates of risk, and (4) quantitative estimates of carcinogenic risk for individuals and populations.

Approaches (1) and (2) are considered hazard-based approaches because they lack the dispersion and/or human exposure modeling steps of an exposure assessment and, therefore, cannot provide quantitative estimates of risk. However, they can provide valuable information, subject to substantial uncertainty, that may be useful in evaluating progress toward risk reduction goals. In contrast, approaches (3) and (4) are considered risk-based approaches because they do incorporate exposure assessments and thereby can provide quantitative risk estimates, although these too are usually subject to substantial uncertainty. Below, we will compare the differences in these approaches.

(1) Weighted emissions or ambient concentrations. Weighting of emissions or ambient concentrations is the least resource-intensive approach of the four in terms of data needs and computational requirements[3]. This hazard-based approach combines HAP emissions or monitored HAP concentrations (acting as surrogates for exposure) with weighting factors (developed from unit risks and reference concentrations) that account for differences in relative toxicity among HAP. Other weighting factors could also potentially be developed to account for differences in dispersion characteristics or variations in population density or behavior.

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[2]RBCs for cancer are ambient concentrations associated with specific levels of cancer risk, assuming 70 years of continuous exposure. RBCs for noncancer effects are ambient concentrations that pose no appreciable risk to humans, assuming continuous exposure. The use of RBCs does not imply a judgment that the concentrations are either acceptable or unacceptable, only that they have been derived in the same way for all HAP.

[3]Peer-reviewed examples of this approach include the EPA/Office of Pollution Prevention and Toxic Substances' Risk-Based Environmental Indicators (Science Advisory Board, 1998), the EPA/Office of Solid Waste's WMPT (U.S. EPA, 1998c), and the EPA/Office of Air Quality Planning and Standards' ranking analysis for urban HAP (Smith et al., 1999).

The toxicity adjustment is intended to account for differences in toxic potency among substances, placing all emissions data on the same scale of hazard potential. For example, acrylamide is approximately 160 times more potent a carcinogen than benzene, such that weighting by potency would consider one ton of acrylamide emissions equivalent to 160 tons of benzene. In a cumulative analysis, emissions or concentrations of each HAP would be weighted by its relative potency to allow for direct comparison and aggregation across HAP (with carcinogenic and noncarcinogenic estimates aggregated separately). This type of analysis permits comparisons of relative hazard between pollutants with large mass emissions and low toxicity (e.g., many non-chlorinated volatile compounds) against pollutants with small mass emissions but high toxicity (e.g., dioxin).

As discussed above, the weighted emissions- or concentration-based approach lacks the last two steps of an exposure assessment, and therefore doesn't provide a quantitative estimate of risks. Also, because of the absence of these important exposure assessment steps, it isn't possible to say how closely changes in weighted emissions or concentrations will be related to changes in health risks. Nevertheless, emissions and ambient concentrations clearly have a strong influence over exposure and risk, and we anticipate that the toxicity-weighting approach will provide useful information to estimate progress where appropriate data for more refined assessment approaches aren't available.

(2) Ratios of ambient concentrations to RBCs. A second type of hazard-based approach is the comparison of ambient HAP concentrations with RBCs[4]. Ambient concentrations may be measured or modeled. Appropriate modeling approaches for estimating ambient concentrations at different spatial scales using emissions data include national-scale and urban- to neighborhood-scale air quality models, as well as multimedia models for urban- to neighborhood-scale analyses.

The RBCs used for comparison are derived from unit risks or reference concentrations. Specifically, cancer RBCs can be defined in terms of a fixed risk level (e.g., HAP concentrations conservatively estimated to result in a 1 in 10,000 or a 1 in 1,000,000 upper-bound risk of contracting cancer from a lifetime exposure at the RBC). Noncancer RBCs can be defined in terms of estimates of continuous exposure levels at which even sensitive subgroups are likely to be without any appreciable risk of adverse effects during a lifetime.

Because it is more complex than emissions-weighting, this type of analysis brings two significant advantages. First, it supports a more complete treatment of ambient HAP concentrations that are already below noncancer RBCs, for which further reductions may not carry significant health benefits. Second, the use of dispersion models to predict ambient concentrations can potentially account for variations in factors such as location of exposed

[4]Peer-reviewed examples of the use of this approach include the concentration-toxicity screen used by EPA's Superfund program to select contaminants and exposures for detailed risk assessment (U.S. EPA, 1989) and EPA's CEP, which compared modeled ambient air concentration estimates with RBCs (termed "health benchmarks" by the authors) for 148 HAP nationwide (Woodruff et al., 1998).

populations relative to sources of HAP, differences in meteorological conditions, and differences in fate and transport characteristics among HAP.

Nevertheless, this approach still lacks the third, human behavior-related step in an exposure assessment. Therefore, it doesn't provide a quantitative estimate of risk, and its use in estimating progress is subject to greater uncertainty than approaches (3) and (4), below. Changes in health risks may not precisely track changes in concentration/RBC ratios. However, because ambient concentrations are important determinants of exposure and risk, we anticipate that the concentration/RBC approach will provide useful information to estimate progress where exposure assessment is not possible.

(3) Ratios of exposures to RBCs. A third type of approach begins with measured or modeled ambient HAP concentrations and adds further refinement by overlaying estimates or measurements of population exposures. Thus, this risk-based approach is qualitatively different from the first two hazard-based approaches, because it incorporates all three steps of an exposure assessment.

While human exposures are directly affected by ambient concentrations, they're also influenced by behavioral factors such as time spent outdoors, periodic movements (such as commuting) within an urban area, and activity levels. Exposures may be estimated with exposure models that simulate the behavioral factors that determine exposure. Human exposure may also be directly measured by personal monitoring, in which subjects wear small air samplers and record their daily activities.

These estimated or measured exposures are then compared to RBCs[5] (as described above for approach (2)). Analogous to the comparisons in approach (2), hazard potential would typically be presented in terms of ratios of the exposure concentrations divided by RBCs. The additional complexity of estimating exposure provides three significant advantages over considering ambient concentrations alone. First, it provides a more realistic comparison with RBCs, which are based on unit risks and reference concentrations usually derived from doses actually received by test organisms. Second, exposure estimates can take into account behavioral differences between populations in different cities, or between different demographic groups. Third, exposure estimates support combining effects of multiple HAP, considering non-additivity and similarities or differences in toxic mechanisms. Comparison of exposures with reference concentrations for noncancer effects (surrogates for RBCs) is currently the most advanced approach used for assessing noncarcinogenic HAP, although this may change in the future for some substances.

(4) Risk estimation. A fourth type of approach that can be used to estimate cancer incidence (but typically not for noncancer assessments) is comprehensive risk estimation,

[5]Peer-reviewed analyses of this type of analysis include many single-substance risk assessments. Several examples concern the fuel additives MMT (Davis et al., 1998; U.S. EPA, 1994b) and MTBE (U.S. EPA, 1993).

focusing on the most exposed individual or on entire populations or subgroups[6]. We'll derive risk estimates by combining exposure estimates with dose-response assessment results in terms of unit cancer risk estimates. Risk estimates will also consider nonstandard dose-response models and complex interactions among different HAP, if information is available. Such risk estimates represent the most refined analysis of the four approaches considered. Comprehensive assessments may contain modeling to account for environmental fate and transport of released pollutants, estimation of exposures to different subpopulations, detailed dose-response assessments for each HAP, and information on complex, nonadditive interactions among HAP. Results are expressed in terms of probabilities of developing cancer during a lifetime. Cancer risks are usually aggregated across HAP by addition, but nonadditive interactions are included if data permit.

In its most complete form, risk estimation produces results in probabilistic form (that is, with calculations considering a range of cancer risks and the likelihood of each), expressed in terms of a frequency distribution rather than as a single deterministic estimate. Of currently available approaches, risk estimation, presented probabilistically, provides the most complete, best-supported, and most accurate presentation of both risk and the variability and uncertainty surrounding it. However, this risk-based approach is much more resource- and calculation-intensive than are simpler approaches, and is often not possible to conduct due to data limitations.

5.3.2 Summary

We anticipate tracking progress in reducing estimated cumulative risks from air toxics in urban areas by relying on estimates of health risk rather than by directly observing reductions in adverse health impacts in human populations. We consider these health risk estimates to be reasonable and appropriate indicators of progress toward meeting the goals of the Strategy. Their use is made necessary by the long latency period for cancer, the high background rate of many health effects (including cancer), and complexities involved in attributing various noncancer health effects to specific environmental causes. Our assessments will use a variety of approaches, including some that do not include all exposure assessment steps. In some cases the information may be too uncertain to support conclusions. We intend to evaluate these approaches against each other, in terms of their ability to estimate risk and their resource and data requirements, when supporting data become available during 2000. These results will assist us in determining the scope, refinement, and precision of future assessments developed to reflect different purposes under the Strategy.

[6]Examples of such multichemical, multipathway risk assessments include many performed by EPA's Superfund program under the Risk Assessment Guidelines for Superfund (U.S. EPA, 1989).

5.4 The Overall Risk Assessment Approach for the Strategy

In previous sections, we discussed the key role that assessing air quality, exposure, and estimated risks will play in assessing progress toward meeting the goals of the Strategy. In addition, these assessment activities will, over time, also serve the following broader purposes:

- Improve the definition of the goal for "substantial" reduction in noncancer risk;
- Support development of national area and mobile source standards;
- Support decisions on how to conduct future risk assessments;
- Evaluate the effectiveness of each of the four approaches to characterizing risk reductions, described above;
- Provide guidance for State, local and Tribal agency efforts in conducting local assessments and developing risk reduction programs at the State, local, and Tribal levels; and
- Guide us in determining significant research needs to better inform future assessments.

Our assessment approach will be generally iterative in nature so as to take advantage of emerging science, new data, and improved tools that become available as future assessments are performed. Consistent with this approach, beginning in mid-2000, we'll conduct an initial set of assessments that will be based on final, updated emissions data. Future assessments will reflect the best available data, methods, and tools.

Our national database of air toxics emissions from major, area, and mobile sources, the NTI, will be a fundamental component of our risk assessments. We are now completing a baseline NTI representing the 1990 to 1993 period, and obtaining State review of a draft 1996 NTI suitable for dispersion and exposure model inputs (scheduled for completion in 1999). We plan to update the NTI every three years and to conduct future risk assessments to coincide with these revisions. Monitored air toxics concentrations will also be an important component of our assessment activities, in part to help us evaluate and refine our air quality models. We are now working with the States to design and implement a national air toxics monitoring network that will provide important information for future assessment activities.

5.4.1 Designing the Assessments

We'll tailor each assessment to the purpose(s) it is to serve (e.g., measuring progress against the 75 percent estimated cancer incidence reduction goal). Accordingly, assessments will vary in scope, level of refinement, and, thus, data and resource requirements. The scope of each assessment will generally be defined by the following characteristics:

- The number of HAP to be evaluated (all 188 or some subset);
- The types of sources included (area, major, mobile);
- The spatial resolution (e.g., aggregation of results on the national, State, urban, or neighborhood scale); and
- The pathways/media to be evaluated (inhalation/air only or multipathway/ multimedia).

Further, for each assessment, we need to specify an appropriate approach to use in estimating progress toward our risk reduction goals, since, as discussed above, it will not be possible to directly measure reduction in cancer incidence or noncancer risks attributable to hazardous air pollutant emissions. Alternative approaches range from rough approximations to more precise risk estimates, with data and resource requirements increasing for more precise assessments that require greater refinement.

5.4.2 Addressing Disproportionate Risks

Disparities in risks from air toxics in the urban environment may exist between different cities, between neighborhoods or demographic groups within a city, or within a similarly-exposed population that includes sensitive groups. In our assessments, we intend to pay particular attention to areas, populations, and sensitive groups with substantially higher-than-average risks.

While differences in risk between different urban areas may be discernible from national screening-level modeling, more refined modeling will generally be needed to evaluate localized disparities within any one urban area. This is because highly localized disparities may be obscured by the simplifying assumptions that are necessarily inherent in national screening-level assessments. For this reason, the ability of EPA or State and local authorities to assess localized risk disparities will depend on the availability of detailed data on emissions and population distribution, local-scale models, and sufficient resources.

5.5 Designing Future Assessments

We'll conduct a series of assessments starting in mid-2000 and periodically thereafter at appropriate times during the implementation of the Strategy. The assessments will include both national-scale and urban-scale analyses. All assessments will incorporate the most current data, information, and assessment tools available. As the Strategy progresses, we may eventually use risk assessment tools that are now only in early development, or perhaps have not yet been envisioned. For this reason, we can't describe in detail the assessments that will be conducted several years from now.

5.5.1 Initial Assessments – National

We'll conduct an initial national assessment in mid-2000 to serve several purposes. First, we'll develop an estimate of progress that has already been made toward the goals of the strategy. Consistent with section 112(k) of the CAA, which focuses on reducing ambient concentrations of HAP to levels "below those currently experienced," we've established 1990 as the base year for assessing progress. To estimate progress since the base year, we'll compare the base year emissions inventory to the inventory for 1996, due to be completed in 1999, using a weighted emissions analysis. This assessment will be limited to the weighted-emissions approach because the 1990 base year inventory, although a comprehensive county-level inventory, will lack the source-specific information necessary to support air quality modeling. Subsequent assessments, however, will not be limited in this way because emission inventory data, beginning in 1996, will include information needed for modeling[7].

Second, the initial national assessment will provide basic information to assist us in prioritizing HAP and source categories for regulatory development, based on their relative importance as contributors of risk. Third, the assessment will provide the clearest and most current picture of inter-urban and demographic disparities in risk and will provide insight on more refined analyses that may be appropriate to identify types of sources associated with particularly high risk levels. Fourth, we intend to use information from the initial assessment to develop a more complete and quantitative goal for a "substantial" reduction in noncancer risk. Finally, we'll use the initial assessment to compare different hazard- and risk-based approaches. In particular, we intend to correlate results of assessment approaches (1) and (2) (which lack exposure assessments) with exposure assessment-based approaches to determine their relative accuracy and to quantify uncertainties. These comparisons, in combination with data and resource availability, will help us to scope the details of future assessments and finalize our estimates of progress from 1990 to 1996.

We'll use all four types of approaches (emissions weighting, comparisons between ambient concentrations and exposure estimates, RBCs, and modeled estimates of risk) in the initial national assessments, to the extent possible. We plan to use the ASPEN model to estimate national air quality concentrations in conjunction with the use of the Hazardous Air Pollutant Exposure Model (HAPEM) to estimate national exposures. We'll conduct screening level analyses before progressing to more refined analyses to ensure that we're allocating appropriate amounts of resources to each assessment, given our information needs. The assessment will

[7]As part of our CEP, the ASPEN model, used to estimate HAP ambient concentrations nationwide, was developed and tested using a 1990 emissions inventory based on the limited HAP information that was available in the mid-1990s (prior to the substantial improvements now reflected in the 1993 NTI). While that first national-scale modeling exercise provided the screening-level information that we've used in conjunction with other information in creating the urban HAP list, we believe that the uncertainties in the CEP's 1990 emission inventory are too large to support a meaningful comparison with modeled concentrations for future years that will result from the application of the ASPEN model using updated emissions inventories. These updated inventories, starting with the 1996 NTI, are specifically designed to include sufficient source-specific information to support air quality modeling.

focus on inhalation exposures, with the expectation of including multipathway exposures, as appropriate, in subsequent assessments. The initial assessment will include all urban areas in the United States, and we anticipate presenting results with county- and/or urban-scale resolution. The assessment will address as many HAP as the data support, but will include at least the 33 HAP considered in the initial national scale assessment.

5.5.2 Initial Assessments – Urban

We plan to conduct urban-scale assessments for a few selected cities over the next few years to serve as case studies that may be particularly useful as guidance for State, local and Tribal program assessments. We'll also provide technical support and risk assessment tools for authorities that wish to conduct their own local assessments to analyze area-specific progress and intra-urban disparities. The experience we gain through these analyses will also help us refine future assessments.

We'll develop these initial urban assessments using the specific approaches that are appropriate for the quality of data available. Each assessment will describe a single urban area, and we anticipate presenting the results with high spatial resolution (e.g., a one kilometer grid). The scope of each assessment will address a subset of HAP that we identify as being priority HAP for the particular urban area being assessed. We plan to consider both inhalation and multipathway exposures as appropriate and as available data permit.

5.5.3 Periodic Assessments

In the years following the initial national assessment, we'll conduct new analyses at appropriate intervals as new data become available. These periodic assessments will serve two principal purposes. First, they'll measure progress toward the goals of the Strategy, considering all actions taken that reduce HAP emissions for any purpose. These include Federal, State, local and Tribal actions, as well as voluntary initiatives by local communities and industry. Second, the new analyses will assist us in prioritizing which future regulatory actions would be most effective in making further progress. We'll develop the periodic assessments using the specific approaches that have proved most efficient (that is, the least resource-intensive approach that accomplishes the purpose of the assessment). Assessments will include all urban areas in the U.S., with results presented on county- and urban-scale level resolution. Assessments will address the full list of 188 HAP, to the extent to which emissions, monitoring, and health data are available. If appropriate tools become available, periodic assessments for bioaccumulative HAP will include multimedia exposures.

By measuring ongoing progress, periodic assessments will also inform us when we have met our goals, and will help us to measure the degree to which we have reduced disparities in risk. The approaches used for such goal-specific comparisons will be determined by the results of earlier assessments and will be developed to fit the Strategy's purposes.

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6. Research Needed to Address Knowledge Gaps

The purpose of this chapter is to summarize the types of scientific information (and related research) needed to better inform future risk assessment and risk management judgments that will be made in carrying out the Strategy. To provide some perspective, we are also providing a summary of planned and/or ongoing EPA research activities[1]. Also, while we have not undertaken a complete inventory of State and local research activities, we mention them in the chapter where we are aware of them. State and local activities are especially important since the Strategy recognizes that the responsibility for reducing health risks from exposure to urban HAP is shared by all levels of government.

This chapter details the development of EPA research strategies and research plans which reflect Agency commitments to specific actions within specified time periods. To aid this process, research needs presented in this chapter are categorized into both short-term (less than five years) and long-term needs (greater than five years). We are now developing, with this chapter as a starting point, an Air Toxics Research Strategy that will identify key questions that need to be answered and the research that needs to be conducted by EPA and others to answer them.

The scientific needs presented in this chapter are organized around the risk assessment/risk management approach described previously, which links the elements of risk assessment (i.e., the description of a health problem, including whether one exists) with risk management (i.e., actions to address the risk). Consistent with this approach, research needs are presented below in four areas:

1. Exposure assessment information needs, which include research into the areas of emission sources, environmental concentrations, and human exposure factors;

2. Health effects information needs, including hazard determinations and dose-response assessments, which include toxicity and mode of action research, as well as development of methods and models for producing probabilistic dose-responses assessments with reduced uncertainty;

3. Risk assessment/characterization information needs, which include development of assessment methods for chemical mixtures and techniques for risk communication; and

[1]EPA research and assessment activities are performed by various EPA offices and laboratories including the Office of Research and Development, the Office of Air Quality Planning and Standards, the Office of Transportation and Air Quality , the Office of Prevention, Pesticides, and Toxic Substances, and Regional Offices.

4. Risk management information needs, which include emission control assessments and pollution prevention alternatives with a focus on categories of area sources.

6.1 Exposure Assessment

An exposure assessment provides estimates of exposures that are occurring or are anticipated to occur under specified conditions. Exposure assessments include:

- An emissions source assessment;
- An evaluation of transformation and fate;
- A determination of environmental concentrations;
- A characterization of pathways that may lead to exposure; and
- An understanding of population characteristics and activity profiles influencing contact between a person and a contaminant, and aggregation of exposure across pathways and chemicals.

In order to assess human exposures to urban HAP, information is needed on emissions (from area, major, and mobile sources), on atmospheric transport and fate, on actual exposures to populations of interest, and on methods to measure the HAP at the places of interest (e.g., at sources, in different media). Also, because it is impossible to measure all the events of interest, models of these events are needed. To be fully effective, the models should encompass the source-to-exposure relationship. Thus, models of contaminant distribution, apportionment, and population activity profiles are needed to assess and predict microenvironmental exposures, preferably on a probabilistic basis. These models should be founded on scientific principles and evaluated using a variety of data. Developing such models is an iterative process, with the scientific foundation improving at each iteration. It is important that the models explicitly address uncertainty and that they be sufficiently detailed so that they can identify the most effective risk reduction approach, should that be necessary. For example, knowledge of which sources and pathways result in the highest exposures can form the basis for optimal risk management. Descriptions of the wide range of exposure-related research needs follow.

Need 1: Improved ambient monitoring methods, characterization, and network design to support a national ambient air toxics monitoring network

Description: The current lack of a national ambient air toxics monitoring network hampers efforts to characterize ambient levels of HAP. Such a network is needed in the Strategy to support efforts to provide information that will assist in:

- Evaluating models;
- Characterizing risk;
- Tracking progress with respect to the risk goals over time; and
- Targeting areas of concern.

Monitoring methods should be developed for those urban HAP for which no methods are currently available. Field (ambient) studies of macro and micro environments require methods that are sensitive to ambient concentrations of HAP. The spatial extent to which such point measurements are valid needs to be determined to allow the assignment of an air quality measurement to a representative area rather than to just a point location in space. These efforts can build on the previous work performed to support the monitoring for the criteria pollutants. Research is needed to evaluate the uncertainties and limitations of current ambient monitoring methods and to improve methods where appropriate. This work should include, for example, an evaluation of current minimum detection limits with respect to expected ambient levels, background concentrations, and health reference levels. Evaluation of "natural background levels" of HAP through ambient monitoring needs to be completed. This should build on existing work and would help define levels of HAP which cannot be reduced through traditional control programs. Research is needed to evaluate the amount of monitoring data (and measurements) needed to develop estimates of annual average concentrations with an appropriate level of confidence. The usefulness of emerging ambient measurement methods for national application (e.g., Light Detecting and Ranging (LIDAR), other optical methods, mobile sampling methods, etc.) need to be evaluated and refined as appropriate.

EPA Activities: We are developing a plan for a national air toxics monitoring network that will build directly on existing monitoring efforts managed by individual State and local air pollution agencies. The network will foster scientific consistency across those existing networks with respect to pollutants measured, methodologies used, and quality assurance techniques employed. Also, it will expand the measurement of air toxics to new areas across the country with the aim of providing a more comprehensive assessment of ambient air toxics levels nationwide, with a particular emphasis on higher population areas. This monitoring network will be designed (in collaboration with the States) to site monitors that will assist in the evaluation of national scale modeling assessments and to facilitate tracking progress with respect to emissions/risks reductions. Other monitors will be sited to support localized assessment activities.

Need 2: Improved area source emissions estimation methodologies and spatial allocation methods

Description: Area source categories present special challenges for estimating emissions. For example, they include stationary emissions sources that are individually too small, too numerous, or too dispersed to be inventoried as individual sources (e.g., landfills, and residential fuel combustion).

We often estimate area source emissions using "top-down" approaches that require a combination of emission factors and source activity data. The available activity data may exist only for large areas, such as the Nation as a whole, or at the State level. Once emissions are estimated at this top level, they must then be spatially allocated down to smaller areas in order to support control strategy development, dispersion and exposure modeling studies, or simply to

permit comparisons of emissions in different geographic areas. A "bottom-up" approach, on the other hand, would involve collection of actual measured emissions from individual sources. This approach more accurately estimates emissions, but often is not practical because of the cost of collecting such data for a large number of area sources and source categories. Emission factors for area sources come from various source tests or other industry specific data (e.g., mass balance). Sometimes emission factors are supported by data from several facilities, but often there are only one or two tests to support them. Therefore, area source emission factors should be improved as new data are collected.

The availability, geographic level of specificity, and overall quality of the activity data for area sources vary from one category to another. Most often, the activity data are obtained from published business and manufacturing sources, governmental statistics publications, and background information from EPA regulatory programs. Examples of sources of activity data are industrial trade associations, the Department of Commerce's Bureau of the Census, the Department of Transportation, the Department of Energy's Energy Information Administration, and various State and local government planning and regulatory agencies. Emissions are allocated geographically by a number of methods. For major sources, the emissions for each facility may be assigned to counties or more specific geographic locations based the address of the facility or its latitude and longitude. Highway passenger vehicle emissions can be assigned to counties based on total county VMT data, which are normally available from State Departments of Transportation (DOTs). Sub-county allocation of these emissions may be based on VMT estimates for specific major roadway links and travel demand model outputs produced by local Metropolitan Planning Organizations (MPOs). Area source emissions are typically more difficult to allocate to counties and sub-county areas. Most often, where facility specific data are not available, emissions are assigned to individual counties or other areas using a surrogate factor for area source activity. Some examples of surrogate approaches include apportioning national emissions to counties based on population, and apportioning emissions from specific industrial sectors to counties based on Standard Industrial Classification (SIC) code-based employment statistics.

These area source estimation methods have several weak points, particularly when the estimates are to be used in dispersion models to predict ambient pollutant concentrations for very small geographic areas, like census tracts. Actual measures of area source activity for small areas are normally not available. Existing methods are thought to produce results with a high degree of uncertainty, but the actual activity data needed to establish credible uncertainty measures are not readily available. New and improved methods for area source emissions estimation and spatial allocation of area source emissions are needed to avoid inaccuracies resulting from the "smearing" effect of the methods described above. Development of such methods requires the completion of rigorous and demanding survey activities to establish credible databases that can be used to develop improved area source methods. While area source needs have been determined to have the higher priority, there is still a need to improve emissions data for major sources over the longer term.

EPA Activities: We have developed a baseline NTI representative of the 1990 - 1993 period, and are now updating these data to a 1996 base year. The objective of the NTI is to provide a compilation of emissions estimates for all CAA listed HAP for point, area, and mobile sources. The NTI therefore will serve as the most comprehensive emissions inventory of air toxics. The NTI incorporates available information from the TRI, State and local inventory data, data from various regulatory programs, and data from other special studies. Also, we have been conducting research to develop an improved method for estimating area source emissions.

Need 3: Methodologies that allow for identification and speciation of important HAP and their combustion and transformation products

Description: Some chemicals are inventoried as compound classes like "mercury compounds" or "chromium compounds." In addition, VOCs include many individual organic species, some of which have been listed as HAP. Some chemical species included in these composite chemical groups are likely to contribute to public health impacts while others may be relatively harmless. There is currently a shortage of data available to characterize individual species, particularly at the source category emissions level.

EPA Activities: We have begun studies to characterize the emissions of mercury and mercury compounds from chlor-alkali manufacturing facilities, believed to be the largest non-combustion source of mercury and speciated mercury compounds (i.e., elemental mercury, mercuric chloride, and mercuric oxide). We also maintain facilities for characterizing HAP emissions from combustion sources, such as boilers, rotary kilns, and municipal waste combustors (MWC). The MWC program performs basic research on MWC pollutant formation and on control mechanisms for acid gas, trace organic, and trace metal emissions. We also have conducted analyses of the products of incomplete combustion of agricultural plastic, and of emissions from the open burning of household waste in barrels.

For mobile sources, we perform in-house vehicle testing programs for determining the effects on emissions of a variety of vehicle operating conditions, including various temperatures, malfunctioning emissions control systems, driving schedules, and fuels. We emphasize such air toxics as benzene and total aromatics, 1,3-butadiene, formaldehyde, acetaldehyde, other aldehydes, MTBE, and primary particles.

Need 4: A more accurate nonroad mobile source emissions characterization

Description: Nonroad mobile sources include a wide variety of mostly gasoline and diesel-powered equipment used for nonroad transportation purposes, industrial and construction activities, agricultural operations, recreational, and other purposes. Examples include aircraft, farm tractors, lawn and garden tractors, snowmobiles, and recreational marine vessels. As is the case for area sources, emissions from nonroad mobile sources are estimated using emission factors and estimates of source activity. As for highway mobile sources, emissions result from the incomplete combustion of motor fuels and evaporation of motor fuel components. In general,

the data needed to estimate emissions include an estimate of the population that exists for a particular class of equipment, an estimate of the average number of hours of use in a year, the average load factor and power requirement for the equipment while in use, and information to spatially and temporally allocate the equipment use. Emission factors for nonroad equipment are based on emissions tests for specific equipment, and may be adjusted to consider deterioration of equipment with age and to account for any applicable emissions controls on the equipment. Emission standards for most nonroad categories have only recently been adopted so that many of the engines in use today were placed in service before controls were applied.

We are currently developing an emissions model for nonroad equipment. This model, NONROAD, estimates VOC and other criteria pollutant emissions using methods like those described above. Draft versions of this model have been released for review. The model does not include methods for aircraft and rail locomotives, or commercial marine vessels. To extend the capabilities of NONROAD to cover air toxics, more research is needed to characterize toxic emission rates (either in absolute terms or as fractions of total VOC emissions). The nonroad mobile source category includes a wide variety of subcategories, each of which may have different emission characteristics because engine sizes and designs, duty cycles, fuel consumption, and approaches to engine cooling and fuel management vary.

Considerable uncertainty is inherent in the methodologies that are used to estimate nonroad engine activity for the temporal and spatial scales needed to support air quality or exposure modeling for urban areas. Typically, there are no State or Federal equipment registration databases that can be used to determine equipment populations. Also, there is no system to measure equipment utilization at either the national or local levels. The national estimates of equipment populations, lifetimes, and utilization are based on limited survey data. To improve the methods for estimating nonroad engine activity in urban areas, more complete information for both national and local equipment population and utilization is needed. Field survey data to better establish nonroad equipment activity levels in urban areas are needed to improve the databases that are needed to develop improved activity level estimation methods, to correlate nonroad equipment activity with other available surrogate parameters that may be better indicators of equipment activity, and to better define the uncertainty bounds of existing methods.

EPA Activities: As discussed above, we are developing a comprehensive nonroad emissions model, called NONROAD, which estimates emissions for criteria pollutants. In addition, our National Exposure Research Laboratory (NERL) is conducting some limited testing to better characterize toxics emissions from some categories of nonroad equipment (e.g., lawnmowers and other lawn and garden equipment, and marine engines).

Need 5: Improved characterization of air toxics from trucks and improvement of modal emissions modeling capabilities for all vehicle classes

Description: The highway vehicle category includes emissions from the operation of all classes of motor vehicles (e.g., light duty gasoline vehicles, light duty gasoline trucks, heavy duty

diesel trucks) on the Nation's highways and streets. Emissions are usually estimated using an emission factor model, such as the EPA MOBILE model or the California EMFAC model, in combination with estimates of VMT, which are developed by State or local transportation planning departments. The EPA's MOBILE5 model calculates fleet average emission factors for specific calendar years, expressed as grams of pollutant emitted per mile of travel. Built into the model are computational methods that will adjust the calculated emission factors to reflect how the age distribution of the vehicle fleet, average vehicle travel speeds, ambient temperatures, the effects of local vehicle Inspection and Maintenance (I/M) programs, and other modal variables, such as movement up a grade, affect emission rates.

For carbon monoxide, VOCs, and nitrogen oxides, basic vehicle emission rates are derived from standard EPA laboratory tests, the Federal Test Procedure (FTP) for highway vehicles. For estimation of air toxic emissions, data to develop emission factors are more limited. However, it is generally accepted that implemented control standards for reduction of VOC emissions can achieve proportional reductions. Some additional research to verify that VOC controls are achieving the expected effects in controlling toxics, especially in unusual driving and ambient conditions, may be appropriate. Relative to other vehicle classes, however, the toxic emissions from light duty gasoline fueled cars and trucks are reasonably well characterized. Not as much information exists to characterize toxic emissions from heavy-duty trucks, which are primarily diesel-fueled vehicles.

The following three research components describe various aspects of work that would be useful to improve the characterization of air toxics from medium and heavy duty trucks. First, a significant research need exists for the development of improved toxics emission factors activity data. In the past, most of our efforts for improving highway vehicle emission models have been focused on passenger vehicles. However, medium and heavy duty truck emissions, most notably PM emissions, may add significantly to the human health risks posed by exposure to motor vehicle emissions. Diesel exhaust is thought to be a likely human carcinogen at ambient levels of exposure. The EPA has prepared a draft health assessment document that was reviewed by CASAC in December 1999. The document is currently being revised to address the review panel's comments and will be reviewed again in late 2000. The temporal and spatial operating patterns for diesel vehicles are significantly different than for personal passenger vehicles. Highway-vehicle-travel-demand forecasting models concentrate on predicting passenger vehicle trips, not truck trips. Thus, there is a need for better characterizations of real world truck activity and emissions rates on current and emerging technologies in urban areas. Second, in addition to research designed to improve emissions characterization (in terms of g/mile and g/min emission factors), work is also needed to construct models that will predict population exposure levels using existing emission factors. This type of work is needed for all air toxics but especially diesel exhaust where questions have been raised about the usefulness of models (such as the HAPEM as developed for mobile sources) which use vehicle carbon monoxide emissions to estimate exposure to diesel exhaust. Third, additional work is needed on size distribution and chemical composition of diesel particulate emissions from new technology engines. While there

is extensive work under way on size distribution of diesel particulates from new technology engines, it is too early to make any conclusions.

The MOBILE5 and total VMT approach is best suited for estimating emissions for county or comparable political subdivision-size areas. Due to the complexity of factors that affect highway vehicle emissions, this approach may yield very uncertain emissions estimates, when used for smaller areas, such as the grid cells needed for atmospheric modeling, or for individual road links. A more sophisticated modeling approach is needed to obtain highway vehicle emission estimates that are accurately resolved in space and time for small areas. Highway vehicle emissions vary considerably based on the operating mode of the engine. For example, following a cold start, hydrocarbon emissions are significantly higher than during hot stabilized operation. This is due primarily to the lower emission control effectiveness of the vehicles's catalytic converter and the need for increased fuel enrichment to promote proper vehicle operation while the engine is cold. Variations in highway vehicle emission rates result from fuel enrichment events caused by "real world" engine loads imposed on vehicles traveling up roadway grades, carrying heavy loads, or hard accelerations by drivers. An alternate modeling approach that employs engine operation mode-based emission factors and uses Geographic Information System (GIS) technology for managing the increased detail of spatial data is capable of producing more accurate estimates of highway vehicle emissions for the detailed temporal and spatial scales that are needed to support air quality dispersion modeling and population exposure studies.

EPA Activities: Pursuant to section 202(l) of the.CAA, in 1993 we released the *Motor Vehicle-Related Air Toxics Study* (U.S. EPA, 1993). This study summarized information on emissions of toxic air pollutants associated with motor vehicles and motor vehicle fuels, as well as estimated exposures and potential risks. The study also provided cancer risk estimates for several air toxics for different years under various control scenarios. We've recently updated the emissions and exposure analyses done for this study to account for new information (U.S. EPA, 1999a).

The MOBILE6 emission factor model, when released, will incorporate additional and improved algorithms for estimation of criteria pollutants.

Also, we have been working with the Georgia Institute of Technology to develop a GIS-based modal emissions model for ozone precursor pollutants for highway vehicles (the Mobile Emissions Assessment System for Urban and Regional Evaluation or MEASURE). By the end of 1999, MEASURE will also include some simple capabilities for estimation of air toxics and PM emissions.

In addition, we have conducted a limited number of on-road emissions measurements for heavy duty diesel trucks, primarily aimed at identifying modal emissions rates and correction factors for nitrogen oxide and PM. This work is being extended to provide for collection of data for PAH and other toxic species.

Additional motor vehicle research focuses on in-house vehicle testing, "real-world" vehicle testing, and human exposure to vehicle emissions in cabin air.

Need 6: Development of source-based urban-scale air quality models for the urban HAP

Description: As mentioned previously, it is necessary to understand the relationship between source emissions and the concentrations of chemicals in the media that may come in contact with humans. Adequate modeling is very important, since measuring all potential exposure scenarios is not feasible. While existing models may be applied to urban areas, no air dispersion model has currently been developed that is tailored specifically to the urban environment. Ultimately, the most effective model (which will actually be a combination of models) should estimate the relationships among the source, the ambient air, and the exposure dose. In this section, we describe the first component of this relationship, from source to the ambient air. A separate **Need 7** describes research that will estimate concentrations in microenvironments for use in exposure studies, the second component of the relationship. It is important to recognize that while **Need 6** and **Need 7** outline needs for exposure assessment in a modeling framework, measurement methods and data collection studies are equally important for the development, evaluation, and use of any model.

In order to develop and operate a numerical simulation model for the fate and transport of any HAP, a scientific understanding of key chemical and physical properties for that pollutant under typical atmospheric conditions is needed. Additionally, some HAP will be transported and dispersed without undergoing any significant chemical transformations (i.e., they are non-reactive). Other HAP undergo significant chemical transformations or are formed in the air as a result of atmospheric transformation of their precursors. For example, formaldehyde is directly emitted from some sources and is created as a result of the atmospheric transformation of other pollutants present. Particle-gas phase partitioning in the atmosphere may also be important for certain HAP. Some HAP are semi-volatile and can exist simultaneously in both gaseous and aerosol forms. The fraction of the total HAP air concentration in each form is a function of the chemical and physical properties of the HAP, the atmospheric conditions, the concentrations of precursors, and the availability of condensate nuclei. Thus, a simulation model for semi-volatile HAP should simulate the behavior of key interacting aerosol materials, not just the gaseous and aerosol fraction of the HAP in question–likewise for HAP that are totally in particulate form with no significant gaseous fraction. These HAP, as particles, may coagulate to form larger particles which deposit through settling out and washout to the earth's surface differently than smaller particles. Therefore, to provide accurate representations of the atmospheric behavior of these HAP, a numerical simulation model should include both chemical and physical behavior of the HAP being considered as well as the surrounding HAP constituents. These processes, together with terrestrial and aquatic fate and transport processes, can be important for assessing non-inhalation pathways of exposure (e.g., ingestion or absorption) that are associated with deposition of these pollutants in soil, water, and various media.

For urban-scale modeling, a comprehensive atmospheric model should also simulate the fate and transport of the pollutant on a local scale. To predict maximum impacts and concentration gradients required to assess human exposure, horizontal simulation may have to have a resolution on the order of hundreds of meters. The vertical resolution of existing simulation models for photochemical oxidants and acidic deposition are expected to be sufficient for urban HAP studies. Further, the model domain size for a typical urban study is on the order of 100 kilometers (km). No such modeling capability currently exists at these resolutions to simulate the necessary physical and chemical processes to predict urban HAP fate and transport. If the HAP in question can be transported long distances (i.e., beyond the 100-km range), then nesting of a larger-scale grid model (or regional-scale model) within the urban study area will be required. Regional-scale models for some HAP do exist, but their usefulness on a local scale is still very much in doubt due to model approximations about small-scale air flows and atmospheric reactions of the HAP in question. Further, model evaluation is difficult because of the lack of any monitoring techniques capable of measuring ambient air concentrations of the HAP in question at temporal and spatial scales of the study.

EPA Activities: We previously developed and applied regional-scale Lagrangian-type models for certain HAP (i.e., mercury, dioxins and furans) with very simple or chemical specific treatments for chemical and physical processes. These Lagrangian models are currently used to model HAP that are transported over long distances, but cannot accurately model many HAP at the spacial scale that need to be considered. Generally, they provide 40-km or larger horizontal resolution, which may be inadequate or inappropriate for some urban assessments.

We have also previously developed and applied a more local-scale, emissions-based Eulerian-type model, the Industrial Source Complex 3 (ISC3) model, for some HAP in candidate urban areas. As mentioned above, while this may have been appropriate for some HAP, there are still many questions associated with the spatial and temporal uncertainties of modeling HAP with this method.

We are now developing a new comprehensive air model of acid deposition, tropospheric oxidants, and aerosols with available horizontal resolutions down to 4 kilometers. This model, the Community Multi-scale Air Quality (CMAQ) model (Byun et al., 1998), is designed to operate within the Models-3 system. Models-3 is a flexible, software system designed to simplify the development and use of environmental assessment and decision support tools for a wide range of applications from regulatory and policy analysis to understanding the interactions of atmospheric chemistry and physics. This effort could serve as a basis for the development of urban-scale HAP models with nesting capabilities within larger-scale models. Current chemical mechanisms of tropospheric chemistry within the CMAQ model are available as a starting point for this work. These mechanisms could probably be expanded to include the many additional reaction pathways and species necessary to describe the detailed transformations of HAP, as well as significant pathways for the production of HAP from non-HAP precursors.

We have developed a set of integrated models, the Integrated Exposure Methodology (IEM), that permits estimation of concentrations of stack-emitted pollutants in various media and associated exposures. This methodology was used in the *Mercury Study Report to Congress* (U.S. EPA, 1997) and in the *Study of Hazardous Air Pollutant Emissions from Electric Utility/Steam Generating Units* (U.S. EPA, 1998), mandated by the 1990 CAA Amendments.

We are developing a modeling system called the Total Risk Integrated Methodology (TRIM), which is intended to provide a framework that is scientifically defensible, flexible, and user-friendly, for assessing human health and ecological risks resulting from multimedia (air, water, soil and food), multipathway (via inhalation, ingestion, and absorption exposure routes) exposure to air toxics and to criteria pollutants. The modeling system will consist of multiple modeling tools from which to select, depending on the level of analysis, data availability, and needed outputs. TRIM will track the movement of pollutant mass through a comprehensive system of compartments. Over time and with additional research, the compartments will attempt to represent all possible locations of the pollutant in the physical and biological environments of a defined study area or species. Also, the modeling system should make use of mass conserving relationships, fugacity, and biokinetics to determine the movement of HAP, and, thus, will be able to provide an inventory of a pollutant throughout the entire system. Also, the modeling system will reflect an integration of uncertainty and variability analysis capabilities.

Need 7: An understanding of the distribution of human exposures (including susceptible subpopulations) and the pathways by which HAP reach humans

Description: Human exposure to HAP occurs at the point of contact between the environmental concentration and the personal receptor. If addressed, previous research needs (see **Need 6**) would enable improved estimation of air quality. However, further refinement in scale may be needed to estimate the population distribution of exposures in an urban environment. For example, a HAP at a 4-km distance may undergo transport and transformation processes in the ambient air during and after penetration into indoor environments before contacting a human. Also, many additional sources could be present within this "4-km grid" and contribute to overall exposure. To account for these possibilities, models developed around sound scientific principles, evaluated with measurements from targeted studies, and capable of providing probabilistic estimates of the number of persons exposed to different concentrations of HAP of interest, should be developed.

Exposure to HAP can more accurately be evaluated in a microenvironmental modeling framework which considers the human as a receptor passing through a series of microenvironments in which exposure occurs. Clearly, there are two critical factors in this approach: (1) characterizing the range and variability of HAP concentrations in each microenvironment, and (2) characterizing the nature of the human exposure in each microenvironment (i.e., when, how long, how often, and with what intensity do people come in contact with the HAP in each microenvironment). Both elements are involved in characterizing susceptible subpopulations. For example, people with low incomes may live closer to sources;

children spend different times in different microenvironments compared to adults; and people with pre-existing diseases (e.g., asthma) also have different activity patterns.

Estimating exposure to HAP is complicated by the range of temporal and spatial scales of emissions that may significantly contribute to personal exposures. Significant HAP emissions may come from a few point sources with high emissions or a collection of sources with relatively low emissions. Exposures of interest may be for an hour or a lifetime. The longer the duration of exposure, the more complicated the assessment, given the variability in the exposure and in personal activities. Although daily exposure may best be evaluated by a model that considers the human receptor as passing through a series of microenvironments of exposure, long-term exposure estimates require development of reliable simplified modeling methods because it is not practical to follow every individual through a daily series of activities.

Research to bridge the gap between available regional-scale models of air pollution transport and stochastic and probabilistic models of personal exposure, include: a) the development of models and data that consider key human exposure microenvironments, b) studies of concentration measurements and activity patterns to support modeling evaluation on selected urban HAP, c) measurements of HAP in various media to which susceptible populations may be exposed to ensure that models adequately capture those populations likely to receive high-end exposures or be more biologically sensitive, and d) development of databases and integration of all data. The data on demography, geography, meteorology, human activity patterns, source emissions, and regional/urban/microenvironmental scale concentrations would need to be integrated. These data support the application of a HAP population-based probabilistic modeling system of personal exposures. It is important that both the inherent variability and the uncertainty of all significant factors for connecting emission sources, environmental concentrations and the magnitude, duration, and frequency of human exposures be understood, and models be developed so that risks may be assessed and managed.

In the context of activity patterns and microenvironments, an existing gap is the need for personal monitoring (e.g., personal monitoring exposure to VOCs and other air toxics through use of gasoline fueled lawn and garden equipment, including commercial equipment which is typically used for many hours per day). The development of biological markers of exposure such as breath, hair, or tissue samples would also help characterize personal exposure of VOCs and other air toxics. An adjunct to the need to determine personal exposure is the long-term need to identify indoor air exposures. In the short-term, this need may be satisfied by knowing the indoor/outdoor ratios of the urban HAP, but in the long-term, more specific data are needed on the movement of HAP between indoors and outdoors. Toxics can absorb onto other items in the indoor environment and then be re-released later as the concentration of the toxic is reduced. Therefore, information on the potential sinks and reservoirs of HAP would add useful information to the indoor characterizations of exposures.

EPA Activities: We have completed some studies, the National Human Activity Pattern Survey (NHAPS) and Total Exposure Assessment Methodology (TEAM), that can contribute

limited human activity and personal exposure data in support of this need. The NHAPS did not evaluate susceptible subpopulations, and TEAM measured only a small number of HAP. Even so, these studies provide valuable direction for the design of necessary follow-up studies. We have developed databases for supporting human exposure modeling [e.g., Consolidated Human Activity Database (CHAD) and Total Human Exposure database and Advanced Simulation Environment (THERdbASE)]. We also have a small ongoing project to develop microenvironmental exposure measurements and models for mobile-source related emissions. These studies will contribute both measurements and models toward developing air pathway, human exposure estimates along and near highways (including urban street canyons). We have sponsored the development of receptor models for source apportionment. Chemical Mass Balance models, and models like UNMIX, have been developed and tested on particulate and other pollutants. Their application to microenvironmental and personal exposure measurements is both feasible and reasonable. These past and present projects are helpful in providing some of the needed data and models.

We are currently using models to estimate ambient levels of air toxics which will subsequently be used as inputs to an exposure model, HAPEM. This exposure model will provide national exposure estimates to air toxics based on the 1996 NTI. This work will be completed in the spring of 2000. We have a small project that develops breath analysis methods for VOCs. Though we currently have no projects on source test methods or ambient methods for the urban HAP, we have recently developed a prototype real-time monitor for formaldehyde. While HAPEM is currently being applied, there are many areas where additional information developed through research is needed to improve the model.

Recently, we sponsored the National Human Exposure Assessment Survey (NHEXAS) which is a multiroute exposure study focusing on metals, pesticides, PAHs, and VOCs. In addition, we recently funded two research centers (New Jersey Medical School and University of California at Berkeley) to develop comprehensive exposure models for a large spectrum of air pollutants, including HAP. Coordination between this particulate matter initiative and the urban air toxics initiative will be beneficial to the urban air toxics program.

6.2 Health Effects and Dose-Response Assessment

Various types of toxicity, mode of action, and interactive (mixture) information are needed to reduce uncertainty in our estimates of risks from exposure to urban air toxics. The needed information includes cancer and noncancer (acute and chronic) toxicity information for HAP and risk assessment techniques that can combine data, produce statistical likelihood of risk from HAP exposure, and reduce uncertainty through the application of better extrapolation models (e.g., animal to human, low dose to high dose).

Need 8: Use alternative sources of human health effects data (chronic and acute) for urban HAP to develop and update dose-response assessments

Description: As described in Chapter 3, a variety of sources of dose-response information was relied upon in identifying the urban HAP.

Additional health effects assessments, including the development of inhalation reference concentrations and oral reference doses for chronic noncancer effects and acute reference exposures for acute effects are needed for a number of the urban HAP. Although enough information exists to raise our concern level and to select urban HAP presenting the greatest threat to public health, more information is needed to complete the knowledge base necessary for quantitative risk assessment, especially for the assessments of mixtures. The EPA's Integrated Risk Information System (IRIS) lacks cancer unit risk estimates for 13, and RfCs and RfDs for 24 and 21, respectively, of the 33 urban HAP identified in the July 19, 1999 *Federal Register* Notice of the Integrated Urban Air Toxics Strategy (U.S. EPA, 1999b). Consequently, unless peer-reviewed, dose-response assessments can be obtained from other sources, significant uncertainty will be present in any risk assessments performed for these pollutants. An important short-term activity is estimation of cancer unit risk and RfCs/RfDs for the HAP that currently lack this information. Our preference is to obtain inhalation and oral data for these assessments through the use of EPA's test rule authority (described below).

When no chronic inhalation dose-response assessments have been available for particular HAP from any source, we have sometimes adapted oral data to inhalation exposure as a short-term solution. Such conversions are not optimal for deriving inhalation dose-response and risk assessments because they involve important uncertainties. For example, confounding features such as portal-of-entry effects and first-pass metabolic effects may play a significant role in altering the concentration of the dose delivered to the target organ and, thereby, attenuating expected responses. Because of the relatively large amount of oral data, the development of validated route-to-route methods and models to extrapolate from oral exposures would expand our ability to perform risk assessments for urban HAP in the near future.

There is a need to develop acute reference exposure values for the short term using methods such as EPA's proposed Acute Reference Exposure (U.S. EPA, 1994a) approach, which is adaptable to any duration of exposure up to 24 hours. These values should be externally peer reviewed, Agency consensus reviewed, and then listed on IRIS for use in developing risk assessments under the Strategy. The methods used to generate the values should be evaluated so that there will be a clearer understanding of the uncertainties associated with each method. Models and software to facilitate acute dose-response assessments should also be developed over the long term whereas developing the methods and data are short-term needs.

Another research need is for information to reduce uncertainty associated with the dose-response assessments now on IRIS. Four HAP (acetaldehyde, acrolein, acrylonitrile, and ethylene dibromide) have RfCs with relatively high associated uncertainty, i.e., with uncertainty

factors greater than or equal to 1000. (The RfC methodology involves the application of uncertainty factors to information in health studies so as to account for chronic noncancer effects on humans, including sensitive subpopulations. For example, a 10-fold uncertainty factor may be needed to account for a lack of understanding of human effects when only subchronic animal studies are available.) Those urban HAP having dose-response assessments on IRIS but that have not been externally peer reviewed should be updated based on current literature and reanalyzed to include external peer review and Agency consensus review. Those pollutants having high uncertainty should be reassessed when test rule data are made available over the longer term. While awaiting test rule data, evaluation of dose-response information developed by States could be useful in deriving interim values for use in the short term.

Where multipathway exposures are deemed relevant to exposures to urban HAP (e.g., mercury, dioxins), RfDs should be developed, as should route-to-route extrapolation methods, that allow their use in assessing inhalation risks. No AREs are available for any of the HAP because the method to calculate them is still being developed. The ARE method currently under development has been reviewed by the EPA Science Advisory Board (SAB) which recognized that large amounts of data are required to support ARE derivation by categorical regression.

Finally, the quantitative structure-toxicity relationship (QSTR) approach is another method for gathering data on the toxicity of urban HAP. By knowing various structural attributes and functions and how these attributes relate to toxicity, QSTR models can predict relative toxicities of urban HAP. Thus far, QSTR model outputs have provided the probability of a compound being carcinogenic and are most appropriate for use in ranking toxicity but not in developing quantitative health assessments themselves (i.e., RfCs or cancer unit risks). Therefore, a short-term research need is to develop the QSTR for the urban HAP and the other HAP on the list in order to expand our knowledge database. A longer-term research need is to be able to use the QSTR to actually predict cancer unit risks or noncancer reference values.

EPA Activities: EPA's authority for acquiring toxicological testing data is found in section 112(b)(4) of the CAA. We have proposed to use the test rule authority under the Toxic Substance Control Act (TSCA) section 4(a) which will require testing of 21 HAP. We noted deficiencies in testing guidelines previously used under TSCA section 4(a) and promulgated eleven harmonized test guidelines. Pharmacokinetic studies and other mechanistic studies were also requested in the test rule protocols to support route-to-route extrapolation and to inform EPA of toxicity by routes other than inhalation. The only urban HAP included in that initial test rule is ethylene dichloride. Additional toxicological testing needs to be conducted, and an amalgamated test rule considered by EPA and ATSDR for the Children's Risk Initiative, Urban HAP, ATSDR VOC, and the metals rule. Testing needs for the urban HAP are candidates for the amalgamated test rule.

Some of the completed assessments and some of the planned assessments have high uncertainty associated with their conclusions based on the underlying toxicological data. In order to significantly reduce the uncertainty of dose-response assessments, future test rule data will be

used for dose-response reanalyses. In addition, only a few of the cancer unit risks on IRIS were developed using the approach described in the Proposed Guidelines for Carcinogen Risk Assessment (U.S. EPA, 1996). An updating of present IRIS cancer unit risk values consistent with the proposed guidelines should be accomplished in the longer term. Exhibit 6-1 presents the current status of activities to update IRIS.

EXHIBIT 6-1
STATUS OF FY00 IRIS ACTIVITIES FOR URBAN HAP

Completed	In Progress	Scheduled New Starts
Arsenic Compounds	Acetaldehyde	Acrolein
Beryllium Compounds	Benzene	Arsenic (inorganic)
Chromium Compounds	1,3-Butadiene	1,2-Dibromoethane
Methylene Diphenyl Diisocyanate (MDI)	Cadmium Compounds	Methylene Chloride
	Chloroform	Methyl Mercury
	1,3-Dichloropropene	
	Dioxin	
	Ethylene Oxide	
	Formaldehyde	
	Nickel Compounds	
	POM	
	Quinoline	
	Styrene	
	Tetrachloroethylene	
	Trichloroethylene	
	Vinyl Chloride	

The IRIS program has recently been altered to provide improved Agency consensus review and external peer review of dose-response assessments. We have ensured that external peer review has been conducted or is planned for the assessments listed in Exhibit 6-1. Although all of the assessment activities for the chemicals in Exhibit 6-1 do not include the development of an RfC, as data are made available (e.g., through test rules), including those relevant to

noncancer dose-response assessments, more RfCs will be derived. Pollutants with high uncertainty factors (>1000) will be reassessed as data become available. No ARE values are available for any HAP, but a framework for their incorporation into IRIS is being considered. The MRLs, acute exposure guidance levels (AEGLs), and levels of concern (LOCs) may be developed as they are necessary to estimate hazard. Work has progressed on using QTSR models to rank 250 disinfection byproducts for the Water Program. This method holds potential for any further ranking of HAP by toxicity as well.

Section 202(l) of the Clean Air Act requires EPA to identify the need for and consider regulation for control of HAP from motor vehicles and motor vehicle fuels. These regulations are at a minimum to apply to emissions of benzene and formaldehyde. The following three ongoing mobile source pollutant health assessment efforts will inform us as we continue our work as part of the Strategy:

- **Benzene health assessment**. Benzene is a carcinogen found in baseline gasoline and reformulated fuels. Calculating the cancer unit risk for benzene will serve to estimate a risk associated with use of fuels containing this hazardous air pollutant. The benzene RfC and RfD are being completed.

- **1,3-Butadiene health assessment**. 1,3-Butadiene is a common emission product and carcinogen resulting from combustion of gasoline and reformulated fuels. The health assessment of 1,3-butadiene was reviewed by the SAB in 1998, and the final assessment document is expected in late 2000.

- **Fuel additive risk assessments**. The health risk assessments of fuel additives, such as methylcyclopentadienyl manganese tricarbonyl MMT (Davis et al., 1998; U.S. EPA, 1994b), are being conducted in support of various EPA mobile source programs. MMT is an organic manganese compound that can be used as an octane enhancer. Questions have been raised about whether there may be inhalation risks associated with exposure to manganese emissions from MMT-fueled vehicles.

Need 9: Development of statistical and mode of action methods for developing acute and chronic dose-response assessments

Description: The lack of toxicity data or the availability of seemingly disparate data often forces the application of uncertainty factors and default assumptions when developing dose-response assessments. Certain cases may arise where multiple toxicity studies are available for developing dose-response assessments. Methods of combining data for cancer and noncancer dose-response assessments that include confidence profiles (Bayesian statistics) or meta-analysis, for example, need to be developed, codified, and incorporated into software packages for easy use. The development of many of these methods can be completed over the shorter term.

The current methodology for developing RfCs divides gases into three classes based on their reactivity and solubility. Developing dose-response assessments on the basis of these classes offers increased certainty and reduces the number of mode of action parameters necessary to define gas behavior. The current RfC methodology utilizes a paradigm which describes gas solubility using mass transfer coefficients. Gas models that can predict the dosimetry of reactive and nonreactive gases and water soluble and insoluble gases are needed. Thus, over the shorter term, mass transfer coefficients are needed for the three categories of gases: Category 1, which are highly water soluble, rapidly reactive, and do not penetrate to blood; Category 2, which are water soluble and show accumulation in the blood; and Category 3, which are water insoluble and perfusion limited. This physical process of mass transfer should also be coupled with chemical reactions in the system.

Estimating risks associated with human exposure to priority urban air toxics under the Strategy will best be done on the basis of probability. The determination of cancer unit risk factors for HAP readily permits such determinations of risk or probability for cancer endpoints. However, for noncancer endpoints, EPA has no definitive methodology for determining risk above reference levels such as the RfC. The RfC is useful in that it indicates a reference concentration below which it can be reasonably expected that no adverse effects will occur, even in the most sensitive subpopulations. The basis of the RfC, which includes the application of either a single point no-observed-adverse-effect level (NOAEL) or a statistical approach such as the benchmark dose (BMD) (U.S. EPA, 1995), does not permit it to be used in probabilistic risk assessments where knowing the probability of the occurrence of a health effect in a population is desired. Though the BMD method utilizes data over a range of doses, the data are normalized to a single effect. If higher exposure/doses are encountered, other endpoints would likely be manifested making the basis of the BMD (dose-response for a single sentinel effect) no longer relevant. It is important to understand that any dose-response method that utilizes a single dose-response function, where response is a single endpoint, cannot provide a probabilistic risk assessment by simply assuming higher doses will produce higher probabilities based on the dose-response function originally chosen. Thus, both the NOAEL and BMD approaches provide deterministic dose-response assessments, but not probabilistic ones. Categorical regression and Bayesian statistics may be useful in developing methods for probabilistic risk assessments, but these methodologies need to be developed on large adequate databases. Probabilistic approaches to dose-response assessments are a longer-term need. Developing noncancer risk as a probability also avoids the problem of having to combine probabilistic exposure assessments with deterministic dose-response assessments. Guidance on the biological motivation and statistical limitations of combining data involving different endpoints would be of added value.

The BMD method and related software are being developed as other tools for developing both acute and chronic noncancer dose-response assessments. This methodology has many similarities to the cancer dose-response method which utilizes curvilinear data fitting. Currently, BMD methods are being used for the development of dose-response assessments entered on IRIS. New software is being readied that will serve to facilitate the selection of models, provide statistical comparisons, and present results in a graphical manner. A finite set of models for

dichotomous data (incidence) are now available, but over the longer term additional models for continuous data (quantitative increases or decreases in a metric) will be needed to develop additional risk assessments. Guidelines for censoring data to develop more relevant dose-response curves and adjusting for poor fit of models are also needed.

The ARE method is a process for developing acute dose response assessments that includes the single point NOAEL approach, the BMD approach, and categorical regression depending on the data availability. The ARE is defined as the exposure (concentration and duration) with an uncertainty spanning an order of magnitude that is not likely to cause adverse effects in a human population, including sensitive subgroups, when exposed on an acute and intermittent basis. Adverse-effect levels are those at which there are increases in frequency, magnitude, or severity of effects due to exposure, which are considered to be adverse. Intermittent implies sufficient time between exposures such that there is no effect of one exposure on the effect of the next, and acute exposure is defined as one of less than 24 hours. Standard methods using the NOAEL and the BMD approaches as used in derivation of RfCs, and RfDs are invoked for ARE derivation with limited amounts of data. When more complete data sets are available encompassing sufficient concentration and duration information, then a categorical regression approach is used to combine the data from different studies and derive the ARE. The ARE methodology uses categorical regression data from many studies. Data are grouped into categories such as no-observed-adverse effects, adverse effects, or frank effects. No-observed-adverse effects and adverse effects have been defined previously. Frank effects are those effects occurring at levels that produce frankly apparent and very severe effects, such as irreversible functional impairment or mortality. Effects data from different experiments, different animals, and different endpoints may be plotted and regressed by category across exposure duration. All the ARE methods sacrifice some certainty. The categorical regression procedure holds the most promise to determine dose-response across various durations of exposure. As a longer-term need, an adaptation of this method or other methods should be developed to reduce uncertainty while still allowing development of dose-response assessments across a duration of exposure.

