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TECHNICAL REPORT

Review of Literature Related to Exposures and Health Effects at Structural Collapse Events

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Prepared for the National Institute for Occupational Safety and Health

INFRASTRUCTURE, SAFETY, AND ENVIRONMENT

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Preface

In 2002, the National Institute for Occupational Safety and Health (NIOSH) asked the RAND Science and Technology Policy Institute (S&TPI) to develop personal protective equipment (PPE) guidelines for emergency responders required to work near or on the remains of recently collapsed tall buildings. With the cessation of the RAND Corporation's management of S&TPI in November 2003, publication of this work is now occurring under the auspices of RAND Infrastructure, Safety, and Environment (ISE).

The evaluation considers the full range of emergency workers who are likely to respond to a large structural collapse, including local fire, medical, and hazardous material teams as well as police officers and urban search and rescue teams. This effort emphasizes incidents at residential or commercial tall buildings but does not address PPE needs for incidents involving chemical, biological, radiological, or nuclear weapons. The project focuses on the first several days following a structural collapse, since that is when the hazards are highest, the response is most intense, and the site-specific exposure monitoring may not be available. It is during these conditions that hazardous exposures are likely to be the greatest and most uncertain.

The NIOSH/RAND team has adopted a four-part approach to develop these guidelines:

1. Characterize the response mission and hazards to emergency responders at building collapse sites.
2. Assess the short- and long-term health effects to emergency responders of exposure to the hazards identified in step 1.
3. Identify PPE options that will protect the various groups of emergency responders from the hazards they are likely to encounter.
4. Provide recommendations for PPE options, highlighting PPE limitations and important training, use, and maintenance issues.

This report is the second of two volumes that describe the results of the research. It addresses the second objective in the above list by reviewing the possible health effects to emergency responders from exposure to conditions following a tall building collapse. The first volume, *Protecting Emergency Responders, Volume 4: Personal Protective Equipment Guidelines for Large Structural Collapses* (MG-425-NIOSH), addresses objectives 1, 3, and 4 in the above list.

The primary purpose of these reports is to serve as a technical source for incident commander guidelines that have been developed by NIOSH for broad distribution to the disaster management and emergency responder communities. In addition, these reports should be of interest to organizations responsible for developing equipment, standards, guidelines, and regulations for the protection of emergency responders.

About the Science and Technology Policy Institute

Originally created by Congress in 1991 as the Critical Technologies Institute and renamed in 1998, the Science and Technology Policy Institute is a federally funded research and development center sponsored by the National Science Foundation. S&TPI was managed by the RAND Corporation from 1992 through November 30, 2003.

The Institute's mission has been to help improve public policy by conducting objective, independent research and analysis on policy issues that involve science and technology. To this end, the Institute

- supported the Office of Science and Technology Policy and other Executive Branch agencies, offices, and councils
- helped science and technology decisionmakers understand the likely consequences of their decisions and choose among alternative policies
- helped improve understanding in both the public and private sectors of the ways in which science and technology can better serve national objectives.

In carrying out its mission, the Institute consulted broadly with representatives from private industry, institutions of higher education, and other nonprofit institutions.

About the RAND Infrastructure, Safety, and Environment Division

Publication of this report was conducted under the auspices of the Safety and Justice Program within the RAND Infrastructure, Safety, and Environment Division. The mission of ISE is to improve the development, operation, use, and protection of society's essential man-made and natural assets and to enhance the related social assets of safety and security of individuals in transit and in their workplaces and community. Safety and Justice Program research addresses occupational safety, transportation safety, food safety, and public safety—including violence, policing, corrections, substance abuse, and public integrity.

Questions or comments about this report should be sent to the project leader, Henry Willis (Henry_Willis@rand.org). Information about the Safety and Justice Program is available online (www.rand.org/ise/safety). Inquiries about research projects should be made to the Program's director, Andrew Morral (Andrew_Morral@rand.org).

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As part of the development of guidelines for personal protective equipment (PPE) for emergency responders, the RAND Corporation assembled information on acute and chronic health effects that might result from working in a structural collapse environment. The rationale for describing the human health risks associated with the post-collapse environment is to better understand the possible consequences of inadequate PPE at the site of a structural collapse.

In the months following the collapse of the World Trade Center (WTC) on September 11, 2001, several federal agencies monitored the air, dust, and water at the collapse site and in the surrounding areas. The air and dust sampled by these agencies were tested for hundreds of substances. Analyses of the dust and smoke aerosol that settled in the areas adjacent to the WTC after its collapse indicated that it was composed of a complicated mixture of pulverized building material and combustion by-products. The topics for the health effect summaries included in this report were selected by focusing on these two components of the mixture. Individual substances were selected that (1) had well-documented adverse health effects, (2) were likely to be present in other structural collapse environments, and (3) represented the full range of hazardous exposures in the structural collapse environment.

The report summarizes data on injuries among emergency responders available from incidents of structural collapse. It also reviews the possible health effects of substances likely to be found in the pulverized building materials, including asbestos, particulate matter, silica, synthetic vitreous fibers, and metals (arsenic, cadmium, chromium, lead, and mercury). Finally, the report describes the possible health effects of several combustion by-products, including benzene, dioxins, polychlorinated biphenyls, and polycyclic aromatic hydrocarbons. For each substance, information is summarized related to the following topics:

- identity, properties, and uses
- possible routes of exposure
- evidence for health effects from human studies
- occupational exposure limits
- carcinogenicity status.

Information about human health effects in these summaries is based primarily on published reviews.

Acknowledgments

This research was conducted collaboratively with the National Personal Protective Technology Laboratory at the National Institute for Occupational Safety and Health. Jon Szalajda, Nadia El Ayouby, Roland BerryAnn, and John Dower provided extensive information and expertise in support of this research.

A panel of emergency responders was assembled to provide guidance to this research effort. Members of the panel gave generously of their time, and their collective expertise was a valuable asset to the project. They included the following:

Rick Bruce, Deputy Chief, San Francisco Police Department

Robert Dubé, Captain, Fairfax County [Virginia] Fire and Rescue

Dario Gonzalez, M.D., F.A.C.E.P., Medical Director, New York City Office of Emergency Management

Barbara McCabe, International Union of Operating Engineers

John Norman, Chief of Rescue Operations, New York Fire Department

Michael Shields, Deputy Chief, Chicago Police Department

Richard Warford, Assistant Chief, Los Angeles City Fire Department.

The authors would like to thank the members of the emergency responder community and federal agencies who generously contributed their time to this research effort. Participants in project review meetings included Mohammad Ayub, John Ferris, Caroline Freeman, Gus Georgiades, Kevin Landkrohn, and Mike Marshall of the Occupational Safety and Health Administration; Philip Goldsmith and Sandy Gross of the Federal Emergency Management Agency; Ronald Burger of the Centers for Disease Control and Prevention; Janice Bradley of the International Safety Equipment Association; Mike Brown, Frank Hearl, Herb Linn, and Ralph Zumwalde of NIOSH; Chip Hughes and Rodney Winchel of the National Institutes of Health; Andy Levinson of the International Association of Fire Fighters; and Bruce Lippy and Kerry Murray of the National Institute of Environmental Health Sciences. Listed affiliations are those at the time of the study.

Finally, the authors thank their RAND colleagues who shared ideas and gave generously of their time: John Baker, Aarti Dalal, Jolene Galegher, Brian Jackson, Timothy LeDean, Jacqueline MacDonald, Amber Moreen, Stuart Olmsted, and Kenneth Shine.

List of Acronyms and Abbreviations

2,3,7,8-TCDD	2,3,7,8-tetrachlorodibenzo-p-dioxin
ACGIH	American Conference of Governmental Industrial Hygienists
ATSDR	Agency for Toxic Substances and Disease Registry
C	ceiling (exposure limit)
cc	cubic centimeter
CNS	central nervous system
COPD	chronic obstructive pulmonary disease
CVS	cardiovascular system
DMAT	Disaster Medical Assistance Team
EPA	Environmental Protection Agency
FDNY	Fire Department of New York City
FEV_1	forced expiratory volume in 1 second
FVC	forced vital capacity
f-yr/ml	fiber-years per milliliter
GI	Gastrointestinal
IARC	International Agency for Research on Cancer
IDLH	immediately dangerous to life or health
L	Liter
LFC	lowest feasible concentration
LOQ	limit of quantitation
m^2/g	square meters per gram
MAK	Federal Republic of Germany Maximum Concentration Values in the Workplace
mg/m^3	milligrams per cubic meter
$\mu g/m^3$	micrograms per cubic meter
µm	Micrometer
MMWR	*Morbidity and Mortality Weekly Report*
mppcf	million particles per cubic foot
NAAQS	National Ambient Air Quality Standards
NIOSH	National Institute for Occupational Safety and Health
NMRD	nonmalignant respiratory disease
NTP	National Toxicology Program
NYCDOH	New York City Department of Health

OCFD	Oklahoma City Fire Department
OSTP	Office of Science and Technology Policy
OSHA	Occupational Safety and Health Administration
PAH	polycyclic aromatic hydrocarbon
PCB	polychlorinated biphenyl
PEL	Permissible Exposure Limit (OSHA)
PM	particulate matter
PM2.5	particulate matter of diameter less than 2.5 micrometers
PM10	particulate matter of diameter less than 10 micrometers
PPE	personal protective equipment
ppb	parts per billion
ppm	parts per million
REL	Recommended Exposure Limit (NIOSH)
S&TPI	Science and Technology Policy Institute
STEL	short-term exposure limit
TB	tuberculosis
TEEL	temporary emergency exposure limit
TLV	threshold limit value
TWA	time-weighted average
USAR	urban search and rescue
VOC	volatile organic compound
WTC	World Trade Center

1. Introduction

As part of the development of guidelines for personal protective equipment (PPE) for emergency responders, the RAND Corporation assembled information on acute and chronic health effects that might result from working in a structural collapse environment. The rationale for describing the human health risks associated with the post-collapse environment is to better understand the possible consequences of inadequate PPE at the site of a structural collapse. The information regarding possible health effects will provide users of the National Institute for Occupational Safety and Health (NIOSH) guidelines an important basis on which to make decisions regarding selection and use of appropriate PPE in the first few days following a structural collapse.

In the months following the collapse of the World Trade Center (WTC) on September 11, 2001, several federal agencies monitored the air, dust, and water at the collapse site and in the surrounding areas. Formal monitoring began several days after. For example, the first asbestos air sample collected by the U.S. Environmental Protection Agency (EPA) at the Albany and Greenwich station was recorded on September 15, 2001. NIOSH, the Occupational Safety and Health Administration (OSHA), and the Agency for Toxic Substances and Disease Registry (ATSDR) also set up monitoring stations and collected samples in the days and weeks following the WTC's collapse. Collectively, the air and dust sampled by these four federal agencies were tested for hundreds of substances. Many of the monitored substances fall into such categories as polycyclic aromatic hydrocarbons (PAHs) and volatile organic compounds (VOCs). Each of the agencies performed tests for a subset of these substances, as indicated in Table 1.1.

Topics of Health Effect Summaries for Structural Collapse PPE Guidelines

Analyses of the dust and smoke aerosol that settled in the areas adjacent to the WTC after its collapse indicated it was composed of a complicated mixture of pulverized building material and combustion by-products (Lioy et al., 2002). Among the substances present in the pulverized building material were common components of construction, including cement, wallboard, office furnishings, and glass fibers. Other substances present in the environment were the products of incomplete combustion produced by the burning of thousands of liters of jet fuel released upon impact as well as that of the contents of the buildings. Lioy and associates (2002) concluded that the toxic materials found in concentrations high enough to be of significant concern included asbestos, glass fibers, lead, and polycyclic aromatic hydrocarbons. Many chemicals detected in these analyses were adhered to the dust and smoke particles, and might have been inhaled on the first and second days following the collapse by those not wearing respiratory protection.

The topics for the health effect summaries included in this report were selected by focusing on two sources of hazardous exposure in the structural collapse environment: pulverized building materials and combustion by-products. Within these two categories, individual substances were selected that (1) had

well-documented adverse health effects, (2) were likely to be present in other structural collapse environments, and (3) represented the full range of hazardous exposures in the structural collapse environment. These criteria were used to select from Table 1.1 substances of particular interest when considering possible health consequences among emergency responders following a structural collapse.

Overview of this Report

In Section 2, we discuss important issues that should be considered in an assessment of possible health effects from exposure to hazardous substances in a structural collapse environment. These include uncertainty regarding the level of risk following exposure, differences in individual susceptibility, and the effects of exposure to multiple chemicals (i.e., mixed exposures).

Sections 3 through 5 provide information relevant to assessing health effects that might occur among emergency responders following a response to a collapse of a tall building. Section 3 summarizes data on injuries among emergency responders available from two incidents of structural collapse, the WTC on September 11, 2001, and Oklahoma City's Murrah building from the bombing on April 19, 1995. Such injuries include respiratory problems, eye injuries, burns, other skin and soft-tissue injuries, musculoskeletal injuries, and exhaustion. Injury data are described from the first few days after the collapse of the WTC collected at the Disaster Medical Assistance Team (DMAT) stations and from medical records at hospital emergency departments visited by the WTC responders reviewed several weeks or months after the collapse. These data provide insight into the injuries that might be preventable by the use of appropriate PPE and, therefore, might inform the decisions about PPE.

Section 4 focuses on the possible health effects of substances likely to be found in the pulverized building materials discussed above. These include asbestos, particulate matter, silica, synthetic vitreous fibers, and metals (arsenic, cadmium, chromium, lead, and mercury). Section 5 describes the possible health effects of several combustion by-products, including benzene, dioxins, polychlorinated biphenyls (PCBs), and PAHs.

Sections 3 through 5 summarize available information on acute and chronic health effects that have been documented in studies of humans following exposure to hazardous substances similar to those known to be, or likely to be, present following the collapse of a building.

For each substance, information is summarized related to the following topics:

- identity, properties, and uses
- possible routes of exposure
- evidence for health effects from human studies
- occupational exposure limits by the American Conference of Governmental Industrial Hygienists (ACGIH), OSHA, and NIOSH, including values for time-weighted average (TWA), short-term exposure limit (STEL), and immediately dangerous to life or health (IDLH)

- carcinogenicity status determined by NIOSH, OSHA, U.S. Environmental Protection Agency (EPA), the International Agency for Research on Cancer (IARC), the Federal Republic of Germany Maximum Concentration Values in the Workplace (MAK), and the U.S. National Toxicology Program (NTP).

Information about human health effects in these summaries is based primarily on reviews published by U.S. and international health organizations, including the

- Toxicological Profile published by ATSDR
- Environmental Health Criteria published by the World Health Organization
- Integrated Risk Information System toxicological reviews published by EPA.

In addition, all other published reports cited in the summaries were reviewed.

Table 1.1 Substances Monitored at the World Trade Center by Four Federal Agencies After September 11, 2001, and Possible Health Effects

Substance	ATSDR[a]	EPA[b]	NIOSH[c]	OSHA[d]	Possible Health Effects[e]
Arsenic, inorganic			X	X	Cancer (lung, skin), lung effects
Asbestos	X	X	X	X	Asbestosis, cancer
Benzene (VOC)		X	X	X	Cancer
Benzo[a]anthracene (PAH)		X	X		Cancer
Benzo[a]pyrene (PAH)		X	X	X	Cancer
Benzo[b]fluoranthene (PAH)		X	X		Cancer
Beryllium (in air)		X	X		Cancer (lung); berylliosis
Cadmium			X	X	Kidney effects
Calcite	X				Not available from source
Carbon monoxide		X	X		Anoxia; CVS effects; CNS effects; reproductive effects
Chromium (in air)		X	X		Metal and Cr III compounds: irritation; dermatitis Water-soluble Cr VI compounds: liver, kidney, and respiratory effects Insoluble Cr VI compounds: cancer; irritation
Chrysene (PAH)			X	X	Skin effects
Coal tar pitch volatiles (VOC)				X	Cancer
Cobalt			X		Asthma; lung and CVS effects
Copper (in air)		X		X	Irritation; GI effects; metal fume fever
Diesel exhaust			X		Diesel fuel, not exhaust: skin effects; irritation
Dioxin (in air) 2,3,7,8-tetrachorodibenzo-*p*-dioxin (2,3,7,8-TCDD)		X			Not available from source
Ethyl benzene (VOC)		X	X		Irritation; CNS effects
Formaldehyde				X	Irritation; cancer
Freon (Chlorodifluoromethane)		X	X	X	CVS effects
Gypsum (calcium sulfate)	X				Irritation
Halite	X				Not available from source
Hydrobromic acid			X		Irritation
Hydrochloric acid			X		Irritation; corrosion
Hydrofluoric acid			X		Irritation; effects on bone and teeth; fluorosis
Hydrogen sulfide			X		Irritation; CNS effects
Iron oxide (in air)		X		X	Pneumoconiosis
Lead (in air)		X	X	X	Effects on CNS; blood; kidney; reproductive
Magnesium			X		Magnesium oxide: Irritation; metal fume fever
Manganese fume (as Mn)			X	X	Effects on CNS (manganism); lung; reproductive
Mercury (vapor) (as Hg)			X	X	Alkyl compounds: CNS effects

Table 1.1 Substances Monitored at the World Trade Center by Four Federal Agencies After September 11, 2001, and Possible Health Effects (cont.)

Substance	ATSDR[a]	EPA[b]	NIOSH[c]	OSHA[d]	Possible Health Effects[e]
					Aryl compounds: CNS effects; neuropathy; vision effects; kidney effects Elemental and inorganic forms: CNS, kidney, and reproductive effects
Mica	X				Pneumoconiosis
Molybdenum			X		Soluble compounds: lung irritation Metal and insoluble compounds: lung and CNS effects
Nickel			X		Elemental: dermatitis; pneumoconiosis Soluble inorganic compounds: CNS effects; irritation; dermatitis Insoluble inorganic compounds: cancer; lung effects; irritation; dermatitis Nickel subsulfide: cancer; lung effects; irritation; dermatitis
Nitric acid			X		Irritation; corrosion; pulmonary edema
Particulate matter (PM10)		X	X		Lung effects
Particulate Matter (PM2.5)		X	X		Lung effects
Phenanthrene (PAH)		X	X		Not available from source
Phosphoric acid			X		Irritation
Phosphorus			X		Irritation; effects on liver; kidney; CVS; GI
Polychlorinated biphenyls (PCBs) (chlorodiphenyls)		X			Irritation; chloracne; liver effects
Polycyclic aromatic hydrocarbons (PAHs)		X			Cancer
Portlandite	X				Portland cement: irritation; dermatitis
Pyrene (PAH)		X	X		Not available from source
Selenium			X		Irritation
Silica (quartz, cristobalite, tridymite)	X	X	X	X	Quartz: silicosis; lung function; lung fibrosis; cancer Cristobalite: lung fibrosis; silicosis Tridymite: lung fibrosis; silicosis
Silver			X		Argyria (skin, eyes, mucosa)
Styrene (PAH)		X	X		Neurotoxicity; irritation; CNS effects
Sulfur dioxide		X			Irritation
Sulfuric acid			X		Irritation; cancer (larynx)
Synthetic vitreous fibers	X				Continuous filament glass fibers: irritation Glass wool fibers: irritation, lung effects Rock wool fibers: irritation, lung effects Slag wool fibers: irritation; lung effects Special purpose glass fibers: irritation; lung effects Refractory ceramic fibers: lung fibrosis; cancer

Table 1.1 Substances Monitored at the World Trade Center by Four Federal Agencies After September 11, 2001, and Possible Health Effects (cont.)

Substance	ATSDR[a]	EPA[b]	NIOSH[c]	OSHA[d]	Possible Health Effects[e]
Tellurium			X		CNS effects; cyanosis; liver effects
Thallium			X		Irritation; CNS and CVS effects
Toluene (VOC)		X	X		CNS effects
Vanadium			X		Vanadium pentoxide: irritation; lung effects
Vinyl chloride (VOC)				X	Cancer (liver)
Volatile organic compounds (VOCs)		X			Not available from source
Xylene (VOC)			X		Irritation
Zinc			X		Zinc chloride fume: irritation; lung edema Zinc chromates: Cancer (lung)
Zinc oxide (in air)		X		X	Fume: lung effects; metal fume fever Dust: lung effects

CVS = cardiovascular system.

CNS = central nervous system.

GI = gastrointestinal.

PAH = polycyclic aromatic hydrocarbon.

VOC = volatile organic compound.

[a] X = Listed in Final Technical Report of the Public Health Investigation to Assess Potential Exposures to Airborne and Settled Surface Dust in Residential Areas of Lower Manhattan (NYCDOHMH and ATSDR, 2002).

[b] X = Listed in Exposure and Human Health Evaluation of Airborne Pollution from the World Trade Center Disaster (External Review Draft) or World Trade Center Disaster Response Air Monitoring Data Summaries (EPA, 2002a; EPA, 2002b).

[c] X = Listed in Summary Report to the New York City Department of Health: NIOSH Air Sample Results for the World Trade Center Disaster Response (NIOSH, 2002b).

[d] X = Listed in OSHA sampling results summary as of October 8, 2002 (OSHA, 2002).

[e] Conditions listed in this column are taken from the TLV Basis-Critical Effects column of the table of Adopted Threshold Limit Values in Threshold Limit Values and Biological Exposure Indices (ACGIH, 2002).

2. Issues Related to Estimating Risk of Health Effects Among Emergency Responders in a Structural Collapse Environment

Differences in Individual Susceptibility

One issue that complicates efforts to estimate risk or exposure and protect emergency responders is the fact that individuals may differ with regard to susceptibility to toxicants. Such differences in response might arise from genetic factors, age, personal habits, medication, or previous exposures.

Nonetheless, a presumed uniformity in the response of humans to various chemicals is the general basis for recommending and promulgating occupational health standards. For example, ACGIH describes threshold limit values (TLVs) as airborne concentrations of substances that represent conditions under which it is believed that nearly all workers may be repeatedly exposed day after day without adverse health effects. In a further description, ACGIH notes that "Because of wide variation in individual susceptibility . . . a small percentage of workers may experience discomfort from some substances at or below the threshold limit; a smaller percentage may be affected more seriously by aggravation of a pre-existing condition or by the development of an occupational illness . . . . Individuals may also be hypersusceptible or otherwise unusually responsive to some industrial chemicals because of genetic factors, age, personal habits (e.g., smoking, alcohol or other drugs), medication, or previous exposures" (ACGIH, 1999).

Genetic differences are an important source of variation in susceptibility. For example, the commonly used insect repellent, DEET, is especially toxic to individuals with genetic or acquired defects in ammonia metabolism, such as carriers of ornithine carbamoyl transferase deficiency (Cecchine et al., 2000). In addition to genetic differences, heterogeneity of many human characteristics may result in differences in susceptibility. However, even "homogeneous" populations of test animals often display a distribution of effects in response to a single toxicant, indicating that other individual differences must also be important. As well as the demographics and personal habits mentioned above, these may include differences in exposure, absorption, and resulting effective doses.

The Effects of Mixed Exposures

Of particular concern to emergency responders in a collapsed environment is the possibility — likely the reality — that they will be exposed not to a single compound but to mixtures of compounds as well as other stressors such as heat and physical exertion. In addition, personal exposures to medicines and behavioral exposures (e.g., smoking, alcohol, and other drug use) can be components of such mixed exposures, further complicating efforts to estimate the effect of even one compound or the mixture of compounds. While some general guidelines have been published for the risk assessment of chemical

mixtures (EPA, 1986; EPA, 2000), the range of potential exposures includes not just chemicals but myriad other exposures. For example, mixed exposures may fall into several categories (Chen and McKone, 2001).[1] Those categories that have been studied include combined chemical exposures such as solvent mixtures (Olsen and Seedorff, 1990; Seedorff and Olsen, 1990); combined physical exposures such as ionizing radiation and ultraviolet light (Sevcova et al., 1978; Shore et al., 1984); combined exposures to biological agents such as pathogenic microorganisms (Straub et al., 1993); combined chemical and physical agents such as solvents and noise (Morata et al., 1994); combined exposures to chemicals and biological agents (e.g., studies on sick-building syndrome) (Witorsch and Schwarts, 1994); and physical agents combined with biological agents such as ultraviolet light and viral infections (Norval and el Ghorr, 1996).

Humans are constantly exposed to mixtures of chemicals and other stressors in the environment. Each component of a mixture has a unique toxic potential and may influence the toxicity of other mixture components by affecting their chemistry and dynamics once in the human body (Simmons, 1994). The toxicology databases maintained generally as the result of academic research and specifically by agencies and organizations concerned with public health consist primarily of the effects of single chemical exposures, based on both empirical data from human and animal studies and the results of risk assessments. Data on the health effects of chemical mixtures, however, are rarely available from human and animal studies. In addition, the risk assessment process is much more difficult for chemical mixtures (Simmons, 1990).

Complicating the study and understanding of mixed exposures is the unfortunate fact that a common terminology has yet to be widely adopted (Greenland, 1993; Samet, 1995). While the following terms may not be universally recognized, they serve to describe potential effects of mixed exposures in this report (Eaton and Klaassen, 1996).

