Appendix
HAP Profiles

OVERVIEW

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

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

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

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

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

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ACETALDEHYDE
75-07-0

Hazard Summary

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

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

Physical Properties

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

Uses

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

Sources and Potential Exposure

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

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

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

Assessing Personal Exposure

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

Health Hazard Information

Acute Effects:

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

Chronic Effects (Noncancer):

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

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

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

Reproductive/Developmental Effects:

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

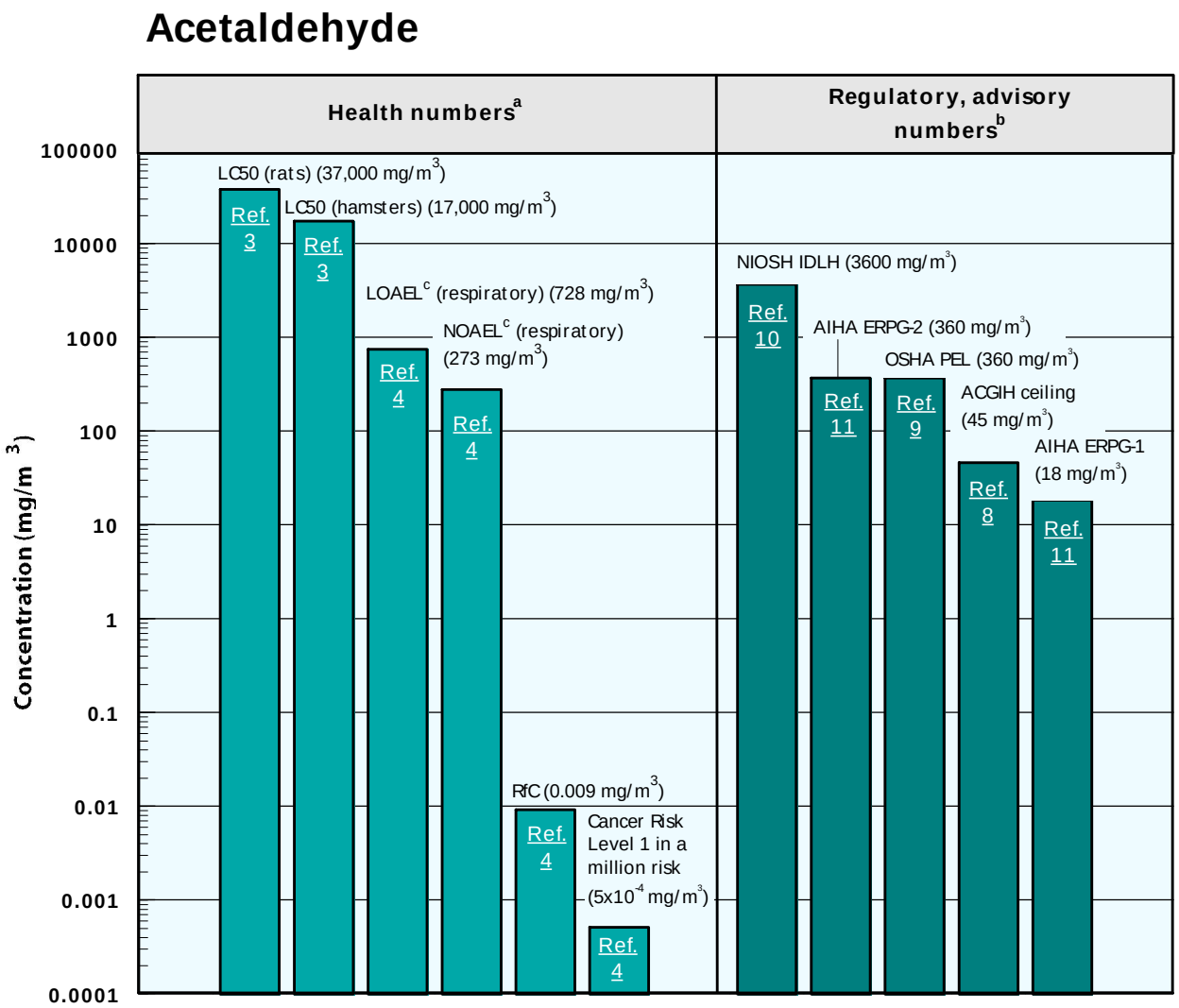
Cancer Risk:

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

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45).
For acetaldehyde: 1 ppm = 1.8 mg/m^3.
To convert from µg/m^3 to mg/m^3: mg/m^3 = (µg/m^3) x (1 mg/1,000 µg).

Health Data from Inhalation Exposure



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

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

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

References

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

2. M. Sittig. *Handbook of Toxic and Hazardous Chemicals and Carcinogens*. 2nd ed. Noyes Publications, Park Ridge, NJ. 1985.

3. U.S. Department of Health and Human Services. Registry of Toxic Effects of Chemical Substances (RTECS, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.

4. U.S. Environmental Protection Agency (EPA). *Integrated Risk Information System (IRIS) on Acetaldehyde*. National Center for Environmental Assessment, Office of Research and Development, Washington, D.C. 1999.

5. *The Merck Index. An Encyclopedia of Chemicals, Drugs, and Biologicals*. 11th ed. Ed. S. Budavari. Merck and Co. Inc., Rahway, NJ. 1989.

6. International Agency for Research on Cancer (IARC). *IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans: Allyl Compounds, Aldehydes, Epoxides and Peroxides*. Volume 36. World Health Organization, Lyon. 1985.

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

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

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

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

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

ACROLEIN
107-02-8

Hazard Summary

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

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

Physical Properties

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

Uses

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

Sources and Potential Exposure

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

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

Assessing Personal Exposure

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

Health Hazard Information

Acute Effects:

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

Chronic Effects (Noncancer):

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

Reproductive/Developmental Effects:

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

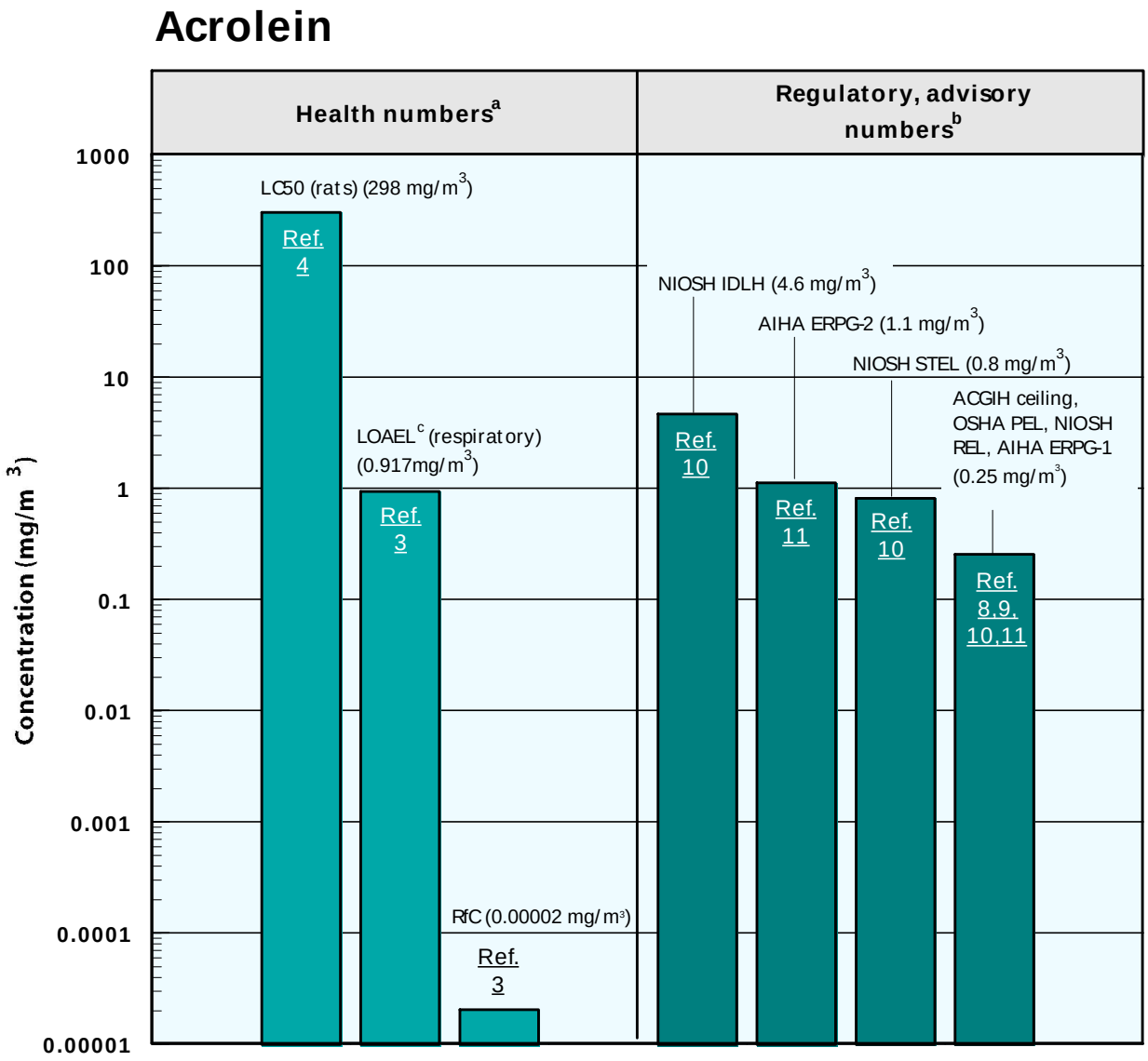
Cancer Risk:

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

Conversion Factors:

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

Health Data from Inhalation Exposure



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

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

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

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

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

References

1. Agency for Toxic Substances and Disease Registry (ATSDR). *Toxicological Profile for Acrolein*. Public Health Service, U.S. Department of Health and Human Services, Atlanta, GA. 1990.

2. U.S. Department of Health and Human Services. Hazardous Substances Data Bank (HSDB, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.

3. U.S. Environmental Protection Agency (EPA). *Integrated Risk Information System (IRIS) on Acrolein*. National Center for Environmental Assessment, Office of Research and Development, Washington, D.C. 1999.

4. U.S. Department of Health and Human Services. Registry of Toxic Effects of Chemical Substances (RTECS). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.

5. E.J. Calabrese and E.M. Kenyon. *Air Toxics and Risk Assessment*. Lewis Publishers, Chelsea, MI. 1991.

6. U.S. Environmental Protection Agency (EPA). *Health Effects Assessment Summary Tables. FY 1997 Update*. Solid Waste and Emergency Response, Office of Emergency and Remedial Response, Cincinnati, OH. EPA/540/R-97-036. 1997.

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

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

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

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

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

ACRYLONITRILE
107-13-1

Hazard Summary

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

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

Physical Properties

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

Uses

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

Sources and Potential Exposure

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

Assessing Personal Exposure

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

Health Hazard Information

Acute Effects:

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

Chronic Effects (Noncancer):

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

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

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

Reproductive/Developmental Effects:

! No information is available on the reproductive or developmental effects of acrylonitrile in humans.

! Fetal malformations (including short tail, missing vertebrae, short trunk, omphalocele, and hemivertebra) have been reported in rats exposed to acrylonitrile by inhalation. (1,4)

! In mice orally exposed to acrylonitrile, degenerative changes in testicular tubules and decreased sperm count were observed. (1)

Cancer Risk:

! A statistically significant increase in the incidence of lung cancer has been reported in several studies of chronically exposed workers. However, some of these studies contain deficiencies such as lack of exposure information, short follow-up, and confounding factors. (1,4,6,8)

! In several studies, an increased incidence of tumors has been observed in rats exposed by inhalation, drinking water, and gavage. Astrocytomas in the brain and spinal cord and tumors of the Zymbal gland (in the ear canal) have been most frequently reported, as well as tumors of the stomach, tongue, small intestine, and mammary gland (in females). (1-4,6,8)

! EPA has classified acrylonitrile as a Group B1, probable human carcinogen. (4)

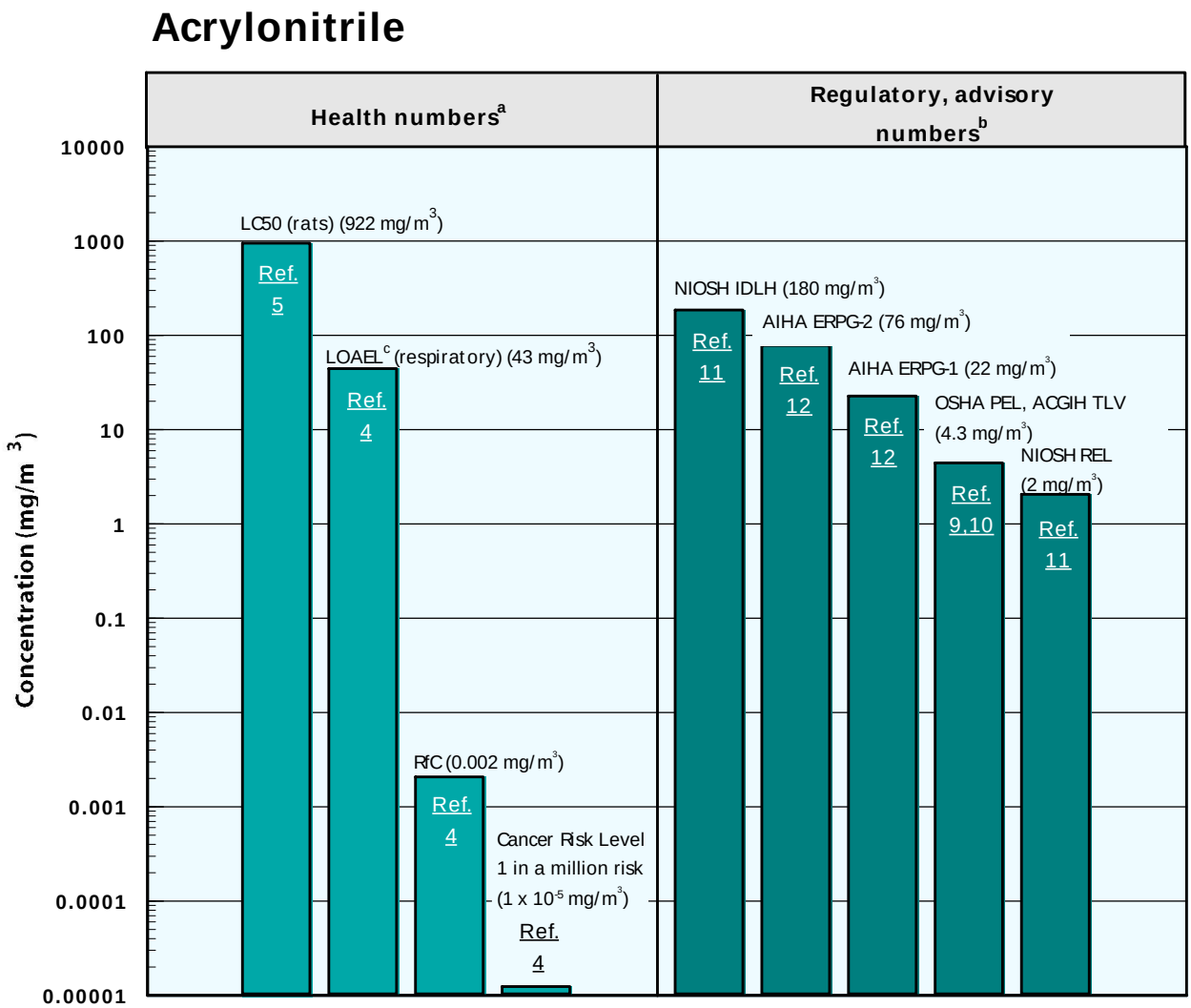
! EPA uses mathematical models, based on human and animal studies, to estimate the probability of a person developing cancer from breathing air containing a specified concentration of a chemical. EPA calculated an inhalation unit risk estimate of 6.8×10^{-5} $(\mu g/m^3)^{-1}$. EPA estimates that, if an individual were to continuously breathe air containing acrylonitrile at an average of 0.01 $\mu g/m^3$ (1×10^{-5} mg/m^3), over his or her entire lifetime, that person would theoretically have no more than a one-in-a-million increased chance of developing cancer as a direct result of breathing air containing this chemical. Similarly, EPA estimates that breathing air containing 0.1 $\mu g/m^3$ (1×10^{-4} mg/m^3) would result in not greater than a one-in-a-hundred thousand increased chance of developing cancer, and air containing 1.0 $\mu g/m^3$ (1×10^{-3} mg/m^3) would result in not greater than a one-in-ten thousand increased chance of developing cancer. For a detailed discussion of confidence in the potency estimates, please see IRIS. (4)

! EPA has calculated an oral cancer slope factor of 0.54 $(mg/kg/d)^{-1}$. (4)

Conversion Factors:

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

Health Data from Inhalation Exposure



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

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

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

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

References

1. Agency for Toxic Substances and Disease Registry (ATSDR). *Toxicological Profile for Acrylonitrile*. Public Health Service, U.S. Department of Health and Human Services, Atlanta, GA. 1990.

2. International Agency for Research on Cancer (IARC). *IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans: Some Monomers, Plastics and Synthetic Elastomers, and Acrolein*. Volume 19. World Health Organization, Lyon. 1979.

3. U.S. Environmental Protection Agency (EPA). *Health Assessment Document for Acrylonitrile* (Revised Draft). EPA/600/8-82-007. Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment, Office of Research and Development, Research Triangle Park, NC. 1982.

4. U.S. Environmental Protection Agency (EPA). *Integrated Risk Information System (IRIS) on Acrylonitrile*, National Center for Environmental Assessment, Office of Research and Development, Washington, D.C. 1999.

5. U.S. Department of Health and Human Services. Registry of Toxic Effects of Chemical Substances (RTECS, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.

6. U.S. Environmental Protection Agency (EPA). *Health Effects Assessment for Acrylonitrile*. EPA/600/8-88/014. Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment, Office of Research and Development, Cincinnati, OH. 1988.

7. U.S. Environmental Protection Agency (EPA). *Health Effects Assessment Summary Tables. FY 1997 Update.* Solid Waste and Emergency Response, Office of Emergency and Remedial Response, Cincinnati, OH. EPA/540/R-97-036. 1997.

8. U.S. Environmental Protection Agency (EPA). *Health and Environmental Effects Profile for Acrylonitrile*. EPA/600/x-85/372. Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment, Office of Research and Development, Cincinnati, OH. 1985.

9. Occupational Safety and Health Administration (OSHA). Occupational Safety and Health Standards, Toxic and Hazardous Substances. *Code of Federal Regulations*. 29 CFR 1910.1045. 1998.

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

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

12. American Industrial Hygiene Association (AIHA). *The AIHA1998 Emergency Response Planning Guidelines and Workplace Environmental Exposure Level Guides Handbook.* 1998.

ARSENIC COMPOUNDS[1]

107-02-8

Hazard Summary

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

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

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

Physical Properties

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

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

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

Uses

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

Sources and Potential Exposure

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

Assessing Personal Exposure

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

Health Hazard Information

Acute Effects:

Inorganic Arsenic

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

Arsine

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

Chronic Effects (Noncancer):

Inorganic arsenic

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

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

Arsine

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

Reproductive/Developmental Effects:

Inorganic arsenic

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

Arsine

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

Cancer Risk:

Inorganic arsenic

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

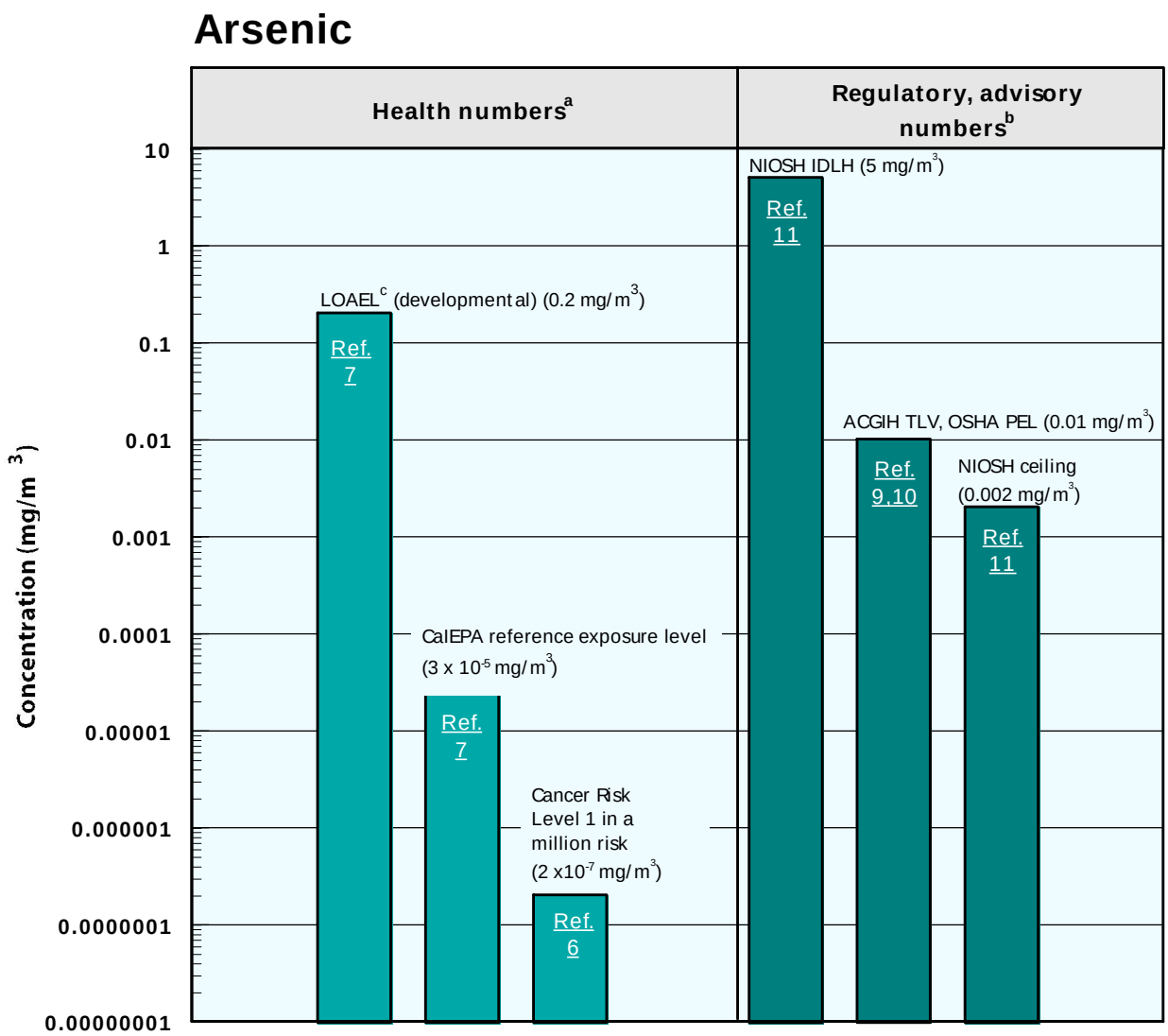
Arsine

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

Conversion Factors:

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

Health Data from Inhalation Exposure (Inorganic Arsenic)



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

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

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

References

1. Agency for Toxic Substances and Disease Registry (ATSDR). *Toxicological Profile for Arsenic* (Draft). U.S. Public Health Service, U.S. Department of Health and Human Services, Atlanta, GA. 1998.

2. Agency for Toxic Substances and Disease Registry (ATSDR). *Case Studies in Environmental Medicine. Arsenic Toxicity.* U.S. Public Health Service, U.S. Department of Health and Human Services, Atlanta, GA. 1990.

3. U.S. Environmental Protection Agency (EPA). *Health Assessment Document for Inorganic Arsenic*. EPA/540/1-86/020. Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment, Office of Research and Development, Washington, DC. 1984.

4. U.S. Environmental Protection Agency (EPA). *Integrated Risk Information System (IRIS) on Arsine*. National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1999.

5. U.S. Department of Health and Human Services. Registry of Toxic Effects of Chemical Substances (RTECS, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.

6. U.S. Environmental Protection Agency (EPA). *Integrated Risk Information System (IRIS) on Arsenic*. National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1999

7. California Environmental Protection Agency (CalEPA). *Technical Support Document for the Determination of Noncancer Chronic Reference Exposure Levels. Draft for Public Comment.* Office of Environmental Health Hazard Assessment, Berkeley, CA. 1997.

8. M. Windolz. *The Merck Index, An Encyclopedia of Chemicals, Drugs, and Biologicals*. 10th ed. Merck and Co., Rahway, NJ. 1983.