The magnitude of response to a toxic chemical exposure is often dependent on both the concentration and the duration of the exposure. The response has been related to their product with an assumption that their product is a constant (a linear assumption). A significant number of RfCs, which are assessments of chronic noncancer effects, are based on subchronic studies in animals with no knowledge of whether a linear relationship exists between the toxic response at greater exposure (considering concentration and duration) and that at lower exposure. Operationally, this lack of understanding is usually accounted for by use of a 10-fold uncertainty factor. Over the longer term, an understanding is needed of the appropriate response metrics (e.g., peak height, area under the curve, peak duration, and frequency of response) to help guide the use of data in developing dose-response assessments of less than chronic exposure durations.

Advances in cancer research leading to proposed changes in EPA's guidelines for cancer risk assessment (U.S. EPA, 1996) have necessitated an improved knowledge of mode of action.

To develop cancer unit risk estimates under the new guidelines, we will have to understand the binding and repair of exogenous agents to DNA on (1) cancer induction, receptor-mediated mechanisms of action, and (2) mechanisms of toxicant interference with critical cellular pathways such as signal transduction and receptors involved in cell growth. Gaps in our knowledge of mode of action as it relates to human susceptibility also present significant uncertainty in cancer and noncancer dose-response assessments. The National Research Council has recognized that with respect to cancer, EPA does not account for person-to-person variations in susceptibility. Factors such as carcinogen metabolism, DNA-adduct formation, DNA-repair rate, synergistic effects of carcinogens, and age may contribute to different modes of action that influence susceptibility to cancer. Research is needed over the longer term to understand the effects of receptor mediation on dose response of toxic chemicals and to model the interaction of environmental chemicals with receptors. In addition, the susceptibility of humans should be compared to human epidemiological and animal toxicological data to validate the assumption of similar susceptibility. Modes of action responsible for increased susceptibility of certain subpopulations (e.g., children, elderly, asthmatics) should be identified and described over the longer term in order to reduce uncertainty in dose-response assessments.

EPA Activities: Some work is ongoing to develop methods for combining data. We are using a meta analysis technique to combine data for health assessments when the available data are directed toward the same endpoint. We have conducted some preliminary research on the use of Bayesian statistics as a way of combining studies to develop a confidence profile around parameters such as a NOAEL. Such a synthesis of data incorporates the uncertainty of parameter estimates and provides visual display of distribution about a central point. Uncertainties in dose-response assessments are also being reduced by research which incorporates mechanistic data. We are also studying a class of chemicals with a common mode of action, endocrine disruptors, which bind to androgenic receptors for reproductive or developmental endpoints in order to determine cumulative risk for multiple chemicals within the same mode-of-action class.

We have several activities which are integral to reducing uncertainty in RfCs and cancer unit risk estimates. Physiologically based pharmacokinetic (PBPK) models for priority HAP (e.g., trichloroethylene and MTBE as shorter-term examples) which permit improved estimation of target tissue concentrations of compounds needed for derivation of RfCs are being developed. A long-term research activity is the development of improved pulmonary dosimetry models for gases and particles. Uptake efficiency data in the upper and lower respiratory tract of nonhuman primates and rodents, which will permit calculation of mass transfer coefficients for certain types of gases, are being gathered. We are compiling a guidance document for use in interspecies adjustments and incorporation of mode of action data that would facilitate development of oral and inhalation cancer and noncancer dose-response assessments. Use of this guide is expected to result in improved risk assessments. We are also developing a more precise model of the regional deposited dose ratio (RDDR) for particles of large and small mass medium aerodynamic diameters. The original model is being altered such that deposition estimates from the existing RDDR model will be based on the ICRP66 model structure with modifications of rate and parameter values as necessary after evaluation and application of new data. This new lung

dosimetry model is being developed to improve precision of dose-response assessments of particles and will soon be available as a software product. We are also upgrading the RDDR model to contain a module for human ventilation activity patterns. Ventilation rates as a function of oro-nasal switching patterns and activity patterns in children are being compared to the patterns in adults to determine susceptibility of children to particle deposition. This work is being conducted in cooperation with the University of North Carolina. New information on particle emission, transport, exposure assessment, and biological mechanisms will be of great value to the urban air toxics research program.

We are conducting some preliminary explorations into statistical methods to develop probabilistic dose-response assessments. Categorical regression is a mathematical tool that can be used to estimate health risk from chemical exposures. Ordered categories of toxics severity or pathological staging can be regressed on exposure-dose to estimate the likelihood of observing any of the categories of severity at any dose level. These estimates can be in the form of incidence. Preliminary work on the toxicity of aldicarb has invoked such a procedure and determined a 0.1 percent probability (risk level) of adverse effects at a dose 10-fold higher than the aldicarb RfD. We have also undertaken a small amount of initial work regarding the application of Bayesian statistics to determining risk above a reference level. Building upon limited Bayesian approaches for estimating dose-response assessments for a single effect, Bayesian statistics have been used to estimate the probability of adverse effects for aldicarb and toluene. The Bayesian approach was used to develop distributions of effects from different sources and then combine these distributions into a single distribution that could be used to provide probability of a given severity of effect at various exposure-doses. Probabilistic dose-response assessments will likely require longer-term research.

Current research in the area of dose-response assessments for acute exposures includes the determination of the effects of the categorical regression model on derived dose-response assessment estimation versus the role of the data. It is important that the available data drive the shape of the regression line and not the mathematical model itself. Idealized data sets are being used to further understand this uncertain aspect of categorical regression of toxicological data. *In vivo* uptake experiments in animals and humans and generic PBPK models for central nervous system (CNS) effects are being studied to determine the magnitude and appropriateness of performing an interspecies dosimetric adjustment for high exposure concentrations at short durations. An additional activity is the development of a framework for utilizing data from a standard acute database previously developed to derive ARE values, bring them to external peer review followed by Agency consensus review, and finally incorporate them in IRIS. Categorical regression software that facilitates ARE value development is also being developed. Usable forms of the ARE methodology will be realized over the shorter term.

We are also conducting research to determine the most appropriate metric for quantifying toxicity from acute exposures. Given that concentration multiplied by time is often not linear, other relationships defining toxicity are being sought. Using endpoints of neurotoxicity and reproductive/developmental toxicity, we are exploring the relevancy of metrics such as peak

height, area under the curve, peak duration, and frequency of response as better predictors of dose-response relationships.

6.3 Risk Assessment/Characterization

After an exposure assessment and a dose-response assessment are completed, it is necessary to combine them into a clear and useful characterization of risk. This section addresses the need to improve risk assessments of chemical mixtures and also the need for better risk communication.

Need 10: Improved risk assessment methods for mixtures

Description: It is possible that the combined exposures to multiple pollutants may produce synergistic or antagonistic effects; effects either more detrimental or less detrimental than exposure to each pollutant individually. Recent epidemiological evidence indicates associations between air pollution and increased illness and death in humans are unlikely to be the result of exposure to a single compound. Rather, exposure to a mixture of pollutants including tropospheric ozone, PM, and other constituents such as HAP, seems to be correlated with adverse effects. There are, however, significant gaps in methods, models, and data that influence the evaluation of the risk to public health from air pollution mixtures. Research is needed on methods of extrapolation from toxicity information about one or more complex mixtures of air pollutants to others. Determination of toxic equivalency factors (TEF) is one approach to gaining information about the toxicity of several compounds within a mixture. More TEF information on mixture components such as polyorganic matter is needed for urban assessments. Short-term toxicity tests of actual mixtures, if performed systematically, would provide information that could be used for priority-setting and risk management.

Other longer-term work that would aid the risk assessment of mixtures is atmospheric fate and dose-response information on mixtures. This should include basic work on chemical characteristics and transformation factors which may affect urban HAP transformation and dispersion in air and other media (e.g., chemical half-life, transformation rates, chemical partition information). Longer-term information is needed concerning the antagonistic, synergistic, or additive nature of risks associated with the components of various mixtures. This kind of information will be useful to EPA as it moves toward enhancing its ability to evaluate cumulative risks. The needs of the urban air toxics program should influence the priority selection of chemicals for which binary and higher order interaction data are developed.

EPA Activities: We are presently developing a strategy to conduct laboratory and clinical studies to identify and quantify the effects associated with exposures to typical mixtures of pollutants in urban areas of the U.S. Particulate matter, ozone and HAP are the primary

pollutants of interest, and the endpoints of interest include both carcinogenicity and noncancer effects, particularly respiratory and immune system responses.

Though resources committed to mixtures research are comparatively small, EPA maintains a mixtures database to help in the development of risk assessments involving more than one chemical. A pilot upgrade of the MIXTOX database is under way. This database is an interaction-based hazard index which can be used to incorporate chemical interactions into risk assessments for mixtures. The MIXTOX database on interactions is available as an easily-used computer program. The current version is years out of date, and the revision project is to establish a priority list of chemical pairs based on their potential interaction and toxicity. Detailed interaction profiles on these priority pairs are being developed. After the revision is complete, a new set of 20 priority chemicals or pairs will be selected and binary mixture interactions data will be gathered, evaluated for binary weight-of-evidence determinations, and entered into the database. Finally, we will update the profiles for 50 more chemicals to be included in the database.

In addition, our original Mixtures Guidelines (U.S. EPA, 1986) are being revised and provide a good first step toward the evaluation and assessment of mixtures. This mixtures risk guidance document includes several methods for addressing different types of data, from whole mixture dose-response data to *in vitro* toxicity data on individual component chemicals. The risk methods include mathematical models for well-understood interactions as well as decision frameworks for handling sparse and qualitative data.

We are studying mode of action for cancer to include receptor-mediated toxicity in humans and model laboratory animals. Research will include studies of polycyclic aromatic hydrocarbons present in urban environments to assess application of the structure-activity-based TEF approach as has been applied to dioxin-like compounds (U.S. EPA, 1989). Future comparative potency research will examine utility of TEF methods to predict biochemical and toxicological responses in animal models to assess potential human health risks.

Need 11: Development of better information for more effective techniques for communicating the results of health risk assessments for urban HAP

Description: The results of health risk assessments for urban HAP should be communicated effectively to those participating in the policy-making process and to various members of the public who may not have technical or scientific backgrounds. For example, the general public needs to be provided with information and the tools to protect their families and communities from exposure to air toxics. Unless a common understanding on the meaning of the assessments is reached between scientists preparing the assessments and persons using the assessments to affect policy, the overall process of risk assessment/risk management may be defeated, sometimes with costly consequences. There are many ideas that can be explored. For example, near real-time measurement, reporting, and access to air toxics ambient air concentrations, together with the actual monitored or modeled data, the estimated risk of health

effects, and the tools for interpreting this information, could be provided to communities throughout the Nation by use of the Internet. Communication of the science to these audiences, however, can pose challenges requiring the development of new scientific information.

Various approaches can be investigated, including: 1) adaption and refinement of state-of-the-art techniques for visualizing air toxics information and evaluating the utility of these techniques for communicating the information to various stakeholders, including the scientific community, regulators, and the public; and 2) development of mechanisms to deliver air toxics information in a timely and easily accessible format (e.g., through the Internet, over radio and television, in the newspaper). Local or regional maps could be provided through the Internet with color-coded air toxics concentrations to match predetermined indices of hazard. In keeping with the Environmental Monitoring for Public Access and Community Tracking (EMPACT) initiative, these risk communication activities should begin over the shorter term.

EPA Activities: We have developed a pollutant standard index (PSI) for ozone. Time-relevant air quality data are provided in an easily accessible and understandable format to the general public for their use in decisionmaking. The approach uses existing air quality monitoring and telemetry technology coupled with the latest Internet technology to provide time-relevant data to the public. This project is intended to expand mapping capabilities for ozone, PM, and air toxics to cover 85 cities across the U.S. Ongoing and completed work includes development of a new ozone PSI format, development of more descriptive ozone health effects messages that can be linked to a map on the Internet, and development of hard copy health effects pamphlets for environmental protection offices (more technical) and doctors' offices (less technical). We may also conduct focus groups to determine whether the most effective process is being used on the Internet and in print to communicate the risks of ozone exposure. Expansion of this approach to air toxics would provide beneficial risk communications to the public and risk managers.

6.4 Risk Management

Engineering information is needed on emissions and emissions reductions over time to support the application of regulatory strategies and compliance programs to achieve HAP emissions reductions. The expanded focus on risk-based activities must be supported by the development of improved risk management tools and information. In large measure, the needs for improved emissions information to support risk management are the same as those discussed under Needs 1 - 5 to support the risk assessment process.

Need 12: Identification of processes contributing to the HAP emissions from area source categories, and listing of control options and pollution prevention (P2) alternatives for these processes

Description: Area source categories considered for regulation under section 112(k) also require technology-based controls, such as GACT standards. More detailed knowledge of the area sources and their emission-producing processes is needed to identify appropriate control

technologies and pollution prevention options. This is a short-term task. To identify applicable control options, it is necessary to identify the processes that produce the HAP emissions.

EPA Activities: Our ongoing pollution prevention (P2) research activities are centered on the identification, evaluation, and demonstration of source reduction options for industrial and commercial surface coating and cleaning operations. Planned activities for FY99 include establishment of an in-house laboratory for testing of low-VOC, low-HAP coating alternatives, demonstration of P2 techniques for autobody refinishing operations, and coating/cleaning research for other metal and plastic substrates. We also maintain software tools showing information on P2 techniques for use by industry, academia, and the regulatory community.

Pollution prevention research areas have included office equipment, aerosol consumer products, textile products, engineered wood products, and conversion varnishes used on wood products. In addition, we have focused on the application of P2 techniques for the improvement of indoor air quality. For example, we have developed a model for analyzing the impact of sources, sinks, ventilation, and air cleaners on indoor air quality. We have studied emissions from various combustion sources, including hazardous waste incineration in boilers, rotary kilns, and other combustors such as municipal waste combustion. The MWC) program supports the development of revised rules for air pollutant emissions from the MWC source category and performs basic research on MWC pollutant formation and control mechanisms for acid gas, trace organic, and trace metal emissions. It also supports field tests, regulation development, and laboratory research for medical waste incinerators (MWI). Much of the MWC regulatory support effort has involved the development of good combustion practices and field evaluations of the performance of air pollution control systems. Additional research has focused on the collection of experimental data and a statistical approach to determine the effect of combustion- and sorbent-injection-related parameters on the mechanism of polychlorinated dibenzo-p-dioxin and polychlorinated dibenzofuran (PCDD and PCDF) formation and prevention in waste combustors. We have also conducted analyses of the products of incomplete combustion of agricultural plastic, as well as the open burning of household waste in barrels.

In a broader perspective, many P2 research opportunities are cross-cutting. Multimedia issues arise with common problems requiring a systems approach. This is why P2 research in the development of tools and technologies for Life Cycle Analysis (LCA), process simulation, P2 measurement, P2 technology, systems integration, cost effectiveness, environmental impact, cleaner production design, and generic decision-making tools for reducing risks fit within and cut across all categories.

Need 13: Identification of pollution prevention alternatives for HAP emissions from mobile sources

Description: Because P2 has been very broadly defined by the Federal Government, many environmental quality and related transportation system management options fit within its scope. Some areas may require an interdisciplinary approach, including emissions control

experts, transportation system experts, economists and behavioral science specialists. Some P2 strategies relate to the actual reduction of emissions, including HAP emissions, from motor vehicles, while others relate to changes in the transportation system infrastructure that will in turn, effect emissions reductions.

EPA Activities: We are involved in a number of activities addressing cleaner fuels and vehicles:

- Partnership for a New Generation of Vehicles (PNGV) -- a joint industry-government research and development agreement to develop a vehicle with three times the fuel efficiency of today's family sedan without sacrificing size, performance, cost, safety, or emissions. As an active partner in PNGV, EPA's interest in high-efficiency vehicles includes efforts to ensure low criteria emissions as well as reduced fuel use and low carbon dioxide..

- Development of technology for clean and efficient engines which operate on renewable alcohol fuels and promotion of the use of advanced technology and emission control equipment to improve air quality.

- Development and evaluation of after-treatment technology to reduce emissions from diesel engines (particularly to reduce PM [soot], NOx, and sulfur emissions). EPA also plans to test different diesel fuel formulations to reduce emissions.

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Appendix
HAP Profiles

OVERVIEW

This Appendix includes fact sheets (or profiles) for each of the 33 urban hazardous air pollutants (HAP). As discussed in Chapter 3 of this Report, these were identified in the Strategy as posing the greatest threat to public health in the largest number of urban areas. The fact sheets for these HAP are arranged in alphabetical order, and each one provides the following information:

- A brief hazard summary;
- Various physical properties (e.g., chemical formula, molecular weight, vapor pressure);
- Uses (e.g., in manufacturing processes, products, etc.);
- Sources and potential for exposure;
- How personal exposure can be assessed;
- Information on health hazards, including
  - acute effects,
  - chronic effects (noncancer),
  - reproductive/developmental effects,
  - cancer risks, and
  - a summary of human health reference values and regulatory and advisory numbers; and
- References.

The main sources of information for the fact sheets include EPA's Integrated Risk Information System (IRIS), Toxicological Profiles from the Agency for Toxic Substances and Disease Registry (ATSDR), EPA's Health Effects Assessment documents and International Agency for Research on Cancer (IARC) monographs, as available. The actual sources for each fact sheet are listed on the sheet. The summary of human health reference values and regulatory and advisory numbers includes values developed by EPA and by ATSDR, the California EPA (CalEPA), the American Conference of Governmental and Industrial Hygienists (ACGIH), the American Industrial Hygiene Association (AIHA), the National Institute of Occupational Safety and Health (NIOSH), and the Occupational Safety and Health Administration (OSHA).

Each fact sheet includes definitions of the acronyms used within the fact sheet, with the exception of the abbreviations for units of measurement (and Hg) listed below.

°C:	degrees Centigrade	m^3:	meters cubed
°F:	degrees Farenheit	mL:	milliliter
d:	day	mm:	millimeter
dL:	deciliter	mg:	milligram
g:	gram	ng:	nanogram
h:	hour	ppb:	parts per billion
Hg:	mercury	ppm:	parts per million
kg:	kilogram	μg:	microgram

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ACETALDEHYDE
75-07-0

Hazard Summary

Acetaldehyde is mainly used as an intermediate in the synthesis of other chemicals. It is ubiquitous in the environment and may be formed in the body from the breakdown of ethanol. Acute (short-term) exposure to acetaldehyde results in effects including irritation of the eyes, skin, and respiratory tract. Symptoms of chronic (long-term) intoxication of acetaldehyde resemble those of alcoholism. The U.S. Environmental Protection Agency (EPA) considers acetaldehyde a probable human carcinogen (Group B2) based on inadequate human cancer studies and animal studies that have shown nasal tumors in rats and laryngeal tumors in hamsters.

Please Note: The main sources of information for this fact sheet are EPA's *Health Assessment Document for Acetaldehyde* and the Integrated Risk Information System (IRIS), which contains information on inhalation chronic toxicity of acetaldehyde and the reference concentration (RfC). Other secondary sources include the International Agency for Research on Cancer (IARC) *Monographs on Chemicals Carcinogenic to Humans*.

Physical Properties

- The chemical formula for acetaldehyde is CH_3CHO, and it has a molecular weight of 44.06 g/mol. (1)
- Acetaldehyde is a colorless mobile liquid that is flammable and miscible with water. (1,6)
- Acetaldehyde has a pungent suffocating odor, but at dilute concentrations, it has a fruity and pleasant odor. The odor threshold of acetaldehyde is 0.05 ppm (0.09 mg/m^3). (1,7)
- The vapor pressure for acetaldehyde is 740 mm Hg at 20 °C, and it has a log octanol/water partition coefficient (log K_{ow}) of 0.43. (1)

Uses

- The predominant use of acetaldehyde is as an intermediate in the synthesis of other chemicals. (1)
- Acetaldehyde is used in the production of perfumes, polyester resins, and basic dyes. Acetaldehyde is also used as a fruit and fish preservative, as a flavoring agent, and as a denaturant for alcohol, in fuel compositions, for hardening gelatin, and as a solvent in the rubber, tanning, and paper industries. (1,2)

Sources and Potential Exposure

- Acetaldehyde is ubiquitous in the ambient environment. It is an intermediate product of higher plant respiration and is formed as a product of incomplete wood combustion in fireplaces and wood stoves, coffee roasting, burning of tobacco, vehicle exhaust fumes,

and coal refining and waste processing. Hence, many individuals are exposed to acetaldehyde by breathing ambient air. It should be noted that residential fireplaces and wood stoves are the two highest sources of emissions, followed by various industrial emissions. (1)

- In Los Angeles, California, levels of acetaldehyde up to 32 ppb have been measured in the ambient environment. (1)
- Exposure may also occur in individuals occupationally exposed to acetaldehyde during its manufacture and use. (1,2)
- In addition, acetaldehyde is formed in the body from the breakdown of ethanol; this would be a source of acetaldehyde among those who consume alcoholic beverages. (1)

Assessing Personal Exposure

- No information was located regarding the measurement of personal exposure to acetaldehyde.

Health Hazard Information

Acute Effects:

- The primary acute effect of inhalation exposure to acetaldehyde is irritation of the eyes, skin, and respiratory tract in humans. At higher exposure levels, erythema, coughing, pulmonary edema, and necrosis may also occur and, at extremely high concentrations, respiratory paralysis and death may occur. (1)
- Acute inhalation of acetaldehyde resulted in a depressed respiratory rate and elevated blood pressure in experimental animals. (1)
- Tests involving acute exposure of animals, such as the LC_{50} and LD_{50} tests in rats, rabbits, and hamsters, have demonstrated acetaldehyde to have low acute toxicity from inhalation and moderate acute toxicity from oral or dermal exposure. (3)

Chronic Effects (Noncancer):

- In hamsters, chronic inhalation exposure to acetaldehyde has produced changes in the nasal mucosa and trachea, growth retardation, slight anemia, and increased kidney weight. (1,4)
- Symptoms of chronic intoxication of acetaldehyde in humans resemble those of alcoholism. (5)
- The RfC for acetaldehyde is 0.009 mg/m^3 based on degeneration of olfactory epithelium in rats. The RfC is an estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure to the human population (including sensitive subgroups), that is likely to be without appreciable risk of deleterious noncancer effects during a lifetime. It is not a direct estimator of risk, but rather a reference point to gauge the potential effects. At exposures increasingly greater than the RfC, the potential for

adverse health effects increases. Lifetime exposure above the RfC does not imply that an adverse health effect would necessarily occur. (4)

- EPA has medium confidence in the principal studies because appropriate histopathology was performed on an adequate number of animals and a no-observed-adverse-effect level (NOAEL) and a lowest-observed-adverse-effect level (LOAEL) were identified, but the exposure duration was short and only one species was tested; low confidence in the database due to the lack of chronic data establishing NOAELs and due to the lack of reproductive and developmental toxicity data; and, consequently, low confidence in the RfC. (4)
- EPA has not established a reference dose (RfD) for acetaldehyde. (4)

Reproductive/Developmental Effects:

- No information is available on the reproductive or developmental effects of acetaldehyde in humans.
- Acetaldehyde has been shown, in animals, to cross the placenta to the fetus. (1,4)
- Data from animal studies suggest that acetaldehyde may be a potential developmental toxin. In one study, a high incidence of embryonic resorptions was observed in mice injected with acetaldehyde. In rats exposed to acetaldehyde by injection, skeletal malformations, reduced birth weight, and increased postnatal mortality have been reported. (1,6)

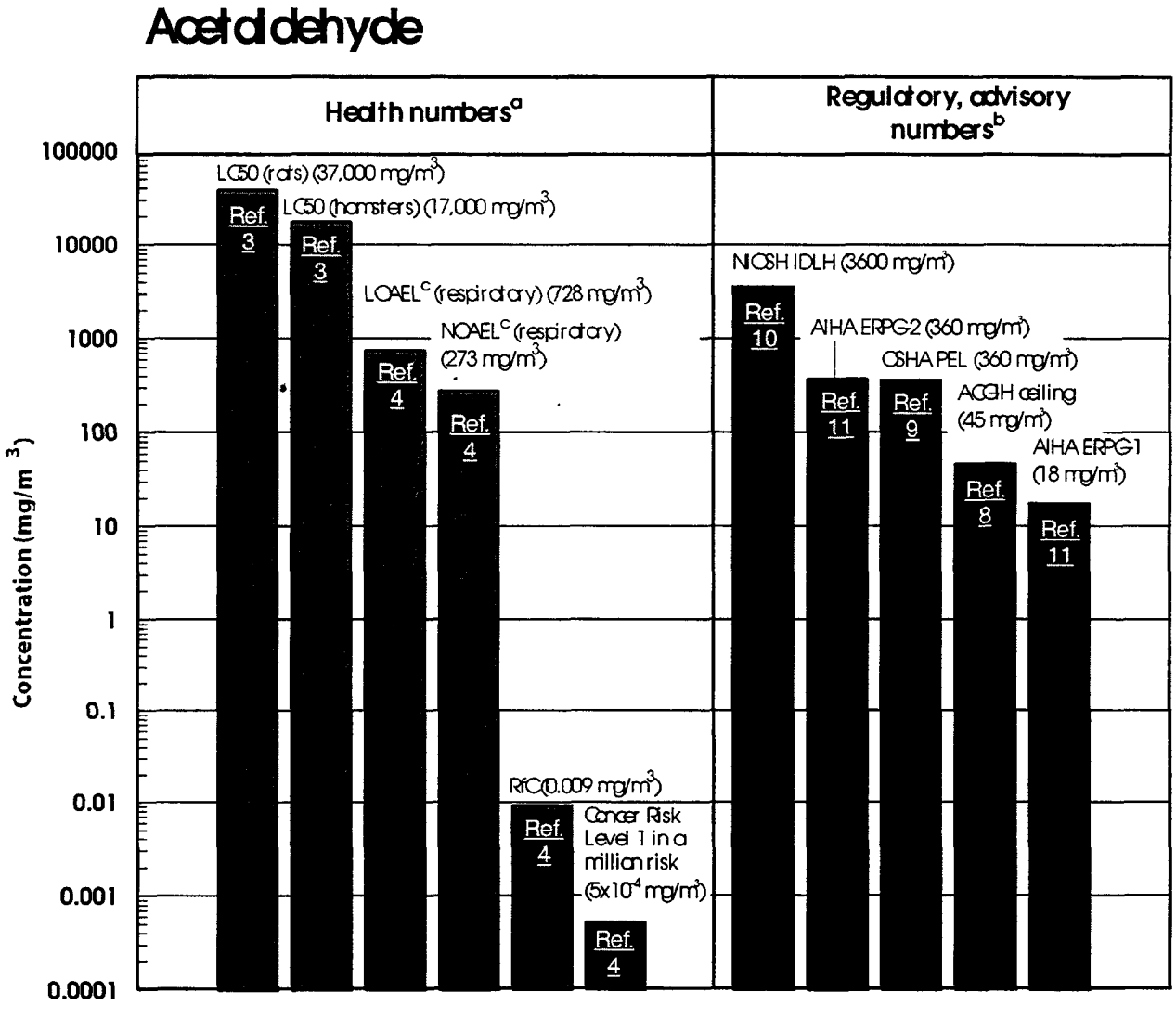
Cancer Risk:

- Human data regarding the carcinogenic effects of acetaldehyde are inadequate. Only one epidemiology study is available that has several limitations including short duration, small number of subjects, and concurrent exposure to other chemicals and cigarettes. (1,4,6)
- Increased incidences of nasal tumors in rats and laryngeal tumors in hamsters have been observed following inhalation exposure to acetaldehyde. (1,4,6)
- EPA has classified acetaldehyde as a Group B2, probable human carcinogen. (1,4)
- EPA uses mathematical models, based on human and animal studies, to estimate the probability of a person developing cancer from breathing air containing a specified concentration of a chemical. EPA calculated an inhalation unit risk of 2.2×10^{-6} $(\mu g/m^3)^{-1}$. EPA estimates that, if an individual were to continuously breathe air containing acetaldehyde at an average of 0.5 $\mu g/m^3$ (5×10^{-4} mg/m^3) over his or her entire lifetime, that person would theoretically have no more than a one-in-a-million increased chance of developing cancer as a direct result of breathing air containing this chemical. Similarly, EPA estimates that breathing air containing 5.0 $\mu g/m^3$ (5×10^{-3} mg/m^3) would result in not greater than a one-in-a-hundred thousand increased chance of developing cancer, and air containing 50.0 $\mu g/m^3$ (5×10^{-2} mg/m^3) would result in not greater than a one-in-ten thousand increased chance of developing cancer. For a detailed discussion of confidence in the potency estimates, please see IRIS. (4)

Conversion Factors:

To convert from ppm to mg/m³: mg/m³ = (ppm) x (molecular weight of the compound)/(24.45).
For acetaldehyde: 1 ppm = 1.8 mg/m³.
To convert from μg/m³ to mg/m³: mg/m³ = (μg/m³) x (1 mg/1,000 μg).

Health Data from Inhalation Exposure



AIHA ERPG –American Industrial Hygiene Association's emergency response planning guidelines. ERPG 1 is the maximum airborne concentration below which it is believed nearly all individuals could be exposed up to one hour without experiencing other than mild transient adverse health effects or perceiving a clearly defined objectionable odor; ERPG 2 is the maximum airborne concentration below which it is believed nearly all individuals could be

exposed up to one hour without experiencing or developing irreversible or other serious health effects that could impair their abilities to take protective action.
ACGIH TLV ceiling – American Conference of Governmental and Industrial Hygienists' threshold limit value ceiling; the concentration of a substance that should not be exceeded during any part of the working exposure.
LC_{50} (Lethal Concentration$_{50}$) – A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.
NIOSH IDLH – National Institute of Occupational Safety and Health's immediately dangerous to life or health limit; NIOSH recommended exposure limit to ensure that a worker can escape from an exposure condition that is likely to cause death or immediate or delayed permanent adverse health effects or prevent escape from the environment.
OSHA PEL – Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.

[a] Health Numbers are toxicological numbers from animal testing or risk assessment values developed by EPA.
[b] Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the Government or other groups as advice.
[c] The LOAEL and NOAEL are from the critical study used as the basis for the EPA RfC.

References

1. U.S. Environmental Protection Agency (EPA). *Health Assessment Document for Acetaldehyde*. EPA/600/8-86-015A. Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment, Office of Research and Development, Research Triangle Park, NC. 1987.

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7. J.E. Amoore and E. Hautala. Odor as an aid to chemical safety: Odor thresholds compared with threshold limit values and volatilities for 214 industrial chemicals in air and water dilution. *Journal of Applied Toxicology*, 3(6):272-290. 1983.

8. American Conference of Governmental Industrial Hygienists (ACGIH). *1999 TLVs and BEIs. Threshold Limit Values for Chemical Substances and Physical Agents, Biological Exposure Indices.* Cincinnati, OH. 1999.

9. Occupational Safety and Health Administration (OSHA). Occupational Safety and Health Standards, Toxic and Hazardous Substances. *Code of Federal Regulations.* 29 CFR 1910.1000. 1998.

10. National Institute for Occupational Safety and Health (NIOSH). *Pocket Guide to Chemical Hazards.* U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention. Cincinnati, OH. 1997.

11. American Industrial Hygiene Association (AIHA). *The AIHA 1998 Emergency Response Planning Guidelines and Workplace Environmental Exposure Level Guides Handbook.* 1998.

ACROLEIN

107-02-8

Hazard Summary

Acrolein is primarily used as an intermediate in the manufacture of acrylic acid. It can be formed from the breakdown of certain pollutants in outdoor air or from burning tobacco or gasoline. It is extremely toxic to humans from inhalation and dermal exposure. Acute (short-term) inhalation exposure may result in upper respiratory tract irritation and congestion. No information is available on its reproductive, developmental, or carcinogenic effects in humans. The animal cancer data are limited, with one study reporting an increased incidence of adrenocortical tumors in rats exposed to acrolein in the drinking water. The U.S. Environmental Protection Agency (EPA) considers acrolein a possible human carcinogen (Group C).

Please Note: The main sources of information for this fact sheet are EPA's Integrated Risk Information System (IRIS), which contains information on inhalation chronic toxicity of acrolein and the reference concentration (RfC), and the Agency for Toxic Substances and Disease Registry's (ATSDR's) *Toxicological Profile for Acrolein.*

Physical Properties

- Acrolein is a water-white or yellow liquid that burns easily and is easily volatilized. (1)
- Acrolein has a disagreeable odor and an odor threshold of 0.2 ppm. (1,8)
- The chemical formula for acrolein is C_3H_4O and the molecular weight is 56.06 g/mol. (1)
- The vapor pressure for acrolein is 220 mm Hg at 20 °C, and its log octanol/water partition coefficient (log K_{ow}) is -0.01. (1)

Uses

- The largest use for acrolein is as an intermediate in the manufacture of acrylic acid. (1)

Sources and Potential Exposure

- Acrolein can be formed from the breakdown of certain pollutants found in outdoor air, from burning tobacco, or from burning gasoline. (1)
- Airborne exposure to acrolein may occur from breathing contaminated air, from smoking tobacco or proximity to someone who is smoking, or from being near automobiles or oil or coal power plants. In several large cities, acrolein has been measured at 9 ppb. (1)
- Occupational exposure to acrolein could occur in industries that use acrolein to make other chemicals. (1)
- Small amounts of acrolein may be found in some foods, such as fried foods, cooking oils, and roasted coffee. (1)

- Acrolein has not been detected in drinking water and is not commonly found in surface water. (1)

Assessing Personal Exposure

- There are currently no tests available to determine personal exposure to acrolein. (1)

Health Hazard Information

Acute Effects:

- Acute inhalation exposure to high levels (10 ppm) of acrolein in humans may result in death. Effects on the lung, such as upper respiratory tract irritation and congestion, have been noted at acrolein levels ranging from 0.17 ppm to 0.43 ppm. (1-3)
- Acrolein is considered to have high acute toxicity, based on short-term animal tests such as the LC_{50} test in rats. (1,4)

Chronic Effects (Noncancer):

- The major effects from chronic (long-term) inhalation exposure to acrolein in humans consist of general respiratory congestion and eye, nose, and throat irritation. (1,2,5)
- Acrolein is a strong dermal irritant, causing skin burns in humans. (1,2,5)
- Animal studies have reported that the respiratory system is the major target organ for acrolein toxicity. (1,2,5)
- The RfC for acrolein is 0.00002 mg/m^3 based on squamous metaplasia and neutrophilic infiltration of nasal epithelium in rats. The RfC is an estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious noncancer effects during a lifetime. It is not a direct estimator of risk but rather a reference point to gauge the potential effects. At exposures increasingly greater than the RfC, the potential for adverse health effects increases. Lifetime exposure above the RfC does not imply that an adverse health effect would necessarily occur. (3)
- EPA has high confidence in the studies on which the RfC was based because adequate numbers of animals were used, careful attention was paid to experimental protocol, and together they demonstrated a consistent profile of histopathological changes in the respiratory system; low to medium confidence in the database due to the lack of chronic data and adequately conducted reproductive or developmental studies; and, consequently, medium confidence in the RfC.
- EPA has not established a reference dose (RfD) for acrolein. (3)
- EPA has calculated a provisional RfD of 0.02 mg/kg/d for acrolein. The provisional RfD is a value that has had some form of Agency review, but it does not appear on IRIS. The EPA announced recently (January 12, 2000, 65 FR 1863) its plan to conduct an IRIS health assessment for acrolein to be completed by FY 2002. (6)

Reproductive/Developmental Effects:

- No information is available on the reproductive or developmental effects of acrolein in humans. (1)
- In the one available reproductive animal study, rats were exposed to acrolein by inhalation, with no effects observed on the number of pregnancies or the number and weights of the fetuses. (1)
- Acrolein has been reported to cause birth defects in rats when injected directly into the embryonic tissue. (1)

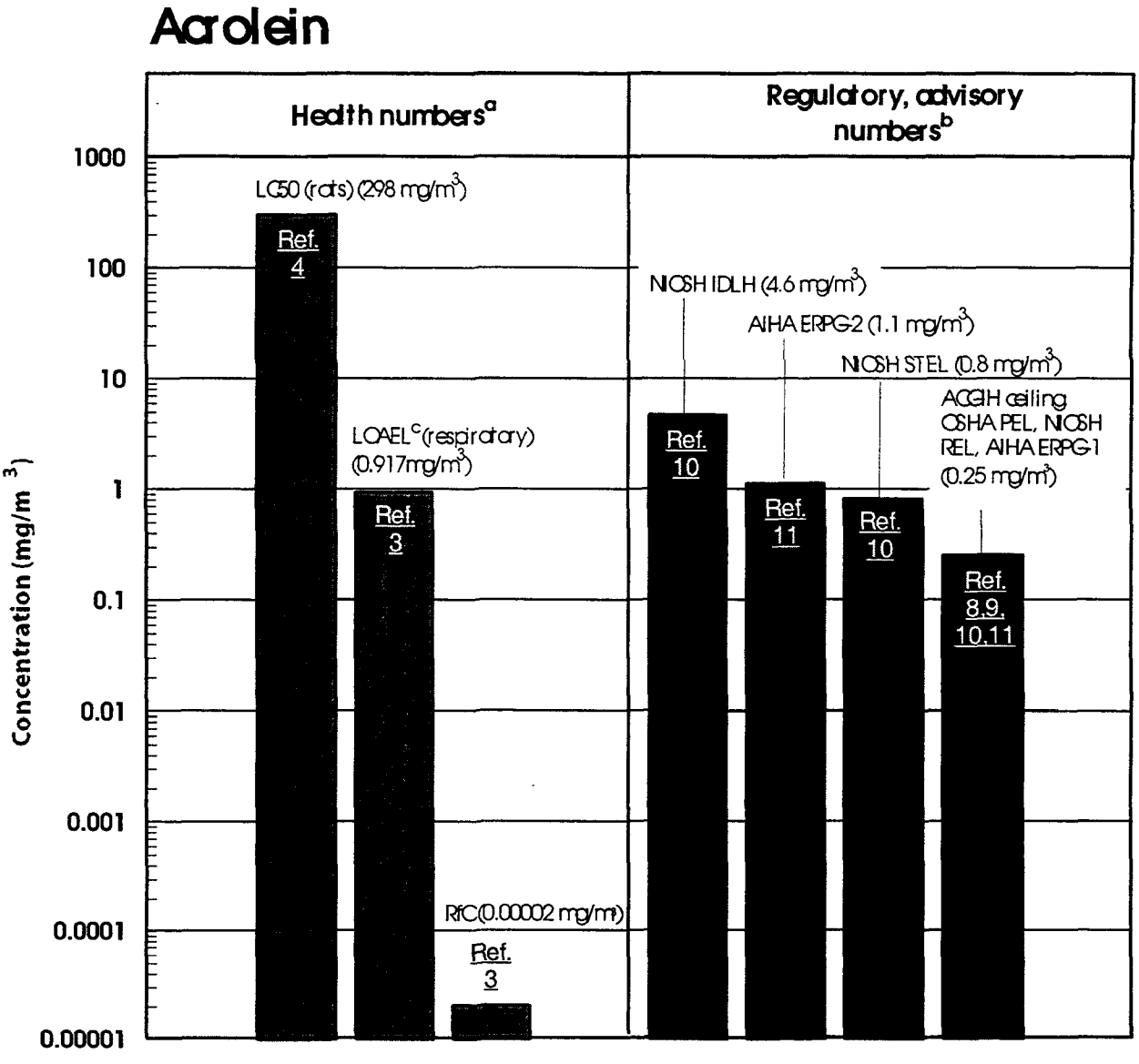
Cancer Risk:

- No information is available on the carcinogenic effects of acrolein in humans. (1,3)
- Limited animal cancer data are available; one inhalation study in rats reported no evidence of tumors in the respiratory tract or in other tissues and organs, while another study reported an increased incidence of adrenocortical tumors in female rats exposed to acrolein in drinking water. (1,3)
- EPA has classified acrolein as a Group C, possible human carcinogen, based on limited evidence of carcinogenicity in animals, the structural similarity of acrolein to substances possibly carcinogenic to humans, the carcinogenic potential of one of its metabolites, and the lack of human data. (3)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45).
For acrolein: 1 ppm = 2.29 mg/m^3.
To convert from $\mu g/m^3$ to mg/m^3: $mg/m^3 = (\mu g/m^3)$ x (1 mg/1,000 μg).

Health Data from Inhalation Exposure



AIHA ERPG –American Industrial Hygiene Association's emergency response planning guidelines. ERPG 1 is the maximum airborne concentration below which it is believed nearly all individuals could be exposed up to one hour without experiencing other than mild transient adverse health effects or perceiving a clearly defined objectionable odor; ERPG 2 is the maximum airborne concentration below which it is believed nearly all individuals could be exposed up to one hour without experiencing or developing irreversible or other serious health effects that could impair their abilities to take protective action

ACGIH ceiling – American Conference of Governmental and Industrial Hygienists' threshold limit value ceiling; the concentration of a substance that should not be exceeded during any part of the working exposure.

LC_{50} (Lethal Concentration$_{50}$) – A calculated concentration of a chemical in air to which

exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.
LOAEL – Lowest-observed-adverse-effect level.
NIOSH IDLH – National Institute of Occupational Safety and Health's immediately dangerous to life or health limit; NIOSH recommended exposure limit to ensure that a worker can escape from an exposure condition that is likely to cause death or immediate or delayed permanent adverse health effects or prevent escape from the environment.
NIOSH REL – NIOSH's recommended exposure limit; NIOSH recommended exposure limit for an 8- or 10-h time-weighted average exposure and/or ceiling.
NIOSH STEL – NIOSH's short term exposure limit; NIOSH recommended exposure limit for a 15-minute period.
OSHA PEL – Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h work week.

[a] Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA.
[b] Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the Government or other groups as advice.
[c] This LOAEL is from the critical study used as the basis for the EPA RfC.

References

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9. Occupational Safety and Health Administration (OSHA). Occupational Safety and Health Standards, Toxic and Hazardous Substances. *Code of Federal Regulations.* 29 CFR 1910.1000. 1998.

10. National Institute for Occupational Safety and Health (NIOSH). *Pocket Guide to Chemical Hazards.* U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention. Cincinnati, OH. 1997.

11. American Industrial Hygiene Association (AIHA). *The AIHA 1998 Emergency Response Planning Guidelines and Workplace Environmental Exposure Level Guides Handbook* 1998.

ACRYLONITRILE
107-13-1

Hazard Summary

Exposure to acrylonitrile is primarily occupational: it is used in the manufacture of acrylic acid and modacrylic fibers. Acute (short-term) exposure of workers to acrylonitrile has been observed to cause mucous membrane irritation, headaches, dizziness, and nausea. No information is available on the reproductive or developmental effects of acrylonitrile in humans. Based on limited evidence in humans and evidence in rats, the U.S. Environmental Protection Agency (EPA) has classified acrylonitrile as a probable human carcinogen (Group B1).

Please Note: The main sources of information for this fact sheet are EPA's Integrated Risk Information System (IRIS), which contains information on inhalation chronic toxicity of acrylonitrile and the reference concentration (RfC) and the carcinogenic effects of acrylonitrile including the unit cancer risk for inhalation exposure, EPA's *Health Effects Assessment for Acrylonitrile*, and the Agency for Toxic Substances and Disease Registry's (ATSDR's) *Toxicological Profile for Acrylonitrile.*

Physical Properties

- The chemical formula for acrylonitrile is C_3H_3N, and its molecular weight is 53.06 g/mol. (1,8)
- Acrylonitrile occurs as a colorless liquid that is soluble in water. (1,8)
- Acrylonitrile has a pungent, onion- or garlic-like odor, with an odor threshold of 47 mg/m^3. (1)
- The vapor pressure for acrylonitrile is 100 mm Hg at 22.8 °C, and its log octanol/water partition coefficient (log K_{ow}) is -0.92. (1)

Uses

- Acrylonitrile is primarily used in the manufacture of acrylic and modacrylic fibers. It is also used as a raw material in the manufacture of plastics (acrylonitrile-butadiene-styrene and styrene-acrylonitrile resins), adiponitrile, acrylamide, and nitrile rubbers and barrier resins. (1,6)

Sources and Potential Exposure

- Human exposure to acrylonitrile appears to be primarily occupational via inhalation. (1)
- Acrylonitrile may be released to the ambient air during its manufacture and use. (1)

Assessing Personal Exposure

- Acrylonitrile can be detected in the blood to determine whether or not exposure has occurred. Metabolites may be detected in the urine, but some breakdown products are not specific to acrylonitrile. (1)

Health Hazard Information

Acute Effects:

- Workers exposed via inhalation to high levels of acrylonitrile for less than an hour experienced mucous membrane irritation, headaches, nausea, feelings of apprehension and nervous irritability; low grade anemia, leukocytosis, kidney irritation, and mild jaundice were also observed in the workers, with these effects subsiding with the ending of exposure. Symptoms associated with acrylonitrile poisoning include limb weakness, labored and irregular breathing, dizziness and impaired judgment, cyanosis, nausea, collapse, and convulsions. (1-4)
- A child died after being exposed to acrylonitrile by inhalation, suffering from respiratory malfunction, lip cyanosis, and tachycardia before death. Several adults exposed to the same concentration of acrylonitrile exhibited eye irritation, but no toxic effects. (1,4)
- Acute dermal exposure may cause severe burns to the skin. (3)
- Acute animal tests, such as the LC_{50} and LD_{50} tests in rats, mice, rabbits, and guinea pigs, have demonstrated acrylonitrile to have high acute toxicity from inhalation and high to extreme acute toxicity from oral or dermal exposure. (5)

Chronic Effects (Noncancer):

- In one study, headaches, fatigue, nausea, and weakness were frequently reported in chronically (long-term) exposed workers. (6)
- In rats chronically exposed by inhalation, degenerative and inflammatory changes in the respiratory epithelium of the nasal turbinates and effects on brain cells have been observed. (1,4,6)
- The RfC for acrylonitrile is 0.002 mg/m^3 based on degeneration and inflammation of nasal respiratory epithelium in rats. The RfC is an estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious noncancer effects during a lifetime. It is not a direct estimator of risk but rather a reference point to gauge the potential effects. At exposures increasingly greater than the RfC, the potential for adverse health effects increases. Lifetime exposure above the RfC does not imply that an adverse health effect would necessarily occur. (4)
- EPA has medium confidence in the study on which the RfC was based because, although it was a well-conducted chronic study in an appropriate number of animals, it was performed on only one species, did not identify a no-observed-adverse-effect level (NOAEL), was confounded by the early sacrifice of rats with large mammary gland

tumors and the target organ (nasal turbinates) was examined only at the end of the study in relatively few animals; medium to low confidence in the database because of the lack of chronic or subchronic inhalation data in a second species, the lack of reproductive data by the inhalation route and the existence of an oral study showing reproductive effects; and, consequently, medium to low confidence in the RfC. (4)

- EPA has calculated a provisional reference dose (RfD) of 0.001 mg/kg/d for acrylonitrile based on decreased sperm counts in mice. The provisional RfD is a value that has had some form of Agency review, but it does not appear on IRIS. (7)

Reproductive/Developmental Effects:

- No information is available on the reproductive or developmental effects of acrylonitrile in humans.
- Fetal malformations (including short tail, missing vertebrae, short trunk, omphalocele, and hemivertebra) have been reported in rats exposed to acrylonitrile by inhalation. (1,4)
- In mice orally exposed to acrylonitrile, degenerative changes in testicular tubules and decreased sperm count were observed. (1)

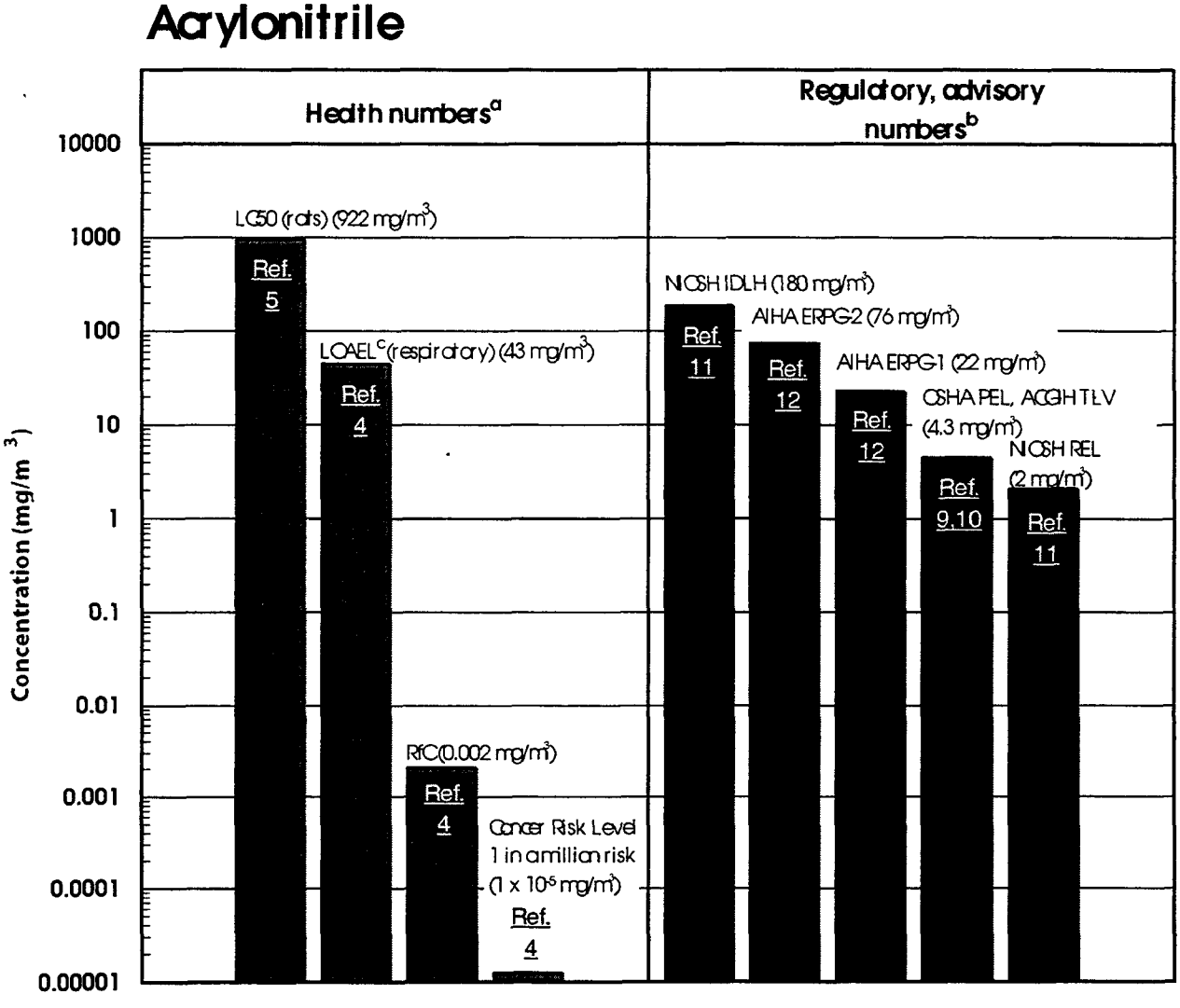
Cancer Risk:

- A statistically significant increase in the incidence of lung cancer has been reported in several studies of chronically exposed workers. However, some of these studies contain deficiencies such as lack of exposure information, short follow-up, and confounding factors. (1,4,6,8)
- In several studies, an increased incidence of tumors has been observed in rats exposed by inhalation, drinking water, and gavage. Astrocytomas in the brain and spinal cord and tumors of the Zymbal gland (in the ear canal) have been most frequently reported, as well as tumors of the stomach, tongue, small intestine, and mammary gland (in females). (1-4,6,8)
- EPA has classified acrylonitrile as a Group B1, probable human carcinogen. (4)
- EPA uses mathematical models, based on human and animal studies, to estimate the probability of a person developing cancer from breathing air containing a specified concentration of a chemical. EPA calculated an inhalation unit risk estimate of 6.8×10^{-5} $(\mu g/m^3)^{-1}$. EPA estimates that, if an individual were to continuously breathe air containing acrylonitrile at an average of 0.01 $\mu g/m^3$ (1×10^{-5} mg/m^3), over his or her entire lifetime, that person would theoretically have no more than a one-in-a-million increased chance of developing cancer as a direct result of breathing air containing this chemical. Similarly, EPA estimates that breathing air containing 0.1 $\mu g/m^3$ (1×10^{-4} mg/m^3) would result in not greater than a one-in-a-hundred thousand increased chance of developing cancer, and air containing 1.0 $\mu g/m^3$ (1×10^{-3} mg/m^3) would result in not greater than a one-in-ten thousand increased chance of developing cancer. For a detailed discussion of confidence in the potency estimates, please see IRIS. (4)
- EPA has calculated an oral cancer slope factor of 0.54 $(mg/kg/d)^{-1}$. (4)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45).
For acrylonitrile: 1 ppm = 2.17 mg/m^3.

Health Data from Inhalation Exposure



ACGIH TLV – American Conference of Governmental and Industrial Hygienists' threshold limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect.

AIHA ERPG – American Industrial Hygiene Association's emergency response planning guidelines. ERPG 1 is the maximum airborne concentration below which it is believed nearly all individuals could be exposed up to one hour without experiencing other than mild transient adverse health effects or perceiving a clearly defined objectionable odor; ERPG 2 is the maximum airborne concentration below which it is believed nearly all individuals could be

exposed up to one hour without experiencing or developing irreversible or other serious health effects that could impair their abilities to take protective action.
LC_{50} (Lethal Concentration$_{50}$) – A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.
LOAEL – Lowest-observed-adverse-effect level.
NIOSH IDLH – National Institute of Occupational Safety and Health's immediately dangerous to life or health limit; NIOSH recommended exposure limit to ensure that a worker can escape from an exposure condition that is likely to cause death or immediate or delayed permanent adverse health effects or prevent escape from the environment.
NIOSH REL – NIOSH's recommended exposure limit; NIOSH-recommended exposure limit for an 8- or 10-h time-weighted-average exposure and/or ceiling.
OSHA PEL – Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.

[a] Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA.
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[c] The LOAEL is from the critical study used as the basis for the EPA RfC.

References

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ARSENIC COMPOUNDS[1]

107-02-8

Hazard Summary

Arsenic, a naturally occurring element, is found throughout the environment; for most people, food is the major source of exposure. Acute (short-term) high-level inhalation exposure to arsenic dust or fumes has resulted in gastrointestinal effects (nausea, diarrhea, abdominal pain); central and peripheral nervous system disorders have occurred in workers acutely exposed to inorganic arsenic. Chronic (long-term) inhalation exposure to inorganic arsenic in humans is associated with irritation of the skin and mucous membranes. Human data suggest a relationship between inhalation exposure of women working at or living near metal smelters and an increased risk of reproductive effects, such as spontaneous abortions. However, as these studies evaluated smelter pollutants in general, arsenic's role is not clear. Chronic oral exposure has resulted in gastrointestinal effects, anemia, peripheral neuropathy, skin lesions, hyperpigmentation, and liver or kidney damage. Inorganic arsenic exposure in humans, by the inhalation route, has been shown to be strongly associated with lung cancer, while ingestion of inorganic arsenic in humans has been linked to a form of skin cancer and also to bladder, liver, and lung cancer. The U.S. Environmental Protection Agency (EPA) has classified inorganic arsenic as a Group A, human carcinogen.

Arsine is a gas consisting of arsenic and hydrogen. It is extremely toxic to humans, with headaches, vomiting, and abdominal pains occurring within a few hours of exposure. Death may occur from kidney failure and pulmonary edema. EPA has not classified arsine for carcinogenicity.

Please Note: The main sources of information for this fact sheet are EPA's Integrated Risk Information System (IRIS), which contains information on inhalation chronic toxicity and the reference concentration (RfC) for arsine, oral chronic toxicity and the reference dose (RfD) for inorganic arsenic, and the carcinogenic effects of inorganic arsenic including the unit cancer risk for inhalation exposure, and the Agency for Toxic Substances and Disease Registry's (ATSDR's) *Toxicological Profile for Arsenic.*

Physical Properties

- Inorganic arsenic is a naturally occurring element in the earth's crust. (1)
- Pure inorganic arsenic is a gray-colored metal, but inorganic arsenic is usually found combined with other elements such as oxygen, chlorine, and sulfur. (1)
- The chemical symbol for inorganic arsenic is As, and it has an atomic weight of 74.92 g/mol. (3)

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[1] This fact sheet addresses the toxicity of the inorganic arsenic compounds as well as the toxicity of the gaseous arsenic trihydride: arsine.