The simplest outcome from mixed exposures is a cumulative effect (e.g., 2 + 2 = 4). However, the observed effects of mixed exposures may in fact be more than or less than that predicted by summing the expected effects of each of the components in the mixture. If the observed effect is slightly more than the expected cumulative effect, the effect of the mixture is additive (2 + 2 = 5). A synergistic effect occurs when the combined effects of the mixture are much greater than the sum of the effects of each component alone (2 + 2 = 20). A situation in which the components of a mixture may interfere with each other to result in a less-than-predicted effect is known as antagonism (2 + 2 = 1). Finally, potentiation occurs when one substance does not have a toxic effect on the target organ or organism in question but makes another substance much more toxic in a mixture (0 + 2 = 10).

Why Mixed Exposures Can Result in Unexpected Effects

As described above, the null hypothesis of mixtures is that effects would be expected to resemble the cumulative effect of each component of the mixture when exposed singularly: If toxicant A produces a hypothetical effect value 1 and toxicant B produces effect value 1, the mixture of A and B would be expected to produce an overall effect value of 2. However, this is not always the case. There are a variety

[1] For a further review of mixed exposures to various chemicals, medicines, alcohol, drugs, heat, and other stressors, see Cecchine et al. (2000).

of mechanisms that could be responsible for significantly higher- or lower-than-expected observations of toxicity caused by a mixture. These mechanisms fall into several general categories.

Concurrent exposures to components of a mixture may enhance their absorption into target tissues. This may occur at the point of exposure, as is the case when one chemical acts as a carrier for another or alters tissues to be more receptive to other chemicals. The enhanced absorption may also occur as a result of altered physiologic action of one or both chemicals. The latter case is exemplified by the hypothesis that a chemical not suspected to reach the brain, pyridostigmine bromide, can enhance the toxicity of chlorpyrifos (a pesticide), which is known to do so (Abou-Donia et al., 1996a; Abou-Donia et al., 1996b). Further, injury to a tissue by one agent may result in greater vulnerability to a second agent, as is the case with cadmium chloride damage to the lungs followed by inhalation of oxygen (Haschek and Witschi, 1991).

Components of mixtures may also interact in a functional manner. In this case, two chemicals may counterbalance each other by producing opposite effects on the same physiological function. This principle is the basis for some pharmaceutical treatments. For example, low blood pressure due to severe barbiturate intoxication is effectively treated by a vasopressor agent such as norepinephrine (Eaton and Klaassen, 1996).

Other chemical interactions that can alter toxicity include alteration of the biotransformation, distribution, or excretion of one or more of the interacting chemicals. For example, dimercaprol bonds chelates with metal ions such as arsenic, mercury, and lead and decreases their toxicity (Eaton and Klaassen, 1996). Further, the chemicals may be competing substrates, resulting in a decreased catabolism of the mixture as a whole. For example, toluene has been shown to be a competitive inhibitor of the metabolism of benzene (Andrews et al., 1977; Sato and Nakajima, 1979). In this and similar cases, the effect of benzene is altered because benzene toxicity is largely dependent upon its metabolites, and an alteration of the rate and pathway by which it is metabolized modifies toxic effects. Such competition may also result in one or more components of the mixture being transported to tissues where it is not normally expected during its metabolism, resulting in unexpected effects (Abou-Donia et al., 1996a; Abou-Donia et al., 1996b). Because the enzyme families that serve to metabolize many toxicants are comprised of similar enzymes,[2] several chemicals can affect the metabolism of themselves and other chemicals because of changes in enzyme levels or activities (Gonzalez, 1988; Lechner, 1994; Snyder and Remmer, 1979). For example, benzene is capable of increasing its own metabolism and that of some other chemicals (Snyder et al., 1967), and polychlorinated biphenyls can increase the metabolism of a wide variety of other chemicals (Snyder and Andrews, 1996).

Challenges in Estimating Risks Posed by Mixed Exposures

Predicting the toxicity of mixtures in general on the basis of the toxicity of single compounds is not feasible (Marinovich et al., 1996). Moreover, the number of possible paired combinations increases exponentially with the number of agents, as 2^n; thus, 10 compounds have more than 1,000 possible paired

[2] For example, the mixed function oxidase system contains a group of related enzymes (epitopes) that are collectively known as cytochrome P450.

combinations that could exert different effects. The problem is further complicated if it is desirable to consider the effects of different exposure durations and routes on different target organs (Simmons, 1994; Simmons, 1995). Even in controlled animal studies, a factorial design to test all possible combinations of only a few compounds at small number of different exposure concentrations is a time- and resource-intensive undertaking (Cecchine, 1997). For example, a full-factorial animal design to examine the interactions of three compounds at five dose levels would require 125 treatment groups and 750 animals, if six animals are included in each treatment group (Simmons et al., 1995). Of course, the effects of mixtures in humans cannot be studied by deliberately exposing people in such a design; the difficulties in determining such effects epidemiologically are even more significant (Samet, 1995).

Most workers who have any occupational chemical exposure have low-level exposures to multiple chemicals and short-term higher exposures to many of these same chemicals (Melius, 1986). However, since the effects of chemical mixtures are not well understood, regulatory standards are based on single agents. Because of the time and resources required to study every possible combination, the U.S. Food and Drug Administration does not require examination of drug combinations in determining approval for an individual drug; it does not even call for examination of combinations that are likely to occur together (Cecchine et al., 2000). Similarly, potential exposures to mixtures of chemicals (and other factors) by emergency responders and other workers are, in general, poorly documented, and "testing even most potential mixtures with the classical toxicological profile is unfeasible" (Marinovich et al., 1996).

Given the inherent difficulties in estimating or empirically measuring the effects of mixed exposures to animals or humans, only limited data are available even for those mixtures that have been recognized to be of significant concern (such as those studies referenced above). For example, multiple animal studies were performed to test the hypothesis that a combination of pesticides and pyridostigmine bromide[3] was a cause of illnesses reported by veterans of combat in the Persian Gulf region in 1990–1991 (see Cecchine et al., 2000). Such studies often provide little useful information because the effects of concern are often due to low-level exposures and an exposure route that do not translate well to short-term animal studies. For example, one study evaluated the lethal interaction of DEET, pyridostigmine bromide, and the pesticide permethrin when given orally to rats by gastric lavage (McCain et al., 1997). Although a significant increase in lethality over expected additive (cumulative) values was observed when all three chemicals were given concurrently, the study used very high doses to produce this effect. In fact, to match the lowest doses used in this study, a 70-kg person (about 155 pounds) would have to simultaneously ingest 107 pyridostigmine tablets, 23 cans of permethrin, and 6.6 tubes of 33 percent DEET. In addition, DEET and permethrin would be administered dermally in humans, not orally, furthering the limitations of this representative study.

How Can the Effects of Mixed Exposures Be Measured?

Ideally, human studies designed to estimate dose-response relationships for specific mixtures of concern would be used for risk assessment because extrapolations are minimal and uncertainties are reduced when these relationships are well described. Such methods have been used for assessing risk due to

[3] Pyridostigmine bromide is a nerve agent chemoprophylaxis.

mixed exposures of cigarette smoke and other exposures (e.g., diesel exhaust); however, except for specific cases of concern, as discussed above, this situation is rarely encountered. Further, risk assessment of mixtures is of the most utility when the expected mixed exposures maintain a fairly consistent composition and exposure level throughout the exposure time frame. A comparable approach is to use information about a well-studied and toxicologically similar surrogate mixture, based on either human or nonhuman data.[4] Existing exposure data are insufficient to determine whether these approaches are worth further consideration for collapsed environments.

Occupational Safety Approach to Estimating Exposure Limits for Mixed Exposures

The approach used by ACGIH and OSHA to consider the combined effects of two or more potentially hazardous agents acting upon the same organ system is to determine a TLV for the mixture by the following equation (ACGIH, 2002):

$$\frac{C_1}{TLV_1} + \frac{C_2}{TLV_2} + \ldots + \frac{C_n}{TLV_n},$$

where C_n indicates the observed atmospheric concentration and TLV_n the corresponding threshold limit for substance *n*. For instances in which the different agents are not expected to interact (e.g., when local effects on different organs are expected from the different agents), the TLV would be exceeded only if one member of the series itself exceeds unity:

$$\frac{C_1}{TLV_1} \geq 1, \quad or \quad \frac{C_2}{TLV_2} \geq 1.$$

[4] The latter method is known as the comparative potency method. In this approach, the human toxicity of the mixture of concern is estimated from that mixture's toxicity in animal studies, by multiplying by a proportionality constant that is estimated from data on other mixtures in the similarity set.

3. Acute Injuries Among Emergency Responders Following a Building Collapse

In the first hours and days following a building collapse, some emergency responders involved in the rescue and recovery operations will likely sustain and seek treatment for acute injuries and illnesses. In an effort to characterize the type of injuries and illnesses that occurred following building collapses in the past, data collected about emergency workers who responded to the World Trade Center attack on September 11, 2001, and the Oklahoma City bombing on April 19, 1995, are summarized in this section. This information is presented to highlight the type of personal protective equipment that should be worn to prevent injuries among emergency responders after future collapses.

Injuries Among Emergency Responders After the World Trade Center Collapse

Within three days of the collapse of the WTC, five DMAT stations[5] were set up at locations around the site to treat individuals who sustained injuries or became ill while performing rescue operations. In addition, four medical facilities near the WTC[6] treated emergency responders who requested care for an injury or illness. A report published by the National Clearinghouse for Worker Safety and Health Training (Elisburg and Moran, 2001) summarizes the injuries and illnesses among rescue workers that were reported to any of these DMAT stations or hospital emergency departments between September 14 and 25, 2001.

Information about each visit to a DMAT station or an emergency room was collected on a standardized Surveillance Form by the clinician responsible for the visit. The checklist of injury and illness types on the form was expanded on three occasions during the time it was used, in response to feedback from clinicians using the form. In addition, on forms issued after September 17, 2001, sections on Activity at the Time of Injury and on use of respirators and eye protection were added (Elisburg and Moran, 2001).

During the first few days after September 11, rescue operations continued 24 hours per day; work shifts varied from 8 to 12 hours. Approximately 5,130 individuals were working at the WTC site on a daily basis: 1,200 firefighters, 2,000 police officers, 495 urban search and rescue team members, 1,350 construction workers, and 85 sanitation department workers (Elisburg and Moran, 2001).

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[5] The DMAT sites are referenced as MS1/North, MS2/West, MS3/Liberty, MS4/Church, and MS5/Vessey in Elisburg and Moran (2001).

[6] The emergency departments included in the data presented here are Bellevue Hospital Emergency Department, Beth Israel Medical Center (Petrie Division) Emergency Department, New York University Downtown Hospital Emergency Department, and St. Vincent's Hospital Emergency Department.

The total number of Surveillance Forms completed between September 14 and 25 was 3,814 (Elisburg and Moran, 2001) (Table 3.1). Of these, the most commonly reported injuries and illnesses were eye injuries (13 percent, N = 509), headaches (9 percent, N = 331), blisters (8 percent, N = 288), respiratory injuries (7 percent, N = 252), and sprains or strains (6 percent, N = 231). The category of Other Injuries included a wide range of injuries and illnesses, as well as requests for medications, supplies, and PPE (see footnote on Table 3.1). Of the 3,814 injuries, 26 percent were reported by construction workers, 24 percent by police officers, 18 percent by firefighters, 4 percent by medical personnel, 4 percent by military personnel, 2 percent by Red Cross personnel, and 23 percent by other and unknown personnel.

In another study of emergency workers with injuries and illnesses following the collapse, the New York City Department of Health (NYCDOH) reviewed records from the emergency departments and inpatient admissions of four hospitals nearest the WTC and a fifth hospital with a burn referral center (MMWR, 2002c). The NYCDOH team collected data from all persons seeking care at these facilities for the 48 hours following the collapse (8:00 a.m. on September 11 until 8:00 a.m. on September 13). The information included demographic and clinical characteristics of each person.

Within the first 48 hours, 279 rescue workers sought emergency care at the four hospitals near the WTC (Table 3.2) (MMWR, 2002c). Of these, 118 (42 percent) had respiratory injuries and 108 (39 percent) had eye injuries. Most of these two types of injuries were caused by exposure to smoke, dust, and fumes. Among those treated at the hospitals, other common injuries were sprain or strain (16 percent), laceration (8 percent), and contusion (16 percent). According to an article in *Morbidity and Mortality Weekly Report* (MMWR), rescue workers seeking care on the second day had been injured by "fires, unstable rubble, sharp-edged building fragments, and exposure to smoke and respirable dust" (MMWR, 2002c).

Table 3.1 Number of Visits at Disaster Medical Assistance Team Stations and Hospital Emergency Departments Following the Collapse of the World Trade Center Towers, by Reason for Visit and Date

	September 2001												
Reason for Visit	**9/14**	**9/15**	**9/16**	**9/17**	**9/18**	**9/19**	**9/20**	**9/21**	**9/22**	**9/23**	**9/24**	**9/25**	**Total**
Abrasion	2	1	2	7	16	15	10	4	7	10	4	3	81
Blister	3	2	3	36	44	42	25	26	29	31	28	19	288
Burn	0	0	2	9	8	10	12	13	9	11	8	6	88
Chest pain	4	1	2	5	1	4	3	1	1	2	2	0	26
Concussion	0	1	0	0	0	0	1	0	1	0	1	0	4
Contusion	3	6	2	5	3	3	2	4	2	6	2	3	41
Crush	0	1	0	1	0	0	1	0	0	2	2	1	8
Dehydration	0	4	0	2	1	3	0	1	0	0	1	0	12
Eye injury, combined[a]	19	13	22	108	72	67	46	40	35	39	24	24	509
Fever	0	0	0	0	0	0	0	0	0	0	1	0	1
Fracture	3	1	2	2	2	2	3	1	2	4	2	3	27
Headache	1	4	4	11	23	40	39	19	39	55	44	52	331
Heat exhaustion	0	0	0	0	0	1	0	0	0	0	0	0	1
Laceration	11	10	5	23	24	25	30	16	20	20	24	5	213
Lung injury, combined[b]	24	16	12	21	18	44	22	23	11	17	20	24	252
Nausea/vomit/diarrhea	1	2	1	3	8	7	9	3	7	16	10	5	72
Other[c]	8	18	20	47	74	93	59	117	110	141	78	126	891
Psychological stress	2	2	1	5	4	0	4	4	3	2	2	20	49
Skin irritation/rash	4	9	2	9	11	17	14	12	16	17	19	30	160
Sprain/strain	27	15	9	17	28	24	23	19	16	24	18	11	231
Unknown	0	1	1	11	15	31	38	37	81	103	97	114	529
Total	112	107	90	322	352	428	341	340	389	500	387	446	3,814

SOURCE: Elisburg and Moran, 2001.

[a] "Eye injury, combined" includes eye irritation and corneal abrasion.

[b] "Lung injury, combined" includes cough, shortness of breath/wheezing, smoke/dust inhalation, and asthma exacerbation.

[c] "Other" includes the following conditions with more than five occurrences between September 14 and 25, shown here with the number of occurrences (in parentheses): allergy (20), back/leg pain (24), animal or insect bite (7), blood pressure check (17), nose or lung congestion (84), dental (13), diabetes (6), wound care (54), ear injury (8), exhaustion/fatigue (8), flu symptoms (10), follow-up care (6), foot infection or injury (61), foreign body (not in eye) (9), request for medication or supplies (141), musculoskeletal (63), respirator/goggles/protective equipment (109), seizure (6), sore throat/throat irritation (50), and stomach ache (39).

Table 3.2 Number and Percentage of Injuries Among Rescue Workers During the 48 Hours[a] After the World Trade Center Attack Reported by Five Hospitals, by Type of Injury

	Rescue Workers with Hospital Visits (N = 279)	
Type of Injury	Number of Injuries	Percentage of Workers[b]
Inhalation	118	42
Ocular	108	39
Sprain or strain	44	16
Laceration	23	8
Contusion	44	16
Fracture	13	5
Burn	6	2
Closed head	3	1
Crush	3	1
All injuries reported by five hospitals	362	—

SOURCE: MMWR, 2002a.

[a] 8:00 a.m. September 11 to 8:00 a.m. September 13.

[b] The sum of the percentages exceeds 100 percent because some rescue workers had more than one injury.

In another report, injury data for the first 24 hours following the WTC collapse were compiled for the rescue workers of the Fire Department of New York City (FDNY) (MMWR, 2002a). Among the FDNY rescue workers responding to the WTC collapse, 240 reported injuries within the first 24 hours. Of those, most injuries were for exposure (27 percent), respiratory irritation (21 percent), and eye irritation (10 percent) (Table 3.3). Exposure is defined as a combination of any or all of the following: exhaustion, dehydration, and eye and respiratory irritation.

Table 3.3 Reasons for Seeking Emergency Medical Care During the 24 Hours After the World Trade Center Collapse Among Fire Department of New York City Rescue Workers, September 11, 2001

	FDNY Rescue Workers with Injuries (N = 240)	
Diagnostic Category	Number of Injuries	Percentage of Workers
Burn	3	1.1
Back pain	10	3.8
Chest pain	8	3.1
Concussion	8	3.1
Contusion	19	7.3
Dehydration	5	1.9
Eye irritation	25	9.5
Fracture	17	6.5
Exposure	70	26.7
Laceration, puncture wounds	4	1.5
Lung injury, combined[a]	54	20.6
Psychological stress	8	3.1
Sprain, strain, meniscus tears	31	11.8
Total	262	—

SOURCE: MMWR, 2002b.

[a] Includes respiratory tract irritation (N = 50), pneumothorax without rib fracture (N = 1), inhalation injury (N = 1), respiratory arrest with bronchospasm (N = 1), and asthma exacerbation (N = 1).

FDNY rescue workers reported certain types of injuries more frequently and others less frequently during the month after September 11 than in the months before the attack. The number of crush injuries, lacerations, and fractures reported by FDNY rescue workers in the month following the WTC collapse increased, compared with the average number per month in the nine months before the attack (Table 3.4). Other types of injuries, however, were reported less frequently after September 11, including contusions, sprains and strains, other orthopedic injuries, and burns (Table 3.4). The incidence of respiratory illnesses requiring medical leave increased dramatically among FDNY rescue workers following the attacks (MMWR, 2002a; MMWR, 2002b). The number of medical leaves due to respiratory illness was 1,876 in the 11 months following the attacks, compared with 393 during the 11 months before (data not shown).

Table 3.4 Average Number of Traumatic Injuries Reported by New York City Fire Department Rescue Workers per Month During the Month After and the Nine Months Before the World Trade Center Collapse

	Average Number of Injuries Reported per Month During	
Nature of Injury	Nine Months Before Attack	One Month After Attack
Crush injuries	3	9
Lacerations	37	50
Fractures	21	27
Contusions	86	67
Strains and sprains	364	200
Other orthopedic injuries	96	61
Burns	43	3

SOURCE: MMWR, 2002b.

In a more detailed report of respiratory illness among rescue workers employed by the FDNY on September 11, the prevalence of respiratory illness was estimated among those with different exposures at the WTC site (Prezant et al., 2002). Patients were evaluated on the basis of a questionnaire, spirometric testing, airway-responsiveness testing, and chest imaging. The main outcome, World Trade Center cough (WTC cough), was defined as "a persistent cough that developed after exposure to the site and was accompanied by respiratory symptoms severe enough to require medical leave for at least four weeks." Prezant et al. (2002) reported the incidence of WTC cough to be 8 percent among those present at the towers' collapse (high exposure), 3 percent among those present within two days (moderate exposure), 1 percent among those present within three to seven days (low exposure), and 0 percent among those not at the WTC within the first two weeks (no exposure) (Table 3.5). When asked about selected upper- and lower-airway symptoms before and after the collapse, rescue workers with WTC cough reported having almost all symptoms more frequently after the collapse than before. Among those with WTC cough, 87 percent reported symptoms of gastroesophageal reflux disease — an unexpected finding. Bronchial hyperreactivity based on methacholine challenge testing was observed in 23 percent of those without WTC cough who were tested in the high-exposure group and in 8 percent of the moderate exposure group without WTC cough. Of those with WTC cough who were tested, 24 percent (47 of 196) were classified as having airway hyperreactivity.

Table 3.5 Number and Percentage of Firefighters Employed by the Fire Department of New York City on September 11, 2001, with World Trade Center Cough,[a] by Level of Exposure to Respiratory Irritants at the Site of the Collapse

Exposure Category	Number in Exposure Category	Number with WTC Cough	Percentage with WTC Cough
High (present at WTC collapse)	1,636	128	7.8
Moderate (present within first two days after WTC collapse)	6,958	187	2.7
Low (present within three to seven days after WTC collapse)	1,320	17	1.3
None (not present first two weeks after collapse)	202	0	0.0
Total	10,116	332	3.3

SOURCE: Prezant et al., 2002.

[a]World Trade Center cough was defined as a persistent cough that developed after exposure to the site of the collapse and was accompanied by respiratory symptoms severe enough to require medical leave for at least four weeks.

Injuries Among Rescue Workers After the Oklahoma City Bombing

In a study of emergency responders responding to the Oklahoma City bombing, injuries were identified among rescue workers from four subgroups: firefighters employed by Oklahoma City Fire Department (OCFD), firefighters employed by other local cities, members of 11 Urban Search and Rescue (USAR) teams from the Federal Emergency Management Agency, and military personnel from a local base (Dellinger et al., 1997). Cases consisted of "rescue workers who were physically injured in the course of performing tasks related to the rescue effort from April 19, 1995 [the day of the bombing] through May 4, 1995 [the last day of recovery activities]." Cases were identified by several methods, including a survey of medical personnel treating rescue workers on-site, review of medical records from 16 local hospital emergency departments and clinics, telephone interviews with fire chiefs from the OCFD and with a representative of 10 of the USAR teams, and a review of the written documentation of the rescue effort for mention of injuries.

A total of 932 rescue workers from the OCFD and 658 USAR team members worked at the bombing site. Based on the case-finding methods described above, 100 persons were identified with a total of 103 injuries. Among these, the most frequent were sprain and strains, eye injuries, and lacerations/punctures (Table 3.6). Sprain and strains were reported for ankle, knee, hand, wrist, elbow, back, and neck.

Synthesis

These injury data are subject to limitations (MMWR, 2002c). Many injuries sustained by emergency responders are probably not included in these estimates because the responders either did not seek treatment or sought their medical care from providers not included in these studies. Therefore, they do not represent all rescue workers who were injured or ill during the rescue and recovery operations; many injured were treated at other medical facilities, DMAT stations, or in physician offices. In addition, many others who were injured probably did not seek treatment at any medical facility. Finally, information on the nature of the injury and other details was missing from many records. These numbers, therefore, serve as a lower bound for the number of injuries that actually occurred at the WTC and Oklahoma City.

Table 3.6 Number and Percentage of Injuries Among Rescue Workers After the Oklahoma City Bombing, by Type of Injury

	Rescue Workers with Injuries (N = 100)	
Injury Category	**Number of Injuries**	**Percentage of Injured Workers**
Burn	5	5
Chemical burn	4	4
Contusion	9	9
Eye injury	20	20
Foot injury[a]	4	4
Fracture	1	1
Laceration, puncture wounds	19	19
Sprain, strain	22	22
Other[b]	19	19
Total	103	

SOURCE: Dellinger et al., 1997.

[a] "Foot injury" includes blisters and sores of the foot.

[b] "Other" includes overheating, inhalation, and other uncommon injuries.

4. Possible Health Effects of Exposure to Substances in Pulverized Building Materials Following a Structural Collapse

Introduction

This section focuses on nine substances (in five categories) that are likely to be present in pulverized building materials produced by the collapse of a large building. They are

- asbestos
- particulate matter
- silica
- synthetic vitreous fibers
- metals (arsenic, cadmium, chromium, lead, and mercury).

The following subsections describe the human health effects that might occur following exposure to each substance, based on studies published in the medical literature.

Asbestos

The term asbestos refers to six types of naturally occurring fibrous silicate minerals that have been used extensively in commercial products around the world (ATSDR, 2001b). The distinguishing property of asbestos, compared with non-asbestiform minerals, is the presence of long, thin fibers that can be easily separated. This property allows asbestiform minerals to be used in a variety of ways.

Based on mineralogical features, these substances are classified as either serpentine asbestos or amphibole asbestos (ATSDR, 2001b). Serpentine asbestos, also known as chrysotile asbestos, is composed of long, bendable fibers that can be woven. More than 99 percent of the asbestos used in the United States is of the chrysotile variety. Amphibole asbestos is made up of crystalline fibers that break easily. Thus, this form of asbestos is used less often in woven form. Amphibole asbestos includes the minerals known as amosite, crocidolite, tremolite, anthophyllite, and actinolite.

All forms of asbestos fibers are essentially chemically inert. The fibers generally do not evaporate, dissolve, burn, or react with other chemicals (ATSDR, 2001b). Among the many desirable properties of asbestos are resistance to heat, fire, wear, and friction; tensile strength; insulation for heat, electricity, and sound; and lack of reaction with chemical and biological agents. Because of these properties, asbestos has been used in a large number of commercial applications and products. In most applications, asbestos is

bonded with Portland cement, plastics, and resins. Less frequently, asbestos is used as a loose fibrous mixture or woven as a textile.

Over the past two decades, the use of asbestos has been decreasing in the United States because of health concerns. By 1999, production had declined from 299 million pounds per year in the late 1960s to 13.2 million pounds (ATSDR, 2001a). In the decades before exposure to asbestos was regulated, however, thousands of workers inhaled airborne asbestos in the manufacture of products containing asbestos, in shipbuilding and repair, and in construction.