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

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

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

BENZENE
71-43-2

Hazard Summary

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

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

Physical Properties

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

Uses

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

Sources and Potential Exposure

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

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

Assessing Personal Exposure

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

Health Hazard Information

Acute Effects:

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

Chronic Effects (Noncancer):

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

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

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

Reproductive/Developmental Effects:

- Several occupational studies suggest that benzene may impair fertility in women exposed to high levels. However, these studies are limited due to lack of exposure history, simultaneous exposure to other substances, and lack of follow-up. (1)
- Available human data on the developmental effects of benzene are inconclusive due to concomitant exposure to other chemicals, inadequate sample size, and lack of quantitative exposure data. (1)
- Adverse effects on the fetus, including low birth weight, delayed bone formation, and bone marrow damage, have been observed where pregnant animals were exposed to benzene by inhalation. (1)

Cancer Risk:

- Increased incidence of leukemia has been observed in humans occupationally exposed to benzene. (1,4)
- EPA has classified benzene as a Group A, known human carcinogen. (4)
- EPA uses mathematical models, based on human and animal studies, to estimate the probability of a person developing cancer from breathing air containing a specified concentration of a chemical. EPA calculated a range of 2.2×10^{-6} to 7.8×10^{-6} as the increase in the lifetime risk of an individual who is continuously exposed to 1 $\mu g/m^3$ of benzene in the air over their lifetime. EPA estimates that, if an individual were to continuously breathe air containing benzene at an average of 0.13 to 0.45 $\mu g/m^3$ (1.3×10^{-4} to 4.5×10^{-4} mg/m^3) over his or her entire lifetime, that person would theoretically have no more than a one-in-a-million increased chance of developing cancer as a direct result of continuously breathing air containing this chemical. Similarly, EPA estimates that continuously breathing air containing 1.3 to 4.5 $\mu g/m^3$ (1.3×10^{-3} to 4.5×10^{-3} mg/m^3) would result in not greater than a one-in-a-hundred thousand increased chance of developing cancer, and air containing 13 to 45 $\mu g/m^3$ (1.3×10^{-2} to 4.5×10^{-2} mg/m^3) would result in not greater than a one-in-ten thousand increased chance of developing

cancer. For a detailed discussion of confidence in the potency estimates, please see IRIS. (4)

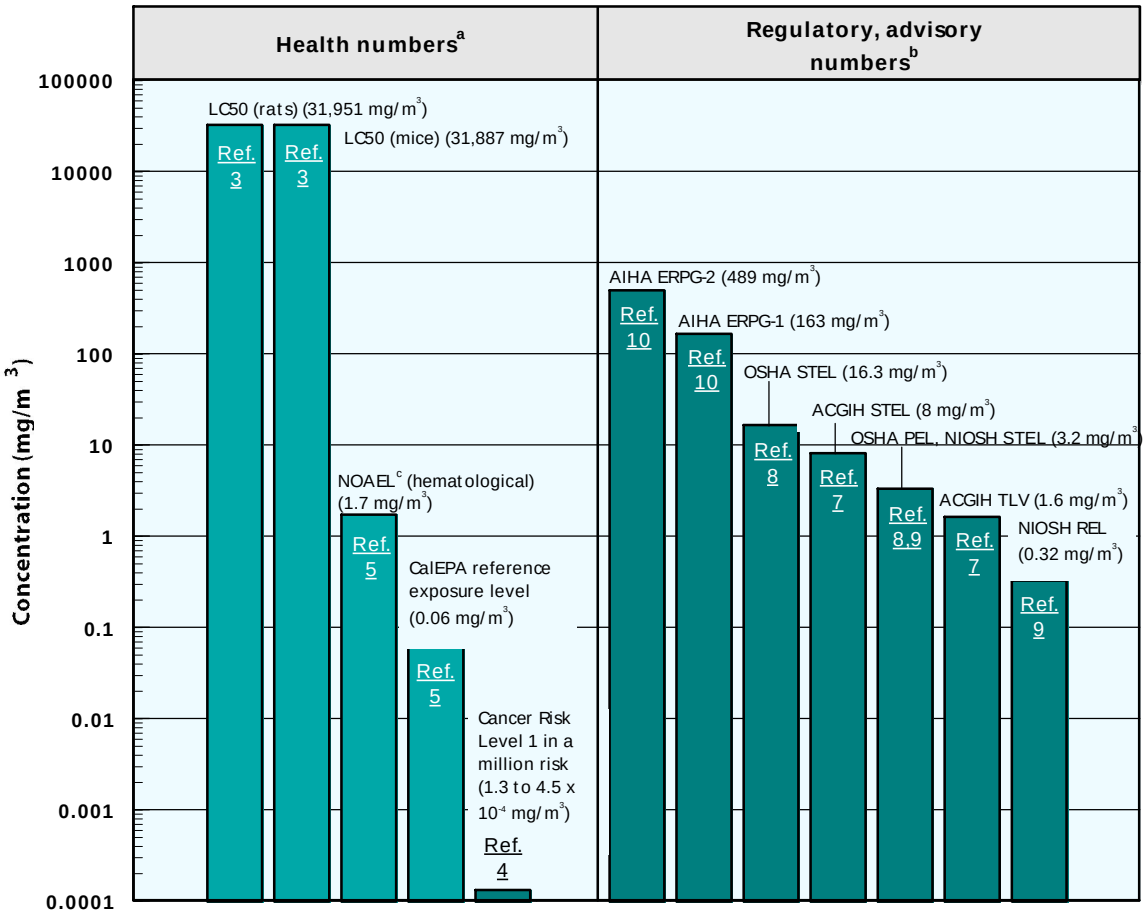
! EPA has calculated an oral cancer slope factor of 2.9 x 10^{-2} $(mg/kg/d)^{-1}$. (4)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45).
For benzene: 1 ppm = 3.26 mg/m^3.
To convert from µg/m^3 to mg/m^3: mg/m^3 = (µg/m^3) x (1 mg/1,000 µg).

Health Data from Inhalation Exposure

Benzene



ACGIH STEL – American Conference of Governmental and Industrial Hygienists' short-term exposure limit.
ACGIH TLV – American Conference of Governmental and Industrial Hygienists' threshold limit value expressed as a time-weighted average; the concentration of a substance to which most

workers can be exposed without adverse effects.
AIHA ERPG – American Industrial Hygiene Association's emergency response planning guidelines. ERPG 1 is the maximum airborne concentration below which it is believed nearly all individuals could be exposed up to one hour without experiencing other than mild transient adverse health effects or perceiving a clearly defined objectionable odor; ERPG 2 is the maximum airborne concentration below which it is believed nearly all individuals could be exposed up to one hour without experiencing or developing irreversible or other serious health effects that could impair their abilities to take protective action.
LC_{50} (Lethal Concentration$_{50}$) – A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.
NIOSH REL – National Institute of Occupational Safety and Health's recommended exposure limit; NIOSH-recommended exposure limit for an 8- or 10-h time-weighted-average exposure and/or ceiling.
NIOSH STEL – NIOSH's short-term exposure limit; NIOSH recommended exposure limit for a 15-minute period.
NOAEL – No-observed-adverse-effect level.
OSHA PEL – Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.
OSHA STEL – Occupational Safety and Health Administration's short-term exposure limit.

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

References

1. Agency for Toxic Substances and Disease Registry (ATSDR). *Toxicological Profile for Benzene* (Update). Public Health Service, U.S. Department of Health and Human Services, Atlanta, GA. 1997.

2. M. Sittig. *Handbook of Toxic and Hazardous Chemicals and Carcinogens*. 2nd ed. Noyes Publications, Park Ridge, NJ. 1985.

3. U.S. Department of Health and Human Services. Registry of Toxic Effects of Chemical Substances (RTECS, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.

4. U.S. Environmental Protection Agency (EPA). *Integrated Risk Information System (IRIS) on Benzene*. National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1999.

5. California Environmental Protection Agency (CalEPA). *Air Toxics Hot Spots Program Risk Assessment Guidelines: Part III. Technical Support Document for the Determination of Noncancer Chronic Reference Exposure Levels. SRP Draft.* Office of Environmental Health Hazard Assessment, Berkeley, CA. 1999.

6. *The Merck Index. An Encyclopedia of Chemicals, Drugs, and Biologicals*. 11th ed. Ed. S. Budavari. Merck and Co. Inc., Rahway, NJ. 1989.

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

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

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

10. American Industrial Hygiene Association (AIHA). *The AIHA1998 Emergency Response Planning Guidelines and Workplace Environmental Exposure Level Guides Handbook*. 1998.

BERYLLIUM COMPOUNDS[1]

107-02-8

Hazard Summary

Inhalation exposure to beryllium primarily occurs in the workplaces where it is mined, processed, or converted into alloys and chemicals, or from the burning of coal or fuel oil and in tobacco smoke. Acute (short-term) inhalation exposure to high levels of beryllium has been observed to cause inflammation of the lungs or acute pneumonitis (reddening and swelling of the lungs) in humans; after exposure ends, these symptoms may be reversible. Chronic (long-term) inhalation exposure of humans to beryllium has been reported to cause chronic beryllium disease (berylliosis), in which granulomatous lesions (noncancerous) develop in the lung. Inadequate information is available on the reproductive or developmental effects of beryllium in humans or animals following inhalation exposure. Inhalation exposure to beryllium has been demonstrated to cause lung cancer in rats and monkeys. Human epidemiology studies are limited, but suggest a causal relationship between beryllium exposure and an increased risk of lung cancer. The U.S. Environmental Protection Agency (EPA) has classified beryllium as a Group B1, probable human carcinogen.

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

Physical Properties

- The chemical symbol for pure beryllium is Be, and its atomic weight is 9.012 g/mol. (1)
- Pure beryllium is a hard gray metal that does not occur naturally but does occur as a chemical component of certain kinds of rocks, coal and oil, soil, and volcanic dust. (1)
- Beryllium is also present in a variety of compounds such as beryllium fluoride, beryllium chloride, beryllium sulfate, beryllium oxide, and beryllium phosphate. (1)
- Pure beryllium is insoluble in water; however, some of its compounds are soluble in water. (1)

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[1] This fact sheet discusses beryllium and beryllium compounds. Most of the information is on beryllium, except in those cases where there are differences in toxicity between beryllium and beryllium compounds. In these cases, information on the beryllium compound is presented.

Uses

- Pure beryllium and its metal alloys have applications in electrical components, tools, structural components for aircraft, missiles, and satellites, and other metal-fabricating uses. (1)
- Beryllium is also used in consumer products, such as televisions, calculators, and personal computers. (1)

Sources and Potential Exposure

- The greatest exposures to beryllium occur in the workplace (i.e., where it is mined, processed, or converted into alloys and chemicals). (1)
- Individuals may also be exposed by inhalation of beryllium dust or fumes from the burning of coal or fuel oil and in tobacco smoke, by the ingestion of many fruits and vegetables and water, or through natural occurrence in soils. (1)
- The average concentration of beryllium measured in the air in the U.S. during the 1980s was 0.03 ng/m^3. Ambient concentrations measured in 50 cities between 1977 and 1981 were 0.1–0.4 ng/m^3. (1)

Assessing Personal Exposure

- Beryllium levels can be measured in urine and blood, but the levels in urine are quite variable, making it difficult to use these levels to assess total exposure. (1)
- Beryllium levels in tissues can be measured through biopsy procedures, however the relationship to exposure is not well documented. (1)
- A medical test, termed the antigen-specific lymphocyte transformation test, can be used to measure hypersensitivity in individuals previously exposed to beryllium and can also be used to diagnose chronic beryllium disease. (1)

Health Hazard Information

Acute Effects:

- Acute inhalation exposure to high levels of beryllium has been observed to cause inflammation of the lungs and acute pneumonitis (reddening and swelling of the lungs) in humans; after exposure ends, these symptoms may be reversible. Acute pneumonitis may cause death. (1-4)
- Acute animal tests, such as the LD_{50} test in rats and mice, have demonstrated beryllium compounds to vary in acute toxicity, ranging from high to extreme acute toxicity from oral exposure. (5)

Chronic Effects (Noncancer):

- Chronic occupational exposure of humans to beryllium by inhalation has been reported to cause chronic beryllium disease (berylliosis), in which granulomatous lesions (noncancerous) develop in the lung. The onset of these effects may be delayed by 3 months to more than 20 years. Symptoms of chronic beryllium disease include irritation of the mucous membranes, reduced lung capacity, shortness of breath, fatigue, anorexia, dyspnea, malaise, and weight loss. In some cases, chronic beryllium disease may cause death. (1-4)
- Animal studies have also reported effects on the lung, such as chronic pneumonitis, from chronic inhalation exposure. (1-3)
- Chronic inhalation exposure has also been observed to cause immunological effects in humans and animals. (1-3)
- A skin allergy may result from dermal exposure to beryllium. Eye contact with beryllium dust has been observed to cause acute conjunctivitis in humans. (1)
- The RfC for beryllium is 0.00002 mg/m^3 based on respiratory effects in humans. The RfC is an estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious noncancer effects during a lifetime. It is not a direct estimator of risk but rather a reference point to gauge the potential effects. At exposures increasingly greater than the RfC, the potential for adverse health effects increases. Lifetime exposure above the RfC does not imply that an adverse health effect would necessarily occur. (3)
- EPA has medium confidence in the RfC due to: medium confidence in the study on which the RfC is based because a no-observed-adverse-affect level (NOAEL) was not identified in the study, but a NOAEL slightly below the lowest-observed-adverse-effect level (LOAEL) was suggested in another study; and medium confidence in the database due to lack of adequate exposure monitoring in the epidemiology studies and some uncertainty regarding the mechanism associated with progression to chronic beryllium disease in beryllium-sensitized individuals. (3)
- The RfD for beryllium is 0.002 mg/kg/d based on small intestinal lesions in dogs. (3)
- EPA has low to medium confidence in the RfD due to: medium confidence in the study on which the RfD was based because it was administered by the oral route with multiple doses for chronic duration, but there were small groups of animals, early mortality at the high dose level, and no control for potential litter effects; and low to medium confidence in the database because there is only one chronic study in dogs showing adverse effect levels. (3)

Reproductive/Developmental Effects:

- The potential for beryllium to induce developmental or reproductive effects has not been adequately assessed.
- Limited information is available on the reproductive or developmental effects of beryllium in humans following inhalation exposure. A case control study found no association between paternal occupational exposure and the risk of stillbirth, pre-term

delivery, or small-for-gestational-age infants, although this study has limited sensitivity. (2,3)

- No data are available on reproductive or developmental effects in animals following inhalation. (2,3)

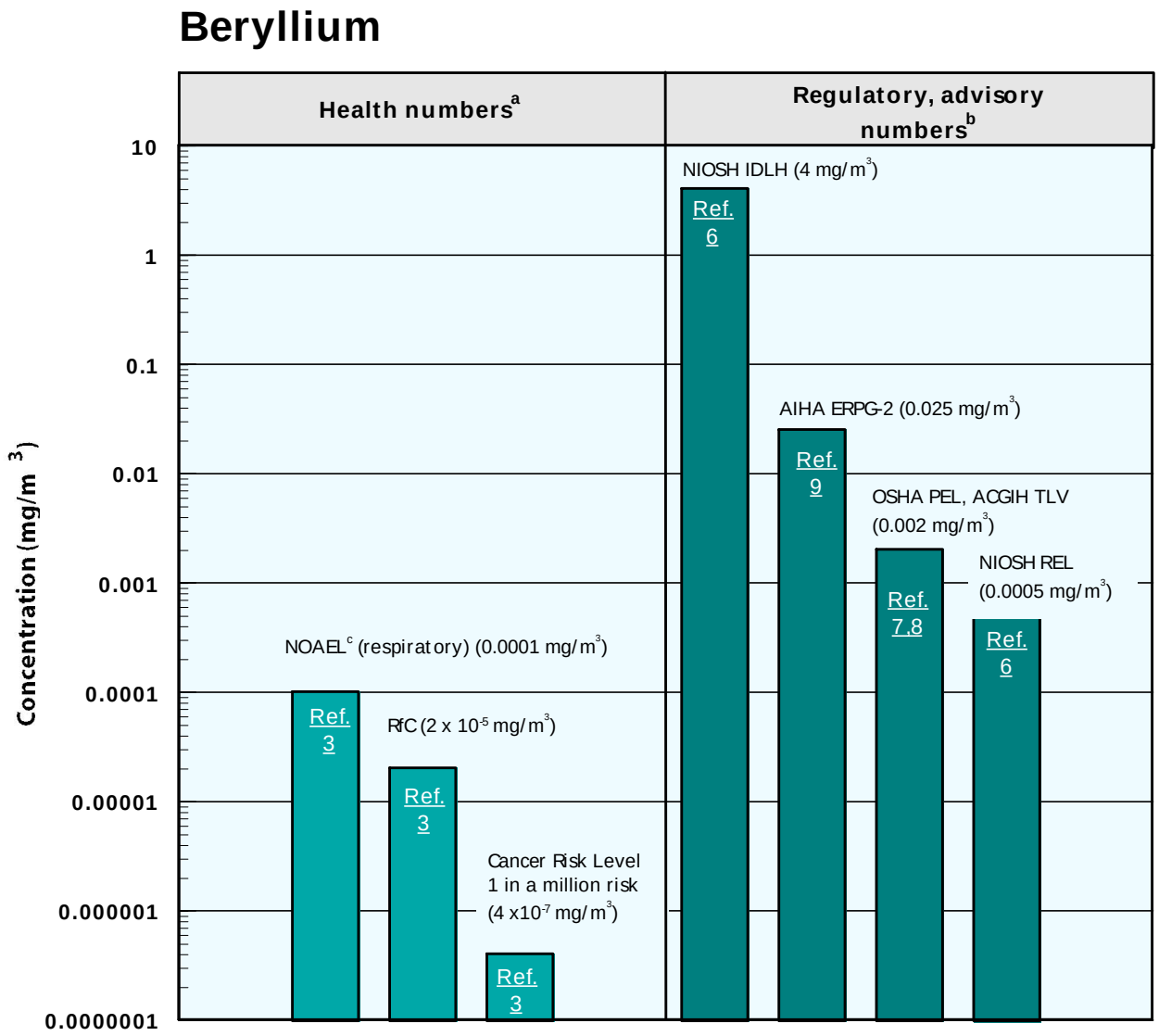
Cancer Risk:

- Several human epidemiological studies have investigated the relationship between beryllium exposure in workers and lung cancer deaths. Although there are shortcomings in all the studies, the results are suggestive of a causal relationship between beryllium exposure and an increased risk of lung cancer. (2,3)
- Beryllium compounds have been shown to cause lung cancer from inhalation exposure in rats and monkeys. (1–3)
- EPA has classified beryllium as a Group B1, probable human carcinogen. (3)
- EPA uses mathematical models, based on human and animal studies, to estimate the probability of a person developing cancer from breathing air containing a specified concentration of a chemical. EPA calculated an inhalation unit risk estimate of 2.4×10^{-3} $(\mu g/m^3)^{-1}$. EPA estimates that, if an individual were to continuously breathe air containing beryllium at an average of 0.0004 $\mu g/m^3$ (4×10^{-7} mg/m^3) over his or her entire lifetime, that person would theoretically have no more than a one-in-a-million increased chance of developing cancer as a direct result of breathing air containing this chemical. Similarly, EPA estimates that continuously breathing air containing 0.004 $\mu g/m^3$ (4×10^{-6} mg/m^3) would result in not greater than a one-in-a-hundred thousand increased chance of developing cancer, and air containing 0.04 $\mu g/m^3$ (4×10^{-5} mg/m^3) would result in not greater than a one-in-ten thousand increased chance of developing cancer. For a detailed discussion of confidence in the potency estimates, please see IRIS. (3)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45). Beryllium and its compounds do not exist in the atmosphere in the vapor phase; therefore, an air conversion factor is not applicable. (1)

Health Data from Inhalation Exposure



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

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

NIOSH IDLH – National Institute of Occupational Safety and Health's immediately dangerous

to life or health concentration; NIOSH recommended exposure limit to ensure that a worker can escape from an exposure condition that is likely to cause death or immediate or delayed permanent adverse health effects or prevent escape from the environment.
NIOSH REL – NIOSH's recommended exposure limit; NIOSH-recommended exposure limit for an 8- or 10-h time-weighted-average exposure and/or ceiling.
OSHA PEL – Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.

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

References

1. Agency for Toxic Substances and Disease Registry (ATSDR). *Toxicological Profile for Beryllium* (Draft). Public Health Service, U.S. Department of Health and Human Services, Altanta, GA. 1992.

2. U.S. Environmental Protection Agency (EPA). *Toxicological Review of Beryllium and Compounds.* In support of summary information on IRIS. National Center for Environmental Assessment, Washington, DC. 1998.

3. U.S. Environmental Protection Agency (EPA). *Integrated Risk Information System (IRIS) on Beryllium*. National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1999.

4. U.S. Department of Health and Human Services. Hazardous Substances Data Bank (HSDB, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.

5. U.S. Department of Health and Human Services. Registry of Toxic Effects of Chemical Substances (RTECS, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.

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

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

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

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

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1,3-BUTADIENE
106-99-0

Hazard Summary

1,3-Butadiene is found in ambient air primarily as a compound of motor vehicle exhaust. Acute (short-term) exposure to 1,3-butadiene by inhalation in humans results in irritation of the eyes, nasal passages, throat, and lungs, and causes neurological effects such as blurred vision, fatigue, headache, and vertigo. Epidemiological studies have reported a possible association between 1,3-butadiene exposure and cardiovascular diseases. No information is available on the reproductive or developmental effects of 1,3-butadiene in humans, while animal studies have reported these type of effects. Epidemiological studies of workers in rubber plants have shown an association between 1,3-butadiene exposure and increased incidence of leukemia. Animal studies have reported tumors at various sites from 1,3-butadiene exposure. The U.S. Environmental Protection Agency (EPA) has classified 1,3-butadiene as a Group B2, probable human carcinogen.

Please Note: The main sources of information for this fact sheet are EPA's Integrated Risk Information System (IRIS), which contains information on the carcinogenic effects of 1,3-butadiene including the unit cancer risk for inhalation exposure, and the Agency for Toxic Substances and Disease Registry's (ATSDR's) *Toxicological Profile for 1,3-Butadiene*.