- The chemical formula for arsine is AsH_3, and it has a molecular weight of 77.95 g/mol. (8)
- Arsine is a colorless gas with a disagreeable garlic odor. (8)
- Arsenic combined with elements such as oxygen, chlorine, and sulfur forms inorganic arsenic; inorganic arsenic compounds include arsenic pentoxide, arsenic trioxide, and arsenic acid. Arsenic combined with carbon and hydrogen forms organic arsenic; organic arsenic compounds include arsanilic acid, arsenobetaine, and dimethylarsinic acid. (1)

Uses

- The major use for inorganic arsenic is in wood preservation; arsine is used in the microelectronics industry and in semiconductor manufacture. (2)
- Until the 1940s, inorganic arsenic solutions were widely used in the treatment of various diseases, such as syphillis and psoriasis. Inorganic arsenic is still used as an antiparasitic agent in veterinary medicine and in homeopathic and folk remedies in the U.S. and other countries. (2)

Sources and Potential Exposure

- Inorganic arsenic is found throughout the environment; it is released into the air by volcanoes, the weathering of arsenic-containing minerals and ores, and by commercial or industrial processes. (1,2)
- For most people, food is the largest source of arsenic exposure (about 25 to 50 μg/d), with lower amounts coming from drinking water and air. Among foods, some of the highest levels are in fish and shellfish; however, this arsenic exists primarily as organic compounds, which are essentially nontoxic. (1)
- Elevated levels of inorganic arsenic may be present in soil, either from natural mineral deposits or contamination from human activities, which may lead to dermal or ingestion exposure. (1)
- Workers in metal smelters and nearby residents may be exposed to above-average inorganic arsenic levels from arsenic released into the air. (1)
- Other sources of inorganic arsenic exposure include burning plywood treated with an arsenic wood preservative or dermal contact with wood treated with arsenic. (2)
- Most arsenic poisoning incidents in industry have involved the production of arsine, a short-lived, extremely toxic gas. (3)

Assessing Personal Exposure

- Measurement of inorganic arsenic in the urine is the best way to determine recent exposure (within the last 1 to 2 days), while measuring inorganic arsenic in hair or fingernails may be used to detect high-level exposures that occurred over the past 6-12 months. (1)

Health Hazard Information

Acute Effects:

Inorganic Arsenic

- Acute inhalation exposure of workers to high levels of arsenic dusts or fumes has resulted in gastrointestinal effects (nausea, diarrhea, abdominal pain), while acute exposure of workers to inorganic arsenic has also resulted in central and peripheral nervous system disorders. (1)
- Acute oral exposure to inorganic arsenic, at doses of approximately 600 μg/kg/d or higher in humans, has resulted in death. Oral exposure to lower levels of inorganic arsenic has resulted in effects on the gastrointestinal tract (nausea, vomiting), central nervous system (CNS) (headaches, weakness, delirium), cardiovascular system (hypotension, shock), liver, kidney, and blood (anemia, leukopenia). (1,2)
- Acute animal tests, such as the LD_{50} test in rats and mice, have shown inorganic arsenic to have moderate to high acute toxicity. (5)

Arsine

- Acute inhalation exposure to arsine by humans has resulted in death; it has been reported that a half-hour exposure to 25 to 50 ppm can be lethal. (4)
- The major effects from acute arsine exposure in humans include headaches, vomiting, abdominal pains, hemolytic anemia, hemoglobinuria, and jaundice; these effects can lead to kidney failure. (4,8)
- Arsine has been shown to have extreme acute toxicity from acute animal tests. (5)

Chronic Effects (Noncancer):

Inorganic arsenic

- Chronic inhalation exposure to inorganic arsenic in humans is associated with irritation of the skin and mucous membranes (dermatitis, conjunctivitis, pharyngitis, and rhinitis). (1,2)
- Chronic oral exposure to inorganic arsenic in humans has resulted in gastrointestinal effects, anemia, peripheral neuropathy, skin lesions, hyperpigmentation, gangrene of the extremities, vascular lesions, and liver or kidney damage. (1,2)
- No chronic inhalation exposure studies have been performed in animals for any inorganic arsenic compound. (1)
- Some studies have suggested that inorganic arsenic is an essential dietary nutrient in goats, chicks, and rats. However, no comparable data are available for humans. EPA has concluded that essentiality, although not rigorously established, is plausible. (1,6)
- EPA has not established an RfC for inorganic arsenic. (6)

- The California Environmental Protection Agency (CalEPA) has established a chronic inhalation reference level of 0.00003 mg/m^3 based on developmental effects in mice. The CalEPA reference exposure level is a concentration at or below which adverse health effects are not likely to occur. It is not a direct estimator of risk, but rather a reference point to gauge the potential effects. At lifetime exposures increasingly greater than the reference exposure level, the potential for adverse health effects increases. (7)
- The RfD for inorganic arsenic is 0.0003 mg/kg/d based on hyperpigmentation, keratosis, and possible vascular complications in humans. The RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious noncancer effects during a lifetime. (6)
- EPA has medium confidence in the study on which the RfD for inorganic arsenic was based because, although an extremely large number of people were included in the assessment (>40,000), the doses were not well characterized and other contaminants were present. The supporting human toxicity database, while extensive, is somewhat flawed and, consequently, EPA has assigned medium confidence to the RfD. (6)

Arsine

- The RfC for arsine is 0.00005 mg/m^3 based on increased hemolysis, abnormal red blood cell morphology, and increased spleen weight in rats, mice, and hamsters. (4)
- EPA has medium confidence in the RfC based on: high confidence in the studies on which the RfC for arsine was based because the sample sizes were adequate, statistical significance was reported, concentration dose-response relationships were documented, three species were investigated, and both a no-observed-adverse-effect level (NOAEL) and a lowest-observed-adverse-effect level (LOAEL) were identified; and medium confidence in the database because there were three inhalation animal studies and a developmental/reproductive study, but no data on human exposure. (4)

Reproductive/Developmental Effects:

Inorganic arsenic

- Several studies have suggested that women who work in, or live near, metal smelters may have higher than normal spontaneous abortion rates, and their children may exhibit lower than normal birth weights. However, these studies are limited because they were designed to evaluate the effects of smelter pollutants in general and are not specific for inorganic arsenic. (1)
- Ingested inorganic arsenic can cross the placenta in humans, exposing the fetus to the chemical. (2)
- Oral animal studies have reported inorganic arsenic at very high doses to be fetotoxic and to cause birth defects. (1)

Arsine

- Human studies have indicated higher than expected spontaneous abortion rates in women in the microelectronics industry who were exposed to arsine. However, these studies have several limitations, including small sample size and exposure to other chemicals in addition to arsine. (4)

Cancer Risk:

Inorganic arsenic

- Human inhalation studies have reported inorganic arsenic exposure to be strongly associated with lung cancer. (1,2,6)
- Ingestion of inorganic arsenic in humans has been associated with an increased risk of nonmelanoma skin cancer and also to an increased risk of bladder, liver, and lung cancer. (1,6)
- Animal studies have not associated inorganic arsenic exposure via the oral route with cancer, and no cancer inhalation studies have been performed in animals for inorganic arsenic. (1)
- EPA has classified inorganic arsenic as a Group A, human carcinogen. (6)
- EPA uses mathematical models, based on human and animal studies, to estimate the probability of a person developing cancer from breathing air containing a specified concentration of a chemical. EPA calculated an inhalation unit risk estimate of 4.3×10^{-3} $(\mu g/m^3)^{-1}$. EPA estimates that, if an individual were to continuously breathe air containing inorganic arsenic at an average of 0.0002 $\mu g/m^3$ (2×10^{-7} mg/m^3) over his or her entire lifetime, that person would theoretically have no more than a one-in-a-million increased chance of developing cancer as a direct result of breathing air containing this chemical. Similarly, EPA estimates that continuously breathing air containing 0.002 $\mu g/m^3$ (2×10^{-6} mg/m^3) would result in not greater than a one-in-a-hundred thousand increased chance of developing cancer, and air containing 0.02 $\mu g/m^3$ (2×10^{-5} mg/m^3) would result in not greater than a one-in-ten thousand increased chance of developing cancer. For a detailed discussion of confidence in the potency estimates, please see IRIS. (6)
- EPA has calculated an oral cancer slope factor of 1.5 $(mg/kg/d)^{-1}$ for inorganic arsenic. (6).

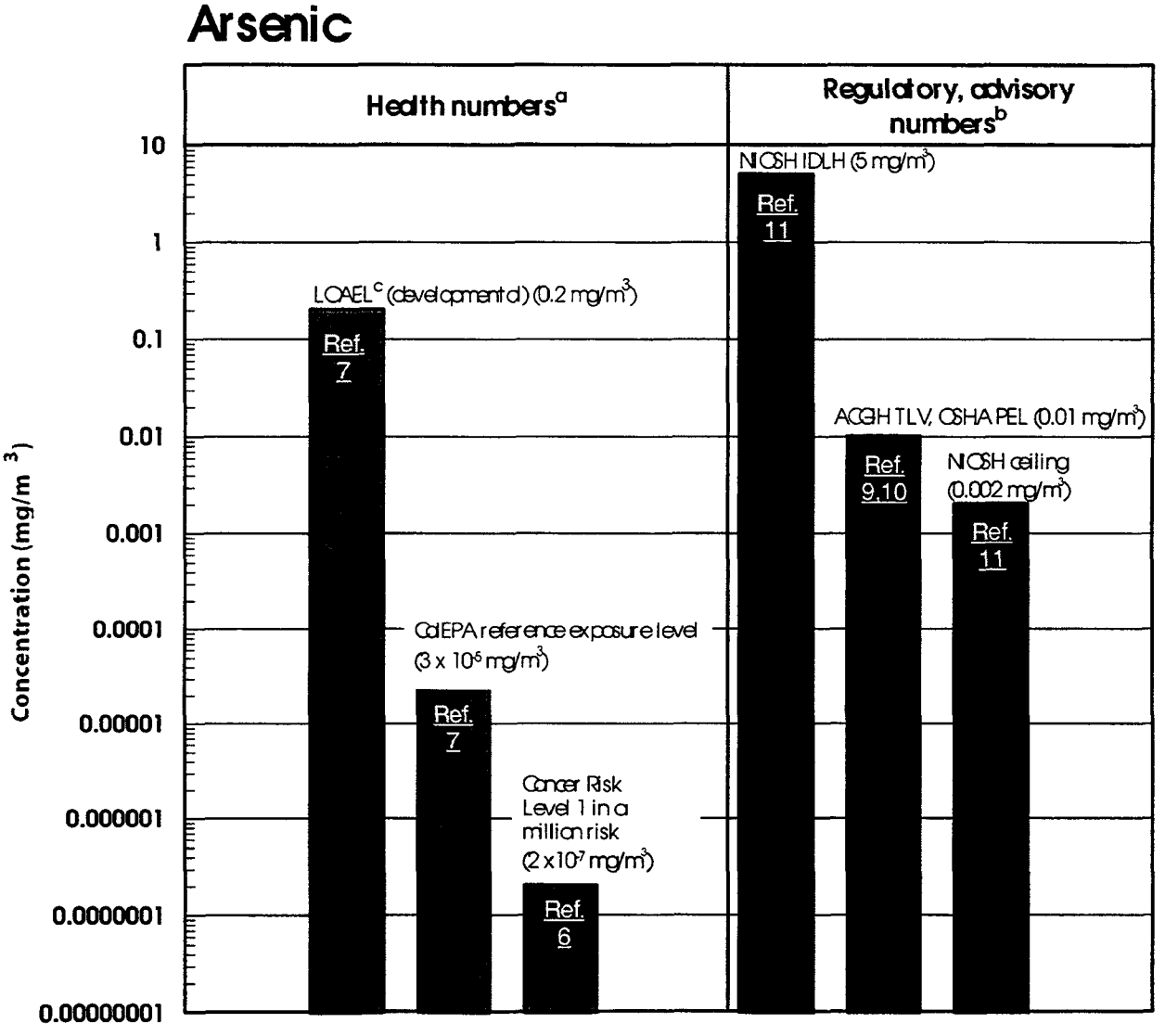
Arsine

- No cancer inhalation studies are available for arsine. (1)
- EPA has not classified arsine for carcinogenicity. (4)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45).
For inorganic arsenic: 1 ppm = 3.06 mg/m^3. For arsine: 1 ppm = 3.19 mg/m^3.
To convert from µg/m^3 to mg/m^3: mg/m^3 = (µg/m^3) x (1 mg/1,000 µg).

Health Data from Inhalation Exposure (Inorganic Arsenic)



ACGIH TLV – American Conference of Governmental and Industrial Hygienists' threshold limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effects.
LOAEL – Lowest-observed-adverse-effect level.
NIOSH IDLH – National Institute of Occupational Safety and Health's immediately dangerous

to life or health concentration; NIOSH recommended exposure limit to ensure that a worker can escape from an exposure condition that is likely to cause death or immediate or delayed permanent adverse health effects or prevent escape from the environment.
NIOSH REL ceiling – NIOSH's recommended exposure limit ceiling; the concentration that should not be exceeded at any time.
OSHA PEL – Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.

[a] Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA.
[b] Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the Government or other groups as advice.
[c] The LOAEL is from the critical study used as the basis for the CalEPA chronic reference exposure level.

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BENZENE
71-43-2

Hazard Summary

Benzene is found in the air from emissions from burning coal and oil, gasoline service stations, and motor vehicle exhaust. Acute (short-term) inhalation exposure of humans to benzene may cause drowsiness, dizziness, headaches, as well as eye, skin, and respiratory tract irritation, and, at high levels, unconsciousness. Chronic (long-term) inhalation exposure has caused various disorders in the blood, including reduced numbers of red blood cells and aplastic anemia, in occupational settings. Reproductive effects have been reported for women exposed by inhalation to high levels, and adverse effects on the developing fetus have been observed in animal tests. Increased incidence of leukemia have been observed in humans occupationally exposed to benzene. The U.S. Environmental Protection Agency (EPA) has classified benzene as a Group A, human carcinogen.

Please Note: The main sources of information for this fact sheet are the Agency for Toxic Substances and Disease Registry's (ATSDR's) *Toxicological Profile for Benzene* and EPA's Integrated Risk Information System (IRIS), which contains information on the carcinogenic effects of benzene including the unit cancer risk for inhalation exposure.

Physical Properties

- The chemical formula for benzene is C_6H_6, and it has a molecular weight of 78.11 g/mol. (4)
- Benzene occurs as a volatile, colorless, highly flammable liquid that dissolves easily in water. (1,7)
- Benzene has a sweet odor with an odor threshold of 1.5 ppm (5 mg/m^3). (1)
- The vapor pressure for benzene is 95.2 mm Hg at 25 °C, and it has a log octanol/water partition coefficient (log K_{ow}) of 2.13. (1)

Uses

- Benzene is used as a constituent in motor fuels; as a solvent for fats, waxes, resins, oils, inks, paints, plastics, and rubber; in the extraction of oils from seeds and nuts; and in photogravure printing. It is also used as a chemical intermediate. Benzene is also used in the manufacture of detergents, explosives, pharmaceuticals, and dyestuffs. (2,6)

Sources and Potential Exposure

- Individuals employed in industries that manufacture or use benzene may be exposed to the highest levels of benzene. (1)

- Benzene is found in emissions from burning coal and oil, motor vehicle exhaust, and evaporation from gasoline service stations and in industrial solvents. These sources contribute to elevated levels of benzene in the ambient air, which may subsequently be breathed by the public. (1)
- Tobacco smoke contains benzene and accounts for nearly half the national exposure to benzene. (1)
- Individuals may also be exposed to benzene by consuming contaminated water. (1)

Assessing Personal Exposure

- Measurement of benzene in an individual's breath or blood or the measurement of breakdown products in the urine (phenol) can provide information on recent personal exposure. (1)

Health Hazard Information

Acute Effects:

- Coexposure to benzene with ethanol (e.g., alcoholic beverages) can increase benzene toxicity. (1)
- Neurological symptoms of inhalation exposure to benzene include drowsiness, dizziness, headaches, and unconsciousness in humans. Death may result from exposure to very high levels of benzene. Ingestion of large amounts of benzene may result in vomiting, dizziness, convulsions, and death in humans. (1)
- Exposure to liquid and vapor may irritate the skin, eyes, and upper respiratory tract. Redness and blisters may result from dermal exposure to benzene. (1,2)
- Animal studies show neurologic, immunologic, and hematologic effects from inhalation and oral exposure to benzene. (1)
- Tests involving acute exposure of animals, such as the LC_{50} and LD_{50} tests in rats, mice, rabbits, and guinea pigs, have demonstrated benzene to have low acute toxicity from inhalation, moderate acute toxicity from ingestion, and low or moderate acute toxicity from dermal exposure. (3)

Chronic Effects (Noncancer):

- Chronic inhalation of certain levels of benzene causes disorders in the blood in humans. Benzene specifically affects bone marrow (the tissues that produce blood cells). Aplastic anemia[1], excessive bleeding, and damage to the immune system (by changes in blood levels of antibodies and loss of white blood cells) may develop. (1)
- In animals, chronic inhalation and oral exposure to benzene produces the same effects as seen in humans. (1)
- Benzene causes both structural and numerical chromosomal aberrations in humans. (1)

[1] Aplastic anemia is a risk factor for developing acute nonlymphocytic leukemia.

- EPA has not established a reference concentration (RfC) or a reference dose (RfD) for benzene. (4)
- The California Environmental Protection Agency (CalEPA) has established a chronic reference exposure level of 0.06 mg/m^3 for benzene based on hematological effects in humans. The CalEPA reference exposure level is a concentration at or below which adverse health effects are not likely to occur. It is not a direct estimator of risk, but rather a reference point to gauge the potential effects. At lifetime exposures increasingly greater than the reference exposure level, the potential for adverse health effects increases. (5)
- ATSDR has established an acute inhalation minimal risk level (MRL) of 0.2 mg/m^3 (0.05 ppm) based on immunological effects in mice and an intermediate MRL of 0.01 mg/m^3 (0.004 ppm) based on neurological effects in mice. The MRL is an estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk of adverse noncancer health effects over a specified duration of exposure. (1)

Reproductive/Developmental Effects:

- Several occupational studies suggest that benzene may impair fertility in women exposed to high levels. However, these studies are limited due to lack of exposure history, simultaneous exposure to other substances, and lack of follow-up. (1)
- Available human data on the developmental effects of benzene are inconclusive due to concomitant exposure to other chemicals, inadequate sample size, and lack of quantitative exposure data. (1)
- Adverse effects on the fetus, including low birth weight, delayed bone formation, and bone marrow damage, have been observed where pregnant animals were exposed to benzene by inhalation. (1)

Cancer Risk:

- Increased incidence of leukemia has been observed in humans occupationally exposed to benzene. (1,4)
- EPA has classified benzene as a Group A, known human carcinogen. (4)
- EPA uses mathematical models, based on human and animal studies, to estimate the probability of a person developing cancer from breathing air containing a specified concentration of a chemical. EPA calculated a range of 2.2×10^{-6} to 7.8×10^{-6} as the increase in the lifetime risk of an individual who is continuously exposed to 1 $\mu g/m^3$ of benzene in the air over their lifetime. EPA estimates that, if an individual were to continuously breathe air containing benzene at an average of 0.13 to 0.45 $\mu g/m^3$ (1.3×10^{-4} to 4.5×10^{-4} mg/m^3) over his or her entire lifetime, that person would theoretically have no more than a one-in-a-million increased chance of developing cancer as a direct result of continuously breathing air containing this chemical. Similarly, EPA estimates that continuously breathing air containing 1.3 to 4.5 $\mu g/m^3$ (1.3×10^{-3} to 4.5×10^{-3} mg/m^3) would result in not greater than a one-in-a-hundred thousand increased chance of developing cancer, and air containing 13 to 45 $\mu g/m^3$ (1.3×10^{-2} to 4.5×10^{-2} mg/m^3) would result in not greater than a one-in-ten thousand increased chance of developing

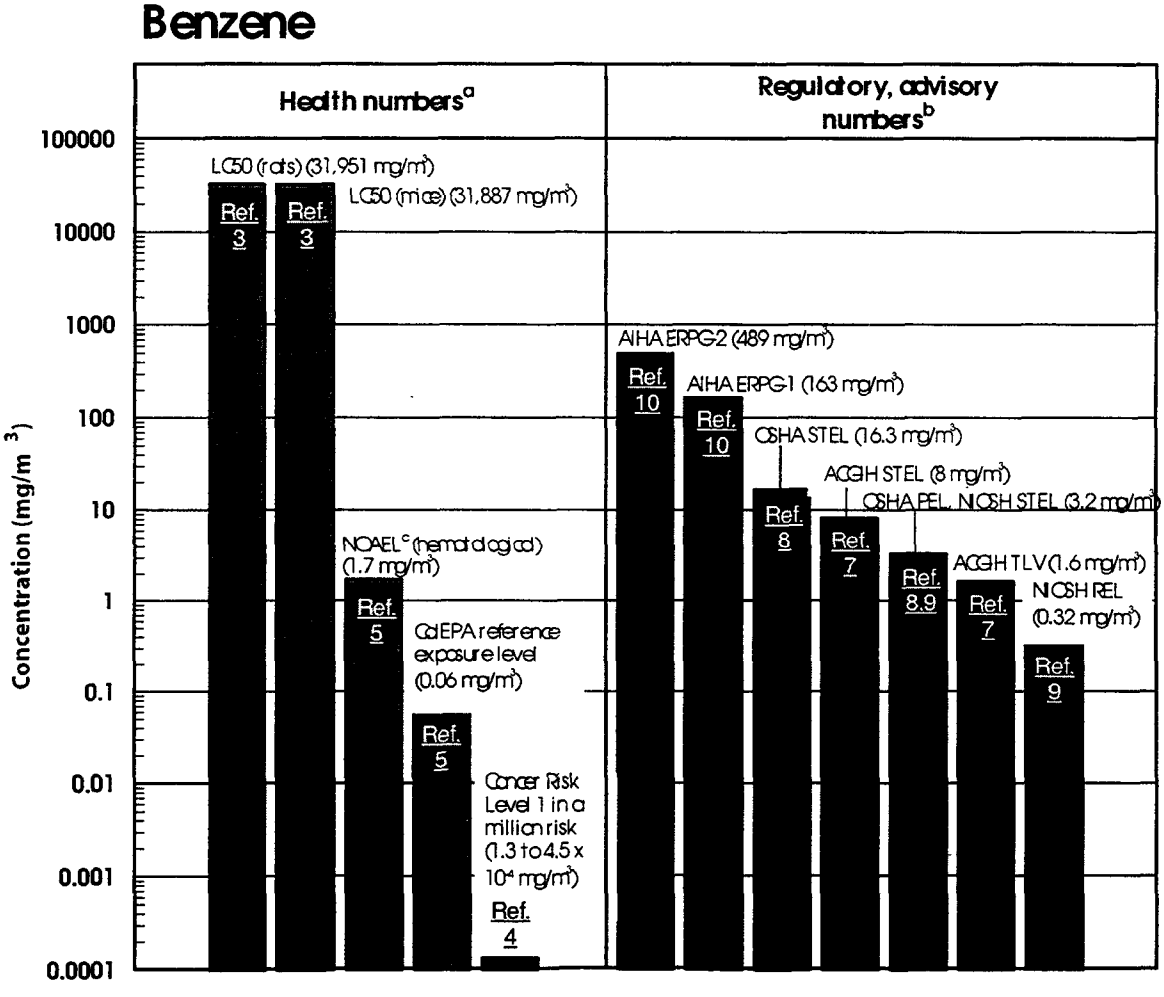
cancer. For a detailed discussion of confidence in the potency estimates, please see IRIS. (4)

- EPA has calculated an oral cancer slope factor of 2.9×10^{-2} $(mg/kg/d)^{-1}$. (4)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45).
For benzene: 1 ppm = 3.26 mg/m^3.
To convert from $\mu g/m^3$ to mg/m^3: mg/m^3 = ($\mu g/m^3$) x (1 mg/1,000 μg).

Health Data from Inhalation Exposure



ACGIH STEL – American Conference of Governmental and Industrial Hygienists' short-term exposure limit.
ACGIH TLV – American Conference of Governmental and Industrial Hygienists' threshold limit value expressed as a time-weighted average; the concentration of a substance to which most

workers can be exposed without adverse effects.
AIHA ERPG – American Industrial Hygiene Association's emergency response planning guidelines. ERPG 1 is the maximum airborne concentration below which it is believed nearly all individuals could be exposed up to one hour without experiencing other than mild transient adverse health effects or perceiving a clearly defined objectionable odor; ERPG 2 is the maximum airborne concentration below which it is believed nearly all individuals could be exposed up to one hour without experiencing or developing irreversible or other serious health effects that could impair their abilities to take protective action.
LC_{50} (Lethal Concentration$_{50}$) – A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.
NIOSH REL – National Institute of Occupational Safety and Health's recommended exposure limit; NIOSH-recommended exposure limit for an 8- or 10-h time-weighted-average exposure and/or ceiling.
NIOSH STEL – NIOSH's short-term exposure limit; NIOSH recommended exposure limit for a 15-minute period.
NOAEL – No-observed-adverse-effect level.
OSHA PEL – Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.
OSHA STEL – Occupational Safety and Health Administration's short-term exposure limit.

[a] Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA.
[b] Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the Government or other groups as advice.
[c] The NOAEL is from the critical study used as the basis for the CalEPA chronic reference exposure level.

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BERYLLIUM COMPOUNDS[1]

107-02-8

Hazard Summary

Inhalation exposure to beryllium primarily occurs in the workplaces where it is mined, processed, or converted into alloys and chemicals, or from the burning of coal or fuel oil and in tobacco smoke. Acute (short-term) inhalation exposure to high levels of beryllium has been observed to cause inflammation of the lungs or acute pneumonitis (reddening and swelling of the lungs) in humans; after exposure ends, these symptoms may be reversible. Chronic (long-term) inhalation exposure of humans to beryllium has been reported to cause chronic beryllium disease (berylliosis), in which granulomatous lesions (noncancerous) develop in the lung. Inadequate information is available on the reproductive or developmental effects of beryllium in humans or animals following inhalation exposure. Inhalation exposure to beryllium has been demonstrated to cause lung cancer in rats and monkeys. Human epidemiology studies are limited, but suggest a causal relationship between beryllium exposure and an increased risk of lung cancer. The U.S. Environmental Protection Agency (EPA) has classified beryllium as a Group B1, probable human carcinogen.

Please Note: The main sources of information for this fact sheet are EPA's Integrated Risk Information System (IRIS), which contains information on oral chronic toxicity and the reference dose (RfD) and inhalation chronic toxicity and the reference concentration (RfC), and the carcinogenic effects of beryllium including the unit cancer risk for inhalation exposure, EPA's *Toxicological Review of Beryllium and Compounds*, and the Agency for Toxic Substances and Disease Registry's (ATSDR's) *Toxicological Profile for Beryllium*.

Physical Properties

- The chemical symbol for pure beryllium is Be, and its atomic weight is 9.012 g/mol. (1)
- Pure beryllium is a hard gray metal that does not occur naturally but does occur as a chemical component of certain kinds of rocks, coal and oil, soil, and volcanic dust. (1)
- Beryllium is also present in a variety of compounds such as beryllium fluoride, beryllium chloride, beryllium sulfate, beryllium oxide, and beryllium phosphate. (1)
- Pure beryllium is insoluble in water; however, some of its compounds are soluble in water. (1)

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[1] This fact sheet discusses beryllium and beryllium compounds. Most of the information is on beryllium, except in those cases where there are differences in toxicity between beryllium and beryllium compounds. In these cases, information on the beryllium compound is presented.

Uses

- Pure beryllium and its metal alloys have applications in electrical components, tools, structural components for aircraft, missiles, and satellites, and other metal-fabricating uses. (1)
- Beryllium is also used in consumer products, such as televisions, calculators, and personal computers. (1)

Sources and Potential Exposure

- The greatest exposures to beryllium occur in the workplace (i.e., where it is mined, processed, or converted into alloys and chemicals). (1)
- Individuals may also be exposed by inhalation of beryllium dust or fumes from the burning of coal or fuel oil and in tobacco smoke, by the ingestion of many fruits and vegetables and water, or through natural occurrence in soils. (1)
- The average concentration of beryllium measured in the air in the U.S. during the 1980s was 0.03 ng/m^3. Ambient concentrations measured in 50 cities between 1977 and 1981 were 0.1–0.4 ng/m^3. (1)

Assessing Personal Exposure

- Beryllium levels can be measured in urine and blood, but the levels in urine are quite variable, making it difficult to use these levels to assess total exposure. (1)
- Beryllium levels in tissues can be measured through biopsy procedures, however the relationship to exposure is not well documented. (1)
- A medical test, termed the antigen-specific lymphocyte transformation test, can be used to measure hypersensitivity in individuals previously exposed to beryllium and can also be used to diagnose chronic beryllium disease. (1)

Health Hazard Information

Acute Effects:

- Acute inhalation exposure to high levels of beryllium has been observed to cause inflammation of the lungs and acute pneumonitis (reddening and swelling of the lungs) in humans; after exposure ends, these symptoms may be reversible. Acute pneumonitis may cause death. (1-4)
- Acute animal tests, such as the LD_{50} test in rats and mice, have demonstrated beryllium compounds to vary in acute toxicity, ranging from high to extreme acute toxicity from oral exposure. (5)

Chronic Effects (Noncancer):

- Chronic occupational exposure of humans to beryllium by inhalation has been reported to cause chronic beryllium disease (berylliosis), in which granulomatous lesions (noncancerous) develop in the lung. The onset of these effects may be delayed by 3 months to more than 20 years. Symptoms of chronic beryllium disease include irritation of the mucous membranes, reduced lung capacity, shortness of breath, fatigue, anorexia, dyspnea, malaise, and weight loss. In some cases, chronic beryllium disease may cause death. (1-4)
- Animal studies have also reported effects on the lung, such as chronic pneumonitis, from chronic inhalation exposure. (1-3)
- Chronic inhalation exposure has also been observed to cause immunological effects in humans and animals. (1-3)
- A skin allergy may result from dermal exposure to beryllium. Eye contact with beryllium dust has been observed to cause acute conjunctivitis in humans. (1)
- The RfC for beryllium is 0.00002 mg/m^3 based on respiratory effects in humans. The RfC is an estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious noncancer effects during a lifetime. It is not a direct estimator of risk but rather a reference point to gauge the potential effects. At exposures increasingly greater than the RfC, the potential for adverse health effects increases. Lifetime exposure above the RfC does not imply that an adverse health effect would necessarily occur. (3)
- EPA has medium confidence in the RfC due to: medium confidence in the study on which the RfC is based because a no-observed-adverse-affect level (NOAEL) was not identified in the study, but a NOAEL slightly below the lowest-observed-adverse-effect level (LOAEL) was suggested in another study; and medium confidence in the database due to lack of adequate exposure monitoring in the epidemiology studies and some uncertainty regarding the mechanism associated with progression to chronic beryllium disease in beryllium-sensitized individuals. (3)
- The RfD for beryllium is 0.002 mg/kg/d based on small intestinal lesions in dogs. (3)
- EPA has low to medium confidence in the RfD due to: medium confidence in the study on which the RfD was based because it was administered by the oral route with multiple doses for chronic duration, but there were small groups of animals, early mortality at the high dose level, and no control for potential litter effects; and low to medium confidence in the database because there is only one chronic study in dogs showing adverse effect levels. (3)

Reproductive/Developmental Effects:

- The potential for beryllium to induce developmental or reproductive effects has not been adequately assessed.
- Limited information is available on the reproductive or developmental effects of beryllium in humans following inhalation exposure. A case control study found no association between paternal occupational exposure and the risk of stillbirth, pre-term

delivery, or small-for-gestational-age infants, although this study has limited sensitivity. (2,3)

- No data are available on reproductive or developmental effects in animals following inhalation. (2,3)

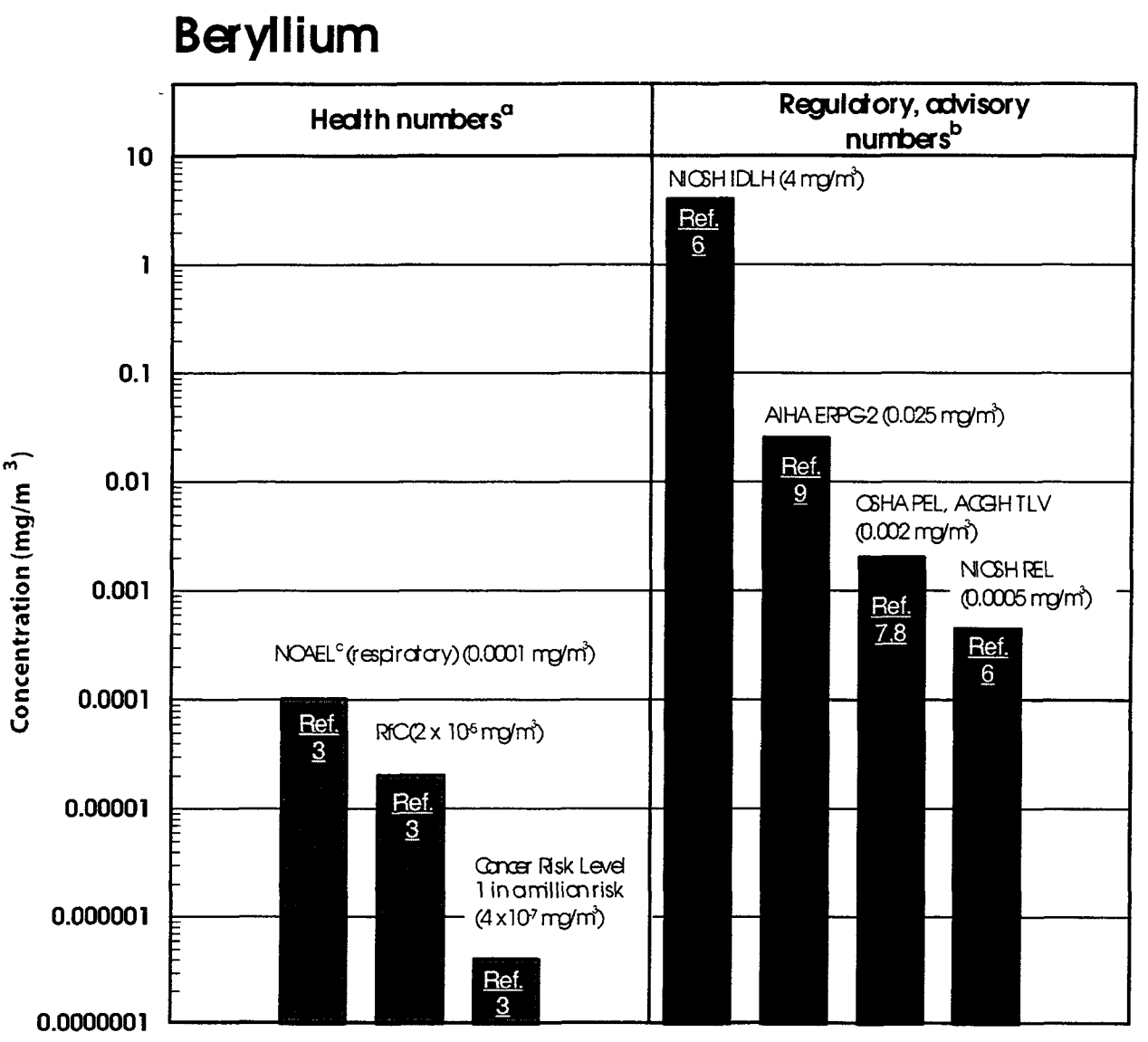
Cancer Risk:

- Several human epidemiological studies have investigated the relationship between beryllium exposure in workers and lung cancer deaths. Although there are shortcomings in all the studies, the results are suggestive of a causal relationship between beryllium exposure and an increased risk of lung cancer. (2,3)
- Beryllium compounds have been shown to cause lung cancer from inhalation exposure in rats and monkeys. (1–3)
- EPA has classified beryllium as a Group B1, probable human carcinogen. (3)
- EPA uses mathematical models, based on human and animal studies, to estimate the probability of a person developing cancer from breathing air containing a specified concentration of a chemical. EPA calculated an inhalation unit risk estimate of 2.4×10^{-3} $(\mu g/m^3)^{-1}$. EPA estimates that, if an individual were to continuously breathe air containing beryllium at an average of 0.0004 $\mu g/m^3$ (4×10^{-7} mg/m^3) over his or her entire lifetime, that person would theoretically have no more than a one-in-a-million increased chance of developing cancer as a direct result of breathing air containing this chemical. Similarly, EPA estimates that continuously breathing air containing 0.004 $\mu g/m^3$ (4×10^{-6} mg/m^3) would result in not greater than a one-in-a-hundred thousand increased chance of developing cancer, and air containing 0.04 $\mu g/m^3$ (4×10^{-5} mg/m^3) would result in not greater than a one-in-ten thousand increased chance of developing cancer. For a detailed discussion of confidence in the potency estimates, please see IRIS. (3)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45). Beryllium and its compounds do not exist in the atmosphere in the vapor phase; therefore, an air conversion factor is not applicable. (1)

Health Data from Inhalation Exposure



ACGIH TLV – American Conference of Governmental and Industrial Hygienists' threshold limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effects.

AIHA ERPG – American Industrial Hygiene Association's emergency response planning guidelines. ERPG 1 is the maximum airborne concentration below which it is believed nearly all individuals could be exposed up to one hour without experiencing other than mild transient adverse health effects or perceiving a clearly defined objectionable odor; ERPG 2 is the maximum airborne concentration below which it is believed nearly all individuals could be exposed up to one hour without experiencing or developing irreversible or other serious health effects that could impair their abilities to take protective action.

NIOSH IDLH – National Institute of Occupational Safety and Health's immediately dangerous

to life or health concentration; NIOSH recommended exposure limit to ensure that a worker can escape from an exposure condition that is likely to cause death or immediate or delayed permanent adverse health effects or prevent escape from the environment.
NIOSH REL – NIOSH's recommended exposure limit; NIOSH-recommended exposure limit for an 8- or 10-h time-weighted-average exposure and/or ceiling.
OSHA PEL – Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.

[a] Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA.
[b] Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the Government or other groups as advice.
[c] This NOAEL is from the critical study used as the basis of the EPA RfC.

References

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3. U.S. Environmental Protection Agency (EPA). *Integrated Risk Information System (IRIS) on Beryllium.* National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1999.

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5. U.S. Department of Health and Human Services. Registry of Toxic Effects of Chemical Substances (RTECS, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.

6. National Institute for Occupational Safety and Health (NIOSH). *Pocket Guide to Chemical Hazards.* U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention. Cincinnati, OH. 1997.

7. Occupational Safety and Health Administration (OSHA). Occupational Safety and Health Standards, Toxic and Hazardous Substances. *Code of Federal Regulations.* 29 CFR 1910.1000. 1998.

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1,3-BUTADIENE

106-99-0

Hazard Summary

1,3-Butadiene is found in ambient air primarily as a compound of motor vehicle exhaust. Acute (short-term) exposure to 1,3-butadiene by inhalation in humans results in irritation of the eyes, nasal passages, throat, and lungs, and causes neurological effects such as blurred vision, fatigue, headache, and vertigo. Epidemiological studies have reported a possible association between 1,3-butadiene exposure and cardiovascular diseases. No information is available on the reproductive or developmental effects of 1,3-butadiene in humans, while animal studies have reported these type of effects. Epidemiological studies of workers in rubber plants have shown an association between 1,3-butadiene exposure and increased incidence of leukemia. Animal studies have reported tumors at various sites from 1,3-butadiene exposure. The U.S. Environmental Protection Agency (EPA) has classified 1,3-butadiene as a Group B2, probable human carcinogen.

Please Note: The main sources of information for this fact sheet are EPA's Integrated Risk Information System (IRIS), which contains information on the carcinogenic effects of 1,3-butadiene including the unit cancer risk for inhalation exposure, and the Agency for Toxic Substances and Disease Registry's (ATSDR's) *Toxicological Profile for 1,3-Butadiene.*

Physical Properties

- 1,3-Butadiene is a colorless gas with a mild gasoline-like odor. (1)
- The odor threshold for 1,3-butadiene is 1.6 ppm. (7)
- The chemical formula for 1,3-butadiene is C_4H_6, and the molecular weight is 54.09 g/mol. (1)
- The vapor pressure for 1,3-butadiene is 2100 mm Hg at 25 °C, and it has an octanol/water partition coefficient (log K_{ow}) of 1.99. (1)

Uses

- 1,3-Butadiene is used in the production of rubber and plastics. It is also used in copolymers including acrylics. (1)

Sources and Potential Exposure

- Sources of 1,3-butadiene released into the air include manufacturing and processing facilities, motor vehicle exhaust, forest fires or other combustion, and cigarette smoke. (1)
- 1,3-Butadiene was detected in ambient air of cities and suburban areas from 1970 to 1982 at an average level of 0.3 ppb. (1)
- Higher levels of 1,3-butadiene may be found in highly industrialized cities or near oil refineries, chemical manufacturing plants, and plastic and rubber factories. (1)

- 1,3-Butadiene has been found in drinking water and in plastic or rubber food containers, but not in food samples. (1)
- Occupational exposure to 1,3-butadiene may occur in the rubber, plastics, and resins industries. (1)

Assessing Personal Exposure

- There is no reliable medical test available at this time to assess personal exposure to 1,3-butadiene. (1)

Health Hazard Information

Acute Effects:

- Acute exposure to 1,3-butadiene by inhalation in humans results in irritation of the eyes, nasal passages, throat, and lungs. Neurological effects, such as blurred vision, fatigue, headache, and vertigo, have also been reported at very high exposure levels. (1,3)
- Dermal exposure to 1,3-butadiene causes a sensation of cold, followed by a burning sensation, which may lead to frostbite. (1)
- Tests involving acute exposure of animals, such as the LC_{50} test in rats and mice, have shown 1,3-butadiene to have low acute toxicity. (1,4)

Chronic Effects (Noncancer):

- One epidemiological study reported that chronic (long-term) exposure to 1,3-butadiene via inhalation resulted in an increase in cardiovascular diseases, such as rheumatic and arteriosclerotic heart diseases, while other human studies have reported effects on the blood. (1)
- Animal studies have reported effects on the respiratory and cardiovascular systems, blood, and liver from chronic, inhalation exposure to 1,3-butadiene. (1)
- EPA has not established a reference concentration (RfC) or a reference dose (RfD) for 1,3-butadiene. (5)
- The California Environmental Protection Agency (CalEPA) has established a chronic reference level of 0.008 mg/m^3 for 1,3-butadiene based on reproductive effects in mice. The CalEPA reference exposure level is a concentration at or below which adverse health effects are not likely to occur. It is not a direct estimator of risk, but rather a reference point to gauge the potential effects. At lifetime exposures increasingly greater than the reference exposure level, the potential for adverse health effects increases. (6)

Reproductive/Developmental Effects:

- No information is available on reproductive or developmental effects of 1,3-butadiene in humans. (1)
- Animal studies using mice have reported developmental effects, such as skeletal abnormalities and decreased fetal weights, and reproductive effects, including an

increased incidence of ovarian atrophy, testicular atrophy, and sperm abnormalities from inhalation exposure to 1,3-butadiene. (1)

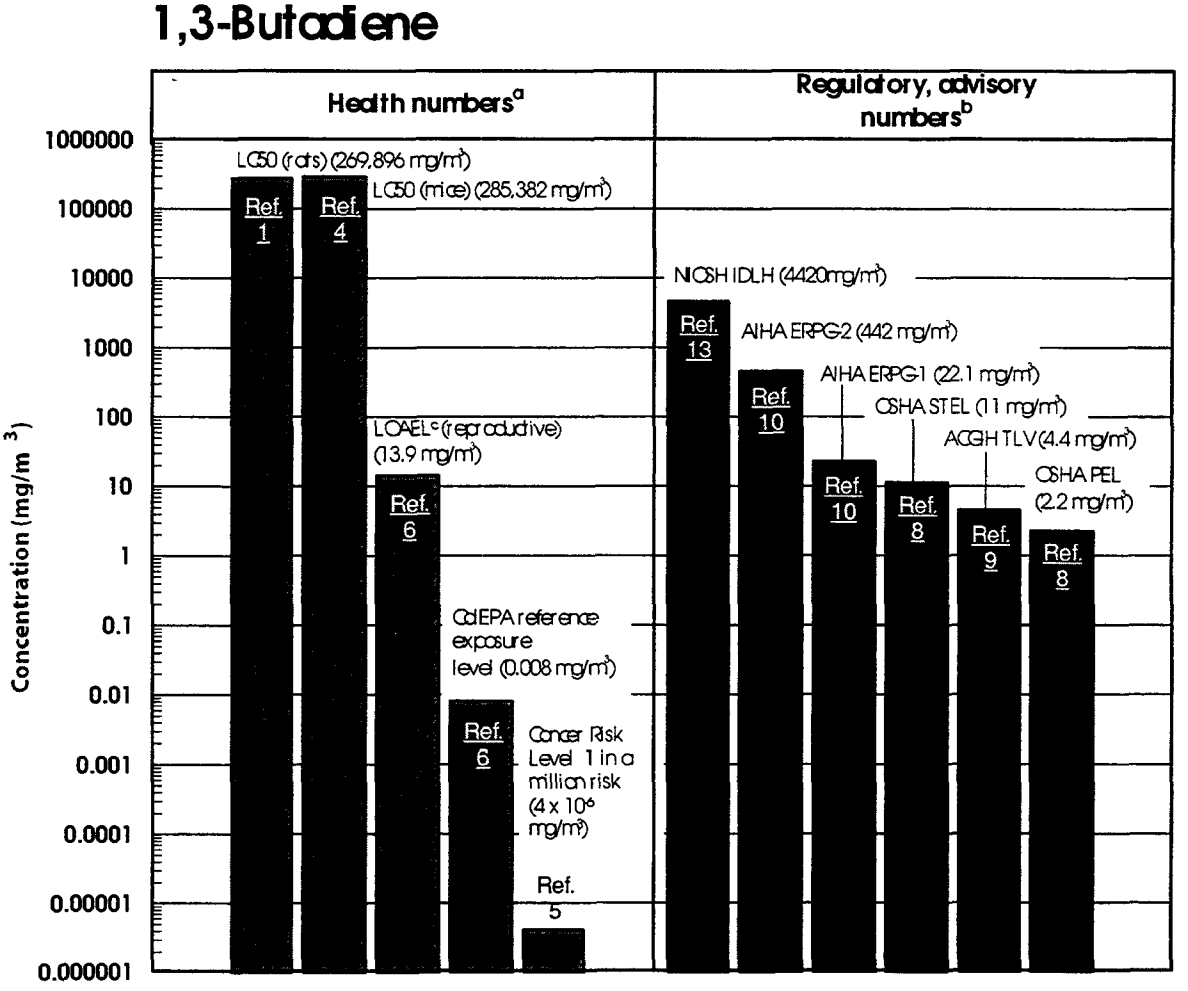
Cancer Risk:

- A large epidemiological study of synthetic rubber industry workers demonstrated a consistent association between 1,3-butadiene exposure and occurrence of leukemia (10, 11).
- Several epidemiological studies of workers in styrene-butadiene rubber factories have shown an increased incidence of respiratory, bladder, stomach, and lymphato-hematopoietic cancers. However, these studies are not sufficient to determine a causal association between 1,3-butadiene exposure and cancer due to possible exposure to other chemicals and other confounding factors. (1,5,6)
- Animal studies have reported tumors at a variety of sites from inhalation exposure to 1,3-butadiene. (1,5,6)
- EPA has classified 1,3-butadiene as a Group B2, probable human carcinogen. However, based on recently available human data, EPA is evaluating a classification of known human carcinogen. (5)
- EPA uses mathematical models, based on human and animal studies, to estimate the probability of a person developing cancer from continuously breathing air containing a specified concentration of a chemical. EPA is currently reevaluating their inhalation unit risk estimate of 2.8×10^{-4} $(\mu g/m^3)^{-1}$ that was derived in 1991. A revised unit risk estimate of 2.1×10^{-6} $(\mu g/m^3)^{-1}$ was presented to EPA's Science Advisory Board (SAB) for review in 1998. As a result of SAB comments, the estimate will be revised and is likely to be lower than the 1991 value. (12)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45).
For 1,3-butadiene: 1 ppm = 2.21 mg/m^3.
To convert from $\mu g/m^3$ to mg/m^3: mg/m^3 = ($\mu g/m^3$) x (1 mg/1,000 μg).

Health Data from Inhalation Exposure



ACGIH TLV – American Conference of Governmental and Industrial Hygienists' threshold limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effects.

AIHA ERPG – American Industrial Hygiene Association's emergency response planning guidelines. ERPG 1 is the maximum airborne concentration below which it is believed nearly all individuals could be exposed up to one hour without experiencing other than mild transient adverse health effects or perceiving a clearly defined objectionable odor; ERPG 2 is the maximum airborne concentration below which it is believed nearly all individuals could be exposed up to one hour without experiencing or developing irreversible or other serious health effects that could impair their abilities to take protective action.

LC_{50} (Lethal Concentration$_{50}$) – A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.

LOAEL – Lowest-observed-adverse-affect level.

NIOSH IDLH – National Institute of Occupational Safety and Health's immediately dangerous to life or health concentration; NIOSH recommended exposure limit to ensure that a worker can escape from an exposure condition that is likely to cause death or immediate or delayed permanent adverse health effects or prevent escape from the environment.
OSHA PEL – Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.
OSHA STEL – OSHA's short-term exposure limit.

[a] Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA.
[b] Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the Government or other groups as advice.
[c] The LOAEL is from the critical study used as the basis for the CalEPA chronic reference exposure level.

References

1. Agency for Toxic Substances and Disease Registry (ATSDR). *Toxicological Profile for 1,3-Butadiene*. Public Health Service, U.S. Department of Health and Human Services, Atlanta, GA. 1992.

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CADMIUM COMPOUNDS[1]

Hazard Summary

The main sources of cadmium in the air are the burning of fossil fuels such as coal or oil and the incineration of municipal waste. The acute (short-term) effects of cadmium in humans through inhalation exposure consist mainly of effects on the lung, such as pulmonary irritation. Chronic (long-term) inhalation or oral exposure to cadmium leads to a build-up of cadmium in the kidneys that can cause kidney disease. Cadmium has been shown to be a developmental toxicant in animals, resulting in fetal malformations and other effects, but no conclusive evidence exists in humans. An association between cadmium exposure and an increased risk of lung cancer has been reported from human studies, but these studies are inconclusive due to confounding factors. Animal studies have demonstrated an increase in lung cancer from long-term inhalation exposure to cadmium. The U.S. Environmental Protection Agency (EPA) has classified cadmium as a Group B1, probable human carcinogen.

Please Note: The main sources of information for this fact sheet are EPA's Integrated Risk Information System (IRIS), which contains information on oral chronic toxicity and the reference dose (RfD), and the carcinogenic effects of cadmium including the unit cancer risk for inhalation exposure, and the Agency for Toxic Substances and Disease Registry's (ATSDR's) *Toxicological Profile for Cadmium.*

Physical Properties

- Cadmium is a soft silver-white metal that is usually found in combination with other elements. (1)
- Cadmium compounds range in solubility in water from quite soluble to practically insoluble. (1)
- The chemical symbol for cadmium is Cd and the atomic weight is 112.41 g/mol. (1)

Uses

- Most cadmium used in the U.S. today is obtained as a byproduct from the smelting of zinc, lead, or copper ores. (1)
- Cadmium is used to manufacture pigments and batteries and in the metal-plating and plastics industries. (1)

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[1] This fact sheet discusses cadmium and cadmium compounds. Most of the information is on cadmium, except in those cases where there are differences in toxicity between cadmium and cadmium compounds. In these cases, information on the cadmium compound is presented.

Sources and Potential Exposure

- The largest sources of airborne cadmium in the environment are the burning of fossil fuels such as coal or oil, and incineration of municipal waste materials. Cadmium may also be emitted into the air from zinc, lead, or copper smelters. (1)
- For nonsmokers, food is generally the largest source of cadmium exposure. Cadmium levels in some foods can be increased by the application of phosphate fertilizers or sewage sludge to farm fields. (1)
- Smoking is another important source of cadmium exposure. Smokers have about twice as much cadmium in their bodies as do nonsmokers. (1)

Assessing Personal Exposure

- The amount of cadmium present in blood or urine can be measured by atomic absorption spectrophotometry and used as an indication of cadmium exposure. (1)
- A more precise method, called neutron activation analysis, can be used to measure cadmium concentrations in the liver or kidney. (1)

Health Hazard Information

Acute Effects:

- Acute inhalation exposure to high levels of cadmium in humans may result in effects on the lung, such as bronchial and pulmonary irritation. A single acute exposure to high levels of cadmium can result in long-lasting impairment of lung function. (1,3,4)
- Cadmium is considered to have high acute toxicity, based on short-term animal tests such as the LC_{50} test in rats. (5)

Chronic Effects (Noncancer):

- Chronic inhalation and oral exposure of humans to cadmium results in a build-up of cadmium in the kidneys that can cause kidney disease, including proteinuria, a decrease in glomerular filtration rate, and an increased frequency of kidney stone formation. (1,3,4)
- Other effects noted in humans from chronic exposure to cadmium in air are effects on the lung, including bronchiolitis and emphysema. (1,3,4)
- Chronic inhalation or oral exposure of animals to cadmium results in effects on the kidney, liver, lung, bone, immune system, blood, and nervous system. (1,3)
- The RfD for cadmium in drinking water is 0.0005 mg/kg/d, and the RfD for dietary exposure to cadmium is 0.001 mg/kg/d; both are based on significant proteinuria in humans. The RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious noncancer effects during a lifetime. It is not a direct estimator of risk, but rather a reference point to gauge the potential effects. At exposures increasingly greater than the RfD, the potential for

adverse health effects increases. Lifetime exposure above the RfD does not imply that an adverse health effect would necessarily occur. (6)

- EPA has high confidence in both RfD values based primarily on a strong database for cadmium toxicity in humans and animals that also permits calculation of pharmacokinetic parameters of cadmium absorption, distribution, metabolism, and elimination. (6)
- EPA has not established a reference concentration (RfC) for cadmium. (6)
- The California Environmental Protection Agency (CalEPA) has established a chronic reference exposure level of 0.00001 mg/m^3 for cadmium based on kidney and respiratory effects in humans. The CalEPA reference exposure level is a concentration at or below which adverse health effects are not likely to occur. (7)

Reproductive/Developmental Effects:

- Limited evidence exists for an association between inhalation exposure and a reduction in sperm number and viability in humans. (1)
- Human developmental studies on cadmium are limited, although there is some evidence to suggest that maternal cadmium exposure may result in decreased birth weights. (1)
- Animal studies provide evidence that cadmium has developmental effects, such as low fetal weight, skeletal malformations, interference with fetal metabolism, and impaired neurological development, via inhalation and oral exposure. (1,3,4)
- Limited animal data are available, although some reproductive effects, such as decreased reproduction and testicular damage, have been noted following oral exposures. (1)

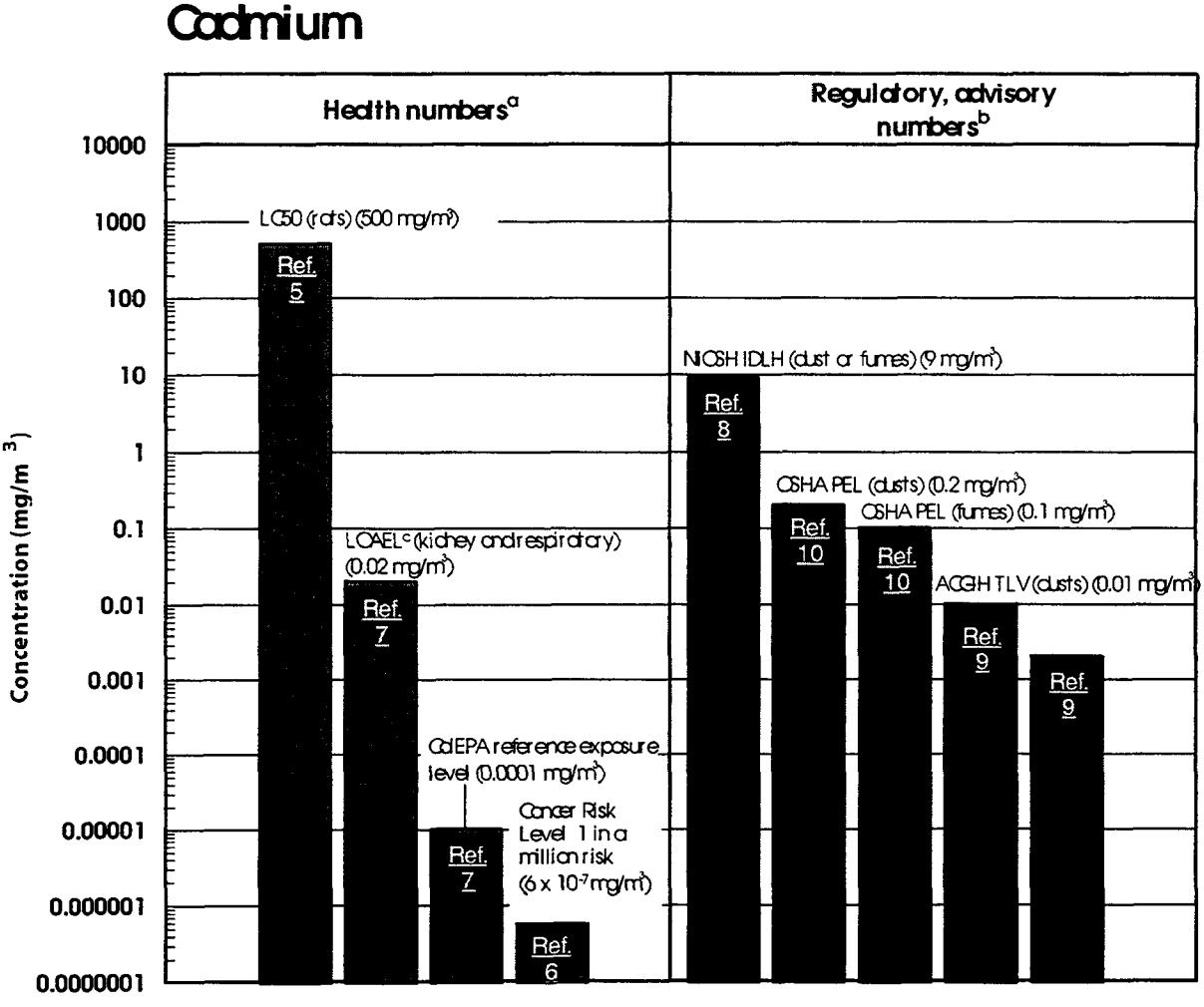
Cancer Risk:

- Several occupational studies have reported an excess risk of lung cancer in humans from exposure to inhaled cadmium. However, the evidence is limited rather than conclusive due to confounding factors. (1,3,6)
- Animal studies have reported cancer resulting from inhalation exposure to several forms of cadmium, while animal ingestion studies have not demonstrated cancer resulting from exposure to cadmium compounds. (1,3,6)
- EPA considers cadmium to be a probable human carcinogen and has classified it as a Group B1 carcinogen. (6)
- EPA uses mathematical models, based on human and animal studies, to estimate the probability of a person developing cancer from breathing air containing a specified concentration of a chemical. EPA calculated an inhalation unit risk estimate of 1.8×10^{-3} $(\mu g/m^3)^{-1}$. EPA estimates that, if an individual were to continuously breathe air containing cadmium at an average of 0.0006 $\mu g/m^3$ (6×10^{-7} mg/m^3) over his or her entire lifetime, that person would theoretically have no more than a one-in-a-million increased chance of developing cancer as a direct result of breathing air containing this chemical. Similarly, EPA estimates that continuously breathing air containing 0.006 $\mu g/m^3$ (6×10^{-6} mg/m^3) would result in not greater than a one-in-a-hundred thousand increased chance of developing cancer, and air containing 0.06 $\mu g/m^3$ (6×10^{-5} mg/m^3) would result in not greater than a one-in-ten thousand increased chance of developing cancer. For a detailed discussion of confidence in the potency estimates, please see IRIS. (6)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45).
For cadmium: 1 ppm = 4.6 mg/m^3.
To convert from µg/m^3 to mg/m^3: mg/m^3 = (µg/m^3) x (1 mg/1000 µg).

Health Data from Inhalation Exposure



ACGIH TLV – American Conference of Governmental and Industrial Hygienists' threshold limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effects.
LC_{50} (Lethal Concentration$_{50}$) – A calculated concentration of a chemical in air to which

exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.
LOAEL – Lowest-observed-adverse-affect level.
NIOSH IDLH – National Institute of Occupational Safety and Health's immediately dangerous to life and health; NIOSH concentration representing the maximum level of a pollutant from which an individual could escape within 30 minutes without escape-impairing symptoms or irreversible health effects.
OSHA PEL – Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.

[a] Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA.
[b] Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the Government or other groups as advice.
[c] The LOAEL is from the critical study used as the basis for the CalEPA chronic reference exposure level.

References

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CARBON TETRACHLORIDE

56-23-5

Hazard Summary

Carbon tetrachloride may be found in both ambient outdoor and indoor air. Human symptoms of acute (short-term) inhalation and oral exposures to carbon tetrachloride include headache, weakness, lethargy, nausea, and vomiting. Depression of the central nervous system (CNS) has also been reported. More severe acute exposures result in kidney and liver damage and extreme exposures have resulted in delayed pulmonary edema (resulting from kidney damage). Chronic (long-term) inhalation or oral exposure to carbon tetrachloride also produces liver and kidney damage in humans. Little information is available on the reproductive or developmental effects of carbon tetrachloride in humans. Reproductive effects have been observed in animals exposed to carbon tetrachloride orally and by inhalation. Human data on the carcinogenic effects of carbon tetrachloride are limited. Studies in animals have shown that ingestion of carbon tetrachloride increases the risk of liver cancer. The U.S. Environmental Protection Agency (EPA) has classified carbon tetrachloride as a Group B2, probable human carcinogen.