Until the early 1970s, asbestos was widely used as a concrete additive, insulation material, and fire retardant. Buildings constructed before 1973, therefore, may contain large amounts of spray-applied asbestos for fire protection. The lower half of the WTC towers contained spray-applied asbestos for fireproofing; other parts of the towers might have also contained asbestos (EPA, 2002a).

In 1973, EPA banned the use of spray-applied asbestos for fireproofing and insulating buildings and other structures. In 1990, the agency revised this to prohibit the spray-on application of materials containing more than 1 percent asbestos, unless the material is encapsulated during spraying and not friable after drying. Currently, spray-on application of materials containing more than 1 percent asbestos is allowed if certain protective conditions are met. In 1975, EPA banned the use of asbestos for pipe insulation and block insulation for boilers and water tanks. In 1978, EPA also banned the use of asbestos for decorative purposes. In 1993, the agency prohibited the use of the following asbestos–containing materials: corrugated paper, roll board, commercial paper, specialty paper, flooring felt, and any new uses of asbestos. The Consumer Product Safety Commission banned the use of asbestos for patching compounds in 1977 and insulation in hair dryers in 1979.

Routes of Exposure

Based on epidemiological studies of workers exposed to asbestos, as well as from animal studies, the primary route of exposure for health effects is inhalation of asbestos fibers. Some studies have indicated, however, that oral exposure to asbestos fibers might also lead to health effects. After asbestos fibers are deposited in lung tissue, they are either removed by mucociliary clearance or macrophages or remain in the lungs for longer periods (ATSDR, 2001b). Most asbestos fibers that are deposited in the lung following inhalation are transported to the pharynx, where they are then swallowed, thereby exposing the gastrointestinal system. Some fibers, however, are left in the respiratory tract and accumulate over time. Asbestos fibers easily penetrate the skin, especially the fingers of those bagging the fiber. Chronic irritation of the skin by asbestos can result in the formation of corns (ATSDR, 2001b).

Air samples for measuring asbestos are collected on an air filter and are analyzed in laboratories using phase contrast microscopy. The exposure levels are usually expressed as fibers per milliliter of air (f/mL). A particle is counted as a fiber if it is at least 5 micrometers (μm) long and has a length-to-thickness ratio of at least 3:1. Because asbestos exposure of the lung is considered to be cumulative over time and health effects seem to correlate with cumulative exposure (concentration in air multiplied by years of exposure), for the health risk assessment the concentration over time is measured as fiber-years per milliliter (f-yr/mL) (ATSDR, 2001b).

All types of asbestos fibers are considered to be fibrogenic (i.e., capable of causing fibrosis) and carcinogenic (capable of causing cancer), but some might be more "potent" than others. Asbestosis, mesothelioma, and lung cancer have been observed in populations exposed to chrysotile, the most commonly used form, but also following exposure to amosite, crocidolite, tremolite, and anthophyllite (ATSDR, 2001b).. The length of fibers might influence the response, with longer fibers being more fibrogenic than shorter fibers. This effect might result from macrophages being unable to surround and eliminate fibers much larger than themselves (ATSDR, 2001b).

Studies of Health Effects Associated with Asbestos Exposure

Results from studies of humans and animals support an association between inhalation exposure to asbestos fibers and malignant and nonmalignant respiratory diseases (ATSDR, 2001a). Studies of asbestos workers have reported that chronic asbestos exposure might result in a higher risk of developing

- asbestosis (Henderson and Enterline, 1979; Nicholson et al., 1979)
- mesothelioma (malignant tumor of the chest or abdominal cavity lining) (Enterline et al., 1987; McDonald et al., 1997; Nicholson et al., 1979)
- pleural plaques (Jakobsson et al., 1995)
- lung cancer (Dement et al., 1994; Enterline et al., 1987; Nicholson et al., 1979).

In addition, exposures for somewhat shorter periods have been reported to be associated with higher risk of asbestosis, lung cancer, and mesothelioma (Levin et al., 1998).

Asbestosis is a fibrotic lung disease defined as a "diffuse interstitial fibrosis of the lungs caused by inhaled asbestos fibers" that can occur after chronic cumulative exposure as low as 15-70 f-yr/mL to asbestos (ATSDR, 2001a). Symptoms of asbestosis include shortness of breath and often a persistent cough. Persons with asbestosis display a decrease in pulmonary function variables, including forced expiratory volume in 1 second (FEV_1) and forced vital capacity (FVC).

Malignant mesothelioma (cancer of the mesothelium) is a malignant disease in which cells of the mesothelium become abnormal and divide without control or order, forming an aggressive tumor of the pleura. The cancer cells can invade and damage nearby tissues and organs, and can also metastasize (spread) from their original site to other parts of the body. Most cases of mesothelioma begin in the pleura or peritoneum (malignant tumor of the chest or abdominal cavity lining). Malignant tumors of the membranes that line the chest (pleural mesothelioma) and abdominal cavities (peritoneal mesothelioma) begin in the pleura or peritoneum (ATSDR, 2001a). Mesotheliomas occur infrequently in the general population, but asbestos workers are at higher risk. Mesothelioma usually occurs after many years of asbestos exposure but has developed many years later in persons exposed for 1–12 months (ATSDR, 2001b).

Lung cancer is a malignant tumor that invades and obstructs the lung's air passages. Cigarette smoking greatly increases the likelihood of a person developing lung cancer as the result of asbestos exposure. The most common symptoms of lung cancer are coughing, wheezing, unexplained weight loss, coughing up blood, and labored breathing. Other symptoms include shortness of breath, persistent chest pain,

hoarseness, and anemia. The risk of lung cancer in asbestos workers is dependent upon cumulative exposure, time since exposure, age at exposure, smoking status, and the type of asbestos (ATSDR, 2001b).

Pleural plaques are "generally oval areas of acellular collagen deposits, usually located on the inferior and posterior surfaces of the pleura" (ATSDR, 2001b). The clinical significance of pleural abnormalities is not generally agreed upon, with some considering them to be benign and others believing that they lead to decreased pulmonary capacity or increased risk of lung cancer (ATSDR, 2001b). Pleural plaques have been observed in persons with cumulative exposures as low as 0.12 f-yr/mL (ATSDR, 2001b).

Noncancer health effects of asbestos generally have not been observed in organs outside the respiratory system, although some cancers of the gastrointestinal system might be related to occupational exposure to asbestos.

Occupational Standards and Recommendations

Workplace standards set by OSHA require that air concentrations of asbestos in occupational settings not exceed a time-weighted average concentration of 0.1 f/mL, assuming exposures of eight hours per day for a 40-hour workweek (OSHA PEL-TWA), and not exceed 1.0 f/mL for any 30-minute period during a workday (OSHA PEL-STEL) (Table 4.1). NIOSH recommends air concentrations of asbestos not exceed a time-weighted average concentration of 0.1 f/mL, assuming exposures of up to a 10-hour workday during a 40-hour workweek (NIOSH REL-TWA). NIOSH has not set an IDLH level for asbestos. These limits are based on the avoidance of asbestosis and cancer (ACGIH, 2002). Asbestos has been classified as a known human carcinogen by several agencies (Table 4.2), including EPA (Group A), IARC (Group 1), MAK (Group 1), and NTP (Group K). These classifications are based on data from occupational studies linking asbestos to malignant mesothelioma and lung cancer.

Table 4.1 Regulatory Standards and Recommendations for Occupational Exposure to Asbestos in Air

Regulatory Measure	Value[a]
ACGIH TLV-TWA	0.1 f/cc
ACGIH TLV-STEL	No value listed
OSHA PEL-TWA	0.1 f/cc
OSHA PEL-STEL	1.0 f/cc (30-min)
NIOSH REL-TWA	0.1 f/cc
NIOSH REL-STEL	No value listed
NIOSH IDLH	Substance not listed

SOURCE: ACGIH, 2002.

NOTE: See Willis et al. (forthcoming) for definitions of exposure limits.

[a] Respirable fibers: Length >5 µm; aspect ratio ≥3:1, as determined by the membrane filter method at 400–450x magnification (4-mm objective), using phase-contrast illumination.

Table 4.2 Carcinogenicity Classifications for Asbestos

Agency	Classification	
ACGIH	A1	(Confirmed human carcinogen)
OSHA	Ca	(Carcinogen defined with no further categorization)
NIOSH	Ca	(Potential occupational carcinogen, with no further categorization)
EPA	A	(Human carcinogen)
IARC	1	(Carcinogenic to humans)
MAK	1	(Substances that cause cancer in man and can be assumed to make a significant contribution to cancer risk)
NTP	K	(Known to be a human carcinogen)

Synthesis

Studies of asbestos workers have established that inhalation of asbestos has led to increased risk of several diseases. Asbestosis (fibrosis of the lung caused by asbestos), malignant mesothelioma, lung cancer, and pleural plaques have been associated with chronic occupational exposure to asbestos. Table 4.3 summarizes the health effects that have been observed in humans following inhalation, oral, and dermal exposure to asbestos.

The OSHA PEL-TWA and NIOSH REL-TWA for air concentration of asbestos in an occupational setting are 0.1 f/mL, and the OSHA PEL-STEL is 1.0 f/mL for any 30-minute period during a workday. These exposure limits are based on the avoidance of asbestosis and cancer (ACGIH, 2002). Asbestos has been classified as a known human carcinogen by several agencies.

Table 4.3 Reported Human Health Effects of Asbestos Exposure by Different Routes

	Route of Exposure		
Health Effect	**Inhalation**	**Oral (Via Drinking Water)**	**Dermal**
Cancer	Mesothelioma[I, C]	Gastric[C]	No known effect
	Lung[I, C]	Kidney[C]	
	Gastrointestinal[C]	Pancreas[C]	
Respiratory	Asbestosis[I, C]	No known effect	No known effect
	Pleural plaques[I, C]		
	Upper airway abnormalities		
Cardiovascular	No known effect	No known effect	No known effect
Gastrointestinal	No known effect	No known effect	No known effect
Immunological	Depressed immune function[C]	No known effect	No known effect
Neurological	No known effect	No known effect	No known effect
Reproductive	No known effect	No known effect	No known effect
Developmental	No known effect	No known effect	No known effect
Other	None	None	Warts or corns on skin[I]

NOTE: This table presents a qualitative survey of reported human health effects associated with asbestos exposure based on the Toxicological Profile for Asbestos (ATSDR, 2001b). The causal relationship between asbestos and health effects is established more for some effects than for others; this table is intended to catalog possible health effects only.

[I] Listed as an effect of intermediate exposure (15–364 days) in ATSDR (2001b).

[C] Listed as an effect of chronic exposure (365 days or more) in ATSDR (2001b).

Particulate Matter

During the collapse of the WTC towers and for four to eight hours after, the level of airborne particulate matter was extremely high, in the range of milligrams per cubic meter (mg/m^3) (EPA, 2002a). For several days after the collapse, the PM levels at the edge of the WTC site continued to exceed EPA's PM2.5 National Ambient Air Quality Standards (NAAQS) 24-hour limit (65 $\mu g/m^3$). Emergency responders present at the time of the collapse or arriving shortly after were exposed to these levels of particulate matter, in combination with other materials.

Particulate matter is a component of air pollution that can consist of solid particles, liquid particles, or a mixture of solid and liquid particles suspended in the air (Brunekreef and Holgate, 2002). Different-sized particles are produced by different processes. Smaller particles (less than 1 µm, ultrafine) are mostly generated from gases, with the smallest of these (<0.1 µm) formed by condensation or chemical reactions that produce new particles. Larger particles are formed mechanically from the breakup of even larger particles. Particulate matter is reported as PM10, PM2.5, and ultrafine particles. PM10 refers to particles less than 10 µm in diameter that are also called "thoracic" particles because they can enter the lower respiratory system of humans. PM2.5 refers to particles less than 2.5 µm in diameter, also called "respirable" particles, that can enter the gas-exchange region of the lung. Ultrafine particles are smaller than 100 nm in diameter and have very little mass, but they represent a large surface area and are the most frequent type of particle in particulate air pollution, with the ability to penetrate deeply into the lung.

Routes of Exposure

Humans are exposed to particulate matter through inhalation of various sizes of particles present in outdoor and indoor air. PM2.5 is produced by many different processes, including industrial combustion, residential combustion, and vehicle exhaust, so their composition varies widely. These particles are also formed by the chemical reaction of gaseous pollutants such as SO_2 and NOx produces fine particles. Larger particles (PM10) arise from airborne dust, and crushing and grinding processes. Different-sized particles can be produced by a variety of sources (e.g., vehicles, woodstoves, power plants). The level of particulate matter in a given air sample depends on whether the location is urban or rural, the season of year, and sources or activities near the sampling site (e.g., highway). The physiological response to particulate matter is determined by the characteristics of the particle, how it is deposited in the respiratory tract, and the response to the particles at the cellular level (Koren, 1995).

Studies of Health Effects Associated with Particulate Matter

Numerous studies have been conducted to investigate the relationship between long-term exposures to particulate matter and health effects. Historically, three episodes of excess mortality have occurred following air pollution episodes (Donaldson et al., 2001). In 1930, five days of fog precipitated 63 deaths among residents of the Meuse Valley in Belgium, most of whom had diagnosed heart or respiratory disease. In 1948, an episode of air pollution in Donora, Pennsylvania, led to 20 deaths and 7,000 reporting acute illness. In 1952, 4,000 excess deaths occurred in London following a pollution episode.

Four well-designed prospective studies have shown an association between increased mortality rates and cities with higher levels of particulate matter. Based on daily mortality rates for 1987–1994 in the 20 largest U.S. counties (or metropolitan areas), PM10 levels were associated with death from all causes and from cardiovascular and respiratory illnesses after controlling for other outdoor-air pollutants (Samet et al., 2000). The populations residing in these metropolitan areas ranged in size from 1.2 million (San Antonio, Texas) to 8.9 million (Los Angeles), with a total study population of more than 50 million. Air pollution data were based on 24-hour mean values from the Aerometric Information Retrieval System operated by EPA. Multiple measurements for a given pollutant for multiple locations within an area were averaged (e.g., there were seven monitors in Los Angeles and two in San Antonio). Levels of particulate matter were recorded on different number of days, ranging from 480 days in Santa Ana–Anaheim, California, to 2,899 days in Pittsburgh. The log-linear regression models controlled for time trends in demographic characteristics, health status, and health care, as well as season of year, day of week, and weather. The relationship between mortality and PM10 was adjusted for the effects of other pollutants (ozone, carbon monoxide, sulfur dioxide, and nitrogen dioxide). For each increase of 10 $\mu g/m^3$ in the level of particulate matter, the relative rate of death increased 0.51 percent for all causes and 0.68 percent for heart and respiratory causes.

In the Six Cities Study, 8,111 white adults living in six cities were followed for about 15 years ending in 1991 (Dockery et al., 1993). Mean concentrations of particulate matter less than 2.5 µm in diameter, and that less than 10 µm (PM10), were used based on data from a centrally located monitor in each city. Increased mortality among the study participants was associated with exposure to higher levels of PM10, in cities where the annual average concentrations were 18.2–46.5 $\mu g/m^3$. These levels are far below the 24-hour PM10 standard of 150 $\mu g/m^3$ and also below the one-year standard of 50 $\mu g/m^3$. Higher mortality rates were also associated with exposure to increased levels of even smaller particles (<2.5 µm). This study reported an association between increased mortality from lung cancer and cardiopulmonary causes and higher exposure to particulate matter.

In a study of subjects recruited by the American Cancer Society, 552,138 adults were followed for seven years (Pope et al., 1995). The authors reported an association between median concentration of fine particulate matter and increased mortality due to all causes, cardiopulmonary causes, and lung cancer. In another study (Abbey et al., 1999), 6,338 nonsmoking adults living in Southern California were followed from 1977 to 1992. They reported a positive association between mortality from all causes of death and the number of days with PM10 concentrations above 100 $\mu g/m^3$. This study also reported that increased mortality from lung cancer in males was associated with higher levels of PM10. All three studies adjusted for individual risk factors in the analyses of mortality.

The results of these studies are consistent with the hypothesis that particulate matter increases the risk of death among persons with serious cardiovascular and pulmonary disease. There are several limitations, however, that should be considered in interpreting the results of these studies. The question of whether exposure to particulate matter and other pollutants decreases life expectancy by a few days or by more substantial periods has been raised (Samet et al., 2000) but has not been addressed adequately by results of current studies. In addition, the analyses measure the association with mortality based on average levels of particulate matter over a large geographic area (i.e., one or more large counties) rather than on levels in a more localized area that might differ markedly from the average. In addition, data on

individual risk factors, including medical conditions, smoking status, and physical activity, are not considered in the analysis and do not reflect variation important in estimating the risk of mortality (Samet et al., 2000).

Measures of morbidity have also been associated with exposure to particulate matter. Decreased lung function (Abbey et al., 1998), increased respiratory symptoms or respiratory illness (Abbey et al., 1995), increased symptoms in asthmatic children (McConnell et al., 1999) and adults (Ostro et al., 1991), and increased pediatric emergency room visits for asthma (Tolbert et al., 2000) have all been reported in areas with higher levels of particulate matter.

Possible mechanisms have been suggested for the health effects of acute and chronic exposure to air pollution in general and particulate matter specifically (Donaldson et al., 2002). The ultrafine component of particulate matter might trigger oxidative stress. Increased blood viscosity, fibrinogen, and C-reactive protein have been observed in populations exposed to higher levels of air pollutants, while heart rate has been shown to increase with a rise in air pollution. Inflammation of lung tissue by ultrafine particles might lead to increased blood coagulability, thereby increasing the risk of myocardial infarction.

Recent studies have suggested that the association between particulate matter and increased mortality is not supported by sound scientific evidence (Gamble, 1998; Gamble and Lewis, 1996). Lack of data on weather conditions, other pollutants, and ambient rather than local and indoor levels of particulate matter might lead to spurious conclusions regarding the role of particulate matter in causing increased mortality rates. In addition, the authors suggest that study results from the same cities at different points in time and from different study designs are inconsistent. In general, the results of studies that correlate average mortality rates and average exposure (i.e., ecologic studies) without using personal measures of exposure suffer from biases that might lead to the conclusion that an association exists at the population level, when, in fact, high levels of exposure to particulate matter might not necessarily correlate with mortality at the individual level.

Occupational and Air Quality Standards

Workplace standards set by OSHA require that air concentrations of particulates (not otherwise regulated) in occupational settings not exceed a time-weighted average concentration of 15 mg/m^3 for total dust and 5 mg/m^3 for the respirable fraction assuming exposures of eight hours per day for a 40-hour workweek (OSHA PEL-TWA) (Table 4.4). The EPA's Office of Air Quality Planning and Standards has set NAAQS for six principal pollutants: carbon monoxide, nitrogen dioxide, ozone, lead, particulate matter, and sulfur dioxide. For PM10, the standards are 150 $\mu g/m^3$ for a 24-hour average and 50 $\mu g/m^3$ for the annual arithmetic mean. For PM2.5, the standards (primary and secondary) are 65 $\mu g/m^3$ for a 24-hour average and 15 $\mu g/m^3$ for the annual arithmetic mean. Particulate matter has not been classified as a carcinogen by any health agency.

Table 4.4 Regulatory Standards and Recommendations for Particulate Matter in Air

Regulatory Measure	Total Dust	Respirable Fraction
ACGIH TLV-TWA	10 mg/m^3 (inhalable)	3 mg/m^3
ACGIH TLV-STEL	No value	No value
OSHA PEL-TWA	15 mg/m^3	5 mg/m^3
OSHA PEL-STEL	No value	No value
NIOSH REL-TWA	No value	No value
NIOSH REL-STEL	No value	No value
NIOSH IDLH	No value	No value

SOURCE: ACGIH, 2002.
NOTE: See Willis et al. (forthcoming) for definitions of exposure limits.

Synthesis

Studies of the general population have established that moderate levels of particulate matter are associated with higher mortality rates among elderly people, decreased lung function, increased respiratory symptoms and illness, and increased symptoms and use of medical care among those with asthma. Table 4.5 summarizes the health effects that have been observed in humans following inhalation exposure to particulate matter.

The OSHA PEL-TWA for air concentration of particulate matter (diameter not specified) in an occupational setting is 10 mg/m^3 (inhalable) and 3 mg/m^3 (respirable). Particulate matter has not been classified as a carcinogen by any health agency.

Table 4.5 Reported Human Health Effects of Particulate Matter Exposure by Inhalation

	Route of Exposure		
Health Effect	**Inhalation**	**Oral**	**Dermal**
Cancer	No known effect	No known effect	No known effect
Respiratory	Increased mortality due to respiratory causes[A,C]	No known effect	No known effect
Cardiovascular	Increased mortality due to cardiovascular causes[A,C]	No known effect	No known effect
Gastrointestinal	No known effect	No known effect	No known effect
Immunological	No known effect	No known effect	No known effect
Neurological	No known effect	No known effect	No known effect
Reproductive	No known effect	No known effect	No known effect
Developmental	No known effect	No known effect	No known effect
Other	No known effect	No known effect	No known effect

NOTE: This table presents a qualitative survey of reported human health effects associated with particulate matter based on published studies described in this section. The causal relationship between particulate matter and health effects is established more for some effects than for others. This table is intended to catalog possible health effects only.
[A] An effect of acute exposure.
[C] An effect of chronic exposure.

Silica

The term silica refers to the chemical compound silicon dioxide (SiO_2). This compound is naturally occurring in both crystalline and noncrystalline forms. Crystalline silica can occur in several forms, including alpha quartz, beta quartz, tridymite, cristobalite, keatite, coesite, stishovite, and moganite.

Alpha quartz is the most commonly occurring form and can be found in soil and rocks. Tridymite and cristobalite are less common, but they are also found in soil and rocks and are also produced when alpha quartz is heated (in industrial operations such as brick and ceramics manufacturing). The other forms are rarely or never observed in nature (NIOSH, 2002a).

Crystalline silica changes its structure in response to changes in temperature and pressure. Quartz changes from alpha to beta form at 573° C. Quartz is found in nearly every mineral deposit, and, as such, exposure to quartz is high. According to NIOSH, at least 1.7 million U.S. workers have been exposed to crystalline silica (NIOSH, 2002a).

Almost any process that involves movement of the earth or other disturbances of products containing silica (bricks, cement, etc.) will expose workers (NIOSH, 2002a). Silica is used to make glass products, including containers, plate and window glass, and fiberglass; molding and core in foundry work; silicon carbide for metallurgical work; fillers for rubber, paints, and putty; ceramics (pottery, brick, and tile); and petroleum manufacturing. Silica is found in many materials that might be used in the construction of buildings, including glass, fiberglass, limestone, concrete, mortar, plaster, and shingles (NIOSH, 2002a).

During the first few days following a tall building collapse, silica (quartz) might be present in airborne and settled dust resulting from pulverized building materials. Analysis of samples of dust collected after the collapse of the WTC indicated that more than 70 percent (by mass) was related to construction materials, "including pulverized cement, wallboard, and office furnishings," much of which were glass fibers (Lioy et al., 2002). Exposure to silica has been documented in many activities performed routinely in the construction industry, including abrasive blasting of buildings, concrete work, demolition, jackhammering, and hauling or dumping silica-containing materials (NIOSH, 2002a). Many of these same tasks would be performed as part of the cleanup activities after a building collapse, resulting in the presence of silica dust in the environment.

Noncrystalline (amorphous) silica is a type of silica whose atoms have no special order or geometric pattern (NIOSH, 2002a). It can be classified into three types: naturally occurring, obtained under uncontrolled conditions, and intentionally manufactured. Intentionally manufactured silica is the only type that does not also contain crystalline silica. This summary will focus primarily on crystalline silica.

Routes of Exposure

Based on epidemiological studies of workers exposed to silica, the primary route of exposure for health effects is inhalation of silica dust (NIOSH, 2002a). When silica dust is inhaled, some dust is deposited in the nasal and oral passageways and on the lungs. Most surface level dust is removed by mucociliary clearance, whereby a mucus layer carries the silica into the throat, where it is then swallowed. Silica deposited in the deepest parts of the lungs is slowly removed by macrophages, which engulf the silica and move it to the mucus layer and then to the throat, where it is swallowed. Because this occurs in the deepest part of the lungs, the process is much slower and some of the silica dissolves in the lung fluid. When silica is partially dissolved in the lung fluid, it can be removed from the lung tissue by the macrophages. Exposure can also occur orally through drinking or eating silica dust. All ingested silica (orally, through macrophages or mucociliary clearance) is eventually excreted in the feces.