Physical Properties

- 1,3-Butadiene is a colorless gas with a mild gasoline-like odor. (1)
- The odor threshold for 1,3-butadiene is 1.6 ppm. (7)
- The chemical formula for 1,3-butadiene is C_4H_6, and the molecular weight is 54.09 g/mol. (1)
- The vapor pressure for 1,3-butadiene is 2100 mm Hg at 25 EC, and it has an octanol/water partition coefficient (log K_{ow}) of 1.99. (1)

Uses

- 1,3-Butadiene is used in the production of rubber and plastics. It is also used in copolymers including acrylics. (1)

Sources and Potential Exposure

- Sources of 1,3-butadiene released into the air include manufacturing and processing facilities, motor vehicle exhaust, forest fires or other combustion, and cigarette smoke. (1)
- 1,3-Butadiene was detected in ambient air of cities and suburban areas from 1970 to 1982 at an average level of 0.3 ppb. (1)
- Higher levels of 1,3-butadiene may be found in highly industrialized cities or near oil refineries, chemical manufacturing plants, and plastic and rubber factories. (1)

- 1,3-Butadiene has been found in drinking water and in plastic or rubber food containers, but not in food samples. (1)
- Occupational exposure to 1,3-butadiene may occur in the rubber, plastics, and resins industries. (1)

Assessing Personal Exposure

- There is no reliable medical test available at this time to assess personal exposure to 1,3-butadiene. (1)

Health Hazard Information

Acute Effects:

- Acute exposure to 1,3-butadiene by inhalation in humans results in irritation of the eyes, nasal passages, throat, and lungs. Neurological effects, such as blurred vision, fatigue, headache, and vertigo, have also been reported at very high exposure levels. (1,3)
- Dermal exposure to 1,3-butadiene causes a sensation of cold, followed by a burning sensation, which may lead to frostbite. (1)
- Tests involving acute exposure of animals, such as the LC_{50} test in rats and mice, have shown 1,3-butadiene to have low acute toxicity. (1,4)

Chronic Effects (Noncancer):

- One epidemiological study reported that chronic (long-term) exposure to 1,3-butadiene via inhalation resulted in an increase in cardiovascular diseases, such as rheumatic and arteriosclerotic heart diseases, while other human studies have reported effects on the blood. (1)
- Animal studies have reported effects on the respiratory and cardiovascular systems, blood, and liver from chronic, inhalation exposure to 1,3-butadiene. (1)
- EPA has not established a reference concentration (RfC) or a reference dose (RfD) for 1,3-butadiene. (5)
- The California Environmental Protection Agency (CalEPA) has established a chronic reference level of 0.008 mg/m^3 for 1,3-butadiene based on reproductive effects in mice. The CalEPA reference exposure level is a concentration at or below which adverse health effects are not likely to occur. It is not a direct estimator of risk, but rather a reference point to gauge the potential effects. At lifetime exposures increasingly greater than the reference exposure level, the potential for adverse health effects increases. (6)

Reproductive/Developmental Effects:

- No information is available on reproductive or developmental effects of 1,3-butadiene in humans. (1)
- Animal studies using mice have reported developmental effects, such as skeletal abnormalities and decreased fetal weights, and reproductive effects, including an

increased incidence of ovarian atrophy, testicular atrophy, and sperm abnormalities from inhalation exposure to 1,3-butadiene. (1)

Cancer Risk:

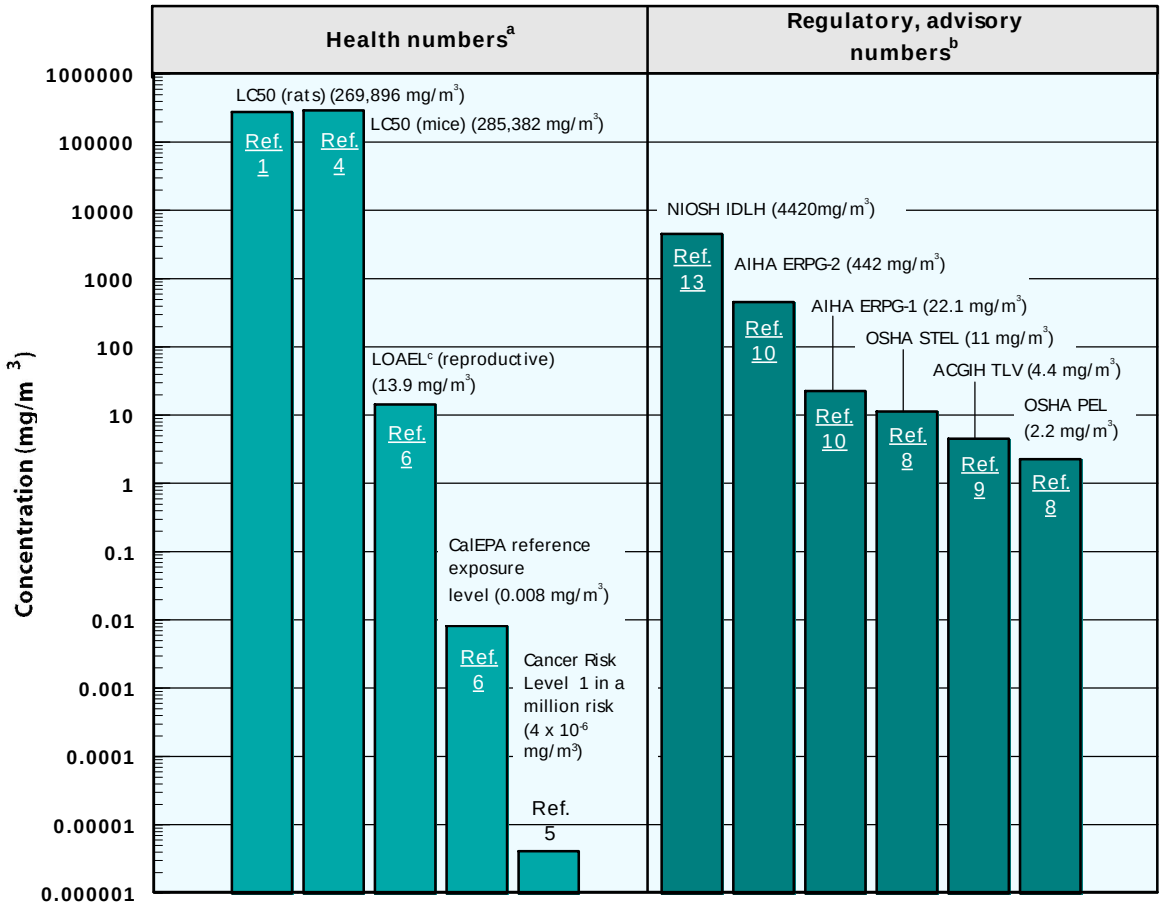
- A large epidemiological study of synthetic rubber industry workers demonstrated a consistent association between 1,3-butadiene exposure and occurrence of leukemia (10, 11).
- Several epidemiological studies of workers in styrene-butadiene rubber factories have shown an increased incidence of respiratory, bladder, stomach, and lymphato-hematopoietic cancers. However, these studies are not sufficient to determine a causal association between 1,3-butadiene exposure and cancer due to possible exposure to other chemicals and other confounding factors. (1,5,6)
- Animal studies have reported tumors at a variety of sites from inhalation exposure to 1,3-butadiene. (1,5,6)
- EPA has classified 1,3-butadiene as a Group B2, probable human carcinogen. However, based on recently available human data, EPA is evaluating a classification of known human carcinogen. (5)
- EPA uses mathematical models, based on human and animal studies, to estimate the probability of a person developing cancer from continuously breathing air containing a specified concentration of a chemical. EPA is currently reevaluating their inhalation unit risk estimate of 2.8×10^{-4} $(\mu g/m^3)^{-1}$ that was derived in 1991. A revised unit risk estimate of 2.1×10^{-6} $(\mu g/m^3)^{-1}$ was presented to EPA's Science Advisory Board (SAB) for review in 1998. As a result of SAB comments, the estimate will be revised and is likely to be lower than the 1991 value. (12)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45).
For 1,3-butadiene: 1 ppm = 2.21 mg/m^3.
To convert from $\mu g/m^3$ to mg/m^3: mg/m^3 = ($\mu g/m^3$) x (1 mg/1,000 µg).

Health Data from Inhalation Exposure

1,3-Butadiene



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

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

LC_{50} (Lethal Concentration$_{50}$) – A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.

LOAEL – Lowest-observed-adverse-affect level.

NIOSH IDLH – National Institute of Occupational Safety and Health's immediately dangerous to life or health concentration; NIOSH recommended exposure limit to ensure that a worker can escape from an exposure condition that is likely to cause death or immediate or delayed permanent adverse health effects or prevent escape from the environment.
OSHA PEL – Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.
OSHA STEL – OSHA's short-term exposure limit.

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

References

1. Agency for Toxic Substances and Disease Registry (ATSDR). *Toxicological Profile for 1,3-Butadiene*. Public Health Service, U.S. Department of Health and Human Services, Atlanta, GA. 1992.

2. E.J. Calabrese and E.M. Kenyon. *Air Toxics and Risk Assessment*. Lewis Publishers. 1991.

3. U.S. Department of Health and Human Services. Hazardous Substances Data Bank (HSDB, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.

4. U.S. Department of Health and Human Services. Registry of Toxic Effects of Chemical Substances (RTECS, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.

5. U.S. Environmental Protection Agency (EPA). *Integrated Risk Information System (IRIS) on 1,3-Butadiene*. National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1999.

6. California Environmental Protection Agency (CalEPA). *Technical Support Document for the Determination of Noncancer Chronic Reference Exposure Levels. Draft for Public Comment.* Office of Environmental Health Hazard Assessment, Berkeley, CA. 1997.

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

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

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

10. Delzell E, Sathiakumar N, Hovinga M, et al. A follow-up study of synthetic rubber workers. *Toxicology* 113:182-9. 1996.

11. Macaluso M, Larson R, Delzell E, et al. Leukemia and cumulative exposure to butadiene, styrene and benzene among workers in the synthetic rubber industry. *Toxicology* 113:190-202. 1996.

12. U.S. Environmental Protection Agency (EPA). *An SAB Report: Review of the Health Risk Assessment of 1,3-Butadiene*. Science Advisory Board, Washington, DC. EPA-SAB-EHC-99-003. 1998.

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

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

CADMIUM COMPOUNDS[1]

Hazard Summary

The main sources of cadmium in the air are the burning of fossil fuels such as coal or oil and the incineration of municipal waste. The acute (short-term) effects of cadmium in humans through inhalation exposure consist mainly of effects on the lung, such as pulmonary irritation. Chronic (long-term) inhalation or oral exposure to cadmium leads to a build-up of cadmium in the kidneys that can cause kidney disease. Cadmium has been shown to be a developmental toxicant in animals, resulting in fetal malformations and other effects, but no conclusive evidence exists in humans. An association between cadmium exposure and an increased risk of lung cancer has been reported from human studies, but these studies are inconclusive due to confounding factors. Animal studies have demonstrated an increase in lung cancer from long-term inhalation exposure to cadmium. The U.S. Environmental Protection Agency (EPA) has classified cadmium as a Group B1, probable human carcinogen.

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

Physical Properties

- Cadmium is a soft silver-white metal that is usually found in combination with other elements. (1)
- Cadmium compounds range in solubility in water from quite soluble to practically insoluble. (1)
- The chemical symbol for cadmium is Cd and the atomic weight is 112.41 g/mol. (1)

Uses

- Most cadmium used in the U.S. today is obtained as a byproduct from the smelting of zinc, lead, or copper ores. (1)
- Cadmium is used to manufacture pigments and batteries and in the metal-plating and plastics industries. (1)

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[1] This fact sheet discusses cadmium and cadmium compounds. Most of the information is on cadmium, except in those cases where there are differences in toxicity between cadmium and cadmium compounds. In these cases, information on the cadmium compound is presented.

Sources and Potential Exposure

- The largest sources of airborne cadmium in the environment are the burning of fossil fuels such as coal or oil, and incineration of municipal waste materials. Cadmium may also be emitted into the air from zinc, lead, or copper smelters. (1)
- For nonsmokers, food is generally the largest source of cadmium exposure. Cadmium levels in some foods can be increased by the application of phosphate fertilizers or sewage sludge to farm fields. (1)
- Smoking is another important source of cadmium exposure. Smokers have about twice as much cadmium in their bodies as do nonsmokers. (1)

Assessing Personal Exposure

- The amount of cadmium present in blood or urine can be measured by atomic absorption spectrophotometry and used as an indication of cadmium exposure. (1)
- A more precise method, called neutron activation analysis, can be used to measure cadmium concentrations in the liver or kidney. (1)

Health Hazard Information

Acute Effects:

- Acute inhalation exposure to high levels of cadmium in humans may result in effects on the lung, such as bronchial and pulmonary irritation. A single acute exposure to high levels of cadmium can result in long-lasting impairment of lung function. (1,3,4)
- Cadmium is considered to have high acute toxicity, based on short-term animal tests such as the LC_{50} test in rats. (5)

Chronic Effects (Noncancer):

- Chronic inhalation and oral exposure of humans to cadmium results in a build-up of cadmium in the kidneys that can cause kidney disease, including proteinuria, a decrease in glomerular filtration rate, and an increased frequency of kidney stone formation. (1,3,4)
- Other effects noted in humans from chronic exposure to cadmium in air are effects on the lung, including bronchiolitis and emphysema. (1,3,4)
- Chronic inhalation or oral exposure of animals to cadmium results in effects on the kidney, liver, lung, bone, immune system, blood, and nervous system. (1,3)
- The RfD for cadmium in drinking water is 0.0005 mg/kg/d, and the RfD for dietary exposure to cadmium is 0.001 mg/kg/d; both are based on significant proteinuria in humans. The RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious noncancer effects during a lifetime. It is not a direct estimator of risk, but rather a reference point to gauge the potential effects. At exposures increasingly greater than the RfD, the potential for

adverse health effects increases. Lifetime exposure above the RfD does not imply that an adverse health effect would necessarily occur. (6)

- EPA has high confidence in both RfD values based primarily on a strong database for cadmium toxicity in humans and animals that also permits calculation of pharmacokinetic parameters of cadmium absorption, distribution, metabolism, and elimination. (6)
- EPA has not established a reference concentration (RfC) for cadmium. (6)
- The California Environmental Protection Agency (CalEPA) has established a chronic reference exposure level of 0.00001 mg/m^3 for cadmium based on kidney and respiratory effects in humans. The CalEPA reference exposure level is a concentration at or below which adverse health effects are not likely to occur. (7)

Reproductive/Developmental Effects:

- Limited evidence exists for an association between inhalation exposure and a reduction in sperm number and viability in humans. (1)
- Human developmental studies on cadmium are limited, although there is some evidence to suggest that maternal cadmium exposure may result in decreased birth weights. (1)
- Animal studies provide evidence that cadmium has developmental effects, such as low fetal weight, skeletal malformations, interference with fetal metabolism, and impaired neurological development, via inhalation and oral exposure. (1,3,4)
- Limited animal data are available, although some reproductive effects, such as decreased reproduction and testicular damage, have been noted following oral exposures. (1)

Cancer Risk:

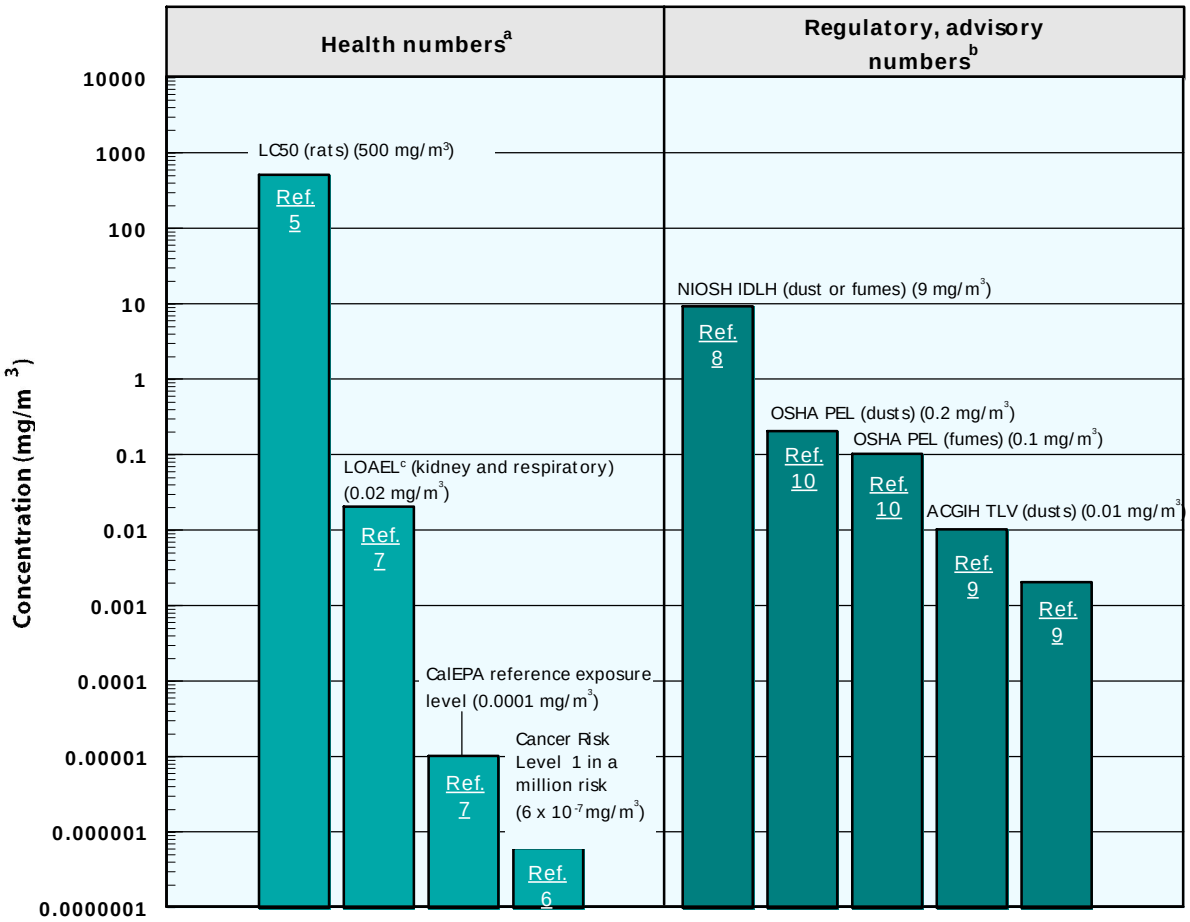
- Several occupational studies have reported an excess risk of lung cancer in humans from exposure to inhaled cadmium. However, the evidence is limited rather than conclusive due to confounding factors. (1,3,6)
- Animal studies have reported cancer resulting from inhalation exposure to several forms of cadmium, while animal ingestion studies have not demonstrated cancer resulting from exposure to cadmium compounds. (1,3,6)
- EPA considers cadmium to be a probable human carcinogen and has classified it as a Group B1 carcinogen. (6)
- EPA uses mathematical models, based on human and animal studies, to estimate the probability of a person developing cancer from breathing air containing a specified concentration of a chemical. EPA calculated an inhalation unit risk estimate of 1.8×10^{-3} $(\mu g/m^3)^{-1}$. EPA estimates that, if an individual were to continuously breathe air containing cadmium at an average of 0.0006 $\mu g/m^3$ (6×10^{-7} mg/m^3) over his or her entire lifetime, that person would theoretically have no more than a one-in-a-million increased chance of developing cancer as a direct result of breathing air containing this chemical. Similarly, EPA estimates that continuously breathing air containing 0.006 $\mu g/m^3$ (6×10^{-6} mg/m^3) would result in not greater than a one-in-a-hundred thousand increased chance of developing cancer, and air containing 0.06 $\mu g/m^3$ (6×10^{-5} mg/m^3) would result in not greater than a one-in-ten thousand increased chance of developing cancer. For a detailed discussion of confidence in the potency estimates, please see IRIS. (6)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45).
For cadmium: 1 ppm = 4.6 mg/m^3.
To convert from µg/m^3 to mg/m^3: mg/m^3 = (µg/m^3) x (1 mg/1000 µg).

Health Data from Inhalation Exposure

Cadmium



ACGIH TLV – American Conference of Governmental and Industrial Hygienists' threshold limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effects.
LC_{50} (Lethal Concentration$_{50}$) – A calculated concentration of a chemical in air to which

exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.
LOAEL – Lowest-observed-adverse-affect level.
NIOSH IDLH – National Institute of Occupational Safety and Health's immediately dangerous to life and health; NIOSH concentration representing the maximum level of a pollutant from which an individual could escape within 30 minutes without escape-impairing symptoms or irreversible health effects.
OSHA PEL – Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.

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

References

1. Agency for Toxic Substances and Disease Registry (ATSDR). *Toxicological Profile for Cadmium*. Draft for Public Comment. Public Health Service, U.S. Department of Health and Human Services, Atlanta, GA. 1997.

2. U.S. Environmental Protection Agency (EPA). *Deposition of Air Pollutants to the Great Waters*. *First Report to Congress*. EPA-453/R-93-055. Office of Air Quality Planning and Standards, Research Triangle Park, NC. 1994.

3. E.J. Calabrese and E.M. Kenyon. *Air Toxics and Risk Assessment*. Lewis Publishers, Chelsea, MI. 1991.

4. U.S. Department of Health and Human Services. Hazardous Substances Data Bank (HSDB, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.

5. U.S. Department of Health and Human Services. Registry of Toxic Effects of Chemical Substances (RTECS, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.

6. U.S. Environmental Protection Agency (EPA). *Integrated Risk Information System (IRIS) on Cadmium*. National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1999.

7. California Environmental Protection Agency (CalEPA). *Technical Support Document for the Determination of Noncancer Chronic Reference Exposure Levels. Draft for Public Comment.* Office of Environmental Health Hazard Assessment, Berkeley, CA. 1997.

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

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

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

CARBON TETRACHLORIDE
56-23-5

Hazard Summary

Carbon tetrachloride may be found in both ambient outdoor and indoor air. Human symptoms of acute (short-term) inhalation and oral exposures to carbon tetrachloride include headache, weakness, lethargy, nausea, and vomiting. Depression of the central nervous system (CNS) has also been reported. More severe acute exposures result in kidney and liver damage and extreme exposures have resulted in delayed pulmonary edema (resulting from kidney damage). Chronic (long-term) inhalation or oral exposure to carbon tetrachloride also produces liver and kidney damage in humans. Little information is available on the reproductive or developmental effects of carbon tetrachloride in humans. Reproductive effects have been observed in animals exposed to carbon tetrachloride orally and by inhalation. Human data on the carcinogenic effects of carbon tetrachloride are limited. Studies in animals have shown that ingestion of carbon tetrachloride increases the risk of liver cancer. The U.S. Environmental Protection Agency (EPA) has classified carbon tetrachloride as a Group B2, probable human carcinogen.

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

Physical Properties

- The chemical formula for carbon tetrachloride is CCl_4, and its molecular weight is 153.8 g/mol. (1,2)
- Carbon tetrachloride is a clear, nonflammable liquid which is almost insoluble in water. (1)
- Carbon tetrachloride has a sweet characteristic odor, with an odor threshold above 10 ppm. (1)
- The vapor pressure for carbon tetrachloride is 91.3 mm Hg at 20 EC, and its log octanol/water partition coefficient (log K_{ow}) is 2.64. (1)

Uses

- Carbon tetrachloride was produced in large quantities to make refrigerants and propellants for aerosol cans, as a solvent for oils, fats, lacquers, varnishes, rubber waxes, and resins, and as a grain fumigant and a dry cleaning agent. Consumer and fumigant uses have been discontinued and only industrial uses remain. (1)

Sources and Potential Exposure

- Individuals may be exposed to carbon tetrachloride in the air from accidental releases from production and uses, and from its disposal in landfills. (1)
- Carbon tetrachloride is also a common contaminant of indoor air; the sources of exposure appear to be building materials or products, such as cleaning agents, used in the home. (1)
- Workers involved in the manufacture or use of carbon tetrachloride are most likely to have significant exposures to carbon tetrachloride. (1)
- Individuals may also be exposed to carbon tetrachloride by drinking contaminated water. (1,2)
- In the past, ingestion of bread or other products made with carbon tetrachloride-fumigated grain may have contributed to dietary exposure, but this route of exposure is no longer of significance. (1)

Assessing Personal Exposure

- Measurement of carbon tetrachloride in exhaled breath has been the most convenient method for determining exposure; measurements in blood, fat, or other tissues have also been used as indicators of exposure. However, these tests are not routinely available and cannot be used to predict whether any health effects will result. (1)

Health Hazard Information

Acute Effects:

- Acute inhalation and oral exposures to high levels of carbon tetrachloride have been observed primarily to damage the liver and kidneys of humans. Depression of the CNS has also been reported. Symptoms of acute exposure in humans include headache, weakness, lethargy, nausea, and vomiting. (1-6)
- Delayed pulmonary edema has been observed in humans exposed to high levels of carbon tetrachloride by inhalation and ingestion, but this is believed to be due to injury to the kidney rather than direct action of carbon tetrachloride on the lung. (1)
- Acute animal exposure tests, such as the LC_{50} and LD_{50} tests in rats, mice, rabbits, and guinea pigs, have demonstrated carbon tetrachloride to have low toxicity from inhalation exposure, low-to-moderate toxicity from ingestion, and moderate toxicity from dermal exposure. (7)

Chronic Effects (Noncancer):

- Chronic inhalation or oral exposure to carbon tetrachloride produces liver and kidney damage in humans and animals. (1,3,6,8)
- EPA has not established a reference concentration (RfC) for carbon tetrachloride. (9)
- The California Environmental Protection Agency (CalEPA) has established a chronic reference exposure level of 0.04 mg/m^3 for carbon tetrachloride based on liver effects in guinea pigs. The CalEPA reference exposure level is a concentration at or below which

adverse health effects are not likely to occur. It is not a direct estimator of risk, but rather a reference point to gauge the potential effects. At lifetime exposures increasingly greater than the reference exposure level, the potential for adverse health effects increases. (10)

- ATSDR has established an acute inhalation minimal risk level (MRL) of 1.3 mg/m^3 (0.2 ppm) based on liver effects in rats, and an intermediate MRL of 0.3 mg/m^3 (0.05 ppm) also based on liver effects in rats. The MRL is an estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk of adverse noncancer health effects over a specified duration of exposure. (1)
- The RfD for carbon tetrachloride is 0.0007 mg/kg/d based on the occurrence of liver lesions in rats. The RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious noncancer effects during a lifetime. (9)
- EPA has medium confidence in the RfD based on: high confidence in the principal study on which the RfD was based because the study was well conducted and good dose-response was observed in the liver, which is the target organ for carbon tetrachloride toxicity; and medium confidence in the database because four additional subchronic studies support the RfD, but reproductive and teratology endpoints are not well investigated; and, consequently, medium confidence in the RfD. (9)

Reproductive/Developmental Effects:

- No information is available on the reproductive effects of carbon tetrachloride in humans. Limited epidemiological data have indicated a possible association between certain birth outcomes (e.g., birth weight, cleft palate) and drinking water exposure. However, as the water contained multiple chemicals, the role of carbon tetrachloride is unclear. (1)
- Decreased fertility and degenerative changes in the testes have been observed in animals exposed to carbon tetrachloride by inhalation. (1,6)
- Birth defects have not been observed in animals exposed to carbon tetrachloride by inhalation or ingestion. (1,2,8)

Cancer Risk:

- Occasional reports have noted the occurrence of liver cancer in workers who had been exposed to carbon tetrachloride by inhalation exposure; however, the data are not sufficient to establish a cause-and-effect relationship. (1,6,8,9,11,12)
- Liver tumors have developed in rats and mice exposed to carbon tetrachloride by gavage. (1-4,6,8,9,11,12)
- EPA has classified carbon tetrachloride as a Group B2, probable human carcinogen. (8,9)
- EPA uses mathematical models, based on human and animal studies, to estimate the probability of a person developing cancer from continuously breathing air containing a specified concentration of a chemical. EPA calculated an inhalation unit risk of 1.5×10^{-5} $(\mu g/m^3)^{-1}$. EPA estimates that, if an individual were to continuously breathe air containing carbon tetrachloride at an average of 0.07 $\mu g/m^3$ (7×10^{-5} mg/m^3) over his or her entire

lifetime, that person would theoretically have no more than a one-in-a-million increased chance of developing cancer as a direct result of breathing air containing this chemical.