Please Note: The main sources of information for this fact sheet are EPA's Integrated Risk Information System (IRIS), which contains information on oral chronic toxicity of carbon tetrachloride and the reference dose (RfD), and the carcinogenic effects of carbon tetrachloride including the unit cancer risk for inhalation exposure, and the Agency for Toxic Substances and Disease Registry's (ATSDR's) *Toxicological Profile for Carbon Tetrachloride.*

Physical Properties

- The chemical formula for carbon tetrachloride is CCl_4, and its molecular weight is 153.8 g/mol. (1,2)
- Carbon tetrachloride is a clear, nonflammable liquid which is almost insoluble in water. (1)
- Carbon tetrachloride has a sweet characteristic odor, with an odor threshold above 10 ppm. (1)
- The vapor pressure for carbon tetrachloride is 91.3 mm Hg at 20 °C, and its log octanol/water partition coefficient (log K_{ow}) is 2.64. (1)

Uses

- Carbon tetrachloride was produced in large quantities to make refrigerants and propellants for aerosol cans, as a solvent for oils, fats, lacquers, varnishes, rubber waxes, and resins, and as a grain fumigant and a dry cleaning agent. Consumer and fumigant uses have been discontinued and only industrial uses remain. (1)

Sources and Potential Exposure

- Individuals may be exposed to carbon tetrachloride in the air from accidental releases from production and uses, and from its disposal in landfills. (1)
- Carbon tetrachloride is also a common contaminant of indoor air; the sources of exposure appear to be building materials or products, such as cleaning agents, used in the home. (1)
- Workers involved in the manufacture or use of carbon tetrachloride are most likely to have significant exposures to carbon tetrachloride. (1)
- Individuals may also be exposed to carbon tetrachloride by drinking contaminated water. (1,2)
- In the past, ingestion of bread or other products made with carbon tetrachloride-fumigated grain may have contributed to dietary exposure, but this route of exposure is no longer of significance. (1)

Assessing Personal Exposure

- Measurement of carbon tetrachloride in exhaled breath has been the most convenient method for determining exposure; measurements in blood, fat, or other tissues have also been used as indicators of exposure. However, these tests are not routinely available and cannot be used to predict whether any health effects will result. (1)

Health Hazard Information

Acute Effects:

- Acute inhalation and oral exposures to high levels of carbon tetrachloride have been observed primarily to damage the liver and kidneys of humans. Depression of the CNS has also been reported. Symptoms of acute exposure in humans include headache, weakness, lethargy, nausea, and vomiting. (1-6)
- Delayed pulmonary edema has been observed in humans exposed to high levels of carbon tetrachloride by inhalation and ingestion, but this is believed to be due to injury to the kidney rather than direct action of carbon tetrachloride on the lung. (1)
- Acute animal exposure tests, such as the LC_{50} and LD_{50} tests in rats, mice, rabbits, and guinea pigs, have demonstrated carbon tetrachloride to have low toxicity from inhalation exposure, low-to-moderate toxicity from ingestion, and moderate toxicity from dermal exposure. (7)

Chronic Effects (Noncancer):

- Chronic inhalation or oral exposure to carbon tetrachloride produces liver and kidney damage in humans and animals. (1,3,6,8)
- EPA has not established a reference concentration (RfC) for carbon tetrachloride. (9)
- The California Environmental Protection Agency (CalEPA) has established a chronic reference exposure level of 0.04 mg/m^3 for carbon tetrachloride based on liver effects in guinea pigs. The CalEPA reference exposure level is a concentration at or below which

adverse health effects are not likely to occur. It is not a direct estimator of risk, but rather a reference point to gauge the potential effects. At lifetime exposures increasingly greater than the reference exposure level, the potential for adverse health effects increases. (10)

- ATSDR has established an acute inhalation minimal risk level (MRL) of 1.3 mg/m^3 (0.2 ppm) based on liver effects in rats, and an intermediate MRL of 0.3 mg/m^3 (0.05 ppm) also based on liver effects in rats. The MRL is an estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk of adverse noncancer health effects over a specified duration of exposure. (1)
- The RfD for carbon tetrachloride is 0.0007 mg/kg/d based on the occurrence of liver lesions in rats. The RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious noncancer effects during a lifetime. (9)
- EPA has medium confidence in the RfD based on: high confidence in the principal study on which the RfD was based because the study was well conducted and good dose-response was observed in the liver, which is the target organ for carbon tetrachloride toxicity; and medium confidence in the database because four additional subchronic studies support the RfD, but reproductive and teratology endpoints are not well investigated; and, consequently, medium confidence in the RfD. (9)

Reproductive/Developmental Effects:

- No information is available on the reproductive effects of carbon tetrachloride in humans. Limited epidemiological data have indicated a possible association between certain birth outcomes (e.g., birth weight, cleft palate) and drinking water exposure. However, as the water contained multiple chemicals, the role of carbon tetrachloride is unclear. (1)
- Decreased fertility and degenerative changes in the testes have been observed in animals exposed to carbon tetrachloride by inhalation. (1,6)
- Birth defects have not been observed in animals exposed to carbon tetrachloride by inhalation or ingestion. (1,2,8)

Cancer Risk:

- Occasional reports have noted the occurrence of liver cancer in workers who had been exposed to carbon tetrachloride by inhalation exposure; however, the data are not sufficient to establish a cause-and-effect relationship. (1,6,8,9,11,12)
- Liver tumors have developed in rats and mice exposed to carbon tetrachloride by gavage. (1-4,6,8,9,11,12)
- EPA has classified carbon tetrachloride as a Group B2, probable human carcinogen. (8,9)
- EPA uses mathematical models, based on human and animal studies, to estimate the probability of a person developing cancer from continuously breathing air containing a specified concentration of a chemical. EPA calculated an inhalation unit risk of 1.5×10^{-5} $(\mu g/m^3)^{-1}$. EPA estimates that, if an individual were to continuously breathe air containing carbon tetrachloride at an average of 0.07 $\mu g/m^3$ (7×10^{-5} mg/m^3) over his or her entire

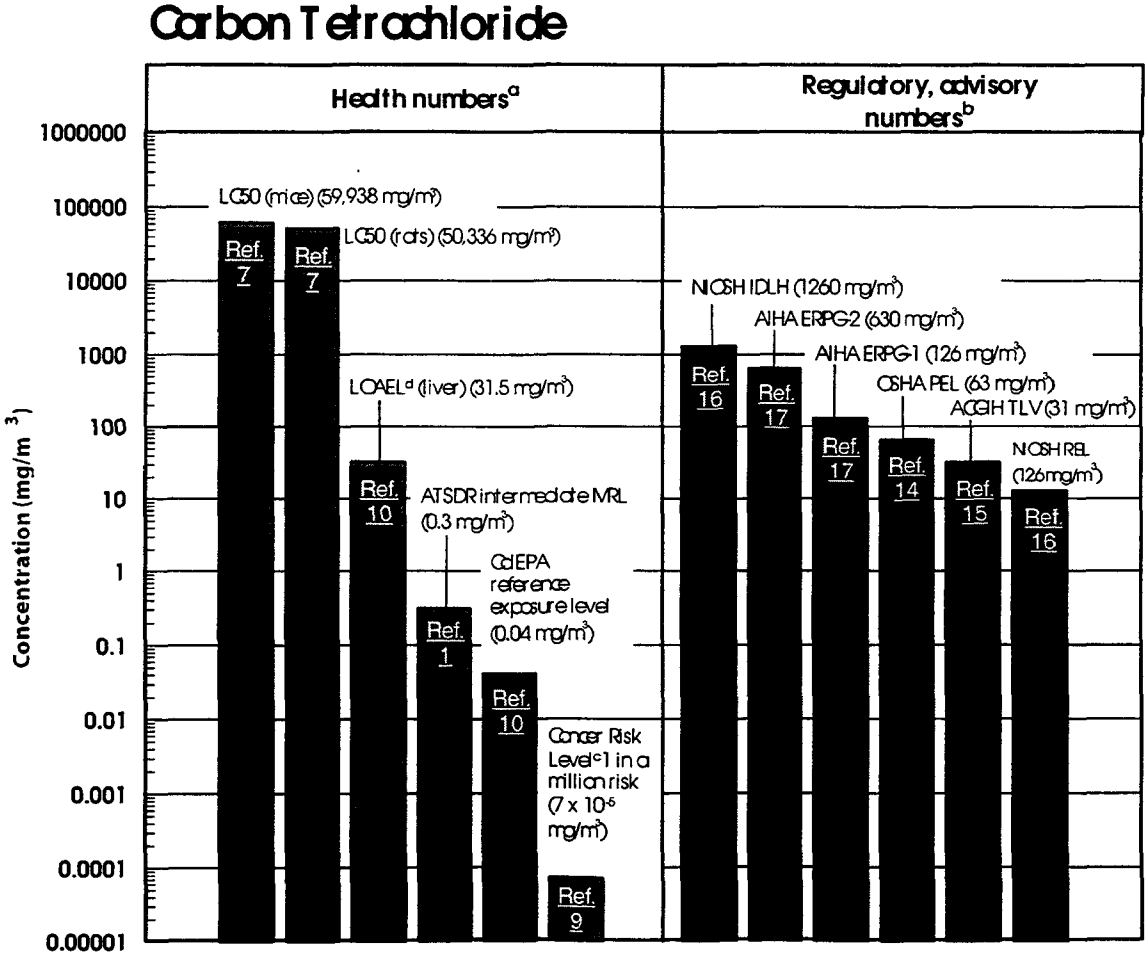
lifetime, that person would theoretically have no more than a one-in-a-million increased chance of developing cancer as a direct result of breathing air containing this chemical.

- Similarly, EPA estimates that continuously breathing air containing 0.7 $\mu g/m^3$ (7×10^{-4} mg/m^3) would result in not greater than a one-in-a-hundred thousand increased chance of developing cancer, and air containing 7.0 $\mu g/m^3$ (7×10^{-3} mg/m^3) would result in not greater than a one-in-a-ten thousand increased chance of developing cancer. (9)
- EPA has calculated an oral cancer slope factor of 1.3×10^{-1} $(mg/kg/d)^{-1}$. For a detailed discussion of confidence in the potency estimates, please see IRIS. (9)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45). For carbon tetrachloride: 1 ppm = 6.3 mg/m^3.

Health Data from Inhalation Exposure



AIHA ERPG – American Industrial Hygiene Association's emergency response planning guidelines. ERPG 1 is the maximum airborne concentration below which it is believed nearly all individuals could be exposed up to one hour without experiencing other than mild transient adverse health effects or perceiving a clearly defined objectionable odor; ERPG 2 is the maximum airborne concentration below which it is believed nearly all individuals could be exposed up to one hour without experiencing or developing irreversible or other serious health effects that could impair their abilities to take protective action.
ACGIH TLV – American Conference of Governmental and Industrial Hygienists' threshold limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effects.
LC_{50} (Lethal Concentration$_{50}$) – A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.
LOAEL – Lowest-observed-adverse-affect level.
NIOSH IDLH – National Institute of Occupational Safety and Health's immediately dangerous to life or health concentration; NIOSH recommended exposure limit to ensure that a worker can escape from an exposure condition that is likely to cause death or immediate or delayed permanent adverse health effects or prevent escape from the environment.
NIOSH REL – NIOSH's recommended exposure limit; NIOSH-recommended exposure limit for an 8- or 10-h time-weighted-average exposure and/or ceiling.
OSHA PEL – Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.

[a] Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA.
[b] Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the Government or other groups as advice.
[c] These cancer risk estimates were derived from oral data and converted to provide the estimated inhalation risk.
[d] The LOAEL is from the critical study used as the basis for the CalEPA chronic reference exposure level.

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CHLOROFORM
67-66-3

Hazard Summary

Chloroform may be released to the air as a result of its formation in the chlorination of drinking water, wastewater and swimming pools. Other sources include pulp and paper mills, hazardous waste sites, and sanitary landfills. The major effect from acute (short-term) inhalation exposure to chloroform is central nervous system (CNS) depression. Chronic (long-term) exposure to chloroform by inhalation in humans has resulted in effects on the liver, including hepatitis and jaundice, and CNS effects, such as depression and irritability. Little information is available on the reproductive or developmental effects of chloroform in humans, while animal studies have reported developmental effects, such as decreased fetal body weight and fetal resorptions, and reproductive effects, such as decreased conception rates, in animals exposed to chloroform by inhalation. No studies are available on the carcinogenic effects of chloroform in humans or animals after inhalation exposure. Chloroform has been shown to be carcinogenic in animals after oral exposure, resulting in an increase in kidney and liver tumors. The U.S. Environmental Protection Agency (EPA) has classified chloroform as a Group B2, probable human carcinogen.

Please Note: The main sources of information for this fact sheet are EPA's Integrated Risk Information System (IRIS), which contains information on oral chronic toxicity and the reference dose (RfD), and the carcinogenic effects of chloroform including the unit cancer risk for inhalation exposure, and the Agency for Toxic Substances and Disease Registry's (ATSDR's) *Toxicological Profile for Chloroform.*

Physical Properties

- Chloroform is a colorless liquid that is not very soluble in water and is very volatile. (1,6)
- Chloroform has a pleasant, nonirritating odor; the odor threshold is 85 ppm. (1)
- The chemical formula for chloroform is $CHCl_3$, and it has a molecular weight of 119.38 g/mol. (1)
- The vapor pressure for chloroform is 159 mm Hg at 20 °C, and it has a log octanol/water partition coefficient (log K_{ow}) of 1.97. (1)

Uses

- The vast majority of the chloroform produced in the U.S. is used to make HCFC-22. The rest is produced for export and for miscellaneous uses. (1)
- Chloroform was used in the past as an extraction solvent for fats, oils, greases, and other products; as a dry cleaning spot remover; in fire extinguishers; as a fumigant; and as an anesthetic. However, chloroform is no longer used in these products. (1)

Sources and Potential Exposure

- Chloroform may be released to the air from a large number of sources related to its manufacture and use, as well as its formation in the chlorination of drinking water, wastewater, and swimming pools. Pulp and paper mills, hazardous waste sites, and sanitary landfills are also sources of air emissions. The background level of chloroform in ambient air in the early 1990's was estimated at 0.00004 ppm. (1)
- Human exposure to chloroform may occur through drinking water, where chloroform is formed as a result of the chlorination of naturally occurring organic materials found in raw water supplies. Measurements of chloroform in drinking water during the 1970's and 1980's ranged from 0.022 to 0.068 ppm. (1)
- Chloroform may also be found in some foods and beverages, largely from the use of tap water during production processes. (1)

Assessing Personal Exposure

- Chloroform can be detected in blood, urine, and body tissues. However, these methods are not very reliable because chloroform is rapidly eliminated from the body, and the tests are not specific for chloroform. (1)

Health Hazard Information

Acute Effects:

- The major effect from acute inhalation exposure to chloroform in humans is CNS depression. At very high levels (40,000 ppm), chloroform exposure may result in death, with concentrations in the range of 1,500 to 30,000 ppm producing anesthesia, and lower concentrations (<1,500 ppm) resulting in dizziness, headache, tiredness, and other effects. (1,2)
- Effects noted in humans exposed to chloroform via anesthesia include changes in respiratory rate, cardiac effects, gastrointestinal effects, such as nausea and vomiting, and effects on the liver and kidney. Chloroform is not currently used as a surgical anesthetic. (1,2)
- In humans, a fatal oral dose of chloroform may be as low as 10 mL (14.8 g), with death due to respiratory or cardiac arrest. (1,2)
- Tests involving acute exposure of animals, such as the LC_{50} and LD_{50} tests in rats, have shown chloroform to have low acute toxicity from inhalation exposure and moderate acute toxicity from oral exposure. (3)

Chronic Effects (Noncancer):

- Chronic exposure to chloroform by inhalation in humans is associated with effects on the liver, including hepatitis and jaundice, and CNS effects, such as depression and irritability. Inhalation exposures of animals have also resulted in effects on the kidney. (1,2)

- Chronic oral exposure to chloroform in humans has resulted in effects on the blood, liver, and kidney. (1,2)
- EPA has not established a reference concentration (RfC) for chloroform. (4)
- The California Environmental Protection Agency (CalEPA) has established a chronic reference exposure level of 0.3 mg/m^3 for chloroform based on exposures resulting in kidney and liver effects in rats. The CalEPA reference exposure level is a concentration at or below which adverse health effects are not likely to occur. It is not a direct estimator of risk, but rather a reference point to gauge the potential effects. At lifetime exposures increasingly greater than the reference exposure level, the potential for adverse health effects increases. (5)
- ATSDR has established an acute inhalation minimal risk level (MRL) of 0.5 mg/m^3 (0.1 ppm) based on exposures resulting in liver effects in mice, an intermediate inhalation MRL of 0.2 mg/m^3 (0.05 ppm) based on worker exposures resulting in liver effects in humans, and a chronic inhalation MRL of 0.1 mg/m^3 (0.02 ppm) also based on liver effects in humans. The MRL is an estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk of adverse noncancer health effects over a specified duration of exposure. (1)
- The RfD for chloroform is 0.01 mg/kg/d based on exposures resulting in fatty cyst formation in the livers of dogs. The RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious noncancer effects during a lifetime. (4)
- EPA has medium to low confidence in the RfD due to: medium confidence in the critical study on which the RfD was based because it was of chronic duration, used a fairly large number of dogs, measured multiple endpoints using only two treatment doses, and a no-observed-effect level (NOEL) was not determined; and medium to low confidence in the database because several studies support the choice of a lowest-observed-adverse-effect level (LOAEL), but a NOEL was not found. (4)

Reproductive/Developmental Effects:

- Little information is available on the reproductive or developmental effects of chloroform in humans, via any route of exposure. A possible association between certain birth outcomes (e.g., low birth weight, cleft palate) and consumption of contaminated drinking water was reported. However, because multiple contaminants were present, the role of chloroform is unclear. (1)
- Animal studies have demonstrated developmental effects, such as decreased fetal body weight, fetal resorptions, and malformations in the offspring of animals exposed to chloroform via inhalation. (1)
- Reproductive effects, such as decreased conception rates, decreased ability to maintain pregnancy, and an increase in the percentage of abnormal sperm were observed in animals exposed to chloroform through inhalation. (1)
- Animal studies have noted decreased fetal weight, increased fetal resorptions, but no evidence of birth defects, in animals orally exposed to chloroform. (1)

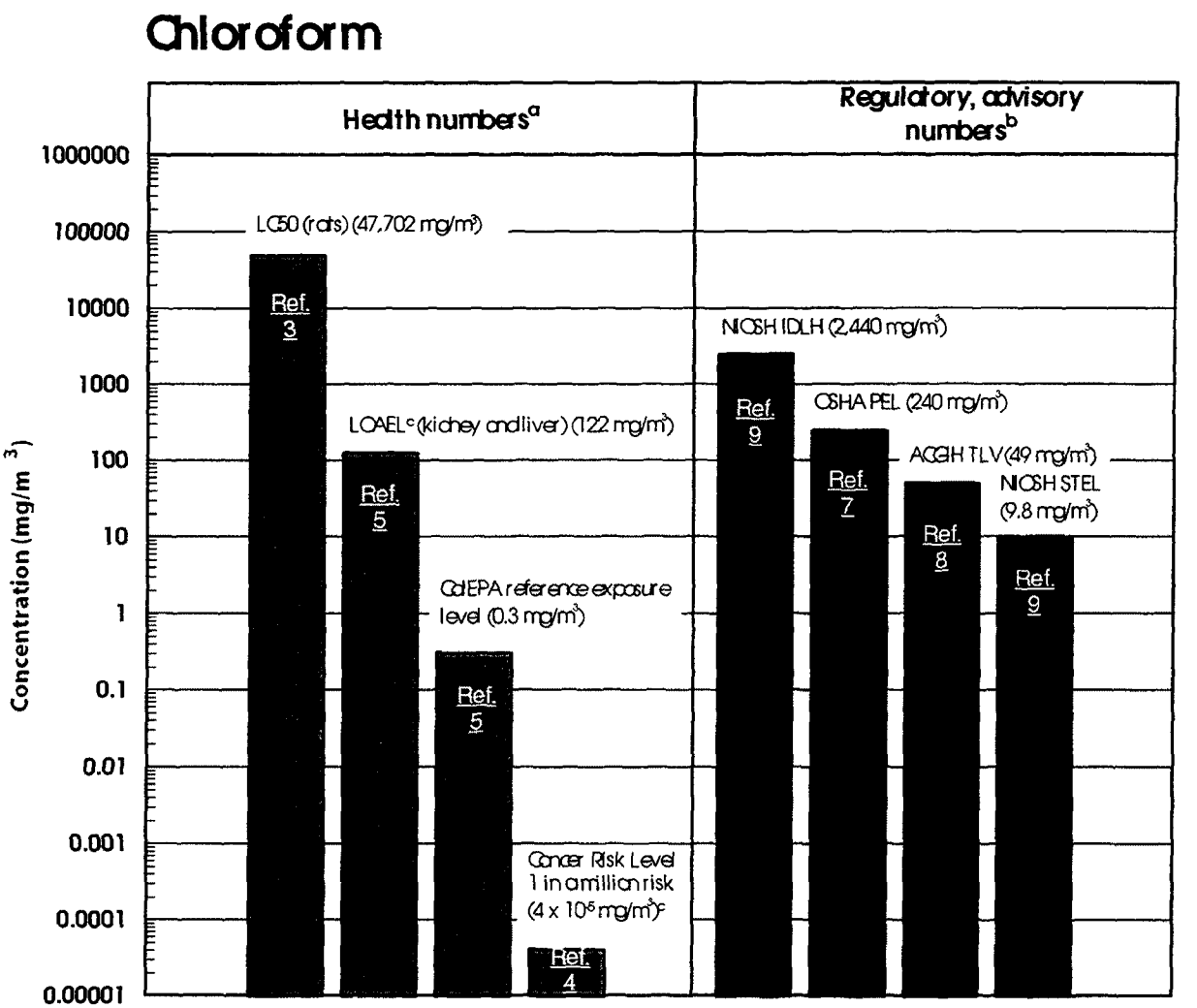
Cancer Risk:

- No information is available regarding cancer in humans or animals after inhalation exposure to chloroform. (1)
- Epidemiologic studies suggest an association between cancer of the large intestine, rectum, and/or bladder and the constituents of chlorinated drinking water, including chloroform. However, there are no epidemiologic studies of water containing only chloroform. (1)
- Chloroform has been shown to be carcinogenic in animals after oral exposure, resulting in an increase in kidney and liver tumors. (1)
- EPA has classified chloroform as a Group B2, probable human carcinogen. (4)
- EPA uses mathematical models, based on human and animal studies, to estimate the probability of a person developing cancer from breathing air containing a specified concentration of a chemical. EPA calculated an inhalation unit risk estimate of 2.3×10^{-5} $(\mu g/m^3)^{-1}$. EPA estimates that, if an individual were to continuously breathe air containing chloroform at an average of 0.04 $\mu g/m^3$ (4×10^{-5} mg/m^3) over his or her entire lifetime, that person would theoretically have no more than a one-in-a-million increased chance of developing cancer as a direct result of breathing air containing this chemical. Similarly, EPA estimates that continuously breathing air containing 0.4 $\mu g/m^3$ (4×10^{-4} mg/m^3) would result in not greater than a one-in-a-hundred thousand increased chance of developing cancer, and air containing 4.0 $\mu g/m^3$ (4×10^{-3} mg/m^3) would result in not greater than a one-in-ten thousand increased chance of developing cancer. For a detailed discussion of confidence in the potency estimates, please see IRIS. (4)
- EPA has calculated an oral cancer slope factor of 6.1×10^{-3} $(mg/kg/d)^{-1}$. (4)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45).
For chloroform: 1 ppm = 4.88 mg/m^3.
To convert from $\mu g/m^3$ to mg/m^3: mg/m^3 = ($\mu g/m^3$) x (1 mg/1,000 μg).

Health Data from Inhalation Exposure



ACGIH TLV – American Conference of Governmental and Industrial Hygienists' threshold limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effects.

LC_{50} (Lethal Concentration$_{50}$) – A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.

LOAEL – Lowest-observed-adverse-effect level.

NIOSH REL – National Institute of Occupational Safety and Health's recommended exposure limit; NIOSH-recommended exposure limit for an 8- or 10-h time-weighted-average exposure and/or ceiling.

OSHA PEL – Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.

[a] Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA.
[b] Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the Government or other groups as advice.
[c] These cancer risk estimates were derived from oral data and converted to provide the estimated inhalation risk.
[d] The LOAEL is from the critical study used as the basis for the CalEPA chronic reference exposure level.

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CHROMIUM COMPOUNDS

Hazard Summary

Chromium occurs in the environment primarily in two valence states, trivalent chromium (Cr III) and hexavalent chromium (Cr VI). Exposure may occur from natural or industrial sources of chromium.

The respiratory tract is the major target organ for chromium (VI) toxicity, for acute (short-term) and chronic (long-term) inhalation exposures. Shortness of breath, coughing, and wheezing were reported from a case of acute exposure to chromium (VI), while perforations and ulcerations of the septum, bronchitis, decreased pulmonary function, pneumonia, and other respiratory effects have been noted from chronic exposure. Limited human studies suggest that chromium (VI) inhalation exposure may be associated with complications during pregnancy and childbirth, while animal studies have not reported reproductive effects from inhalation exposure to chromium (VI). The U.S. Environmental Protection Agency (EPA) has classified chromium (VI) as a Group A, known human carcinogen. Human studies have clearly established that inhaled chromium (VI) is a human carcinogen, resulting in an increased risk of lung cancer. Animal studies have shown chromium (VI) to cause lung tumors via inhalation exposure.

Chromium III is much less toxic than chromium (VI). The respiratory tract is also the major target organ for chromium (III) toxicity, similar to chromium (VI). Chromium (III) is an essential element in humans, with a daily intake of 50 to 200 μg/d recommended for an adult. The body can detoxify some amount of chromium (VI) to chromium (III).

Please Note: The main sources of information for this fact sheet are EPA's Integrated Risk Information System (IRIS), which contains information on inhalation chronic toxicity and the reference concentration (RfC) and oral chronic toxicity and the reference dose (RfD), and the carcinogenic effects of chromium including the unit cancer risk for inhalation exposure, EPA's *Toxicological Review of Trivalent Chromium* and *Toxicological Review of Hexavalent Chromium,* and the Agency for Toxic Substances and Disease Registry's (ATSDR's) *Toxicological Profile for Chromium.*

Physical Properties

- The metal, chromium (Cr), is a steel-gray solid with a high melting point and an atomic weight of 51.996 g/mol. Chromium has oxidation states ranging from chromium (-II) to chromium (+VI). (1)
- Chromium forms a large number of compounds, in both the chromium (III) and the chromium (VI) forms. Chromium compounds are stable in the trivalent state, with the hexavalent form being the second most stable state. (1)
- The chromium (III) compounds are sparingly soluble in water and may be found in water bodies as soluble chromium (III) complexes, while the chromium (VI) compounds are readily soluble in water. (1)

Uses

- The metal chromium is used mainly for making steel and other alloys. (1)
- Chromium compounds, in either the chromium (III) or chromium (VI) forms, are used for chrome plating, the manufacture of dyes and pigments, leather and wood preservation, and treatment of cooling tower water. Smaller amounts are used in drilling muds, textiles, and toner for copying machines. (1)

Sources and Potential Exposure

- Chromium is a naturally occurring element in rocks, animals, plants, soil, and volcanic dust and gases. (1)
- Chromium occurs in the environment predominantly in one of two valence states: trivalent chromium (Cr III), which occurs naturally and is an essential nutrient, and hexavalent chromium (Cr VI), which, along with the less common metallic chromium (Cr 0), is most commonly produced by industrial processes. (1)
- Chromium (III) is essential to normal glucose, protein, and fat metabolism and is thus an essential dietary element. The body has several systems for reducing chromium (VI) to chromium (III). This chromium (VI) detoxification leads to increased levels of chromium (III). (1)
- Air emissions of chromium are predominantly of trivalent chromium, and in the form of small particles or aerosols. (1, 2)
- The most important industrial sources of chromium in the atmosphere are those related to ferrochrome production. Ore refining, chemical and refractory processing, cement-producing plants, automobile brake lining and catalytic converters for automobiles, leather tanneries, and chrome pigments also contribute to the atmospheric burden of chromium. (3)
- The general population is exposed to chromium (generally chromium [III]) by eating food, drinking water, and inhaling air that contains the chemical. The average daily intake from air, water, and food is estimated to be approximately less than 0.2 to 0.4 μg, 2.0 μg, and 60 μg, respectively. (1)
- Dermal exposure to chromium may occur during the use of consumer products that contain chromium, such as wood treated with copper dichromate or leather tanned with chromic sulfate. (1)
- Occupational exposure to chromium occurs from chromate production, stainless-steel production, chrome plating, and working in tanning industries; occupational exposure can be two orders of magnitude higher than exposure to the general population. (1)
- People who live in the vicinity of chromium waste disposal sites or chromium manufacturing and processing plants have a greater probability of elevated chromium exposure than the general population. These exposures are generally to mixed chromium (VI) and chromium (III). (1)

Assessing Personal Exposure

- Laboratory tests can detect chromium in the blood, urine, and hair of exposed individuals. (1, 5)
- Laboratory tests find it difficult to separate chromium VI from chromium III; in many cases analysis is done for total chromium. (1)

Health Hazard Information

Acute Effects:

Chromium VI

- Chromium (VI) is much more toxic than chromium (III), for both acute and chronic exposures. (1,3,4)
- The respiratory tract is the major target organ for chromium (VI) following inhalation exposure in humans. Shortness of breath, coughing, and wheezing were reported in cases where an individual inhaled very high concentrations of chromium trioxide. (1,4)
- Other effects noted from acute inhalation exposure to very high concentrations of chromium (VI) include gastrointestinal and neurological effects, while dermal exposure causes skin burns. (1,4,5)
- Ingestion of high amounts of chromium (VI) causes gastrointestinal effects in humans and animals, including abdominal pain, vomiting, and hemorrhage. (1)
- Acute animal tests, such as the LC_{50} and LD_{50} tests in rats, have shown chromium (VI) to have extreme toxicity from inhalation (LC_{50} = 30-140 mg/m^3) and oral (LD_{50} <100 mg/kg) exposure. (1,6)

Chromium III

- Chromium (III) is an essential element in humans, with a daily intake of 50 to 200 μg/d recommended for adults. (1)
- Acute animal tests have shown chromium (III) to have moderate toxicity from oral exposure, with LD_{50} values of 200-2000 mg/kg and much lower toxicity from acute dietary exposures. (1,6)

Chronic Effects (Noncancer):

Chromium VI

- Chronic inhalation exposure to chromium (VI) in humans results in effects on the respiratory tract, with perforations and ulcerations of the septum, bronchitis, decreased pulmonary function, pneumonia, asthma, and nasal itching and soreness reported. (1,4,5)
- Chronic human exposure to high levels of chromium (VI) by inhalation or oral exposure may produce effects on the liver, kidney, gastrointestinal and immune systems, and possibly the blood. (1,4,5)

- Rat studies have shown that, following inhalation exposure, the lung and kidney have the highest tissue levels of chromium. (1,4,5)
- Dermal exposure to chromium (VI) may cause contact dermatitis, sensitivity, and ulceration of the skin. (1,4,5)
- The RfC for chromium (VI) (particulates) is 0.0001 mg/m^3 based on respiratory effects in rats. The RfC is an estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious noncancer effects during a lifetime. It is not a direct estimator of risk but rather a reference point to gauge the potential effects. At exposures increasingly greater than the RfC, the potential for adverse health effects increases. Lifetime exposure above the RfC does not imply that an adverse health effect would necessarily occur. (7)
- EPA has medium confidence in the RfC for chromium VI (particulates) based on medium confidence in the study on which it was based because of uncertainties regarding upper respiratory tract, reproductive, and renal effects resulting from the exposures. (7)
- The RfC for chromium (VI) (chromic acid mists and dissolved Cr (VI) aerosols) is 0.000008 mg/m^3 based on respiratory effects in humans. (7)
- EPA has low confidence in the RfC based on low confidence in the study on which the RfC for chromium (VI) (chromic acid mists and dissolved Cr (VI) aerosols) is based because of uncertainties regarding the exposure characterization and the role of direct contact for the critical effect; and low confidence in the database because the supporting studies are equally uncertain regarding the exposure characterization. (7)
- The RfD for chromium (VI) is 0.003 mg/kg/d based on the exposure at which no effects were noted in rats exposed to chromium in the drinking water. (7)
- EPA has low confidence in the RfD based on: low confidence in the study on which the RfD for chromium (VI) was based because a small number of animals were tested, a small number of parameters were measured, and no toxic effects were noted at the highest dose tested; and low confidence in the database because the supporting studies are of equally low quality and developmental endpoints are not well studied. (7)

Chromium III

- Although data from animal studies have identified the respiratory tract as the major target organ for chronic chromium exposure, these data do not demonstrate that the effects observed following inhalation of chromium (VI) particulates are relevant to inhalation of chromium (III). (8)
- EPA has not established an RfC for chromium (III). (8)
- The RfD for chromium (III) is 1.5 mg/kg/d based on the exposure level at which no effects were observed in rats exposed to chromium (III) in the diet. (8)
- EPA has low confidence in the RfD based on: low confidence in the study on which the RfD for chromium (III) was based due to the lack of explicit detail on study protocol and results; and low confidence in the database due to the lack of high-dose supporting data. (8)

Reproductive/Developmental Effects:

Chromium VI

- Limited information on the reproductive effects of chromium (VI) in humans exposed by inhalation suggest that exposure to chromium (VI) may result in complications during pregnancy and childbirth. (1)
- Animal studies have not reported reproductive or developmental effects from inhalation exposure to chromium (VI). Oral studies have reported severe developmental effects in mice such as gross abnormalities and reproductive effects including decreased litter size, reduced sperm count, and degeneration of the outer cellular layer of the seminiferous tubules. (1,4)

Chromium III

- No information is available on the reproductive or developmental effects of chromium (III) in humans. (3)
- A study of mice fed high levels of chromium (III) in their drinking water has suggested a potential for reproductive effects, although various study characteristics preclude a definitive finding. (3)
- No developmental effects were reported in the offspring of rats fed chromium (III) during their developmental period. (1,3)

Cancer Risk:

Chromium VI

- Epidemiological studies of workers have clearly established that inhaled chromium is a human carcinogen, resulting in an increased risk of lung cancer. Although chromium-exposed workers were exposed to both chromium (III) and chromium (VI) compounds, only chromium (VI) has been found to be carcinogenic in animal studies, so EPA has concluded that only chromium (VI) should be classified as a human carcinogen. (1,7)
- Animal studies have shown chromium (VI) to cause lung tumors via inhalation exposure. (1,5)
- EPA has classified chromium (VI) as a Group A, known human carcinogen by the inhalation route of exposure. Carcinogenicity by the oral route of exposure cannot be determined and has been classified by EPA as a Group D. (7)
- EPA uses mathematical models, based on human and animal studies, to estimate the probability of a person developing cancer from breathing air containing a specified concentration of a chemical. EPA calculated an inhalation unit risk estimate of 1.2×10^{-2} $(\mu g/m^3)^{-1}$. EPA estimates that, if an individual were to continuously breathe air containing chromium at an average of 0.00008 $\mu g/m^3$ (8×10^{-8} mg/m^3) over his or her entire lifetime, that person would theoretically have no more than a one-in-a-million increased chance of developing cancer as a direct result of breathing air containing this chemical. Similarly, EPA estimates that continuously breathing air containing 0.0008 $\mu g/m^3$ (8×10^{-7} mg/m^3)

would result in not greater than a one-in-a-hundred thousand increased chance of developing cancer during their lifetime, and air containing 0.008 $\mu g/m^3$ (8×10^{-6} mg/m^3) would result in not greater than a one-in-ten-thousand increased chance of developing cancer during their lifetime. For a detailed discussion of confidence in the potency estimates, please see IRIS. (7)

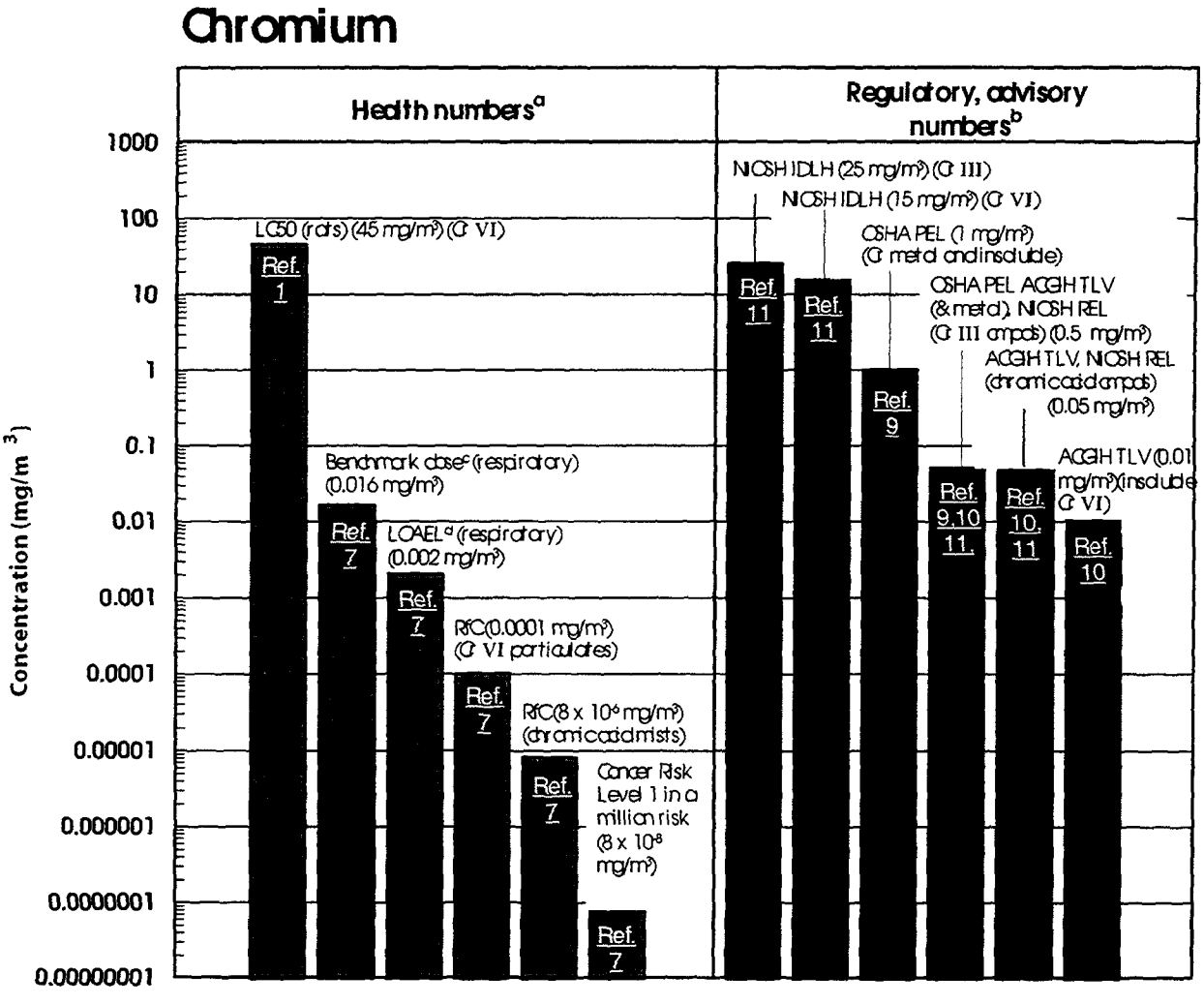
Chromium III

- No data are available on the carcinogenic potential of chromium (III) compounds alone. (1,8)
- EPA has classified chromium (III) as a Group D carcinogen, not classifiable as to carcinogenicity in humans. (8)
- EPA has stated that "the classification of chromium (VI) as a known human carcinogen raises a concern for the carcinogenic potential of chromium (III)." (8)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45).
For chromium: 1 ppm = 2.12 mg/m^3.
To convert from $\mu g/m^3$ to mg/m^3: mg/m^3 = ($\mu g/m^3$) x (1 mg/1,000 μg).

Health Data from Inhalation Exposure



ACGIH TLV – American Conference of Governmental and Industrial Hygienists' threshold limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effects.

LC_{50} (Lethal Concentration$_{50}$) – A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.

LOAEL – Lowest-observed-adverse-affect level.

NIOSH IDLH – National Institute of Occupational Safety and Health's immediately dangerous to life or health concentration; NIOSH recommended exposure limit to ensure that a worker can escape from an exposure condition that is likely to cause death or immediate or delayed permanent adverse health effects or prevent escape from the environment.

NIOSH REL – NIOSH's recommended exposure limit; NIOSH-recommended exposure limit for an 8- or 10-h time-weighted-average exposure and/or ceiling.

OSHA PEL – Occupational Safety and Health Administration's permissible exposure limit

expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.

[a] Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA.
[b] Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the Government or other groups as advice.
[c] The benchmark dose is from the critical study used as the basis for the EPA's RfC for Cr(VI) particulates.
[d] The LOAEL is from the critical study used as the basis for the EPA's RfC for chromic acid mists and dissolved Cr (VI) aerosols.

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COKE OVEN EMISSIONS[1]

Hazard Summary

Exposure to coke oven emissions may occur for workers in the aluminum, steel, graphite, electrical, and construction industries. No information is available on the effects of coke oven emissions in humans from acute (short-term) exposure. Animal studies have reported weakness, depression, shortness of breath, general edema, and effects on the liver from acute oral exposure to coke oven emissions. Chronic (long-term) exposure to coke oven emissions in humans results in conjunctivitis, severe dermatitis, and lesions of the respiratory system and digestive system. No information is available on the reproductive or developmental effects of coke oven emissions in humans or animals. Cancer is the major concern from exposure to coke oven emissions. Epidemiologic studies of coke oven workers have reported an increase in cancer of the lung, trachea, bronchus, kidney, prostate, and other sites. Animal studies have reported tumors of the lung and skin from inhalation exposure to coal tar. The U.S. Environmental Protection Agency (EPA) has classified coke oven emissions as a Group A, known human carcinogen.

Please Note: The main source of information for this fact sheet is EPA's Integrated Risk Information System (IRIS), which contains information on the carcinogenic effects of coke oven emissions including the unit cancer risk for inhalation exposure. Other secondary sources include the Hazardous Substances Data Bank (HSDB), a database of summaries of peer-reviewed literature, and *The Handbook of Toxic and Hazardous Chemicals and Carcinogens,* a reference book that summarizes the key effects from exposure to hazardous chemicals.

Physical Properties

- Coke oven emissions are a mixture of coal tar, coal tar pitch, and creosote and contain chemicals such as benzo(*a*)pyrene, benzanthracene, chrysene, and phenanthrene. (1)
- Condensed coke oven emissions are a brownish, thick liquid or semisolid with a naphthalene-like odor, while uncondensed coke oven emissions are vapors that escape when the ovens are changed and emptied. (2)
- The odor threshold for coke oven emissions is not available. The actual chemical content of the emissions depends on the process variables.

Uses

- Chemicals recovered from coke oven emissions are used as a raw material for plastics, solvents, dyes, drugs, waterproofing, paints, pipecoating, roads, roofing, insulation, and as pesticides and sealants. (2)

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[1] Coke oven emissions include coal tar, creosote, and coal tar pitch.

Sources and Potential Exposure

- Occupational exposure to coke oven emissions may occur for those workers in the aluminum, steel, graphite, electrical, and construction industries. (1)

Assessing Personal Exposure

- No information is available on the assessment of personal exposure to coke oven emissions.

Health Hazard Information

Acute Effects:

- No information is available on the effects of coke oven emissions from acute exposure in humans.
- Animal studies have reported weakness, depression, shortness of breath, general edema, and effects on the liver from acute oral exposure to coke oven emissions. (2)

Chronic Effects (Noncancer):

- Chronic exposure to coke oven emissions in humans results in conjunctivitis, severe dermatitis, and lesions of the respiratory and digestive systems. (2)
- Animal studies have reported effects on the liver from chronic oral exposure to coke oven emissions. (2)
- EPA has not established a reference concentration (RfC) or a reference dose (RfD) for coke oven emissions. (3)

Reproductive/Developmental Effects:

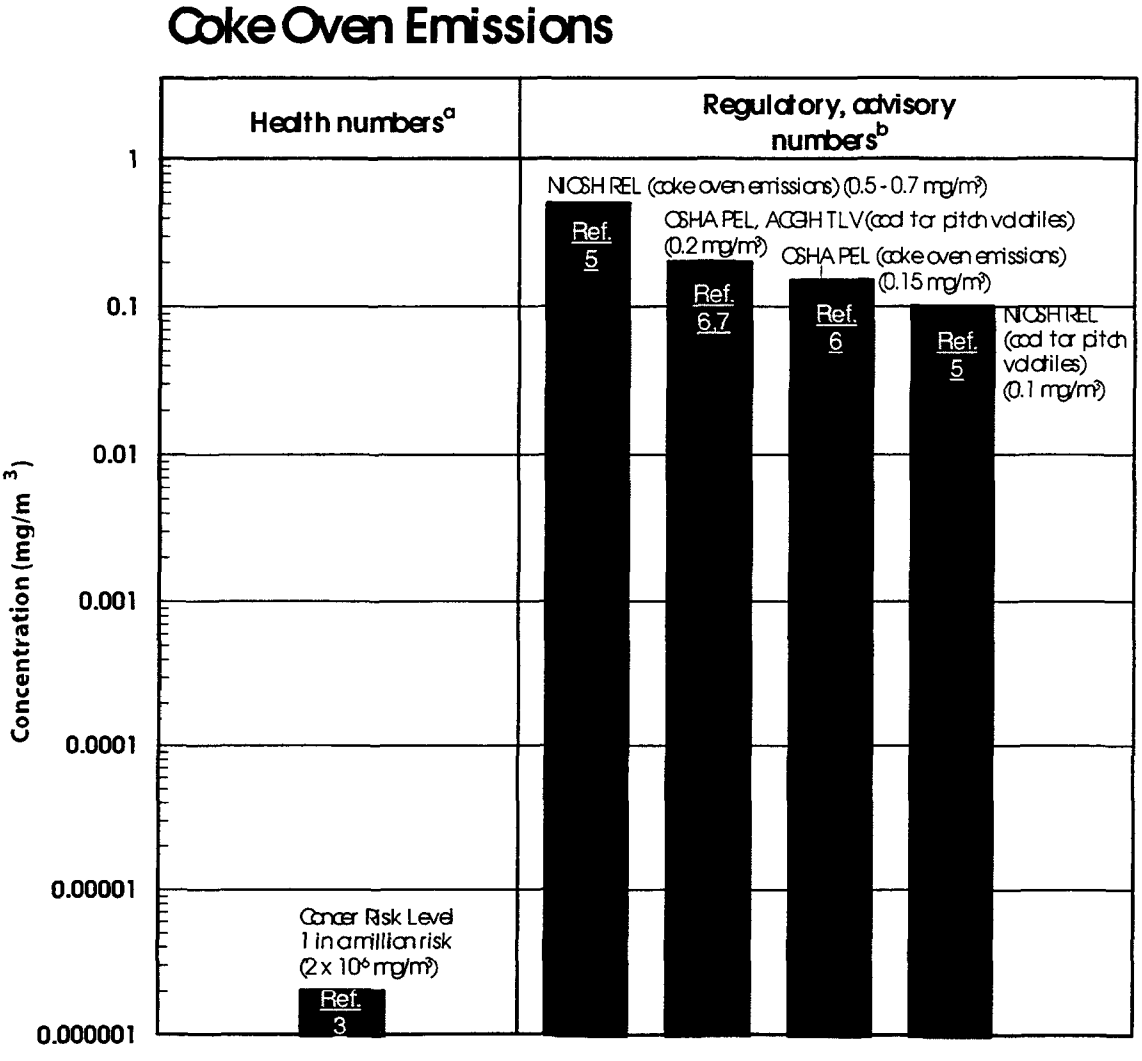
- No information is available on the reproductive or developmental effects of coke oven emissions in humans or animals.

Cancer Risk:

- Epidemiologic studies of coke oven workers have reported an increase in cancer of the lung, trachea, bronchus, kidney, prostate, and other sites. (3)
- Animal studies have reported tumors of the lung and skin from inhalation exposure to coal tar. (3)
- EPA has classified coke oven emissions as a Group A, known human carcinogen. (3)
- EPA uses mathematical models, based on human and animal studies, to estimate the probability of a person developing cancer from breathing air containing a specified concentration of a chemical. EPA calculated an inhalation unit risk estimate of 6.2×10^{-4} $(\mu g/m^3)^{-1}$. EPA estimates that, if an individual were to continuously breathe air containing coke oven emissions at an average of 0.002 $\mu g/m^3$ (2×10^{-6} mg/m^3) over his or her entire

lifetime, that person would theoretically have no more than a one-in-a-million increased chance of developing cancer as a direct result of continuously breathing air containing this chemical. Similarly, EPA estimates that breathing air containing 0.02 $\mu g/m^3$ (2×10^{-5} mg/m^3) would result in not greater than a one-in-a-hundred-thousand increased chance of developing cancer during a lifetime, and air containing 0.2 $\mu g/m^3$ (2×10^{-4} mg/m^3) would result in not greater than a one-in-ten-thousand increased chance of developing cancer during a lifetime. For a detailed discussion of confidence in the potency estimates, please see IRIS. (3)

Health Data from Inhalation Exposure



ACGIH TLV – American Conference of Governmental and Industrial Hygienists' threshold limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effects.

NIOSH REL – National Institute of Occupational Safety and Health's recommended exposure

limit; NIOSH-recommended exposure limit for an 8- or 10-h time-weighted-average exposure and/or ceiling.
OSHA PEL – Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effects averaged over a normal 8-h workday or a 40-h workweek.

[a] Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA.
[b] Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the Government or other groups as advice.

References

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3. U.S. Environmental Protection Agency (EPA). *Integrated Risk Information System (IRIS) on Coke Oven Emissions.* National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1999.

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1,2-DICHLOROETHANE (ETHYLENE DICHLORIDE)

107-06-2

Hazard Summary

Exposure to low levels of 1,2-dichloroethane can occur from breathing ambient or workplace air. Inhalation of concentrated 1,2-dichloroethane vapor can induce effects on the human nervous system, liver, and kidneys, as well as respiratory distress, cardiac arrhythmia, nausea, and vomiting. Similar effects have been reported in animals exposed by inhalation. Clouding of the cornea and eye irritation have been observed in animals. Chronic (long-term) inhalation exposure to 1,2-dichloroethane produced effects on the liver and kidneys in animals. No information is available on the reproductive or developmental effects of 1,2-dichloroethane in humans. Decreased fertility and increased embryo mortality have been observed in inhalation studies of rats. The U.S. Environmental Protection Agency (EPA) has classified 1,2-dichloroethane as a Group B2, probable human carcinogen. Epidemiological studies are not conclusive regarding the carcinogenic effects of 1,2-dichloroethane, due to concomitant exposure to other chemicals. Following treatment by gavage, several tumor types were induced in rats and mice.

Please Note: The main sources of information for this fact sheet are EPA's Integrated Risk Information System (IRIS), which contains information on the carcinogenic effects of 1,2-dichloroethane including the unit cancer risk for inhalation exposure, and the Agency for Toxic Substances and Disease Registry's (ATSDR's) *Toxicological Profile for 1,2-Dichloroethane.*

Physical Properties

- The chemical formula for 1,2-dichloroethane is $C_2H_4Cl_2$, and its molecular weight is 98.96 g/mol. (1)
- 1,2-Dichloroethane occurs as a colorless, oily, heavy liquid that is slightly soluble in water. (1)
- 1,2-Dichloroethane has a pleasant chloroform-like odor, with an odor threshold of 6-10 ppm. (1)
- The vapor pressure for 1,2-dichloroethane is 64 mm Hg at 20 °C, and its log octanol/water partition coefficient (log K_{ow}) is 1.48. (1)

Uses

- 1,2-Dichloroethane is primarily used in the production of vinyl chloride as well as other chemicals. It is used in solvents in closed systems for various extraction and cleaning purposes in organic synthesis. It is also added to leaded gasoline as a lead scavenger. (1)
- It is also used as a dispersant in rubber and plastics, as a wetting and penetrating agent. (1)

- It was formerly used in ore flotation, as a grain fumigant, as a metal degreaser, and in textile and PVC cleaning. (1)

Sources and Potential Exposure

- Inhalation of 1,2-dichloroethane in the ambient or workplace air is generally the main route of human exposure. The compound may be released during its production, storage, use, transport, and disposal. (1)
- Exposure may also occur through the consumption of contaminated water. But usually 1,2-dichloroethane will evaporate quickly into the air from the water or soil. (1)
- The average levels of 1,2-dichloroethane in the air of seven urban locations in 1980-1981 ranged from 0.1 to 1.5 ppb. (1)

Assessing Personal Exposure

- Breath samples may be used to determine whether or not someone has been recently exposed to 1,2-dichloroethane. (1)

Health Hazard Information

Acute Effects:

- Inhaling concentrated 1,2-dichloroethane can be lethal to humans. An occupationally exposed man died from cardiac arrhythmia after acute (short-term) inhalation exposure to concentrated vapors of 1,2-dichloroethane; congestion of the lungs, degenerative changes in the myocardium, and damage to the liver, kidneys, and nerve cells in the brain were also observed. (1)
- Acute inhalation exposure to 1,2-dichloroethane can affect the nervous system, with effects including narcosis, nausea, and vomiting. (1)
- Effects reported in animals exposed by inhalation are similar to those for humans. (1)
- Clouding of the cornea and eye irritation have been observed in animals and are thought to be the result of vapor contact with the eyes. (1)
- Cardiac arrhythmia, pulmonary edema, bronchitis, hemorrhagic gastritis and colitis, depression, and changes in the brain tissue have been reported in humans that ingested large amounts of 1,2-dichloroethane. (1)
- Acute animal tests, such as the LC_{50} and LD_{50} tests in rats, mice, and rabbits, have demonstrated 1,2-dichloroethane to have moderate acute toxicity from inhalation or dermal exposure and moderate to high acute toxicity from oral exposure. (2)

Chronic Effects (Noncancer):

- Chronic inhalation exposure to 1,2-dichloroethane produced effects on the liver and kidneys in animals. (1)

- Some studies have reported changes in the liver and kidneys and effects on the immune system and central nervous system (CNS) in animals chronically exposed by ingestion. (1)
- EPA has not established a reference dose (RfD) or a reference concentration (RfC) for 1,2-dichloroethane. (3)
- ATSDR has established an intermediate oral minimal risk level (MRL) of 0.2 mg/kg/d based on kidney effects in animals. The MRL is an estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk of adverse noncancer health effects over a specified duration of exposure. Exposure to a level above the MRL does not mean that adverse health effects will occur. The MRL is intended to serve as a screening tool. (1)
- ATSDR has established a chronic inhalation MRL of 0.8 mg/m^3 (0.2 ppm) based on liver effects in animals and an acute inhalation MRL of 0.8 mg/m^3 (0.2 ppm) based on immunological effects in animals. (1)
- The California Environmental Protection Agency (CalEPA) has established a chronic reference exposure level of 0.4 mg/m^3 for 1,2-dichloroethane based on liver effects in rats. The CalEPA reference exposure level is a concentration at or below which adverse health effects are not likely to occur. (5)

Reproductive/Developmental Effects:

- No information is available on the reproductive or developmental effects of 1,2-dichloroethane in humans.
- Decreased fertility and increased embryo mortality have been observed in inhalation studies of rats. (1)

Cancer Risk:

- Epidemiological occupational studies could not link exposure to 1,2-dichloroethane specifically with excess cancer incidence. (1)
- An increased incidence of colon and rectal cancer in men over 55 years of age exposed to 1,2-dichloroethane in the drinking water has been reported. However, the study population was concomitantly exposed to other chemicals. (1)
- Following treatment by gavage, several tumor types (including increased incidences of forestomach squamous-cell carcinomas, circulatory system hemangiosarcomas, mammary adenocarcinoma, alveolar/bronchiolar adenomas, endometrial stromal polyps and sarcomas, and hepatocellular carcinomas) were induced in rats and mice. (1,3,4)
- An increased incidence of lung papillomas has been reported in mice after topical application. (1,3)
- EPA has classified 1,2-dichloroethane as a Group B2, probable human carcinogen. (3)
- EPA uses mathematical models, based on human and animal studies, to estimate the probability of a person developing cancer from breathing air containing a specified concentration of a chemical. EPA calculated an inhalation unit cancer risk estimate of 2.6 x 10^{-5} $(\mu g/m^3)^{-1}$. EPA estimates that, if an individual were to continuously breathe air containing 1,2-dichloroethane at an average of 0.04 $\mu g/m^3$ (4 x 10^{-5} mg/m^3) over his or

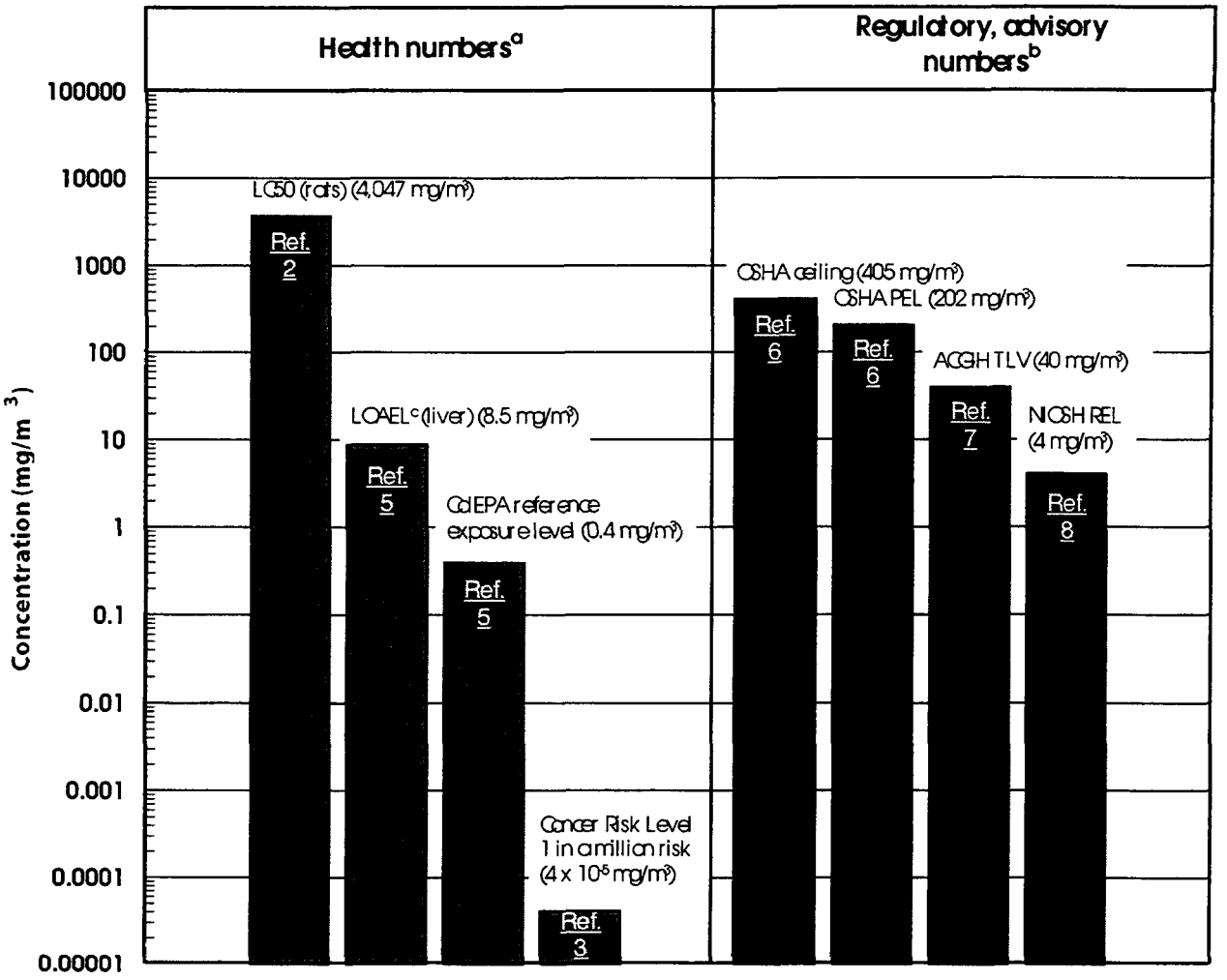
her entire lifetime, that person would theoretically have no more than a one-in-a-million increased chance of developing cancer as a direct result of breathing air containing this chemical. Similarly, EPA estimates that breathing air containing 0.4 $\mu g/m^3$ (4×10^{-4} mg/m^3) would result in not greater than a one-in-a-hundred thousand increased chance of developing cancer, and air containing 4.0 $\mu g/m^3$ (4×10^{-3} mg/m^3) would result in not greater than a one-in-ten thousand increased chance of developing cancer. For a detailed discussion of confidence in the potency estimates, please see IRIS. (3)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45). For 1,2-dichloroethane: 1 ppm = 4.05 mg/m^3. To convert from $\mu g/m^3$ to mg/m^3: mg/m^3 = ($\mu g/m^3$) x (1 mg/1,000 μg).

Health Data from Inhalation Exposure

1,2-Dichloroethane



ACGIH TLV – American Conference of Governmental and Industrial Hygienists' threshold limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effects.

LC_{50} (Lethal Concentration$_{50}$) – A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.

LOAEL – Lowest-observed-adverse-affect level.

NIOSH REL – National Institute of Occupational Safety and Health recommended exposure limit; NIOSH-recommended exposure limit for an 8- or 10-h time-weighted-average exposure and/or ceiling.