Studies of Health Effects Associated with Silica Exposure

Results from studies of humans and animals support a causal relationship between inhalation exposure to silica and increased risk of developing several health effects:

- Silicosis (Hessel et al., 1998; Hnizdo and Sluis-Cremer, 1993): Epidemiological studies of workers exposed to silica dust have shown a connection between inhalation of silica dust and development of silicosis. Silicosis is a progressive lung disease that can develop long after workers discontinue exposure to silica dust.
- Pulmonary tuberculosis (TB) (Cowie, 1994; Kleinschmidt and Churchyard, 1997): Cowie (1994) found that black South African gold miners with chronic silicosis had three times the incidence of TB than did non-silica-exposed workers of similar age and race. Another study of South African mine workers found that incidence of TB was highest in workers with silicosis, older workers, and those who had high exposure to dust (Kleinschmidt and Churchyard, 1997).
- Lung cancer (McDonald, 1995; McLaughlin et al., 1992): Evidence of lung cancer caused by exposure to silica dust has been mixed. Many epidemiologic studies have found an association between occupational exposure to crystalline silica and lung cancer (McDonald, 1995; McLaughlin et al., 1992). These studies indicate that the risk for lung cancer increases with cumulative exposure to respirable silica, duration of exposure, peak intensity of exposure, presence of radiographically defined silicosis, and length of follow-up time from date of silicosis diagnosis.
- Chronic obstructive pulmonary disease, including chronic bronchitis and emphysema: Exposure to respirable silica has also been associated with many other nonmalignant respiratory diseases. Nonmalignant respiratory disease (NMRD) is a catchall category that includes silicosis and other pneumoconiosis, chronic bronchitis, emphysema, asthma, and other respiratory conditions. In a review of the 13 studies of silica-exposed workers, Oxman et al. (1993) concluded that exposure to gold mine dust containing silica may cause chronic obstructive pulmonary disease (COPD) and that smokers are at an increased risk.

Silicosis is the lung disease most commonly associated with exposure to silica. It is a nodular pulmonary fibrosis caused by inhalation of silica particles. There are three types of silicosis: chronic silicosis (exposure to low concentrations of silica for 10 or more years), accelerated silicosis (develops 5–10 years after the first exposure to silica), and acute silicosis (develops shortly after exposure to high concentrations of silica). The development and severity of silicosis depends on the dose of respirable dust to which one is exposed. It also depends upon the particle size, the crystalline or noncrystalline nature of the silica, the duration of exposure, and the varying time period from first exposure to diagnosis (NIOSH, 2002a). Long periods might elapse between exposure to silica and diagnosis of silicosis. Development and progression of the disease may occur after exposure to silica has ceased.

Pulmonary tuberculosis is a severe mycobacterial infection that can complicate silicosis. This condition is caused by the infectious organism *Mycobacterium tuberculosis*. When one is exposed to silica dust, the macrophages in the lungs can be overwhelmed by the dust and unable to kill the *Mycobacterium* organism. Other similar infectious diseases are caused by the nontuberculous mycobacteria: *Mycobacterium kansasii*, *Mycobacterium avium-intracellulare* or *Nocardia asteroids* and *Cryptococcus*.

Silica has been deemed a potential human carcinogen based on an increased risk of lung cancer among workers exposed to silica (IARC, 1997; NIOSH, 2002a). Studies regarding its carcinogenicity, however, remain controversial.

COPD refers to an irreversible airflow limitation. Common symptoms of COPD include shortness of breath, coughing, wheezing, and recurrent respiratory infections. Patients diagnosed with COPD usually exhibit some combination of chronic bronchitis, emphysema, asthma, and peripheral airways disease.

In addition to the diseases listed above, exposure to silica can also affect outcomes on pulmonary function tests, which measure lung function, including lung volume, airflow, and blood gas exchange. Decreased pulmonary function has been associated with increased mortality from diseases such as COPD.

Emphysema is caused by destruction of the lung parenchyma and results in abnormal enlargement of the air spaces distal to the terminal bronchiole with destructive changes in the alveolar walls.

Autoimmune diseases associated with inhalation of silica include scleroderma, systemic lupus erythematosus (lupus), rheumatoid arthritis, autoimmune hemolytic anemia, and dermatomyositis or dermatopolymyositis. Studies have also shown association with chronic renal disease, ataxic sensory neuropathy, chronic thyroiditis, hyperthyroidism, monoclonal gammopathy, polyarteritis nodosa, and end-stage renal disease morbidity (NIOSH, 2002a). The connection between autoimmune diseases and chronic renal failure following exposure to silica is unclear. One theory is that the immune system is activated by fibrogenic proteins and growth factors generated by the macrophages produced to extricate the respirable silica particles. Others theorize a direct toxic effect of silica or an immunologic injury by immune complex formation (NIOSH, 2002a).

Other possible health effects from exposure to silica include extrapulmonary deposits of silica, hepatic changes, hepatic or hepatosplenic silicosis, hepatocellular carcinoma, cutaneous silica granuloma, cor pulmonale, pulmonary arterial hypertension, pulmonary alveolar proteinosis, development of nonfilarial tropical elephantiasis, and abrasion-related deterioration of dental health (NIOSH, 2002a).

Occupational Standards and Recommendations

Workplace standards have been set by ACGIH, OSHA, and NIOSH. ACGIH has set a threshold limit for air concentrations where respirable silica does not exceed a time-weighted average concentration of 0.05 mg/m^3 assuming exposures of eight hours per day for a 40-hour workweek (ACGIH TLV-TWA) (Table 4.6). Standards set by OSHA vary by type of silica. OSHA requires that air concentrations of quartz in occupational settings not exceed a time-weighted average concentration of 250 mppcf ÷ ($\%SiO_2 + 2$), assuming exposures of eight hours per day for a 40-hour workweek (OSHA PEL-TWA), and not exceed 30 mg/m^3 ÷ ($\%SiO_2 + 2$) for any 30-minute period during a workday (OSHA PEL-STEL). These exposure limits are halved for crystobalite and tridymite. NIOSH recommends air concentrations of silica not exceed a time-weighted average concentration of 0.05 mg/m^3, assuming exposures of up to a 10-hour workday during a 40-hour workweek (NIOSH REL-TWA). These limits are based on the avoidance of silicosis, lung fibrosis, and cancer (ACGIH, 2002). Silica has been classified as a suspected or possible human carcinogen by ACGIH and NIOSH. IARC, MAK, and NTP have classified silica as a known human carcinogen (Table 4.7). These classifications are based on human data from occupational studies linking silica to lung cancer (ACGIH, 2002).

Table 4.6 Regulatory Standards and Recommendations for Occupational Exposure to Three Forms of Silica in Air

Regulatory Measure	Quartz	Cristobalite	Tridymite
ACGIH TLV-TWA	0.05 mg/m^3 **R**[a]	0.05 mg/m^3 **R**[a]	0.05 mg/m^3 **R**[a]
ACGIH TLV-STEL	No value listed	No value listed	No value listed
OSHA PEL-TWA	See formula below[b,c]	½ the value calculated from the respirable dust formulae for quartz[b]	½ the value calculated from the respirable dust formulae for quartz[b]
OSHA PEL-STEL	See formula below[d]	See above	See above
NIOSH REL-TWA	0.05 mg/m^3	0.05 mg/m^3 [e]	0.05 mg/m^3
NIOSH REL-STEL	No value listed	No value listed	No value listed
NIOSH IDLH	50 mg/m^3	25 mg/m^3	25 mg/m^3

SOURCE: ACGIH, 2002.
NOTE: See Willis et al. (forthcoming) for definitions of exposure limits.

[a] R = Measured as a respirable fraction of the aerosol

[b] Formula for OSHA PEL-TWA (respirable dust) = $\frac{250 \text{ mppcf}}{\% SiO_2 + 2}$

[c] Formula for OSHA PEL-TWA (total dust) = $\frac{30 \text{ mg/m}^3}{\% SiO_2 + 2}$

[d] Formula for OSHA PEL-STEL (respirable dust) = $\frac{30 \text{ mg/m}^3}{\% SiO_2 + 2}$ =

[e] Respirable dust

mppcf = million particles per cubic foot

Table 4.7 Carcinogenicity Classifications for Three Forms of Silica

Agency	Cristobalite	Quartz	Tridymite
ACGIH	No value listed	A2 "Suspected Human Carcinogen"	No value listed
OSHA	No value listed	No value listed	No value listed
NIOSH	Ca "Potential occupational carcinogen, with no further categorization"	Ca "Potential occupational carcinogen, with no further categorization"	Ca "Potential occupational carcinogen, with no further categorization"
EPA	Substance not listed	Substance not listed	Substance not listed
IARC	1 "Carcinogenic to Humans"	1 "Carcinogenic to Humans"	1 "Carcinogenic to Humans"
MAK	1 "Substances that cause cancer in man and can be assumed to make a significant contribution to cancer risk"	1 "Substances that cause cancer in man and can be assumed to make a significant contribution to cancer risk"	1 "Substances that cause cancer in man and can be assumed to make a significant contribution to cancer risk"
NTP	K "Known To Be A Human Carcinogen"	K "Known To Be A Human Carcinogen"	K "Known To Be A Human Carcinogen"

Synthesis

Studies of workers exposed to silica dust have established that inhalation exposure has led to increased risk of several diseases, including silicosis, pulmonary tuberculosis, chronic bronchitis, COPD, lung cancer, and autoimmune diseases. Data from human and animal studies have shown that silica might have carcinogenic potential. Risk factors other than silica, notably cigarette smoking, increase the risk of lung cancer, emphysema, and COPD among those exposed to silica. Table 4.8 summarizes the health effects that have been observed following inhalation, oral, and dermal exposure to silica.

The NIOSH REL-TWA for air concentration of respirable silica in an occupational setting is 0.05 mg/m^3, assuming exposures of up to a 10-hour workday during a 40-hour workweek. These exposure limits are based on the avoidance of silicosis, lung fibrosis, and lung cancer (ACGIH, 2002). Silica has been classified as a possible or known human carcinogen by several agencies.

Table 4.8 Reported Human Health Effects of Silica Exposure by Different Routes

	Route of Exposure		
Health Effect	**Inhalation**	**Oral**	**Dermal**
Cancer	Lung[a]	No known effect	No known effect
Respiratory	Silicosis[b]	No known effect	No known effect
	Chronic obstructive pulmonary disease[c]		
	Chronic bronchitis		
	Abnormalities in pulmonary function tests		
	Emphysema		
	Nonmalignant respiratory disease		
Cardiovascular	No known effect	No known effect	No known effect
Gastrointestinal	No known effect	No known effect	No known effect
Immunological	Autoimmune diseases (including Scleroderma, lupus, arthritis, anemia)	No known effect	No known effect
Neurological	No known effect	No known effect	No known effect
Reproductive	No known effect	No known effect	No known effect
Developmental	No known effect	No known effect	No known effect
Other	Pulmonary tuberculosis	None	None
	Chronic renal disease		

NOTE: This table presents a qualitative survey of reported human health effects associated with silica exposure. The causal relationship between silica and health effects is established more for some effects than for others; this table is intended to catalog possible health effects only.

[a] The relationship between lung cancer and silica is still under debate. "Further research is needed to determine the exposure-response relationship between lung cancer and nonsmokers and occupational silica dust exposure. . ." (NIOSH, 2002a).

[b] Silicosis can occur after acute, intermediate, and chronic exposure.

[c] Listed as an effect of chronic exposure in NIOSH (2002a).

Synthetic Vitreous Fibers

Synthetic vitreous fibers can be found in residential and industrial insulation (ATSDR, 2002). They are used to insulate heat and sound as well as to reinforce other materials. Most exposure occurs to workers who produce or use products that contain synthetic vitreous fibers. When materials containing the fibers are disturbed, the fibers are released into the air, where they can be inhaled. Those who produce, install, demolish, or maintain materials containing synthetic vitreous fibers are at risk for exposure.

Synthetic vitreous fibers such as fiberglass may provide a large source of particulate matter in cases of full or extensive building collapse. Studies at the WTC collapse indicate that fibers, including mineral wool, fiberglass, asbestos, wood, paper, and cotton, comprised the majority of the mass of dust created by the collapse of the two towers (Lioy et al., 2002).

The term synthetic vitreous fibers refers to a group of fibrous, inorganic materials that contain aluminum or calcium silicates, and are made from rock, clay, slag, or glass (ATSDR, 2002). They are categorized in three groups: (1) glass fibers, including glass wool and continuous (textile) glass; (2) mineral wool, which contains stone wool and slag wool; and (3) refractory ceramic fibers. Special-purpose glass fibers are also used in high-technology industries, and their properties are adjusted to the specific purpose of the fiber. Glass wool, rock wool, and slag wool account for 80 percent of the synthetic vitreous fibers produced in the United States, while refractory ceramic fibers make up about 2 percent. Synthetic vitreous fibers have an amorphous molecular structure, unlike other natural mineral fibers such as asbestos. Found in the air, water, and soil, they are fairly resistant to environmental forces. They can be moved great distances by the wind and water currents, but they do not evaporate, dissolve, break down, or change over time.

Synthetic vitreous fibers are used primarily for insulation and reinforcement of other materials, often substituting for the use of asbestos. Glass fibers and mineral fibers have similar properties and provide high electrical, heat, water, and chemical resistance (ATSDR, 2002). Glass wool, rock wool, and slag wool are used for insulation, while continuous filament fibers are used primarily to reinforce plastics, cement, papers, and roofing materials. Refractory ceramic fibers are highly heat resistant and are used for very high temperature insulation (e.g., furnaces).

The production of synthetic vitreous fibers has occurred in the United States at significant levels since World War I. Currently, the United States produces more than 3 million tons of synthetic vitreous fibers annually, the majority of them being glass fibers (ATSDR, 2002). In 1985, there were 58 facilities in the United States producing synthetic vitreous fibers.

Routes of Exposure

The primary route of exposure for health effects of synthetic vitreous fibers is through inhalation, but exposure also occurs through the skin and eyes as well as by oral consumption (ATSDR, 2002). When synthetic vitreous fibers are inhaled, some fibers are deposited in the nasal and oral passageways and on the lungs. Most surface level fibers are removed by mucociliary clearance, whereby a mucus layer carries the fibers into the throat, where they are then swallowed. Fibers deposited in the deepest parts of the lungs are slowly removed by macrophages, which engulf the fibers and move them to the mucus layer and then to the throat, where they are swallowed. Because these fibers are in the deepest part of the lungs, the process is much slower and some of the fibers partially dissolve in the lung fluid. When fibers are partially dissolved in the lung fluid, they can be broken down and carried away by the macrophages. Exposure can also occur orally through drinking or eating fibers. All ingested fibers (orally, through macrophages or mucociliary clearance) are eventually excreted in the feces. If exposure occurs through the skin or eyes, it is unlikely that synthetic vitreous fibers will enter the body (ATSDR, 2002). However, adverse reactions may occur.

Studies of Health Effects Associated with Synthetic Vitreous Fiber Exposure

Results from studies of humans and animals have shown various health effects following exposure to synthetic vitreous fibers. Reversible acute irritation of the skin, eyes, and upper respiratory tract are common reactions following direct dermal and inhalation exposure to various synthetic vitreous fibers in construction and manufacturing (Albin et al., 1998; Bjornberg, 1985; Clausen et al., 1993; Kiec-Swierczynska and Wojtczak, 2000; Petersen and Sabroe, 1991). Respiratory symptoms (including decreased pulmonary function, coughing, and bronchitis) have been consistently reported following chronic exposure of workers to continuous filament glass fibers, glass wool, and rock and slag wool (Albin et al., 1998; Clausen et al., 1993) and refractory ceramic fibers (Lemasters et al., 1998; Trethowan et al., 1995). Epidemiologic studies of workers who manufacture synthetic vitreous fibers have not found consistent evidence of increased mortality from respiratory disease, lung cancer, or mesothelioma associated with long-term exposure to synthetic vitreous fibers (Marsh et al., 2001; Shannon et al., 1990). They did find pleural changes on workers who make refractory ceramic fibers (Cowie et al., 2001; Lockey et al., 1996). Most of the health effects associated with exposure to synthetic vitreous fibers have been observed in animal studies with high-level inhalation exposure. In studies of hamsters and rats, refractory ceramic fibers have induced malignant lung tumors and mesotheliomas following inhalation exposure (Davis, 1986; McConnell et al., 1995).

The health hazards associated with exposure to synthetic vitreous fibers have also been associated with the hazards of occupational exposure to asbestos. However, the studies have shown that synthetic vitreous fibers are far less potent than asbestos. To summarize, synthetic vitreous fibers have been associated with the following health effects:

- "fiberglass itch" and irritation of the skin and eyes
- irritation of the upper respiratory tract
- pleural plaques: refractory ceramic fibers only
- pulmonary inflammation
- bronchiolization
- pulmonary fibrosis: animal studies only
- lung cancer: animal studies only
- mesothelioma: animal studies only.

The severity of the health effects of synthetic vitreous fibers is associated with the level of exposure. Those who are not exposed to high levels of fibers may experience mild effects. In addition, health effects vary by type of synthetic vitreous fiber. Some types, called durable or biopersistent synthetic vitreous fibers, stay in the lung for longer periods than others, thus creating more long-lasting effects. Generally, the commonly used glass wools, stone wools, and slag wools are less durable than refractory ceramic fibers.

A minor health effect associated with synthetic vitreous fibers is "fiberglass itch," an irritation of the skin and eyes resulting from contact with synthetic vitreous fibers. Other mild effects include the irritation of

the upper respiratory tract and lungs, causing sore throat, congestion, and cough. These effects usually go away with time and do not lead to serious health effects because of the low exposure to synthetic vitreous fibers.

Pleural plaques are "generally oval areas of acellular collagen deposits, usually located on the inferior and posterior surfaces of the pleura" (ATSDR, 2002). The clinical significance of pleural abnormalities is not generally agreed, with some considering them to be benign and others believing that they lead to decreased pulmonary capacity or increased risk of lung cancer. In studies on the health effects of pleural plaques on workers who make synthetic vitreous fibers, the pleural plaques did not seem to harm the workers.

Pulmonary inflammation occurs when synthetic vitreous fibers are continuously deposited in the deepest part of the lung in high numbers. Macrophages attempt to engulf the fibers and move them out of the lungs, but because there are so many, they get clumped together. If this continues, it can result in bronchiolization, which is a thickening of the cells lining the lung. Bronchiolization can limit the oxygen intake to the body. Although these health effects are possible, the conditions will disappear when exposure stops.

Repeatedly breathing high levels of synthetic vitreous fibers may cause pulmonary fibrosis. This occurs when scar tissue slowly builds up in the lungs and in the membrane that surrounds the lungs, rendering the lungs unable to expand and contract as usual. This can cause difficulty in breathing. Pulmonary fibrosis is caused primarily by durable synthetic vitreous fibers.

Exposure to durable synthetic vitreous fibers has been associated with increased risk of cancer of the lung and mesotheliomas in animals. Malignant mesotheliomas are malignant tumors of the membranes that line the chest (pleural mesothelioma) and abdominal cavities (peritoneal mesothelioma) (ATSDR, 2002). In the cases of pulmonary fibrosis, lung cancer, and mesotheliomas, studies have shown that development of these conditions following exposure to synthetic vitreous fibers depends on exposure dose and duration, as well as dimension and durability of the fibers.

Occupational Standards and Recommendations

OSHA has not set workplace standards for air concentrations and exposure of synthetic vitreous fibers in occupational settings. ACGIH has set a threshold limit for air concentrations where respirable synthetic vitreous fibers, except refractory ceramic fibers, do not exceed a time-weighted average concentration of 1 f/cc, assuming exposures of eight hours per day for a 40-hour workweek (ACGIH TLV-TWA), and do not exceed 1 f/cc for any 15-minute period during a workday (ACGIH TLV-STEL) (Table 4.9). For refractory ceramic fibers, the ACGIH TLV-TWA and ACGIH TLV-STEL are both 0.2 f/cc. NIOSH recommends air concentrations of continuous filament glass fibers and glass wool fibers not exceed a time-weighted average concentration of 5 mg/m^3, assuming exposures of up to a 10-hour workday during a 40-hour workweek (NIOSH REL-TWA). These limits are based on the avoidance of irritation (continuous filament glass fibers); lung effects and irritation (glass wool, rock wool, slag wool, and special-purpose glass fibers), and lung fibrosis and cancer (refractory ceramic fibers) (ACGIH, 2002). ACGIH has classified glass wool, rock wool, slag wool and special-purpose glass fibers as confirmed animal carcinogens but is

unable to determine the relevance to humans (Table 4.10). The organization has classified refractory ceramic fibers as a suspected human carcinogen. IARC and MAK have classified glass wool, rock wool, slag wool, and refractory ceramic fibers as possible human carcinogens. NTP notes only glass wool and refractory ceramic fibers as reasonably anticipated to be human carcinogens.

Table 4.9 Regulatory Standards and Recommendations for Occupational Exposure to Synthetic Vitreous Fibers in Air

Regulatory Measure	Continuous Filament Glass Fibers	Glass Wool Fibers	Rock Wool Fibers	Slag Wool Fibers	Special Purpose Glass Fibers	Refractory Ceramic Fibers
ACGIH TLV-TWA	5 mg/m^3 I[a]; 1 f/cc[(F) b]	1 f/cc[(F) b]	1 f/cc[(F)]	1 f/cc[(F)]	1 f/cc[(F)]	0.2 f/cc
ACGIH TLV-STEL	1 f/cc[(F)]	1 f/cc[(F)]	1 f/cc[(F)]	1 f/cc[(F)]	1 f/cc[(F)]	0.2 f/cc[(F)]
OSHA PEL-TWA	No value listed	No value listed	No value listed	No value listed	No value listed	No value listed
OSHA PEL-STEL	No value listed	No value listed	No value listed	No value listed	No value listed	No value listed
NIOSH REL-TWA	5 mg/m^3 [c]	5 mg/m^3 [c]	No value listed	No value listed	No value listed	No value listed
NIOSH REL-STEL	No value listed	No value listed	No value listed	No value listed	No value listed	No value listed
NIOSH IDLH	Substance not listed	Substance not listed	Substance not listed	Substance not listed	Substance not listed	Substance not listed

SOURCE: ACGIH, 2002.

NOTE: See Willis et al. (forthcoming) for definitions of exposure limits.

[a] Measured as inhalable fraction of the aerosol.

[b] (F) = Respirable fibers: length >5 µm; aspect ratio ≥3:1, as determined by the membrane filter method at 400–450x magnification (4-mm objective), using phase-contrast illumination.

[c] Total fibrous glass, or 3 f/cc TWA (fib ≤ 3.5 µm length).

Synthesis

Epidemiological studies on human exposure to synthetic vitreous fibers have shown an increased risk of respiratory irritation, pulmonary inflammation, and fibrosis. Studies of animals have established that inhalation exposure to synthetic vitreous fibers has led to increased risk of several diseases, including malignant mesothelioma, lung cancer, and pulmonary fibrosis. No studies have been conducted on the oral or dermal exposure to synthetic vitreous fibers, but irritation of the skin and eyes following exposure to all types of synthetic vitreous fibers is well documented. Table 4.11 summarizes the health effects that have been observed following inhalation, oral, and dermal exposure to synthetic vitreous fibers.

The ACGIH TLV-TWA for air concentration of all types of synthetic vitreous fibers except refractory ceramic fibers in an occupational setting is 1 f/cc and the ACGIH TLV-STEL is 1 f/cc for any 15-minute period during a workday. These exposure limits are protective of irritation and lung effects (ACGIH, 2002). The ACGIH TLV-TWA for air concentration of refractory ceramic fibers in an occupational setting is 0.2 f/cc, and the ACGIH TLV-STEL is 0.2 f/cc for any 15-minute period during a workday. These exposure limits are protective of effects on the lung (fibrosis and cancer) (ACGIH, 2002). All types of synthetic vitreous fibers except continuous glass filament fibers have been classified as possible carcinogens by several agencies.

Table 4.10 Carcinogenicity Classifications for Synthetic Vitreous Fibers

Agency	Continuous Filament Glass Fibers	Glass Wool Fibers	Rock Wool Fibers
ACGIH	A4 "Not Classifiable as a Human Carcinogen"	A3 "Confirmed Animal Carcinogen with Unknown Relevance to Humans"	A3 "Confirmed Animal Carcinogen with Unknown Relevance to Humans"
OSHA	No value listed	No value listed	No value listed
NIOSH	No value listed	No value listed	No value listed
EPA	No value listed	No value listed	No value listed
IARC	3 "Unclassifiable as to the Carcinogenicity in Humans"[a]	2B "Possibly Carcinogenic to Humans"	2B "Possibly Carcinogenic to Humans"
MAK	No value listed	2 "Substances that are considered to be carcinogenic for man because sufficient data from long-term animal studies or limited evidence from animal studies substantiated by evidence from epidemiological studies indicate that they can make a significant contribution to cancer risk"	2 "Substances that are considered to be carcinogenic for man because sufficient data from long-term animal studies or limited evidence from animal studies substantiated by evidence from epidemiological studies indicate that they can make a significant contribution to cancer risk"
NTP	No value listed	R "Reasonably Anticipated To Be A Human Carcinogen"	No value listed

[a] Glass filament.