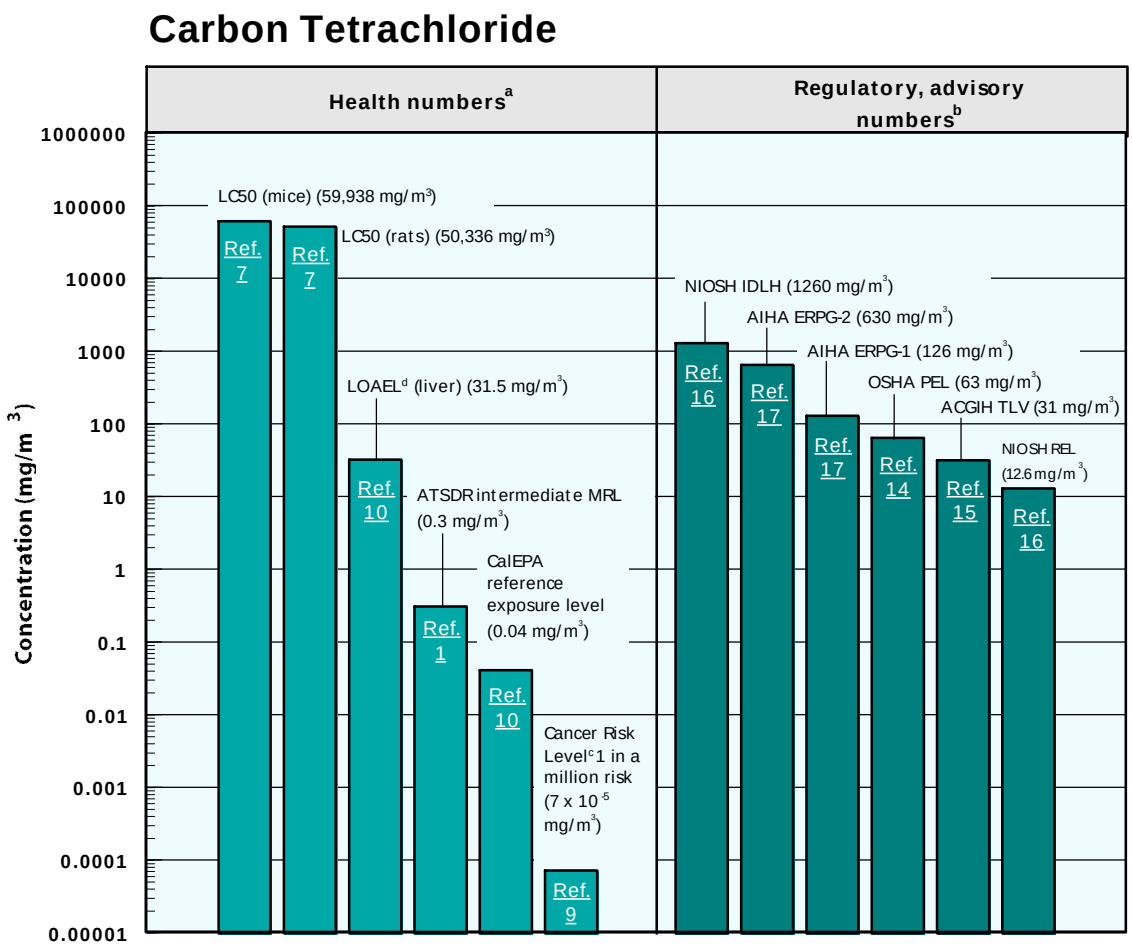
! Similarly, EPA estimates that continuously breathing air containing 0.7 µg/m^3 (7 x 10^{-4} mg/m^3) would result in not greater than a one-in-a-hundred thousand increased chance of developing cancer, and air containing 7.0 µg/m^3 (7 x 10^{-3} mg/m^3) would result in not greater than a one-in-a-ten thousand increased chance of developing cancer. (9)

! EPA has calculated an oral cancer slope factor of 1.3 x 10^{-1} (mg/kg/d)$^{-1}$. For a detailed discussion of confidence in the potency estimates, please see IRIS. (9)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45). For carbon tetrachloride: 1 ppm = 6.3 mg/m^3.

Health Data from Inhalation Exposure



AIHA ERPG – American Industrial Hygiene Association's emergency response planning guidelines. ERPG 1 is the maximum airborne concentration below which it is believed nearly all individuals could be exposed up to one hour without experiencing other than mild transient adverse health effects or perceiving a clearly defined objectionable odor; ERPG 2 is the maximum airborne concentration below which it is believed nearly all individuals could be exposed up to one hour without experiencing or developing irreversible or other serious health effects that could impair their abilities to take protective action.
ACGIH TLV – American Conference of Governmental and Industrial Hygienists' threshold limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effects.
LC_{50} (Lethal Concentration$_{50}$) – A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.
LOAEL – Lowest-observed-adverse-affect level.
NIOSH IDLH – National Institute of Occupational Safety and Health's immediately dangerous to life or health concentration; NIOSH recommended exposure limit to ensure that a worker can escape from an exposure condition that is likely to cause death or immediate or delayed permanent adverse health effects or prevent escape from the environment.
NIOSH REL – NIOSH's recommended exposure limit; NIOSH-recommended exposure limit for an 8- or 10-h time-weighted-average exposure and/or ceiling.
OSHA PEL – Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.

[a] Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA.
[b] Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the Government or other groups as advice.
[c] These cancer risk estimates were derived from oral data and converted to provide the estimated inhalation risk.
[d] The LOAEL is from the critical study used as the basis for the CalEPA chronic reference exposure level.

References

1. Agency for Toxic Substances and Disease Registry (ATSDR). *Toxicological Profile for Carbon Tetrachloride (Update)*. Public Health Service, U.S. Department of Health and Human Services, Atlanta, GA. 1994.

2. U.S. Environmental Protection Agency (EPA). *Carbon Tetrachloride Health Advisory*. Office of Drinking Water, Washington, DC. 1987.

3. U.S. Department of Health and Human Services. Hazardous Substances Databank (HSDB, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.

4. International Agency for Research on Cancer (IARC). *IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans: Some Halogenated Hydrocarbons*. Volume 20. World Health Organization, Lyon. 1979.

5. M. Sittig. *Handbook of Toxic and Hazardous Chemicals and Carcinogens*. 2nd ed. Noyes Publications, Park Ridge, NJ. 1985.

6. U.S. Environmental Protection Agency (EPA). *Health Affects Document for Carbon Tetrachloride*. EPA/600/8-82-001F. Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment, Office of Research and Development, Cincinnati, OH. 1984.

7. U.S. Department of Health and Human Services. Registry of Toxic Effects of Chemical Substances (RTECS, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.

8. U.S. Environmental Protection Agency (EPA). *Updated Health Effects Assessment for Carbon Tetrachloride*. EPA/600/8-89/088. Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment, Office of Research and Development, Cincinnati, OH. 1989.

9. U.S. Environmental Protection Agency (EPA). *Integrated Risk Information System (IRIS) on Carbon Tetrachloride*. National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1999.

10. California Environmental Protection Agency (CalEPA). *Technical Support Document for the Determination of Noncancer Chronic Reference Exposure Levels. Draft for Public Comment.* Office of Environmental Health Hazard Assessment, Berkeley, CA. 1997.

11. International Agency for Research on Cancer (IARC). *IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans: Chemicals, Industrial Processes and Industries Associated with Cancer in Humans.* Supplement 4. World Health Organization, Lyon. 1982.

12. International Agency for Research on Cancer (IARC). *IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man*. Volume 1. World Health Organization, Lyon. 1972.

13. *The Merck Index. An Encyclopedia of Chemicals, Drugs, and Biologicals*. 11th ed. Ed. S. Budavari. Merck and Co. Inc., Rahway, NJ. 1989.

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

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

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

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

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CHLOROFORM
67-66-3

Hazard Summary

Chloroform may be released to the air as a result of its formation in the chlorination of drinking water, wastewater and swimming pools. Other sources include pulp and paper mills, hazardous waste sites, and sanitary landfills. The major effect from acute (short-term) inhalation exposure to chloroform is central nervous system (CNS) depression. Chronic (long-term) exposure to chloroform by inhalation in humans has resulted in effects on the liver, including hepatitis and jaundice, and CNS effects, such as depression and irritability. Little information is available on the reproductive or developmental effects of chloroform in humans, while animal studies have reported developmental effects, such as decreased fetal body weight and fetal resorptions, and reproductive effects, such as decreased conception rates, in animals exposed to chloroform by inhalation. No studies are available on the carcinogenic effects of chloroform in humans or animals after inhalation exposure. Chloroform has been shown to be carcinogenic in animals after oral exposure, resulting in an increase in kidney and liver tumors. The U.S. Environmental Protection Agency (EPA) has classified chloroform as a Group B2, probable human carcinogen.

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

Physical Properties

- Chloroform is a colorless liquid that is not very soluble in water and is very volatile. (1,6)
- Chloroform has a pleasant, nonirritating odor; the odor threshold is 85 ppm. (1)
- The chemical formula for chloroform is $CHCl_3$, and it has a molecular weight of 119.38 g/mol. (1)
- The vapor pressure for chloroform is 159 mm Hg at 20 EC, and it has a log octanol/water partition coefficient (log K_{ow}) of 1.97. (1)

Uses

- The vast majority of the chloroform produced in the U.S. is used to make HCFC-22. The rest is produced for export and for miscellaneous uses. (1)
- Chloroform was used in the past as an extraction solvent for fats, oils, greases, and other products; as a dry cleaning spot remover; in fire extinguishers; as a fumigant; and as an anesthetic. However, chloroform is no longer used in these products. (1)

Sources and Potential Exposure

- Chloroform may be released to the air from a large number of sources related to its manufacture and use, as well as its formation in the chlorination of drinking water, wastewater, and swimming pools. Pulp and paper mills, hazardous waste sites, and sanitary landfills are also sources of air emissions. The background level of chloroform in ambient air in the early 1990's was estimated at 0.00004 ppm. (1)
- Human exposure to chloroform may occur through drinking water, where chloroform is formed as a result of the chlorination of naturally occurring organic materials found in raw water supplies. Measurements of chloroform in drinking water during the 1970's and 1980's ranged from 0.022 to 0.068 ppm. (1)
- Chloroform may also be found in some foods and beverages, largely from the use of tap water during production processes. (1)

Assessing Personal Exposure

- Chloroform can be detected in blood, urine, and body tissues. However, these methods are not very reliable because chloroform is rapidly eliminated from the body, and the tests are not specific for chloroform. (1)

Health Hazard Information

Acute Effects:

- The major effect from acute inhalation exposure to chloroform in humans is CNS depression. At very high levels (40,000 ppm), chloroform exposure may result in death, with concentrations in the range of 1,500 to 30,000 ppm producing anesthesia, and lower concentrations (<1,500 ppm) resulting in dizziness, headache, tiredness, and other effects. (1,2)
- Effects noted in humans exposed to chloroform via anesthesia include changes in respiratory rate, cardiac effects, gastrointestinal effects, such as nausea and vomiting, and effects on the liver and kidney. Chloroform is not currently used as a surgical anesthetic. (1,2)
- In humans, a fatal oral dose of chloroform may be as low as 10 mL (14.8 g), with death due to respiratory or cardiac arrest. (1,2)
- Tests involving acute exposure of animals, such as the LC_{50} and LD_{50} tests in rats, have shown chloroform to have low acute toxicity from inhalation exposure and moderate acute toxicity from oral exposure. (3)

Chronic Effects (Noncancer):

- Chronic exposure to chloroform by inhalation in humans is associated with effects on the liver, including hepatitis and jaundice, and CNS effects, such as depression and irritability. Inhalation exposures of animals have also resulted in effects on the kidney. (1,2)

- Chronic oral exposure to chloroform in humans has resulted in effects on the blood, liver, and kidney. (1,2)
- EPA has not established a reference concentration (RfC) for chloroform. (4)
- The California Environmental Protection Agency (CalEPA) has established a chronic reference exposure level of 0.3 mg/m^3 for chloroform based on exposures resulting in kidney and liver effects in rats. The CalEPA reference exposure level is a concentration at or below which adverse health effects are not likely to occur. It is not a direct estimator of risk, but rather a reference point to gauge the potential effects. At lifetime exposures increasingly greater than the reference exposure level, the potential for adverse health effects increases. (5)
- ATSDR has established an acute inhalation minimal risk level (MRL) of 0.5 mg/m^3 (0.1 ppm) based on exposures resulting in liver effects in mice, an intermediate inhalation MRL of 0.2 mg/m^3 (0.05 ppm) based on worker exposures resulting in liver effects in humans, and a chronic inhalation MRL of 0.1 mg/m^3 (0.02 ppm) also based on liver effects in humans. The MRL is an estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk of adverse noncancer health effects over a specified duration of exposure. (1)
- The RfD for chloroform is 0.01 mg/kg/d based on exposures resulting in fatty cyst formation in the livers of dogs. The RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious noncancer effects during a lifetime. (4)
- EPA has medium to low confidence in the RfD due to: medium confidence in the critical study on which the RfD was based because it was of chronic duration, used a fairly large number of dogs, measured multiple endpoints using only two treatment doses, and a no-observed-effect level (NOEL) was not determined; and medium to low confidence in the database because several studies support the choice of a lowest-observed-adverse-effect level (LOAEL), but a NOEL was not found. (4)

Reproductive/Developmental Effects:

- Little information is available on the reproductive or developmental effects of chloroform in humans, via any route of exposure. A possible association between certain birth outcomes (e.g., low birth weight, cleft palate) and consumption of contaminated drinking water was reported. However, because multiple contaminants were present, the role of chloroform is unclear. (1)
- Animal studies have demonstrated developmental effects, such as decreased fetal body weight, fetal resorptions, and malformations in the offspring of animals exposed to chloroform via inhalation. (1)
- Reproductive effects, such as decreased conception rates, decreased ability to maintain pregnancy, and an increase in the percentage of abnormal sperm were observed in animals exposed to chloroform through inhalation. (1)
- Animal studies have noted decreased fetal weight, increased fetal resorptions, but no evidence of birth defects, in animals orally exposed to chloroform. (1)

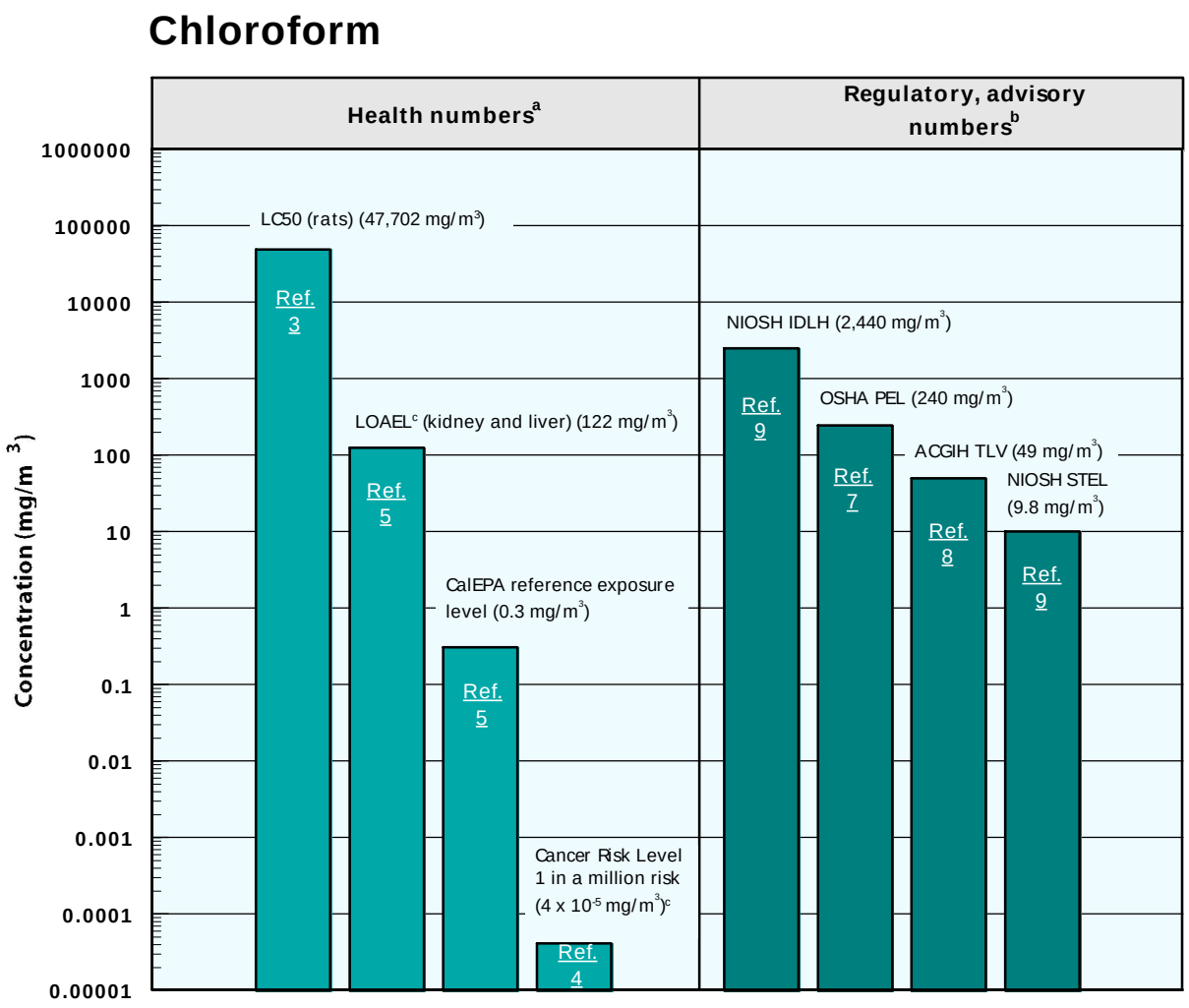
Cancer Risk:

- No information is available regarding cancer in humans or animals after inhalation exposure to chloroform. (1)
- Epidemiologic studies suggest an association between cancer of the large intestine, rectum, and/or bladder and the constituents of chlorinated drinking water, including chloroform. However, there are no epidemiologic studies of water containing only chloroform. (1)
- Chloroform has been shown to be carcinogenic in animals after oral exposure, resulting in an increase in kidney and liver tumors. (1)
- EPA has classified chloroform as a Group B2, probable human carcinogen. (4)
- EPA uses mathematical models, based on human and animal studies, to estimate the probability of a person developing cancer from breathing air containing a specified concentration of a chemical. EPA calculated an inhalation unit risk estimate of 2.3×10^{-5} $(\mu g/m^3)^{-1}$. EPA estimates that, if an individual were to continuously breathe air containing chloroform at an average of 0.04 $\mu g/m^3$ (4×10^{-5} mg/m^3) over his or her entire lifetime, that person would theoretically have no more than a one-in-a-million increased chance of developing cancer as a direct result of breathing air containing this chemical. Similarly, EPA estimates that continuously breathing air containing 0.4 $\mu g/m^3$ (4×10^{-4} mg/m^3) would result in not greater than a one-in-a-hundred thousand increased chance of developing cancer, and air containing 4.0 $\mu g/m^3$ (4×10^{-3} mg/m^3) would result in not greater than a one-in-ten thousand increased chance of developing cancer. For a detailed discussion of confidence in the potency estimates, please see IRIS. (4)
- EPA has calculated an oral cancer slope factor of 6.1×10^{-3} $(mg/kg/d)^{-1}$. (4)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45).
For chloroform: 1 ppm = 4.88 mg/m^3.
To convert from $\mu g/m^3$ to mg/m^3: mg/m^3 = ($\mu g/m^3$) x (1 mg/1,000 μg).

Health Data from Inhalation Exposure



ACGIH TLV – American Conference of Governmental and Industrial Hygienists' threshold limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effects.
LC_{50} (Lethal Concentration$_{50}$) – A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.
LOAEL – Lowest-observed-adverse-effect level.
NIOSH REL – National Institute of Occupational Safety and Health's recommended exposure limit; NIOSH-recommended exposure limit for an 8- or 10-h time-weighted-average exposure and/or ceiling.
OSHA PEL – Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.

[a] Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA.
[b] Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the Government or other groups as advice.
[c] These cancer risk estimates were derived from oral data and converted to provide the estimated inhalation risk.
[d] The LOAEL is from the critical study used as the basis for the CalEPA chronic reference exposure level.

References

1. Agency for Toxic Substances and Disease Registry (ATSDR). *Toxicological Profile for Chloroform*. Public Health Service, U.S. Department of Health and Human Services, Atlanta, GA. 1997.

2. U.S. Department of Health and Human Services. Hazardous Substances Data Bank (HSDB, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.

3. U.S. Department of Health and Human Services. Registry of Toxic Effects of Chemical Substances (RTECS, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.

4. U.S. Environmental Protection Agency (EPA). *Integrated Risk Information System (IRIS) on Chloroform*. National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1999.

5. California Environmental Protection Agency (CalEPA). *Technical Support Document for the Determination of Noncancer Chronic Reference Exposure Levels. Draft for Public Comment.* Office of Environmental Health Hazard Assessment, Berkeley, CA. 1997.

6. *The Merck Index. An Encyclopedia of Chemicals, Drugs, and Biologicals*. 11th ed. Ed. S. Budavari. Merck and Co. Inc., Rahway, NJ. 1989.

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

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

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

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CHROMIUM COMPOUNDS

Hazard Summary

Chromium occurs in the environment primarily in two valence states, trivalent chromium (Cr III) and hexavalent chromium (Cr VI). Exposure may occur from natural or industrial sources of chromium.

The respiratory tract is the major target organ for chromium (VI) toxicity, for acute (short-term) and chronic (long-term) inhalation exposures. Shortness of breath, coughing, and wheezing were reported from a case of acute exposure to chromium (VI), while perforations and ulcerations of the septum, bronchitis, decreased pulmonary function, pneumonia, and other respiratory effects have been noted from chronic exposure. Limited human studies suggest that chromium (VI) inhalation exposure may be associated with complications during pregnancy and childbirth, while animal studies have not reported reproductive effects from inhalation exposure to chromium (VI). The U.S. Environmental Protection Agency (EPA) has classified chromium (VI) as a Group A, known human carcinogen. Human studies have clearly established that inhaled chromium (VI) is a human carcinogen, resulting in an increased risk of lung cancer. Animal studies have shown chromium (VI) to cause lung tumors via inhalation exposure.

Chromium III is much less toxic than chromium (VI). The respiratory tract is also the major target organ for chromium (III) toxicity, similar to chromium (VI). Chromium (III) is an essential element in humans, with a daily intake of 50 to 200 µg/d recommended for an adult. The body can detoxify some amount of chromium (VI) to chromium (III).