OSHA PEL – Occupational Safety and Health Administration's permissible exposure limit

expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.
OSHA PEL ceiling – OSHA's permissible exposure limit ceiling value; the concentration of a substance that should not be exceeded at any time.

[a] Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA.
[b] Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the Government or other groups as advice.
[c] The LOAEL is from the critical study used as the basis for the CalEPA chronic reference exposure level.
[d] These cancer risk estimates were derived from oral data and converted to provide the estimated inhalation risk.

References

1. Agency for Toxic Substances and Disease Registry (ATSDR). *Toxicological Profile for 1,2-Dichloroethane.* Public Health Service, U.S. Department of Health and Human Services, Atlanta, GA. 1992.

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3. U.S. Environmental Protection Agency (EPA). *Integrated Risk Information System (IRIS) on 1,2-Dichloroethane.* National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1999.

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7. American Conference of Governmental Industrial Hygienists (ACGIH). *1999 TLVs and BEIs. Threshold Limit Values for Chemical Substances and Physical Agents. Biological Exposure Indices.* Cincinnati, OH. 1999.

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1,2-DICHLOROPROPANE (PROPYLENE DICHLORIDE)

78-87-5

Hazard Summary

1,2-Dichloropropane is used as a chemical intermediate in several industries. Acute (short-term) inhalation exposure to high levels of 1,2-dichloropropane by humans results in effects on the lungs, gastrointestinal system, blood, liver, kidneys, central nervous system (CNS), and eyes. No information is available on the chronic (long-term) effects of 1,2-dichloropropane in humans, and animal studies have reported effects on the respiratory system and blood from chronic inhalation exposure. Limited information is available on the reproductive or developmental effects of 1,2-dichloropropane in humans. Animal studies have reported reproductive and developmental effects from 1,2-dichloropropane exposure by gavage. No information is available regarding the carcinogenic effects of 1,2-dichloropropane in humans from inhalation or oral exposure. Animal studies have reported an increased incidence of mammary gland tumors in female rats and liver tumors in male and female mice given 1,2-dichloropropane by gavage. The U.S. Environmental Protection Agency (EPA) has provisionally classified 1,2-dichloropropane as a Group B2, probable human carcinogen.

Please Note: The main sources of information for this fact sheet are the Agency for Toxic Substances and Disease Registry's (ATSDR's) *Toxicological Profile for 1,2-Dichloropropane* and EPA's Integrated Risk Information System (IRIS), which contains information on inhalation chronic toxicity of 1,2-dichloropropane and the reference concentration (RfC).

Physical Properties

- The chemical formula for 1,2-dichloropropane is $C_3H_6Cl_2$, and the molecular weight is 112.99 g/mol. (1)
- 1,2-Dichloropropane is a colorless liquid which evaporates quickly at room temperature. (1)
- 1,2-Dichloropropane has a chloroform-like odor and an odor threshold of 0.25 ppm. (1)
- The vapor pressure for 1,2-dichloropropane is 49.67 mm Hg at 25 °C, and it has a log octanol/water partition coefficient (log K_{ow}) of 1.99. (1)
- 1,2-Dichloropropane has a half-life in air ranging from 16 to greater than 23 days. (1)

Uses

- 1,2-Dichloropropane is used as a chemical intermediate in the production of chlorinated organic chemicals, as an industrial solvent, in ion exchange manufacture, in toluene diisocyanate production, in photographic film manufacture, for paper coating, and for petroleum catalyst regeneration. (1)

- 1,2-Dichloropropane was used in the past as a soil fumigant for a variety of crops. This use has been discontinued, and pesticide formulations containing 1,2-dichloropropane are no longer available in the U.S.. (1)

Sources and Potential Exposure

- 1,2-Dichloropropane has been detected at low levels in ambient air, with an average level in air of about 0.022 ppb. (1)
- An early 1980s nationwide survey of water supplies derived from groundwater found that 13 of 945 water supplies contained 1,2-dichloropropane at levels around 1 ppb. (1)
- Occupational exposure to 1,2-dichloropropane may occur during its production, during its use in chemical reactions or as an industrial solvent, or from evaporation from wastewater that contains the chemical. (1)

Assessing Personal Exposure

- Medical tests can detect 1,2-dichloropropane in urine and blood. 1,2-Dichloropropane leaves the body quickly, and thus the tests should be done soon after the exposure. (1)

Health Hazard Information

Acute Effects:

- Acute exposure of humans to very high levels of 1,2-dichloropropane from inhalation and oral exposure results in effects on the gastrointestinal system, blood, liver, kidneys, and CNS. Additional effects noted in humans, from inhalation exposure only, are effects on the lung (chest discomfort, shortness of breath, and cough) and the eyes (conjunctival hemorrhages). (1)
- Animal studies have reported effects on the respiratory system, liver, kidneys, eyes, and CNS from acute inhalation exposure to 1,2-dichloropropane. (1)
- Tests involving acute exposure of animals, such as the LC_{50} and LD_{50} tests in rats, have shown 1,2-dichloropropane to have moderate acute toxicity from inhalation and oral exposure. (1,2)

Chronic Effects (Noncancer):

- No information is available on the effects from chronic exposure to 1,2-dichloropropane in humans from inhalation or oral exposure. (1)
- Chronic animal studies, via inhalation exposure, have reported effects on the respiratory system and blood, while oral animal studies have noted effects on the blood, liver, and CNS. (1,3)
- The RfC for 1,2-dichloropropane is 0.004 mg/m^3 based on hyperplasia of the nasal mucosa in rats. The RfC is an estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious noncancer

effects during a lifetime. It is not a direct estimator of risk but rather a reference point to gauge the potential effects. At exposures increasingly greater than the RfC, the potential for adverse health effects increases. Lifetime exposure above the RfC does not imply that an adverse health effect would necessarily occur. (4)

- EPA has high confidence in the RfC based on: high confidence in the study on which the RfC was based because it used an adequate number of animals, exposure concentrations, and controls, examined three species, focused on known target organs, and the incidence and severity of the nasal lesions were exposure-related, and medium confidence in the database because there are no chronic inhalation studies. (4)
- EPA has not established a reference dose (RfD) for 1,2-dichloropropane. (4)
- ATSDR has established an acute oral minimal risk level (MRL) of 0.1 mg/kg/d based on neurological effects in rats; an intermediate oral MRL of 0.07 mg/kg/d based on hematological effects in rats; and a chronic oral MRL of 0.09 mg/kg/d based on liver effects in mice. The MRL is an estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk of adverse noncancer health effects over a specified duration of exposure. (1)

Reproductive/Developmental Effects:

- A case was reported of a woman who was hospitalized with metrorrhagia (bleeding from the uterus between menstrual periods) after acute inhalation exposure to 1,2-dichloropropane. No other information is available on the reproductive or developmental effects of 1,2-dichloropropane in humans. (1)
- No reproductive effects were noted in several animal inhalation studies. (1)
- Developmental effects, such as an increased incidence of delayed ossification of the bones of the skull, and reproductive effects such as testicular degeneration and increased incidences of infection of the ovary, uterus, or other organs, have been observed in animals exposed to 1,2-dichloropropane by gavage. It is not known if the infections observed were related to 1,2-dichloropropane treatment since controls were also infected. (1)

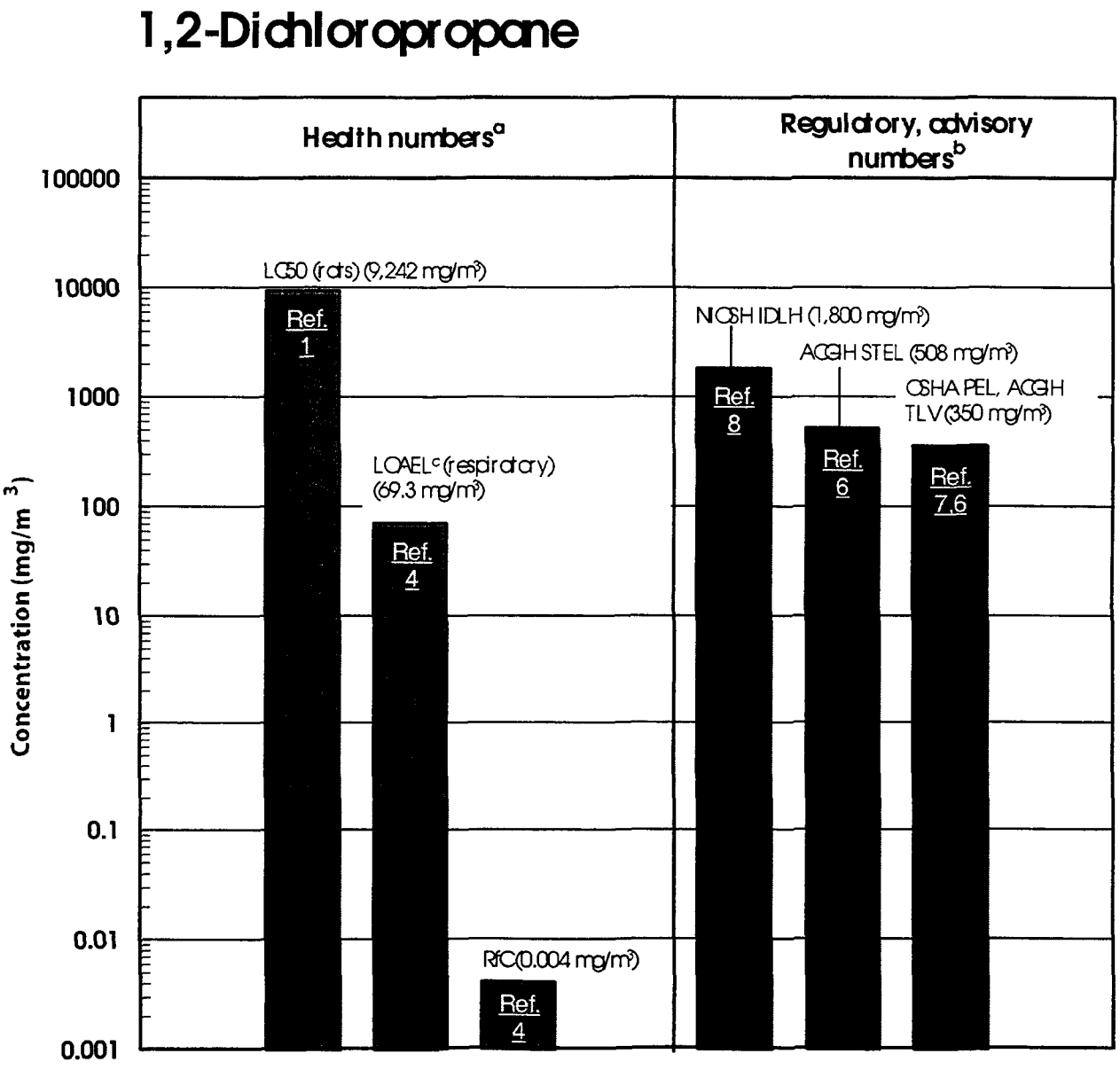
Cancer Risk:

- No studies are available regarding carcinogenic effects in humans from inhalation or oral exposure to 1,2-dichloropropane. (1)
- An increased incidence of mammary gland tumors in female rats and liver tumors in male and female mice were reported in studies in which 1,2-dichloropropane was given by gavage. (1)
- EPA has provisionally classified 1,2-dichloropropane as a Group B2, probable human carcinogen, with an oral cancer slope factor of 6.8×10^{-2} $(mg/kg/d)^{-1}$. (5)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45).
For dichloropropane: 1 ppm = 4.62 mg/m^3.

Health Data from Inhalation Exposure



ACGIH STEL – American Conference of Governmental and Industrial Hygienists' short-term exposure limit; 15-min time-weighted-average exposure that should not be exceeded at any time during a workday even if the 8-h time-weighted-average is within the threshold limit value.

ACGIH TLV – American Conference of Governmental and Industrial Hygienists' threshold limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effects.
LC_{50} (Lethal Concentration$_{50}$) – A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.
LOAEL – Lowest-observed-adverse-effect level.
NIOSH IDLH – National Institute of Occupational Safety and Health's immediately dangerous to life or health concentration; NIOSH recommended exposure limit to ensure that a worker can escape from an exposure condition that is likely to cause death or immediate or delayed permanent adverse health effects or prevent escape from the environment.
OSHA PEL – Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.
[a] Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA.
[b] Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the Government or other groups as advice.
[c] This LOAEL is from the critical study used as the basis for the EPA RfC.

References

1. Agency for Toxic Substances and Disease Registry (ATSDR). *Toxicological Profile for 1,2-Dichloropropane* (Draft). Public Health Service, U.S. Department of Health and Human Services. 1989.

2. U.S. Department of Health and Human Services. Registry of Toxic Effects of Chemical Substances (RTECS, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.

3. U.S. Department of Health and Human Services. Hazardous Substances Data Bank (HSDB, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.

4. U.S. Environmental Protection Agency(EPA). *Integrated Risk Information System (IRIS) on 1,2-Dichloropropane.* National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1999.

5. U.S. Environmental Protection Agency (EPA). *Health Effects Assessment Summary Tables. FY-1997 Update.* National Center for Environmental Assessment, Office of Research and Development, Office of Emergency Response and Remedial Response, Washington, DC. 1997.

6. American Conference of Governmental Industrial Hygienists (ACGIH). *1999 TLVs and BEIs. Threshold Limit Values for Chemical Substances and Physical Agents, Biological Exposure Indices.* Cincinnati, OH. 1999.

7. Occupational Safety and Health Administration (OSHA). Occupational Safety and Health Standards, Toxic and Hazardous Substances. *Code of Federal Regulations.* 29 CFR 1910.1000. 1998.

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1,3-DICHLOROPROPENE

542-75-6

Hazard Summary

1,3-Dichloropropene is used as a component in formulations for soil fumigants. Acute (short-term) inhalation exposure of humans following a spill caused mucous membrane irritation, chest pain, and breathing difficulties. Effects on the lung have been observed in rats acutely exposed to 1,3-dichloropropene by inhalation. Chronic (long-term) dermal exposure may result in skin sensitization in humans. Damage to the nasal mucosa and urinary bladder are the primary health effects of rodents chronically exposed to 1,3-dichloropropene by inhalation. A study of male workers engaged in the manufacture of 1,3-dichloropropene indicated no significant effect on fertility at exposure levels occurring in the work environment. The only developmental effect seen in animal studies was fewer fetuses per litter in rats exposed to high levels by inhalation, and no reproductive effects have been noted. Information on the carcinogenic effects of 1,3-dichloropropene in humans is limited; two cases of histiocytic lymphomas and one case of leukemia have been reported in humans accidentally exposed by inhalation to concentrated vapors during cleanup of a tank truck spill. An increased incidence of bronchioalveolar adenomas has been reported in male mice exposed by inhalation but not in rats or female mice. The U.S. Environmental Protection Agency (EPA) has classified 1,3-dichloropropene as a Group B2, probable human carcinogen.

Please Note: The main sources of information for this fact sheet are EPA's Integrated Risk Information System (IRIS), which contains information on inhalation chronic toxicity of 1,3-dichloropropene and the reference concentration (RfC), oral chronic toxicity and the reference dose (RfD), and the carcinogenic effects of 1,3-dichloropropene, and the Agency for Toxic Substances and Disease Registry's (ATSDR's) *Toxicological Profile for 1,3-Dichloropropene.*

Physical Properties

- The chemical formula for 1,3-dichloropropene is $C_3H_4Cl_2$, and its molecular weight is 110.98 g/mol. (1)
- 1,3-Dichloropropene occurs as a colorless liquid that dissolves in water. (1)
- 1,3-Dichloropropene has a sweet chloroform-like odor, with an odor threshold of 1 ppm. (1)
- The vapor pressure for 1,3-dichloropropene is 34 to 43 mm Hg at 25 °C, and its log octanol/water partition coefficient (log K_{ow}) is 1.60. (1)
- The half-life of 1,3-dichloropropene in ambient air may range from 7 to 50 hours. (1)

Uses

- 1,3-Dichloropropene is the predominant component of several formulations used in agriculture as soil fumigants for parasitic nematodes. (1,4)

Sources and Potential Exposure

- Workers may be occupationally exposed to 1,3-dichloropropene, dermally or by inhalation, during its manufacture, formulation, or application as a soil fumigant. (1, 2)
- The general public may be exposed via inhalation near source areas or from the consumption of contaminated drinking water from wells near some hazardous waste sites. (1,2)

Assessing Personal Exposure

- 1,3-Dichloropropene or its breakdown products can be detected in blood and urine to determine whether or not exposure has occurred. However, metabolites measured in blood and urine are not specific to 1,3-dichloropropene. (1)

Health Hazard Information

Acute Effects:

- Acute inhalation exposure of humans after a tank truck spill resulted in mucous membrane irritation, cough, chest pain, and breathing difficulties. (1)
- Effects on the lung, including emphysema and edema, have been observed in rats acutely exposed to 1,3-dichloropropene by inhalation. (1)
- Lung congestion and hemorrhage, ulcerations of the glandular stomach, hemorrhage of the small intestine, dark and patchy liver, and hemorrhage of the liver have been observed in rats acutely exposed to 1,3-dichloropropene in their diet or via gavage. Neurotoxic effects, including hunched posture, lethargy, ptosis, ataxia, and decreased respiratory rate, have also been observed in orally exposed rats. (1)
- Acute animal tests, such as the LC_{50} and LD_{50} tests in rats, mice, and rabbits, have demonstrated 1,3-dichloropropene to have moderate acute toxicity from inhalation, moderate to high acute toxicity from oral exposure, and high acute toxicity from dermal exposure. (3)

Chronic Effects (Noncancer):

- Chronic dermal exposure may result in skin sensitization in humans. (1)
- Damage to the nasal mucosa and urinary bladder are the primary health effects of rodents chronically exposed to 1,3-dichloropropene by inhalation. Hyperplastic lesions of the upper respiratory tract and degeneration of the olfactory epithelium in the nasal turbinates have been observed in chronically exposed rats and mice. Chronic inhalation exposure of mice has resulted in changes in the urinary bladder. (1,4,5)
- In one study, reversible cloudy swelling of the renal tubular epithelium was reported in rats chronically exposed by inhalation. (1,4,5)
- In rats and mice chronically exposed by inhalation, hyperplasia and hyperkeratosis of the forestomach have been observed, while hyperplasia of the forestomach and of the urinary bladder have resulted from chronic oral exposure. (1,4)

- The RfC for 1,3-dichloropropene is 0.02 mg/m^3 based on hypertrophy/hyperplasia of the nasal respiratory epithelium in mice. The RfC is an estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious noncancer effects during a lifetime. It is not a direct estimator of risk but rather a reference point to gauge the potential effects. At exposures increasingly greater than the RfC, the potential for adverse health effects increases. Lifetime exposure above the RfC does not imply that an adverse health effect would necessarily occur. (5)
- EPA has high confidence in the RfC based on: high confidence in the study on which the RfC was based because it is a well-designed study using two species of animals (both sexes) and including detailed histopathological examinations of numerous tissues with extensive analysis of the respiratory system and corroborative studies performed in both rats and mice have also shown this to be a sensitive endpoint; and high confidence in the database because several studies reported similar effects on the respiratory system at comparable exposure levels, and acute effects observed in humans were similar to the animal effects. (5)
- The RfD for 1,3-dichloropropene is 0.0003 mg/kg/d based on increased organ weights in rats. (5)
- EPA has low confidence in the RfD based on: low confidence in the study on which the RfD was based because it is of low quality and of short duration (90 days), and low confidence in the database because of the remaining studies, only two teratology studies were considered acceptable. (5)

Reproductive/Developmental Effects:

- A study of male workers engaged in the manufacture of 1,3-dichloropropene indicated no significant effect on fertility at exposure levels occurring in the work environment. (4)
- No evidence of developmental toxicity was observed in rats or rabbits exposed to 1,3-dichloropropene by inhalation, but significant maternal toxicity was seen in both species. (4)
- In one study of rats exposed by inhalation, fewer fetuses per litter were reported at the highest exposure concentration. (1)
- In other studies, no adverse reproductive effects were observed in rats and mice exposed by inhalation. (1,5)

Cancer Risk:

- Information on the carcinogenic effects of 1,3-dichloropropene in humans is limited. Two cases of histiocytic lymphomas and one case of leukemia have been reported in emergency response personnel exposed to concentrated 1,3-dichloropropene vapors during cleanup of a tank truck spill. (1,4,5)
- An increased incidence of bronchioalveolar adenomas has been reported in male mice exposed by inhalation but not in rats or female mice. (1,4)

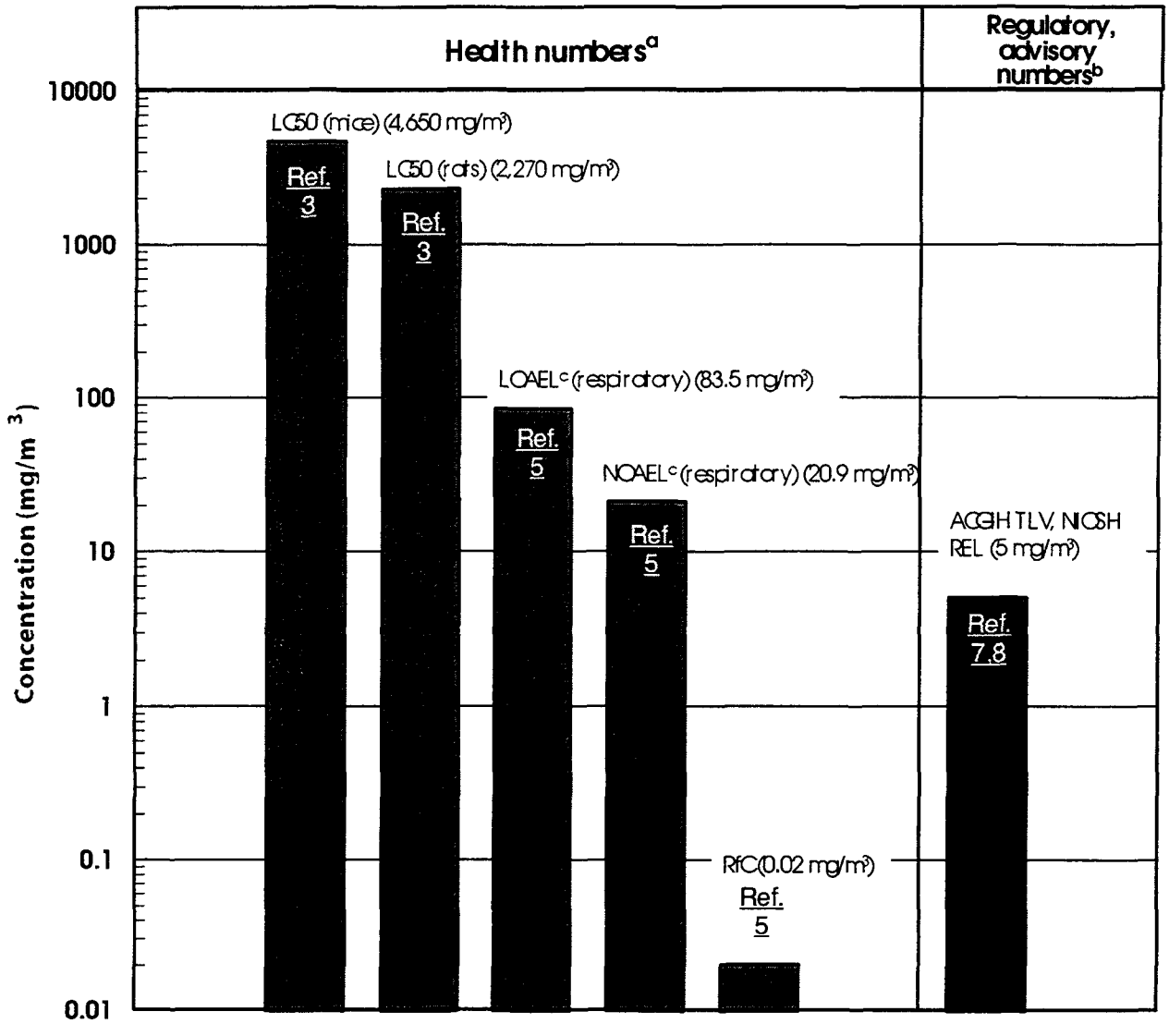
- Forestomach, adrenal and thyroid tumors, and liver nodules in rats and forestomach, urinary bladder, and lung tumors in mice have been observed in rodents exposed to 1,3-dichloropropene via gavage. (1,4,5)
- EPA has classified 1,3-dichloropropene as a Group B2, probable human carcinogen. (5)
- EPA uses mathematical models, based on human and animal studies, to estimate the probability of a person developing cancer from breathing air containing a specified concentration of a chemical. EPA has calculated a provisional inhalation unit risk estimate of $3.7. \times 10^{-5}$ $(\mu g/m^3)^{-1}$. (6)
- EPA has calculated a provisional oral cancer slope factor of 0.18 $(mg/kg/d)^{-1}$. (6)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45).
For 1,3-dichloropropene: 1 ppm = 4.54 mg/m^3.

Health Data from Inhalation Exposure

1,3-Dichloropropene



ACGIH TLV – American Conference of Governmental and Industrial Hygienists' threshold limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effects.

LC_{50} (Lethal Concentration$_{50}$) – A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.

LOAEL – Lowest-observed-adverse-effect level.

NIOSH REL – National Institute of Occupational Safety and Health's recommended exposure limit; NIOSH-recommended exposure limit for an 8- or 10-h time-weighted-average exposure and/or ceiling.

NOAEL – No-observed-adverse-effect level.
OSHA PEL – Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.

[a] Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA.
[b] Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the Government or other groups as advice.
[c] The LOAEL and NOAEL are from the critical study used as the basis for the EPA RfC.

References

1. Agency for Toxic Substances and Disease Registry (ATSDR). *Toxicological Profile for 1,3-Dichloropropene*. Public Health Service, U.S. Department of Health and Human Services. 1992.

2. U.S. Department of Health and Human Services. Hazardous Substances Data Bank (HSDB, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.

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ETHYLENE DIBROMIDE (1,2-DIBROMOETHANE)

106-93-4

Hazard Summary

Exposure to ethylene dibromide primarily occurs from its past use as an additive to leaded gasoline and as a fumigant. Ethylene dibromide is extremely toxic to humans. Changes in the liver and kidney have been noted in humans who died from ingestion of ethylene dibromide. The chronic (long-term) effects of exposure to ethylene dibromide have not been well documented in humans. Animal studies indicate that chronic exposure to ethylene dibromide may result in toxic effects to the liver, kidney, and the testis, irrespective of the route of exposure. Limited data on men occupationally exposed to ethylene dibromide indicate that long-term exposure to ethylene dibromide can impair reproduction by damaging sperm cells in the testicles. Animal studies have demonstrated reproductive and developmental effects from ethylene dibromide exposure. Human data are considered inadequate in providing evidence of cancer by exposure to ethylene dibromide. Several animal studies indicate that long-term exposure to ethylene dibromide increases the incidences of a variety of tumors in rats and mice in both sexes by all routes of exposure. The U.S. Environmental Protection Agency (EPA) has classified ethylene dibromide as a Group B2, probable human carcinogen.

Please Note: The main sources of information for this fact sheet EPA's Integrated Risk Information System (IRIS), which contains information on the carcinogenic effects of ethylene dibromide including the unit cancer risk for inhalation exposure, and the Agency for Toxic Substances and Disease Registry's (ATSDR's) *Toxicological Profile for 1,2-Dibromoethane.*

Physical Properties

- Ethylene dibromide is a colorless liquid with a mild sweet odor, like chloroform. (1,7)
- Ethylene dibromide is slightly soluble in water. (1,7)
- The chemical formula for ethylene dibromide is $C_2H_4Br_2$, and it has a molecular weight of 187.88 g/mol. (1,7)
- The vapor pressure for ethylene dibromide is 11.0 mm Hg at 25 °C, and it has a log octanol/water partition coefficient (log K_{ow}) of 86. (1).
- Ethylene dibromide reacts with hydroxyl radicals in the atmosphere, with a half-life for this reaction of approximately 40 days. In water, its half-life ranges from 2.5 to 13.2 years, and in soil it was detected 19 years after it had been applied. (1)

Uses

- Ethylene dibromide was used in the past as an additive to leaded gasoline; however, since leaded gasoline is now banned, it is no longer used for this purpose. (1)

- Ethylene dibromide was used as a fumigant to protect against insects, pests, and nematodes in citrus, vegetable, and grain crops, and as a fumigant for turf, particularly on golf courses. In 1984, EPA banned its use as a soil and grain fumigant. (1)
- Ethylene dibromide is currently used in the treatment of felled logs for bark beetles and termites, and control of wax moths in beehives. (1)
- Ethylene dibromide is also used as an intermediate for dyes, resins, waxes, and gums. (1)

Sources and Potential Exposure

- Possible sources of ethylene dibromide emissions to the ambient air are production and processing facilities. (1)
- Exposure could occur from inhalation of ambient air near industries that use ethylene dibromide or through the ingestion of contaminated drinking water. (1)

Assessing Personal Exposure

- There is no known reliable medical test to determine whether someone has been exposed to ethylene dibromide. (1)

Health Hazard Information

Acute Effects:

- Clinical signs in humans and animals related to acute inhalation exposure to ethylene dibromide are depression and collapse. Ethylene dibromide is a severe skin irritant that can cause blistering. (1,2)
- Exposure to high concentrations of ethylene dibromide through inhalation, ingestion, or skin contact can result in death. Changes in the liver and kidney are reported in humans who died from ingestion of ethylene dibromide. (1,2)
- Tests involving acute exposure of animals, such as the LD_{50} test in rats, have shown ethylene dibromide to have high acute toxicity from oral exposure, while the LC_{50} test in rats has demonstrated moderate acute toxicity from inhalation exposure. (3)

Chronic Effects (Noncancer):

- The chronic effects of exposure to ethylene dibromide have not been extensively documented in humans. In one case in which a worker breathed ethylene dibromide for several years, he developed bronchitis, headache, and depression. His health improved after he stopped breathing air contaminated with ethylene dibromide. (1,2)
- Animal studies indicate that prolonged exposure to ethylene dibromide may result in toxic effects to the liver, kidney, and the testis whether by inhalation, ingestion, or skin contact. (1,2)
- EPA has not established a reference dose (RfD) or a reference concentration (RfC) for ethylene dibromide. (4)

- EPA has calculated a provisional RfC of 0.0002 mg/m^3 for ethylene dibromide based on reproductive effects in humans. The RfC is an estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious noncancer effects during a lifetime. It is not a direct estimator of risk but rather a reference point to gauge the potential effects. At exposures increasingly greater than the RfC, the potential for adverse health effects increases. Lifetime exposure above the RfC does not imply that an adverse health effect would necessarily occur. The provisional RfC is a value that has had some form of Agency review, but it does not appear on IRIS. (5)

Reproductive Effects/Developmental:

- Developmental effects have not been documented in humans. Limited data on men occupationally exposed to ethylene dibromide indicate that long-term exposure to ethylene dibromide can impair reproduction by damaging sperm cells in the testicles. (1,2)
- Animals that breathed or ate food containing ethylene dibromide for short or long periods were less fertile than control animals or had abnormal sperm. Pregnant animals that were sick from exposure to ethylene dibromide have had pups with birth defects. (1,2)

Cancer Risk:

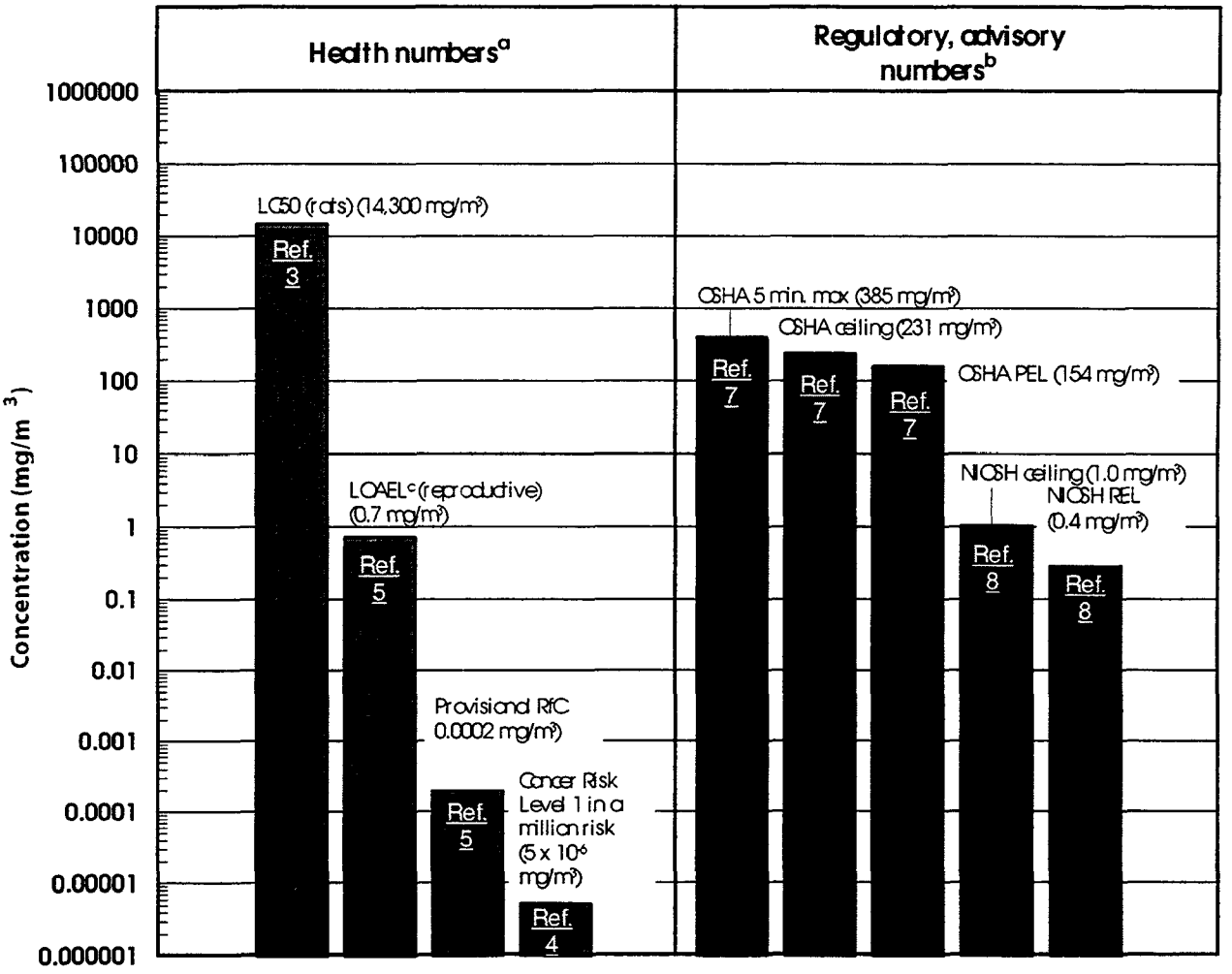
- Two cancer studies on workers exposed to ethylene dibromide have been carried out. Neither study reported a statistically significant increase in cancer mortality; however these studies are considered inadequate due to confounding factors. (4)
- Several animal studies indicate that long-term exposure to ethylene dibromide increases the incidences of a variety of tumors in rats and mice in both sexes by inhalation, by gavage, or by administration to the skin. (4)
- EPA has classified ethylene dibromide as a Group B2, probable human carcinogen. (4)
- EPA uses mathematical models, based on animal studies, to estimate the probability of a person developing cancer from breathing air containing a specified concentration of a chemical. EPA has calculated an inhalation unit risk estimate of 2.2×10^{-4} $(\mu g/m^3)^{-1}$. EPA estimates that, if an individual were to continuously breathe air containing ethylene dibromide at an average of 0.005 $\mu g/m^3$ (5×10^{-6} mg/m^3) over his or her entire lifetime, that person would theoretically have no more than a one-in-a-million increased chance of developing cancer as a direct result of breathing air containing this chemical. Similarly, EPA estimates that continuously breathing air containing 0.05 $\mu g/m^3$ (5×10^{-5} mg/m^3) would result in not greater than a one-in-hundred thousand increased chance of developing cancer, and air containing 0.5 $\mu g/m^3$ (5×10^{-4} mg/m^3) would result in not greater than a one-in-ten thousand increased chance of developing cancer in their lifetime. For a detailed discussion of confidence in the potency estimates, please see IRIS. (4)
- EPA has calculated an oral cancer slope factor of 85 $(mg/kg/d)^{-1}$. (4)

Conversion Factors:

To convert from ppm to mg/m³: mg/m³ = (ppm) x (molecular weight of the compound)/(24.45).
For ethylene dibromide: 1 ppm = 7.7 mg/m³.
To convert from μg/m³ to mg/m³: mg/m³ = (μg/m³) x (1 mg/1,000 μg).

Health Data from Inhalation Exposure

1,2-Dibromoethane



LC_{50} (Lethal Concentration$_{50}$) – A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.
LOAEL – Lowest-observed-adverse-affect level.
NIOSH ceiling – National Institute of Occupational Safety and Health's ceiling limit; NIOSH--recommended 15-min exposure limit, which should not be exceeded.

NIOSH REL – NIOSH's recommended exposure limit; NIOSH-recommended exposure limit for an 8- or 10-h time-weighted-average exposure and/or ceiling.
OSHA PEL – Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.

[a] Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA.
[b] Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the Government or other groups as advice.
[c] The LOAEL is from the critical study used as the basis for the EPA Provisional RfC.

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ETHYLENE OXIDE
75-21-8

Hazard Summary

The major use for ethylene oxide is as a chemical intermediate in industry. The acute (short-term) effects of ethylene oxide in humans consist mainly of central nervous system (CNS) depression and irritation of the eyes and mucous membranes. High concentrations of ethylene oxide produce weakness, nausea, bronchitis, pulmonary edema, emphysema, and death. Chronic (long-term) exposure to ethylene oxide in humans can cause irritation of the eyes, skin, and mucous membranes; and problems in the functioning of the brain and nerves. Limited evidence in both animal and human studies indicate that inhalation exposure to ethylene oxide may result in adverse reproductive effects such as an increased rate of miscarriages. These effects could be seen from acute as well as chronic exposures. Some human cancer data show an increase in the incidence of leukemia, stomach cancer, cancer of the pancreas, and Hodgkin's disease in workers exposed to ethylene oxide. However these data are considered to be limited and inconclusive due to uncertainties in the studies. Ethylene oxide has been shown to cause lung, gland, and uterine tumors in laboratory animals. The U.S. Environmental Protection Agency (EPA) has classified ethylene oxide as a Group B1, probable human carcinogen.

Please Note: The main source of information for this fact sheet is the Agency for Toxic Substances and Disease Registry's (ATSDR's) *Toxicological Profile for Ethylene Oxide*. Other secondary sources include the Hazardous Substances Data Bank (HSDB), a database of summaries of peer-reviewed literature, and the Registry of Toxic Effects of Chemical Substances (RTECS), a database of toxic effects that are not peer reviewed.

Physical Properties

- Ethylene oxide is a colorless gas with a sweet odor. (1,6)
- The chemical formula for ethylene oxide is C_2H_4O and the molecular weight is 44.1 g/mol. (6)
- The vapor pressure for ethylene oxide is 1,095 mm Hg at 20 °C, and it has an octanol/water partition coefficient (log K_{ow}) of -0.30. (6)
- Ethylene oxide is very soluble in water and is flammable. (1)
- Ethylene oxide has an odor threshold of 430 ppm. (7)
- Ethylene oxide has an estimated half-life in air ranging from 69 to 149 days, while its half-life in water is about 50 years. (1).

Uses

- Ethylene oxide is used mainly as a chemical intermediate in the manufacture of textiles, detergents, polyurethane foam, antifreeze, solvents, medicinals, adhesives, and other products. (1)

- Relatively small amounts of ethylene oxide are used as a fumigant, a sterilant for food (spices) and cosmetics, and in hospital sterilization of surgical equipment and plastic devices that cannot be sterilized by steam. (1)

Sources and Potential Exposure

- Sources of ethylene oxide emissions into the air include uncontrolled emissions or venting with other gases in industrial settings. (1)
- Other sources of ethylene oxide air emissions include automobile exhaust and its release from commodity-fumigated materials, as well as its use as a sterilizer of medical equipment. (1)
- The general population may be exposed to ethylene oxide through breathing contaminated air or from smoking tobacco or being in the proximity to someone who is smoking. Certain occupational groups (e.g., workers in ethylene oxide manufacture or processing plants, sterilization technicians, and workers involved in fumigation) may be exposed in the workplace. (1)

Assessing Personal Exposure

- There are tests currently available to determine personal exposure to ethylene oxide, such as the determination of ethylene oxide in the blood or the amount breathed out of the lungs. (1)

Health Hazard Information

Acute Effects:

- Acute inhalation exposure of workers to high levels of ethylene oxide has resulted in nausea, vomiting, neurological disorders, bronchitis, pulmonary edema, emphysema, and even death at very high concentrations. (1,2)
- Dermal or ocular contact with solutions of ethylene oxide has caused irritation of the eyes and skin in humans. (1,2)
- Tests involving acute exposure of animals, such as the LD_{50} test in rats, has shown ethylene oxide to have high acute toxicity from oral exposure. LC_{50} tests in rats, mice, dogs, and guinea pigs have also shown high acute toxicity from ethylene oxide exposure. (3)

Chronic Effects (Noncancer):

- Major effects observed in workers exposed to ethylene oxide at low levels for several years are irritation of the eyes, skin, and mucous membranes and problems in the functioning of the brain and nerves. (1,2)
- There is evidence suggesting that long-term exposure to high levels of ethylene oxide, at a level of 700 ppm, can result in cataracts in humans. (2)

- EPA has not established a reference dose (RfD) or a reference concentration (RfC) for ethylene oxide.
- The California Environmental Protection Agency (CalEPA) has established a chronic reference exposure level of 0.005 mg/m^3 for ethylene oxide based on hematological effects in humans. The CalEPA reference exposure level is a concentration at or below which adverse health effects are not likely to occur. It is not a direct estimator of risk, but rather a reference point to gauge the potential effects. At lifetime exposures increasingly greater than the reference exposure level, the potential for adverse health effects increases. (4)
- ATSDR has an established an intermediate inhalation minimal risk level (MRL) of 0.2 mg/m^3 (0.09 ppm) based on respiratory effects in humans. The MRL is an estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk of adverse noncancer health effects over a specified duration of exposure. (1)

Reproductive/Developmental Effects:

- Some evidence exists indicating that inhalation exposure to ethylene oxide can cause an increased rate of miscarriages in female workers. These effects could be seen from acute, as well as chronic, exposure. (1,2)
- Various adverse reproductive effects have been noted in inhalation exposure studies of animals including decreased number of implantation sites, decreased testicular weights and sperm concentration, and testicular degeneration. (1,2)

Cancer Risk:

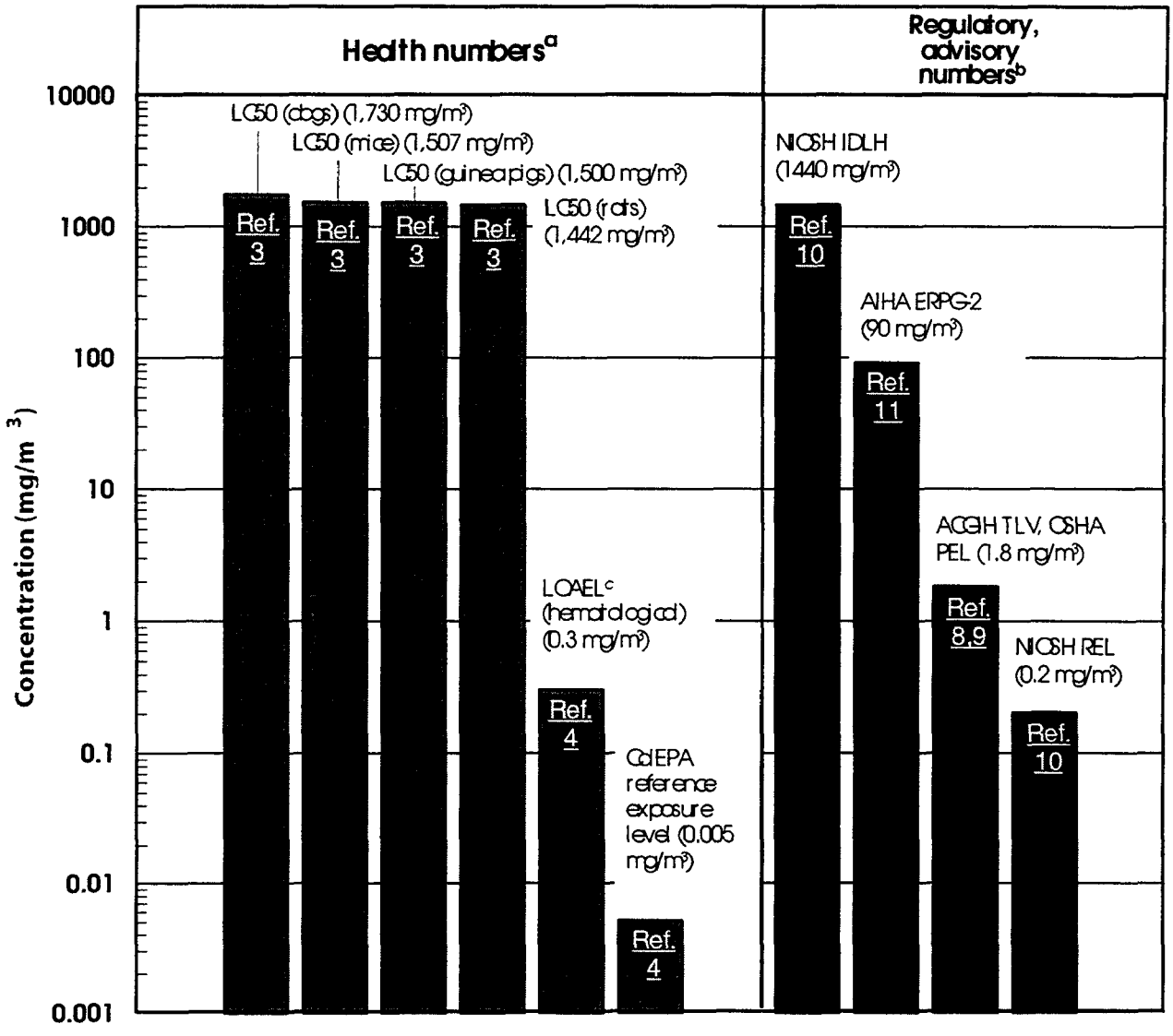
- Human occupational studies have shown elevated cases of leukemia, stomach and pancreatic cancer, and Hodgkin's disease in workers exposed to ethylene oxide by inhalation. However, the data are considered to be limited and inconclusive due to the small number of individuals studied and uncertainties about the exposure levels. (1,2)
- Animal studies have shown lung, gland, and uterine tumors caused by inhalation exposure to ethylene oxide. (1,2)
- EPA has classified ethylene oxide as a Group B1, probable human carcinogen. (5)
- EPA uses mathematical models, based on human and animal studies, to estimate the probability of a person developing cancer from breathing air containing a specified concentration of a chemical. EPA has calculated a provisional inhalation unit cancer risk estimate of 1.0×10^{-4} $(\mu g/m^3)^{-1}$. A provisional value is one that has not received Agencywide review. (5)
- EPA has calculated a provisional oral cancer slope factor of 1.0 $(mg/kg/d)^{-1}$. (5)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45).
For ethylene oxide: 1 ppm = 1.8 mg/m^3.

Health Data from Inhalation Exposure

Ethylene Oxide



ACGIH TLV – American Conference of Governmental and Industrial Hygienists' threshold limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effects.

AIHA ERPG – American Industrial Hygiene Association's emergency response planning guidelines. ERPG 1 is the maximum airborne concentration below which it is believed nearly all individuals could be exposed up to one hour without experiencing other than mild transient adverse health effects or perceiving a clearly defined objectionable odor; ERPG 2 is the maximum airborne concentration below which it is believed nearly all individuals could be exposed up to one hour without experiencing or developing irreversible or other serious health effects that could impair their abilities to take protective action.

LC_{50} (Lethal Concentration$_{50}$) – A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.
LOAEL – Lowest-observed-no-adverse-affect level.
NIOSH IDLH – National Institute of Occupational Safety and Health's immediately dangerous to life or health concentration; NIOSH recommended exposure limit to ensure that a worker can escape from an exposure condition that is likely to cause death or immediate or delayed permanent adverse health effects or prevent escape from the environment.
NIOSH REL – NIOSH's recommended exposure limit; NIOSH-recommended exposure limit for an 8- or 10-h time-weighted-average exposure and/or ceiling.
OSHA PEL – Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.

[a] Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA.
[b] Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the Government or other groups as advice.
[c] The LOAEL is from the critical study used as the basis for the CalEPA chronic reference exposure level.

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FORMALDEHYDE

50-00-0

Hazard Summary

Formaldehyde is used mainly to produce resins used in particle board products and as an intermediate in the synthesis of other chemicals. Exposure to formaldehyde may occur by breathing contaminated indoor air, tobacco smoke, or ambient urban air. Acute (short-term) and chronic (long-term) inhalation exposure to formaldehyde in humans can result in respiratory symptoms, and eye, nose, and throat irritation. Reproductive effects, such as menstrual disorders and pregnancy problems, have been reported in female workers exposed to formaldehyde. Limited human studies have reported an association between formaldehyde exposure and lung and nasopharyngeal cancer. Animal inhalation studies have reported an increased incidence of nasal squamous cell cancer. The U.S. Environmental Protection Agency (EPA) has classified formaldehyde as a Group B2, probable human carcinogen.

Please Note: The main sources of information for this fact sheet are EPA's *Health and Environmental Effects Profile for Formaldehyde* and the Integrated Risk Information System (IRIS), which contains information on oral chronic toxicity and the reference dose (RfD), and the carcinogenic effects of formaldehyde including the unit cancer risk for inhalation exposure.

Physical Properties

- The chemical formula for formaldehyde is CH_2O, and the molecular weight is 30.03 g/mol. (1)
- The vapor pressure for formaldehyde is 10 mm Hg at -88 °C, and its log octanol/water partition coefficient (log K_{ow}) is -0.65. (1)
- Formaldehyde is a colorless gas with a pungent, suffocating odor at room temperature; the odor threshold for formaldehyde is 0.83 ppm. (1,8)
- Formaldehyde is readily soluble in water at room temperature. (1)
- Commercial formaldehyde is produced and sold as an aqueous solution containing 37 to 50 percent formaldehyde by weight. (1)

Uses

- Formaldehyde is used predominantly as a chemical intermediate. It also has minor uses in agriculture, as an analytical reagent, in concrete and plaster additives, cosmetics, disinfectants, fumigants, photography, and wood preservation. (1,2)
- One of the most common uses of formaldehyde in the U.S. is manufacturing urea-formaldehyde resins, used in particle board products. (7)
- Formaldehyde (as urea formaldehyde foam) was extensively used as an insulating material until 1982 when it was banned by the U.S. Consumer Product Safety Commission. (1,2)

Sources and Potential Exposure

- The highest levels of airborne formaldehyde have been detected in indoor air, where it is released from various consumer products such as building materials and home furnishings. One survey reported formaldehyde levels ranging from 0.10 to 3.68 ppm in homes. Higher levels have been found in new manufactured or mobile homes than in older conventional homes. (1)
- Formaldehyde has also been detected in ambient air; the average concentrations reported in U.S. urban areas were in the range of 11 to 20 ppb. The major sources appear to be power plants, manufacturing facilities, incinerators, and automobile exhaust emissions. (7)
- Smoking is another important source of formaldehyde. (1)
- Formaldehyde may also be present in food, either naturally or as a result of contamination. (1)

Assessing Personal Exposure

- Blood levels of formaldehyde can be measured. However, these measurements are only useful when exposure by inhalation to relatively large amounts of formaldehyde has occurred. (2)

Health Hazard Information

Acute Effects:

- The major toxic effects caused by acute formaldehyde exposure via inhalation are eye, nose, and throat irritation and effects on the nasal cavity. (1,2)
- Other effects seen from exposure to high levels of formaldehyde in humans are coughing, wheezing, chest pains, and bronchitis. (1,2)
- Ingestion exposure to formaldehyde in humans has resulted in corrosion of the gastrointestinal tract and inflammation and ulceration of the mouth, esophagus, and stomach. (1,2)
- Acute animal tests, such as the LC_{50} and LD_{50} tests in rats and rabbits have shown formaldehyde to have high acute toxicity from inhalation, oral, and dermal exposure. (3)

Chronic Effects (Noncancer):

- Chronic exposure to formaldehyde by inhalation in humans has been associated with respiratory symptoms and eye, nose, and throat irritation. (1,2,4,5)
- Repeated contact with liquid solutions of formaldehyde has resulted in skin irritation and allergic contact dermatitis. (5)
- Animal studies have reported effects on the nasal respiratory epithelium and lesions in the respiratory system from chronic inhalation exposure to formaldehyde. (1,2,4,5)

- The RfD for formaldehyde is 0.2 mg/kg/d based on a decrease in body weight gain and effects on the stomach in rats. The RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious noncancer effects during a lifetime. It is not a direct estimator of risk but rather a reference point to gauge the potential effects. At exposures increasingly greater than the RfD, the potential for adverse health effects increases. Lifetime exposure above the RfD does not imply that an adverse health effect would necessarily occur. (6)
- EPA has high confidence in the study on which the RfD was based since it consisted of an adequate number of animals of both sexes, as well as a thorough examination of toxicological and histological parameters; medium confidence in the database as several additional chronic bioassays and reproductive and developmental studies support the critical effect and study; and, consequently, medium confidence in the RfD. (6)
- EPA has not established a reference concentration (RfC) for formaldehyde. (6)
- The Agency for Toxic Substances and Disease Registry (ATSDR) has established a chronic inhalation minimal risk level (MRL) of 0.003 ppm (0.004 mg/m^3) based on respiratory effects in humans. The MRL is an estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk of adverse noncancer health effects over a specified duration of exposure. (7)

Reproductive/Developmental Effects:

- An increased incidence of menstrual disorders were observed in female workers using urea-formaldehyde resins. However, possible confounding factors were not evaluated in this study. (1,2)
- A study of hospital workers who sterilize equipment did not report an association between formaldehyde exposure and increased spontaneous abortions. (1,2)
- Developmental effects, such as birth defects, have not been observed in animal studies with formaldehyde. (1,2)

Cancer Risk:

- Occupational studies have noted statistically significant associations between exposure to formaldehyde and increased incidence of lung and nasopharyngeal cancer. This evidence is considered to be "limited," rather than "sufficient," due to possible exposure to other agents that may have contributed to the excess cancers. (1,6)
- Animal studies have reported an increased incidence of nasal squamous cell carcinomas by inhalation exposure. (1,6)
- EPA has classified formaldehyde as a Group B1, probable human carcinogen. (6)
- EPA uses mathematical models, based on human and animal studies, to estimate the probability of a person developing cancer from breathing air containing a specified concentration of a chemical. EPA calculated an inhalation unit risk estimate of 1.3×10^{-5} $(\mu g/m^3)^{-1}$. EPA estimates that, if an individual were to continuously breathe air containing formaldehyde at an average of 0.08 $\mu g/m^3$ (8.0×10^{-5} mg/m^3) over his or her entire lifetime, that person would theoretically have no more than a one-in-a-million increased

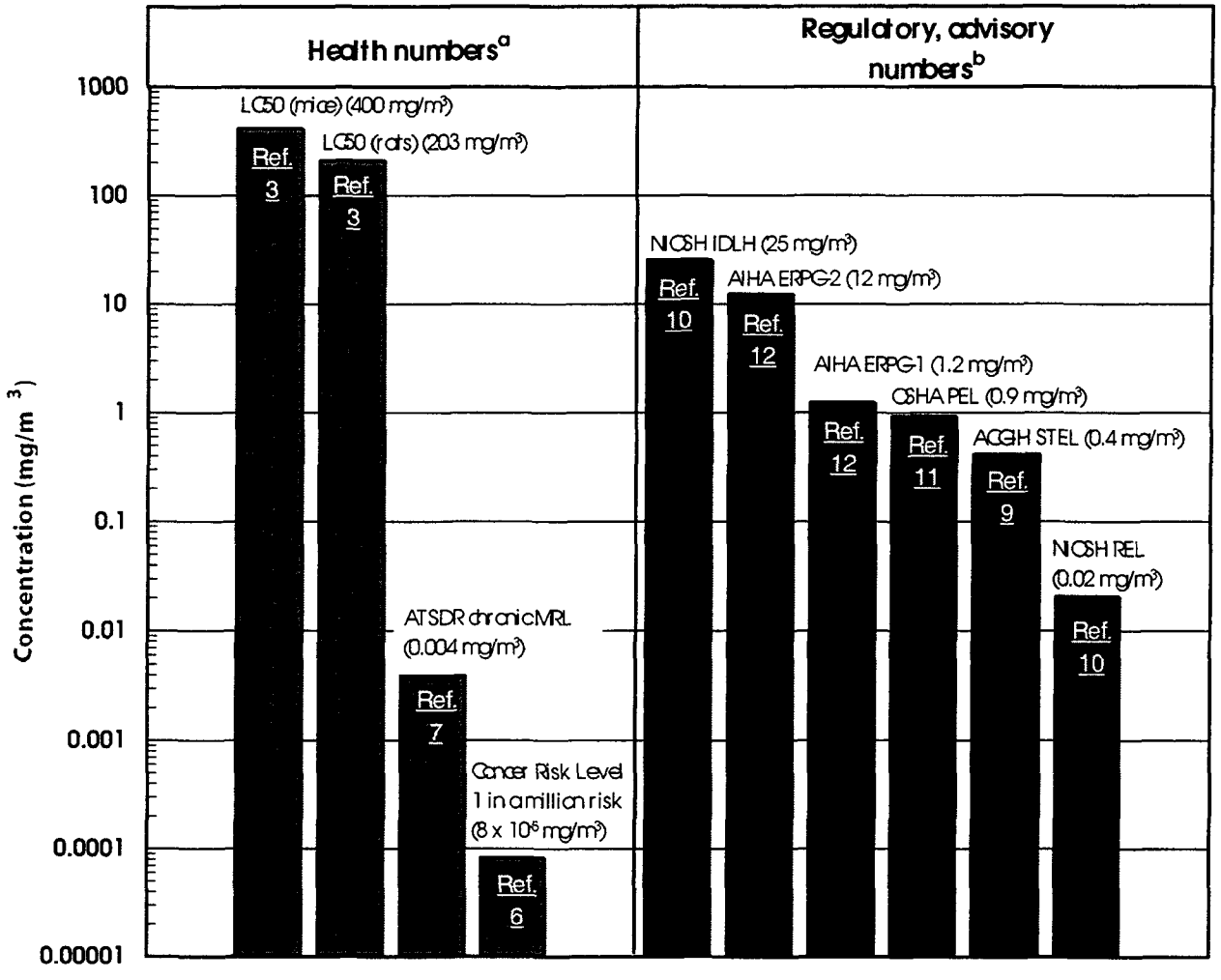
chance of developing cancer as a direct result of breathing air containing this chemical. Similarly, EPA estimates that breathing air containing 0.8 $\mu g/m^3$ (8.0×10^{-4} mg/m^3) would result in not greater than a one-in-a-hundred thousand increased chance of developing cancer, and air containing 8.0 $\mu g/m^3$ (8.0×10^{-3} mg/m^3) would result in not greater than a one-in-ten-thousand increased chance of developing cancer. For a detailed discussion of confidence in the potency estimates, please see IRIS. (6)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45). For formaldehyde: 1 ppm = 1.23 mg/m^3.

Health Data from Inhalation Exposure

Formaldehyde



AIHA ERPG – American Industrial Hygiene Association's emergency response planning guidelines. ERPG 1 is the maximum airborne concentration below which it is believed nearly all individuals could be exposed up to one hour without experiencing other than mild transient adverse health effects or perceiving a clearly defined objectionable odor; ERPG 2 is the maximum airborne concentration below which it is believed nearly all individuals could be exposed up to one hour without experiencing or developing irreversible or other serious health effects that could impair their abilities to take protective action.