Agency	Slag Wool Fibers	Special-Purpose Glass Fibers	Refractory Ceramic Fibers
ACGIH	A3 "Confirmed Animal Carcinogen with Unknown Relevance to Humans"	A3 "Confirmed Animal Carcinogen with Unknown Relevance to Humans"	A2 "Suspected Human Carcinogen"
OSHA	No value listed	No value listed	No value listed
NIOSH	No value listed	No value listed	No value listed
EPA	No value listed	No value listed	B2 "Probably Human Carcinogen, Sufficient evidence from animal studies; inadequate evidence or no data from epidemiologic studies"
IARC	2B "Possibly Carcinogenic to Humans"	No value listed	2B "Possibly Carcinogenic to Humans"
MAK	3B "Substances for which in vitro tests or animal studies have yielded evidence of carcinogenic effects that is not sufficient for classification of the substance in one of the other categories. Further studies are required before a final classification can be made"	No value listed	2 "Substances that are considered to be carcinogenic for man because sufficient data from long-term animal studies or limited evidence from animal studies substantiated by evidence from epidemiological studies indicate that they can make a significant contribution to cancer risk"
NTP	No value listed	No value listed	R "Reasonably Anticipated To Be A Human Carcinogen"

Table 4.11 Reported Human Health Effects of Synthetic Vitreous Fiber Exposure, by Different Routes

	Route of Exposure		
Health Effect	**Inhalation**	**Oral**	**Dermal**
Cancer	Mesothelioma [C, R, G] Lung [R, E, I, C]	No known effect	No known effect
Respiratory	Pleural changes [C] Decreased pulmonary function [C] Upper airway abnormalities [C]	No known effect	No known effect
Cardiovascular	Mortality from ischemic heart disease [F]	No known effect	No known effect
Gastrointestinal	No known effect	No known effect	No known effect
Immunological	No known effect	No known effect	No known effect
Neurological	No known effect	No known effect	No known effect
Reproductive	No known effect	No known effect	No known effect
Developmental	No known effect	No known effect	No known effect
Other	None	None	Strong itching Contact dermatitis Acute eye irritation

NOTE: This table presents a qualitative survey of reported human health effects associated with synthetic vitreous fiber exposure based on the Toxicological Profile for Synthetic Vitreous Fibers (ATSDR, 2002). The causal relationship between synthetic vitreous fibers and health effects is established more for some effects than for others; this table is intended to catalog possible health effects only.

[I] Listed as an effect of intermediate exposure (15–364 days) in ATSDR (2002a).

[C] Listed as an effect of chronic exposure (365 days or more) in ATSDR (2002a).

[R] Listed as an effect of exposure to refractory ceramic fibers in ATSDR (2002a).

[E] Listed as an effect of exposure to 104E-glass in ATSDR (2002a).

[G] Listed as an effect of exposure to glass wool, rock wool, and slag wool and continuous filament glass fibers in ATSDR (2002a).

[F] Listed as an effect of exposure to continuous filament glass fibers in ATSDR (2002a).

Arsenic

Arsenic is a naturally occurring element found in the soil. It occurs in two basic classes of compounds: inorganic and organic (ATSDR, 2000a). Inorganic arsenic is generally found as arsenic combined with oxygen, chlorine, or sulfur. Organic arsenic is arsenic combined with carbon and hydrogen. In general, inorganic and organic arsenic compounds have no smell or taste. Most toxic effects come from exposure to inorganic arsenic. Inorganic arsenic has been used as a poison for many centuries (ATSDR, 2000a).

Arsenic is not produced in the United States but is an imported product. Most arsenic in the United States (90 percent) is used as a wood preservative (called pressure-treating). Chromated copper arsenate is added to wood to make it resistant to decay. A further use of arsenic is as an additive to other metals, primarily those used in lead-acid batteries (commonly found in automobiles). Of significance to emergency responders at a building collapse, arsenic is also used in light-emitting diodes and semiconductors (ATSDR, 2000a). In this case, the specific compound is Gallium arsenide.

Routes of Exposure

Many different compounds containing arsenic exist, which can complicate examinations of toxic effects. However, the ATSDR *Toxicological Profile* (2000a) does not make distinctions between different arsenic compounds because (1) the potency differences are small, (2) arsenic may be converted to different forms during or after exposure, and (3) for human exposure, the type of arsenic is often not known.

Based on human studies, health effects can result from both inhalation and ingestion of arsenic. Atmospheric sources of arsenic include volcanic eruptions, smelting of copper and lead, and coal-fired power plants. Human activities worldwide — mining and smelting of ores for metals and incineration of coal and waste products — release small amounts of arsenic into the air from these sources. Arsenic is released into the environment as very small particles that can stay airborne for days. Inhalation exposure to low levels of arsenic might occur among workers in metal refineries and smelters and in the manufacturing of lead-acid vehicle batteries, semiconductors, and light-emitting diodes (ATSDR, 2000a). The general population might be exposed to arsenic in air from hazardous waste sites or manufacturing plants.

Humans are also exposed to arsenic through ingestion of water, soil, and food containing arsenic. Arsenic (inorganic and organic) can dissolve in water. As such, fish and shellfish may ingest the substance and produce arsenobetaine and arsenochlorine (called "fish arsenic"). These substances have been found to be nontoxic (Brown et al., 1990).

Studies of Health Effects Associated with Arsenic Exposure

Results from studies of humans exposed to arsenic support an association between oral exposure to arsenic and numerous health effects (ATSDR, 2000a). Ingestion of different levels of arsenic might result in

- death, following serious gastrointestinal symptoms and damage to several organ systems (Quatrehomme et al., 1992)
- gastrointestinal symptoms, including nausea, diarrhea, and vomiting following ingestion of higher doses (Armstrong et al., 1984; Kingston et al., 1993) and lower doses (Cebrian et al., 1988)
- skin changes, including hyperkeratosis, warts, corns, and hyper- and hypopigmentation (Bickley and Papa, 1989; Cebrian et al., 1988)
- skin cancer (both squamous cell and basal cell carcinomas) (Bickley and Papa, 1989; Cebrian et al., 1988).

Studies of workers in smelters and chemical plants have concluded that chronic inhalation exposure to arsenic dust in air results in a higher risk of developing

- irritation of the nose and throat (Morton and Caron, 1989) and perforation of the nasal septum (Sandstrom et al., 1989)
- lung cancer (Enterline and Marsh, 1982; Welch et al., 1982).

Inhalation Exposure

Many of the data for inhalation exposure come from studies of workers in smelters and chemical plants and relate to exposure to inorganic arsenic trioxide (As_2O_3) dust. These studies have some external validity because arsenic trioxide is the most common arsenic compound in the air. Inhalation exposure is measured as milligrams of arsenic per cubic meter of air (mg As/m^3).

Several studies have identified gastrointestinal health effects associated with inhalation exposure to arsenic. These health effects include nausea, vomiting, and diarrhea (Beckett et al., 1986). However, in general, gastrointestinal effects of inhaled arsenic have not been identified — or at least are not typical in the studies listed in the ADSTR report.

Inhalation of low levels of arsenic is likely to cause a sore throat (Morton and Caron, 1989). Arsenic dusts are irritating to the mucous membranes of the respiratory tract. Higher doses of airborne arsenic (about 1 mg/m^3) can cause skin conditions mentioned below and perforation of the nasal septum. However, pulmonary function does not seem to be affected (ATSDR, 2000a).

Longer inhalation exposure to arsenic has been linked to hematological and nerve problems. Arsenic causes a decrease in both red and white blood cell production (Morton and Caron, 1989). This can lead to blood-vessel damage and an abnormal heart rhythm. Arsenic can also cause nerve damage. Typical symptoms include tingling and numbness ("pins and needles") in feet and hands (Morton and Caron, 1989). Smelter workers have been shown to have an increased incidence of Raynaud's phenomenon, which manifests itself as spasms of the digital arteries (i.e., those in the fingers) and finger numbness (Morton and Caron, 1989).

Inhaled arsenic has been associated with an increased risk of lung cancer in humans (Enterline and Marsh, 1982; Jarup et al., 1989; Lee-Feldstein, 1989; Welch et al., 1982). This association occurs with multiple types of lung cancer, indicating that arsenic is a nonspecific lung cancer agent.

Oral Exposure

A large number of studies describe the toxic effects of ingested arsenic exposures. Many of these studies come from accidental, suicidal, homicidal, or medical exposure. Exposure is measured as milligrams of arsenic per kilogram body weight per day (mg As/Kg/day).

Ingested arsenic, both organic and inorganic, is excreted from the body in urine. In fact, most of the small amounts of arsenic to which humans are naturally exposed are eliminated within several days. Some evidence (from animal studies) would even suggest that small amounts of arsenic could be beneficial to health, although no such evidence exists for human exposure (ATSDR, 2000a).

Because low doses of arsenic are not problematic, ATSDR (2000a) presents estimates of levels of arsenic that present minimal risk to humans (termed Minimal Risk Levels). These are defined as "an estimate of daily human exposure to a substance that is likely to be without an appreciable risk of adverse effects (noncarcinogenic) over a specified duration of exposure" (ATSDR, 2000a). This is given as 0.0008 mg As/kg/day.

Ingestion of small amounts of arsenic (300–30,000 ppb in food or water) will cause intestinal problems, including nausea, vomiting, and diarrhea (ATSDR, 2000a). After a single exposure, these symptoms are usually of short duration, and decline after exposure ceases.

Oral arsenic doses of 8 mg/As/Kg cause respiratory problems in humans, including bronchitis and pulmonary edema (Civantos et al., 1995). Serious effects occur on the cardiovascular system. After exposure to 93 mg of arsenic, cardiac arrhythmias occur (Quatrehomme et al., 1992). At levels as low as 0.1-50 μg/L in drinking water, loss of circulation to the extremities occurs, leading to hand and foot necrosis and gangrene (Chiou et al., 1997) — called Blackfoot disease. Anemia is common following acute, intermediate, and chronic oral exposure to arsenic (Chiou et al., 1997). This can occur at doses as low as 0.05 mg As/Kg/day.

Another common symptom after oral exposure to arsenic is dermal effects. Chronic doses of about 0.01 mg As/Kg/day can cause corns and hyperpigmentation (mainly on the face, neck, and back) (Bickley and Papa, 1989; Cebrian et al., 1988). Long-term arsenic exposure also causes the skin to darken and produce "corns." These in turn can develop into skin cancer.

A large number of studies have shown an association between ingestion of arsenic and skin cancer. For example, Cebrian et al. (1988) identified a cancer effect level with exposure to 0.022 mg As/Kg/day (continuous exposure for an unknown period). In most cases, chronic exposure is necessary, but a few instances are recorded of skin cancer development after less than one year of exposure — although no exposure levels are given (ATSDR, 2000a). Recent evidence would also suggest that an association with prostate cancer might also exist (Lewis et al., 1999).

The lethal dose to arsenic is between 22 and 121 mg As/Kg (Civantos et al., 1995). However, death from lower doses over a more prolonged period can also occur. For example, water containing 128 ppm of arsenic can cause death after one week (Armstrong et al., 1984).

Dermal Exposure

Dermal exposure to arsenic has not been extensively studied (ATSDR, 2000a). Although, the results of the few studies that exist are consistent with the fact that absorption through the skin is limited — thus health effects are limited.

With high levels of arsenic exposure (1.034 mg/m^3), dermatitis has been reported (Lagerkvist et al., 1986). The effects of dermal exposure are consistent, causing few health problems (ATSDR, 2000a).

Occupational Standards and Recommendations

Workplace standards set by OSHA require that air concentrations of arsenic in occupational settings not exceed a time-weighted average concentration of 0.01 mg/m^3, assuming exposures of eight hours per day for a 40-hour workweek (OSHA PEL-TWA) (Table 4.12). NIOSH recommends air concentrations of arsenic not exceed 0.002 mg/m^3 for any 15-minute period during a workday (NIOSH REL-STEL) (Table 4.12). These limits are based on the avoidance of lung cancer and skin cancer and other respiratory effects

(ACGIH, 2002). Arsenic has been classified as a confirmed human carcinogen by several agencies (Table 4.13), including EPA (Group A), IARC (Group 1), MAK (Group 1), and NTP (Group K). These classifications are based on data from human studies linking arsenic to lung and skin cancer.

Synthesis

Studies of arsenic workers have established that inhalation exposure has led to increased risk of several health effects, including lung cancer, irritation of the nose and throat, and perforation of the nasal septum. Ingestion of high doses of arsenic can lead to death with failure of all organ systems and severe gastrointestinal symptoms. Chronic exposure to lower doses of arsenic increases the risk of skin changes and skin cancer. Table 4.14 summarizes the health effects that have been observed following inhalation, oral, and dermal exposure to arsenic.

The OSHA PEL-TWA for air concentration of arsenic in an occupational setting is 0.01 mg/m^3, and the NIOSH REL-STEL is 0.002 mg/m^3 for any 15-minute period during a workday. These exposure limits are based on the avoidance of cancer (ACGIH, 2002). Arsenic has been classified as a known human carcinogen by several agencies.

Table 4.12 Regulatory Standards and Recommendations for Occupational Exposure to Arsenic (and Inorganic Compounds as Arsenic) in Air

Regulatory Measure	Value
ACGIH TLV-TWA	0.01 mg/m^3
ACGIH TLV-STEL	No value listed
OSHA PEL-TWA	0.01 mg/m^3
OSHA PEL-STEL	No value listed
NIOSH REL-TWA	No value listed
NIOSH REL-STEL	C 0.002 mg/m^3 (15-min)
NIOSH IDLH	5 mg As/m^3

SOURCE: ACGIH, 2002.
NOTE: See Willis et al. (forthcoming) for definitions of exposure limits.
C = ceiling concentration that must not be exceeded during any part of the workday.

Table 4.13 Carcinogenicity Classifications for Arsenic (and Inorganic Compounds as Arsenic)

Agency		Classification
ACGIH	A1	"Confirmed human carcinogen"
OSHA	Ca	"Carcinogen defined with no further categorization"
NIOSH	Ca	"Potential occupational carcinogen, with no further categorization"[a]
EPA	A	"Human carcinogen"
IARC	1	"Carcinogenic to humans"
MAK	1	"Substances that cause cancer in man and can be assumed to make a significant contribution to cancer risk"
NTP	K	"Known to be a human carcinogen"[a]

[a] Inorganic compounds.

Table 4.14 Reported Human Health Effects of Arsenic Exposure by Different Routes

	Route of Exposure		
Health Effect	**Inhalation**	**Oral (Via Drinking Water and Food)**	**Dermal**
Cancer	Lung[C]	Lung[C] Skin[A,C] Bladder[C] Kidney[C] Urinary tract[C]	No known effect
Respiratory	No known effect	Respiratory distress[A] Lung hemorrhage[A] Edema[A] Sore throat[A] Rhinorrhea[A]	No known effect
Cardiovascular	Vasospasticity[C] Raynaud's phenomenon[C]	Hypotension[A] Ventricular fibrillation[A] Tachycardia[A] Cardiac arrest[A] Pulmonary edema[A] Gangrene of feet[C] Raynaud's phenomenon[C] Ischemic heart disease[C]	No known effect
Gastrointestinal	No known effect	Vomiting[A, C] Diarrhea[A, I, C] Abdominal pain[A] Inflammation of GI tract[A] Ulceration of GI tract[A] Gastrointestinal hemorrhages[C]	No known effect
Immunological	No known effect	Anemia[A, I, C] Leukopenia[A, I]	No known effect
Neurological	Decreased nerve conduction velocity[C]	Encephalopathy[A] Confusion[A, I] Brain edema[A] Weakness[A, I] Paresthesia[A, I] Periperal neuropathy[A] Severe polyneuropathy[A] Lethargy[A] Agitation[A] Paranoia[A] Hypesthesia in legs[A] Disorientation[I] Functional denervation[C] Tingling hands/feet[C]	No known effect

Table 4.14 Reported Human Health Effects of Arsenic Exposure by Different Routes (cont.)

	Route of Exposure		
Health Effect	**Inhalation**	**Oral (Via Drinking Water and Food)**	**Dermal**
Reproductive	No known effect	No known effect	No known effect
Developmental	Increased risk of stillbirth[C]		No known effect
Other	Warts[C]	Severe pulmonary hemorrhage[A]	Contact
	Skin pigmentation[C]	Renal failure[A]	dermatitis[A]
	Dermatitis[C]	Hepatic damage[A]	
	Hyperkeratinization[C]	Anuria[A]	
		Atrophy of distal muscle group[A]	
		Hemolysis[A]	
		Edema of eyelids[A, I]	
		Conjunctivitis[A, C]	
		Central scotoma[A]	
		Neuro-retinitis[A]	
		Scaley rash[I]	
		Diffuse erythematous[I]	
		Skin pigmentation[I]	
		Dermatitis[I]	
		Hyperkeratinization[I,C]	
		Cirrhosis[C]	
		Ascites[C]	
		Leukoderma[C]	

NOTE: This table presents a qualitative survey of reported human health effects associated with arsenic exposure based on the Toxicological Profile for Arsenic (ATSDR, 2000a). The causal relationship between arsenic and health effects is established more for some effects than for others. This table is intended to catalog *possible* health effects only.

[A] Listed as an effect of acute exposure in ATSDR (2000a).

[I] Listed as an effect of intermediate exposure in ATSDR (2000a).

[C] Listed as an effect of chronic exposure in ATSDR (2000a).

Cadmium

Cadmium is a naturally occurring element found in the earth's crust and soil, usually as a mineral combined with other elements: oxygen (cadmium oxide), chlorine (cadmium chloride), or sulfur (cadmium sulfate, cadmium sulfide) (ATSDR, 1999a). Cadmium is especially prevalent in association with zinc ores, and for every ton of zinc produced, 3 kilograms of cadmium are produced.

Cadmium is used in the United States for the electrode component in nickel-cadmium batteries, welding materials, pigments in plastics and glasses, and metal alloys (World Health Organization et al., 1992). Increased demand for cadmium has resulted from its use in batteries — 70 percent of cadmium is used to produce batteries (ATSDR, 1999a). Cadmium is also used as a fungicide (cadmium chloride), stabilizer in polyvinyl chloride, and as protective plating on some steel products. Cadmium is released into the air when fossil fuels (e.g., coal-fired electrical plants) and household waste are burned. Cadmium was likely to be released into the WTC collapse environment from combustion of the building components and contents. Cadmium compounds are commonly found in, or attached to, airborne particulates.

Routes of Exposure

Based on occupational studies and animal studies, health effects can result from both inhalation and ingestion of cadmium. Humans are exposed to cadmium primarily through inhalation. Human activities worldwide — mining, burning fossil fuels, burning household waste — release approximately 4,000–13,000 tons per year (termed anthropogenic emissions). Inhalation exposure to low levels of cadmium might occur among workers in metal refineries and smelters or in plants that manufacture products that contain cadmium, such as batteries, metal plating, or plastics (ATSDR, 1999a). The general population might be exposed to cadmium in air from hazardous waste sites or manufacturing plants.

Humans are also exposed to cadmium through food and cigarettes. Cadmium levels in food range from 2 to 40 ppb, although levels are higher in so-called organ meats (liver and kidney). Each cigarette contains between 1 and 2 µg of cadmium, of which about 40–60 percent can pass into the lungs of the smoker. Exposure to secondhand smoke probably does not increase cadmium levels in the air (ATSDR, 1999a). In general, water is not an important route of exposure to cadmium.

Studies of Health Effects Associated with Cadmium Exposure

Results from studies of workers exposed to cadmium support an association between inhalation exposure to cadmium and several health outcomes (ATSDR, 2001a). Studies of workers have reported that chronic inhalation exposure to cadmium might result in a higher risk of developing

- impaired lung function (Davison et al., 1988; Leduc et al., 1993; Smith et al., 1976), including emphysema (Davison et al., 1988)
- kidney damage (Friberg, 1950; Gompertz et al., 1983; Smith et al., 1976).

In addition, acute inhalation exposures to high levels of cadmium have been reported to result in respiratory failure (Beton et al., 1966).

Ingestion of high levels of cadmium (i.e., oral exposure) might result in gastrointestinal symptoms (Buckler et al., 1986; Wisniewska-Knypl et al., 1971). Chronic oral exposure to cadmium in food might also result in musculoskeletal effects, such as osteoporosis and osteomalacia (Kido et al., 1989).

Inhalation Exposure

Results from studies of humans and animals support an association between acute and chronic inhalation exposure to cadmium and respiratory disease (ATSDR, 1999a). Many of these studies examine workers exposed to cadmium dusts in the smelting, battery, soldering, and pigment production industries (ATSDR, 1999a).

Acute exposure to high levels of cadmium can lead to respiratory failure and death (Beton et al., 1966). The initial symptoms of exposure are mild but progress over the course of a couple of days to respiratory failure. Chronic exposures to lower levels of cadmium can also be fatal. One human case of 14 years of exposure to 6.8 mg Cd/m^3 was reported to be fatal (Friberg, 1950).

Cadmium dust (or fumes) is irritating to the respiratory system. With levels of cadmium at 8.63 mg/m^3, irritation of the throat occurs within 5 hours; after about 10 hours, influenza-like symptoms appear; and after this time, severe pulmonary responses occur (e.g., chest pain, malaise, anorexia) (Beton et al., 1966). A single high dose can cause impaired lung functioning for years (Beton et al., 1966).

After controlling for smoking, little evidence is found for an association between cadmium and an increased risk of lung cancer. There is, however, some evidence that emphysema in smokers may be accelerated after cadmium exposure (Leduc et al., 1993). Studies have also examined prostate cancer and have not found any association with cadmium exposure (ATSDR, 1999a).

Oral Exposure

Ingestion of cadmium has been used as a suicide method. This causes widespread organ destruction, but death is not immediate. With 25 mg Cd/Kg (estimated) ingestion, death takes 33 hours (Wisniewska-Knypl et al., 1971).

In humans, high concentrations of oral cadmium exposure cause nausea, vomiting, salivation, abdominal pain, cramps, and diarrhea (Buckler et al., 1986). Anemia may also occur following chronic cases of cadmium exposure (Buckler et al., 1986).

Dermal Exposure

With high levels of dermal exposure to cadmium (2 percent cadmium chloride), eczema can occur (Wahlberg, 1977). No other health effects from dermal exposure to cadmium have been identified (ATSDR, 1999a).

Occupational Standards and Recommendations

Workplace standards set by OSHA require that air concentrations of cadmium in occupational settings not exceed a time-weighted average concentration of 0.005 mg/m^3, assuming exposures of eight hours per day for a 40-hour workweek (OSHA PEL-TWA) (Table 4.15). These limits are protective of effects on the kidney (ACGIH, 2002). Cadmium has been classified as a known or suspected human carcinogen by several agencies (Table 4.16), including EPA (Group B1), IARC (Group 1), MAK (Group 2), and NTP (Group K). These classifications are based on data from animal studies possibly linking cadmium to lung cancer.

Synthesis

Studies of workers have established that inhalation exposure to cadmium has led to increased risk of impaired lung function and kidney damage. Table 4.17 summarizes the health effects that have been observed in humans following inhalation, oral, and dermal exposure to cadmium.

The OSHA PEL-TWA for air concentration of cadmium in an occupational setting is 0.005 mg/m^3. This exposure limit is protective of effects on the kidney (ACGIH, 2002). The NIOSH IDLH value is 9 mg Cd/m^3 for cadmium dust and cadmium fume. Cadmium has been classified as a known or possible human carcinogen by several agencies.

Table 4.15 Regulatory Standards and Recommendations for Occupational Exposure to Cadmium in Air

Regulatory Measure	Value
ACGIH TLV-TWA	0.01 mg/m^3 **I** [a], 0.002 mg/m^3 **R** [b]
ACGIH TLV-STEL	No value listed
OSHA PEL-TWA	0.005 mg/m^3
OSHA PEL-STEL	No value listed
NIOSH REL-TWA	LFC (LOQ 0.1 mg/m^3)
NIOSH REL-STEL	LFC (LOQ 0.1 mg/m^3)
NIOSH IDLH	Dust — 9 mg Cd/m^3
	Fume — 9 mg Cd/m^3

SOURCE: ACGIH, 2002.

NOTE: See Willis et al. (forthcoming) for definitions of exposure limits.

[a] Measured as inhalable fraction of the aerosol.

[b] Measured as a respirable fraction of the aerosol.

LFC = lowest feasible concentration.

LOQ = limit of quantitation.

Table 4.16 Carcinogenicity Classifications for Cadmium

Agency		Classification
ACGIH	A2	"Suspected Human Carcinogen"
OSHA	Ca	"Carcinogen defined with no further categorization"
NIOSH	Ca	"Potential occupational carcinogen, with no further categorization"
EPA	B1	"Limited evidence of Carcinogenicity from epidemiologic studies"
IARC	1	"Carcinogenic to humans"
MAK	2	"Substances that are considered to be carcinogenic for man because sufficient data from long-term animal studies or limited evidence from animal studies substantiated by evidence from epidemiological studies indicate that they can make a significant contribution to cancer risk"
NTP	K	"Known to be a human carcinogen"

Table 4.17 Reported Human Health Effects of Cadmium Exposure by Different Routes

	Route of Exposure		
Health Effect	**Inhalation**	**Oral (Via Drinking Water and Food)**	**Dermal**
Cancer	Lung (possible)[C]	No known effects	No known effect
Respiratory	Impaired pulmonary function[C]	No known effect	No known effect
	Respiratory failure [A]		
Cardiovascular	No known effect	No known effect	No known effect
Gastrointestinal	No known effect	Nausea, vomiting, diarrhea [A]	No known effect
Immunological	No known effect	No known effect	No known effect
Neurological	No known effect	No known effect	No known effect
Reproductive	No known effect	No known effect	No known effect
Developmental	No known effect	No known effect	No known effect
Other	Kidney disease [C]	Kidney damage[C]	Skin irritation[A]
	Bone effects[C]	Renal tubule interstitial lesions[C]	
	Pronounced proteinuria (protein in urine)[C]	Widespread organ failure at high doses[A]	

NOTE: This table presents a qualitative survey of reported human health effects associated with cadmium exposure based on the Toxicological Profile for Cadmium (ATSDR, 1999a). The causal relationship between cadmium and health effects is established more for some effects than for others. This table is intended to catalog *possible* health effects only.