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

Physical Properties

- The metal, chromium (Cr), is a steel-gray solid with a high melting point and an atomic weight of 51.996 g/mol. Chromium has oxidation states ranging from chromium (-II) to chromium (+VI). (1)
- Chromium forms a large number of compounds, in both the chromium (III) and the chromium (VI) forms. Chromium compounds are stable in the trivalent state, with the hexavalent form being the second most stable state. (1)
- The chromium (III) compounds are sparingly soluble in water and may be found in water bodies as soluble chromium (III) complexes, while the chromium (VI) compounds are readily soluble in water. (1)

Uses

- The metal chromium is used mainly for making steel and other alloys. (1)
- Chromium compounds, in either the chromium (III) or chromium (VI) forms, are used for chrome plating, the manufacture of dyes and pigments, leather and wood preservation, and treatment of cooling tower water. Smaller amounts are used in drilling muds, textiles, and toner for copying machines. (1)

Sources and Potential Exposure

- Chromium is a naturally occurring element in rocks, animals, plants, soil, and volcanic dust and gases. (1)
- Chromium occurs in the environment predominantly in one of two valence states: trivalent chromium (Cr III), which occurs naturally and is an essential nutrient, and hexavalent chromium (Cr VI), which, along with the less common metallic chromium (Cr 0), is most commonly produced by industrial processes. (1)
- Chromium (III) is essential to normal glucose, protein, and fat metabolism and is thus an essential dietary element. The body has several systems for reducing chromium (VI) to chromium (III). This chromium (VI) detoxification leads to increased levels of chromium (III). (1)
- Air emissions of chromium are predominantly of trivalent chromium, and in the form of small particles or aerosols. (1, 2)
- The most important industrial sources of chromium in the atmosphere are those related to ferrochrome production. Ore refining, chemical and refractory processing, cement-producing plants, automobile brake lining and catalytic converters for automobiles, leather tanneries, and chrome pigments also contribute to the atmospheric burden of chromium. (3)
- The general population is exposed to chromium (generally chromium [III]) by eating food, drinking water, and inhaling air that contains the chemical. The average daily intake from air, water, and food is estimated to be approximately less than 0.2 to 0.4 µg, 2.0 µg, and 60 µg, respectively. (1)
- Dermal exposure to chromium may occur during the use of consumer products that contain chromium, such as wood treated with copper dichromate or leather tanned with chromic sulfate. (1)
- Occupational exposure to chromium occurs from chromate production, stainless-steel production, chrome plating, and working in tanning industries; occupational exposure can be two orders of magnitude higher than exposure to the general population. (1)
- People who live in the vicinity of chromium waste disposal sites or chromium manufacturing and processing plants have a greater probability of elevated chromium exposure than the general population. These exposures are generally to mixed chromium (VI) and chromium (III). (1)

Assessing Personal Exposure

- Laboratory tests can detect chromium in the blood, urine, and hair of exposed individuals. (1, 5)
- Laboratory tests find it difficult to separate chromium VI from chromium III; in many cases analysis is done for total chromium. (1)

Health Hazard Information

Acute Effects:

Chromium VI

- Chromium (VI) is much more toxic than chromium (III), for both acute and chronic exposures. (1,3,4)
- The respiratory tract is the major target organ for chromium (VI) following inhalation exposure in humans. Shortness of breath, coughing, and wheezing were reported in cases where an individual inhaled very high concentrations of chromium trioxide. (1,4)
- Other effects noted from acute inhalation exposure to very high concentrations of chromium (VI) include gastrointestinal and neurological effects, while dermal exposure causes skin burns. (1,4,5)
- Ingestion of high amounts of chromium (VI) causes gastrointestinal effects in humans and animals, including abdominal pain, vomiting, and hemorrhage. (1)
- Acute animal tests, such as the LC_{50} and LD_{50} tests in rats, have shown chromium (VI) to have extreme toxicity from inhalation (LC_{50} = 30-140 mg/m^3) and oral (LD_{50} <100 mg/kg) exposure. (1,6)

Chromium III

- Chromium (III) is an essential element in humans, with a daily intake of 50 to 200 µg/d recommended for adults. (1)
- Acute animal tests have shown chromium (III) to have moderate toxicity from oral exposure, with LD_{50} values of 200-2000 mg/kg and much lower toxicity from acute dietary exposures. (1,6)

***Chronic Effects (Noncancer)*:**

Chromium VI

- Chronic inhalation exposure to chromium (VI) in humans results in effects on the respiratory tract, with perforations and ulcerations of the septum, bronchitis, decreased pulmonary function, pneumonia, asthma, and nasal itching and soreness reported. (1,4,5)
- Chronic human exposure to high levels of chromium (VI) by inhalation or oral exposure may produce effects on the liver, kidney, gastrointestinal and immune systems, and possibly the blood. (1,4,5)

- Rat studies have shown that, following inhalation exposure, the lung and kidney have the highest tissue levels of chromium. (1,4,5)
- Dermal exposure to chromium (VI) may cause contact dermatitis, sensitivity, and ulceration of the skin. (1,4,5)
- The RfC for chromium (VI) (particulates) is 0.0001 mg/m^3 based on respiratory effects in rats. The RfC is an estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious noncancer effects during a lifetime. It is not a direct estimator of risk but rather a reference point to gauge the potential effects. At exposures increasingly greater than the RfC, the potential for adverse health effects increases. Lifetime exposure above the RfC does not imply that an adverse health effect would necessarily occur. (7)
- EPA has medium confidence in the RfC for chromium VI (particulates) based on medium confidence in the study on which it was based because of uncertainties regarding upper respiratory tract, reproductive, and renal effects resulting from the exposures. (7)
- The RfC for chromium (VI) (chromic acid mists and dissolved Cr (VI) aerosols) is 0.000008 mg/m^3 based on respiratory effects in humans. (7)
- EPA has low confidence in the RfC based on low confidence in the study on which the RfC for chromium (VI) (chromic acid mists and dissolved Cr (VI) aerosols) is based because of uncertainties regarding the exposure characterization and the role of direct contact for the critical effect; and low confidence in the database because the supporting studies are equally uncertain regarding the exposure characterization. (7)
- The RfD for chromium (VI) is 0.003 mg/kg/d based on the exposure at which no effects were noted in rats exposed to chromium in the drinking water. (7)
- EPA has low confidence in the RfD based on: low confidence in the study on which the RfD for chromium (VI) was based because a small number of animals were tested, a small number of parameters were measured, and no toxic effects were noted at the highest dose tested; and low confidence in the database because the supporting studies are of equally low quality and developmental endpoints are not well studied. (7)

Chromium III

- Although data from animal studies have identified the respiratory tract as the major target organ for chronic chromium exposure, these data do not demonstrate that the effects observed following inhalation of chromium (VI) particulates are relevant to inhalation of chromium (III). (8)
- EPA has not established an RfC for chromium (III). (8)
- The RfD for chromium (III) is 1.5 mg/kg/d based on the exposure level at which no effects were observed in rats exposed to chromium (III) in the diet. (8)
- EPA has low confidence in the RfD based on: low confidence in the study on which the RfD for chromium (III) was based due to the lack of explicit detail on study protocol and results; and low confidence in the database due to the lack of high-dose supporting data. (8)

Reproductive/Developmental Effects:

Chromium VI

- Limited information on the reproductive effects of chromium (VI) in humans exposed by inhalation suggest that exposure to chromium (VI) may result in complications during pregnancy and childbirth. (1)
- Animal studies have not reported reproductive or developmental effects from inhalation exposure to chromium (VI). Oral studies have reported severe developmental effects in mice such as gross abnormalities and reproductive effects including decreased litter size, reduced sperm count, and degeneration of the outer cellular layer of the seminiferous tubules. (1,4)

Chromium III

- No information is available on the reproductive or developmental effects of chromium (III) in humans. (3)
- A study of mice fed high levels of chromium (III) in their drinking water has suggested a potential for reproductive effects, although various study characteristics preclude a definitive finding. (3)
- No developmental effects were reported in the offspring of rats fed chromium (III) during their developmental period. (1,3)

Cancer Risk:

Chromium VI

- Epidemiological studies of workers have clearly established that inhaled chromium is a human carcinogen, resulting in an increased risk of lung cancer. Although chromium-exposed workers were exposed to both chromium (III) and chromium (VI) compounds, only chromium (VI) has been found to be carcinogenic in animal studies, so EPA has concluded that only chromium (VI) should be classified as a human carcinogen. (1,7)
- Animal studies have shown chromium (VI) to cause lung tumors via inhalation exposure. (1,5)
- EPA has classified chromium (VI) as a Group A, known human carcinogen by the inhalation route of exposure. Carcinogenicity by the oral route of exposure cannot be determined and has been classified by EPA as a Group D. (7)
- EPA uses mathematical models, based on human and animal studies, to estimate the probability of a person developing cancer from breathing air containing a specified concentration of a chemical. EPA calculated an inhalation unit risk estimate of 1.2×10^{-2} $(\mu g/m^3)^{-1}$. EPA estimates that, if an individual were to continuously breathe air containing chromium at an average of 0.00008 $\mu g/m^3$ (8×10^{-8} mg/m^3) over his or her entire lifetime, that person would theoretically have no more than a one-in-a-million increased chance of developing cancer as a direct result of breathing air containing this chemical. Similarly, EPA estimates that continuously breathing air containing 0.0008 $\mu g/m^3$ (8×10^{-7} mg/m^3)

would result in not greater than a one-in-a-hundred thousand increased chance of developing cancer during their lifetime, and air containing 0.008 µg/m^3 (8 x 10^{-6} mg/m^3) would result in not greater than a one-in-ten-thousand increased chance of developing cancer during their lifetime. For a detailed discussion of confidence in the potency estimates, please see IRIS. (7)

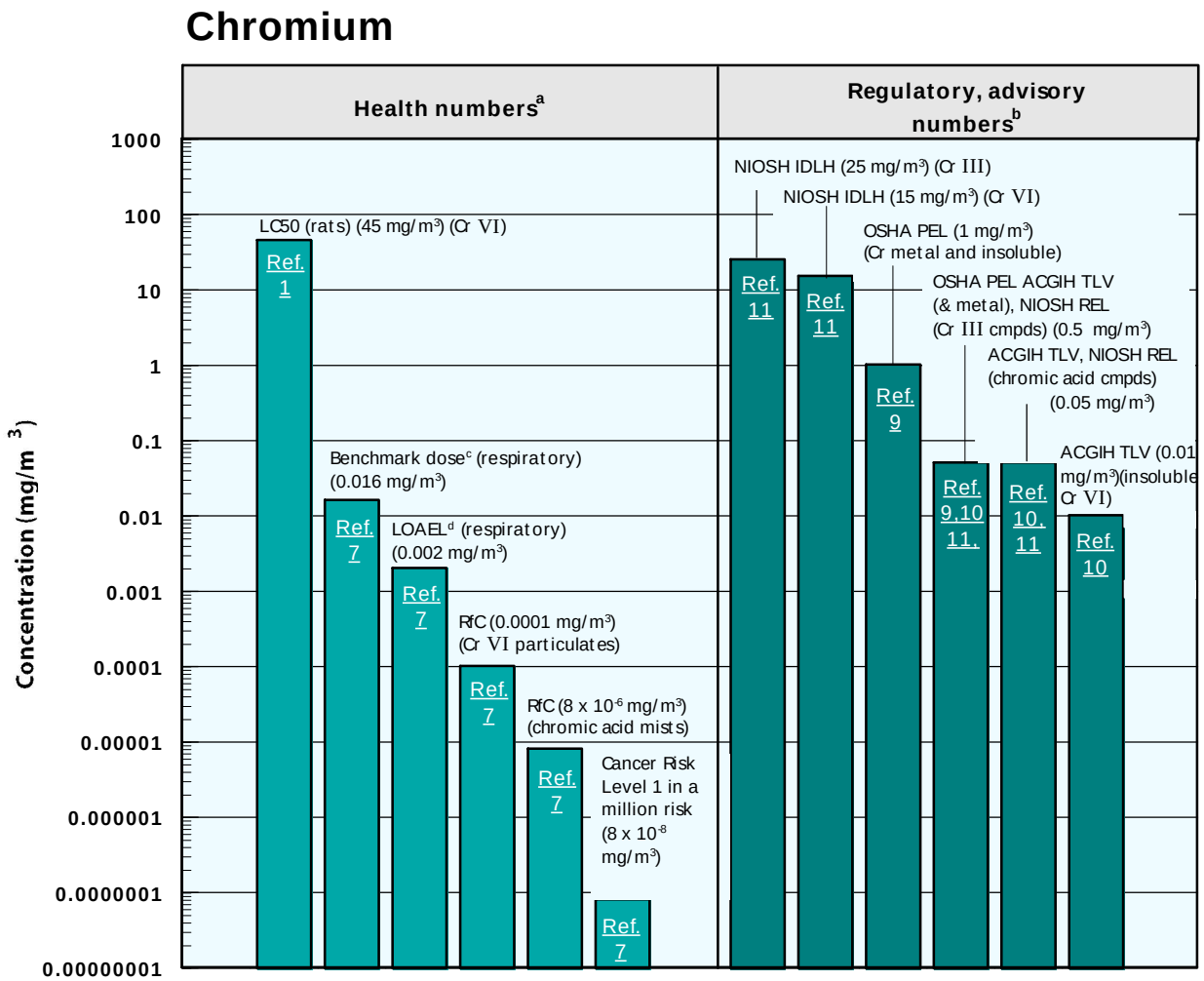
Chromium III

- **!** No data are available on the carcinogenic potential of chromium (III) compounds alone. (1,8)
- **!** EPA has classified chromium (III) as a Group D carcinogen, not classifiable as to carcinogenicity in humans. (8)
- **!** EPA has stated that "the classification of chromium (VI) as a known human carcinogen raises a concern for the carcinogenic potential of chromium (III)." (8)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45).
For chromium: 1 ppm = 2.12 mg/m^3.
To convert from µg/m^3 to mg/m^3: mg/m^3 = (µg/m^3) x (1 mg/1,000 µg).

Health Data from Inhalation Exposure



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

LC_{50} (Lethal Concentration$_{50}$) – A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.

LOAEL – Lowest-observed-adverse-affect level.

NIOSH IDLH – National Institute of Occupational Safety and Health's immediately dangerous to life or health concentration; NIOSH recommended exposure limit to ensure that a worker can escape from an exposure condition that is likely to cause death or immediate or delayed permanent adverse health effects or prevent escape from the environment.

NIOSH REL – NIOSH's recommended exposure limit; NIOSH-recommended exposure limit for an 8- or 10-h time-weighted-average exposure and/or ceiling.

OSHA PEL – Occupational Safety and Health Administration's permissible exposure limit

expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.

[a] Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA.
[b] Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the Government or other groups as advice.
[c] The benchmark dose is from the critical study used as the basis for the EPA's RfC for Cr(VI) particulates.
[d] The LOAEL is from the critical study used as the basis for the EPA's RfC for chromic acid mists and dissolved Cr (VI) aerosols.

References

1. Agency for Toxic Substances and Disease Registry (ATSDR). *Toxicological Profile for Chromium*. Public Health Service, U.S. Department of Health and Human Services, Atlanta, GA. 1998.

2. SAIC. *PM/Toxics Integration: Addressing Co-Control Benefits*. Submitted to U.S. Environmental Protection Agency, Office of Air Quality Planning and Standards, Research Triangle Park, NC. 1998.

3. U.S. Environmental Protection Agency (EPA). *Toxicological Review of Trivalent Chromium*. National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1998.

4. U.S. Environmental Protection Agency (EPA). *Toxicological Review of Hexavalent Chromium*. National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1998.

5. World Health Organization (WHO). Chromium. *Environmental Health Criteria 61*. Geneva, Switzerland. 1988.

6. U.S. Department of Health and Human Services. Registry of Toxic Effects of Chemical Substances (RTECS, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.

7. U.S. Environmental Protection Agency (EPA). *Integrated Risk Information System (IRIS) on Chromium VI*. National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1993.

8. U.S. Environmental Protection Agency (EPA). *Integrated Risk Information System (IRIS) on Chromium III*. National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1993.

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

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

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

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COKE OVEN EMISSIONS[1]

Hazard Summary

Exposure to coke oven emissions may occur for workers in the aluminum, steel, graphite, electrical, and construction industries. No information is available on the effects of coke oven emissions in humans from acute (short-term) exposure. Animal studies have reported weakness, depression, shortness of breath, general edema, and effects on the liver from acute oral exposure to coke oven emissions. Chronic (long-term) exposure to coke oven emissions in humans results in conjunctivitis, severe dermatitis, and lesions of the respiratory system and digestive system. No information is available on the reproductive or developmental effects of coke oven emissions in humans or animals. Cancer is the major concern from exposure to coke oven emissions. Epidemiologic studies of coke oven workers have reported an increase in cancer of the lung, trachea, bronchus, kidney, prostate, and other sites. Animal studies have reported tumors of the lung and skin from inhalation exposure to coal tar. The U.S. Environmental Protection Agency (EPA) has classified coke oven emissions as a Group A, known human carcinogen.

Please Note: The main source of information for this fact sheet is EPA's Integrated Risk Information System (IRIS), which contains information on the carcinogenic effects of coke oven emissions including the unit cancer risk for inhalation exposure. Other secondary sources include the Hazardous Substances Data Bank (HSDB), a database of summaries of peer-reviewed literature, and *The Handbook of Toxic and Hazardous Chemicals and Carcinogens,* a reference book that summarizes the key effects from exposure to hazardous chemicals.

Physical Properties

- Coke oven emissions are a mixture of coal tar, coal tar pitch, and creosote and contain chemicals such as benzo(*a*)pyrene, benzanthracene, chrysene, and phenanthrene. (1)
- Condensed coke oven emissions are a brownish, thick liquid or semisolid with a naphthalene-like odor, while uncondensed coke oven emissions are vapors that escape when the ovens are changed and emptied. (2)
- The odor threshold for coke oven emissions is not available. The actual chemical content of the emissions depends on the process variables.

Uses

- Chemicals recovered from coke oven emissions are used as a raw material for plastics, solvents, dyes, drugs, waterproofing, paints, pipecoating, roads, roofing, insulation, and as pesticides and sealants. (2)

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[1] Coke oven emissions include coal tar, creosote, and coal tar pitch.

Sources and Potential Exposure

- Occupational exposure to coke oven emissions may occur for those workers in the aluminum, steel, graphite, electrical, and construction industries. (1)

Assessing Personal Exposure

- No information is available on the assessment of personal exposure to coke oven emissions.

Health Hazard Information

Acute Effects:

- No information is available on the effects of coke oven emissions from acute exposure in humans.
- Animal studies have reported weakness, depression, shortness of breath, general edema, and effects on the liver from acute oral exposure to coke oven emissions. (2)

Chronic Effects (Noncancer):

- Chronic exposure to coke oven emissions in humans results in conjunctivitis, severe dermatitis, and lesions of the respiratory and digestive systems. (2)
- Animal studies have reported effects on the liver from chronic oral exposure to coke oven emissions. (2)
- EPA has not established a reference concentration (RfC) or a reference dose (RfD) for coke oven emissions. (3)

Reproductive/Developmental Effects:

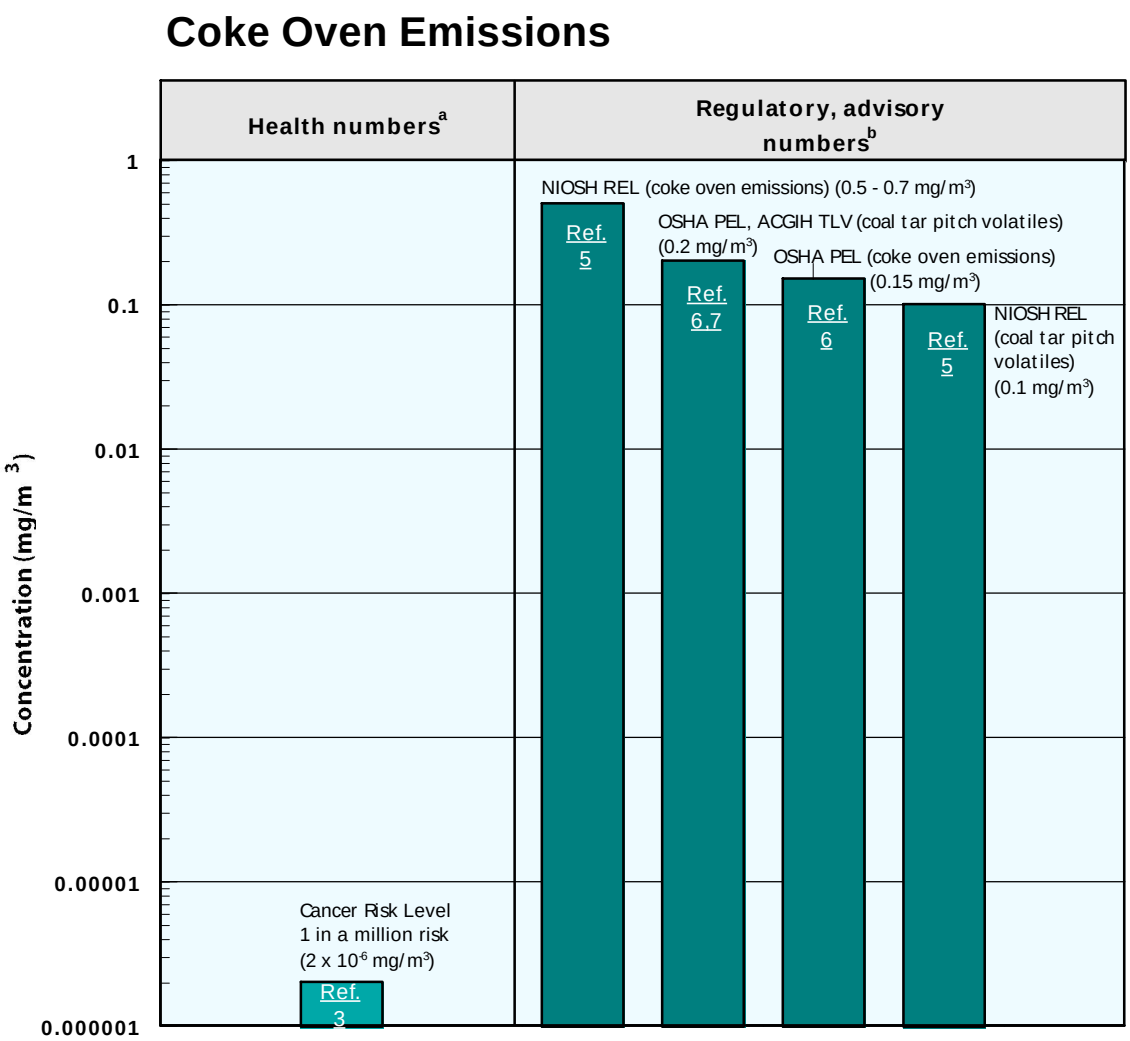
- No information is available on the reproductive or developmental effects of coke oven emissions in humans or animals.

Cancer Risk:

- Epidemiologic studies of coke oven workers have reported an increase in cancer of the lung, trachea, bronchus, kidney, prostate, and other sites. (3)
- Animal studies have reported tumors of the lung and skin from inhalation exposure to coal tar. (3)
- EPA has classified coke oven emissions as a Group A, known human carcinogen. (3)
- EPA uses mathematical models, based on human and animal studies, to estimate the probability of a person developing cancer from breathing air containing a specified concentration of a chemical. EPA calculated an inhalation unit risk estimate of 6.2×10^{-4} $(\mu g/m^3)^{-1}$. EPA estimates that, if an individual were to continuously breathe air containing coke oven emissions at an average of 0.002 $\mu g/m^3$ (2×10^{-6} mg/m^3) over his or her entire

lifetime, that person would theoretically have no more than a one-in-a-million increased chance of developing cancer as a direct result of continuously breathing air containing this chemical. Similarly, EPA estimates that breathing air containing 0.02 µg/m^3 (2 x 10^{-5} mg/m^3) would result in not greater than a one-in-a-hundred-thousand increased chance of developing cancer during a lifetime, and air containing 0.2 µg/m^3 (2 x 10^{-4} mg/m^3) would result in not greater than a one-in-ten-thousand increased chance of developing cancer during a lifetime. For a detailed discussion of confidence in the potency estimates, please see IRIS. (3)

Health Data from Inhalation Exposure



ACGIH TLV – American Conference of Governmental and Industrial Hygienists' threshold limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effects.
NIOSH REL – National Institute of Occupational Safety and Health's recommended exposure

limit; NIOSH-recommended exposure limit for an 8- or 10-h time-weighted-average exposure and/or ceiling.
OSHA PEL – Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effects averaged over a normal 8-h workday or a 40-h workweek.

[a] Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA.
[b] Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the Government or other groups as advice.

References

1. M. Sittig. *Handbook of Toxic and Hazardous Chemicals and Carcinogens*. 2nd ed. Noyes Publications, Park Ridge, NJ. 1985.

2. U.S. Department of Health and Human Services. Hazardous Substances Data Bank (HSDB, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.

3. U.S. Environmental Protection Agency (EPA). *Integrated Risk Information System (IRIS) on Coke Oven Emissions*. National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1999.

4. U.S. Department of Health and Human Services. Registry of Toxic Effects of Chemical Substances (RTECS, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.

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

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

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

1,2-DICHLOROETHANE (ETHYLENE DICHLORIDE)

107-06-2

Hazard Summary

Exposure to low levels of 1,2-dichloroethane can occur from breathing ambient or workplace air. Inhalation of concentrated 1,2-dichloroethane vapor can induce effects on the human nervous system, liver, and kidneys, as well as respiratory distress, cardiac arrhythmia, nausea, and vomiting. Similar effects have been reported in animals exposed by inhalation. Clouding of the cornea and eye irritation have been observed in animals. Chronic (long-term) inhalation exposure to 1,2-dichloroethane produced effects on the liver and kidneys in animals. No information is available on the reproductive or developmental effects of 1,2-dichloroethane in humans. Decreased fertility and increased embryo mortality have been observed in inhalation studies of rats. The U.S. Environmental Protection Agency (EPA) has classified 1,2-dichloroethane as a Group B2, probable human carcinogen. Epidemiological studies are not conclusive regarding the carcinogenic effects of 1,2-dichloroethane, due to concomitant exposure to other chemicals. Following treatment by gavage, several tumor types were induced in rats and mice.

Please Note: The main sources of information for this fact sheet are EPA's Integrated Risk Information System (IRIS), which contains information on the carcinogenic effects of 1,2-dichloroethane including the unit cancer risk for inhalation exposure, and the Agency for Toxic Substances and Disease Registry's (ATSDR's) *Toxicological Profile for 1,2-Dichloroethane*.