ACGIH STEL – American Conference of Governmental and Industrial Hygienists' short-term exposure limit expressed as a time-weighted average exposure; the concentration of a substance which should not be exceeded at any time during a workday.

LC_{50} (Lethal Concentration$_{50}$) – A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined

experimental animal population.
NIOSH IDLH – National Institute of Occupational Safety and Health's immediately dangerous to life or health limit; NIOSH recommended exposure limit to ensure that a worker can escape from an exposure condition that is likely to cause death or immediate or delayed permanent adverse health effects or prevent escape from the environment.
NIOSH REL – NIOSH's recommended exposure limit; NIOSH recommended exposure limit for an 8- or 10-h time-weighted average exposure and/or ceiling.
OSHA PEL – Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.

[a] Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA.
[b] Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the Government or other groups as advice.

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HEXACHLOROBENZENE
118-74-1

Hazard Summary

Hexachlorobenzene is formed as a byproduct during the manufacture of other chemicals. It was widely used as a pesticide until 1965. Chronic (long-term) oral exposure to hexachlorobenzene in humans results in a liver disease with associated skin lesions. Animal studies have reported effects on the liver, skin, kidneys, immune system, and blood from chronic oral exposure to hexachlorobenzene. Hexachlorobenzene may cause developmental effects in humans and has been found to decrease the survival rates of newborn animals. Epidemiologic studies of persons orally exposed to hexachlorobenzene have not shown an increased cancer incidence. However, based on animal studies that have reported cancer of the liver, thyroid, and kidney from oral exposure to hexachlorobenzene, the U.S. Environmental Protection Agency (EPA) has classified hexachlorobenzene as a Group B2, probable human carcinogen. Very little inhalation data are available.

Please Note: The main sources of information for this fact sheet are EPA's Integrated Risk Information System (IRIS), which contains information on oral chronic toxicity and the reference dose (RfD), and the carcinogenic effects of hexachlorobenzene including the unit cancer risk for inhalation exposure, and the Agency for Toxic Substances and Disease Registry's (ATSDR's) *Toxicological Profile for Hexachlorobenzene.*

Physical Properties

- Hexachlorobenzene is a white crystalline solid that is not very soluble in water. (1)
- The odor threshold for hexachlorobenzene is not available.
- The chemical formula for hexachlorobenzene is C_6Cl_6, and the molecular weight is 284.8 g/mol. (1)
- The vapor pressure for hexachlorobenzene is 1.09×10^{-5} mm Hg at 20 °C, and it has a log octanol/water partition coefficient (log K_{ow}) of 6.18. (1)

Uses

- There are currently no commercial uses of hexachlorobenzene in the U.S.. (1)
- Hexachlorobenzene was used as a pesticide until 1965 and was also used in the production of rubber, aluminum, and dyes and in wood preservation. (1)
- Hexachlorobenzene is currently formed as a byproduct during the manufacture of other chemicals (mainly solvents) and pesticides. (1)

Sources and Potential Exposure

- Inhalation exposure to hexachlorobenzene may occur through proximity to industrial sites where it is formed as a byproduct or to waste facilities where it is disposed. (1)

- Occupational exposure, via inhalation and dermally, can occur at industries where hexachlorobenzene is produced as a byproduct. (1)
- Exposure to hexachlorobenzene can also occur through consuming foods tainted with hexachlorobenzene. (1)
- Hexachlorobenzene has been listed as a pollutant of concern in EPA's Great Waters Program due to its persistence in the environment, potential to bioaccumulate, and toxicity to humans and the environment (2).

Assessing Personal Exposure

- Medical tests can measure levels of hexachlorobenzene in the fat or blood. (1)

Health Hazard Information

Acute Effects:

- No information is available on the acute (short-term) effects of hexachlorobenzene in humans. (1,3)
- Acute animal tests, such as the LD_{50} tests in rats and mice, have shown hexachlorobenzene to have low-to-moderate acute toxicity from oral exposure. (4)

Chronic Effects (Noncancer):

- Humans who ingested hexachlorobenzene in heavily contaminated bread during a 4-year poisoning incident were sickened with a liver disease with associated skin lesions (porphyria cutanea tarda). (1)
- Animal studies have reported effects on the liver, skin, immune system, kidneys, and blood from chronic oral exposure to hexachlorobenzene. (1,3)
- Very little data are available on the health effects of hexachlorobenzene in humans or animals following inhalation exposure.
- EPA has determined that there are inadequate data to establish a reference concentration (RfC) for hexachlorobenzene. (5)
- The California Environmental Protection Agency (CalEPA) has established a chronic inhalation reference exposure level of 0.003 mg/m^3 for hexachlorobenzene. The CalEPA reference exposure level is a concentration at or below which adverse health effects are not likely to occur. It is not a direct estimator of risk but rather a reference point to gauge the potential effects. At lifetime exposures increasingly greater than the reference exposure level, the potential for adverse health effects increases. (6)
- The RfD for hexachlorobenzene is 0.0008 mg/kg/d based on liver effects in rats. The RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious noncancer effects during a lifetime. (5)
- EPA has medium confidence in the study used as the basis for the RfD because it had an unusual dosing scheme making it difficult to determine the true doses received by each

experimental group; high confidence in the database due to the extensive number of quality research studies available; and consequently medium confidence in the RfD. (5)

Reproductive/Developmental Effects:

- One human study reported abnormal physical development in young children who ingested contaminated bread during a 4-year poisoning incident. (1)
- Hexachlorobenzene has been found to decrease the survival rates of newborn animals and to cross the placenta and accumulate in fetal tissue in several animal species. (3)
- Neurological, teratogenic, liver, and immune system effects have been reported in the offspring of animals orally exposed to hexachlorobenzene while they were pregnant. (1)

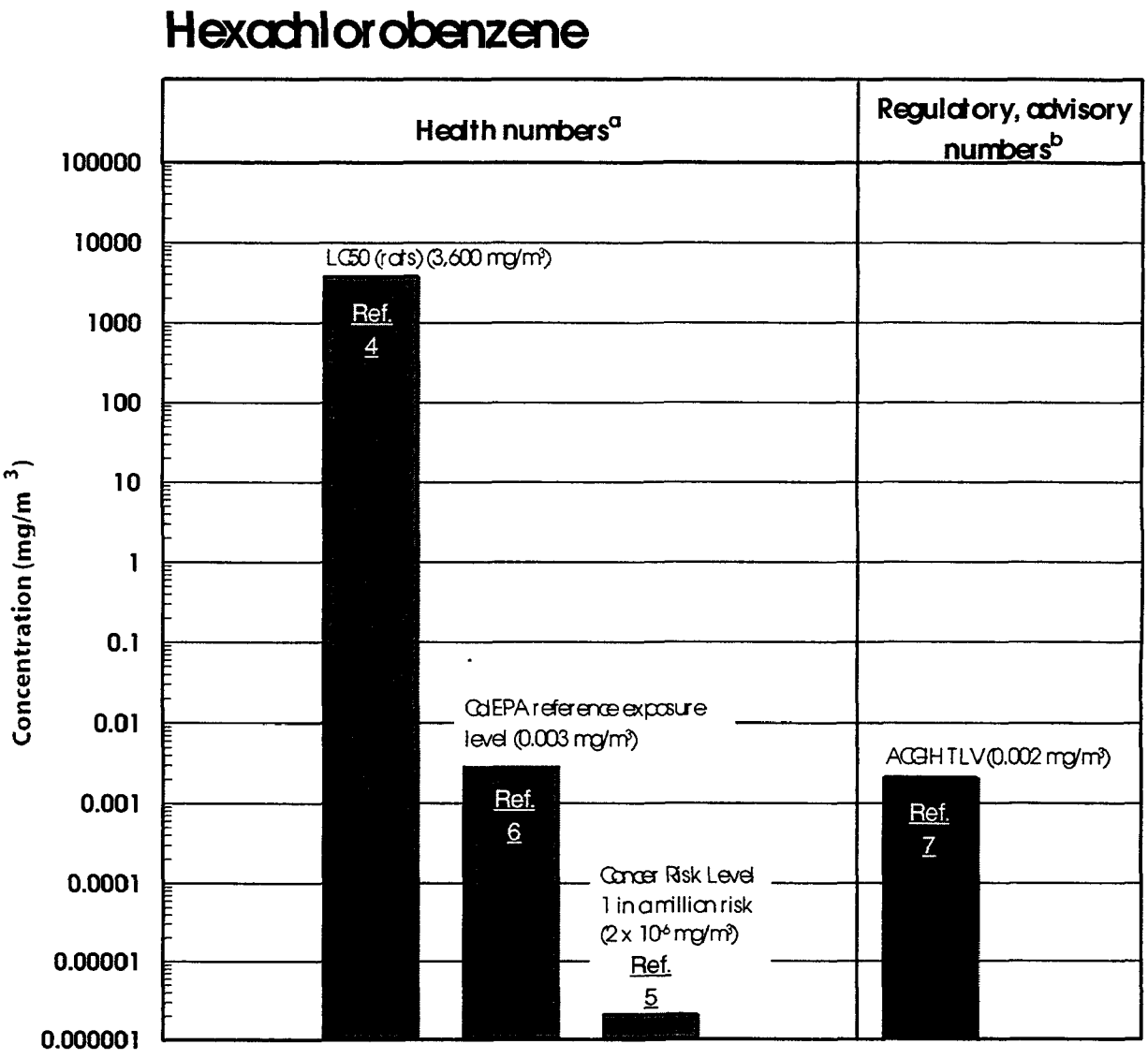
Cancer Risk:

- Human data regarding the carcinogenic effects of hexachlorobenzene are inadequate. (5)
- Hexachlorobenzene, when administered orally, has been shown to induce tumors of the liver, thyroid, and kidney in several animal species. (1,3,5)
- EPA has classified hexachlorobenzene as a Group B2, probable human carcinogen. (5)
- EPA uses mathematical models, based on human and animal studies to estimate the probability of a person developing cancer from breathing air containing a specified concentration of a chemical. EPA calculated an inhalation unit risk estimate of 4.6×10^{-4} $(\mu g/m^3)^{-1}$. EPA estimates that, if an individual were to continuously breathe air containing hexachlorobenzene at an average of 0.002 $\mu g/m^3$ (2.0×10^{-6} mg/m^3) over his or her entire lifetime, that person would theoretically have no more than a one-in-a-million increased chance of developing cancer as a direct result of breathing air containing this chemical. Similarly, EPA estimates that breathing air containing 0.02 $\mu g/m^3$ (2.0×10^{-5} mg/m^3) would result in not greater than a one-in-a-hundred thousand increased chance of developing cancer, and air containing 0.2 $\mu g/m^3$ (2.0×10^{-4} mg/m^3) would result in not greater than a one-in-ten thousand increased chance of developing cancer. For a detailed discussion of confidence in the potency estimates, please see IRIS. (5)
- EPA has calculated an oral cancer slope factor of $1.6\ (mg/kg/d)^{-1}$. (5)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45).
For hexachlorobenzene: 1 ppm = 11.6 mg/m^3.

Health Data from Inhalation Exposure



ACGIH TLV – American Conference of Governmental and Industrial Hygienists' threshold limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effects.

LC_{50} (Lethal Concentration$_{50}$) – A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.

[a] Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA.

[b] Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the Government or other groups as advice.

[c] These cancer risk estimates were derived from oral data and converted to provide the estimated inhalation risk.

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HYDRAZINE

302-01-2

Hazard Summary

Individuals may be exposed to hydrazine in the workplace or to small amounts in tobacco smoke. Symptoms of acute (short-term) exposure to high levels of hydrazine may include irritation of the eyes, nose, and throat, dizziness, headache, nausea, pulmonary edema, seizures, and coma in humans. Acute exposure can also damage the liver, kidneys, and central nervous system (CNS) in humans. The liquid is corrosive and may produce dermatitis from skin contact. Effects to the lungs, liver, spleen, and thyroid have been reported in animals chronically (long-term) exposed to hydrazine via inhalation. Exposure of rodents to hydrazine has resulted in fetotoxicity and damage to reproductive organs. Increased incidences of lung and liver tumors have been observed in mice exposed to hydrazine. Tumors in the nasal cavity were observed in rats and hamsters exposed by inhalation. The U.S. Environmental Protection Agency (EPA) has classified hydrazine as a Group B2, probable human carcinogen.

Please Note: The main sources of information for this fact sheet are EPA's Integrated Risk Information System (IRIS), which contains information on the carcinogenic effects of hydrazine including the unit cancer risk for inhalation exposure, EPA's *Health and Environmental Effects Profile for Hydrazine,* and the Agency for Toxic Substances and Disease Registry's (ATSDR's) *Toxicological Profile for Hydrazines.*

Physical Properties

- The chemical formula for hydrazine is H_4N_2, and its molecular weight is 32.05 g/mol. (6)
- Hydrazine occurs as a colorless, oily, flammable liquid that is miscible with water. (6,8)
- Hydrazine has a penetrating odor, resembling that of ammonia, with an odor threshold of 3.7 ppm. (8,9)
- The vapor pressure for hydrazine is 14.4 mm Hg at 25 °C, and its log octanol/water partition coefficient (log K_{ow}) is 0.08. (6)

Uses

- Hydrazine is used in agricultural chemicals (pesticides), chemical blowing agents, pharmaceutical intermediates, photography chemicals, boiler water treatment for corrosion protection, textile dyes, and as fuel for rockets and spacecraft. (4,6,8,10)

Sources and Potential Exposure

- Individuals may be occupationally exposed to hydrazine in the workplace. (1,2,10)
- Accidental discharge into water, air, and soil may occur during storage, handling, transport, and improper waste disposal. However, hydrazine rapidly degrades in the environment and is rarely encountered. (2,3)

- Small amounts of hydrazine have been detected in tobacco smoke. (2,10)

Assessing Personal Exposure

- Hydrazine may be detected in the blood of exposed individuals. (1,2)

Health Hazard Information

Acute Effects:

- Symptoms of acute exposure to high levels of hydrazine include irritation of the eyes, nose, and throat, temporary blindness, dizziness, headache, nausea, pulmonary edema, seizures, and coma in humans. Acute exposure can also damage the liver, kidneys, and the CNS in humans. (2-4)
- The liquid is corrosive and may produce chemical burns and severe dermatitis from skin contact. (1,4)
- Acute animal tests, such as the LC_{50} and LD_{50} tests in rats, mice, rabbits, and guinea pigs, have demonstrated hydrazine to have high acute toxicity from inhalation and ingestion and extreme acute toxicity from dermal exposure. (5)

Chronic Effects (Noncancer):

- Information is not available on the chronic effects of hydrazine in humans.
- In animals chronically exposed to hydrazine by inhalation, effects on the respiratory system, liver, spleen, and thyroid have been observed. (10)
- EPA has not established a reference concentration (RfC) or a reference dose (RfD) for hydrazine. (4)
- The California Environmental Protection Agency (CalEPA) has calculated a chronic inhalation reference exposure level of 0.0002 mg/m^3 based on liver and thyroid effects in hamsters. The CalEPA reference exposure level is a concentration at or below which adverse health effects are not likely to occur. It is not a direct estimator of risk but rather a reference point to gauge the potential effects. At lifetime exposures increasingly greater than the reference exposure level, the potential for adverse health effects increases. (11)
- ATSDR has calculated an intermediate inhalation minimal risk level (MRL) of 0.005 mg/m^3 (0.004 ppm) based on liver effects in mice. The MRL is an estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk of adverse noncancer health effects over a specified duration of exposure. (10)

Reproductive/Developmental Effects:

- Information is not available on the reproductive or developmental effects of hydrazine in humans.
- Data regarding developmental effects in animals are limited to a study in which hydrazine injected into pregnant rats resulted in fetotoxicity including increased fetal and neonatal mortality. (6,10)

- Inhalation of hydrazine for a year resulted in effects to the ovaries, endometrium, and uterus in female rats and to the testes in male hamsters. (10)

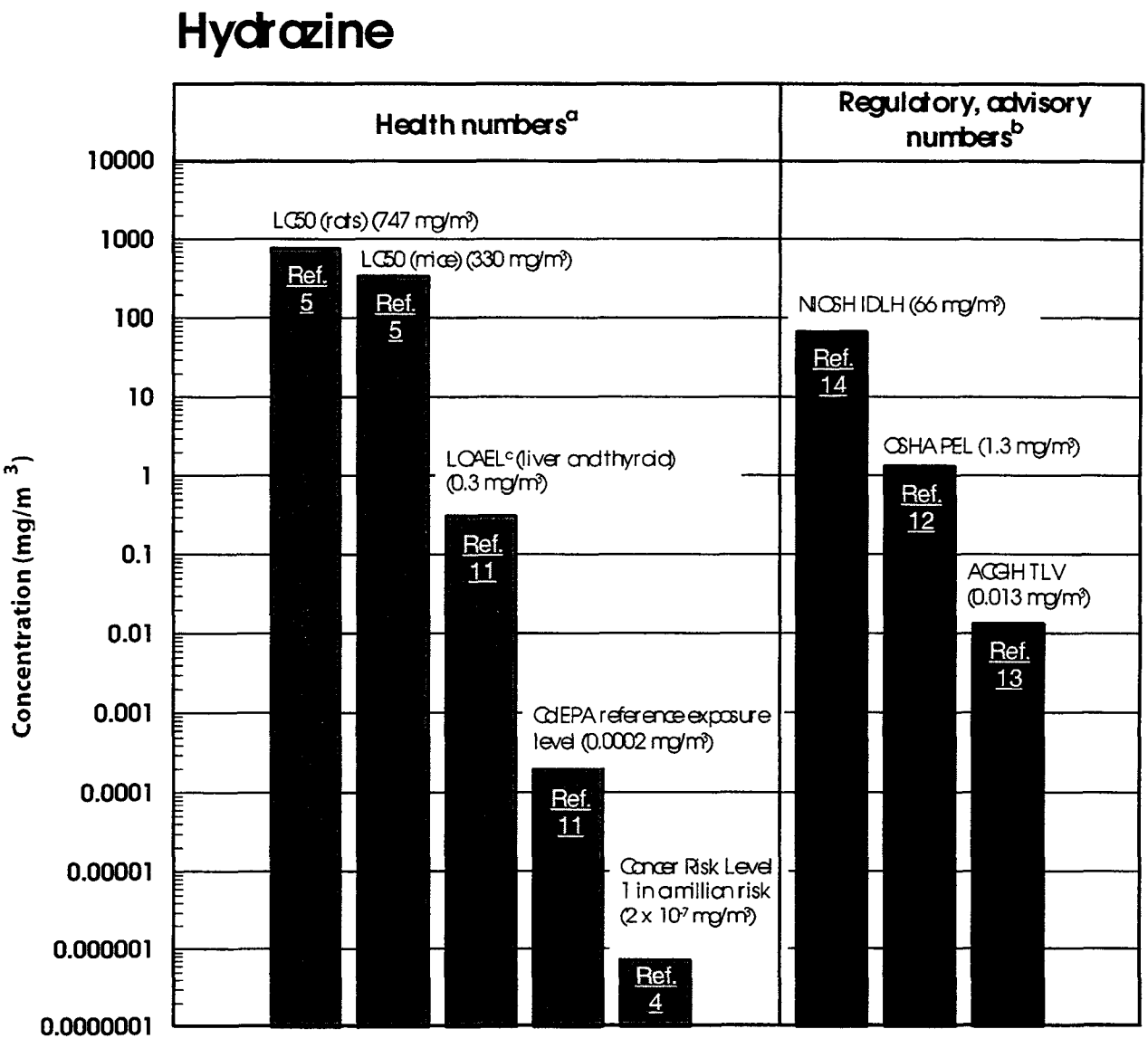
Cancer Risk:

- Adequate information is not available on the carcinogenic effects of hydrazine in humans. (4)
- Increased incidences of lung and liver tumors have been observed in mice exposed to hydrazine by inhalation, in their drinking water, via gavage and injection. Tumors in the nasal cavity were observed in rats and hamsters exposed by inhalation. (4,6,7)
- EPA has classified hydrazine as a Group B2, probable human carcinogen. (4)
- EPA uses mathematical models, based on human and animal studies, to estimate the probability of a person developing cancer from breathing air containing a specified concentration of a chemical. EPA calculated an inhalation unit risk estimate of 4.9×10^{-3} $(\mu g/m^3)^{-1}$. EPA estimates that, if an individual were to continuously breathe air containing hydrazine at an average of 0.0002 $\mu g/m^3$ (2.0×10^{-7} mg/m^3) over his or her entire lifetime, that person would theoretically have no more than a one-in-a-million increased chance of developing cancer as a direct result of breathing air containing this chemical. Similarly, EPA estimates that breathing air containing 0.002 $\mu g/m^3$ (2.0×10^{-6} mg/m^3) would result in not greater than a one-in-a-hundred thousand increased chance of developing cancer, and air containing 0.02 $\mu g/m^3$ (2.0×10^{-5} mg/m^3) would result in not greater than a one-in-ten thousand increased chance of developing cancer. For a detailed discussion of confidence in the potency estimates, please see IRIS. (4)
- EPA has calculated an oral cancer slope factor of 3.0 $(mg/kg/d)^{-1}$. (4)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45).
For hydrazine: 1 ppm = 1.31 mg/m^3.

Health Data from Inhalation Exposure



ACGIH TLV – American Conference of Governmental and Industrial Hygienists' threshold limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effects.

LC_{50} (Lethal Concentration$_{50}$) – A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.

LOAEL – Lowest-observed-adverse-effect level

NIOSH IDLH – National Institute of Occupational Safety and Health's immediately dangerous to life or health limit; NIOSH recommended exposure limit to ensure that a worker can escape from an exposure condition that is likely to cause death or immediate or delayed permanent adverse health effects or prevent escape from the environment.

OSHA PEL – Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.

[a] Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA.
[b] Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the Government or other groups as advice.
[c] The LOAEL is from the critical study used as the basis for the CalEPA chronic reference exposure level.

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LEAD COMPOUNDS[1]

Hazard Summary

Lead is used in the manufacture of batteries, metal products, paints, and ceramic glazes. Exposure to lead can occur from breathing contaminated workplace air or dust or eating lead-based paint chips or contaminated dirt. Lead is a very toxic element, causing a variety of effects at low dose levels. Brain damage, kidney damage, and gastrointestinal distress are seen from acute (short-term) exposure to high levels of lead in humans. Chronic (long-term) exposure to lead in humans results in effects on the blood, central nervous system (CNS), blood pressure, kidneys, and Vitamin D metabolism. Children are particularly sensitive to the chronic effects of lead, with slowed cognitive development, reduced growth and other effects reported. Reproductive effects, such as decreased sperm count in men and spontaneous abortions in women, have been associated with lead exposure. The developing fetus is at particular risk from maternal lead exposure, with low birth weight and slowed postnatal neurobehavioral development noted. Human studies are inconclusive regarding lead exposure and cancer, while animal studies have reported an increase in kidney cancer from lead exposure by the oral route. The U.S. Environmental Protection Agency (EPA) considers lead to be a Group B2, probable human carcinogen.

Please Note: The main sources of information for this fact sheet are EPA's Integrated Risk Information System (IRIS), which contains information on the carcinogenic effects of lead, and the Agency for Toxic Substances and Disease Registry's (ATSDR's) *Toxicological Profile for Lead.*

Physical Properties

- Lead is a naturally occurring, bluish-gray metal that is found in small quantities in the earth's crust. (1,2)
- Lead is present in a variety of compounds such as lead acetate, lead chloride, lead chromate, lead nitrate, and lead oxide. (1,2)
- Pure lead is insoluble in water; however, the lead compounds vary in solubility from insoluble to water soluble. (1,2)
- The chemical symbol for lead is Pb, and the atomic weight is 207.2 g/mol. (1)
- The vapor pressure for lead is 1.0 mm Hg at 980 °C. (1)

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[1] Human exposure to lead occurs through a combination of inhalation and oral exposure, with inhalation generally contributing a greater proportion of the dose for occupationally exposed groups, and the oral route generally contributing a greater proportion of the dose for the general population. The effects of lead are the same regardless of the route of exposure (inhalation or oral) and are correlated with internal exposure as blood lead levels. For this reason, this fact sheet will not discuss the exposure in terms of route but will present it in terms of blood lead levels.

Uses

- The primary use of lead is in the manufacture of batteries. (1)
- Lead is also used in the production of metal products, such as sheet lead, solder (but no longer in food cans), and pipes, and in ceramic glazes, paint, ammunition, cable covering, and other products. (1)
- Tetraethyl lead was used in gasoline to increase the octane rating until lead additives were phased out and eventually banned from use in gasoline by the EPA beginning in 1973. (1)

Sources and Potential Exposure

- The largest source of lead in the atmosphere has been from leaded gasoline combustion, but with the phase down of lead in gasoline, air lead levels have decreased considerably. Other airborne sources include combustion of solid waste, coal, and oils, emissions from iron and steel production and lead smelters, and tobacco smoke. (1,2)
- Exposure to lead can also occur from food and soil. Children are at particular risk to lead exposure since they commonly put hands, toys, and other items in their mouths, which may come in contact with lead-containing dust and dirt. (1,2)
- Lead-based paints were commonly used for many years and flaking paint, paint chips, and weathered paint powder may be a major source of lead exposure, particularly for children. (1,2)
- Lead in drinking water is due primarily to the presence of lead in certain pipes, solder, and fixtures. (1,2)
- Exposure to lead may also occur in the workplace, such as lead smelting and refining industries, steel and iron factories, gasoline stations, and battery manufacturing plants. (1,2)
- Lead has been listed as a pollutant of concern to EPA's Great Waters Program due to its persistence in the environment, potential to bioaccumulate, and toxicity to humans and the environment. (3)

Assessing Personal Exposure

- The amount of lead in the blood can be measured to determine if exposure to lead has occurred. (1,2)
- The level of lead in the blood is measured in μg/dL.
- The Centers for Disease Control concluded in 1993 that blood lead concentrations at or around 10 μg/dL present a public health risk to sensitive populations.
- Exposure to lead can also be evaluated by measuring erythrocyte protoporphyrin (EP), a component of red blood cells known to increase when the amount of lead in the blood is high. This method was commonly used to screen children for potential lead poisoning. (1,2)
- Methods to measure lead in teeth or bones by X-ray fluorescence techniques are not widely available. (1)

Health Hazard Information

Acute Effects:

- Death from lead poisoning may occur in children who have blood lead levels greater than 125 μg/dL, and brain and kidney damage have been reported at blood lead levels of approximately 100 μg/dL in adults and 80 μg/dL in children. (1,2)
- Gastrointestinal symptoms, such as colic, have also been noted in acute exposures at blood lead levels of approximately 60 μg/dL in adults and children. (1,2)
- Short-term (acute) animal tests, such as the LC_{50} test in rats, have shown lead to have moderate to high acute toxicity. (4)

Chronic Effects (Noncancer):

- Chronic exposure to lead in humans can affect the blood. Anemia has been reported in adults at blood lead levels of 50 to 80 μg/dL, and in children at blood lead levels of 40 to 70 μg/dL. (1,2)
- Lead also affects the nervous system. Neurological symptoms have been reported in workers with blood lead levels of 40 to 60 μg/dL, and slowed nerve conduction in peripheral nerves in adults occurs at blood lead levels of 30 to 40 μg/dL. (1,2)
- Children are particularly sensitive to the neurotoxic effects of lead. A greatly expanded body of research has shown that even low levels of lead exposure can result in neurobehavioral changes, such as lowered IQ, in developing children. There is evidence that blood lead levels of 10 to 30 μg/dL, or lower, may affect the hearing threshold and growth in children. (1,2)
- Other effects from chronic lead exposure in humans include effects on blood pressure and kidney function, and interference with vitamin D metabolism. (1,2,5)
- Animal studies have reported effects similar to those found in humans, with effects on the blood, kidneys, and nervous, immune, and cardiovascular systems noted. (1,2,5)
- EPA has not established a reference concentration (RfC) or a reference dose (RfD) for elemental lead or inorganic lead compounds. (6)
- EPA has established an RfD for tetraethyl lead (an organometallic form of lead) of 1 x 10^{-7} mg/kg/d based on effects in the liver and thymus of rats. The RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious noncancer effects during a lifetime. It is not a direct estimator of risk, but rather a reference point to gauge the potential effects. At exposures increasingly greater than the RfD, the potential for adverse health effects increases. Lifetime exposure above the RfD does not imply that an adverse health effect would necessarily occur. (7)
- EPA has medium to low confidence in the RfD due to: medium to low confidence in the study on which the RfD for tetraethyl lead was based because, although only a few animals per sex per dose level were tested, a good histopathologic exam was conducted and a dose-severity was observed; and medium to low confidence in the database because some supporting information was available. (7)

- The EPA has set a national ambient air quality standard (NAAQS) for lead at 1.5 μg/m3 as a quarterly average concentration. The NAAQS was set on the basis of evidence that numerous health effects were associated with lead exposure, including impairment of heme synthesis, and in recognition that young children (age 1-5 years) were a particularly sensitive group to lead effects. (11,12)

Reproductive/Developmental Effects:

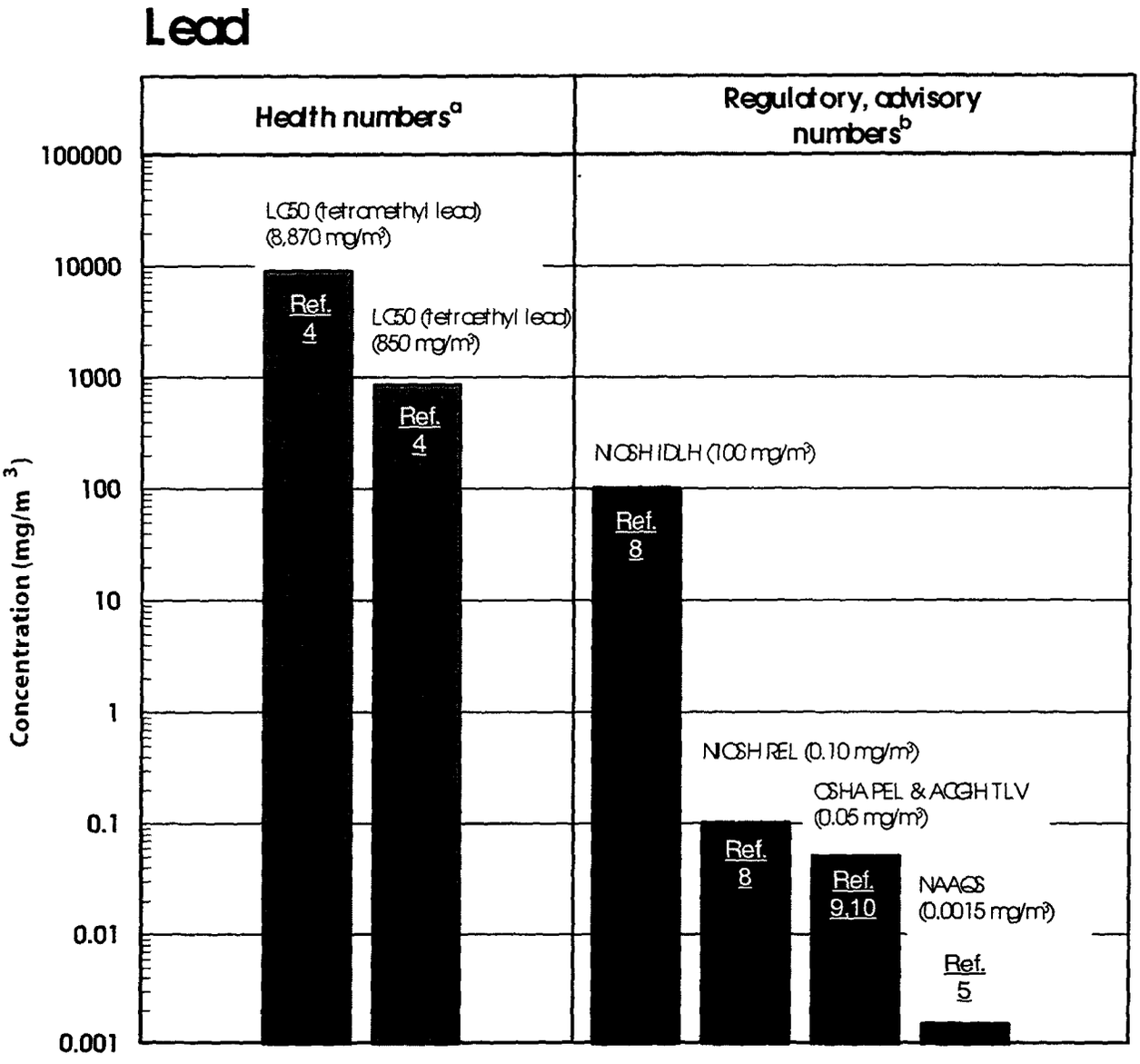
- Studies on male lead workers have reported severe depression of sperm count and decreased function of the prostate and/or seminal vesicles at blood lead levels of 40 to 50 μg/dL. These effects may be seen from acute as well as chronic exposures. (1,5)
- Occupational exposure to high levels of lead has been associated with a high likelihood of spontaneous abortion in pregnant women. However, the lowest blood lead levels at which this occurs has not been established. These effects may be seen from acute as well as chronic exposures. (1,5)
- Exposure to lead during pregnancy produces toxic effects on the human fetus, including increased risk of preterm delivery, low birth weight, and impaired mental development. These effects have been noted at maternal blood lead levels of 10 to 15 μg/dL, and possibly lower. Decreased IQ scores have been noted in children at blood lead levels of approximately 10 to 50 μg/dL. (1,2)
- Human studies are inconclusive regarding the association between lead exposure and other birth defects, while animal studies have shown a relationship between high lead exposure and birth defects. (1,5)

Cancer Risk:

- Human studies are inconclusive regarding lead exposure and an increased cancer risk. Four major human studies of workers exposed to lead have been carried out; two studies did not find an association between lead exposure and cancer, one study found an increased incidence of respiratory tract and kidney cancers, and the fourth study found excesses for lung and stomach cancers. However, all of these studies are limited in usefulness because the route(s) of exposure and levels of lead to which the workers were exposed were not reported. In addition, exposure to other chemicals probably occurred. (1,2,6)
- Animal studies have reported kidney tumors in rats and mice exposed to lead via the oral route. (1,2,5,6)
- EPA considers lead to be a Group B2, probable human carcinogen. (6)

Conversion Factors:
To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45).
For lead: 1 ppm = 8.5 mg/m^3.

Health Data from Inhalation Exposure



ACGIH TLV – American Conference of Governmental and Industrial Hygienists' threshold limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effects.

LC_{50} (Lethal Concentration$_{50}$) – A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.

NIOSH REL – National Institute of Occupational Safety and Health's recommended exposure limit; NIOSH-recommended exposure limit for an 8- or 10-h time-weighted-average exposure and/or ceiling.

NIOSH IDLH – NIOSH's immediately dangerous to life or health concentration; NIOSH

recommended exposure limit to ensure that a worker can escape from an exposure condition that is likely to cause death or immediate or delayed permanent adverse health effects or prevent escape from the environment.
NAAQS – National Ambient Air Quality Standard. NAAQS set by EPA for pollutants that are considered to be harmful to public health and the environment; the NAAQS for lead is 1.5 $\mu g/m^3$, maximum arithmetic mean averaged over a calendar quarter.
OSHA PEL – Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.

[a] Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA.
[b] Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the Government or other groups as advice.

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MANGANESE COMPOUNDS

Hazard Summary

Manganese is naturally ubiquitous in the environment. Manganese is essential for normal physiologic functioning in humans and animals. Health effects in humans have been associated with both deficiencies and excess intakes of manganese. Chronic (long-term) exposure to low levels of manganese in the diet is considered to be nutritionally essential in humans, with a recommended daily allowance of 2 to 5 mg/d. Chronic exposure to high levels of manganese by inhalation in humans results primarily in central nervous system (CNS) effects. Visual reaction time, hand steadiness, and eye-hand coordination were affected in chronically-exposed workers. A syndrome named manganism may result from chronic exposure to higher levels; manganism is characterized by feelings of weakness and lethargy, tremors, a mask-like face, and psychological disturbances. Respiratory effects have also been noted in workers chronically exposed by inhalation. Impotence and loss of libido have been noted in male workers afflicted with manganism attributed to high-level inhalation exposures to manganese. No studies are available regarding the carcinogenic effects of manganese in humans, and animal studies are inadequate. The U.S. Environmental Protection Agency (EPA) has classified manganese as a Group D, not classifiable as to carcinogenicity in humans.

Please Note: The main sources of information for this fact sheet are EPA's Integrated Risk Information System (IRIS), which contains information on inhalation chronic toxicity of manganese and the reference concentration (RfC), oral chronic toxicity and the reference dose (RfD), and the Agency for Toxic Substances and Disease Registry's (ATSDR's) *Toxicological Profile for Manganese.*

Physical Properties

- Manganese is a silver-colored metal that forms compounds in the environment with chemicals such as oxygen, sulfur, and chlorine. (1)
- Manganese compounds are solids that do not evaporate; however, small dust particles can become suspended in air. (1)
- Manganese can dissolve in water. (1)
- The chemical symbol for manganese is Mn, and elemental manganese has an atomic weight of 54.94 g/mol. (1)
- Some manganese compounds are: manganese dioxide (MnO_2), manganese tetraoxide (Mn_3O_4), manganese salts (chloride, sulfate, carbonate, and nitrate), manganese silicate, and potassium permanganate ($KMnO_4$).

Uses

- Metallic manganese is used primarily in steel production to improve hardness, stiffness, and strength. It is also used in carbon steel, stainless steel, and high-temperature steel, along with cast iron and superalloys. (1)

- Manganese compounds have a variety of uses. Manganese dioxide is used in the production of dry-cell batteries, matches, fireworks, and the production of other manganese compounds. (1)
- Manganese chloride is used as a catalyst in the chlorination of organic compounds, in animal feed, and in dry-cell batteries, while manganese sulfate is used as a fertilizer, livestock nutritional supplement, in glazes and varnishes, and in ceramics. (1)
- Potassium permanganate is used for water purification purposes in water and waste-treatment plants. (1)

Sources and Potential Exposure

- Manganese is a naturally occurring substance found in many types of rock and soil; it is ubiquitous in the environment and found in low levels in water air, soil, and food. (1)
- Manganese can also be released into the air by iron and steel production plants, power plants, and coke ovens. (1)
- The average manganese levels in various media are as follows: levels in drinking water are approximately 0.004 ppm; average air levels are approximately 0.02 $\mu g/m^3$; levels in soil range from 40 to 900 ppm; the average daily intake from food ranges from 1 to 5 mg/d. (1)
- People who work in factories where manganese metal is produced from manganese ore or where manganese compounds are used to make steel or other products are most likely to be exposed through inhalation to higher than normal levels of manganese. (1)

Assessing Personal Exposure

- Several tests are available for measuring manganese in blood, urine, hair, or feces. As manganese is naturally present in the body, some manganese is always found in these materials. In addition, excess manganese is usually removed from the body within a few days, making it difficult to measure past exposure to manganese. (1)

Health Hazard Information

Acute Effects:

- No reports of effects in humans following acute (short-term) effects of exposure to manganese are available.
- Effects to the lung have been reported following acute exposure of rats to manganese via inhalation. (1)
- Manganese is considered to have moderate acute toxicity based on short-term tests, such as the LD_{50} test given by gavage in rats. However, other animal tests in which manganese has been given orally have indicated that manganese has low acute oral toxicity. (1)

Chronic Effects (Noncancer):

- Chronic exposure to manganese at low levels is nutritionally essential in humans. The recommended daily intake of manganese is 2 to 5 mg/d for adults and adolescents. (1)
- No cases of manganese deficiency have been observed in the general population. However, manganese deficiency in animals has been associated with impaired growth, skeletal abnormalities, impaired reproductive function in females, and testicular degeneration in males. (1)
- Chronic inhalation exposure of humans to manganese results primarily in effects on the nervous system. Slower visual reaction time, poorer hand steadiness, and impaired eye-hand coordination were reported in several studies of workers occupationally exposed to manganese dust in air. (1,3)
- Chronic inhalation exposure of humans to high levels may result in a syndrome called manganism and typically begins with feelings of weakness and lethargy and progresses to other symptoms such as gait disturbances, clumsiness, tremors, speech disturbances, a mask-like facial expression, and psychological disturbances. (1,3)
- Other chronic effects reported in humans from inhalation exposure to manganese are respiratory effects such as an increased incidence of cough, bronchitis, dyspnea during exercise, and an increased susceptibility to infectious lung disease. (1,3)
- The RfC for manganese is 0.00005 mg/m^3 based on impairment of neurobehavioral function in humans. The RfC is an estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious noncancer effects during a lifetime. It is not a direct estimator of risk but rather a reference point to gauge the potential effects. At exposures increasingly greater than the RfC, the potential for adverse health effects increases. Lifetime exposure above the RfC does not imply that an adverse health effect would necessarily occur. (3)
- EPA has medium confidence in the RfC due to medium confidence in the principal studies on which the RfC was based and medium confidence in the database. Neither of the principal studies identified a no-observed-adverse-effect level (NOAEL) for neurobehavioral effects, nor did either study directly measure particle size or provide information on the particle size distribution. These limitations of the studies are mitigated by the fact that the principal studies found similar indications of neurobehavioral dysfunction, and these findings were consistent with the results of other human studies. EPA has medium confidence in the database because the duration of exposure was relatively limited in the principal and supporting studies, the majority of studies did not specify the species of manganese, and the reproductive and developmental effects have not been adequately studied. (3)
- EPA has established a RfD for manganese of 0.14 mg/kg/d based on CNS effects in humans. The RfD is estimated to be an intake for the general population that is not associated with adverse health effects; this is not meant to imply that intakes above the RfD are necessarily associated with toxicity. Some individuals may, in fact, consume a diet that contributes more than 10 mg Mn/day without any cause for concern. When assessing risk from manganese in drinking water or soil, a modified RfD of 0.05 mg/kg/d is recommended. (3)

- EPA has medium confidence in the RfD due to medium confidence in the studies on which the RfD for manganese was based; and medium confidence in the database. (3)

Reproductive/Developmental Effects:

- Reproductive effects, such as impotence and loss of libido, have been noted in male workers afflicted with manganism attributed to occupational exposure to high levels of manganese by inhalation. No information is available on developmental effects of manganese in humans. (1,3)
- Animal studies have reported degenerative changes in the seminiferous tubules leading to sterility from intratracheal instillation of high doses of manganese (experimentally delivering the manganese directly to the trachea). In young animals exposed to manganese orally, decreased testosterone production and retarded growth of the testes were reported. (1)
- Decreased activity levels and a decrease in average pup weight have been noted in the offspring of mice exposed to manganese by inhalation. (1)

Cancer Risk:

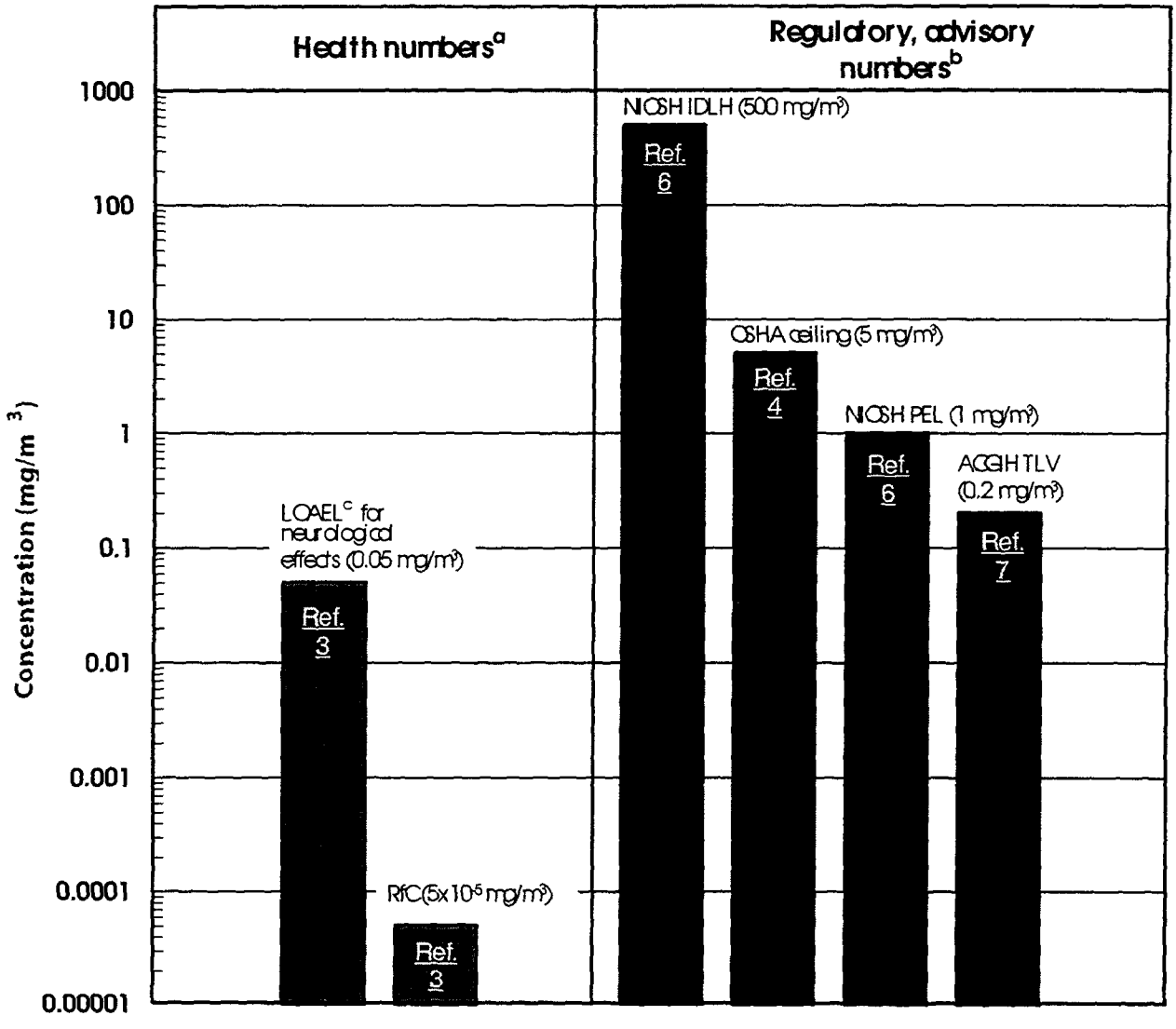
- No studies are available regarding carcinogenic effects in humans or animals from inhalation exposure to manganese. (1,3)
- No studies are available regarding cancer in humans from oral exposure to manganese. Oral animal studies on manganese sulfate are inadequate, with several studies reporting negative results, one study reporting an increased incidence of thyroid gland follicular cell adenomas and hyperplasia, and one study noting an increased incidence of pancreatic tumors. (1,3)
- EPA has classified manganese as a Group D, not classifiable as to carcinogenicity in humans. (3)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45).
For manganese: 1 ppm = 2.25 mg/m^3.
To convert from $\mu g/m^3$ to mg/m^3: mg/m^3 = ($\mu g/m^3$) x (1 mg/1,000 μg).

Health Data from Inhalation Exposure

Manganese



ACGIH TLV – American Conference of Governmental and Industrial Hygienists' threshold limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effects.

LOAEL – Lowest-observed-adverse-effect level.

NIOSH REL – National Institute of Occupational Safety and Health's recommended exposure limit; NIOSH-recommended exposure limit for an 8- or 10-h time-weighted-average exposure and/or ceiling.

NIOSH IDLH – NIOSH's immediately dangerous to life or health concentration; NIOSH recommended exposure limit to ensure that a worker can escape from an exposure condition that is likely to cause death or immediate or delayed permanent adverse health effects or prevent escape from the environment.

OSHA PEL – Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.
OSHA ceiling – OSHA's short-term exposure limit ceiling; an exposure that should not be exceeded at any time during a workday even if the 8-h time-weighted-average is within the threshold limit value.

[a] Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA.
[b] Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the Government or other groups as advice.
[c] This LOAEL is from the critical study used as the basis for the EPA RfC.

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MERCURY COMPOUNDS

Hazard Summary

Mercury exists in three forms: elemental mercury, inorganic mercury compounds (primarily mercuric chloride), and organic mercury compounds (primarily methyl mercury). All forms of mercury are quite toxic, and each form exhibits different health effects.

Acute (short-term) exposure to high levels of elemental mercury in humans results in central nervous system (CNS) effects such as tremors, mood changes, and slowed sensory and motor nerve function. High inhalation exposures can also cause kidney damage. Effects on the gastrointestinal tract and respiratory system have also been noted in humans from acute inhalation exposure. Chronic (long-term) exposure to elemental mercury in humans also affects the CNS, with effects such as erethism (increased excitability), irritability, excessive shyness, and tremors. Human studies are inconclusive regarding elemental mercury and cancer. The U.S. Environmental Protection Agency (EPA) has classified elemental mercury as a Group D, not classifiable as to human carcinogenicity.

Acute exposure to inorganic mercury by the oral route may result in effects such as nausea, vomiting, and severe abdominal pain. The major effect from chronic exposure to inorganic mercury is kidney damage. Animal studies have reported effects such as alterations in testicular tissue, increased resorption rates, and abnormalities of development. Mercuric chloride (an inorganic mercury compound) exposure has been shown to result in forestomach, thyroid, and renal tumors in experimental animals. EPA has classified inorganic mercury as Group C, possible human carcinogen.

Acute exposure of humans to very high levels of methyl mercury results in CNS effects such as blindness, deafness, and impaired level of consciousness. Chronic exposure to methyl mercury in humans also affects the CNS with symptoms such as paresthesia (a sensation of pricking on the skin), blurred vision, malaise, speech difficulties, and constriction of the visual field. Methyl mercury exposure, via the oral route, has led to significant developmental effects. Infants born to women who ingested high levels of methyl mercury exhibited mental retardation, ataxia, constriction of the visual field, blindness, and cerebral palsy. No human studies are available on the carcinogenic effects of methyl mercury, and one animal study reported renal tumors in mice. EPA has classified methyl mercury as Group C, possible human carcinogen.

Please Note: The main sources of information for this fact sheet are EPA's Integrated Risk Information System (IRIS), which contains information on inhalation chronic toxicity and the reference concentration (RfC) for elemental mercury, oral chronic toxicity and the reference dose (RfD) for inorganic and methyl mercury, EPA's *Mercury Study Report to Congress*, and the Agency for Toxic Substances and Disease Registry's (ATSDR's)

Toxicological Profile for Mercury. Other secondary sources include the World Health Organization's *Environmental Health Criteria Documents on Methyl Mercury and Inorganic Mercury.*

Physical Properties

- Elemental mercury is a silver-white metal with an atomic weight of 200.59 g/mol. (1)
- Mercury is a liquid at room temperature and has a vapor pressure of 0.002 mm Hg at 25 °C. (1)
- Mercury can exist in three oxidation states — elemental, mercurous, and mercuric — and it can be part of both inorganic and organic compounds. (1)
- Inorganic mercury compounds include mercuric chloride, mercuric sulfide, mercurous chloride. Organic mercury compounds include mercuric acetate, methylmercuric chloride, dimethyl mercury, and phenylmercuric acetate. (1)

Uses

Elemental Mercury

- Elemental mercury is used in thermometers, barometers, and pressure-sensing devices. It is also used in batteries, lamps, industrial processes, refining, lubrication oils, and dental amalgams. (1)

Inorganic Mercury

- Inorganic mercury was used in the past in laxatives, skin-lightening creams and soaps, and in latex paint. In 1990, EPA canceled registration for all interior paints that contained mercury. Mercury use in exterior paint was discontinued after 1991. (1)

Methyl Mercury

- Methyl mercury has no industrial uses; it is formed in the environment from the methylation of the inorganic mercurial ion. (1)

Sources and Potential Exposure

Elemental Mercury

- A major source of exposure for elemental mercury is through inhalation in occupational settings. (1,3,4)
- Another source of exposure to low levels of elemental mercury in the general population is elemental mercury released in the mouth from dental amalgam fillings. (3-5)

Inorganic Mercury

- The general population is usually not exposed to inorganic mercury compounds to any significant extent today, as most products containing these compounds have now been banned. Limited exposure could occur through the use of old cans of latex paint, which until 1990, could contain mercury compounds to prevent bacterial and fungal growth. (1,4)

Methyl Mercury

- The most important organic mercury compound, in terms of human exposure, is methyl mercury. Methyl mercury exposure occurs primarily through the diet, with fish and fish products as the dominant source. Sources of past exposure to methyl mercury include fungicide-treated grains and meat from animals fed such grain. However, fungicides containing mercury are banned in the U.S. today, and this source of exposure is now negligible. (1)
- Mercury has been listed as a pollutant of concern to EPA's Great Waters Program due to its persistence in the environment, potential to bioaccumulate, and toxicity to humans and the environment. (6)

Assessing Personal Exposure

- Laboratory tests can detect mercury in blood, urine, and hair samples. (1)

Health Hazard Information

Acute Effects:

Elemental Mercury

- The major systems impacted by human inhalation of elemental mercury are the kidneys and CNS. Acute exposure to high levels of elemental mercury in humans results in CNS effects, such as tremors, irritability, insomnia, memory loss, neuromuscular changes, headaches, slowed sensory and motor nerve function, and reduction in cognitive function. (1,2)
- Acute inhalation exposure of humans to high concentrations has resulted in kidney effects ranging from mild transient proteinuria to acute renal failure. (1,2)
- Gastrointestinal effects and respiratory effects, such as chest pains, dyspnea, cough, pulmonary function impairment, and interstitial pneumonitis have also been noted from human inhalation exposure to elemental mercury. (1,2)

Inorganic Mercury

- Symptoms noted after acute oral exposure to inorganic mercury compounds include a metallic taste in the mouth, nausea, vomiting, and severe abdominal pain. (1,2,7)

- The acute lethal dose for most inorganic mercury compounds for an adult is 1 to 4 g or 14 to 57 mg/kg for a 70-kg person. (1,7)

Methyl Mercury

- Acute inhalation exposure to high levels of methyl mercury, which is extremely rare, has resulted in severe CNS effects, including blindness, deafness, impaired level of consciousness, and death. (8)
- It has been estimated that the minimum lethal dose of methyl mercury for a 70-kg person ranges from 20 to 60 mg/kg. (8)

Chronic Effects (Noncancer):

Elemental Mercury

- The CNS is the major target organ for elemental mercury toxicity in humans. Effects noted include erethism (increased excitability), irritability, excessive shyness, insomnia, severe salivation, gingivitis, and tremors. (1,2,9)
- Chronic exposure to elemental mercury also affects the kidney in humans, with the development of proteinuria. (1,2,9)
- Acrodynia is a rare syndrome found in children exposed to elemental mercury compounds. It is characterized by severe leg cramps, irritability, paresthesia (a sensation of prickling on the skin), and painful pink fingers and peeling hands, feet, and nose. (1,2)
- EPA has not established an RfD for elemental mercury. (11)
- The RfC for elemental mercury is 0.0003 mg/m^3 based on CNS effects in humans. The RfC is an estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious noncancer effects during a lifetime. It is not a direct estimator of risk but rather a reference point to gauge the potential effects. At exposures increasingly greater than the RfC, the potential for adverse health effects increases. Lifetime exposure above the RfC does not imply that an adverse health effect would necessarily occur. (11)
- EPA has medium confidence in the RfC due to: medium confidence in the studies on which the RfC was based because there were sufficient number of human subjects, inclusion of appropriate control groups, and exposure levels in a number of the studies had to be extrapolated from blood mercury levels; and medium confidence in the database due to a lack of human or multispecies reproductive/developmental studies. (11)

Inorganic Mercury

- The primary effect from chronic exposure to inorganic mercury is kidney damage, primarily due to mercury-induced autoimmune glomerulonephritis (induction of an immune response to the body's kidney tissue). (1,2,9,10)
- Acrodynia may also occur from exposure to inorganic mercury compounds. (1,2,9,10)

- The RfD for inorganic mercury (mercuric chloride) is 0.0003 mg/kg/d based on autoimmune effects in rats. (12)
- EPA has high confidence in the RfD based on the weight of evidence from the studies using Brown-Norway rats and the entirety of the mercuric chloride database. (12)
- EPA has not established an RfC for inorganic mercury. (12)

Methyl Mercury

- The primary effect from chronic exposure to methyl mercury in humans is damage to the CNS. The earliest effects are symptoms such as paresthesia, blurred vision, and malaise. Effects at higher doses include deafness, speech difficulties, and constriction of the visual field. (1,2,8)
- The RfD for methyl mercury is 0.0001 mg/kg/d based on CNS effects in humans. (13)
- EPA has medium confidence in the RfD due to: (1) medium confidence in the studies on which the RfD was based because the benchmark dose approach allowed use of the entire dose-response assessment, and the results of laboratory studies with nonhuman primates support the quantitative estimate of the no-observed-adverse-effect level (NOAEL)/ lowest-observed-adverse-effect level (LOAEL) range of the benchmark dose that was indicated by the human studies; and (2) medium confidence in the database. (13)
- EPA has not established an RfC for methyl mercury. (13)

Reproductive/Developmental Effects:

Elemental Mercury

- Studies on the reproductive and developmental effects of elemental mercury in humans have shown mixed results. One study did not see an association between mercury exposure and miscarriages, while another revealed an increase in the rate of spontaneous abortions. Another study showed a higher than expected frequency of birth defects, which was not confirmed in a fourth study. (1,9)

Inorganic Mercury

- No information is available on the reproductive or developmental effects of inorganic mercury in humans.
- Animal studies have reported effects including alterations in testicular tissue, increased resorption rates, and abnormalities of development. (1,7,9)

Methyl Mercury

- A large number of human studies on the systemic effects of methyl mercury have been carried out. This is the result of two large scale poisoning incidents in Japan and Iraq and several epidemiologic studies investigating populations that consume large quantities of fish. (1,2)

- Oral exposure to methyl mercury has been observed to produce significant developmental effects in humans. Infants born to women who ingested high concentrations of methyl mercury exhibited CNS effects, such as mental retardation, ataxia, deafness, constriction of the visual field, blindness, and cerebral palsy. At lower methyl mercury concentrations, developmental delays and abnormal reflexes were noted. (1,2,8)
- Considerable new data on the health effects of methyl mercury are becoming available. Large studies of fish and marine mammal consuming populations in Seychelles and Faroe Islands are being carried out. Smaller scale studies also describe effects around the U.S. Great Lakes. (1,2)

Cancer Risk:

Elemental Mercury

- Several studies have been carried out regarding elemental mercury and cancer in humans. These studies are inconclusive due to lack of valid exposure data and confounding factors. (1,2,9)
- EPA has classified elemental mercury as a Group D, not classifiable as to human carcinogenicity. (12)

Inorganic Mercury

- No studies are available on the carcinogenic effects of inorganic mercury in humans.
- A chronic study on mercuric chloride in rats and mice reported an increased incidence of forestomach and thyroid tumors in rats, and an increased incidence of renal tumors in mice. (14)
- EPA has classified inorganic mercury as Group C, possible human carcinogen. (12)

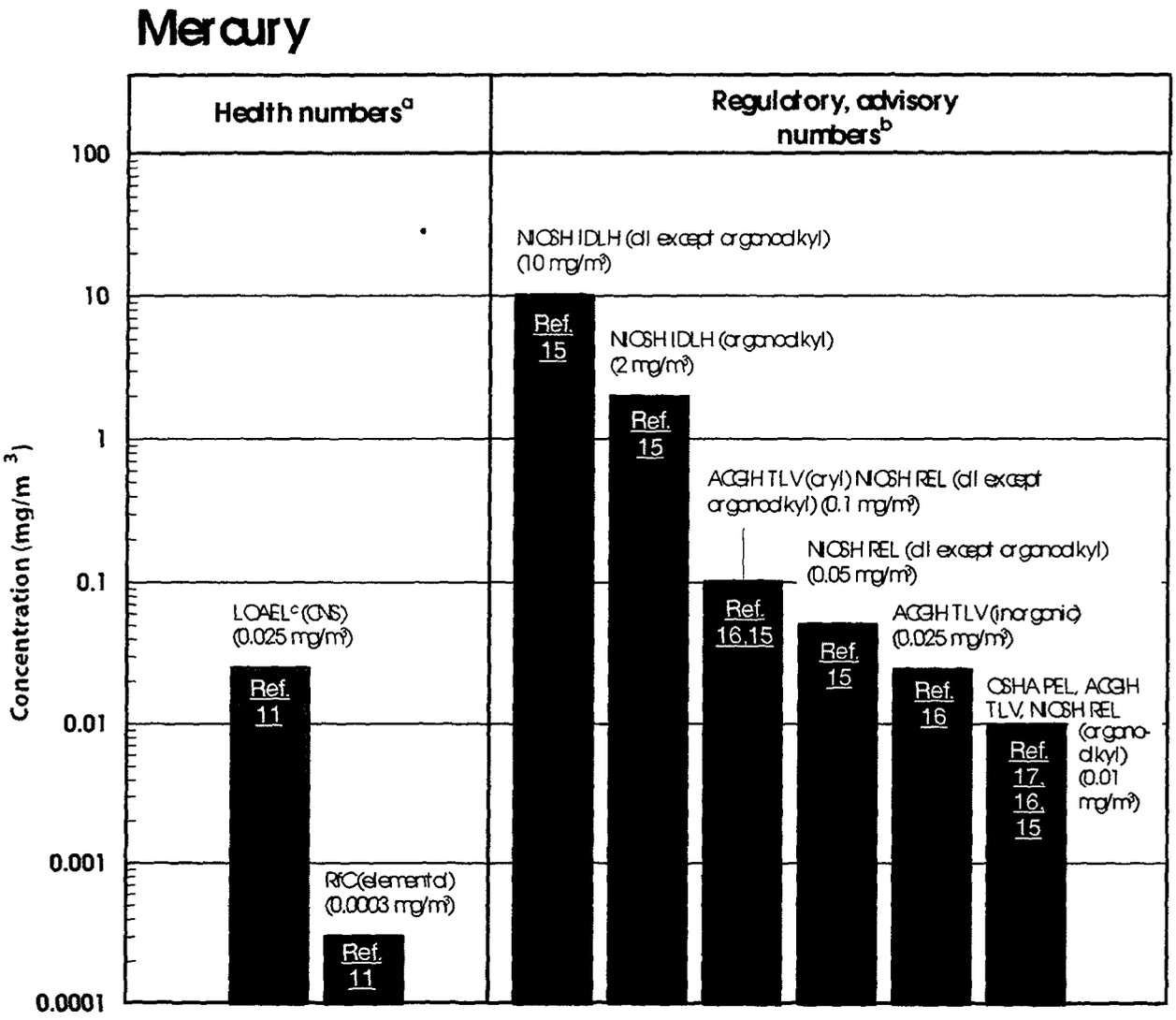
Methyl Mercury

- No studies are available on the carcinogenic effects of methyl mercury in humans, and the one available animal study reported renal tumors in mice. (1,2,13)
- EPA has classified methyl mercury as Group C, possible human carcinogen. (13)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45). For elemental mercury: 1 ppm = 8.2 mg/m^3. For mercuric chloride: 1 ppm = 11.1 mg/m^3. For methyl mercuric chloride: 1 ppm = 10.3 mg/m^3.