[A] Listed as an effect of acute exposure in ATSDR (1999a).

[I] Listed as an effect of intermediate exposure in ATSDR (1999a).

[C] Listed as an effect of chronic exposure in ATSDR (1999a).

Chromium

Chromium is a naturally occurring element found in the earth's crust and soil (ranging from 0.1 to 1.0 ppm) and also in animals and plants. It is usually present as chromium (0), chromium (III), or chromium (VI). Chromium (0) and chromium (VI), also known as hexavalent chromium, are generally produced by industry (i.e., anthropogenic sources). Chromium (III), also known as trivalent chromium, occurs naturally and is an essential nutrient used by the body to promote the action of insulin (ATSDR, 2000b).

Atmospheric sources of chromium (VI) are chromate chemicals used as rust inhibitors in cooling towers released as mists, particulate matter released during the production of metal chromates, and chromic acid mist from the plating industry (ATSDR, 2000b). Chromium is primarily used in the United States for wood preservation (52 percent), leather tanning (13 percent), and metals finishing (13 percent), such as in making stainless steel (ATSDR, 2000b). Of significance to a structural collapse, chromium is also found in cement, paint, rubber, and toner powder in copying machines. Chromium (III) is released into the air as a result of emissions from burning fossil fuels (coal and oil) and producing steel, while chromium (VI) is produced by welding of stainless steel and manufacturing of chemicals (ATSDR, 2000b). Both types of chromium compounds might be suspended in the air as fine dust particles for a long period. During suspension, chromium (VI) reacts with dust and pollutants to form chromium (III). Because chromium is used in the production of stainless steel and other metal alloys (U.S. Environmental Protection Agency et al., 2002), it was likely to be present in the WTC post-collapse environment.

Routes of Exposure

Based on human and animal studies, the documented health effects of chromium (III) and chromium (VI) occur following exposure through inhalation and ingestion. Most health studies have focused on chromium (VI), produced by anthropogenic sources, because it is more toxic than other forms of chromium. Humans are exposed to chromium from both inhalation and water/food consumption. Ambient air concentrations of chromium are 0.01–0.03 ug/m^3 (chromium [III] and chromium [VI] combined) and about 2 ppb in water (primarily chromium [III]) (ATSDR, 2000b). In food, small amounts of chromium can leach from stainless steel cans elevating exposure levels; but most fresh foods contain extremely low levels of chromium.

Studies of Health Effects Associated with Chromium Exposure

Results from occupational studies support an association between inhalation exposure to chromium (VI) and chromium (III) and several health outcomes (ATSDR, 2000b). As stated above, chromium (VI) is considered to be more highly toxic than chromium (III), but many studies of the health effects are not able to separate the effects of the two forms. Workers in the chromate manufacturing and ferrochromium industries have been exposed to both chromium (VI) and chromium (III) for many years. Based on these studies, it is generally thought that inhalation exposure to chromium in an occupational setting might result in a higher risk of developing

- nasal mucosal irritation and perforation (Cohen et al., 1974; Lindberg and Hedenstierna, 1983)
- lung cancer (Hayes et al., 1989; Rosenman and Stanbury, 1996).

Ingestion of water containing a high level of chromium (VI) has been observed to cause a range of gastrointestinal symptoms and conditions (Zhang and Li, 1997). Occupational contact dermatitis has been reported to result following dermal exposure to chromium, especially chromate (Thormann et al., 1979).

Inhalation Exposure

Possible health effects associated with human studies of inhalation exposure to chromium (VI) are shown in Table 4.22. Chromium dust is irritating to the lungs. With high levels of chromium (VI), irritation occurs with symptoms of coughing, sneezing, rhinorrhea, nosebleed, and asthma. One of the most common symptoms following chronic exposure to air containing chromium is nasal septum perforation (Cohen et al., 1974).

Chromium (VI) has gastrointestinal effects following inhalation. This includes stomach pains, duodenal ulcers, gastritis, and indigestion (Lucas and Kramkowski, 1975). Exposure can occur by workers breathing chromium-containing air through the mouth, thereby swallowing chromate dust.

Chromium (VI) is associated with hepatic health problems, including cirrhosis of the liver (Moulin et al., 1993). However, these studies are confounded by occupational variables, such as exposure to other chemicals, and personal exposure variables, such as alcohol consumption, and are not generally supported by animal studies.

Chromium (VI) is also associated with respiratory system cancers, especially bronchogenic and nasal. In a study of 3,408 workers exposed to chromium dust, the risk of lung cancer was found to be elevated compared with those not exposed to chromium (Rosenman and Stanbury, 1996).

Oral Exposure

Possible health effects associated with human studies of oral exposure to chromium (VI) are shown in Table 4.22. Ingestion of chromium (VI) can cause death, but the quantity of the lethal dose is unknown (ATSDR, 2000b). Ingestion causes generalized edema, pulmonary edema, severe bronchitis, and necrosis of the liver. However, these identified health effects come from case studies, not from large-scale occupational studies (e.g., Clochesy, 1984). For this reason, they should be interpreted with some caution.

Ingestion of chromium (VI) can cause gastrointestinal problems. From a dose of 20 mg chromium (VI)/L in water, abdominal pain and vomiting were observed (Zhang and Li, 1997). It is uncertain whether chronic exposure to ingestion of chromium is associated with stomach cancer. Elevated levels of cancer incidence are found in regions exposed to chromium. However, no dose-response relationship was identified, and confounding variables related to lifestyle were not controlled (Zhang and Li, 1997).

Dermal Exposure

Some chromium (VI) compounds are caustic. These include chromium trioxide (chromic acid), potassium dichromate, and sodium dichromate. These compounds can cause burns and adsorption, and lead to systemic toxicity (ATSDR, 2000b). Occupational contact dermatitis has been reported to result following exposure to chromium, especially chromate (Thormann et al., 1979).

Occupational Standards and Recommendations

Chromium (VI). Workplace standards set by OSHA require that air concentrations of chromium (VI) (water soluble and water insoluble) in occupational settings not exceed a ceiling of 0.1 mg/m^3 during a workday (OSHA PEL-STEL) (Table 4.18). NIOSH recommends that air concentrations of chromium (VI) (water soluble and water insoluble compounds) in occupational settings not exceed a time-weighted average concentration of 0.001 mg/m^3 assuming exposures of up to a 10-hour workday during a 40-hour workweek (NIOSH REL-TWA) (Table 4.18). These limits are protective of effects on the liver, kidney, and respiratory system for water-soluble chromium (VI) compounds, and against lung cancer and respiratory irritation for water-insoluble chromium (VI) compounds (ACGIH, 2002).

Chromium (VI) compounds (water soluble and water insoluble) have been classified as a known human carcinogens by several agencies (Table 4.19), including EPA (Group A), IARC (Group 1), MAK (Group 2), and NTP (Group K). These classifications are based on human data from occupational studies linking chromium (VI) compounds to lung cancer.

Table 4.18 Regulatory Standards and Recommendations for Occupational Exposure to Chromium (VI) in Air

Regulatory Measure	Chromium (VI) Water Soluble	Chromium (VI) Water Insoluble
ACGIH TLV-TWA	0.05 mg/m^3	0.01 mg/m^3
ACGIH TLV-STEL	No value listed [BEI]	No value listed
OSHA PEL-TWA	No value listed	No value listed
OSHA PEL-STEL	C 0.1 mg/m^3	C 0.1 mg/m^3
NIOSH REL-TWA	0.001 mg/m^3	0.001 mg/m^3
NIOSH REL-STEL	No value listed	No value listed
NIOSH IDLH	15 mg Cr (VI)/ m^3	15 mg Cr (VI)/ m^3

SOURCE: ACGIH, 2002.
NOTE: See Willis et al. (forthcoming) for definitions of exposure limits.

Chromium (III) and Chromium Metal. Workplace standards set by OSHA require that air concentrations of chromium (III) and chromium metal in occupational settings not exceed a time-weighted average concentration of 0.5 mg/m^3 and 1 mg/m^3, respectively, assuming exposures of eight hours per day for a 40-hour workweek (OSHA PEL-TWA) (Table 4.20). NIOSH recommends that air concentrations of chromium (III) and chromium metal in occupational settings not exceed a time-weighted average concentration of 0.5 mg/m^3, assuming exposures of up to a 10-hour workday during a 40-hour workweek (NIOSH REL-TWA) (Table 4.20). These limits are based on the avoidance of respiratory irritation and dermatitis (ACGIH, 2002). Chromium (III) and chromium metal are not classified as carcinogens by any health agency (Table 4.21).

Table 4.19 Carcinogenicity Classifications for Chromium (VI)

Agency	Chromium (VI) Water Soluble		Chromium (VI) Water Insoluble	
ACGIH	A1	"Confirmed Human Carcinogen"	A1	"Confirmed Human Carcinogen"
OSHA	No value listed		No value listed	
NIOSH	Ca	"Potential occupational carcinogen, with no further categorization"	Ca	"Potential occupational carcinogen, with no further categorization"
EPA	A	"Human Carcinogen"	A	"Human Carcinogen"
	K	"Known Human Carcinogens"	K	"Known Human Carcinogens"
IARC	1	"Carcinogenic to Humans"	1	"Carcinogenic to Humans"
MAK	2	"Substances that are considered to be carcinogenic for man because sufficient data from long-term animal studies or limited evidence from animal studies substantiated by evidence from epidemiological studies indicate that they can make a significant contribution to cancer risk"	No value listed	
NTP	K	"Known To Be A Human Carcinogen"	K	"Known To Be A Human Carcinogen"

Table 4.20 Regulatory Standards and Recommendations for Occupational Exposure to Chromium (III and Metal) in Air

Regulatory Measure	Chromium (III)	Chromium Metal
ACGIH TLV-TWA	0.5 mg/m^3	0.5 mg/m^3
ACGIH TLV-STEL	No value listed	No value listed
OSHA PEL-TWA	0.5 mg/m^3	1.0 mg/m^3
OSHA PEL-STEL	No value listed	No value listed
NIOSH REL-TWA	0.5 mg/m^3	0.5 mg/m^3
NIOSH REL-STEL	No value listed	No value listed
NIOSH IDLH	25 mg Cr (III)/m^3	250 mg Cr/m^3

SOURCE: ACGIH, 2002.
NOTE: See Willis et al. (forthcoming) for definitions of exposure limits.

Table 4.21 Carcinogenicity Classifications for Chromium (III and Metal)

Agency	Chromium (III)	Chromium Metal
ACGIH	A4 "Not Classifiable as a Human Carcinogen"	A4 "Not Classifiable as a Human Carcinogen"
OSHA	No value listed	No value listed
NIOSH	No value listed	No value listed
EPA	D "Not Classifiable as to Human Carcinogenicity"	No value listed
	CBD "Cannot Be Determined"	
IARC	3 "Unclassifiable as to the Carcinogenicity in Humans"	3 "Unclassifiable as to the Carcinogenicity in Humans"
MAK	No value listed	No value listed
NTP	No value listed	No value listed

Synthesis

Studies of workers have established that inhalation exposure to chromium has led to increased risk of nasal mucosal irritation and perforation as well as lung cancer. Table 4.22 summarizes the possible health effects that have been observed in humans following inhalation, oral, and dermal exposure to chromium.

The NIOSH REL-TWA for air concentration in an occupational setting is 0.001 mg/m^3 for chromium (VI) (water soluble and water insoluble compounds) and 0.5 mg/m^3 for chromium (III) and chromium metal. The exposure limit for chromium (VI) (water soluble compounds) is protective of effects on the liver, kidney, and respiratory system (ACGIH, 2002). The exposure limit for chromium (VI) (water insoluble compounds) is protective against lung cancer and irritation (ACGIH, 2002). The exposure limit for chromium metal and chromium (III) compounds is protective against irritation and dermatitis (ACGIH, 2002). Chromium (VI) has been classified as a known human carcinogen by several agencies. Chromium (III) and chromium metal are not classified as carcinogens by any health agency.

Table 4.22 Reported Human Health Effects of Chromium (VI and III) Exposure by Different Routes

	Route of Exposure		
		Oral	
Health Effect	**Inhalation**	**(Via Drinking Water and Food)**	**Dermal**
Cancer	Lung[C]	No known effect	No known effect
Respiratory	Epitaxis[I] rhinorrhea	Congested lungs[A]	Nasal septum ulceration
	Nasal ulceration[I]	Pleural effusions[A]	Nasal septum perforation[C]
	Chronic tonsillitis[C]		
	Mild decreased lung function[I]		
	Nasal mucosa atrophy [I]		
	Atrophy of larynx[C]		
	Nasal septum perforation[C]		
	Chronic pharyngitis[C]		
Cardiovascular	No known effect	Hemorrhage[A]	No known effect
		Cardiac arrest[A]	
Gastrointestinal	Stomach pains[C]	Hemorrhage[A]	Ulcers[C]
	Cramps[C]	Diarrhea[C]	Gastritis (possible)[C]
	Ulcers[C]	Abdominal pain[C]	
	Gastric irritation ulcer[C]	Indigestion[C]	
		Vomiting[C]	
Immunological	No known effect	No known effect	No known effect
Neurological	No known effect	No known effect	No known effect
Reproductive	No known effect	No known effect	No known effect
Developmental	No known effect	No known effect	No known effect
Other	Death[A]	Death[A]	Death
	Increase in retinal binding	Acute tubular necrosis[A]	Erythema[A]
	protein and tubular antigen[C]	Necrosis of the liver [A]	Chromium allergy[A]
	Increased urinary beta-2-	Inhibited coagulation[A]	Chrome holes[C]
	microglobulin[C]	Dermatitis[A]	
		Leukocytosis[C]	
		Immature neutrophils[C]	

NOTE: This table presents a qualitative survey of reported human health effects associated with chromium exposure based on the Toxicological Profile for Chromium (ATSDR, 2000b). The causal relationship between chromium and health effects is established more for some effects than for others. This table is intended to catalog *possible* health effects only.

[A] Listed as an effect of acute exposure in ATSDR (2000b).

[I] Listed as an effect of intermediate exposure in ATSDR (2000b).

[C] Listed as an effect of chronic exposure in ATSDR (2000b).

Lead

Lead is soft, silver-gray metal that occurs naturally in its elemental form in the earth's crust. Elemental lead is resistant to corrosion and does not dissolve in water or burn. Lead can react with other elements to form compounds such as lead sulfide, lead oxides, and lead salts. Sources of lead in the air include burning fuel, lead smelters, and industrial processes. Lead in the air also arose from emissions from leaded gasoline until that type of fuel was banned in 1996 (ATSDR, 1999b).

Lead in the soil comes from sources such as lead-based paint from buildings and from lead settling from the air. The use of these paints was banned in 1978; now paint cannot contain more than 0.06 percent lead. Lead in water primarily comes from soil, solder in pipes carrying water, or from wastewater from industry; although, most water contains less than 0.005 ppm (ATSDR, 1999b). Many foods contain small amounts of lead (meats, seafood, fruits, vegetables). Cigarette smoke also contains lead as do some cosmetics.

Some lead that enters the body is stored in the bones and teeth (called the lead "sinks"). In fact, 94 percent of all lead in our bodies is found in the bones and teeth. However, most lead (99 percent) that enters the human body is not stored in this way but rather is eliminated in about two weeks through urine and feces. These rates are different for children, who store 73 percent of lead in their bones and teeth and eliminate only 32 percent in waste in two weeks (ATSDR, 1999b).

Lead is used in the United States for a variety of purposes. The two most common uses are for making batteries and ammunition. Lead is also used in many types of metal products such as solder, brass and bronze products, and pipes, as well as ceramic glazes. In addition, lead is used in components of medical, scientific, and military equipment. As mentioned above, lead was added to gasoline to increase the octane rating until it was phased out in the 1980s and eventually banned in 1996. In the 1960s and 1970s, lead was commonly used in paint and in the solder used for indoor plumbing, electrical wiring, computer circuit boards, and electrical appliances (Environmental Protection Agency, 2002b). After the WTC collapse, lead might have been produced, therefore, as a by-product of the fires or in the pulverized materials, attached to particulate matter or in the settled dust.

Routes of Exposure

Humans are exposed to lead from both inhalation and water/food consumption. Most health effects studies have examined lead found in inorganic compounds (salts, oxides, sulfides). Most of these studies are unusual in that exposures are expressed as PbB levels (levels of lead in the blood measured in µg/dL) rather than mg/Kg/day (which are generally not available from human studies) (ATSDR, 1999b). Because exposure to lead occurs from all three exposure routes (inhalation, oral, and dermal), estimating the magnitude of exposure and resulting health effects from each route is impossible. Therefore, the information on health effects presented below includes "internal doses of lead" representing multiple routes of exposure.

Studies of Health Effects Associated with Lead Exposure

The multiple health effects of lead exposure observed in humans vary based on the magnitude of the dose and the length of exposure. The generally accepted effects of lead exposure include the following:

- lead poisoning characterized by gastrointestinal symptoms (abdominal pain, constipation, cramps, nausea, vomiting, anorexia, and weight loss) (Awad el Karim et al., 1986; Baker et al., 1979)
- decreased hemoglobin synthesis and anemia (Alessio et al., 1976; Gennart et al., 1992a)

- neurologic effects (Campara et al., 1984), including encephalopathy (Campara et al., 1984; Zimmermann-Tansella et al., 1983)
- peripheral neuropathy (causing weakness in fingers, wrists, and ankles) among workers chronically exposed to high levels of lead (Ehle, 1986; Triebig et al., 1984)
- kidney damage, including reversible changes after short-term exposures, and altered kidney function due to sclerosis and fibrosis following long-term exposure to high lead levels (Cramer et al., 1974; Wedeen et al., 1979)
- reduced sperm count in men (Gennart et al., 1992b).

Colic (i.e., abdominal pain, constipation, cramps, nausea, vomiting, anorexia, and weight loss) is considered to be an early symptom of lead poisoning (in children and adults) and can occur with exposures as low as 40–60 µg/dL (Awad el Karim et al., 1986). Lead also has hematological effects, including anemia, basophilic stippling of erythrocytes, and lower mean corpuscular values. These effects occur primarily because enzymes essential to heme biosynthesis are inhibited by lead. A dose-response relationship between some of these enzymes and lead exposure has been documented (Herber, 1980).

The most prominent symptoms of lead poisoning are neurological. Lead encephalopathy (a disease that affects brain function) can occur. Milder symptoms include headaches, muscular tremors, memory loss, and hallucinations. More severe symptoms include delirium, convulsions, paralysis, coma, and even death (Kumar et al., 1987). These symptoms are thought to occur at high lead exposure levels (ATSDR, 1999b). At lower lead levels, the effects of lead exposure are generally described as behavioral effects. These include impaired visual motor performance, hand dexterity, IQ, cognitive performance, and nervousness. Some of these symptoms (e.g., impaired attention, concentration, and psychomotor performance) can occur at PbB levels of 35–50 µg/dL (Arnvig et al., 1980).

Many studies of neurological symptoms of lead poisoning show decreased nerve conduction velocities. Effects have been identified with exposures as low as 30–48 µg/dL (Seppalainen et al., 1983).

The association between lead exposure and cancer is tenuous because many studies are confounded because of exposure to other known carcinogens (e.g., other metals and smoking). The ATSDR report (1999b) concludes that studies "are not sufficient to determine the carcinogenicity of lead in humans."

Although the above studies considered all routes of exposure, it has been demonstrated that lead can enter the bloodstream via inhalation. Exposure of human volunteers to 0.003–0.01 mg lead/m^3 in the air for three months increased mean PbB levels from 20 to 27 µg/dL (Griffin et al., 1975). Animal studies show that oral exposure to lead acetate and lead phosphate is associated with cancer (mostly renal cancer). However, the doses involved are extremely high and cumulative (Azar et al., 1973).

Occupational Standards and Recommendations

Workplace standards set by OSHA require that air concentrations of lead in occupational settings not exceed a time-weighted average concentration of 0.05 mg/m^3, assuming exposures of eight hours per day for a 40-hour workweek (OSHA PEL-TWA) (Table 4.23). NIOSH recommends air concentrations of lead not exceed a time-weighted average concentration of 0.1 mg/m^3, assuming exposures of up to a 10-hour

workday during a 40-hour workweek (NIOSH REL-TWA). These limits are protective of effects on the central nervous system, blood, kidney, and reproductive system (ACGIH, 2002). Lead has been classified as a probable or possible human carcinogen by several agencies (Table 4.24), including EPA (Group B2), IARC (Group 2B), and MAK (Group 3B). These classifications are based on data from animal studies possibly linking lead to cancer. OSHA, NIOSH, and NTP have not classified lead as a carcinogen.

Synthesis

Studies of persons exposed to lead in an occupational setting and in the general population have established that lead exposure has been associated with an increased risk of several diseases. Lead poisoning; decreased hemoglobin synthesis and anemia; neurologic effects, including encephalopathy and peripheral neuropathy; kidney damage; and reduced sperm count in men have been reported in studies of the health effects of lead exposure. Table 4.25 summarizes the health effects that have been observed in humans following inhalation, oral, and dermal exposure to lead.

The OSHA PEL-TWA for air concentration of lead in an occupational setting is 0.05 mg/m^3. These exposure limits are protective of effects on the central nervous system, blood, kidney, and reproductive system (ACGIH, 2002). Lead has been classified as a possible human carcinogen by several agencies.

Table 4.23 Regulatory Standards and Recommendations for Occupational Exposure to Lead (and Inorganic Compounds as Lead) in Air

Regulatory Measure	Value
ACGIH TLV-TWA	0.05 mg/m^3
ACGIH TLV-STEL	No value listed
OSHA PEL-TWA	0.05 mg/m^3
OSHA PEL-STEL	No value listed
NIOSH REL-TWA	<0.1 mg/m^3 (blood Pb < mg/100 g whole blood)
NIOSH REL-STEL	No value listed
NIOSH IDLH	100 mg Pb/m^3

SOURCE: ACGIH, 2002.
NOTE: See Willis et al. (forthcoming) for definitions of exposure limits.

Table 4.24 Carcinogenicity Classifications for Lead (and Inorganic Compounds as Lead)

Agency	Classification	
ACGIH	A3	"Confirmed Animal Carcinogen with Unknown Relevance to Humans"
OSHA	No value listed	
NIOSH	No value listed	
EPA	B2	"Probably Human Carcinogen, Sufficient evidence from animal studies; inadequate evidence or no data from epidemiologic studies"
IARC	2B	"Possibly Carcinogenic to Humans"
MAK	3B	"Substances for which in vitro tests or animal studies have yielded evidence of carcinogenic effects that is not sufficient for classification of the substance in one of the other categories"
NTP	No value listed	

Table 4.25 Reported Human Health Effects of Lead Exposure by Different Routes

Health Effect	Internal (Inhalation, Oral, and Dermal Combined)
Cancer	Lung (possible)[NS]
Respiratory	Respiratory failure[NS]
Cardiovascular	Increased blood pressure[NS]
	Ischemic electrocardiogram changes[NS]
Gastrointestinal	Colic[A]
Immunological	Depression of cellular immune function[NS]
Neurological	Encephalopathy[A]
	Decreased peripheral nerve function[NS]
	Decreased visual-motor function[NS]
	Decreased IQ[NS]
	Irritability[NS]
	Lethargy[A, C]
	Headache[A, C]
	Fatigue[A, C]
	Impotence[A, C]
	Weakness[A, C]
	Paresthesia[A, C]
	Impaired memory[NS]
Reproductive	Reduced birth weight[NS]
	Increased incidence of stillbirth[NS]
	Low sperm count[NS]
Developmental	Growth retardation in children[NS]
	Decreased growth rate[NS]
	Impaired motor development[NS]
Other	Decreased hemoglobin[NS]
	Anemia[NS]
	Chronic nephropathy[NS]
	Impaired renal function[C]
	Gout[C]

NOTE: This table presents a qualitative survey of reported human health effects associated with lead exposure based on the Toxicological Profile for Lead (ATSDR, 1999b). The causal relationship between lead and health effects is established more for some effects than for others. This table is intended to catalog possible health effects only.

[A] Listed as an effect of acute exposure in ATSDR (1999b).

[I] Listed as an effect of intermediate exposure in ATSDR (1999b).

[C] Listed as an effect of chronic exposure in ATSDR (1999b).

[NS] Listed as unknown exposure time in ATSDR (1999b).

Mercury

Mercury is a naturally occurring substance that exists in three forms: metallic mercury (Hg), inorganic mercury, and organic mercury. Metallic mercury is an element that is liquid at room temperature. Inorganic mercury compounds are generally made up of mercury combined with chlorine, sulfur, or oxygen. Organic mercury compounds are mercury combined with carbon (the most common is methylmercury) (ATSDR, 1999c). Metallic mercury is derived through mining cinnabar ore (contains mercury sulfide). The ore is heated, vaporizing the mercury, which is then cooled and captured as metallic mercury.

Mercury is used in the United States for producing chlorine gas and caustic soda, extracting gold, and as a component of fungicides and paints. Of significance to emergency responders at a building collapse, mercury is also found in electrical switches, batteries, thermostats, and fluorescent light bulbs (ATSDR, 1999c).