Physical Properties

- The chemical formula for 1,2-dichloroethane is $C_2H_4Cl_2$, and its molecular weight is 98.96 g/mol. (1)
- 1,2-Dichloroethane occurs as a colorless, oily, heavy liquid that is slightly soluble in water. (1)
- 1,2-Dichloroethane has a pleasant chloroform-like odor, with an odor threshold of 6-10 ppm. (1)
- The vapor pressure for 1,2-dichloroethane is 64 mm Hg at 20 EC, and its log octanol/water partition coefficient (log K_{ow}) is 1.48. (1)

Uses

- 1,2-Dichloroethane is primarily used in the production of vinyl chloride as well as other chemicals. It is used in solvents in closed systems for various extraction and cleaning purposes in organic synthesis. It is also added to leaded gasoline as a lead scavenger. (1)
- It is also used as a dispersant in rubber and plastics, as a wetting and penetrating agent. (1)

- It was formerly used in ore flotation, as a grain fumigant, as a metal degreaser, and in textile and PVC cleaning. (1)

Sources and Potential Exposure

- Inhalation of 1,2-dichloroethane in the ambient or workplace air is generally the main route of human exposure. The compound may be released during its production, storage, use, transport, and disposal. (1)
- Exposure may also occur through the consumption of contaminated water. But usually 1,2-dichloroethane will evaporate quickly into the air from the water or soil. (1)
- The average levels of 1,2-dichloroethane in the air of seven urban locations in 1980-1981 ranged from 0.1 to 1.5 ppb. (1)

Assessing Personal Exposure

- Breath samples may be used to determine whether or not someone has been recently exposed to 1,2-dichloroethane. (1)

Health Hazard Information

Acute Effects:

- Inhaling concentrated 1,2-dichloroethane can be lethal to humans. An occupationally exposed man died from cardiac arrhythmia after acute (short-term) inhalation exposure to concentrated vapors of 1,2-dichloroethane; congestion of the lungs, degenerative changes in the myocardium, and damage to the liver, kidneys, and nerve cells in the brain were also observed. (1)
- Acute inhalation exposure to 1,2-dichloroethane can affect the nervous system, with effects including narcosis, nausea, and vomiting. (1)
- Effects reported in animals exposed by inhalation are similar to those for humans. (1)
- Clouding of the cornea and eye irritation have been observed in animals and are thought to be the result of vapor contact with the eyes. (1)
- Cardiac arrhythmia, pulmonary edema, bronchitis, hemorrhagic gastritis and colitis, depression, and changes in the brain tissue have been reported in humans that ingested large amounts of 1,2-dichloroethane. (1)
- Acute animal tests, such as the LC_{50} and LD_{50} tests in rats, mice, and rabbits, have demonstrated 1,2-dichloroethane to have moderate acute toxicity from inhalation or dermal exposure and moderate to high acute toxicity from oral exposure. (2)

Chronic Effects (Noncancer):

- Chronic inhalation exposure to 1,2-dichloroethane produced effects on the liver and kidneys in animals. (1)

- Some studies have reported changes in the liver and kidneys and effects on the immune system and central nervous system (CNS) in animals chronically exposed by ingestion. (1)
- EPA has not established a reference dose (RfD) or a reference concentration (RfC) for 1,2-dichloroethane. (3)
- ATSDR has established an intermediate oral minimal risk level (MRL) of 0.2 mg/kg/d based on kidney effects in animals. The MRL is an estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk of adverse noncancer health effects over a specified duration of exposure. Exposure to a level above the MRL does not mean that adverse health effects will occur. The MRL is intended to serve as a screening tool. (1)
- ATSDR has established a chronic inhalation MRL of 0.8 mg/m^3 (0.2 ppm) based on liver effects in animals and an acute inhalation MRL of 0.8 mg/m^3 (0.2 ppm) based on immunological effects in animals. (1)
- The California Environmental Protection Agency (CalEPA) has established a chronic reference exposure level of 0.4 mg/m^3 for 1,2-dichloroethane based on liver effects in rats. The CalEPA reference exposure level is a concentration at or below which adverse health effects are not likely to occur. (5)

Reproductive/Developmental Effects:

- No information is available on the reproductive or developmental effects of 1,2-dichloroethane in humans.
- Decreased fertility and increased embryo mortality have been observed in inhalation studies of rats. (1)

Cancer Risk:

- Epidemiological occupational studies could not link exposure to 1,2-dichloroethane specifically with excess cancer incidence. (1)
- An increased incidence of colon and rectal cancer in men over 55 years of age exposed to 1,2-dichloroethane in the drinking water has been reported. However, the study population was concomitantly exposed to other chemicals. (1)
- Following treatment by gavage, several tumor types (including increased incidences of forestomach squamous-cell carcinomas, circulatory system hemangiosarcomas, mammary adenocarcinoma, alveolar/bronchiolar adenomas, endometrial stromal polyps and sarcomas, and hepatocellular carcinomas) were induced in rats and mice. (1,3,4)
- An increased incidence of lung papillomas has been reported in mice after topical application. (1,3)
- EPA has classified 1,2-dichloroethane as a Group B2, probable human carcinogen. (3)
- EPA uses mathematical models, based on human and animal studies, to estimate the probability of a person developing cancer from breathing air containing a specified concentration of a chemical. EPA calculated an inhalation unit cancer risk estimate of 2.6 x 10^{-5} $(\mu g/m^3)^{-1}$. EPA estimates that, if an individual were to continuously breathe air containing 1,2-dichloroethane at an average of 0.04 $\mu g/m^3$ (4 x 10^{-5} mg/m^3) over his or

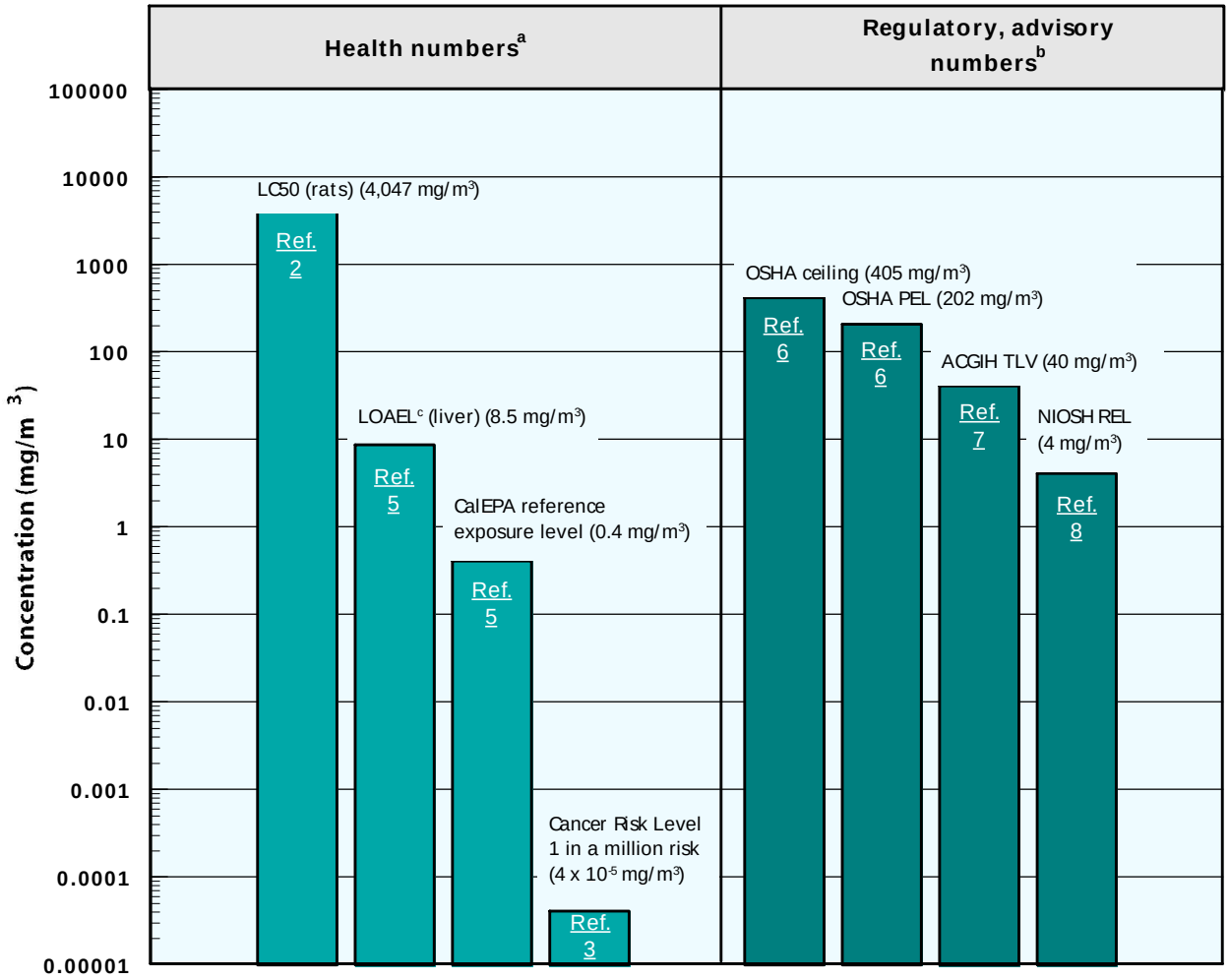
her entire lifetime, that person would theoretically have no more than a one-in-a-million increased chance of developing cancer as a direct result of breathing air containing this chemical. Similarly, EPA estimates that breathing air containing 0.4 $\mu g/m^3$ (4×10^{-4} mg/m^3) would result in not greater than a one-in-a-hundred thousand increased chance of developing cancer, and air containing 4.0 $\mu g/m^3$ (4×10^{-3} mg/m^3) would result in not greater than a one-in-ten thousand increased chance of developing cancer. For a detailed discussion of confidence in the potency estimates, please see IRIS. (3)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45). For 1,2-dichloroethane: 1 ppm = 4.05 mg/m^3. To convert from $\mu g/m^3$ to mg/m^3: mg/m^3 = ($\mu g/m^3$) x (1 mg/1,000 μg).

Health Data from Inhalation Exposure

1,2-Dichloroethane



ACGIH TLV – American Conference of Governmental and Industrial Hygienists' threshold limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effects.
LC_{50} (Lethal Concentration$_{50}$) – A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.
LOAEL – Lowest-observed-adverse-affect level.
NIOSH REL – National Institute of Occupational Safety and Health recommended exposure limit; NIOSH-recommended exposure limit for an 8- or 10-h time-weighted-average exposure and/or ceiling.
OSHA PEL – Occupational Safety and Health Administration's permissible exposure limit

expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.
OSHA PEL ceiling – OSHA's permissible exposure limit ceiling value; the concentration of a substance that should not be exceeded at any time.

[a] Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA.
[b] Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the Government or other groups as advice.
[c] The LOAEL is from the critical study used as the basis for the CalEPA chronic reference exposure level.
[d] These cancer risk estimates were derived from oral data and converted to provide the estimated inhalation risk.

References

1. Agency for Toxic Substances and Disease Registry (ATSDR). *Toxicological Profile for 1,2-Dichloroethane.* Public Health Service, U.S. Department of Health and Human Services, Atlanta, GA. 1992.

2. U.S. Department of Health and Human Services. Registry of Toxic Effects of Chemical Substances (RTECS, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.

3. U.S. Environmental Protection Agency (EPA). *Integrated Risk Information System (IRIS) on 1,2-Dichloroethane*. National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1999.

4. U.S. Environmental Protection Agency (EPA). *Health Effects Assessment for 1,2-Dichloroethane*. EPA/540/1-86/002. Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment, Office of Research and Development, Cincinnati, OH. 1986.

5. California Environmental Protection Agency (CalEPA). *Technical Support Document for the Determination of Noncancer Chronic Reference Exposure Levels. Draft for Public Comment.* Office of Environmental Health Hazard Assessment, Berkeley, CA. 1997.

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

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

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

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1,2-DICHLOROPROPANE (PROPYLENE DICHLORIDE)

78-87-5

Hazard Summary

1,2-Dichloropropane is used as a chemical intermediate in several industries. Acute (short-term) inhalation exposure to high levels of 1,2-dichloropropane by humans results in effects on the lungs, gastrointestinal system, blood, liver, kidneys, central nervous system (CNS), and eyes. No information is available on the chronic (long-term) effects of 1,2-dichloropropane in humans, and animal studies have reported effects on the respiratory system and blood from chronic inhalation exposure. Limited information is available on the reproductive or developmental effects of 1,2-dichloropropane in humans. Animal studies have reported reproductive and developmental effects from 1,2-dichloropropane exposure by gavage. No information is available regarding the carcinogenic effects of 1,2-dichloropropane in humans from inhalation or oral exposure. Animal studies have reported an increased incidence of mammary gland tumors in female rats and liver tumors in male and female mice given 1,2-dichloropropane by gavage. The U.S. Environmental Protection Agency (EPA) has provisionally classified 1,2-dichloropropane as a Group B2, probable human carcinogen.

Please Note: The main sources of information for this fact sheet are the Agency for Toxic Substances and Disease Registry's (ATSDR's) *Toxicological Profile for 1,2-Dichloropropane* and EPA's Integrated Risk Information System (IRIS), which contains information on inhalation chronic toxicity of 1,2-dichloropropane and the reference concentration (RfC).

Physical Properties

- The chemical formula for 1,2-dichloropropane is $C_3H_6Cl_2$, and the molecular weight is 112.99 g/mol. (1)
- 1,2-Dichloropropane is a colorless liquid which evaporates quickly at room temperature. (1)
- 1,2-Dichloropropane has a chloroform-like odor and an odor threshold of 0.25 ppm. (1)
- The vapor pressure for 1,2-dichloropropane is 49.67 mm Hg at 25 EC, and it has a log octanol/water partition coefficient (log K_{ow}) of 1.99. (1)
- 1,2-Dichloropropane has a half-life in air ranging from 16 to greater than 23 days. (1)

Uses

- 1,2-Dichloropropane is used as a chemical intermediate in the production of chlorinated organic chemicals, as an industrial solvent, in ion exchange manufacture, in toluene diisocyanate production, in photographic film manufacture, for paper coating, and for petroleum catalyst regeneration. (1)

- 1,2-Dichloropropane was used in the past as a soil fumigant for a variety of crops. This use has been discontinued, and pesticide formulations containing 1,2-dichloropropane are no longer available in the U.S.. (1)

Sources and Potential Exposure

- 1,2-Dichloropropane has been detected at low levels in ambient air, with an average level in air of about 0.022 ppb. (1)
- An early 1980s nationwide survey of water supplies derived from groundwater found that 13 of 945 water supplies contained 1,2-dichloropropane at levels around 1 ppb. (1)
- Occupational exposure to 1,2-dichloropropane may occur during its production, during its use in chemical reactions or as an industrial solvent, or from evaporation from wastewater that contains the chemical. (1)

Assessing Personal Exposure

- Medical tests can detect 1,2-dichloropropane in urine and blood. 1,2-Dichloropropane leaves the body quickly, and thus the tests should be done soon after the exposure. (1)

Health Hazard Information

Acute Effects:

- Acute exposure of humans to very high levels of 1,2-dichloropropane from inhalation and oral exposure results in effects on the gastrointestinal system, blood, liver, kidneys, and CNS. Additional effects noted in humans, from inhalation exposure only, are effects on the lung (chest discomfort, shortness of breath, and cough) and the eyes (conjunctival hemorrhages). (1)
- Animal studies have reported effects on the respiratory system, liver, kidneys, eyes, and CNS from acute inhalation exposure to 1,2-dichloropropane. (1)
- Tests involving acute exposure of animals, such as the LC_{50} and LD_{50} tests in rats, have shown 1,2-dichloropropane to have moderate acute toxicity from inhalation and oral exposure. (1,2)

Chronic Effects (Noncancer):

- No information is available on the effects from chronic exposure to 1,2-dichloropropane in humans from inhalation or oral exposure. (1)
- Chronic animal studies, via inhalation exposure, have reported effects on the respiratory system and blood, while oral animal studies have noted effects on the blood, liver, and CNS. (1,3)
- The RfC for 1,2-dichloropropane is 0.004 mg/m^3 based on hyperplasia of the nasal mucosa in rats. The RfC is an estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious noncancer

effects during a lifetime. It is not a direct estimator of risk but rather a reference point to gauge the potential effects. At exposures increasingly greater than the RfC, the potential for adverse health effects increases. Lifetime exposure above the RfC does not imply that an adverse health effect would necessarily occur. (4)

- EPA has high confidence in the RfC based on: high confidence in the study on which the RfC was based because it used an adequate number of animals, exposure concentrations, and controls, examined three species, focused on known target organs, and the incidence and severity of the nasal lesions were exposure-related, and medium confidence in the database because there are no chronic inhalation studies. (4)
- EPA has not established a reference dose (RfD) for 1,2-dichloropropane. (4)
- ATSDR has established an acute oral minimal risk level (MRL) of 0.1 mg/kg/d based on neurological effects in rats; an intermediate oral MRL of 0.07 mg/kg/d based on hematological effects in rats; and a chronic oral MRL of 0.09 mg/kg/d based on liver effects in mice. The MRL is an estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk of adverse noncancer health effects over a specified duration of exposure. (1)

Reproductive/Developmental Effects:

- A case was reported of a woman who was hospitalized with metrorrhagia (bleeding from the uterus between menstrual periods) after acute inhalation exposure to 1,2-dichloropropane. No other information is available on the reproductive or developmental effects of 1,2-dichloropropane in humans. (1)
- No reproductive effects were noted in several animal inhalation studies. (1)
- Developmental effects, such as an increased incidence of delayed ossification of the bones of the skull, and reproductive effects such as testicular degeneration and increased incidences of infection of the ovary, uterus, or other organs, have been observed in animals exposed to 1,2-dichloropropane by gavage. It is not known if the infections observed were related to 1,2-dichloropropane treatment since controls were also infected. (1)

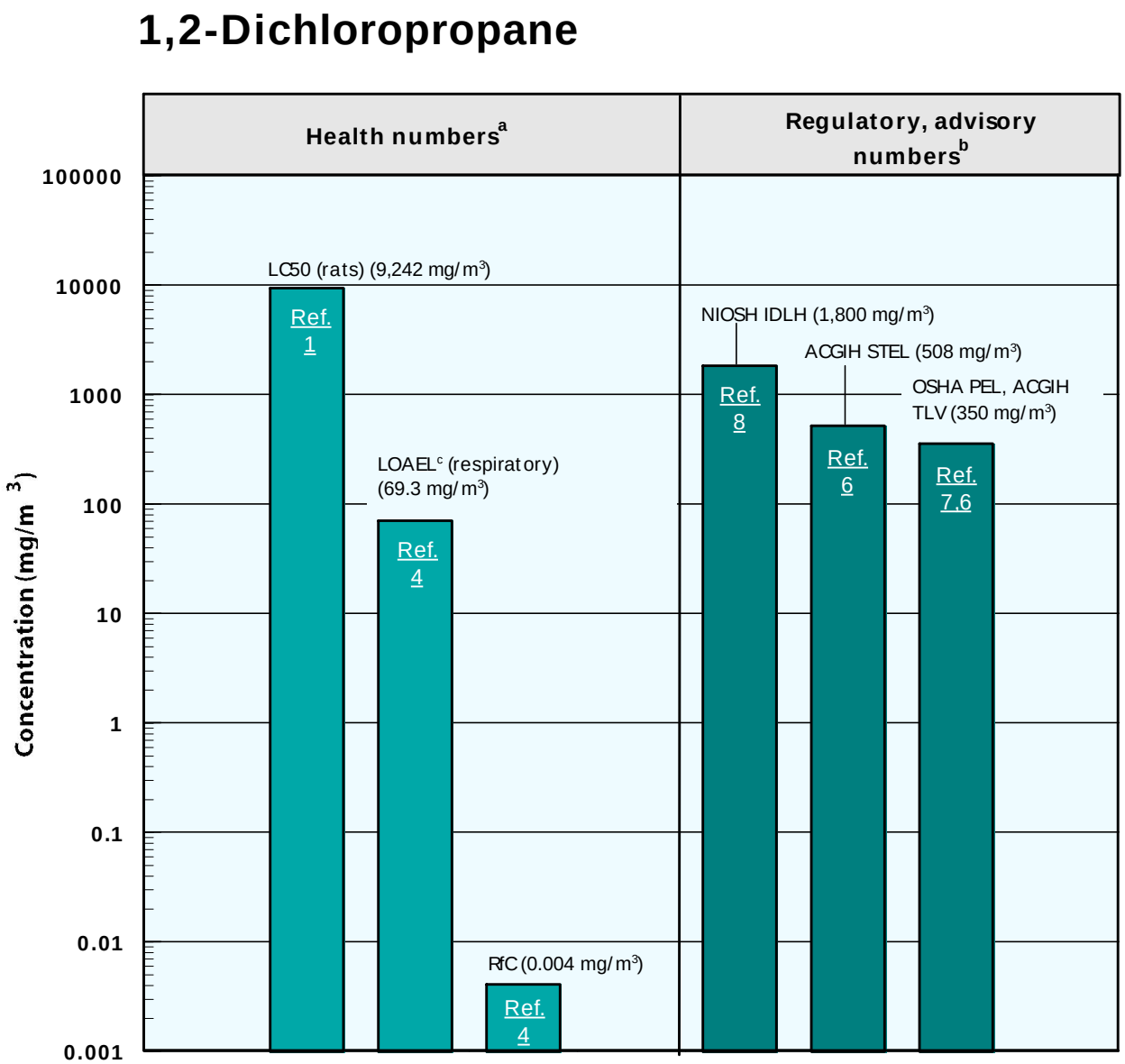
Cancer Risk:

- No studies are available regarding carcinogenic effects in humans from inhalation or oral exposure to 1,2-dichloropropane. (1)
- An increased incidence of mammary gland tumors in female rats and liver tumors in male and female mice were reported in studies in which 1,2-dichloropropane was given by gavage. (1)
- EPA has provisionally classified 1,2-dichloropropane as a Group B2, probable human carcinogen, with an oral cancer slope factor of 6.8×10^{-2} $(mg/kg/d)^{-1}$. (5)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45).
For dichloropropane: 1 ppm = 4.62 mg/m^3.

Health Data from Inhalation Exposure



ACGIH STEL – American Conference of Governmental and Industrial Hygienists' short-term exposure limit; 15-min time-weighted-average exposure that should not be exceeded at any time during a workday even if the 8-h time-weighted-average is within the threshold limit value.

ACGIH TLV – American Conference of Governmental and Industrial Hygienists' threshold limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effects.
LC_{50} (Lethal Concentration$_{50}$) – A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.
LOAEL – Lowest-observed-adverse-effect level.
NIOSH IDLH – National Institute of Occupational Safety and Health's immediately dangerous to life or health concentration; NIOSH recommended exposure limit to ensure that a worker can escape from an exposure condition that is likely to cause death or immediate or delayed permanent adverse health effects or prevent escape from the environment.
OSHA PEL – Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.
[a] Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA.
[b] Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the Government or other groups as advice.
[c] This LOAEL is from the critical study used as the basis for the EPA RfC.

References

1. Agency for Toxic Substances and Disease Registry (ATSDR). *Toxicological Profile for 1,2-Dichloropropane* (Draft). Public Health Service, U.S. Department of Health and Human Services. 1989.

2. U.S. Department of Health and Human Services. Registry of Toxic Effects of Chemical Substances (RTECS, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.

3. U.S. Department of Health and Human Services. Hazardous Substances Data Bank (HSDB, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.

4. U.S. Environmental Protection Agency(EPA). *Integrated Risk Information System (IRIS) on 1,2-Dichloropropane.* National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1999.

5. U.S. Environmental Protection Agency (EPA). *Health Effects Assessment Summary Tables. FY-1997 Update*. National Center for Environmental Assessment, Office of Research and Development, Office of Emergency Response and Remedial Response, Washington, DC. 1997.

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

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

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

1,3-DICHLOROPROPENE

542-75-6

Hazard Summary

1,3-Dichloropropene is used as a component in formulations for soil fumigants. Acute (short-term) inhalation exposure of humans following a spill caused mucous membrane irritation, chest pain, and breathing difficulties. Effects on the lung have been observed in rats acutely exposed to 1,3-dichloropropene by inhalation. Chronic (long-term) dermal exposure may result in skin sensitization in humans. Damage to the nasal mucosa and urinary bladder are the primary health effects of rodents chronically exposed to 1,3-dichloropropene by inhalation. A study of male workers engaged in the manufacture of 1,3-dichloropropene indicated no significant effect on fertility at exposure levels occurring in the work environment. The only developmental effect seen in animal studies was fewer fetuses per litter in rats exposed to high levels by inhalation, and no reproductive effects have been noted. Information on the carcinogenic effects of 1,3-dichloropropene in humans is limited; two cases of histiocytic lymphomas and one case of leukemia have been reported in humans accidentally exposed by inhalation to concentrated vapors during cleanup of a tank truck spill. An increased incidence of bronchioalveolar adenomas has been reported in male mice exposed by inhalation but not in rats or female mice. The U.S. Environmental Protection Agency (EPA) has classified 1,3-dichloropropene as a Group B2, probable human carcinogen.

Please Note: The main sources of information for this fact sheet are EPA's Integrated Risk Information System (IRIS), which contains information on inhalation chronic toxicity of 1,3-dichloropropene and the reference concentration (RfC), oral chronic toxicity and the reference dose (RfD), and the carcinogenic effects of 1,3-dichloropropene, and the Agency for Toxic Substances and Disease Registry's (ATSDR's) *Toxicological Profile for 1,3-Dichloropropene*.