Health Data from Inhalation Exposure



ACGIH TLV – American Conference of Governmental and Industrial Hygienists' threshold limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect.

NIOSH IDLH – National Institute of Occupational Safety and Health's immediately dangerous to life or health value; the maximum environmental concentration of a contaminant from which one could escape within 30 min without any escape-impairing symptoms or irreversible health

effects.
NIOSH REL – National Institute of Occupational Safety and Health's recommended exposure limit; NIOSH-recommended exposure limit for an 8- or 10-h time-weighted-average exposure and/or ceiling.
OSHA PEL – Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.

[a] Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA.
[b] Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the Government or other groups as advice.
[c] The LOAEL is from the critical study used as the basis for the EPA RfC for elemental mercury.

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METHYLENE CHLORIDE

75-09-2

Hazard Summary

Methylene chloride is predominantly used as a solvent. The acute (short-term) effects of methylene chloride inhalation in humans consist mainly of nervous system effects including decreased visual, auditory, and motor functions, but these effects are reversible once exposure ceases. The effects of chronic (long-term) exposure to methylene chloride suggest that the central nervous system (CNS) is a potential target in humans and animals. Limited animal studies have reported developmental effects. Human data are inconclusive regarding methylene chloride and cancer. Animal studies have shown increases in liver and lung cancer and benign mammary gland tumors following the inhalation of methylene chloride. The U.S. Environmental Protection Agency (EPA) has classified methylene chloride as a Group B2, probable human carcinogen.

Please Note: The main sources of information for this fact sheet are the Agency for Toxic Substances and Disease Registry's (ATSDR's) *Toxicological Profile for Methylene Chloride* and EPA's Integrated Risk Information System (IRIS), which contains information on oral chronic toxicity and the reference dose (RfD), and the carcinogenic effects of methylene chloride including the unit cancer risk for inhalation exposure.

Physical Properties

- A common synonym for methylene chloride is dichloroethane. (1,4)
- Methylene chloride is a colorless liquid with a sweetish odor. (1,6)
- The chemical formula for methylene chloride is CH_2Cl_2, and the molecular weight is 84.93 g/mol. (1)
- The vapor pressure for methylene chloride is 349 mm Hg at 20 °C, and it has an octanol/water coefficient (log K_{ow}) of 1.30. (1)
- Methylene chloride has an odor threshold of 250 ppm. (7)
- Methylene chloride is slightly soluble in water and is nonflammable. (1,6)

Uses

- Methylene chloride is predominantly used as a solvent in paint strippers and removers; as a process solvent in the manufacture of drugs, pharmaceuticals, and film coatings; as a metal cleaning and finishing solvent in electronics manufacturing; and as an agent in urethane foam blowing. (1)
- Methylene chloride is also used as a propellant in aerosols for products such as paints, automotive products, and insect sprays. (1)
- It is used as an extraction solvent for spice oleoresins, hops, and for the removal of caffeine from coffee. However, due to concern over residual solvent, most decaffeinators no longer use methylene chloride. (1)

- Methylene chloride is also approved for use as a postharvest fumigant for grains and strawberries and as a degreening agent for citrus fruit. (1)

Sources and Potential Exposure

- The principal route of human exposure to methylene chloride is inhalation of ambient air. (1)
- Occupational and consumer exposure to methylene chloride in indoor air may be much higher, especially from spray painting or other aerosol uses. People who work in these places can breathe in the chemical or it may come in contact with the skin. (1)
- Methylene chloride has been detected in both surface water and groundwater samples taken at hazardous waste sites and in drinking water at very low concentrations. (1)

Assessing Personal Exposure

- Several tests exist for determining exposure to methylene chloride. These tests include measurement of methylene chloride in the breath, blood, and urine. It is noted that smoking and exposure to other chemicals may affect the results of these tests. (1)

Health Hazard Information

Acute Effects:

- Case studies of methylene chloride poisoning during paint stripping operations have demonstrated that inhalation exposure to extremely high levels can be fatal to humans. (1,2)
- Acute inhalation exposure to high levels of methylene chloride in humans has resulted in effects on the CNS including decreased visual, auditory, and psychomotor functions, but these effects are reversible once exposure ceases. Methylene chloride also irritates the nose and throat at high concentrations. (1,2)
- Tests involving acute exposure of animals, such as the LD_{50} and LC_{50} tests in rats, have shown methylene chloride to have moderate acute toxicity from oral and inhalation exposure. (3)

Chronic Effects (Noncancer):

- The major effects from chronic inhalation exposure to methylene chloride in humans are effects on the CNS, such as headaches, dizziness, nausea, and memory loss. (1,2)
- Animal studies indicate that the inhalation of methylene chloride causes effects on the liver, kidney, CNS, and cardiovascular system. (1,2)
- EPA has calculated a provisional reference concentration (RfC) of 3 mg/m^3 based on liver effects in rats. The RfC is an estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious noncancer effects during a lifetime. It is not a direct estimator of risk but rather a reference point to

gauge the potential effects. At exposures increasingly greater than the RfC, the potential for adverse health effects increases. Lifetime exposure above the RfC does not imply that an adverse health effect would necessarily occur. (5)

- The RfD for methylene chloride is 0.06 mg/kg/d based on liver toxicity in rats. (4)
- EPA has medium confidence in the RfD based on: high confidence in the study on which the RfD is based because a large number of animals of both sexes were tested in four dose groups, with a large number of controls, many effects were monitored, and a dose-related increase in severity was observed; and medium to low confidence in the database because only a few studies support the no-observed-adverse-effect level (NOAEL). (4)

Reproductive/Developmental Effects:

- No studies were located regarding developmental or reproductive effects in humans from inhalation or oral exposure. (1,2)
- Animal studies have demonstrated that methylene chloride crosses the placental barrier, and minor skeletal variations and lowered fetal body weights have been noted. (1,2)

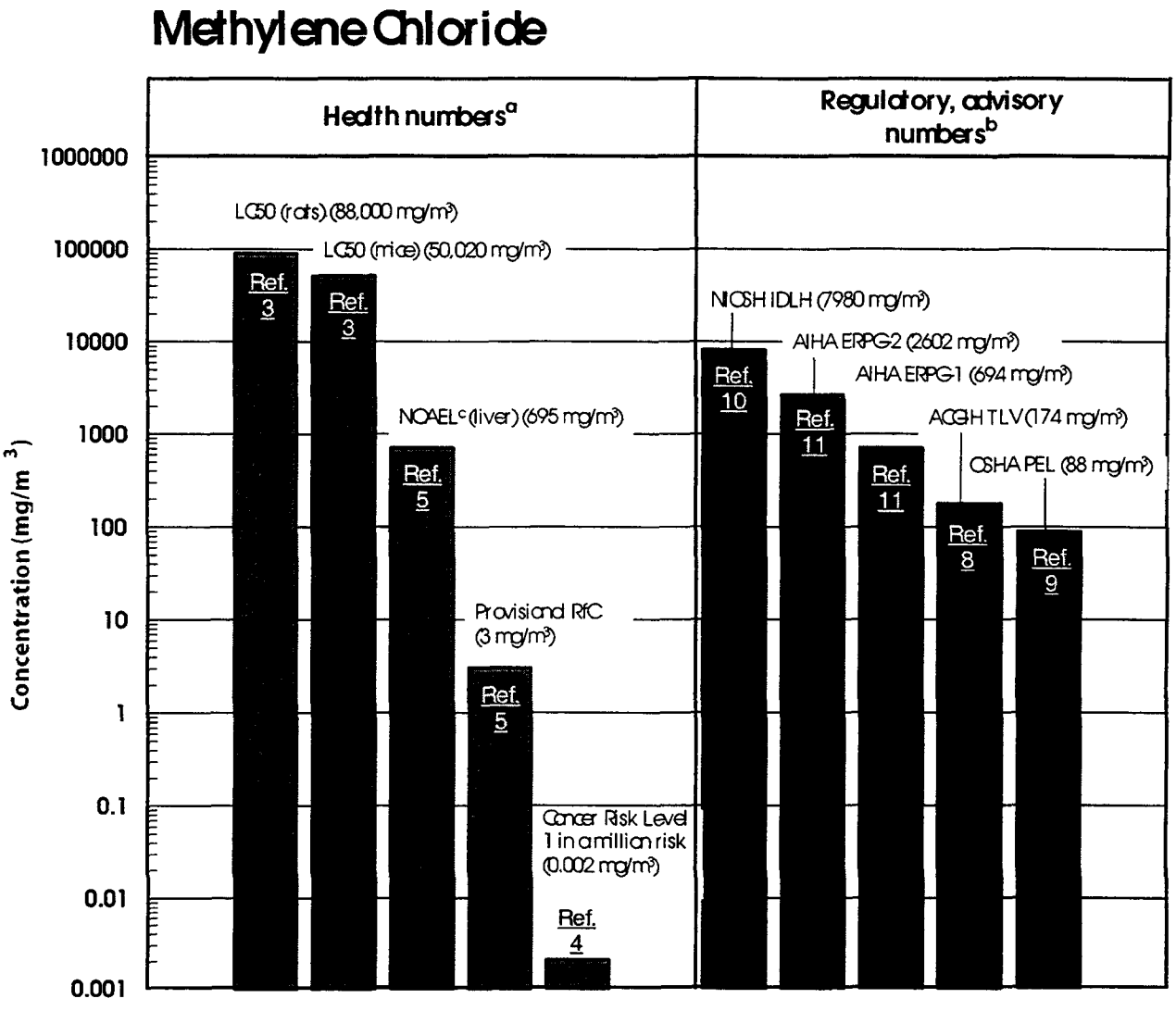
Cancer Risk:

- Several studies did not report a statistically significant increase in deaths from cancer among workers exposed to methylene chloride. (1,2)
- Animal studies have shown an increase in liver and lung cancer and benign mammary gland tumors following inhalation exposure to methylene chloride. (1,2,4)
- EPA has classified methylene chloride as a Group B2, probable human carcinogen. (4)
- EPA uses mathematical models, based on human and animal studies, to estimate the probability of a person developing cancer from breathing air containing a specified concentration of a chemical. EPA calculated an inhalation unit risk estimate of 4.7×10^{-7} $(\mu g/m^3)^{-1}$. EPA estimates that, if an individual were to continuously breathe air containing methylene chloride at an average of 2.0 $\mu g/m^3$ (0.002 mg/m^3) over his or her entire lifetime, that person would theoretically have no more than a one-in-a-million increased chance of developing cancer as a direct result of breathing air containing this chemical. Similarly, EPA estimates that breathing air containing 20 $\mu g/m^3$ (0.02 mg/m^3) would result in not greater than a one-in-a-hundred thousand increased chance of developing cancer, and air containing 200 $\mu g/m^3$ (0.2 mg/m^3) would result in not greater than a one-in-ten thousand increased chance of developing cancer. For a detailed discussion of confidence in the potency estimates, please see IRIS. (4)
- EPA calculated an oral cancer slope factor of 7.5×10^{-3} $(mg/kg/d)^{-1}$. (4)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45). For methylene chloride: 1 ppm = 3.5 mg/m^3. To convert from $\mu g/m^3$ to mg/m^3: mg/m^3 = ($\mu g/m^3$) x (1 mg/1,000 μg).

Health Data from Inhalation Exposure



ACGIH TLV – American Conference of Governmental and Industrial Hygienists' threshold limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effects.

AIHA ERPG – American Industrial Hygiene Association's emergency response planning guidelines. ERPG 1 is the maximum airborne concentration below which it is believed nearly all individuals could be exposed up to one hour without experiencing other than mild transient adverse health effects or perceiving a clearly defined objectionable odor; ERPG 2 is the maximum airborne concentration below which it is believed nearly all individuals could be exposed up to one hour without experiencing or developing irreversible or other serious health effects that could impair their abilities to take protective action.

LC_{50} (Lethal Concentration$_{50}$)--A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.

NIOSH IDLH – National Institute of Occupational Safety and Health's immediately dangerous to life or health concentration; NIOSH recommended exposure limit to ensure that a worker can escape from an exposure condition that is likely to cause death or immediate or delayed permanent adverse health effects or prevent escape from the environment.
NOAEL – No-observed-adverse-effects level.
OSHA PEL – Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average: the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.

[a] Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA.
[b] Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the Government or other groups as advice.
[c] The NOAEL is from the critical study used as the basis for the provisional RfC.

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NICKEL COMPOUNDS

Hazard Summary

Nickel occurs naturally in the environment at low levels. Nickel is an essential element in some animal species, and it has been suggested it may be essential for human nutrition. Nickel dermatitis, consisting of itching of the fingers, hands, and forearms, is the most common effect in humans from chronic (long-term) skin contact with nickel. Respiratory effects have also been reported in humans from inhalation exposure to nickel. No information is available regarding the reproductive or developmental effects of nickel in humans, but animal studies have reported reproductive and developmental effects. The U.S. Environmental Protection Agency (EPA) has not evaluated soluble salts of nickel as a class of compounds for potential human carcinogenicity. Human and animal studies have reported an increased risk of lung and nasal cancers from exposure to nickel refinery dusts and nickel subsulfide. EPA has classified nickel refinery dust and nickel subsulfide as Group A, human carcinogens. Animal studies of soluble nickel compounds (i.e., nickel carbonyl) have reported lung tumors. EPA has classified nickel carbonyl as a Group B2, probable human carcinogen.

Please Note: The main sources of information for this fact sheet are EPA's Integrated Risk Information System (IRIS), which contains information on oral chronic toxicity and the reference dose (RfD), and the carcinogenic effects of nickel including the unit cancer risk for inhalation exposure, EPA's *Health Assessment Document for Nickel*, and the Agency for Toxic Substances and Disease Registry's (ATSDR's) *Toxicological Profile for Nickel*.

Physical Properties

- Nickel is a silvery-white metal that is found in nature as a component of silicate, sulfide, or arsenide ores. (1)
- In the environment, nickel is found primarily combined with oxygen or sulfur as oxides or sulfides. (1)
- Each form of nickel exhibits different physical properties. (1,6)
- Soluble nickel salts include nickel chloride, nickel sulfate, and nickel nitrate. (6)
- Nickel carbonyl, a highly unstable form, is not found naturally and decomposes rapidly. (1)
- The chemical symbol for nickel is Ni, and it has an atomic weight of 58.71 g/mol. (1)

Uses

- Nickel is used for nickel alloys, electroplating, batteries, coins, industrial plumbing, spark plugs, machinery parts, stainless-steel, nickel-chrome resistance wires, and catalysts. (1,6)
- Nickel carbonyl has severely limited use in nickel refining. (1)

Sources and Potential Exposure

- Nickel is a natural element of the earth's crust; therefore, small amounts are found in food, water, soil, and air. (6)
- Food is the major source of nickel exposure, with an average intake for adults estimated to be approximately 100 to 300 μg/d. (1,6)
- Individuals also may be exposed to nickel in occupations involved in its production, processing, and use, or through contact with everyday items such as nickel-containing jewelry and stainless steel cooking and eating utensils, and by smoking tobacco. (1)
- Nickel is found in ambient air at very low levels as a result of releases from oil and coal combustion, nickel metal refining, sewage sludge incineration, manufacturing facilities, and other sources. (2,6)
- Given its high instability, nickel carbonyl exposure is extremely rare.

Assessing Personal Exposure

- Laboratory tests can detect nickel in blood, urine, feces, and hair samples. (1,6)

Health Hazard Information

Acute Effects:

- One person exposed to an extremely high level of nickel by inhalation suffered severe damage to the lungs and kidneys. (6)
- Gastrointestinal distress (e.g., nausea, vomiting, diarrhea) and neurological effects were reported in workers who drank water on one shift that was contaminated with nickel as nickel sulfate and nickel chloride. (1,6)
- Pulmonary fibrosis and renal edema were reported in humans and animals following acute (short-term) exposure to nickel carbonyl. (1)
- Acute animal tests, such as the LD_{50} test in rats, have shown nickel compounds to exhibit acute toxicity values ranging from low to high. The soluble compounds, such as nickel acetate, were the most toxic, and the insoluble forms, such as nickel powder, were the least toxic. (6)

Chronic Effects (Noncancer):

- Dermatitis is the most common effect in humans from chronic dermal exposure to nickel. Cases of nickel dermatitis have been reported following occupational and non-occupational exposure, with symptoms of eczema (rash, itching) of the fingers, hands, wrists, and forearms. (1,2,6,7)
- Chronic inhalation exposure to nickel in humans also results in respiratory effects, including a type of asthma specific to nickel, decreased lung function, and bronchitis. (6,7)

- Animal studies have reported effect on the lungs and immune system from inhalation exposure to soluble and insoluble nickel compounds (nickel oxide, subsulfide, sulfate heptahydrate). (1,6)
- Soluble nickel compounds are more toxic to the respiratory tract than less soluble compounds. (6)
- EPA has not established a reference concentration (RfC) for nickel. (2-5)
- The RfD for nickel (soluble salts) is 0.02 mg/kg/d based on decreased body and organ weights in rats. The RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious noncancer effects during a lifetime. It is not a direct estimator of risk, but rather a reference point to gauge the potential effects. At exposures increasingly greater than the RfD, the potential for adverse health effects increases. Lifetime exposure above the RfD does not imply that an adverse health effect would necessarily occur. (5)
- EPA has medium confidence in the RfD due to: low confidence in the study on which the RfD for nickel (soluble salts) was based because, although it was properly designed and provided adequate toxicological endpoints, high mortality occurred in the controls; and medium confidence in the database because it provided adequate supporting subchronic studies, one by gavage and the other in drinking water, but inadequacies in the remaining reproductive data. (5)
- Nickel is an essential nutrient for some mammalian species and has been suggested to be essential for human nutrition. By extrapolation from animal data, it is estimated that a 70-kg person would have a daily requirement of 50 μg per kg diet of nickel. (6)
- The California Environmental Protection Agency (CalEPA) has calculated a chronic inhalation reference exposure level of 0.00005 mg/m^3 for nickel based on respiratory and immune system effects reported in rats exposed to a soluble nickel salt. The CalEPA reference exposure level is a concentration at or below which adverse health effects are not likely to occur. (7)
- ATSDR has calculated a chronic-duration inhalation minimal risk level (MRL) of 0.0002 mg/m^3 for nickel based on respiratory effects reported in rats exposed to a soluble nickel salt. The MRL is an estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk of adverse noncancer health effects over a specified duration of exposure. (6)

Reproductive/Developmental Effects:

- No information is available regarding the reproductive or developmental effects of nickel in humans. (6)
- Animal studies have reported reproductive and developmental effects, such as a decreased number of live pups per litter, increased pup mortality, and reduction in fetal body weight, and effects to the female from oral exposure to soluble salts of nickel. (5,6)
- Sperm abnormalities and decreased sperm count have been reported in animals exposed to nickel nitrate orally and nickel oxide by inhalation, respectively. (6)

Cancer Risk:

Nickel Salts

- Nickel sulfate via inhalation and nickel acetate in drinking water were not carcinogenic in either rats or mice. (6)
- EPA has not evaluated soluble salts of nickel as a class of compounds for potential human carcinogenicity. (5)

Nickel Refinery Dust and Nickel Subsulfide

- Human studies have reported an increased risk of lung and nasal cancers among nickel refinery workers exposed to nickel refinery dust. Nickel refinery dust is a mixture of many nickel compounds, with nickel subsulfide being the major constituent. (3,4,6)
- Animal studies have also reported lung tumors from inhalation exposure to nickel refinery dusts and to nickel subsulfide. (3,4)
- EPA has classified nickel refinery dust and nickel subsulfide as Group A, human carcinogens. (3,4)
- EPA uses mathematical models, based on human and animal studies, to estimate the probability of a person developing cancer from breathing air containing a specified concentration of a chemical. EPA calculated an inhalation unit risk estimate of 2.4×10^{-4} $(\mu g/m^3)^{-1}$ for nickel refinery dusts. EPA estimates that, if an individual were to continuously breathe air containing nickel refinery dusts at an average of 0.004 $\mu g/m^3$ (4×10^{-6} mg/m^3) over his or her entire lifetime, that person would theoretically have no more than a one-in-a-million increased chance of developing cancer as a direct result of breathing air containing this chemical. Similarly, EPA estimates that continuously breathing air containing 0.04 $\mu g/m^3$ would result in not greater than a one-in-a-hundred thousand increased chance of developing cancer, and air containing 0.4 $\mu g/m^3$ would result in not greater than a one-in-ten thousand increased chance of developing cancer. For a detailed discussion of confidence in the potency estimates, please see IRIS. (3)
- For nickel subsulfide, EPA calculated an inhalation unit risk estimate of 4.8×10^{-4} $(\mu g/m^3)^{-1}$. EPA estimates that, if an individual were to continuously breathe air containing this nickel compound at an average of 0.002 $\mu g/m^3$ (2×10^{-6} mg/m^3) over his or her entire lifetime, that person would theoretically have no more than a one-in-a-million increased chance of developing cancer as a direct result of breathing air containing this chemical. Similarly, EPA estimates that continuously breathing air containing 0.02 $\mu g/m^3$ would result in not greater than a one-in-a-hundred thousand increased chance of developing cancer, and air containing 0.2 $\mu g/m^3$ would result in not greater than a one-in-ten thousand increased chance of developing cancer. (4)

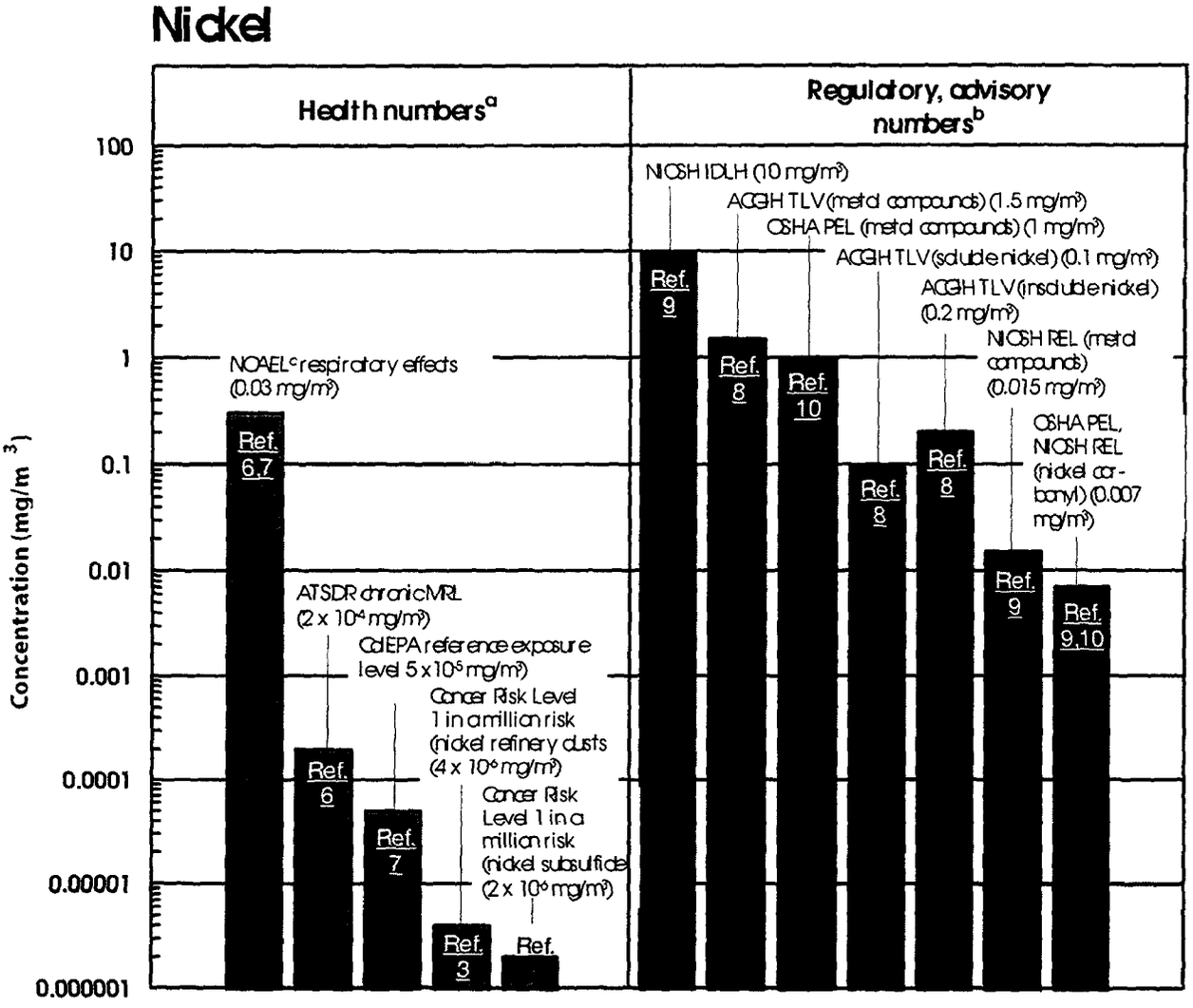
Nickel Carbonyl

- Nickel carbonyl has been reported to produce lung tumors in rats exposed via inhalation. (2)
- EPA has classified nickel carbonyl as a Group B2, probable human carcinogen. (2)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45).
For nickel: 1 ppm = 2.4 mg/m^3.
To convert from µg/m^3 to mg/m^3: mg/m^3 = (µg/m^3) x (1 mg/1,000 µg).

Health Data from Inhalation Exposure



ACGIH TLV – American Conference of Governmental and Industrial Hygienists' threshold limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effects.
NIOSH REL – National Institute of Occupational Safety and Health's recommended exposure limit; NIOSH-recommended exposure limit for an 8- or 10-h time-weighted-average exposure and/or ceiling.

NIOSH IDLH – NIOSH's immediately dangerous to life or health concentration; NIOSH recommended exposure limit to ensure that a worker can escape from an exposure condition that is likely to cause death or immediate or delayed permanent adverse health effects or prevent escape from the environment.
NOAEL – No-observed-adverse-effect level.
OSHA PEL – Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.

[a] Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA.
[b] Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the Government or other groups as advice.
[c] The NOAEL is from the critical study used as the basis for both the ATSDR chronic MRL and CalEPA chronic reference exposure level.

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POLYCHLORINATED BIPHENYLS (PCBs)

1336-36-3

Hazard Summary

PCBs are a group of chemicals that contain 209 individual compounds (known as congeners) with varying harmful effects. Information on specific congener toxicity is very limited. Most toxicity testing has been done on specific commercial mixtures; however, PCB mixtures found in the environment will differ in composition from the commercial mixtures because of biotransformation and bioaccumulation. The U.S. Environmental Protection Agency (EPA) treats all PCBs as being potentially hazardous based on results from some formulations. However, this can have large uncertainty for any given mixture situation.

PCBs are no longer produced or used in the U.S. today; the major source of exposure to PCBs today is the redistribution of PCBs already present in soil and water. No information is available on the acute (short-term) effects of PCBs in humans, and animal studies have reported effects on the liver, kidney, and central nervous system (CNS) from oral exposure to PCBs. Chronic (long-term) exposure to some PCB formulations by inhalation in humans results in respiratory tract symptoms, gastrointestinal effects, mild liver effects, and effects on the skin and eyes such as chloracne, skin rashes, and eye irritation. Epidemiological studies suggest an association between dietary PCB exposures and developmental effects; human reproductive studies are inconclusive. Human studies provide inconclusive, yet suggestive, evidence of an association between PCBs exposure and liver cancer. Animal studies have reported an increase in liver tumors in rats and mice exposed orally to some PCB formulations. EPA has classified PCBs as a Group B2, probable human carcinogen.

Please Note: The main sources of information for this fact sheet are EPA's Integrated Risk Information System (IRIS), which contains information on the carcinogenic effects of PCBs including the unit cancer risk for oral exposure, and the Agency for Toxic Substances and Disease Registry's (ATSDR's) *Toxicological Profile for PCBs*.

Physical Properties

- PCBs are a class of industrial chemicals that contain 209 individual compounds or congeners. (1)
- PCBs made in the U.S. were marketed under the trade name Aroclor and are identified by a four-digit numbering code in which the first two digits indicate that the parent molecule is a biphenyl and for the 1200 series Aroclors the last two digits indicate the chlorine content by weight. For example, Aroclor 1260 has 60 percent chlorine. (1)
- Commercial trade names for PCBs not manufactured in the U.S. include Kanechlor, Clophen, Fenclor, and Phenoclor. (1)
- PCBs are either oily liquids or solids and are colorless to light yellow in color with no known smell or taste. (1)

- The molecular weight for one particular PCB (Aroclor 1260) is 375.7 g/mol; the vapor pressure is 4.05 x 10^{-5} mm Hg at 25 °C; the octanol/water partition coefficient (log K_{ow}) is 6.8. (1)
- PCB mixtures found in environmental media (air, water, sediment, foods) will differ in composition from the commercial mixtures due to differential biotransformation and bioaccumulation among the individual compounds. (1)

Uses

- Before 1974, PCBs were used in capacitors, transformers, plasticizers, surface coatings, inks, adhesives, pesticide extenders, and carbonless duplicating paper. After 1974, use of PCBs was restricted to the production of capacitors and transformers, and after 1979 PCBs were no longer used in the production of capacitors and transformers. (1)

Sources and Potential Exposure

- PCBs are no longer produced in the U.S. and are no longer used in the manufacture of new products; the major source of air exposure to PCBs today is the redistribution of PCBs already present in soil and water. Smaller amounts of PCBs may be released to the air from disposal sites containing transformers, capacitors, and other PCB wastes, incineration of PCB-containing wastes, and improper disposal of the compounds to open areas. (1)
- PCBs have been detected in indoor air at concentrations of an order of magnitude greater than ambient air. It has been suggested that certain electrical appliances and devices, such as fluorescent lighting ballasts, which have PCB-containing components, may emit PCBs to the indoor air. (1)
- In the past, PCBs were released to wastewater from its industrial uses. Today, PCBs are still detected in water due to the environmental recycling of the compound. Most of the PCBs in water are bound to the soil and sediments and may be released to the water slowly over a long period of time. (1)
- PCBs have been detected in food; they bioaccumulate through the food chain, with some of the highest concentrations found in fish. (1)
- PCBs have been listed as a pollutant of concern to EPA's Great Waters Program due to their persistence in the environment, potential to bioaccumulate, and toxicity to humans and the environment. (3)

Assessing Personal Exposure

- Laboratory analyses can detect PCBs in blood, body fat, and breast milk. (1)

Health Hazard Information

Acute Effects:

- No reports of effects in humans following acute exposure to PCBs are available. (1)

- Animal studies have reported acute effects on the liver, kidney, and CNS from oral exposure to PCBs. (1)
- Acute animal tests, such as the LD_{50} test in rats, have shown PCBs to have moderate acute toxicity from oral exposure. (1,4)

Chronic Effects (Noncancer):

- Chronic inhalation exposure of workers to PCBs has been reported to result in respiratory tract symptoms, such as cough and tightness of the chest, gastrointestinal effects including anorexia, weight loss, nausea, vomiting, and abdominal pain, mild liver effects, and effects on the skin and eyes, such as chloracne, skin rashes, and eye irritation. (1,5)
- EPA has not established a reference concentration (RfC) or a reference dose (RfD) for all PCB mixtures. (6)
- The RfD for Aroclor 1016 is 0.00007 mg/kg/d based on reduced birth weights in monkeys. The RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious noncancer effects during a lifetime. It is not a direct estimator of risk, but rather a reference point to gauge the potential effects. At exposures increasingly greater than the RfD, the potential for adverse health effects increases. Lifetime exposure above the RfD does not imply that an adverse health effect would necessarily occur. (7)
- EPA has medium confidence in the RfD based on: medium confidence in the study on which the RfD was based because this was a well-conducted study, but only one group of monkeys was examined; and medium confidence in the database because an extensive amount of data are available but mixtures of PCBs in the environment do not match the pattern of congeners found in Aroclor 1016. (7)
- The RfD for Aroclor 1254 is 0.00002 mg/kg/d based on immunological effects in monkeys. (8)
- EPA has medium confidence in the RfD based on: (1) medium confidence in the study on which the RfD was based because groups of monkeys were tested at four dose levels and a lowest-observed-adverse-effect level (LOAEL) was established; and (2) medium confidence in the database because an extensive number of laboratory animal and human studies were available for review, but human data are available for PCB mixtures in general but not specifically for Aroclor 1254. (8)
- EPA has not established an RfC for Aroclor 1016 or Aroclor 1254. (7,8)

Reproductive/Developmental Effects:

- An epidemiological study of women occupationally exposed to high levels of PCBs suggested a relationship between PCB exposure and reduced birth weight and shortened gestational age of their babies; however, limitations of the study limit the strength of the conclusion. (1)
- Two human studies that investigated exposure to PCBs through the consumption of contaminated fish suggest that exposure to PCBs may cause developmental effects in humans. Both studies reported an association between consumption of fish with high

PCB levels by pregnant women and an increased incidence of neurodevelopmental effects, such as motor deficits at birth, impaired psychomotor index, impaired visual recognition, and deficits in short-term memory in infants. (1)

- Human studies are not conclusive on the reproductive effects of PCBs. One study of men who were occupationally exposed to PCBs showed no fertility abnormalities, while another study of men with low sperm counts found elevated levels of PCBs in the blood and an association between certain PCB compounds in semen and decreased sperm motility. (1)
- Animal studies have reported developmental effects, such as learning deficits, impaired immune functions, focal liver necrosis, and cellular alterations of the thyroid, in the offspring of animals exposed orally to PCBs. Reproductive effects, such as decreased fertility, decreased conception, and prolonged menstruation have also been noted in animal studies of dietary PCB exposures. (1)

Cancer Risk:

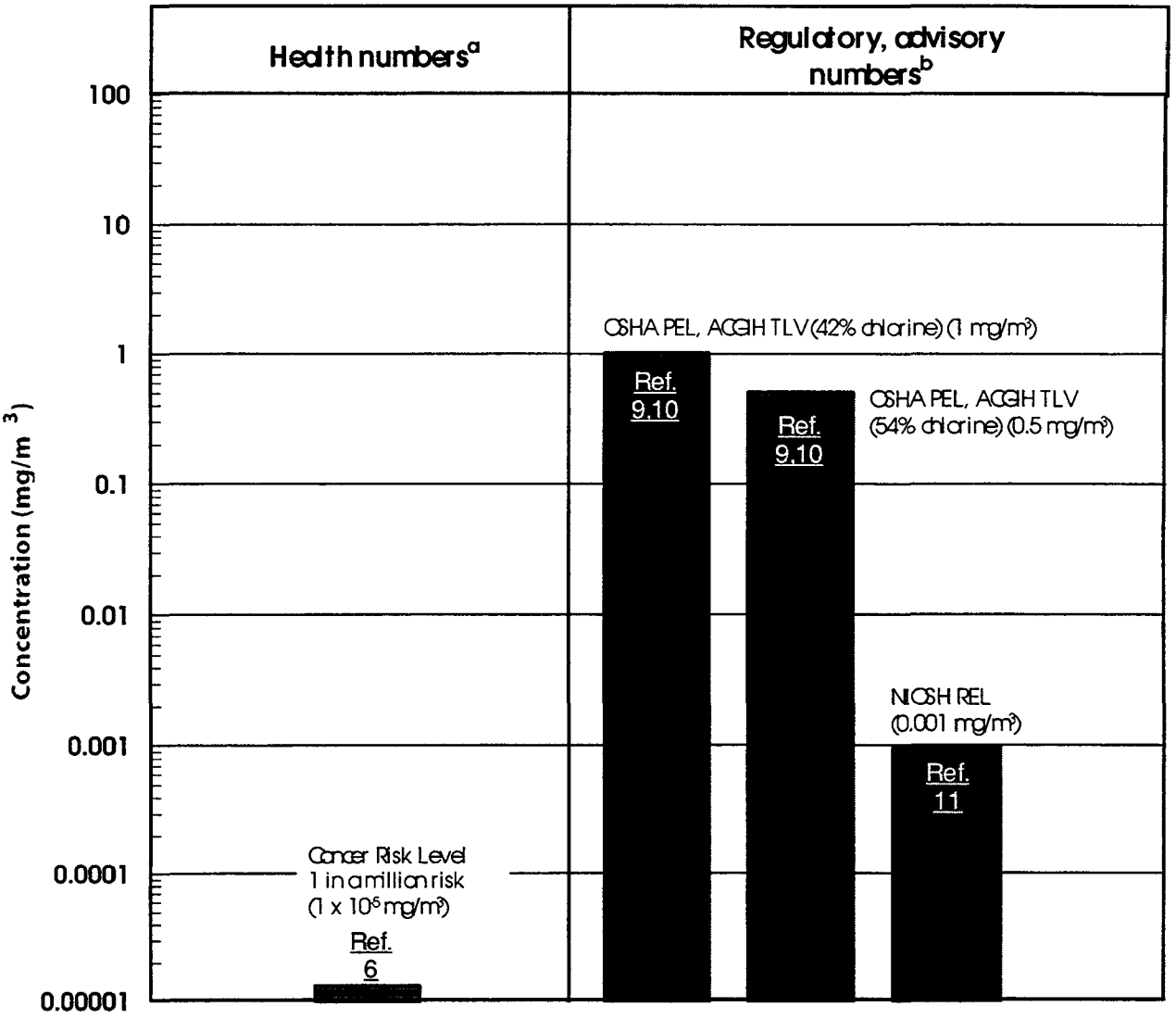
- Human studies provide inconclusive, yet suggestive evidence of an association between PCBs' exposure and liver cancer. Several studies have reported an increase in liver cancer among persons occupationally exposed to some PCB formulations. However, the studies are inconclusive due to confounding exposures and lack of exposure quantification. (1,6)
- Oral exposure studies in animals show an increase in liver tumors in rats and mice exposed to several commercial mixtures of PCBs and to several specific congeners. (1,6)
- No animal inhalation studies are available on PCBs. (1)
- EPA has classified PCBs as a Group B2, probable human carcinogen. (6)
- EPA uses mathematical models, based on human and animal studies, to estimate the probability of a person developing cancer from ingesting water containing a specified concentration of a chemical. EPA calculated an upper bound inhalation unit cancer risk estimate of 1.0×10^{-4} $(\mu g/m^3)^{-1}$ for inhalation of evaporated PCB congeners. EPA estimates that, if an individual were to continuously breathe air containing PCBs at an average of 0.01 $\mu g/m^3$ (1×10^{-5} mg/m^3) over his or her entire lifetime, that person would theoretically have no more than a one-in-a-million increased chance of developing cancer as a direct result of breathing air containing this chemical. Similarly, EPA estimates that breathing air containing 0.1 $\mu g/m^3$ (1×10^{-4} mg/m^3) would result in not greater than a one-in-a-hundred thousand increased chance of developing cancer, and air containing 1.0 $\mu g/m^3$ (1×10^{-3} mg/m^3) would result in not greater than a one-in-ten thousand increased chance of developing cancer. For a detailed discussion of confidence in the potency estimates, please see IRIS. (6)
- EPA has calculated an upperbound oral cancer slope factor of 0.4 $(mg/kg/d)^{-1}$ for ingestion of water soluble congeners, an upperbound oral cancer slope factor of 2.0 $(mg/kg/d)^{-1}$ for food chain exposure, and an upperbound oral cancer slope factor of 0.07 $(mg/kg/d)^{-1}$ for PCB exposures where congeners with more than 4 chlorines comprise less than 5 percent of the total. (6)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45). For Aroclor 1260: 1 ppm = 15.4 mg/m^3. To convert from µg/m^3 to mg/m^3: mg/m^3 = (µg/m^3) x (1 mg/1,000 µg).

Health Data from Inhalation Exposure

Polychlorinated biphenyls



ACGIH TLV – American Conference of Governmental and Industrial Hygienists' threshold limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effects.

NIOSH REL – National Institute of Occupational Safety and Health's recommended exposure limit; NIOSH-recommended exposure limit for an 8- or 10-h time-weighted-average exposure and/or ceiling.

OSHA PEL – Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.

[a] Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA.
[b] Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the Government or other groups as advice.

References

1. Agency for Toxic Substances and Disease Registry (ATSDR). *Toxicological Profile for Polychlorinated Biphenyls*. Public Health Service, U.S. Department of Health and Human Services, Atlanta, GA. 1997.

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4. U.S. Department of Health and Human Services. Registry of Toxic Effects of Chemical Substances (RTECS, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.

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10. American Conference of Governmental Industrial Hygienists (ACGIH). *1999 TLVs and BEIs. Threshold Limit Values for Chemical Substances and Physical Agents, Biological Exposure Indices.* Cincinnati, OH. 1999.

11. National Institute for Occupational Safety and Health (NIOSH). *Pocket Guide to Chemical Hazards.* U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention. Cincinnati, OH. 1997.

POLYCYCLIC ORGANIC MATTER (POM)[1]

Hazard Summary

The term POM defines a broad class of compounds that includes the polycyclic aromatic hydrocarbon compounds (PAHs), of which benzo[a]pyrene is a member. POM compounds are formed primarily from combustion and are present in the atmosphere predominantly in particulate form with a smaller amount as vapor. Sources of air emissions are diverse and include cigarette smoke, vehicle exhaust, home heating, laying tar, and grilling meat. Skin exposures to mixtures of carcinogenic PAHs cause skin disorders in humans and animals. No information is available on the reproductive or developmental effects of POM in humans, while animal studies have reported that benzo[a]pyrene, via oral exposure, causes reproductive and developmental effects. Cancer is the major concern from exposure to POM. Epidemiologic studies have reported an increase in lung cancer in humans exposed to coke oven emissions, roofing tar emissions, and cigarette smoke; all of these mixtures contain POM compounds. Animal studies have reported respiratory tract tumors from inhalation exposure to benzo[a]pyrene and forestomach tumors, leukemia, and lung tumors from oral exposure to benzo[a]pyrene. The U.S. Environmental Protection Agency (EPA) has classified seven PAHs (benzo[*a*]pyrene, benz[a]anthracene, chrysene, benzo[b]fluoranthene, benzo[k]fluoranthene, dibenz[a,h]anthracene, and indeno[1,2,3-cd]pyrene) as Group B2, probable human carcinogens.

Please Note: The main sources of information for this fact sheet are EPA's Integrated Risk Information System (IRIS), which contains information on the carcinogenic effects of benzo(*a*)pyrene including the unit cancer risk for oral exposure, and the Agency for Toxic Substances and Disease Registry's (ATSDR's) *Toxicological Profile for Polycyclic Aromatic Hydrocarbons (PAHs).*

Physical Properties

- The term POM generally defines a broad class of compounds that includes all organic structures having two or more fused aromatic rings (i.e., rings that share a common border), and that have a boiling point greater than or equal to 212 °F (100 °C). The 1990 Amendments to the Clean Air Act describes POM as including "organic compounds with more than one benzene ring, and which have a boiling point greater than or equal to 100 degrees C." (11)
- POM has been identified with up to seven fused rings and, theoretically, millions of POM compounds could be formed; however, only about 100 species have been identified and studied. (11)

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[1] Polycyclic organic matter consists of polycyclic aromatic hydrocarbons (PAHs), including benzo(*a*)pyrene (CAS#50-32-8), their nitrogen analogs, and a small number of oxygen-containing polycyclic organic matter compounds.

- Eight major categories of compounds have been defined by the EPA to constitute the class known as POM. The most common category is the polycyclic aromatic hydrocarbons (PAHs), also known as polynuclear aromatics, which include benzo[a]pyrene. (11)
- Most POM compounds are solids with high melting and boiling points, and are extremely insoluble in water. The PAHs are primarily planar, nonpolar compounds with melting points considerably over 212 °F (100 °C). Phenanthrene, with a melting point of 214 °F (101 °C), and benzo[c]phenanthrene, with a melting point of 154 °F (68 °C), are two exceptions. (11)
- POM is present in the atmosphere predominantly in the particulate form with a smaller amount in the vapor phase. (11)
- The chemical formula for benzo[a]pyrene is $C_{20}H_{12}$, and the molecular weight is 252.3 g/mol. (1)
- The vapor pressures of POM compounds vary, depending upon the ring size and molecular weight, from 6.8×10^{-4} mm Hg for phenanthrene, to 1.5×10^{-12} for coronene. The vapor pressure for benzo[a]pyrene is 5.6×10^{-9} mm Hg at 25 °C, and it has a log octanol/water partition coefficient (log K_{ow}) of 6.06. (1,11)

Uses

- The majority of the polycyclic organic compounds have no commercial uses. (11)
- Solutions containing mixtures of some PAHs are used to treat some skin disorders in humans. (1)

Sources and Potential Exposure

- The primary source of POM is formation during combustion. A less significant formation mechanism is the volatilization of lightweight POM compounds, which occurs in the production and use of naphthalene. (11)
- Polycyclic organic compounds have been detected in ambient air from sources including cigarette smoke, vehicle exhausts, asphalt road paving, coal burning, application of coal tar, agricultural burning, residential wood burning, and hazardous waste sites. The compounds present in POM and their relative amounts differ among different sources (e.g, POM from diesel exhaust is chemically different than POM from wood burning). (1,2)
- Benzo[a]pyrene, one of the more commonly monitored PAHs, has been detected in urban air at levels approximately twice as high as those in rural areas (e.g., 0.6 ng/m^3 versus 0.3 ng/m^3). Seasonal variations have also been observed from monitoring in the Northeast U.S. during the early 1980's, with mean benzo[a]pyrene concentrations during the winter more than an order of magnitude greater than during the summer. (11)
- PAHs have been found in some drinking water supplies. (1)
- Cooking meat or other foods at high temperatures increases the amount of PAHs in the food. (1)
- Occupational exposure to PAHs may occur in coal tar production plants, coking plants, coal-gasification sites, smokehouses, municipal trash incinerators, and other facilities. (1)

- POM has been listed as a pollutant of concern in EPA's Great Waters Program due to its persistence in the environment, potential to bioaccumulate, and toxicity to humans and the environment (2).

Assessing Personal Exposure

- PAHs or their breakdown products can be measured in urine, blood, or body tissues. (1)

Health Hazard Information

Acute Effects:

- No reports of effects to humans following acute (short-term) exposure to POM are available.
- Acute animal tests, such as the LD_{50} test in rats, have shown benzo[a]pyrene to have high acute toxicity from oral exposure. (3)

Chronic Effects (Noncancer):

- Skin exposures to mixtures of carcinogenic PAHs cause skin disorders in humans and animals, and adverse skin effects have been noted in humans and animals following application of solutions containing benzo[a]pyrene. (1)
- An epidemiological study of workers exposed by inhalation to benzo[a]pyrene and other particulate matter reported some respiratory effects. The role of benzo[a]pyrene in this association, however, is unclear. (1)
- Animal studies have reported effects on the blood and liver from oral exposure to benzo[a]pyrene and a slight hypersensitivity response from dermal exposure to benzo[a]pyrene. (1)
- EPA has not established a reference concentration (RfC) or a reference dose (RfD) for POM or for benzo[a]pyrene. (4,5)

Reproductive/Developmental Effects:

- No information is available on the reproductive or developmental effects of POM in humans.
- Animal studies have indicated that benzo[a]pyrene, via oral exposure, induces reproductive toxicity, including a reduced incidence of pregnancy and decreased fertility. Developmental effects, such as a reduced viability of litters and reduced mean pup weight, have also been noted from oral exposure to benzo[a]pyrene in animals. (1,6)

Cancer Risk:

- Epidemiologic studies have reported an increase in lung cancer in humans exposed to coke oven emission, roofing tar emissions, and cigarette smoke. Each of these mixtures contains a number of POM compounds (e.g., certain PAHs). (1,6)

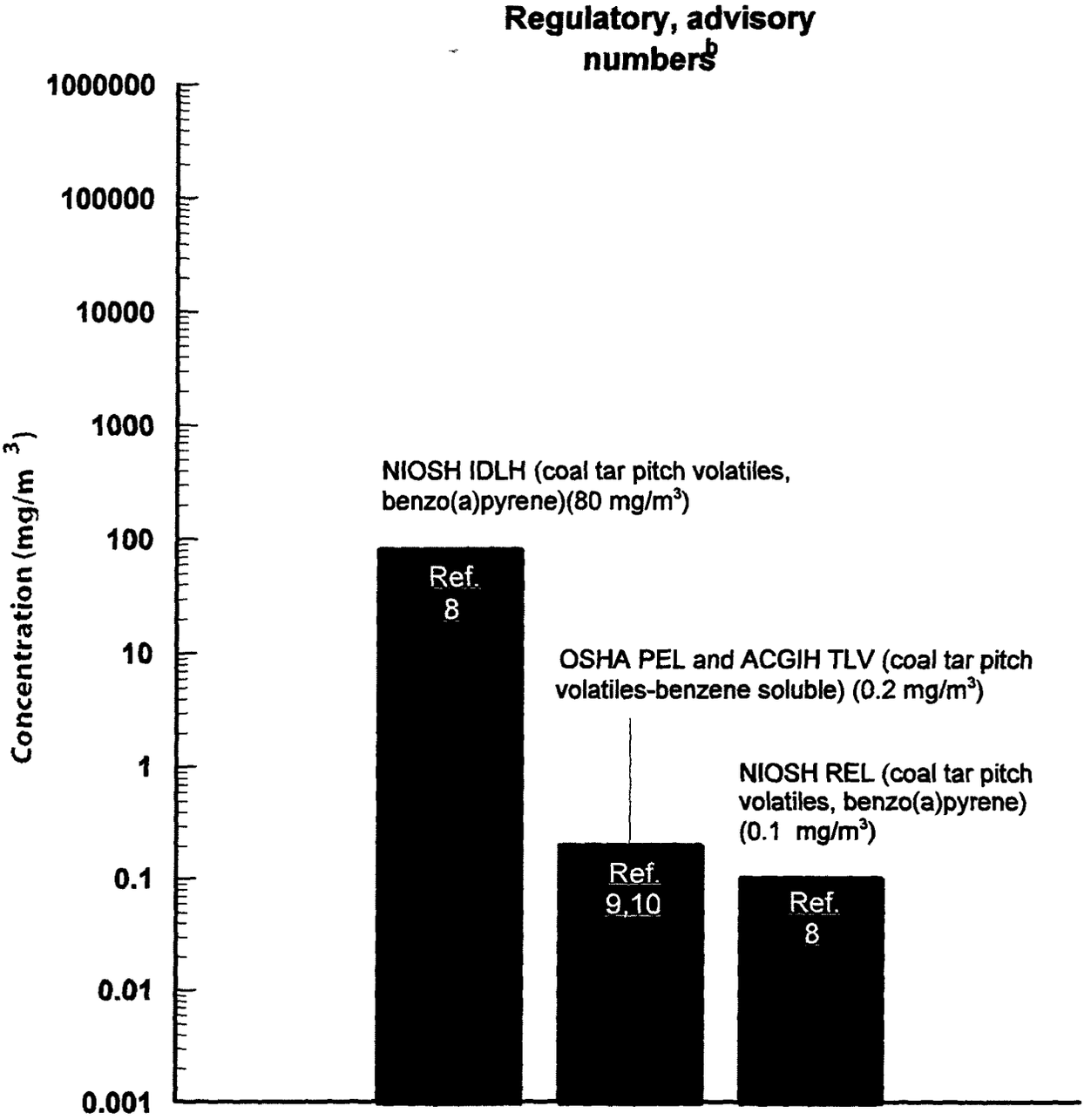
- Animal studies have reported respiratory tract tumors from inhalation exposure to benzo(*a*)pyrene and forestomach tumors, leukemia, and lung tumors from oral exposure to benzo[a]pyrene. (1,5,7)
- EPA has classified seven PAHs (benzo[*a*]pyrene, benz[a]anthracene, chrysene, benzo[b]fluoranthene, benzo[k]fluoranthene, dibenz[a,h]anthracene, and indeno[1,2,3-cd]pyrene) as Group B2, probable human carcinogens. (4,5,12-17)
- EPA uses mathematical models, based on human and animal studies, to estimate the probability of a person developing cancer from ingesting water containing a specified concentration of a chemical. Although a quantitative cancer risk estimate for the mixture of POM has not been derived, EPA has calculated an oral cancer slope factor of 7.3 $(mg/kg/d)^{-1}$ for benzo[a]pyrene, one of the many constituents of POM. For a detailed discussion of the confidence in the potency estimates, please see IRIS. (5)
- The California Environmental Protection Agency (CalEPA) has calculated an inhalation unit risk estimate of 1.1×10^{-3} $(\mu g/m^3)^{-1}$ for benzo[a]pyrene, one of the many constituents of POM. (7)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45).
For benzo(a)pyrene: 1 ppm = 10.3 mg/m^3.
To convert from $\mu g/m^3$ to mg/m^3: mg/m^3 = ($\mu g/m^3$) x (1 mg/1,000 μg).

Health Data from Inhalation Exposure

Coal Tar Pitch Volatiles[a]



ACGIH TLV – American Conference of Governmental and Industrial Hygienists' threshold limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effects.

NIOSH REL – National Institute of Occupational Safety and Health's recommended exposure limit; NIOSH-recommended exposure limit for an 8- or 10-h time-weighted-average exposure and/or ceiling.

NIOSH IDLH – NIOSH's recommended exposure limit; NIOSH-recommended immediately dangerous to health level.
OSHA PEL – Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effects averaged over a normal 8-h workday or a 40-h workweek.

[a] These chemicals, a subset of POM, are emitted from the application of hot coal tar pitch.
[b] Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the Government or other groups as advice.

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12. U.S. Environmental Protection Agency (EPA). *Integrated Risk Information System (IRIS) on Benz[a]anthracene.* National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1999.

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14. U.S. Environmental Protection Agency (EPA). *Integrated Risk Information System (IRIS) on Benzo[k]fluoranthene.* National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1999.

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16. U.S. Environmental Protection Agency (EPA). *Integrated Risk Information System (IRIS) on Dibenz[a,h]anthracene.* National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1999.

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QUINOLINE
91-22-5

Hazard Summary

Quinoline is used mainly as an intermediate in the manufacture of other products. Potential exposure to quinoline may occur from the inhalation of cigarette smoke and, to a much lesser extent, ambient air contaminated by emissions from the petroleum and coal industries. Acute (short-term) inhalation exposure to quinoline vapors irritates the eyes, nose, and throat and may cause headaches, dizziness, and nausea in humans. Information on the chronic (long-term), reproductive, developmental, or carcinogenic effects of quinoline in humans is not available. Liver damage has been observed in rats chronically exposed to quinoline by ingestion. An increased incidence of liver vascular tumors has been observed in rats and mice orally exposed to quinoline. The U.S. Environmental Protection Agency (EPA) has provisionally classified quinoline as a Group C, possible human carcinogen.

Please Note: The main source of information for this fact sheet is EPA's *Health and Environmental Effects Profile for Quinoline*. Other secondary sources include the Hazardous Substances Data Bank (HSDB), a database of summaries of peer-reviewed literature, and the Registry of Toxic Effects of Chemical Substances (RTECS), a database of toxic effects that are not peer reviewed.

Physical Properties

- The chemical formula for quinoline is C_9H_7N, and it has a molecular weight of 129.15 g/mol. (7)
- Quinoline occurs as a colorless, hygroscopic liquid that darkens with age and is sparingly soluble in water but is more easily soluble in hot water. (3,7)
- Quinoline has a penetrating, pungent odor. (3,7)
- The vapor pressure of quinoline is 0.0091 mm Hg at 25 °C and its log octanol/water partition coefficient (log K_{ow}) is 2.03. (3)

Uses

- Quinoline is used mainly as an intermediate in the manufacture of other products. (3)
- Quinoline is also used as a catalyst, a corrosion inhibitor, in metallurgical processes, in the manufacture of dyes, as a preservative for anatomical specimens, in polymers and agricultural chemicals, and as a solvent for resins and terpenes. It is also used as an antimalarial medicine. (2,3,7)

Sources and Potential Exposure

- Workers in certain industries may be occupationally exposed to quinoline by inhalation, ingestion of particulates, or dermal contact. (1,2)

- A potential source of very low exposure to quinoline includes the inhalation of ambient air contaminated by emissions from petroleum refining, coal mining, quenching and coking, and release in shale oil, synthetic coal conversion wastewaters, and wood preservative wastewaters. Levels of 2-7 $\mu g/m^3$ have been measured in ambient air. (1,3)
- Quinoline is found at higher levels in cigarette smoke (1-20 μg/cigarette). (1,3)
- Underground coal gasification has been a source of quinoline contamination of groundwater. Individuals may be exposed by consumption of contaminated water. (1)

Assessing Personal Exposure

- No information was located regarding the measurement of personal exposure to quinoline.

Health Hazard Information

Acute Effects:

- Acute inhalation exposure to quinoline vapor irritates the eyes, nose, and throat, and may cause headaches, dizziness, and nausea, and, at high concentrations, coma in humans. (3)
- Tests involving acute exposure of animals, such as the LD_{50} test in rats and rabbits, have demonstrated quinoline to have high acute toxicity by oral or dermal exposure. (4)

Chronic Effects (Noncancer):

- Information on the chronic effects of quinoline in humans is not available. (3)
- Liver damage has been observed in rats chronically exposed to quinoline by ingestion. (3)
- EPA has not established a reference concentration (RfC) or reference dose (RfD) for quinoline. (5)

Reproductive/Developmental Effects:

- No information is available on the reproductive or developmental effects of quinoline in humans or animals. (3)

Cancer Risk:

- No human studies are available on the carcinogenicity of quinoline. (3)
- An increased incidence of liver hemangioendotheliomas (liver vascular tumors) has been observed in rats and mice orally exposed to quinoline. (3)
- EPA has provisionally classified quinoline as a Group C, possible human carcinogen. (3,6)
- EPA has calculated a provisional oral cancer slope factor of 12 $(mg/kg/d)^{-1}$. A provisional value is one which has not received Agency-wide review. (6)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45).
For quinoline: 1 ppm = 5.3 mg/m^3.