Routes of Exposure

Humans are exposed to mercury primarily from inhalation. In general, 20 ng/m^3 of mercury is found in the air — which is several hundred times below occupational safety standards (ATSDR, 1999c). Mercury is released into the air from natural processes, including weathering rocks, volcanic eruptions, and forest fires. Human activities such as mining and smelting of mercury and other metal ores, production of cement, and burning fossil fuels and household waste also release mercury into the air (termed anthropogenic emissions). Metallic mercury is also released through fertilizers and fungicides, and by discarding mercury-containing waste and medical equipment (e.g., thermometers and blood pressure measuring equipment). From air, water, and food, animals and plants can take mercury into their bodies. Microorganisms convert inorganic mercury to methylmercury. This compound can accumulate up the "food chain," especially in large fish (e.g., sharks) and marine mammals (e.g., seals).

This summary focuses on studies of the health effects following exposure to inorganic mercury (i.e., metallic mercury and inorganic mercury compounds) because these types of mercury are the most likely forms to which emergency responders will be exposed.

Studies of Health Effects Associated with Mercury Exposure

Results from studies of humans and animals support an association between inhalation exposure to mercury and numerous health effects (ATSDR, 1999c). Metallic mercury and inorganic mercury compounds have similar toxic effects and are therefore considered together in this section as "mercury." The main target organs for toxicity induced by mercury vapor are the kidney and central nervous system (World Health Organization, 1995). Acute inhalation exposure to high levels of mercury vapor has been associated with effects on many organ systems (Bluhm et al., 1992; Kanluen and Gottlieb, 1991; Rowens et al., 1991; Taueg et al., 1992), including the following:

- kidney damage, ranging from transient effects to acute renal failure
- nervous system disorders, including hand tremors, emotional instability, loss of sleep, memory loss, muscle weakness, and decreased nerve conduction velocity
- respiratory irritation, including cough, shortness of breath, and chest pain
- increased heart rate and blood pressure
- gastrointestinal effects, including abdominal pains, nausea and vomiting, and diarrhea.

Occupational studies of workers with chronic inhalation exposure to lower levels of mercury vapor have shown some of the same effects, most notably symptoms related to the nervous system and kidneys (Langworth et al., 1992a; Langworth et al., 1992b; Roels et al., 1982).

Ingesting inorganic mercury compounds has been associated with toxicity in multiple organ systems in humans and animals, based primarily on studies of mercuric chloride (ATSDR, 1999c). Metallic mercury is not absorbed by the digestive system and therefore has little or no effect. The most important effects of oral exposure to inorganic mercury salts are related to the kidneys and central nervous system, similar to inhalation exposure.

Inhalation Exposure

Death can occur following acute exposure to mercury, primarily from respiratory failure (Soni et al., 1992). Mercury vapor mercury associated with particulates is irritating to the lungs. Exposure can result in cough, shortness of breath, respiratory distress, pulmonary edema, lobar pneumonia, fibrosis, and desquamation of the bronchiolar epithelium. Most of these health effects were observed with exposure to mercury vapor for four to eight hours (Soni et al., 1992). Cardiovascular effects from exposure to mercury vapor have also been observed. These health effects include increased blood pressure and heart rate/palpitations (Soni et al., 1992). However, levels of mercury vapor were not recorded in these studies. One study of workers exposed to 0.27 mg/m^3 mercury vapor for seven years showed no cardiovascular effects (Schuckmann, 1979).

Gastrointestinal effects are associated with acute inhalation exposure to mercury vapor. These include stomatitis (inflammation of the oral mucosa), excessive salivation, difficulty swallowing, nausea, vomiting, and diarrhea (Bluhm et al., 1992). Acute inhalation exposure to mercury vapor has also been associated with hematological effects, including fatigue, fever, chills, and elevated leukocyte count — symptoms consistent with a syndrome called "metal fume fever" (Rowens et al., 1991).

Renal effects are associated with acute inhalation exposure to mercury vapor, including changes in urinary acid excretion, proteinuria, hematuria, and acute renal failure (Rowens et al., 1991). This is also confirmed by animal studies, most of which show serious kidney degenerative effects from inhalation exposure to mercury vapor (Ashe et al., 1953). Dermal effects are associated with acute inhalation exposure to mercury vapor, including skin rashes, heavy perspiration, and reddened and/or peeling skin (Aronow et al., 1990).

Neurological effects are associated with acute inhalation exposure to mercury vapor including cognitive, personality, sensory, and motor disturbances. The ATSDR report (1999c) lists approximately 30 specific neurological effects, and the central nervous system is described as "probably the most sensitive target organ for metallic mercury vapor exposure" (ATSDR, 1999c). Effects following short-term exposure have been observed. For example, irritability, lack of ambition, and lack of sexual desire were observed for workers exposed to 44 mg/m^3 mercury vapor for less than eight hours (McFarland and Reigel, 1978). This is also confirmed by animal studies, most of which show serious neurological effects following inhalation of mercury vapor.

Oral Exposure

Ingestion of inorganic mercury compounds has been used as a suicide method because it causes widespread organ damage, including cardiovascular collapse, acute renal failure, and severe

gastrointestinal damage (Troen et al., 1951). However, doses to cause effects are high; swallowing small amounts of mercury causes few symptoms. For example, ingestion of 204 g of metallic mercury caused no symptoms (Wright et al., 1980). This is congruent with negligible absorption of mercury that occurs in the gastrointestinal tract.

The systemic, respiratory, and cardiovascular effects of oral exposure to mercury are similar to those described above for inhalation exposure. The organ systems most affected include the kidneys and central nervous system. However, few human studies of oral exposure to mercury have been conducted.

Dermal Exposure

Few studies have been identified for dermal exposure to mercury (ATSDR, 1999c). No studies were identified examining systemic effects. One study found cardiovascular effects (tachycardia) from contact with mercuric chloride solution after a child treated with a mercury-containing ointment developed anorexia (Warkany and Hubbard, 1953). Contact dermatitis is a dermal effect documented in numerous case studies (ATSDR, 1999c); however, few other effects were identified.

Occupational Standards and Recommendations

Workplace standards set by ACGIH require that air concentrations of elemental mercury and inorganic mercury compounds in occupational settings not exceed a time-weighted average concentration of 0.025 mg/m^3, assuming exposures of eight hours per day for a 40-hour workweek (ACGIH TLV-TWA) (Table 4.26). Workplace standards set by OSHA require that air concentrations of the same forms of mercury in occupational settings not exceed 0.1 mg/m^3 for any 15-minute period during a workday (OSHA PEL-STEL) (Table 4.26). NIOSH recommends that air concentrations of mercury not exceed 0.1 mg/m^3 for any 15-minute period during a workday (NIOSH REL-STEL) (Table 4.26). These limits are protective of effects on the central nervous system and kidneys, as well as reproductive effects (ACGIH, 2002). Mercury has not been classified as a human carcinogen by any health agency (Table 4.27).

Table 4.26 Regulatory Standards and Recommendations for Occupational Exposure to Mercury in Air

Regulatory Measure	Elemental and Inorganic Compounds, as Mercury	Alkyl Compounds, as Mercury
ACGIH TLV-TWA	0.025 mg/m^3 (skin)	0.01 mg/m^3 (skin)
ACGIH TLV-STEL	No value listed (skin)	0.03 mg/m^3 (skin)
OSHA PEL-TWA	No value listed	0.01 mg/m^3
OSHA PEL-STEL	C 0.1 mg/m^3	C 0.04 mg/m^3
NIOSH REL-TWA	No value listed	0.01 mg/m^3 (skin)
NIOSH REL-STEL	C 0.1 mg/m^3 (skin)	0.03 mg/m^3 (skin)
NIOSH IDLH	10 mg Hg/m^3	2 mg Hg/m^3

SOURCE: ACGIH, 2002.
NOTE: See Willis et al. (forthcoming) for definitions of exposure limits.
Skin = danger of cutaneous absorption.

Table 4.27 Carcinogenicity Classifications for Mercury (Elemental and Inorganic Compounds, as Mercury)

Agency	Classification	
ACGIH	A4	"Not Classifiable as a Human Carcinogen"
OSHA	No value listed	
NIOSH	No value listed	
EPA	D	"Not Classifiable as to Human Carcinogenicity"
IARC	3	"Unclassifiable as to the Carcinogenicity in Humans"
MAK	3B	"Substances for which in vitro tests or animal studies have yielded evidence of carcinogenic effects that is not sufficient for classification of the substance in one of the other categories"
NTP	No value listed	

Synthesis

Studies of workers and other persons exposed to inorganic mercury have established that breathing mercury vapor over short and long periods leads to effects on multiple organ systems. Effects on kidney function and the central nervous system are most pronounced. Table 4.28 summarizes the health effects that have been observed in humans following inhalation, oral, and dermal exposure to mercury.

The ACGIH TLV-TWA for air concentration of mercury in an occupational setting is 0.025 mg/m^3, and the OSHA PEL-STEL is 0.1 mg/m^3 for any 15-minute period during a workday. These exposure limits are protective of effects on the central nervous system and kidneys, as well as reproductive effects (ACGIH, 2002). Mercury has not been classified as a carcinogen by any health agency.

Table 4.28 Reported Human Health Effects of Mercury Exposure by Different Routes

	Route of Exposure		
Health Effect	**Inhalation**	**Oral (Via Drinking Water and Food)**	**Dermal**
Cancer	No known effect	No known effect	No known effect
Respiratory	Cough[NS]	No known effect	No known effect
	Dyspnea[NS]		
	Respiratory distress[NS]		
	Pulmonary edema[NS]		
	Lobar pneumonia[NS]		
	Fibrosis[NS]		
	Desquamation of the bronchiolar epithelium[NS]		
Cardiovascular	Increased blood pressure[NS]	No known effect	Tachycardia[NS]
	Heart rate/palpitations[NS]		Anorexia[NS]
Gastrointestinal	Stomatitis[NS]	Nausea[A]	No known effect
	Excessive salivation[NS]	Vomiting[A]	
	Difficulty swallowing[NS]	Diarrhea[A]	
	Nausea[NS]	Abdominal cramps[A]	
	Vomiting[NS]		
	Diarrhea[NS]		
Immunological	Fatigue[NS]	No known effect	No known effect
	Fever[NS]		
	Chills[NS]		
	Elevated leukocyte count[NS]		
Neurological	Cognitive disturbances[NS]	Cognitive disturbances[NS]	No known effect
	Personality disturbances[NS]	Personality disturbances[NS]	
	Sensory disturbances[NS]	Sensory disturbances[NS]	
	Motor disturbances[NS]		
Reproductive	No known effect	No known effect	No known effect
Developmental	No known effect	Delayed walking [A]	No known effect
		Abnormal motor scores [A]	
Other	Changes in urinary acid excretion[NS]	Changes in urinary acid excretion[A]	Contact dermatitis[NS]
	Frank proteinuria[NS]	Proteinuria[A]	
	Hematuria[NS]	Hematuria[A]	
	Acute renal failure[NS]	Acute renal failure[A]	
		Oliguria[A]	
		Proteinuria[A]	

NOTE: This table presents a qualitative survey of reported human health effects associated with mercury exposure based on the Toxicological Profile for Mercury (ATSDR, 1999c). The causal relationship between mercury and health effects is established more for some effects than for others. This table is intended to catalog *possible* health effects only.

[A] Listed as an effect of acute exposure in ATSDR (1999c).

[I] Listed as an effect of intermediate exposure in ATSDR (1999c).

[C] Listed as an effect of chronic exposure in ATSDR (1999c).

[NS] Listed as unknown exposure time in ATSDR (1999c).

5. Possible Health Effects of Exposure to Combustion By-Products Following a Structural Collapse

Introduction

This section focuses on four combustion by-products that are likely to be present after the collapse of a large building if a fire is burning. They are

- benzene
- dioxins
- polychlorinated biphenyls (PCBs)
- polycyclic aromatic hydrocarbons (PAHs).

The following subsections describe the human health effects that might occur following exposure to each substance, based on studies published in the medical literature.

Benzene

Benzene is also commonly known as benzol. It is a highly flammable, colorless liquid that readily evaporates into air and is slightly soluble in water (ATSDR, 1997). Benzene was first produced in significant quantities as a by-product of coke production in the steel industry during the 19th century. Later, it was produced as a fuel component and as a by-product of petroleum refining. Benzene is a product of the incomplete combustion of petroleum and coal. It is found in crude oil, gasoline, vehicle exhaust, cigarette smoke, and products in which it is used during manufacturing.

Because of its utility, benzene is one of the top 20 chemicals produced in the United States, by volume. It remains a widely used solvent and is employed in the production of many materials, including rubber, inks and other dyes, lubricants, drugs, detergents, and pesticides (ATSDR, 1997; Snyder and Andrews, 1996). A simple aromatic hydrocarbon, benzene is commonly used as a starting point for chemical synthesis, including for the production of styrene (present in Styrofoam and other plastics) as well as many resins and synthetic fibers, such as nylon.

Benzene is found in emissions from burning coal, oil, and gasoline. Benzene is used in the manufacturing process of many products — in the production of starting materials and intermediates, including phenol, aniline, benzidine, sulphonic acid, diphenyl, and acetone, nylon, and synthetic detergents. In a post-collapse environment, benzene may be present in air due to the partial combustion of these products.

Routes of Exposure

Of particular importance to emergency responders, structural fires have been reported as a source of benzene release to air (Lowry et al., 1985). Occupational and nonoccupational exposures to benzene are primarily via inhalation, with some probable though undefined contribution from dermal absorption (Snyder and Andrews, 1996). Exposure to benzene often occurs via several routes simultaneously, but Hattemer-Frey et al. (1990) report that inhalation accounts for more than 99 percent of the total human daily intake of benzene. Further, it is difficult to determine the contribution of the less-significant oral and dermal routes of exposure, given the overwhelming contribution of inhalational exposures, especially for non-acute exposures. Because the largest source at a building collapse will likely be from combustion by-products, inhalation exposure to benzene will be of greatest concern in a collapsed building environment.

Vehicle exhaust and industrial emissions account for approximately 20 percent of the total U.S. nationwide exposure to benzene. About 50 percent of benzene exposure nationwide results from smoking tobacco or being exposed to tobacco smoke. Benzene exposure from tobacco smoke far exceeds background levels. The average smoker (32 cigarettes per day) is exposed to approximately 10 times the average daily benzene intake of nonsmokers. In fact, while individuals occupationally exposed to benzene may have the greatest magnitude of exposure, smoking has been reported as the largest anthropogenic source of background human exposure to benzene (ATSDR, 1997; Hattemer-Frey et al., 1990). Other releases of benzene to the atmosphere include off-gassing from particle board (Glass et al., 1986), vaporization from oil spills, vehicles burning petroleum products, and emissions from landfills (ATSDR, 1997). Natural sources of benzene include volcanoes and forest fires (ATSDR, 1997).

Studies of Health Effects Associated with Benzene Exposure

Acute exposure to high concentrations of benzene may cause unconsciousness and death by depressing the central nervous system, and death may also be caused by fatal cardiac arrhythmia (Snyder and Andrews, 1996). Brief exposure to very high levels of benzene in air can result in death. While the amount of benzene exposure in such fatal cases is often not known, it has been estimated that minutes of exposure to 20,000 ppm benzene in air is usually fatal (Sullivan and Krieger, 1992). Exposure to lower levels of benzene (700–3,000 ppm) can cause drowsiness, dizziness, rapid heart rate, headaches, tremors, confusion, and unconsciousness (ATSDR, 1997).

Unlike other simple aromatic hydrocarbons, the most significant effect of chronic benzene exposure is hematopoietic[7] toxicity. Results from studies of humans and animals support an association between benzene exposure and various diseases, primarily those involving the blood and blood-forming organs. A review of benzene toxicity by Snyder and Andrews (1996) indicates that bone marrow depression associated with benzene exposure is dose-dependent. Studies of workers exposed to benzene have reported that chronic benzene exposure might result in a higher risk of developing

[7] Pertaining to the formation of blood cells.

- anemia[8] (Kipen et al., 1989)
- leukopenia[9] (Xia et al., 1995)
- leukemia[10] (Snyder and Kalf, 1994).

Intermittent exposures to benzene can make it difficult to assume that average concentrations of benzene measured in a workplace and included in epidemiological studies indicate the true exposure experience by each worker. However, ATSDR (1997) concluded that, "A cause-effect relationship between benzene and leukemia is sufficiently clear." A qualitative summary of potential health effects associated with benzene exposure is provided in Table 5.3.

Occupational Standards and Recommendations

Workplace standards set by OSHA require that air concentrations of benzene in occupational settings not exceed a time-weighted average concentration of 1 ppm or 3 mg/m^3, assuming exposures of eight hours per day for a 40-hour workweek (OSHA PEL-TWA), and not exceed 5 ppm or 15 mg/m^3 for any 15-minute period during a workday (OSHA PEL-STEL) (Table 5.1). NIOSH recommends air concentrations of benzene not exceed a time-weighted average concentration of 0.1 ppm or 0.32 mg/m^3, assuming exposures of up to a 10-hour workday during a 40-hour workweek (NIOSH REL-TWA), and not exceed 1 ppm or 3.2 mg/m^3 for any 15-minute period during a workday (NIOSH REL-STEL) (Table 5.1). These limits are based on the avoidance of cancer (ACGIH, 2002). Benzene has been classified as a known human carcinogen by several agencies (Table 5.2), including EPA (Group A), IARC (Group 1), MAK (Group 1), and NTP (Group K). These classifications are based on human data from occupational studies linking benzene to leukemia.

Synthesis

Because benzene has been studied for more than a century, its associated health effects are fairly well documented. Acute exposures to benzene can cause neurological depression and related symptoms, rapid heart rates, unconsciousness, and, in cases of high exposures, death. Studies of benzene workers have shown that inhalation of benzene at concentrations lower than those that produce acute effects is associated with increased risk of several diseases, including such cancers as leukemia and lymphoma. Table 5.3 summarizes the health effects that have been observed in humans following benzene exposure.

The OSHA PEL-TWA and NIOSH REL-TWA for air concentration of benzene in an occupational setting are 3 mg/m^3 and 0.32 mg/m^3, respectively. The OSHA PEL-STEL is 15 mg/m^3 for any 15-minute period during a workday. These exposure limits are based on the avoidance of cancer (ACGIH, 2002). Benzene has been classified as a known human carcinogen by several agencies.

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[8] A condition in which the number of red blood cells or hemoglobin per unit volume is decreased below normal.

[9] A condition in which the total number of leukocytes in the circulating blood is less than normal.

[10] Leukemia is a cancer of the tissues that form white blood cells. More specifically, it is characterized by a progressive proliferation of abnormal leukocytes and is classified by the dominant cell type proliferated (e.g., myelogenous leukemia, one type associated with benzene exposure).

Table 5.1 Regulatory Standards and Recommendations for Occupational Exposure to Benzene in Air

Regulatory Standard or Recommendation	Value
ACGIH TLV-TWA	0.5 ppm; 1.6 mg/m^3 (skin)
ACGIH TLV-STEL	2.5 ppm; 8 mg/m^3 (skin)
OSHA PEL-TWA	1 ppm; 3 mg/m^3
OSHA PEL-STEL	5 ppm; 15 mg/m^3 (15-minute average)
NIOSH REL-TWA	0.1 ppm; 0.32 mg/m^3
NIOSH REL-STEL	1 ppm; 3.2 mg/m^3
NIOSH IDLH	500 ppm

SOURCE: ACGIH, 2002.
NOTE: See Willis et al. (forthcoming) for definitions of exposure limits.
Skin = danger of cutaneous absorption.

Table 5.2 Carcinogenicity Classifications for Benzene

Agency		Classification
ACGIH	A1	"Confirmed human carcinogen"
OSHA	Ca	"Carcinogen defined with no further categorization"
NIOSH	Ca	"Potential occupational carcinogen, with no further categorization"
EPA	A	"Human carcinogen"
IARC	1	"Carcinogenic to humans"
MAK	1	"Substances that cause cancer in man and can be assumed to make a significant contribution to cancer risk"
NTP	K	"Known to be a human carcinogen"

Table 5.3 Reported Human Health Effects of Benzene Exposure by Different Routes

	Route of Exposure		
Health Effect	**Inhalation**	**Oral (Food or Water)**	**Dermal**
Cancer	Leukemia(s) Lymphoma Chronic erythroid leukemia Chronic myeloid leukemia Acute myeloid leukemia	—	—
Respiratory	Respiratory irritation Respiratory arrest Pulmonary edema Pneumonia Dyspnea Tracheitis Laryngitis Bronchitis	Respiratory arrest	—
Cardiovascular/ Immunological/ Hematological	Anemia Lymphocytosis Thrombocytopenia Leukopenia Leukocytosis Macrocytosis Pancytopenia Cyanosis Hemolysis Organ hemorrhage Hypocellular to hypercellular bone marrow	Rapid heart rate	—
Gastrointestinal	Nausea Gastric irritation Congestive Gastritis	Vomiting Gastric irritation	—
Neurological/ Musculoskeletal	CNS depression Myelofibrosis Myalgia Dizziness Euphoria Headache Staggering gait Weakness Fatigue Convulsions Paralysis	CNS depression Dizziness Fatigue Convulsions	—
Reproductive	Irregular menstruation[a]	—	—
Developmental	—	—	—
Other	Anemia Cyanosis Hemolysis Organ hemorrhage Death	Coma Death	Skin, eye irritation Dermatitis Blurred vision Corneal damage

NOTE: This table presents a qualitative survey of reported human health effects associated with benzene exposure based on the Toxicological Profile for Benzene (ATSDR, 1997). The causal relationship between benzene and health effects is established more for some effects than for others; this table is intended to catalog possible health effects only.

[a] Limited, inconclusive evidence exists of reproductive effects such as ovarian atrophy and of development effects associated with benzene exposure.

Dioxins

Chlorinated dibenzo-p-dioxins are a group of about 75 compounds, often called "dioxins." These chemicals are produced from the incomplete combustion naturally — for example, during forest fires or volcanic activity. Most dioxins, however, come from human activities — such as the burning of fossil fuels (ATSDR, 1988). In general, dioxins are not purposefully manufactured but might occur as a contaminant in the manufacture of other chemicals.

2,3,7,8-tetrachlorodibenzo-p-dioxin (2,3,7,8-TCDD) is often used as a "prototype" dioxin when examining health effects, primarily because it is the most toxic. Other dioxins are reported to have half to one-tenth the toxicity of 2,3,7,8-TCDD (ATSDR, 1988). This toxicity difference between 2,3,7,8-TCDD and other dioxins is often called the Toxic Equivalent Factor. Dioxins also often coexist with other toxic chemicals such as PCBs. Thus, in occupational studies and environmental studies, human exposure to a mixture of chemicals occurs in most situations, rather than exposure to dioxins exclusively. Simultaneous exposure to dioxins and other potentially toxic compounds makes it difficult to establish a causal relationship between dioxins and specific health effects.

Anthropogenic sources of dioxin include waste incinerators, vehicle exhaust, and cigarette smoke (ATSDR, 1988). Dioxins attach themselves to very small particles (such as ash) that can stay airborne for days. Wastewater from the bleaching process used in pulp and paper mills contains dioxins and, when released, can contaminate other water sources. Dioxins can attach to microscopic plants and animals, and make their way up the food chain. Because animals are generally unable to metabolize dioxins, the concentrations of dioxins can increase in larger animals (called biomagnification). Because dioxins are formed during combustion, the fires at the WTC would have been expected to produce them throughout the weeks and months of burning. Seventeen compounds related to dioxins were measured at the WTC (EPA, 2002a).

Dioxins are contained in fish and milk products. Lower levels are found in fruits and vegetables. Most drinking water in the United States does not contain dioxins — at least at levels that are can be detected as parts per quadrillion (ppq). Once in the body, body fat and the liver store dioxins — often for many years. The half-life of dioxins in the body is between 7 and 12 years (ATSDR, 1988).

Routes of Exposure

Occupational exposure to dioxins usually occurs by inhalation of air contaminated with dioxins or by dermal contact with dioxin-containing materials (ATSDR, 1988). Occupational exposure is quite limited, occurring primarily in herbicide manufacture (Holmstedt, 1980). Persons employed in industries that produce chlorinated phenols or chlorinated pesticides or herbicides might be exposed to dioxins. Other occupations with possible exposure include those working with pressure treatment of wood with chlorinated phenols, chlorination of pulp and paper, or incineration of solid waste or hazardous waste. Emergency responders might be exposed to dioxins when fighting fires involving PCB transformers or capacitors. Veterans of the Vietnam War might have been exposed to dioxins as a result of aerial spraying

from 1962 to 1970 of 19 million gallons of herbicides, 11 million gallons of which were Agent Orange (Wolfe et al., 1985). Agent Orange is a 1:1 mixture of herbicides and diesel oil that contained, as a contaminant, less than 1–20 ppm 2,3,7,8-TCDD only.