Physical Properties

- The chemical formula for 1,3-dichloropropene is $C_3H_4Cl_2$, and its molecular weight is 110.98 g/mol. (1)
- 1,3-Dichloropropene occurs as a colorless liquid that dissolves in water. (1)
- 1,3-Dichloropropene has a sweet chloroform-like odor, with an odor threshold of 1 ppm. (1)
- The vapor pressure for 1,3-dichloropropene is 34 to 43 mm Hg at 25 EC, and its log octanol/water partition coefficient (log K_{ow}) is 1.60. (1)
- The half-life of 1,3-dichloropropene in ambient air may range from 7 to 50 hours. (1)

Uses

- 1,3-Dichloropropene is the predominant component of several formulations used in agriculture as soil fumigants for parasitic nematodes. (1,4)

Sources and Potential Exposure

- Workers may be occupationally exposed to 1,3-dichloropropene, dermally or by inhalation, during its manufacture, formulation, or application as a soil fumigant. (1, 2)
- The general public may be exposed via inhalation near source areas or from the consumption of contaminated drinking water from wells near some hazardous waste sites. (1,2)

Assessing Personal Exposure

- 1,3-Dichloropropene or its breakdown products can be detected in blood and urine to determine whether or not exposure has occurred. However, metabolites measured in blood and urine are not specific to 1,3-dichloropropene. (1)

Health Hazard Information

Acute Effects:

- Acute inhalation exposure of humans after a tank truck spill resulted in mucous membrane irritation, cough, chest pain, and breathing difficulties. (1)
- Effects on the lung, including emphysema and edema, have been observed in rats acutely exposed to 1,3-dichloropropene by inhalation. (1)
- Lung congestion and hemorrhage, ulcerations of the glandular stomach, hemorrhage of the small intestine, dark and patchy liver, and hemorrhage of the liver have been observed in rats acutely exposed to 1,3-dichloropropene in their diet or via gavage. Neurotoxic effects, including hunched posture, lethargy, ptosis, ataxia, and decreased respiratory rate, have also been observed in orally exposed rats. (1)
- Acute animal tests, such as the LC_{50} and LD_{50} tests in rats, mice, and rabbits, have demonstrated 1,3-dichloropropene to have moderate acute toxicity from inhalation, moderate to high acute toxicity from oral exposure, and high acute toxicity from dermal exposure. (3)

Chronic Effects (Noncancer):

- Chronic dermal exposure may result in skin sensitization in humans. (1)
- Damage to the nasal mucosa and urinary bladder are the primary health effects of rodents chronically exposed to 1,3-dichloropropene by inhalation. Hyperplastic lesions of the upper respiratory tract and degeneration of the olfactory epithelium in the nasal turbinates have been observed in chronically exposed rats and mice. Chronic inhalation exposure of mice has resulted in changes in the urinary bladder. (1,4,5)
- In one study, reversible cloudy swelling of the renal tubular epithelium was reported in rats chronically exposed by inhalation. (1,4,5)
- In rats and mice chronically exposed by inhalation, hyperplasia and hyperkeratosis of the forestomach have been observed, while hyperplasia of the forestomach and of the urinary bladder have resulted from chronic oral exposure. (1,4)

- The RfC for 1,3-dichloropropene is 0.02 mg/m^3 based on hypertrophy/hyperplasia of the nasal respiratory epithelium in mice. The RfC is an estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious noncancer effects during a lifetime. It is not a direct estimator of risk but rather a reference point to gauge the potential effects. At exposures increasingly greater than the RfC, the potential for adverse health effects increases. Lifetime exposure above the RfC does not imply that an adverse health effect would necessarily occur. (5)
- EPA has high confidence in the RfC based on: high confidence in the study on which the RfC was based because it is a well-designed study using two species of animals (both sexes) and including detailed histopathological examinations of numerous tissues with extensive analysis of the respiratory system and corroborative studies performed in both rats and mice have also shown this to be a sensitive endpoint; and high confidence in the database because several studies reported similar effects on the respiratory system at comparable exposure levels, and acute effects observed in humans were similar to the animal effects. (5)
- The RfD for 1,3-dichloropropene is 0.0003 mg/kg/d based on increased organ weights in rats. (5)
- EPA has low confidence in the RfD based on: low confidence in the study on which the RfD was based because it is of low quality and of short duration (90 days), and low confidence in the database because of the remaining studies, only two teratology studies were considered acceptable. (5)

Reproductive/Developmental Effects:

- A study of male workers engaged in the manufacture of 1,3-dichloropropene indicated no significant effect on fertility at exposure levels occurring in the work environment. (4)
- No evidence of developmental toxicity was observed in rats or rabbits exposed to 1,3-dichloropropene by inhalation, but significant maternal toxicity was seen in both species. (4)
- In one study of rats exposed by inhalation, fewer fetuses per litter were reported at the highest exposure concentration. (1)
- In other studies, no adverse reproductive effects were observed in rats and mice exposed by inhalation. (1,5)

Cancer Risk:

- Information on the carcinogenic effects of 1,3-dichloropropene in humans is limited. Two cases of histiocytic lymphomas and one case of leukemia have been reported in emergency response personnel exposed to concentrated 1,3-dichloropropene vapors during cleanup of a tank truck spill. (1,4,5)
- An increased incidence of bronchioalveolar adenomas has been reported in male mice exposed by inhalation but not in rats or female mice. (1,4)

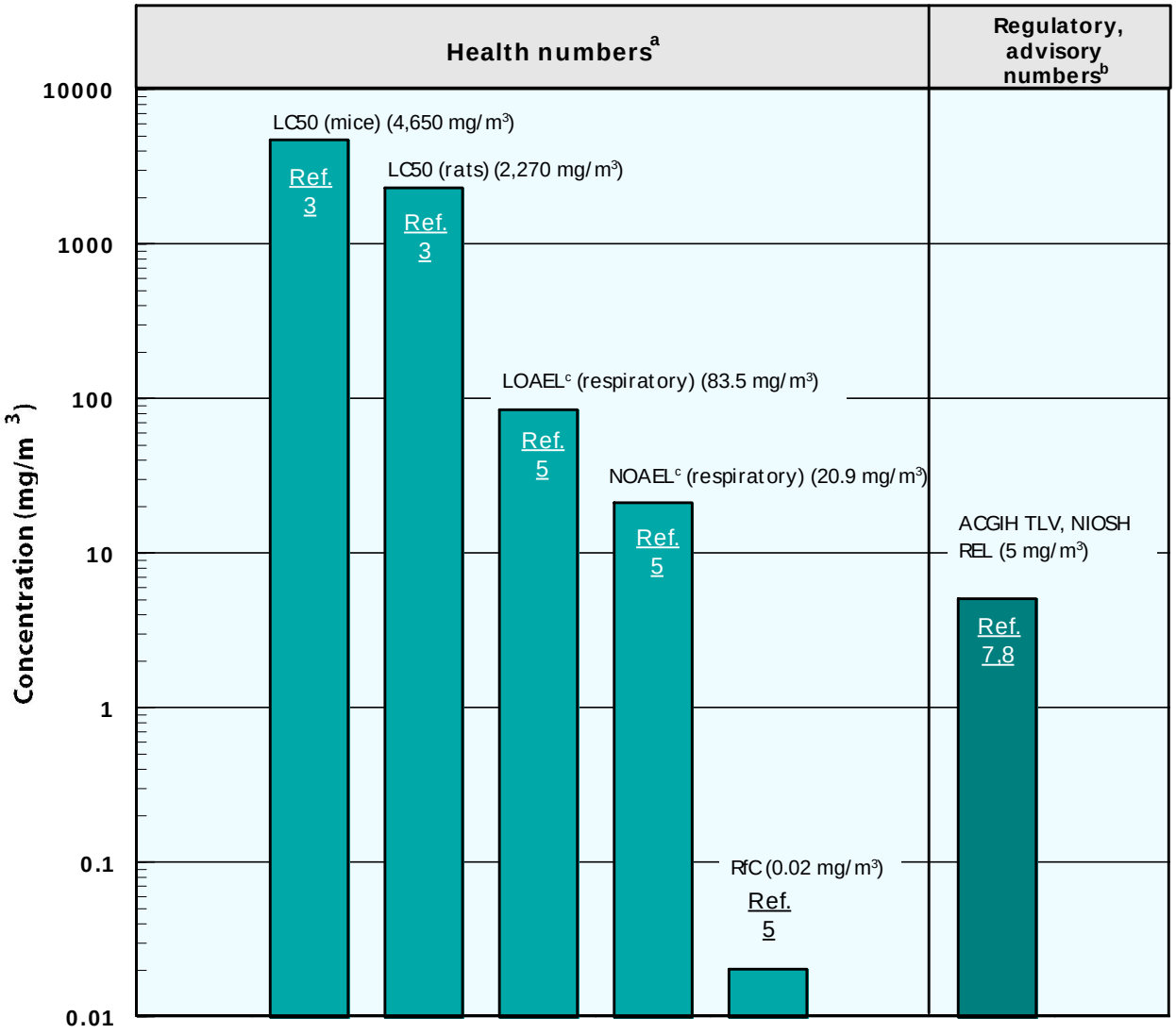
- Forestomach, adrenal and thyroid tumors, and liver nodules in rats and forestomach, urinary bladder, and lung tumors in mice have been observed in rodents exposed to 1,3-dichloropropene via gavage. (1,4,5)
- EPA has classified 1,3-dichloropropene as a Group B2, probable human carcinogen. (5)
- EPA uses mathematical models, based on human and animal studies, to estimate the probability of a person developing cancer from breathing air containing a specified concentration of a chemical. EPA has calculated a provisional inhalation unit risk estimate of $3.7. \times 10^{-5}$ $(\mu g/m^3)^{-1}$. (6)
- EPA has calculated a provisional oral cancer slope factor of 0.18 $(mg/kg/d)^{-1}$. (6)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45).
For 1,3-dichloropropene: 1 ppm = 4.54 mg/m^3.

Health Data from Inhalation Exposure

1,3-Dichloropropene



ACGIH TLV – American Conference of Governmental and Industrial Hygienists' threshold limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effects.
LC_{50} (Lethal Concentration$_{50}$) – A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.
LOAEL – Lowest-observed-adverse-effect level.
NIOSH REL – National Institute of Occupational Safety and Health's recommended exposure limit; NIOSH-recommended exposure limit for an 8- or 10-h time-weighted-average exposure and/or ceiling.

NOAEL – No-observed-adverse-effect level.
OSHA PEL – Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.

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

References

1. Agency for Toxic Substances and Disease Registry (ATSDR). *Toxicological Profile for 1,3-Dichloropropene*. Public Health Service, U.S. Department of Health and Human Services. 1992.

2. U.S. Department of Health and Human Services. Hazardous Substances Data Bank (HSDB, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.

3. U.S. Department of Health and Human Services. Registry of Toxic Effects of Chemical Substances (RTECS, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.

4. U.S. Environmental Protection Agency (EPA). *Health and Environmental Effects Profile for 1,3-Dichloropropene*. ECAO-CIN-G074. Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment, Office of Research and Development, Cincinnati, OH. 1989.

5. U.S. Environmental Protection Agency (EPA). *Integrated Risk Information System (IRIS) on 1,3-Dichloropropene*. National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1999.

6. U.S. Environmental Protection Agency (EPA). *Health Effects Assessment Summary Tables. FY-1997 Update*. National Center for Environmental Assessment, Office of Research and Development, Office of Emergency and Remedial Response, Washington, DC. 1997.

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

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

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ETHYLENE DIBROMIDE (1,2-DIBROMOETHANE)

106-93-4

Hazard Summary

Exposure to ethylene dibromide primarily occurs from its past use as an additive to leaded gasoline and as a fumigant. Ethylene dibromide is extremely toxic to humans. Changes in the liver and kidney have been noted in humans who died from ingestion of ethylene dibromide. The chronic (long-term) effects of exposure to ethylene dibromide have not been well documented in humans. Animal studies indicate that chronic exposure to ethylene dibromide may result in **t**oxic effects to the liver, kidney, and the testis, irrespective of the route of exposure. Limited data on men occupationally exposed to ethylene dibromide indicate that long-term exposure to ethylene dibromide can impair reproduction by damaging sperm cells in the testicles. Animal studies have demonstrated reproductive and developmental effects from ethylene dibromide exposure. Human data are considered inadequate in providing evidence of cancer by exposure to ethylene dibromide. Several animal studies indicate that long-term exposure to ethylene dibromide increases the incidences of a variety of tumors in rats and mice in both sexes by all routes of exposure. The U.S. Environmental Protection Agency (EPA) has classified ethylene dibromide as a Group B2, probable human carcinogen.

Please Note: The main sources of information for this fact sheet EPA's Integrated Risk Information System (IRIS), which contains information on the carcinogenic effects of ethylene dibromide including the unit cancer risk for inhalation exposure, and the Agency for Toxic Substances and Disease Registry's (ATSDR's) *Toxicological Profile for 1,2-Dibromoethane*.

Physical Properties

- Ethylene dibromide is a colorless liquid with a mild sweet odor, like chloroform. (1,7)
- Ethylene dibromide is slightly soluble in water. (1,7)
- The chemical formula for ethylene dibromide is $C_2H_4Br_2$, and it has a molecular weight of 187.88 g/mol. (1,7)
- The vapor pressure for ethylene dibromide is 11.0 mm Hg at 25 EC, and it has a log octanol/water partition coefficient (log K_{ow}) of 86. (1).
- Ethylene dibromide reacts with hydroxyl radicals in the atmosphere, with a half-life for this reaction of approximately 40 days. In water, its half-life ranges from 2.5 to 13.2 years, and in soil it was detected 19 years after it had been applied. (1)

Uses

- Ethylene dibromide was used in the past as an additive to leaded gasoline; however, since leaded gasoline is now banned, it is no longer used for this purpose. (1)

- Ethylene dibromide was used as a fumigant to protect against insects, pests, and nematodes in citrus, vegetable, and grain crops, and as a fumigant for turf, particularly on golf courses. In 1984, EPA banned its use as a soil and grain fumigant. (1)
- Ethylene dibromide is currently used in the treatment of felled logs for bark beetles and termites, and control of wax moths in beehives. (1)
- Ethylene dibromide is also used as an intermediate for dyes, resins, waxes, and gums. (1)

Sources and Potential Exposure

- Possible sources of ethylene dibromide emissions to the ambient air are production and processing facilities. (1)
- Exposure could occur from inhalation of ambient air near industries that use ethylene dibromide or through the ingestion of contaminated drinking water. (1)

Assessing Personal Exposure

- There is no known reliable medical test to determine whether someone has been exposed to ethylene dibromide. (1)

Health Hazard Information

Acute Effects:

- Clinical signs in humans and animals related to acute inhalation exposure to ethylene dibromide are depression and collapse. Ethylene dibromide is a severe skin irritant that can cause blistering. (1,2)
- Exposure to high concentrations of ethylene dibromide through inhalation, ingestion, or skin contact can result in death. Changes in the liver and kidney are reported in humans who died from ingestion of ethylene dibromide. (1,2)
- Tests involving acute exposure of animals, such as the LD_{50} test in rats, have shown ethylene dibromide to have high acute toxicity from oral exposure, while the LC_{50} test in rats has demonstrated moderate acute toxicity from inhalation exposure. (3)

Chronic Effects (Noncancer):

- The chronic effects of exposure to ethylene dibromide have not been extensively documented in humans. In one case in which a worker breathed ethylene dibromide for several years, he developed bronchitis, headache, and depression. His health improved after he stopped breathing air contaminated with ethylene dibromide. (1,2)
- Animal studies indicate that prolonged exposure to ethylene dibromide may result in toxic effects to the liver, kidney, and the testis whether by inhalation, ingestion, or skin contact. (1,2)
- EPA has not established a reference dose (RfD) or a reference concentration (RfC) for ethylene dibromide. (4)

- EPA has calculated a provisional RfC of 0.0002 mg/m^3 for ethylene dibromide based on reproductive effects in humans. The RfC is an estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious noncancer effects during a lifetime. It is not a direct estimator of risk but rather a reference point to gauge the potential effects. At exposures increasingly greater than the RfC, the potential for adverse health effects increases. Lifetime exposure above the RfC does not imply that an adverse health effect would necessarily occur. The provisional RfC is a value that has had some form of Agency review, but it does not appear on IRIS. (5)

Reproductive Effects/Developmental:

- Developmental effects have not been documented in humans. Limited data on men occupationally exposed to ethylene dibromide indicate that long-term exposure to ethylene dibromide can impair reproduction by damaging sperm cells in the testicles. (1,2)
- Animals that breathed or ate food containing ethylene dibromide for short or long periods were less fertile than control animals or had abnormal sperm. Pregnant animals that were sick from exposure to ethylene dibromide have had pups with birth defects. (1,2)

Cancer Risk:

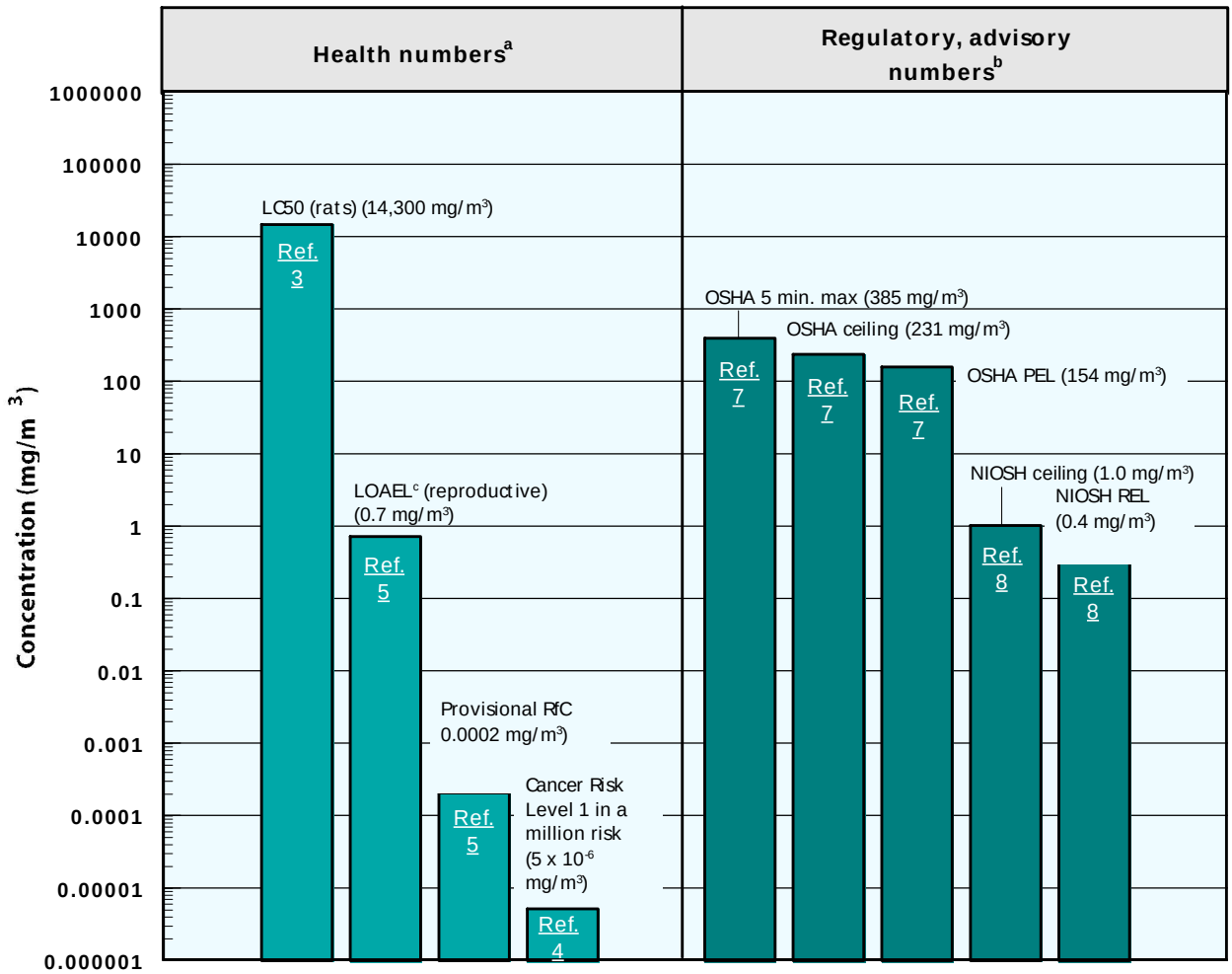
- Two cancer studies on workers exposed to ethylene dibromide have been carried out. Neither study reported a statistically significant increase in cancer mortality; however these studies are considered inadequate due to confounding factors. (4)
- Several animal studies indicate that long-term exposure to ethylene dibromide increases the incidences of a variety of tumors in rats and mice in both sexes by inhalation, by gavage, or by administration to the skin. (4)
- EPA has classified ethylene dibromide as a Group B2, probable human carcinogen. (4)
- EPA uses mathematical models, based on animal studies, to estimate the probability of a person developing cancer from breathing air containing a specified concentration of a chemical. EPA has calculated an inhalation unit risk estimate of 2.2×10^{-4} $(\mu g/m^3)^{-1}$. EPA estimates that, if an individual were to continuously breathe air containing ethylene dibromide at an average of 0.005 $\mu g/m^3$ (5×10^{-6} mg/m^3) over his or her entire lifetime, that person would theoretically have no more than a one-in-a-million increased chance of developing cancer as a direct result of breathing air containing this chemical. Similarly, EPA estimates that continuously breathing air containing 0.05 $\mu g/m^3$ (5×10^{-5} mg/m^3) would result in not greater than a one-in-hundred thousand increased chance of developing cancer, and air containing 0.5 $\mu g/m^3$ (5×10^{-4} mg/m^3) would result in not greater than a one-in-ten thousand increased chance of developing cancer in their lifetime. For a detailed discussion of confidence in the potency estimates, please see IRIS. (4)
- EPA has calculated an oral cancer slope factor of 85 $(mg/kg/d)^{-1}$. (4)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45).
For ethylene dibromide: 1 ppm = 7.7 mg/m^3.
To convert from µg/m^3 to mg/m^3: mg/m^3 = (µg/m^3) x (1 mg/1,000 µg).

Health Data from Inhalation Exposure

1,2-Dibromoethane



LC_{50} (Lethal Concentration$_{50}$) – A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.
LOAEL – Lowest-observed-adverse-affect level.
NIOSH ceiling – National Institute of Occupational Safety and Health's ceiling limit; NIOSH--recommended 15-min exposure limit, which should not be exceeded.

NIOSH REL – NIOSH's recommended exposure limit; NIOSH-recommended exposure limit for an 8- or 10-h time-weighted-average exposure and/or ceiling.
OSHA PEL – Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.

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

References

1. Agency for Toxic Substances and Disease Registry (ATSDR). *Toxicological Profile for 1,2-Dibromoethane*. Public Health Service, U.S. Department of Health and Human Services, Atlanta, GA. 1992.

2. U.S. Department of Health and Human Services. Hazardous Substances Data Bank (HSDB, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.

3. U.S. Department of Health and Human Services. Registry of Toxic Effects of Chemical Substances (RTECS, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.

4. U.S. Environmental Protection Agency (EPA). *Integrated Risk Information System (IRIS) on 1,2-Dibromoethane*. National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1999.

5. U.S. Environmental Protection Agency (EPA). *Health Effects Assessment Summary Tables. FY-1997 Update*. National Center for Environmental Assessment, Office of Research and Development, Office of Emergency and Remedial Response, Washington, DC. 1997.

6. *The Merck Index. An Encyclopedia of Chemicals, Drugs, and Biologicals*. 11th ed. Ed. S. Budavari. Merck and Co. Inc., Rahway, NJ. 1989.

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

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

ETHYLENE OXIDE

75-21-8

Hazard Summary

The major use for ethylene oxide is as a chemical intermediate in industry. The acute (short-term) effects of ethylene oxide in humans consist mainly of **c**entral nervous system (CNS) depression and irritation of the eyes and mucous membranes. High concentrations of ethylene oxide produce weakness, nausea, bronchitis, pulmonary edema, emphysema, and death. Chronic (long-term) exposure to ethylene oxide in humans can cause irritation of the eyes, skin, and mucous membranes; and problems in the functioning of the brain and nerves. Limited evidence in both animal and human studies indicate that inhalation exposure to ethylene oxide may result in adverse reproductive effects such as an increased rate of miscarriages. These effects could be seen from acute as well as chronic exposures. Some human cancer data show an increase in the incidence of leukemia, stomach cancer, cancer of the pancreas, and Hodgkin's disease in workers exposed to ethylene oxide. However these data are considered to be limited and inconclusive due to uncertainties in the studies. Ethylene oxide has been shown to cause lung, gland, and uterine tumors in laboratory animals. The U.S. Environmental Protection Agency (EPA) has classified ethylene oxide as a Group B1, probable human carcinogen.

Please Note: The main source of information for this fact sheet is the Agency for Toxic Substances and Disease Registry's (ATSDR's) *Toxicological Profile for Ethylene Oxide*. Other secondary sources include the Hazardous Substances Data Bank (HSDB), a database of summaries of peer-reviewed literature, and the Registry of Toxic Effects of Chemical Substances (RTECS), a database of toxic effects that are not peer reviewed.

Physical Properties

- Ethylene oxide is a colorless gas with a sweet odor. (1,6)
- The chemical formula for ethylene oxide is C_2H_4O and the molecular weight is 44.1 g/mol. (6)
- The vapor pressure for ethylene oxide is 1,095 mm Hg at 20 EC, and it has an octanol/water partition coefficient (log K_{ow}) of -0.30. (6)
- Ethylene oxide is very soluble in water and is flammable. (1)
- Ethylene oxide has an odor threshold of 430 ppm. (7)
- Ethylene oxide has an estimated half-life in air ranging from 69 to 149 days, while its half-life in water is about 50 years. (1).