Note: There are very few health numbers or regulatory/advisory numbers for quinoline; thus, a graph has not been prepared for this compound.

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2,3,7,8-TETRACHLORODIBENZO-p-DIOXIN (2,3,7,8-TCDD)

1746-01-6

Hazard Summary

2,3,7,8-Tetrachlorodibenzo-p-dioxin (2,3,7,8-TCDD) is formed as an unintentional by-product of incomplete combustion. It may be released to the environment during the combustion of fossil fuels and wood, and during the incineration of municipal and industrial wastes. It causes chloracne in humans, a severe acne-like condition, and has been shown to be very toxic in animals studies. It is known to be a developmental toxicant in animals, causing skeletal deformities, kidney defects, and weakened immune responses in the offspring of animals exposed to 2,3,7,8-TCDD during pregnancy. Human studies have shown an association between 2,3,7,8-TCDD and soft-tissue sarcomas, lymphomas, and stomach carcinomas. The U.S. Environmental Protection Agency (EPA) has classified 2,3,7,8- TCDD as a Group B2, probable human carcinogen.

Please Note: The main source of information for this fact sheet is the Agency for Toxic Substances and Disease Registry's (ATSDR's) *Toxicological Profile for Chlorinated Dibenzo-p-Dioxins*.

Physical Properties

- 2,3,7,8-TCDD is a colorless solid with no distinguishable odor. (1)
- The chemical formula for 2,3,7,8-TCDD is $C_{12}H_4Cl_4O_2$, and the molecular weight is 322 g/mol. (1)
- The vapor pressure for 2,3,7,8-TCDD is 7.4 $x10^{-10}$ at 25 °C, and it has an octanol/water partition coefficient (log K_{ow}) of 6.8 - 7.58. (1)

Uses

- 2,3,7,8-TCDD is not intentionally produced by industry. It can be inadvertently produced in very small amounts as an impurity during the incineration of municipal and industrial wastes and during the manufacture of certain chemicals. (1)
- The only present use for 2,3,7,8-TCDD is in chemical research. (1)

Sources and Potential Exposure

- 2,3,7,8-TCDD may be formed during the chlorine bleaching process used by pulp and paper mills, and as a by-product from the manufacture of certain chlorinated organic chemicals, such as chlorinated phenols. (1)
- 2,3,7,8-TCDD is primarily released to the environment during the combustion of fossil fuels (including motor vehicles) and wood, and during incineration processes. (1)
- Very low levels of 2,3,7,8-TCDD are found throughout the environment, including air, food, and soil. (1)

- Most of the exposure of the general population to 2,3,7,8-TCDD is from food, mainly meat, dairy products, and fish. (1)

Assessing Personal Exposure

- Body fat, blood, and breast milk may be analyzed for 2,3,7,8-TCDD. (1)

Health Hazard Information

Acute Effects:

- The major acute (short-term) effect from exposure of humans to high levels of 2,3,7,8-TCDD in air is chloracne, a severe acne-like condition that can develop within months of first exposure. (1,2)
- Acute animal tests, such as the LD_{50} test in dogs, monkeys, and guinea pigs, have shown 2,3,7,8-TCDD to have extreme toxicity from oral exposure. (1)

Chronic Effects (Noncancer):

- Chloracne is also the major effect seen from chronic (long-term) exposure to 2,3,7,8-TCDD. (1)
- Animal studies have reported hair loss, loss of body weight, and a weakened immune system from oral exposure to 2,3,7,8-TCDD. (1)
- EPA has not established a reference concentration (RfC) or a reference dose (RfD) for 2,3,7,8-TCDD.
- ATSDR has calculated a chronic oral minimal risk level (MRL) of 1×10^{-9} mg/kg/d based on neurological effects in monkeys. The MRL is an estimate of daily exposure to a dose of a chemical that is likely to be without appreciable risk of adverse noncancerous effects over a specified duration of exposure. Exposure to a level above the MRL does not mean that adverse effects will occur. The MRL is used by public health professionals as a screening tool. (1)

Reproductive/Developmental Effects:

- The results of available reproductive and developmental studies in humans are inconclusive. (1)
- Animal studies have reported developmental effects, such as skeletal deformities, kidney defects, and weakened immune responses in the offspring of animals exposed to 2,3,7,8-TCDD during pregnancy. (1)
- Reproductive effects, including altered levels of sex hormones, reduced production of sperm, and increased rates of miscarriages, have been seen in animals exposed to 2,3,7,8-TCDD. (1)

Cancer Risk:

- Human studies, primarily of workers occupationally exposed to 2,3,7,8-TCDD by inhalation, have found an association between 2,3,7,8-TCDD and lung cancer, soft-tissue sarcomas, lymphomas, and stomach carcinomas, although for malignant lymphomas, the increase in risk is not consistent. (1)
- No information is available on the carcinogenic effects of 2,3,7,8-TCDD in animals following inhalation exposure. (1)
- Animal studies have reported tumors of the liver, lung, tongue, thyroid, and nasal turbinates from oral exposure to 2,3,7,8-TCDD. (1)
- EPA has classified 2,3,7,8-TCDD as a Group B2, probable human carcinogen. (2,3)
- EPA has calculated a provisional inhalation cancer slope factor of 1.5×10^{5} $(mg/kg/d)^{-1}$ and an inhalation unit risk estimate of 3.3×10^{-5} $(pg/m^3)^{-1}$ for 2,3,7,8-TCDD. The provisional slope factor is a value that has had some form of Agency review, but it does not appear on IRIS. (2,3)
- EPA has calculated a provisional oral cancer slope factor of 1.5×10^{5} $(mg/kg/d)^{-1}$ and an oral unit risk factor of 4.5 $(\mu g/L)^{-1}$ for 2,3,7,8-TCDD. (2,3)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45). For 2,3,7,8-TCDD: 1 ppm = 13.2 mg/m^3.

Note: There are very few health numbers or regulatory/advisory numbers for 2,3,7,8-TCDD; thus, a graph has not been prepared for this compound.

References

1. Agency for Toxic Substances and Disease Registry (ATSDR). *Toxicological Profile for Chlorinated Dibenzo-p-Dioxins*. Public Health Service, U.S. Department of Health and Human Services, Atlanta, GA. 1998.

2. U.S. Environmental Protection Agency (EPA). *Health Effects Assessment Summary Tables. FY 1997 Update.* Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment, Office of Research and Development, Cincinnati, OH. 1997.

3. U.S. Environmental Protection Agency (EPA). *Health Assessment Document for Polychlorinated Dibenzo-p-Dioxin.* Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment, Office of Research and Development, Cincinnati, OH. EPA 600/8-84-014F. 1985.

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1,1,2,2-TETRACHLOROETHANE

79-34-5

Hazard Summary

As 1,1,2,2-tetrachloroethane is no longer used much in the U.S., current air emissions predominantly result from its use as a chemical intermediate during the manufacture of other chemicals. Low levels have been detected in air. The main effects of 1,1,2,2-tetrachloroethane are liver and neurological effects. Acute (short-term) inhalation exposure to very high levels of 1,1,2,2-tetrachloroethane has resulted in effects on the liver and respiratory, central nervous, and gastrointestinal systems in humans. Chronic (long-term) inhalation exposure to 1,1,2,2-tetrachloroethane in humans results in jaundice and an enlarged liver, headaches, tremors, dizziness, numbness, and drowsiness. Animal studies have shown a significantly increased incidence of liver tumors in mice orally exposed to 1,1,2,2-tetrachloroethane. The U.S. Environmental Protection Agency (EPA) has classified 1,1,2,2-tetrachloroethane as a Group C possible human carcinogen.

Please Note: The main sources of information for this fact sheet are EPA's Integrated Risk Information System (IRIS), which contains information on the carcinogenic effects of 1,1,2,2-tetrachloroethane, and the Agency for Toxic Substances and Disease Registry's (ATSDR's) *Toxicological Profile for 1,1,2,2-Tetrachloroethane.*

Physical Properties

- 1,1,2,2-Tetrachloroethane is a colorless, dense liquid that has a sweet, chloroform like odor. (1,6)
- The odor threshold for 1,1,2,2-tetrachloroethane is 1.5 ppm. (6)
- The chemical formula for 1,1,2,2-tetrachloroethane is $C_2H_2Cl_4$, and the molecular weight is 167.85 g/mol. (1,2)
- The vapor pressure for 1,1,2,2-tetrachloroethane is 5.95 mm Hg at 25 °C, and it has a log octanol/water partition coefficient (log K_{ow}) of 2.39. (1)
- The half-life in air is about 60 days. (1)

Uses

- The production of 1,1,2,2-tetrachloroethane has decreased significantly in the U.S. (1)
- In the past, 1,1,2,2-tetrachloroethane was used in large amounts to produce trichloroethylene, tetrachloroethylene, and 1,2,-dichloroethylene. (1)
- It was also used as a solvent, in cleaning and degreasing metals, in paint removers, varnishes and lacquers, in photographic films, as an extractant for oils and fats, and in pesticides. (1)

Sources and Potential Exposure

- As it is no longer used much in the U.S., present sources of 1,1,2,2-tetrachloroethane are chemical production activities in which it is an intermediate product. (1)
- Low levels of 1,1,2,2-tetrachloroethane can be present in both indoor and outdoor air. In the early 1980s, average ambient air concentrations were around 0.005 ppb, and average concentrations in the indoor air of several homes measured 1.8 ppb. (1)
- 1,1,2,2-Tetrachloroethane has been found, in trace amounts, in adhesives, oils, greases, and lubricants; these household products may contaminate indoor air. (1)
- Limited occupational exposure to 1,1,2,2-tetrachloroethane may occur through inhalation of the vapors or through skin contact due to spills or accidents in the workplace. (1)
- 1,1,2,2-Tetrachloroethane has been detected in surface water and groundwater; however, a nationwide survey of drinking water supplies in the 1980s did not find any supplies containing 1,1,2,2-tetrachloroethane. (1)

Assessing Personal Exposure

- No specific medical tests are available to determine exposure to 1,1,2,2-tetrachloroethane. (1)

Health Hazard Information

Acute Effects:

- Acute exposure to very high levels of 1,1,2,2-tetrachloroethane has caused death in humans; the autopsies revealed severe liver destruction. (1,2)
- Respiratory and eye irritation, dizziness, nausea, and vomiting have been noted in humans exposed to fumes in the workplace. (1)
- Animal studies have reported effects on the liver, eyes, and central nervous system (CNS) from acute inhalation exposure to 1,1,2,2,-tetrachloroethane. (1)
- Tests involving acute exposure of animals, such as the LC_{50} and LD_{50} tests in rats and mice, have shown 1,1,2,2-tetrachloroethane to have moderate acute toxicity. (3)

Chronic Effects (Noncancer):

- Chronic exposure of humans to high levels of 1,1,2,2-tetrachloroethane results in effects on the liver (jaundice and an enlarged liver), central and peripheral nervous system (headaches, tremors, dizziness, and drowsiness), and gastrointestinal effects (pain, nausea, vomiting, and loss of appetite). (1)
- Liver effects have also been observed in animals exposed via inhalation. (1)
- EPA has not established a reference concentration (RfC) or reference dose (RfD) for 1,1,2,2-tetrachloroethane. (4)
- ATSDR has calculated an intermediate-duration inhalation minimal risk level (MRL) of 0.4 ppm (3 mg/m^3) for 1,1,2,2-tetrachloroethane based on liver effects in rats. The MRL is an estimate of the daily human exposure to a hazardous substance that is likely to be

without appreciable risk of adverse noncancer health effects over a specified duration of exposure. Exposure to a level above the MRL does not mean that adverse health effects will occur. The MRL is intended to serve as a screening tool. (1)

Reproductive/Developmental Effects:

- No studies are available regarding developmental or reproductive effects in humans from inhalation or oral exposure to 1,1,2,2-tetrachloroethane. (1)
- Animal studies have not reported reproductive effects from inhalation exposure to 1,1,2,2-tetrachloroethane, while an oral study in rats reported histopathological changes in the testes. (1)
- No effects to the offspring of male rats exposed to 1,1,2,2-tetrachloroethane via inhalation were reported. (1)

Cancer Risk:

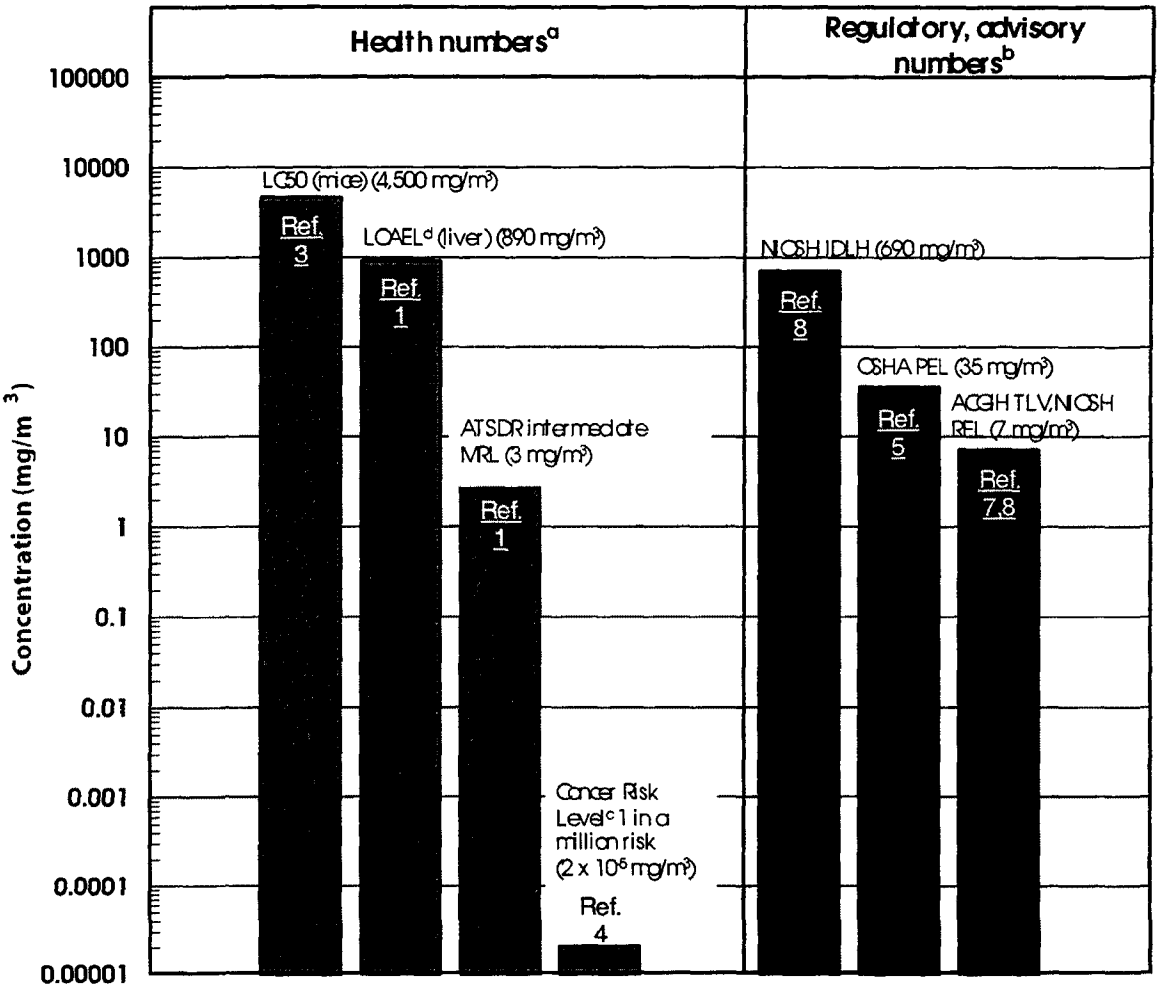
- Oral exposure to 1,1,2,2-tetrachloroethane in mice resulted in an increased incidence of hepatocellular carcinomas, while no increase in tumors was reported in rats. (1,4)
- EPA has classified 1,1,2,2-tetrachloroethane as a Group C, possible human carcinogen. (4)
- EPA uses mathematical models, based on human and animal studies, to estimate the probability of a person developing cancer from breathing air containing a specified concentration of a chemical. EPA has calculated an inhalation unit risk estimate of 5.8 x 10^{-5} $(\mu g/m^3)^{-1}$. EPA estimates that, if an individual were to continuously breathe air containing 1,1,2,2-tetrachloroethane at an average of 0.02 $\mu g/m^3$ (2.0 x 10^{-5} mg/m^3) over his or her entire lifetime, that person would theoretically have no more than a one-in-a-million increased chance of developing cancer as a direct result of breathing air containing this chemical. Similarly, EPA estimates that continuously breathing air containing 0.2 $\mu g/m^3$ (2.0 x 10^{-4} mg/m^3) would result in not greater than a one-in-a-hundred thousand increased chance of developing cancer over a lifetime, and air containing 2.0 $\mu g/m^3$ (2.0 x 10^{-3} mg/m^3) would result in not greater than a one-in-ten thousand increased chance of developing cancer. For a detailed discussion of confidence in the potency estimates, please see IRIS. (4)
- EPA has also calculated an oral cancer slope factor of 0.2 $(mg/kg/d)^{-1}$. (4)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45).
For 1,1,2,2-tetrachloroethane: 1 ppm = 6.86 mg/m^3.
To convert from $\mu g/m^3$ to mg/m^3: mg/m^3 = ($\mu g/m^3$) x (1 mg/1,000 μg).

Health Data from Inhalation Exposure

1,1,2,2-Tetrachloroethane



ACGIH TLV – American Conference of Governmental and Industrial Hygienists' threshold limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effects.

LC_{50} (Lethal Concentration$_{50}$) – A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.

LOAEL – Lowest-observed-no-adverse-affect level.

NIOSH REL – National Institute of Occupational Safety and Health's recommended exposure limit; NIOSH-recommended exposure limit for an 8- or 10-h time-weighted-average exposure and/or ceiling.

NIOSH IDLH – NIOSH's immediately dangerous to life or health concentration; NIOSH recommended exposure limit to ensure that a worker can escape from an exposure condition that is likely to cause death or immediate or delayed permanent adverse health effects or prevent escape from the environment.

OSHA PEL – Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average: the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.

[a] Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA.
[b] Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the Government or other groups as advice.
[c] These cancer risk estimates were derived from oral data and converted to provide the estimated inhalation risk.
[d] The LOAEL is from the critical study used as the basis for the ATSDR intermediate MRL.

References

1. Agency for Toxic Substances and Disease Registry (ATSDR). *Toxicological Profile for 1,1,2,2-Tetrachloroethane (Update).* U.S. Public Health Service, U.S. Department of Health and Human Services, Atlanta, GA. 1996.

2. U.S. Department of Health and Human Services. Hazardous Substances Data Bank (HSDB, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.

3. U.S. Department of Health and Human Services. Registry of Toxic Effects of Chemical Substances (RTECS, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.

4. U.S. Environmental Protection Agency (EPA). *Integrated Risk Information System (IRIS) on 1,1,2,2-Tetrachloroethane.* National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1999.

5. Occupational Safety and Health Administration (OSHA). Occupational Safety and Health Standards, Toxic and Hazardous Substances. *Code of Federal Regulations* 29 CFR 1910.1000. 1998.

6. J.E. Amoore and E. Hautala. Odor as an aid to chemical safety: Odor thresholds compared with threshold limit values and volatilities for 214 industrial chemicals in air and water dilution. *Journal of Applied Toxicology*, 3(6):272-290. 1983.

7. American Conference of Governmental Industrial Hygienists (ACGIH). *1999 TLVs and BEIs. Threshold Limit Values for Chemical Substances and Physical Agents, Biological Exposure Indices.* Cincinnati, OH. 1999.

8. National Institute for Occupational Safety and Health (NIOSH). *Pocket Guide to Chemical Hazards.* U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention. Cincinnati, OH. 1997.

TETRACHLOROETHYLENE (PERCHLOROETHYLENE)

127-18-4

Hazard Summary

Tetrachloroethylene is widely used for dry-cleaning fabrics and metal degreasing operations. The main effects of tetrachloroethylene in humans are neurological, liver, and kidney effects following acute (short-term) and chronic (long-term) inhalation exposure. Dizziness, sleepiness, and impaired coordination have been reported. Some adverse reproductive effects, such as menstrual disorders and spontaneous abortions, have been reported from occupational exposure to tetrachloroethylene; however, no definite conclusions can be made because of the limitations of the studies. Results from epidemiological studies of tetrachloroethylene and cancer incidence have been mixed; some studies reported an increased incidence of a variety of tumors, while other studies did not report any carcinogenic effects. Animal studies have reported an increased incidence of liver cancer in mice, via inhalation and gavage, and kidney and mononuclear cell leukemia in rats. The U.S. Environmental Protection Agency (EPA) considers trichloroethylene as intermediate between a probable and possible human carcinogen (Group B/C). The Agency is currently reassessing its potential carcinogenicity.

Please Note: The main sources of information for this fact sheet are EPA's Integrated Risk Information System (IRIS), which contains information on oral chronic toxicity and the reference dose (RfD), and the Agency for Toxic Substances and Disease Registry's (ATSDR's) *Toxicological Profile for Tetrachloroethylene.* Another secondary source is EPA's *Health Effects Assessment for Tetrachloroethylene.*

Physical Properties

- Tetrachloroethylene is a nonflammable colorless liquid with a sharp sweet odor; the odor threshold is 1 ppm. (1)
- The chemical formula for tetrachloroethylene is C_2Cl_4, and the molecular weight is 165.83 g/mol. (1)
- The vapor pressure for tetrachloroethylene is 18.47 mm Hg at 25 °C, and it has a log octanol/water partition coefficient (log K_{ow}) of 3.40. (1)

Uses

- Tetrachloroethylene is used for dry cleaning and textile processing, as a chemical intermediate, and for vapor degreasing in metal-cleaning operations. (1)

Sources and Potential Exposure

- Prior to 1981, tetrachloroethylene was detected in ambient air at average levels of 0.16 ppb in rural and remote areas, 0.79 ppb in urban and suburban areas, and 1.3 ppb in areas near emission sources. (1)

- Tetrachloroethylene has also been detected in drinking water; one survey prior to 1984 of water supplies from groundwater sources reported a median concentration of 0.75 ppb for the samples in which tetrachloroethylene was detected, with a maximum level of 69 ppb. (1)
- Occupational exposure to tetrachloroethylene may occur, primarily in dry cleaning establishments and at industries manufacturing or using the chemical. (1)

Assessing Personal Exposure

- Tetrachloroethylene can be measured in the breath, and breakdown products of tetrachloroethylene can be measured in the blood and urine. (1)

Health Hazard Information

Acute Effects:

- Acute exposure to very high levels of tetrachloroethylene in humans has caused death. Effects noted from short-term, inhalation exposure to tetrachloroethylene vapors include irritation of the upper respiratory tract and eyes, kidney dysfunction, and at lower concentrations, neurological effects, such as reversible mood and behavioral changes, impairment of coordination, dizziness, headache, sleepiness, and unconsciousness. (1)
- Animal studies have reported effects on the liver, kidney, and central nervous system (CNS) from acute inhalation exposure to tetrachloroethylene. (1)
- Acute animal tests, such as the LC_{50} and LD_{50} tests in mice have shown tetrachloroethylene to have low toxicity from inhalation and oral exposure. (1)

Chronic Effects (Noncancer):

- The major effects from chronic inhalation exposure to tetrachloroethylene in humans are neurological effects, including headaches, and impairment of memory, concentration, and intellectual function. Other effects noted in humans include cardiac arrhythmia, liver damage, and possible kidney effects. (1,5)
- Animal studies have reported effects on the liver, kidney, and CNS from chronic inhalation exposure to tetrachloroethylene. (1,5)
- EPA has not established a reference concentration (RfC) for tetrachloroethylene. (4)
- The RfD for tetrachloroethylene is 0.01 mg/kg/d based on hepatotoxicity in mice and weight gain in rats. The RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious noncancer effects during a lifetime. It is not a direct estimator of risk, but rather a reference point to gauge the potential effects. At exposures increasingly greater than the RfD, the potential for adverse health effects increases. Lifetime exposure above the RfD does not imply that an adverse health effect would necessarily occur. (4)
- EPA has medium confidence in the RfD based on low confidence in the study on which the RfD was based due to the lack of complete histopathological examination at the

no-observed-adverse-effect level (NOAEL) in the mouse; and medium confidence in the database because it is relatively complete but lacks studies of reproductive and teratology endpoints subsequent to oral exposure. (4)

- ATSDR has calculated a chronic-duration inhalation minimal risk level (MRL) of 0.04 ppm (0.3 mg/m^3) for tetrachloroethylene based on neurological effects in humans. The MRL is an estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk of adverse noncancer health effects over a specified duration of exposure. (1)
- Repeated skin contact may cause irritation. (1)

Reproductive/Developmental Effects:

- Some adverse reproductive effects, such as menstrual disorders and spontaneous abortions, have been reported in women occupationally exposed to tetrachloroethylene. However, no definitive conclusions can be made because of the limitations of the studies. (1)
- In a study of residents exposed to drinking water contaminated with solvents, including tetrachloroethylene, there was a suggestion that birth defects were associated with exposure. However, no firm conclusions can be drawn from this study due to multiple chemical exposures and problems with the analysis. (1)
- Increased fetal resorptions and effects to the fetus have been reported in animals exposed to high levels of tetrachloroethylene by inhalation. (1)

Cancer Risk:

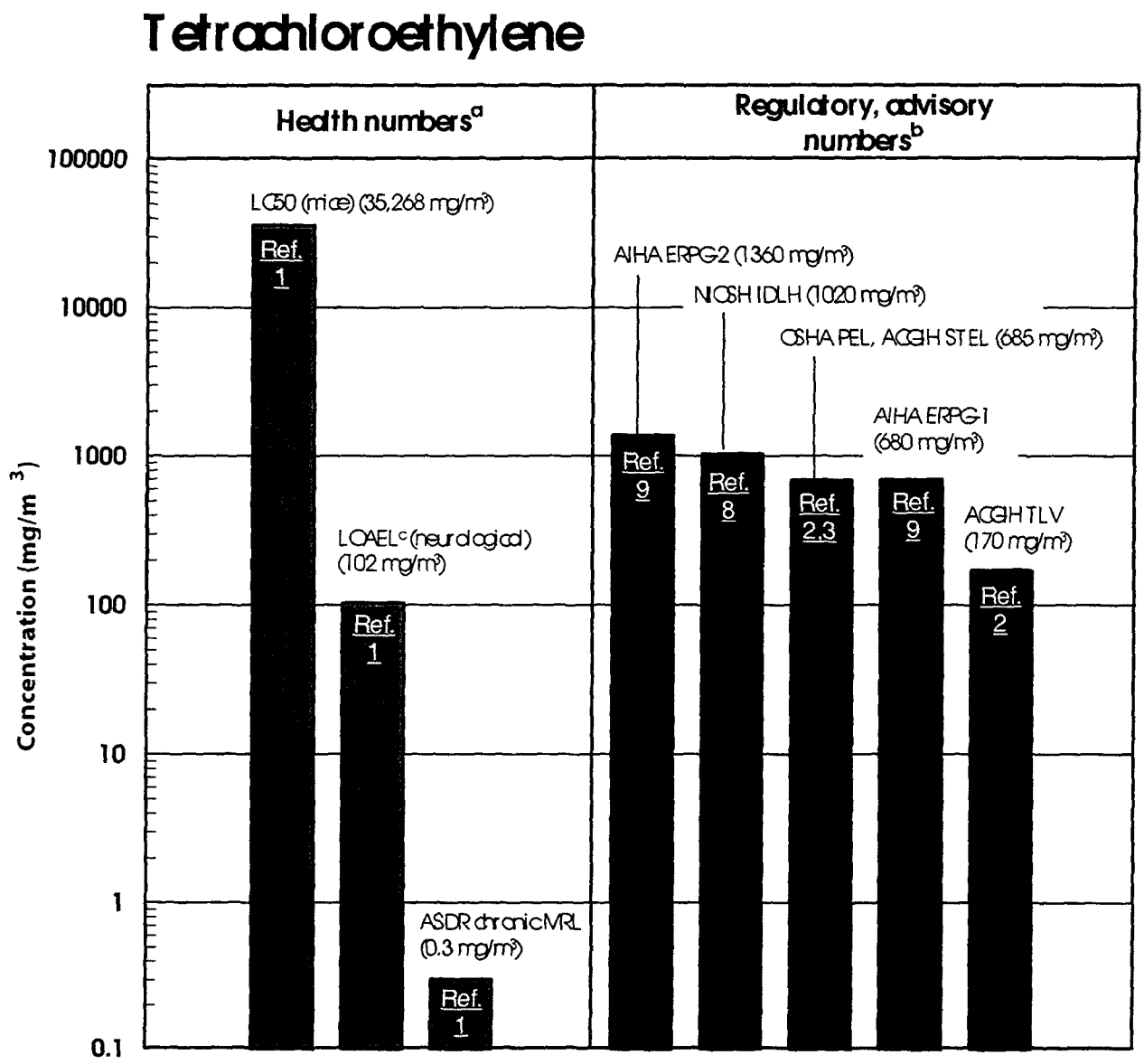
- Epidemiological studies of dry cleaning workers exposed to tetrachloroethylene and other solvents have shown mixed results; some studies reported an increased incidence of a variety of tumors, while other studies did not show any carcinogenic effects. All of these studies are complicated by potential exposure to numerous chemicals. (1,5,6)
- One human study reported that there was a potential association between drinking water contaminated with tetrachloroethylene and other chemicals and an increased risk of childhood leukemia. Other studies reexamined the data and did not agree with the association because the people were exposed to multiple chemicals and the statistical significance of the incidence of leukemia has not been resolved. (1)
- Animal studies have reported an increased incidence of liver tumors in mice, from inhalation and gavage exposure, and kidney and mononuclear cell leukemias in rats, via inhalation exposure. (1,5,6)
- Regardless of exposure route, less than 5 percent of absorbed tetrachloroethylene is metabolized by humans to trichloroacetic acid (TCA), with the remainder being exhaled unchanged. Trichloroacetic acid is classified as a Group C, possible human carcinogen based on limited evidence of liver tumors in mice (but not rats). (4,7)
- EPA considers trichloroethylene as intermediate between a probable and possible human carcinogen (Group B/C). The Agency is currently reassessing its potential carcinogenicity. (10)

- EPA uses mathematical models, based on animal studies, to estimate the probability of a person developing cancer from breathing air containing a specified concentration of a chemical. EPA has calculated a provisional inhalation unit risk estimate of 5.8×10^{-7} $(\mu g/m^3)^{-1}$. A provisional value is one which has not received Agency-wide review. (7)
- EPA has calculated a provisional oral cancer slope factor of 0.051 $(mg/kg/d)^{-1}$. (5)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45).
For tetrachloroethylene: 1 ppm = 6.78 mg/m^3.
To convert from $\mu g/m^3$ to mg/m^3: $mg/m^3 = (\mu g/m^3) \times (1\ mg/1{,}000\ \mu g)$.

Health Data from Inhalation Exposure



AIHA ERPG – American Industrial Hygiene Association's emergency response planning guidelines. ERPG 1 is the maximum airborne concentration below which it is believed nearly all individuals could be exposed up to one hour without experiencing other than mild transient adverse health effects or perceiving a clearly defined objectionable odor; ERPG 2 is the maximum airborne concentration below which it is believed nearly all individuals could be exposed up to one hour without experiencing or developing irreversible or other serious health effects that could impair their abilities to take protective action.

ACGIH STEL – American Conference of Governmental and Industrial Hygienists' short-term exposure limit; 15-min time-weighted-average exposure that should not be exceeded at any time during a workday even if the 8-h time-weighted-average is within the threshold limit value.

ACGIH TLV – American Conference of Governmental and Industrial Hygienists' threshold

limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effects.
LC_{50} (Lethal Concentration$_{50}$) – A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.
LOAEL – Lowest-observed-no-adverse-affect level.
NIOSH IDLH – National Institute of Occupational Safety and Health's immediately dangerous to life or health concentration; NIOSH recommended exposure limit to ensure that a worker can escape from an exposure condition that is likely to cause death or immediate or delayed permanent adverse health effects or prevent escape from the environment.
OSHA PEL – Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.

[a] Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA.
[b] Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the Government or other groups as advice.
[c] The LOAEL is from the critical study used as the basis for the ATSDR chronic inhalation MRL.

References

1. Agency for Toxic Substances and Disease Registry (ATSDR). *Toxicological Profile for Tetrachloroethylene (Update).* U.S. Public Health Service, U.S. Department of Health and Human Services, Atlanta, GA. 1997.

2. American Conference of Governmental and Industrial Hygienists (ACGIH). *1999 TLVs and BEIs: Threshold Limit Values for Chemical Substances and Physical Agents, Biological Exposure Indices. Cincinnati, OH.* 1999.

3. Occupational Safety and Health Administration (OSHA). Occupational Safety and Health Standards, Toxic and Hazardous Substances. *Code of Federal Regulations* 29 CFR 1910.1000. 1998.

4. U.S. Environmental Protection Agency (EPA). *Integrated Risk Information System (IRIS) on Tetrachloroethylene.* National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1999.

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6. U.S. Environmental Protection Agency (EPA). *Updated Health Assessment Document for Tetrachloroethylene*. EPA/600/8-82/005B. Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment, Office of Research and Development, Cincinnati, OH. 1988.

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10. U.S. Environmental Protection Agency (EPA). National Emission Standards for Hazardous Air Pollutants: Wood Furniture Manufacturing Operations. *Federal Register* 63 FR 34336-346. June 24, 1998.

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TRICHLOROETHYLENE

79-01-6

Hazard Summary

Most of the trichloroethylene (TCE) used in the U.S. is released into the atmosphere from industrial degreasing operations. Acute (short-term) and chronic (long-term) inhalation exposure to trichloroethylene can affect the human central nervous system (CNS), with symptoms such as dizziness, headaches, confusion, euphoria, facial numbness, and weakness. High, short-term exposures of humans by inhalation also have been associated with effects on the liver, kidneys, gastrointestinal system, and skin. Although several epidemiological studies have investigated a possible link between trichloroethylene exposure and reproductive or developmental effects, no conclusive evidence has been identified. Similarly, the existence of a relationship between trichloroethylene exposure and cancer is also not clear from the epidemiological studies that have been performed. Animal studies have reported increases in lung, liver, and testicular tumors, via inhalation exposure. The U.S. Environmental Protection Agency (EPA) considers trichloroethylene as intermediate between a probable and possible human carcinogen (Group B/C). The Agency is currently reassessing its potential carcinogenicity.

Please Note: The main source of information for this fact sheet is the Agency for Toxic Substances and Disease Registry's (ATSDR's) *Toxicological Profile for Trichloroethylene*. Another secondary source used is EPA's *Health Assessment Document for Trichloroethylene*.

Physical Properties

- Trichloroethylene is a nonflammable colorless liquid with a sweet odor similar to ether or chloroform. (1)
- The odor threshold for trichloroethylene is 28 ppm. (6)
- The chemical formula for trichloroethylene is C_2HCl_3, and the molecular weight is 131.40 g/mol. (1)
- The vapor pressure for trichloroethylene is 74 mm Hg at 25 °C, and it has a log octanol/water partition coefficient (log K_{ow}) of 2.42. (1)
- Trichloroethylene is not a persistent chemical in the atmosphere; its half-life in air is about 7 days. (1)

Uses

- The main use of trichloroethylene is in the vapor degreasing of metal parts. (1)
- Trichloroethylene is also used as an extraction solvent for greases, oils, fats, waxes, and tars, a chemical intermediate in the production of other chemicals, and as a refrigerant. (1)
- Trichloroethylene is used in consumer products such as typewriter correction fluids, paint removers/strippers, adhesives, spot removers, and rug-cleaning fluids. (1)
- Trichloroethylene was used in the past as a general anesthetic. (1)

Sources and Potential Exposure

- Trichloroethylene has been detected in ambient air at levels less than 1 ppb. (1)
- Drinking water supplies relying on contaminated groundwater sources may contain trichloroethylene. A monitoring study in the early 1980s of drinking water systems relying groundwater sources detected TCE in 10 percent of the systems sampled. The median level among the systems where detected was 1 ppb. (1)
- Workers may be exposed to trichloroethylene in the factories where it is manufactured or used. In addition, persons breathing air around these factories may be exposed to trichloroethylene. (1)
- Persons may also be exposed to trichloroethylene through the use of products containing the chemical and from evaporation and leaching from waste disposal sites. (1)

Assessing Personal Exposure

- Trichloroethylene can be measured in the breath, and breakdown products of trichloroethylene can be measured in urine or blood. (1)

Health Hazard Information

Acute Effects:

- Acute exposure to extremely high levels of trichloroethylene (approximately 10,000 ppm) in humans has caused death. A few of these reports have cited cardiac arrhythmias as the cause of death, and one report noted massive liver damage. (1)
- CNS effects are the primary effects noted from acute inhalation exposure to trichloroethylene in humans, with symptoms including sleepiness, fatigue, headache, confusion, and feelings of euphoria. Effects on the liver, kidneys, gastrointestinal system, and skin have also been noted. (1)
- Neurological, lung, kidney, and heart effects have been reported in animals acutely exposed to trichloroethylene. (1)
- Tests involving acute exposure of animals, such as the LC_{50} and LD_{50} tests in rats and mice, have shown trichloroethylene to have low toxicity from inhalation exposure and moderate toxicity from oral exposure. (1,2)

Chronic Effects (Noncancer):

- As with acute exposure, chronic exposure to trichloroethylene by inhalation also affects the human CNS. Case reports of intermediate and chronic occupational exposures included effects such as dizziness, headache, sleepiness, nausea, confusion, blurred vision, facial numbness, and weakness. (1)
- Studies have shown that simultaneous alcohol consumption and trichloroethylene inhalation increases the toxicity of trichloroethylene in humans. (1)
- Neurological, liver, and kidney effects were reported in chronically-exposed animals. (1)

- EPA has not calculated a reference concentration (RfC) or reference dose (RfD) for trichloroethylene. (3)
- ATSDR has calculated an intermediate-duration inhalation minimal risk level (MRL) of 0.1 ppm (0.5 mg/m^3) for trichloroethylene based on neurological effects in rats. The MRL is an estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk of adverse noncancer health effects over a specified duration of exposure. Exposure to a level above the MRL does not mean that adverse health effects will occur. The MRL is intended to serve as a screening tool. (1)
- The California Environmental Protection Agency (CalEPA) has calculated a chronic inhalation reference exposure level of 0.6 mg/m^3 based on neurological effects in humans. The CalEPA reference exposure level is a concentration at or below which adverse health effects are not likely to occur. (5)

Reproductive/Developmental Effects:

- A study of nurses occupationally exposed by inhalation to trichloroethylene along with other chemicals in operating rooms, and another epidemiological study of women exposed occupationally or nonoccupationally to trichloroethylene and other solvents, have reported increases in the incidence of miscarriages. The presence of other chemicals, however, limits the ability to draw conclusions specific to trichloroethylene. (1)
- An epidemiological study of 2,000 male and female workers exposed to trichloroethylene via inhalation found no increase in malformations in babies born following exposure. (1)
- Several studies have evaluated and not found an association between adverse reproductive effects in humans and exposure to trichloroethylene in contaminated drinking water. An association was found between the occurrence of congenital heart disease in children and a drinking water supply contaminated with trichloroethylene and other similar chemicals; however, no causal relationship with trichloroethylene could be concluded. (1)
- In one animal study, an increase in abnormal sperm morphology was observed following very high inhalation exposures of mice; however, other animal studies have not reported reproductive or developmental effects from either inhalation or ingestion exposures. (1,4)

Cancer Risk:

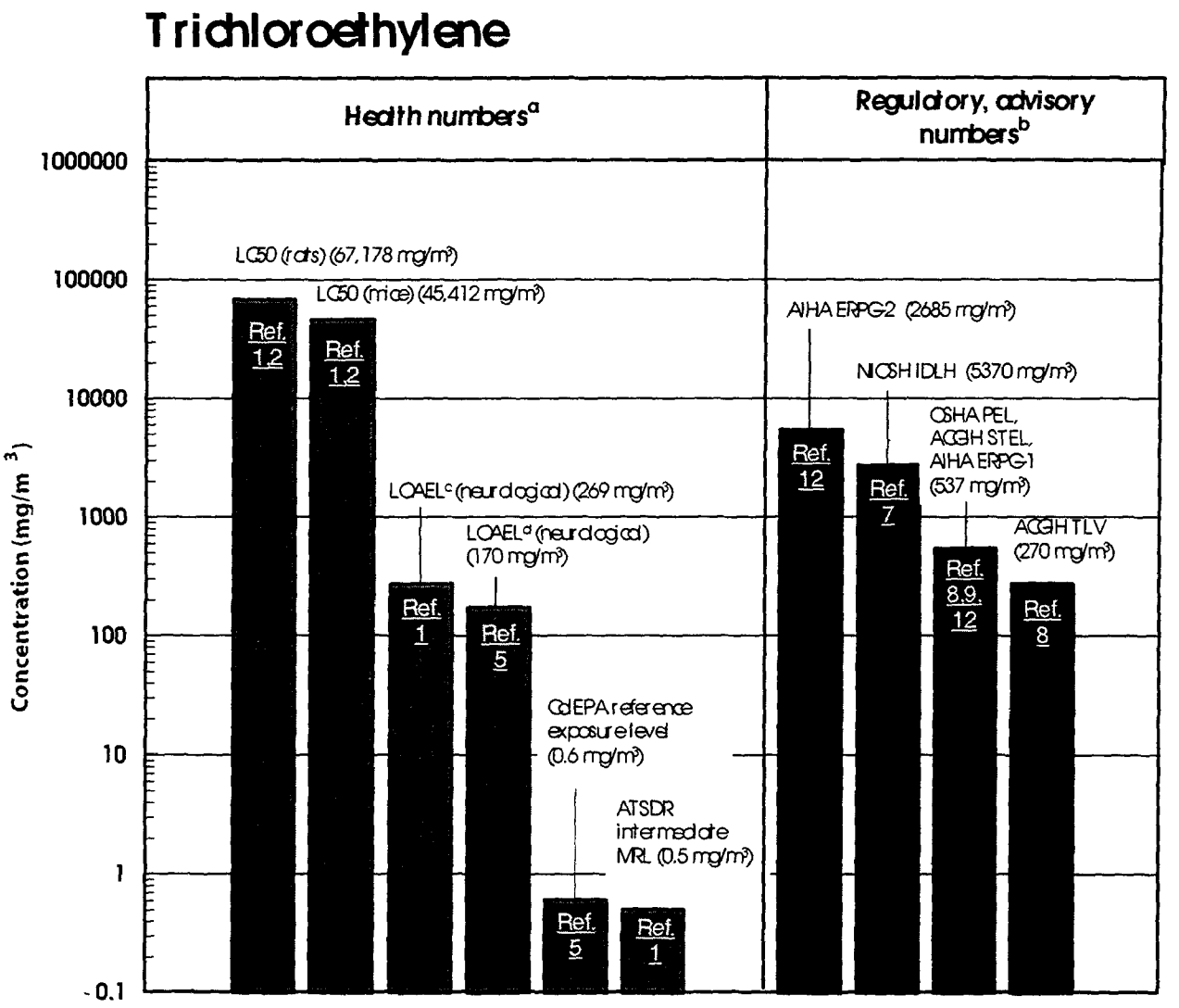
- Several human studies have investigated the relationship between inhalation exposure to trichloroethylene and cancer, some finding weak relationships and others finding none; however, each has limitations that restrict its usefulness. None of the studies found strong evidence of an association between trichloroethylene exposure and cancer incidence. (1,4)
- The existence of a relationship between oral exposure to trichloroethylene and cancer incidence is also not clear. One human study reported that there was a potential association between drinking water contaminated with trichloroethylene and an increased risk of childhood leukemia. Other studies reexamined the data and did not agree with the association because the people were exposed to chemicals other than trichloroethylene, and the statistical significance of the incidence of leukemia has not been resolved. (1)

- Animal studies, via inhalation exposure, have reported increases in lung, liver, and testicular tumors and increases in liver tumors via gavage. (1,4)
- EPA considers trichloroethylene as intermediate between a probable and possible human carcinogen (Group B/C). The Agency is currently reassessing its potential carcinogenicity. (11)
- EPA uses mathematical models, based on animal studies, to estimate the probability of a person developing cancer from continuously breathing air containing a specified concentration of a chemical. EPA has calculated a provisional inhalation unit risk estimate of 1.7 x 10-6 $(\mu g/m^3)^{-1}$. A provisional value is one which has not received Agency-wide review. (10)
- EPA has also calculated a provisional oral cancer slope factor of 0.011 $(mg/kg/d)^{-1}$. (10)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45). For trichloroethylene: 1 ppm = 5.37 mg/m^3. To convert from $\mu g/m^3$ to mg/m^3: mg/m^3 = ($\mu g/m^3$) x (1 mg/1,000 μg).

Health Data from Inhalation Exposure



ACGIH STEL – American Conference of Governmental and Industrial Hygienists' short-term exposure limit; 15-min time-weighted-average exposure that should not be exceeded at any time during a workday even if the 8-h time-weighted-average is within the threshold limit value.
ACGIH TLV – ACGIH's threshold limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effects.
AIHA ERPG – American Industrial Hygiene Association's emergency response planning guidelines. ERPG 1 is the maximum airborne concentration below which it is believed nearly all individuals could be exposed up to one hour without experiencing other than mild transient adverse health effects or perceiving a clearly defined objectionable odor; ERPG 2 is the maximum airborne concentration below which it is believed nearly all individuals could be exposed up to one hour without experiencing or developing irreversible or other serious health effects that could impair their abilities to take protective action.
LC_{50} (Lethal Concentration$_{50}$) – A calculated concentration of a chemical in air to which

exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.
LOAEL – Lowest-observed-adverse-affect level
NIOSH IDLH – National Institute of Occupational Safety and Health's immediately dangerous to life or health concentration; NIOSH recommended exposure limit to ensure that a worker can escape from an exposure condition that is likely to cause death or immediate or delayed permanent adverse health effects or prevent escape from the environment.
OSHA PEL – Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.

[a] Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA.
[b] Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the Government or other groups as advice.
[c] The LOAEL is from the critical study used as the basis for the ATSDR intermediate MRL.
[d] The LOAEL is from the critical study used as the basis for the CalEPA chronic reference exposure level.

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VINYL CHLORIDE

75-01-4

Hazard Summary

Most vinyl chloride is used to make polyvinyl chloride (PVC) plastic and vinyl products. Acute (short-term) exposure to high levels of vinyl chloride in air has resulted in central nervous system(CNS) effects, such as dizziness, drowsiness, and headaches in humans. Chronic (long-term) exposure to vinyl chloride through inhalation and oral exposure in humans has resulted in liver damage. There are positive human and animal studies showing adverse effects which raise a concern about potential reproductive and developmental hazards to humans from exposure to vinyl chloride. Cancer is a major concern from exposure to vinyl chloride via inhalation, as vinyl chloride exposure has been shown to increase the risk of a rare form of liver cancer in humans. The U.S. Environmental Protection Agency (EPA) has classified vinyl chloride as a Group A, human carcinogen.

Please Note: The main sources of information for this fact sheet are the Agency for Toxic Substances and Disease Registry's (ATSDR's) *Toxicological Profile for Vinyl Chloride* and *Case Studies in Environmental Medicine. Vinyl Chloride Toxicity.*

Physical Properties

- Vinyl chloride is a colorless gas with a mild, sweet odor. (1)
- The odor threshold for vinyl chloride is 3,000 ppm. (5)
- Vinyl chloride is slightly soluble in water and is quite flammable. (1)
- The chemical formula for vinyl chloride is C_2H_3Cl, and the molecular weight is 62.5 g/mol. (1)
- The vapor pressure for vinyl chloride is 2,600 mm Hg at 25 °C, and it has a log octanol/water partition coefficient (log K_{ow}) of 1.36. (1)
- The half-life of vinyl chloride in air is a few hours. (1)

Uses

- Most of the vinyl chloride produced in the U.S. is used to make polyvinyl chloride (PVC), a material used to manufacture a variety of plastic and vinyl products including pipes, wire and cable coatings, and packaging materials. (1)
- Smaller amounts of vinyl chloride are used in furniture and automobile upholstery, wall coverings, housewares, and automotive parts. (1)
- Vinyl chloride has been used in the past as a refrigerant. (1)

Sources and Potential Exposure

- Ambient air concentrations of vinyl chloride are generally quite low, with exposure occurring from the discharge of exhaust gases from factories that manufacture or process vinyl chloride, or evaporation from areas where chemical wastes are stored. (1,2)
- Air inside new cars may contain vinyl chloride at higher levels than detected in ambient air because vinyl chloride may outgas into the air from the new plastic parts. (1,2)
- Drinking water may contain vinyl chloride released from contact with polyvinyl pipes. (1,2)
- Vinyl chloride is a microbial degradation product of trichloroethylene in groundwater, and thus can be found in groundwater affected by trichloroethylene contamination. (3)
- Occupational exposure to vinyl chloride may occur in those workers concerned with the production, use, transport, storage, and disposal of the chemical. (1,2)

Assessing Personal Exposure

- Vinyl chloride can be detected in urine and body tissues, but the tests are not reliable indicators of total exposure. (1,2)

Health Hazard Information

Acute Effects:

- Acute exposure of humans to high levels of vinyl chloride via inhalation in humans has resulted in effects on the CNS, such as dizziness, drowsiness, headaches, and giddiness. (1,2)
- Vinyl chloride is reported to be slightly irritating to the eyes and respiratory tract in humans. (1,2)
- Acute exposure to extremely high levels of vinyl chloride has caused loss of consciousness, lung and kidney irritation, and inhibition of blood clotting in humans and cardiac arrhythmias in animals. (1)
- Tests involving acute exposure of animals, such as the LC_{50} test in mice, have shown vinyl chloride to have high acute toxicity from inhalation exposure. (5)

Chronic Effects (Noncancer):

- Liver damage may result in humans from chronic exposure to vinyl chloride, through both inhalation and oral exposure. (1,2)
- A small percentage of individuals occupationally exposed to high levels of vinyl chloride in air have developed a set of symptoms termed "vinyl chloride disease," which is characterized by Raynaud's phenomenon (fingers blanch and numbness and discomfort are experienced upon exposure to the cold), changes in the bones at the end of the fingers, joint and muscle pain, and scleroderma-like skin changes (thickening of the skin, decreased elasticity, and slight edema). (1,2)

- CNS effects (including dizziness, drowsiness, fatigue, headache, visual and/or hearing disturbances, memory loss, and sleep disturbances) as well as peripheral nervous system symptoms (peripheral neuropathy, tingling, numbness, weakness, and pain in fingers) have also been reported in workers exposed to vinyl chloride. (1)
- Animal studies have reported effects on the liver, kidney, and CNS from chronic exposure to vinyl chloride. (1,6)
- EPA has not established a reference concentration (RfC) or a reference dose (RfD) for vinyl chloride. (8)
- ATSDR has calculated an intermediate-duration inhalation minimal risk level (MRL) of 0.03 ppm (0.08 mg/m^3) for vinyl chloride based on liver effects in rats. The MRL is an estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk of adverse noncancer health effects over a specified duration of exposure. Exposure to a level above the MRL does not mean that adverse health effects will occur. The MRL is intended to serve as a screening tool. (1)
- The California Environmental Protection Agency (CalEPA) has calculated a chronic inhalation reference exposure level of 0.005 mg/m^3 based on liver effects in humans. The CalEPA reference exposure level is a concentration at or below which adverse health effects are not likely to occur. (15)

Reproductive/Developmental Effects:

- Several case reports suggest that male sexual performance may be affected by vinyl chloride. However, these studies are limited by lack of quantitative exposure information and possible co-occurring exposure to other chemicals. (1)
- Several epidemiological studies have reported an association between vinyl chloride exposure in pregnant women and an increased incidence of birth defects, while other studies have not reported similar findings. (1,2)
- Epidemiological studies have suggested an association between men occupationally exposed to vinyl chloride and miscarriages in their wives' pregnancies although other studies have not supported these findings. (1,2)
- Testicular damage and decreased male fertility have been reported in rats exposed to low levels for up to 12 months. (1)
- Animal studies have reported decreased fetal weight and birth defects at levels that are also toxic to maternal animals in the offspring of rats exposed to vinyl chloride through inhalation. (1)

Cancer Risk:

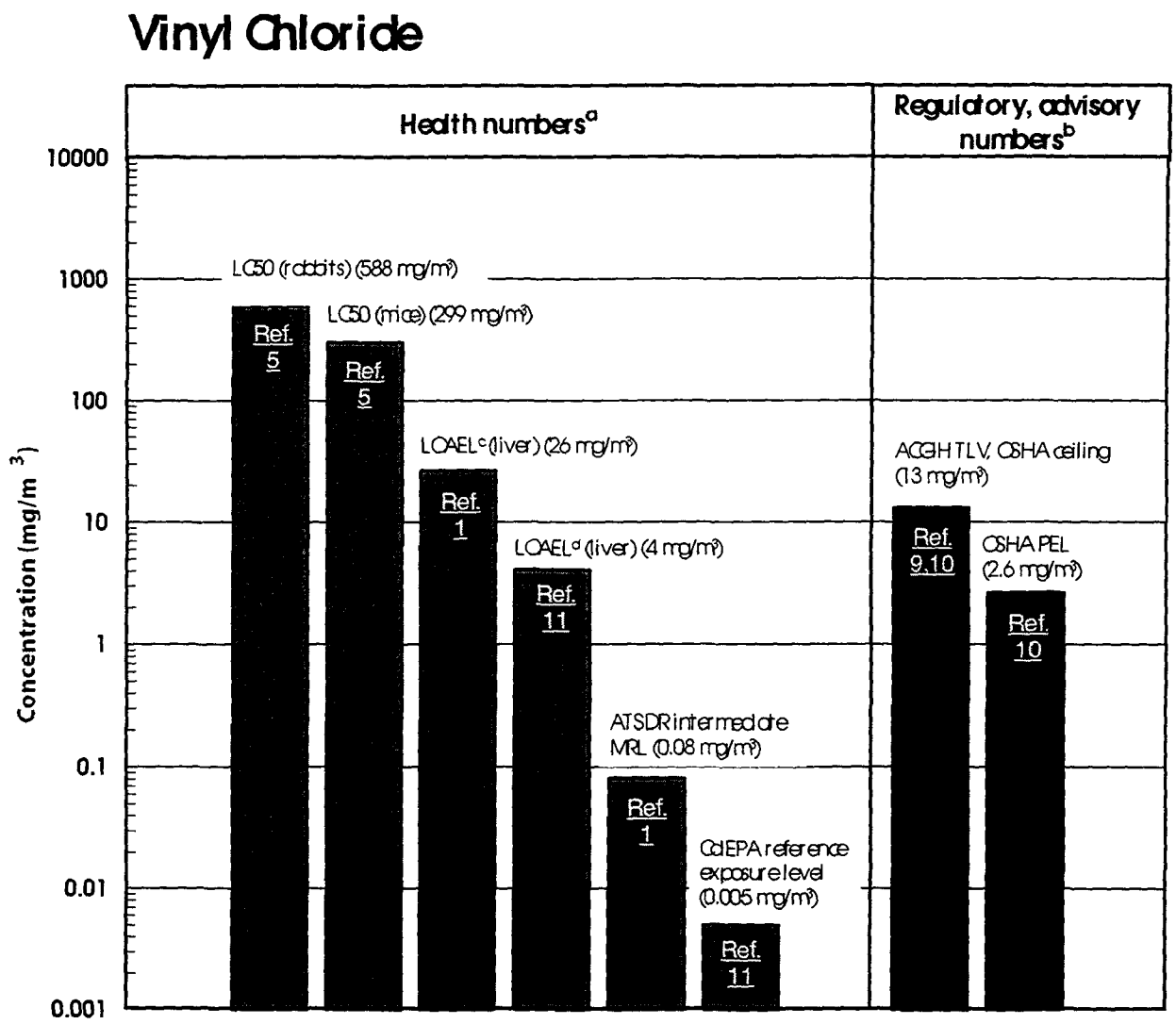
- Inhaled vinyl chloride has been shown to increase the risk of a rare form of liver cancer (angiosarcoma of the liver) in humans. (1,2,6)
- Vinyl chloride exposure, through inhalation, has also been associated with cancer of the brain, CNS, lung, respiratory tract, and the lymphatic/hematopoietic system in humans. (1,2)
- Animal studies have shown that vinyl chloride, via inhalation, increases the incidence of angiosarcoma of the liver and cancer of the liver and brain. (1,2,6)

- Several rat studies show a pronounced early-life susceptibility to the carcinogenic effect of vinyl chloride, i.e., early exposures are associated with higher cancer incidence than much longer exposures that occur after maturity. (1)
- EPA has classified vinyl chloride as a Group A, human carcinogen. (8)
- EPA uses mathematical models, based on human and animal studies, to estimate the probability of a person developing cancer from breathing air containing a specified concentration of a chemical. EPA has calculated a provisional inhalation unit risk estimate of 8.4×10^{-5} $(\mu g/m^3)^{-1}$ for vinyl chloride. A provisional value is one which has not received Agency-wide review. (8)
- EPA has calculated a provisional oral cancer slope factor of 1.9 $(mg/kg/d)^{-1}$ for vinyl chloride. (8)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45).
For vinyl chloride: 1 ppm = 2.6 mg/m^3.
To convert from $\mu g/m^3$ to mg/m^3: mg/m^3 = ($\mu g/m^3$) x (1 mg/1,000 μg).

Health Data from Inhalation Exposure



ACGIH TLV – American Conference of Governmental and Industrial Hygienists' threshold limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effects.

LC_{50} (Lethal Concentration$_{50}$) – A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.

LOAEL – Lowest-observed-no-adverse-affect level.

OSHA PEL – Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average: the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.

OSHA PEL ceiling value – OSHA's permissible exposure limit ceiling value; the concentration of a substance that should not be exceeded at any time.

[a] Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA.
[b] Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the Government or other groups as advice.
[c] The LOAEL is from the critical study used as the basis for the ATSDR intermediate-duration inhalation MRL.
[d] The LOAEL is from the critical study used as the basis for the CalEPA chronic inhalation reference exposure level.

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TECHNICAL REPORT DATA

(Please read Instructions on reverse before completing)

1. REPORT NO.	2.	3. RECIPIENT'S ACCESSION NO.
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4. TITLE AND SUBTITLE	5. REPORT DATE
National Air Toxics Program: The Integrated Urban Strategy Report to Congress	2000
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9. PERFORMING ORGANIZATION NAME AND ADDRESS U.S. Environmental Protection Agency Office of Air Quality Planning and Standards Research Triangle Park, NC 27711	10. PROGRAM ELEMENT NO.
	11. CONTRACT/GRANT NO.
12. SPONSORING AGENCY NAME AND ADDRESS Director Office of Air Quality Planning and Standards Office of Air and Radiation U.S. Environmental Protection Agency Research Triangle Park, NC 27711	13. TYPE OF REPORT AND PERIOD COVERED
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15. SUPPLEMENTARY NOTES

16. ABSTRACT

The report is the first one of two that are required by section 112(k) of the Clean Air Act. It summarizes EPA's strategy to reduce risk to public health posed by the release of hazardous air pollutants from area sources. The report contains information similar to that provided in the Federal Register notice titled *National Air Toxics Program: The Integrated Urban Strategy* ("Strategy") that was published on July 19, 1999. However, this report contains more details on the information and assessments conducted to comple the Strategy. Furthermore, the report summarizes existing information on risk assessments which have bee conducted in various urban areas and provides a detailed description of 13 research needs to carry out the goals of the Strategy.

17. KEY WORDS AND DOCUMENT ANALYSIS

a. DESCRIPTORS	b. IDENTIFIERS/OPEN ENDED TERMS	c. COSATI Field/Group
Air Toxics Hazardous Air Pollutants	Air Pollution control	

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