Studies of Health Effects Associated with Dioxin Exposure

Numerous studies have been conducted on workers exposed to dioxins through the manufacture of herbicides, persons accidentally exposed in a residential setting, and veterans of the Vietnam War (ATSDR, 1998). From these studies, the primary health effects of dioxins are considered to be the following:

- Chloracne (Kimbrough et al., 1977; Moses et al., 1984; Reggiani, 1980). Chloracne is a serious skin condition characterized by disfiguring acne-like lesions that occur primarily on the face and upper body, but can occur elsewhere (ATSDR, 1988). Mild cases of chloracne might disappear shortly after exposure ends, while serious cases might persist for years.
- Other skin disorders, including hyperpigmentation and abnormal hair growth (Poland et al., 1971; Suskind and Hertzberg, 1984).
- Altered glucose metabolism and thyroid function (Henriksen et al., 1997) and liver abnormalities based on changes in blood and urine (Calvert et al., 1996).
- Neurological symptoms (Moses et al., 1984).
- Cancer (soft-tissue sarcoma, non-Hodgkin's lymphoma, and respiratory cancer) (Bertazzi et al., 1997; Eriksson et al., 1990).

These and other health effects are discussed further below.

Chloracne (follicular hyperkeratosis) is associated with dermal exposure to dioxin. This can be disfiguring and persist for 30 years (Crow, 1978). Varying degrees of chloracne were identified in almost all studies of dermal exposure reviewed by the ATSDR (1998), including those from herbicide exposure, exposure to Agent Orange, and industrial accidents. In addition, studies identifying acute, chronic, and intermediate exposure times all identified chloracne to be associated with dermal exposure.

Using Vietnam veterans exposed to Agent Orange (containing dioxins), a strong positive association with endocrine health effects was identified (Henriksen et al., 1997). This includes the incidence of diabetes and glucose metabolism abnormalities. This study used 989 exposed subjects and 1,276 controls, and controlled for age, race, and military occupation.

Dioxin exposure is associated with hepatic effects (Calvert et al., 1996). In most studies, no liver disease was identified, but lipid metabolism was affected (resulting in high HDL cholesterol and high triglyceride concentrations, for example). These effects are described as "mild," and for the most part, "transient" (ATSDR, 1988). Respiratory effects (bronchitis, laryngitis, and hemorrhagic pleuritis) have been reported following acute exposure to high levels of dioxins resulting from an industrial accident (Suskind and Hertzberg, 1984).

Numerous studies of herbicide exposure, exposure to Agent Orange, and industrial accidents have examined the carcinogenicity of dioxins. Most studies are limited because of the lack of exposure data

and adequate control of exposure to other potential carcinogens. The largest study included 21,863 workers exposed to herbicides (Kogevinas et al., 1997) and identified a significant increase in cancer deaths. Several other studies also found a significant increase in cancer risk (ATSDR, 1988). Although these risks are all low and evidence for site-specific cancers is lacking, it would appear that enough evidence exists for at least a presumptive association between dioxins and cancer.

Occupational Standards and Recommendations

OSHA and NIOSH have not set time-weighted averages or short-term exposure limits for dioxin compounds (Table 5.4). 2,3,7,8-TCDD, the most toxic dioxin compound, has been classified as a known human carcinogen by two health agencies (Table 5.5): IARC (Group 1) and NTP (Group K). These classifications are based on human studies linking dioxins to cancer.

Synthesis

Studies of workers exposed to dioxins in an industrial setting and of Vietnam veterans exposed to Agent Orange indicate that inhalation and dermal exposures lead to increased risk of chloracne and other dermatologic effects, endocrine effects, liver abnormalities, and cancer. Table 5.6 summarizes the health effects that have been observed in humans following exposure to dioxins.

OSHA and NIOSH have not set time-weighted averages or short-term exposure limits. Dioxins have been classified as known human carcinogens by two health agencies.

Table 5.4 Regulatory Standards and Recommendations for Occupational Exposure to Dioxins (2,3,7,8–Tetrachlorodibenzo-p-dioxin)

Regulatory Measure	Value
ACGIH TLV-TWA	No value listed
ACGIH TLV-STEL	No value listed
OSHA PEL-TWA	No value listed
OSHA PEL-STEL	No value listed
NIOSH REL-TWA	LFC
NIOSH REL-STEL	LFC
NIOSH IDLH	No value listed

SOURCE: ACGIH, 2002.
NOTE: See Willis et al. (forthcoming) for definitions of exposure limits.
LFC = lowest feasible concentration.

Table 5.5 Carcinogenicity Classifications for Dioxins (2,3,7,8–Tetrachlorodibenzo-p-dioxin)

Agency	Classification	
ACGIH	No value listed	
OSHA	No value listed	
NIOSH	Ca	"Potential occupational carcinogen, with no further categorization"
EPA	No value listed	
IARC	1	"Carcinogenic to Humans"
MAK	4	"Substances with carcinogenic potential for which genotoxicity plays no or at most a minor role"
NTP	K	"Known To Be A Human Carcinogen"

Table 5.6 Possible Human Health Effects Following Dioxin Exposure by "Mixed" Routes

Health Effect	Inhalation/Oral/Dermal
Cancer	Cancer (soft-tissue sarcoma, non-Hodgkin's lymphoma, and respiratory)
Respiratory	Bronchitis
	Laryngitis
	Hemorrhagic pleuritis
Cardiovascular	No known effect
Gastrointestinal	No known effect
Immunological	No known effect
Neurological	Lassitude
	Weakness
	Muscular pains
	Sleepiness
	Sleeplessness
	Increased perspiration
	Loss of appetite
	Headaches
	Mental disorders
	Sexual disorders
Reproductive	No known effect
Developmental	No known effect
Other	Chloracne
	Lipid metabolism
	Diabetes
	Glucose metabolism abnormalities

NOTE: This table presents a qualitative survey of reported human health effects associated with dioxin exposure based on the Toxicological Profile for Chlorinated Dibenzo-p-Dioxins (ATSDR, 1988). The causal relationship between dioxins and health effects is established more for some effects than for others. This table is intended to catalog *possible* health effects only.

Polychlorinated Biphenyls

Polychlorinated biphenyls are a group of synthetic organic chemical compounds referred to as PCBs. These chemicals were commercially produced as mixtures of individual chlorinated biphenyl compounds in the United States from about 1930 to 1977 under the trade name Aroclor, or by their chemical name chlorodiphenyl. Two common mixtures are chlorodiphenyl 42% and chlorodiphenyl 54%, which contain 42% and 54% chlorine by weight, respectively. The production of PCBs in the United States was discontinued in 1977 because of PCBs' tendency to build up in the environment without breaking down. PCBs do not occur naturally in the environment, but they continue to be released into the environment as a by-product of some manufacturing processes (ATSDR, 2000c).

PCBs do not burn easily, are chemically inert, and, therefore, are effective coolants and insulators. Because of these properties, they were commonly used in electrical equipment, such as transformers and capacitors. They are generally oily liquids or solids, but some PCBs are volatile and can become vapors. The ATSDR (2000c) lists many uses for PCBs: capacitors, transformers, hydraulic fluids, vacuum pumps, rubbers, synthetic resins, carbonless paper, adhesives, wax extenders, de-dusting agents, inks, cutting oils, pesticide extenders, and sealants.

In the early 1970s, when the WTC was constructed, PCBs were commonly used for many of the applications listed above. When the WTC collapsed, these PCB-containing products were crushed, burned, or pulverized, thereby releasing the PCBs into the post-collapse environment (EPA, 2002a).

Routes of Exposure

Because PCBs are found in air, water, and soil, humans are exposed by breathing contaminated air and eating contaminated food. PCBs are consumed by microscopic plants and animals, and make their way up the food chain. Because animals are generally unable to synthesize PCBs, their concentration can increase in larger animals (called biomagnification), especially seals and whales. Indeed, fish are a major dietary source of PCBs for humans, with concentrations of about 2 ppm. Dairy products and meat also contain PCBs, with concentrations of about 1 ppm (ATSDR, 2000c).

Studies of Health Effects Associated with PCB Exposure

Evaluating the health effects of PCBs is a challenge due to the fact that PCBs occur as mixtures of many compounds, and the studies, therefore, reflect effects of the mixtures rather than the individual compounds. Given this limitation, occupational studies and human consumption of contaminated food provide evidence supporting an association between PCBs and several health effects (ATSDR, 2000c).

The toxic effects of PCBs have been studied based on accidental exposure to PCBs that occurred following consumption of contaminated rice oil; these are known as the Yusho and Yu-Cheng poisoning incidents (World Health Organization et al., 1993). The observed effects consisted of the following:

- dermatologic effects, including skin irritation, chloracne, and discoloration of nails and skin (Kuratsune, 1989; Rogan, 1989)
- ocular abnormalities, including abnormal conjunctiva, swollen eyelids, and excessive secretions (Kuratsune, 1989; Rogan, 1989)
- swelling of arms and legs, enlarged liver, and liver dysfunction (Kuratsune, 1989)
- cognitive and behavioral abnormalities in offspring of those exposed (Chen et al., 1992)
- suppression of the immune system (Chang et al., 1981)
- liver cancer (Kuratsune et al., 1987).

Occupational studies have observed similar effects following chronic exposure in an industrial setting (World Health Organization et al., 1993), consisting of the following:

- skin conditions, including rashes, itching, burning, pigmentation of nails and skin, and chloracne (Fischbein et al., 1979; Cohen and Rice, 2001; Smith et al., 1982)
- liver toxicity, including increased serum levels of liver enzymes and possible liver damage in humans (Emmett et al., 1988b; Smith et al., 1982)
- irritation, watering, and burning of eyes (Emmett et al., 1988a; Smith et al., 1982)

- cancer of the liver, biliary tract, intestines, and skin (melanoma) (Bertazzi et al., 1987; Gustavsson and Hogstedt, 1997; Sinks et al., 1992).

The target organs for the toxicity of PCB exposure are considered to be the skin and liver (World Health Organization , 1993).

PCB exposure is associated with some hepatic effects. Liver enzyme abnormalities have been detected indicating liver damage (Kuratsune, 1989). These effects could not, however, be attributed solely to PCB exposure (ATSDR, 2000c). A consistent finding from animal studies is hepatotoxicity (ATSDR, 2000c). Other metabolic effects include elevation of serum cholesterol and triglycerides (Emmett, 1985).

Chloracne (follicular hyperkeratosis) is associated with dermal exposure to PCBs (Bertazzi et al., 1987). However, there appears to be a varied human dermal response to PCBs. The response seems to occur when high doses of PCBs are present, and no studies were identified identifying chloracne associated with consumption of PCBs in foods (e.g., Great Lakes fish contaminated with PCBs) (ATSDR, 2000c).

Numerous studies have examined the carcinogenicity of PCBs. The ATSDR report (2000c) concludes, "the human studies provide some evidence that PCBs are carcinogenic." In addition, a strong association with cancer is found in animal studies. Occupational exposure and environmental exposure studies have shown an increased risk of liver, biliary tract, intestine, and skin cancers. Probably the most significant is the retrospective study of approximately 1,700 patients from the Yusho incident (Kuratsune et al., 1987).

Occupational Standards and Recommendations

OSHA workplace standards for chlorodiphenyl require that air concentrations of chlorodiphenyl 42% and chlorodiphenyl 54% not exceed time-weighted average concentrations of 1 mg/m^3 and 0.5 mg/m^3, respectively, assuming exposures of eight hours per day for a 40-hour workweek (OSHA PEL-TWA) (Table 5.7). NIOSH recommends air concentrations of chlorodiphenyl 42% and chlorodiphenyl 54% not exceed a time-weighted average concentration of 0.001 mg/m^3, assuming exposures of up to a 10-hour workday during a 40-hour workweek (NIOSH REL-TWA). NIOSH has set an IDLH level of 5 mg/m^3 for chlorodiphenyl 42% and chlorodiphenyl 54%. These limits are protective of effects on the liver, as well as skin irritation and chloracne (ACGIH, 2002). Chlorodiphenyl 42% and chlorodiphenyl 54% have been classified as a possible or probable human carcinogen by several agencies (Table 5.8), including EPA (Group B2), IARC (Group 2A), MAK (Group 3B), and NTP (Group R). These classifications are based on animal data linking chlorodiphenyl 42% and chlorodiphenyl 54% to cancer.

Synthesis

Studies of workers and persons who accidentally ingested PCBs have established that exposure to PCBs over short and long periods leads to effects on multiple organ systems. Effects on the skin and the liver are most pronounced. Table 5.9 summarizes the health effects that have been observed in humans following inhalation, oral, and dermal exposure to PCBs.

The OSHA PEL-TWA for air concentrations of chlorodiphenyl 42% and chlorodiphenyl 54% in an occupational setting are 1 mg/m^3 and 0.5 mg/m^3, respectively. These exposure limits are protective of

skin irritation, chloracne, and effects on the liver (ACGIH, 2002). PCBs have been classified as an animal carcinogen and a probable human carcinogen by several agencies.

Table 5.7 Regulatory Standards and Recommendations for Occupational Exposure to Polychlorinated Biphenyls (Chlorodiphenyl)[a] in Air

Regulatory Measure	Chlorodiphenyl 42%	Chlorodiphenyl 54%
ACGIH TLV-TWA	1 mg/m^3 (skin)	0.5 mg/m^3 (skin)
ACGIH TLV-STEL	No value (skin)	No value (skin)
OSHA PEL-TWA	1 mg/m^3 (skin)	0.5 mg/m^3 (skin)
OSHA PEL-STEL	No value (skin)	No value (skin)
NIOSH REL-TWA	0.001 mg/m^3	0.001 mg/m^3
NIOSH REL-STEL	No value listed	No value listed
NIOSH IDLH	5 mg/m^3	5 mg/m^3

SOURCE: ACGIH, 2002.

NOTE: See Willis et al. (forthcoming) for definitions of exposure limits.

[a] According to the ACGIH manual, the synonym for polychlorinated biphenyls is chlorodiphenyls. They are listed as 2 categories, 42% chlorine and 54% chlorine.

Skin = danger of cutaneous absorption.

Table 5.8 Carcinogenicity Classifications for Polychlorinated Biphenyls (Chlorodiphenyl)

Agency	Polychlorinated Biphenyls	Chlorodiphenyl 42%	Chlorodiphenyl 54%
ACGIH	No value listed	No value listed	A3 "Confirmed Animal Carcinogen with Unknown Relevance to Humans"
OSHA	No value listed	No value listed	No value listed
NIOSH	No value listed	Ca "Potential occupational carcinogen, with no further categorization"	Ca "Potential occupational carcinogen, with no further categorization"
EPA	B2 "Sufficient evidence from animal studies; inadequate evidence or no data from epidemiologic studies"	B2 "Sufficient evidence from animal studies; inadequate evidence or no data from epidemiologic studies"	B2 "Sufficient evidence from animal studies; inadequate evidence or no data from epidemiologic studies"
IARC	2A "Probably Carcinogenic to Humans"	2A "Probably Carcinogenic to Humans"	2A "Probably Carcinogenic to Humans"
MAK	No value listed	3B "Substances for which in vitro tests or animal studies have yielded evidence of carcinogenic effects that is not sufficient for classification of the substance in one of the other categories"	3B "Substances for which in vitro tests or animal studies have yielded evidence of carcinogenic effects that is not sufficient for classification of the substance in one of the other categories"
NTP	R "Reasonably Anticipated To Be A Human Carcinogen"	R "Reasonably Anticipated To Be A Human Carcinogen"	R "Reasonably Anticipated To Be A Human Carcinogen"

Table 5.9 Reported Human Health Effects of Polychlorinated Biphenyl Exposure by Different Routes

	Route of Exposure		
Health Effect	**Inhalation**	**Oral**	**Dermal**
Cancer	Liver[C] Biliary tract[C] Intestine[C] Skin[C]	Liver[A,C] Biliary tract[A,C] Intestine[A,C] Skin[A,C]	No known effect
Respiratory	Chest pain[C]	Respiratory infections [A] Persistent cough[A] Chronic bronchitis [A]	No known effect
Cardiovascular	No known effect	Hypertension [C]	No known effect
Gastrointestinal	Loss of appetite[C] Anorexia [C] Nausea [C]	Vomiting [A] Abdominal pain [A]	No known effect
Immunological	No known effect	No known effect	No known effect
Neurological	No known effect	No known effect	No known effect
Reproductive	No known effect	No known effect	No known effect
Developmental	No known effect	No known effect	No known effect
Other	Liver enzyme abnormalities[C] Chloracne[I,C]	Liver enzyme abnormalities[A] Elevated serum cholesterol[A,C] Elevated triglycerides[A,C]	Chloracne [A,C]

NOTE: This table presents a qualitative survey of reported human health effects associated with PCB exposure based on the Toxicological Profile for Polychlorinated Biphenyls (ATSDR, 2000c). The causal relationship between PCBs and health effects is established more for some effects than for others. This table is intended to catalog *possible* health effects only.

[A] Listed as an effect of acute exposure in ATSDR (2000c).

[I] Listed as an effect of intermediate exposure in ATSDR (2000c).

[C] Listed as an effect of chronic exposure in ATSDR (2000c).

Polycyclic Aromatic Hydrocarbons

Polycyclic aromatic hydrocarbons are compounds formed during incomplete burning of organic substances such as gas, wood, coal, and oil. PAHs are a group of approximately 100 chemicals. PAHs generally occur as a mixture of these chemicals and are seldom found as single compounds (ATSDR, 1995). Most studies of the health effects of PAHs have considered mixtures of PAHs rather than a single compound. This summary contains occupational standards for two of the PAH compounds, chrysene and benzo[a]pyrene. Although chrysene and benzo[a]pyrene might be more harmful to human health than other PAHs, their effects can be considered representative of the effects of other PAHs.

PAHs encountered by the general population arise primarily from natural sources, such as forest fires, and man-made sources, such as vehicle emissions and cigarette smoke. PAHs exist in the air as vapors or attached to small particles. In general, PAHs are not readily water soluble (ATSDR, 1995). Ambient levels of PAHs in the air in urban areas are around 0.15–19.3 ng/m^3 and 0.02–1.2 ng/m^3 in rural areas. Ambient levels of PAHs in drinking water are around 4–24 ng/L.

PAHs are also found in occupational settings such as manufacturing plants that produce coal tar, bitumen, asphalt, and aluminum (ATSDR, 1995). Other industries that use PAH-containing products include mining, oil refining, metalworking, transportation, and petroleum. Because PAHs are typically not readily biodegradable or soluble in water, they are well suited for waterproofing and asphalt applications. PAHs are produced as a by-product of burning jet fuel and combustion of other materials and, therefore, might have been present after the WTC collapse.

Routes of Exposure

Humans can be exposed to PAHs by breathing air that contains PAH vapor or particles contaminated with one or more PAH compounds. Exposure to PAHs might also occur by ingesting contaminated food and water or by dermal contact with PAH-containing solids (e.g., contaminated soil) or liquids (e.g., creosote).

Studies of Health Effects Associated with PAH Exposure

Acute exposure to high levels of PAHs can result in cough, throat irritation, chest irritation, chest pains, breathing problems, bloody vomit, or significant decrements in ventilatory function (Gupta et al., 1993).

Evidence exists from human and animal studies to support the carcinogenicity of PAHs following chronic exposure to lower levels of PAHs. Occupational studies of workers have observed the following effects of PAH mixtures:

- increased lung cancer mortality rates among workers exposed to coke-oven emissions (Lloyd, 1971; Mazumdar et al., 1975; Redmond et al., 1976) and roofing-tar emissions (Hammond et al., 1976)
- decreased levels of serum immunoglobins and among coke-oven workers (Szczeklik et al., 1994)
- increased risk of scrotal cancer among chimney sweeps exposed to high levels of PAH-containing soot (Pott, 1973)
- skin disorders following dermal exposure to PAH mixtures, including warts, blisters, disseminated pigment discolorations, ulcers, and cutaneous and muscular atrophy (Cottini and Mazzone, 1939)
- skin cancer among shale workers from dermal exposure (Purde and Etlin, 1980).

Occupational Standards

Workplace standards set by OSHA require that air concentrations of chrysene and benzo[a]pyrene in occupational settings not exceed a time-weighted average concentration of 0.2 mg/m^3, assuming exposures of eight hours per day for a 40-hour workweek (OSHA PEL-TWA). NIOSH recommends air concentrations of chrysene and benzo[a]pyrene not exceed a time-weighted average concentration of 0.1 mg/m^3, assuming exposures of up to a ten-hour workday during a 40-hour workweek (NIOSH REL-TWA) (Table 5.10). These limits are based on the avoidance of skin effects (chrysene) and cancer (benzo[a]pyrene)(ACGIH, 2002). Chrysene has been classified as a probable human carcinogen by several

agencies (Table 5.11), including EPA (Group B2), IARC (Group 3), and MAK (Group 2). Benzo[a]pyrene has also been classified as a probable human carcinogen by several agencies (Table 5.11), including EPA (Group B2), IARC (Group 2A), MAK (Group 2), and NTP (Group R). These classifications are based on data from animal studies linking these compounds to cancer.

Synthesis

Studies of workers exposed to PAH-containing emissions in the coke and roofing-tar industries suggest that inhalation of such emissions has led to increased risk of mortality due to lung cancer. In addition, various skin disorders, including skin cancer, have been observed following repeated dermal exposure to PAHs. Table 5.12 summarizes the health effects that have been observed in humans following inhalation, oral, and dermal exposure to PAHs.

The OSHA PEL-TWA for air concentration of chrysene and benzo[a]pyrene in an occupational setting is 0.2 mg/m^3. This exposure limit is based on the avoidance of skin effects (chrysene) and avoidance of cancer (benzo[a]pyrene)(ACGIH, 2002). Chrysene and benzo[a]pyrene have been classified as possible human carcinogens by several agencies.

Table 5.10 Regulatory Standards and Recommendations for Occupational Exposure to Selected Polycyclic Aromatic Hydrocarbons in Air

Regulatory Measure	Chrysene	Benzo[a]pyrene
ACGIH TLV-TWA	No value listed; (L)[a]	No value listed; (L)[a]
ACGIH TLV-STEL	No value listed; (L)	No value listed; (L)
OSHA PEL-TWA	0.2 mg/m^3	0.2 mg/m^3
OSHA PEL-STEL	No value listed	No value listed
NIOSH REL-TWA	0.1 mg/m^3 (LFC)	0.1 mg/m^3
NIOSH REL-STEL	No value listed (LFC)	No value listed
NIOSH IDLH	Substance not listed	Substance not listed

SOURCE: ACGIH, 2002.
NOTE: See Willis et al. (forthcoming) for definitions of exposure limits.
[a] Exposure by all routes should be carefully controlled to levels as low as possible.
LFC = lowest feasible concentration.

Table 5.11 Carcinogenicity Classifications for Chrysene and Benzo[a]pyrene

Agency	Chrysene		Benzo[a]pyrene	
ACGIH	A3	"Confirmed Animal Carcinogen with Unknown Relevance to Humans"	A2	"Suspected Human Carcinogen"
OSHA	No value listed		No value listed	
NIOSH	Ca	"Potential occupational carcinogen, with no further categorization"	Ca	"Potential occupational carcinogen, with no further categorization"
EPA	B2	"Probably Human Carcinogen, Sufficient evidence from animal studies; inadequate evidence or no data from epidemiologic studies"	B2	"Probably Human Carcinogen, Sufficient evidence from animal studies; inadequate evidence or no data from epidemiologic studies"
IARC	3	"Unclassifiable as to the Carcinogenicity in Humans"	2A	"Probably Carcinogenic to Humans"
MAK	2	"Substances that are considered to be carcinogenic for man because sufficient data from long-term animal studies or limited evidence from animal studies substantiated by evidence from epidemiological studies indicate that they can make a significant contribution to cancer risk"	2	"Substances that are considered to be carcinogenic for man because sufficient data from long-term animal studies or limited evidence from animal studies substantiated by evidence from epidemiological studies indicate that they can make a significant contribution to cancer risk"
NTP	No value listed		R	"Reasonably Anticipated To Be A Human Carcinogen"

Table 5.12 Reported Health Effects of Polycyclic Aromatic Hydrocarbon Exposure by Different Routes

	Route of Exposure		
		Oral	
Health Effect	**Inhalation**	**(Via Drinking Water and Food)**	**Dermal**
Cancer	Lung (possible)[C]	No known effects	Skin (possible)[C] Scrotal[C]
Respiratory	Cough[NS] Throat irritation[NS] Chest irritation [NS] Chest pains[NS] Breathing problems[NS] Decreased respiratory function[NS]	No known effect	No known effect
Cardiovascular	No known effect	No known effect	No known effect
Gastrointestinal	No known effect	No known effect	No known effect
Immunological	No known effect	No known effect	No known effect
Neurological	No known effect	No known effect	No known effect
Reproductive	No known effect	No known effect	No known effect
Developmental	No known effect	No known effect	No known effect
Other	None	None	Warts[NS] Blisters[NS] Disseminated pigment discolorations[NS] Ulcers[NS] Cutaneous atrophy [NS] Muscular atrophy[NS]

NOTE: This table presents a qualitative survey of reported human health effects associated with polycyclic aromatic hydrocarbon exposure based on the Toxicological Profile for Polycyclic Aromatic Hydrocarbons (ATSDR, 1995). The causal relationship between polycyclic aromatic hydrocarbons and health effects is established more for some effects than for others; this table is intended to catalog possible health effects only.

[A] Listed as an effect of acute exposure in ATSDR (1995).

[I] Listed as an effect of intermediate exposure in ATSDR (1995).

[C] Listed as an effect of chronic exposure in ATSDR (1995).

[NS] Listed as unknown exposure time in ATSDR (1995).

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