Uses

- Ethylene oxide is used mainly as a chemical intermediate in the manufacture of textiles, detergents, polyurethane foam, antifreeze, solvents, medicinals, adhesives, and other products. (1)

- Relatively small amounts of ethylene oxide are used as a fumigant, a sterilant for food (spices) and cosmetics, and in hospital sterilization of surgical equipment and plastic devices that cannot be sterilized by steam. (1)

Sources and Potential Exposure

- Sources of ethylene oxide emissions into the air include uncontrolled emissions or venting with other gases in industrial settings. (1)
- Other sources of ethylene oxide air emissions include automobile exhaust and its release from commodity-fumigated materials, as well as its use as a sterilizer of medical equipment. (1)
- The general population may be exposed to ethylene oxide through breathing contaminated air or from smoking tobacco or being in the proximity to someone who is smoking. Certain occupational groups (e.g., workers in ethylene oxide manufacture or processing plants, sterilization technicians, and workers involved in fumigation) may be exposed in the workplace. (1)

Assessing Personal Exposure

- There are tests currently available to determine personal exposure to ethylene oxide, such as the determination of ethylene oxide in the blood or the amount breathed out of the lungs. (1)

Health Hazard Information

Acute Effects:

- Acute inhalation exposure of workers to high levels of ethylene oxide has resulted in nausea, vomiting, neurological disorders, bronchitis, pulmonary edema, emphysema, and even death at very high concentrations. (1,2)
- Dermal or ocular contact with solutions of ethylene oxide has caused irritation of the eyes and skin in humans. (1,2)
- Tests involving acute exposure of animals, such as the LD_{50} test in rats, has shown ethylene oxide to have high acute toxicity from oral exposure. LC_{50} tests in rats, mice, dogs, and guinea pigs have also shown high acute toxicity from ethylene oxide exposure. (3)

Chronic Effects (Noncancer):

- Major effects observed in workers exposed to ethylene oxide at low levels for several years are irritation of the eyes, skin, and mucous membranes and problems in the functioning of the brain and nerves. (1,2)
- There is evidence suggesting that long-term exposure to high levels of ethylene oxide, at a level of 700 ppm, can result in cataracts in humans. (2)

- EPA has not established a reference dose (RfD) or a reference concentration (RfC) for ethylene oxide.
- The California Environmental Protection Agency (CalEPA) has established a chronic reference exposure level of 0.005 mg/m^3 for ethylene oxide based on hematological effects in humans. The CalEPA reference exposure level is a concentration at or below which adverse health effects are not likely to occur. It is not a direct estimator of risk, but rather a reference point to gauge the potential effects. At lifetime exposures increasingly greater than the reference exposure level, the potential for adverse health effects increases. (4)
- ATSDR has an established an intermediate inhalation minimal risk level (MRL) of 0.2 mg/m^3 (0.09 ppm) based on respiratory effects in humans. The MRL is an estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk of adverse noncancer health effects over a specified duration of exposure. (1)

Reproductive/Developmental Effects:

- Some evidence exists indicating that inhalation exposure to ethylene oxide can cause an increased rate of miscarriages in female workers. These effects could be seen from acute, as well as chronic, exposure. (1,2)
- Various adverse reproductive effects have been noted in inhalation exposure studies of animals including decreased number of implantation sites, decreased testicular weights and sperm concentration, and testicular degeneration. (1,2)

Cancer Risk:

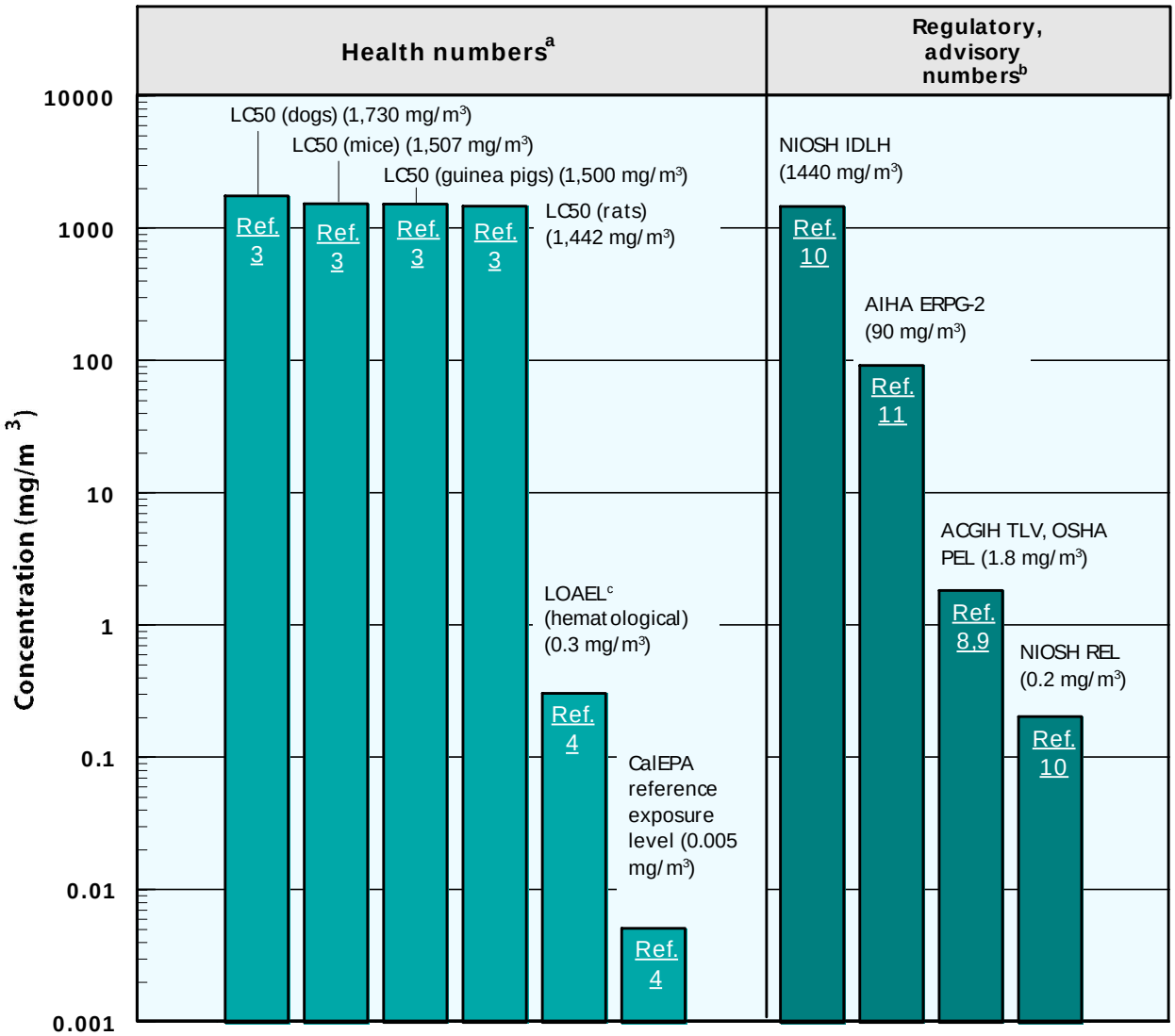
- Human occupational studies have shown elevated cases of leukemia, stomach and pancreatic cancer, and Hodgkin's disease in workers exposed to ethylene oxide by inhalation. However, the data are considered to be limited and inconclusive due to the small number of individuals studied and uncertainties about the exposure levels. (1,2)
- Animal studies have shown lung, gland, and uterine tumors caused by inhalation exposure to ethylene oxide. (1,2)
- EPA has classified ethylene oxide as a Group B1, probable human carcinogen. (5)
- EPA uses mathematical models, based on human and animal studies, to estimate the probability of a person developing cancer from breathing air containing a specified concentration of a chemical. EPA has calculated a provisional inhalation unit cancer risk estimate of 1.0×10^{-4} $(\mu g/m^3)^{-1}$. A provisional value is one that has not received Agencywide review. (5)
- EPA has calculated a provisional oral cancer slope factor of 1.0 $(mg/kg/d)^{-1}$. (5)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45). For ethylene oxide: 1 ppm = 1.8 mg/m^3.

Health Data from Inhalation Exposure

Ethylene Oxide



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

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

LC_{50} (Lethal Concentration$_{50}$) – A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.
LOAEL – Lowest-observed-no-adverse-affect level.
NIOSH IDLH – National Institute of Occupational Safety and Health's immediately dangerous to life or health concentration; NIOSH recommended exposure limit to ensure that a worker can escape from an exposure condition that is likely to cause death or immediate or delayed permanent adverse health effects or prevent escape from the environment.
NIOSH REL – NIOSH's recommended exposure limit; NIOSH-recommended exposure limit for an 8- or 10-h time-weighted-average exposure and/or ceiling.
OSHA PEL – Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.

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

References

1. Agency for Toxic Substances and Disease Registry (ATSDR). *Toxicological Profile for Ethylene Oxide*. U.S. Public Health Service, U.S. Department of Health and Human Services. 1990.

2. U.S. Department of Health and Human Services. Hazardous Substances Data Bank (HSDB, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.

3. U.S. Department of Health and Human Services. Registry of Toxic Effects of Chemical Substances (RTECS, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.

4. California Environmental Protection Agency (CalEPA). *Technical Support Document for the Determination of Noncancer Chronic Reference Exposure Levels. Draft for Public Comment.* Office of Environmental Health Hazard Assessment, Berkeley, CA. 1997.

5. U.S. Environmental Protection Agency (EPA). *Health Effects Assessment Summary Tables. FY 1997 Update.* National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1997.

6. *The Merck Index. An Encyclopedia of Chemicals, Drugs, and Biologicals*. 11th ed. Ed. S. Budavari. Merck and Co. Inc., Rahway, NJ. 1989.

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

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

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

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

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

FORMALDEHYDE
50-00-0

Hazard Summary

Formaldehyde is used mainly to produce resins used in particle board products and as an intermediate in the synthesis of other chemicals. Exposure to formaldehyde may occur by breathing contaminated indoor air, tobacco smoke, or ambient urban air. Acute (short-term) and chronic (long-term) inhalation exposure to formaldehyde in humans can result in respiratory symptoms, and eye, nose, and throat irritation. Reproductive effects, such as menstrual disorders and pregnancy problems, have been reported in female workers exposed to formaldehyde. Limited human studies have reported an association between formaldehyde exposure and lung and nasopharyngeal cancer. Animal inhalation studies have reported an increased incidence of nasal squamous cell cancer. The U.S. Environmental Protection Agency (EPA) has classified formaldehyde as a Group B2, probable human carcinogen.

Please Note: The main sources of information for this fact sheet are EPA's *Health and Environmental Effects Profile for Formaldehyde* and the Integrated Risk Information System (IRIS), which contains information on oral chronic toxicity and the reference dose (RfD), and the carcinogenic effects of formaldehyde including the unit cancer risk for inhalation exposure.

Physical Properties

- The chemical formula for formaldehyde is CH_2O, and the molecular weight is 30.03 g/mol. (1)
- The vapor pressure for formaldehyde is 10 mm Hg at -88 EC, and its log octanol/water partition coefficient (log K_{ow}) is -0.65. (1)
- Formaldehyde is a colorless gas with a pungent, suffocating odor at room temperature; the odor threshold for formaldehyde is 0.83 ppm. (1,8)
- Formaldehyde is readily soluble in water at room temperature. (1)
- Commercial formaldehyde is produced and sold as an aqueous solution containing 37 to 50 percent formaldehyde by weight. (1)

Uses

- Formaldehyde is used predominantly as a chemical intermediate. It also has minor uses in agriculture, as an analytical reagent, in concrete and plaster additives, cosmetics, disinfectants, fumigants, photography, and wood preservation. (1,2)
- One of the most common uses of formaldehyde in the U.S. is manufacturing urea-formaldehyde resins, used in particle board products. (7)
- Formaldehyde (as urea formaldehyde foam) was extensively used as an insulating material until 1982 when it was banned by the U.S. Consumer Product Safety Commission. (1,2)

Sources and Potential Exposure

- The highest levels of airborne formaldehyde have been detected in indoor air, where it is released from various consumer products such as building materials and home furnishings. One survey reported formaldehyde levels ranging from 0.10 to 3.68 ppm in homes. Higher levels have been found in new manufactured or mobile homes than in older conventional homes. (1)
- Formaldehyde has also been detected in ambient air; the average concentrations reported in U.S. urban areas were in the range of 11 to 20 ppb. The major sources appear to be power plants, manufacturing facilities, incinerators, and automobile exhaust emissions. (7)
- Smoking is another important source of formaldehyde. (1)
- Formaldehyde may also be present in food, either naturally or as a result of contamination. (1)

Assessing Personal Exposure

- Blood levels of formaldehyde can be measured. However, these measurements are only useful when exposure by inhalation to relatively large amounts of formaldehyde has occurred. (2)

Health Hazard Information

Acute Effects:

- The major toxic effects caused by acute formaldehyde exposure via inhalation are eye, nose, and throat irritation and effects on the nasal cavity. (1,2)
- Other effects seen from exposure to high levels of formaldehyde in humans are coughing, wheezing, chest pains, and bronchitis. (1,2)
- Ingestion exposure to formaldehyde in humans has resulted in corrosion of the gastrointestinal tract and inflammation and ulceration of the mouth, esophagus, and stomach. (1,2)
- Acute animal tests, such as the LC_{50} and LD_{50} tests in rats and rabbits have shown formaldehyde to have high acute toxicity from inhalation, oral, and dermal exposure. (3)

Chronic Effects (Noncancer):

- Chronic exposure to formaldehyde by inhalation in humans has been associated with respiratory symptoms and eye, nose, and throat irritation. (1,2,4,5)
- Repeated contact with liquid solutions of formaldehyde has resulted in skin irritation and allergic contact dermatitis. (5)
- Animal studies have reported effects on the nasal respiratory epithelium and lesions in the respiratory system from chronic inhalation exposure to formaldehyde. (1,2,4,5)

- The RfD for formaldehyde is 0.2 mg/kg/d based on a decrease in body weight gain and effects on the stomach in rats. The RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious noncancer effects during a lifetime. It is not a direct estimator of risk but rather a reference point to gauge the potential effects. At exposures increasingly greater than the RfD, the potential for adverse health effects increases. Lifetime exposure above the RfD does not imply that an adverse health effect would necessarily occur. (6)
- EPA has high confidence in the study on which the RfD was based since it consisted of an adequate number of animals of both sexes, as well as a thorough examination of toxicological and histological parameters; medium confidence in the database as several additional chronic bioassays and reproductive and developmental studies support the critical effect and study; and, consequently, medium confidence in the RfD. (6)
- EPA has not established a reference concentration (RfC) for formaldehyde. (6)
- The Agency for Toxic Substances and Disease Registry (ATSDR) has established a chronic inhalation minimal risk level (MRL) of 0.003 ppm (0.004 mg/m^3) based on respiratory effects in humans. The MRL is an estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk of adverse noncancer health effects over a specified duration of exposure. (7)

Reproductive/Developmental Effects:

- An increased incidence of menstrual disorders were observed in female workers using urea-formaldehyde resins. However, possible confounding factors were not evaluated in this study. (1,2)
- A study of hospital workers who sterilize equipment did not report an association between formaldehyde exposure and increased spontaneous abortions. (1,2)
- Developmental effects, such as birth defects, have not been observed in animal studies with formaldehyde. (1,2)

Cancer Risk:

- Occupational studies have noted statistically significant associations between exposure to formaldehyde and increased incidence of lung and nasopharyngeal cancer. This evidence is considered to be "limited," rather than "sufficient," due to possible exposure to other agents that may have contributed to the excess cancers. (1,6)
- Animal studies have reported an increased incidence of nasal squamous cell carcinomas by inhalation exposure. (1,6)
- EPA has classified formaldehyde as a Group B1, probable human carcinogen. (6)
- EPA uses mathematical models, based on human and animal studies, to estimate the probability of a person developing cancer from breathing air containing a specified concentration of a chemical. EPA calculated an inhalation unit risk estimate of 1.3×10^{-5} $(\mu g/m^3)^{-1}$. EPA estimates that, if an individual were to continuously breathe air containing formaldehyde at an average of 0.08 $\mu g/m^3$ (8.0×10^{-5} mg/m^3) over his or her entire lifetime, that person would theoretically have no more than a one-in-a-million increased

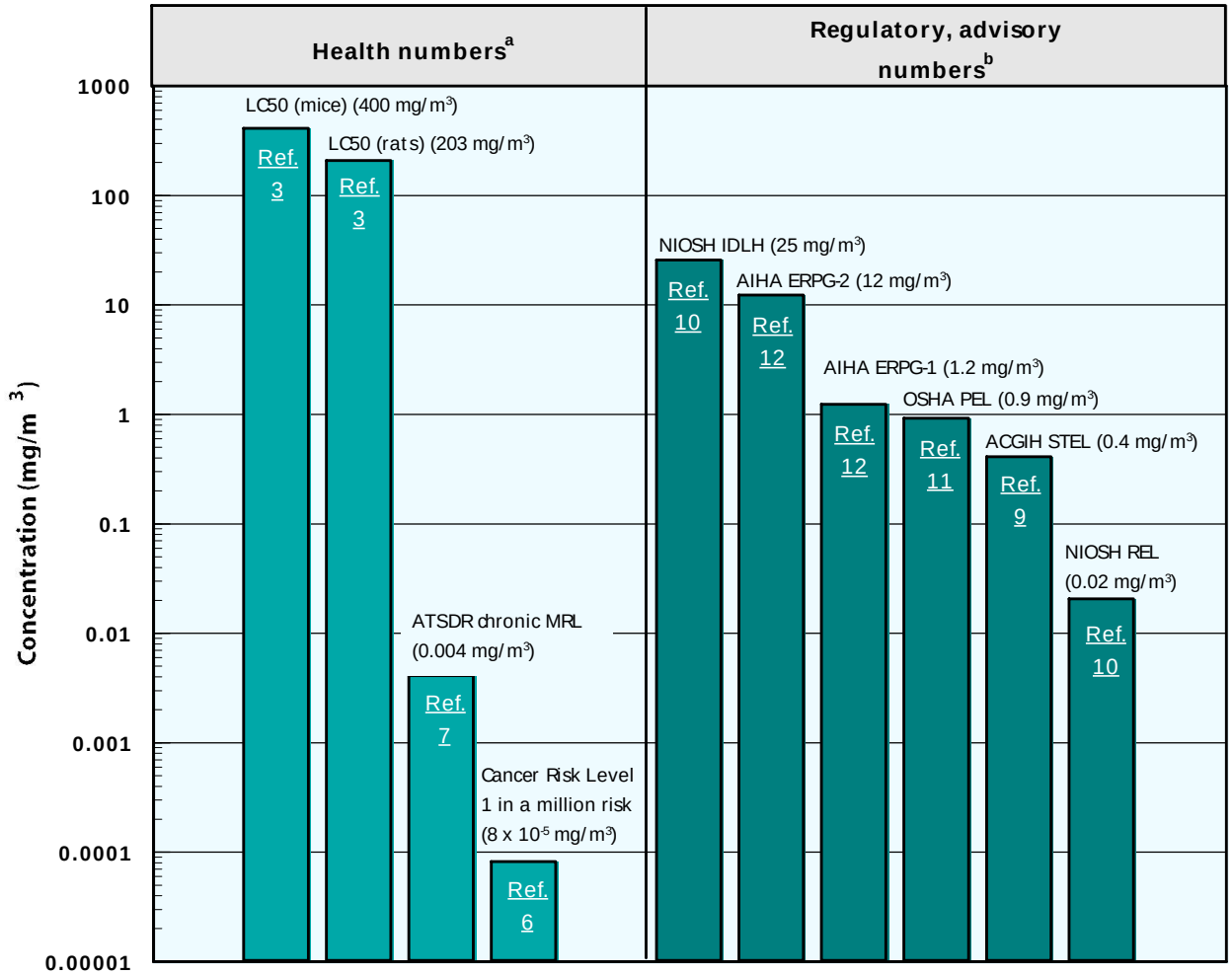
chance of developing cancer as a direct result of breathing air containing this chemical. Similarly, EPA estimates that breathing air containing 0.8 µg/m^3 (8.0 x 10^{-4} mg/m^3) would result in not greater than a one-in-a-hundred thousand increased chance of developing cancer, and air containing 8.0 µg/m^3 (8.0 x 10^{-3} mg/m^3) would result in not greater than a one-in-ten-thousand increased chance of developing cancer. For a detailed discussion of confidence in the potency estimates, please see IRIS. (6)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45).
For formaldehyde: 1 ppm = 1.23 mg/m^3.

Health Data from Inhalation Exposure

Formaldehyde



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

ACGIH STEL – American Conference of Governmental and Industrial Hygienists' short-term exposure limit expressed as a time-weighted average exposure; the concentration of a substance which should not be exceeded at any time during a workday.

LC_{50} (Lethal Concentration$_{50}$) – A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined

experimental animal population.
NIOSH IDLH – National Institute of Occupational Safety and Health's immediately dangerous to life or health limit; NIOSH recommended exposure limit to ensure that a worker can escape from an exposure condition that is likely to cause death or immediate or delayed permanent adverse health effects or prevent escape from the environment.
NIOSH REL – NIOSH's recommended exposure limit; NIOSH recommended exposure limit for an 8- or 10-h time-weighted average exposure and/or ceiling.
OSHA PEL – Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.

[a] Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA.
[b] Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the Government or other groups as advice.

References

1. U.S. Environmental Protection Agency (EPA). *Health and Environmental Effects Profile for Formaldehyde*. EPA/600/x-85/362. Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment, Office of Research and Development, Cincinnati, OH. 1988.

2. World Health Organization (WHO). *Environmental Health Criteria for Formaldehyde*. Volume 89. World Health Organization, Geneva, Switzerland. 1989.

3. U.S. Department of Health and Human Services. Registry of Toxic Effects of Chemical Substances (RTECS, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.

4. E.J. Calabrese and E.M. Kenyon. *Air Toxics and Risk Assessment*. Lewis Publishers, Chelsea, MI. 1991.

5. U.S. Department of Health and Human Services. Hazardous Substances Databank (HSDB, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.

6. U.S. Environmental Protection Agency (EPA). *Integrated Risk Information System (IRIS) on Formaldehyde*. National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1999.

7. Agency for Toxic Substances and Disease Registry (ATSDR). *Toxicological Profile for Formaldehyde* (Draft). Public Health Service, U.S. Department of Health and Human Services, Atlanta, GA. 1997.

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

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

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

11. Occupational Safety and Health Administration (OSHA). Occupational Safety and Health Standards, Toxic and Hazardous Substances. *Code of Federal Regulations* 29 CFR 1910.1048. 1998.

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

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HEXACHLOROBENZENE

118-74-1

Hazard Summary

Hexachlorobenzene is formed as a byproduct during the manufacture of other chemicals. It was widely used as a pesticide until 1965. Chronic (long-term) oral exposure to hexachlorobenzene in humans results in a liver disease with associated skin lesions. Animal studies have reported effects on the liver, skin, kidneys, immune system, and blood from chronic oral exposure to hexachlorobenzene. Hexachlorobenzene may cause developmental effects in humans and has been found to decrease the survival rates of newborn animals. Epidemiologic studies of persons orally exposed to hexachlorobenzene have not shown an increased cancer incidence. However, based on animal studies that have reported cancer of the liver, thyroid, and kidney from oral exposure to hexachlorobenzene, the U.S. Environmental Protection Agency (EPA) has classified hexachlorobenzene as a Group B2, probable human carcinogen. Very little inhalation data are available.

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

Physical Properties

- Hexachlorobenzene is a white crystalline solid that is not very soluble in water. (1)
- The odor threshold for hexachlorobenzene is not available.
- The chemical formula for hexachlorobenzene is C_6Cl_6, and the molecular weight is 284.8 g/mol. (1)
- The vapor pressure for hexachlorobenzene is 1.09×10^{-5} mm Hg at 20 EC, and it has a log octanol/water partition coefficient (log K_{ow}) of 6.18. (1)

Uses

- There are currently no commercial uses of hexachlorobenzene in the U.S.. (1)
- Hexachlorobenzene was used as a pesticide until 1965 and was also used in the production of rubber, aluminum, and dyes and in wood preservation. (1)
- Hexachlorobenzene is currently formed as a byproduct during the manufacture of other chemicals (mainly solvents) and pesticides. (1)

Sources and Potential Exposure

- Inhalation exposure to hexachlorobenzene may occur through proximity to industrial sites where it is formed as a byproduct or to waste facilities where it is disposed. (1)

- Occupational exposure, via inhalation and dermally, can occur at industries where hexachlorobenzene is produced as a byproduct. (1)
- Exposure to hexachlorobenzene can also occur through consuming foods tainted with hexachlorobenzene. (1)
- Hexachlorobenzene has been listed as a pollutant of concern in EPA's Great Waters Program due to its persistence in the environment, potential to bioaccumulate, and toxicity to humans and the environment (2).

Assessing Personal Exposure

- Medical tests can measure levels of hexachlorobenzene in the fat or blood. (1)

Health Hazard Information

Acute Effects:

- No information is available on the acute (short-term) effects of hexachlorobenzene in humans. (1,3)
- Acute animal tests, such as the LD_{50} tests in rats and mice, have shown hexachlorobenzene to have low-to-moderate acute toxicity from oral exposure. (4)

Chronic Effects (Noncancer):

- Humans who ingested hexachlorobenzene in heavily contaminated bread during a 4-year poisoning incident were sickened with a liver disease with associated skin lesions (porphyria cutanea tarda). (1)
- Animal studies have reported effects on the liver, skin, immune system, kidneys, and blood from chronic oral exposure to hexachlorobenzene. (1,3)
- Very little data are available on the health effects of hexachlorobenzene in humans or animals following inhalation exposure.
- EPA has determined that there are inadequate data to establish a reference concentration (RfC) for hexachlorobenzene. (5)
- The California Environmental Protection Agency (CalEPA) has established a chronic inhalation reference exposure level of 0.003 mg/m^3 for hexachlorobenzene. The CalEPA reference exposure level is a concentration at or below which adverse health effects are not likely to occur. It is not a direct estimator of risk but rather a reference point to gauge the potential effects. At lifetime exposures increasingly greater than the reference exposure level, the potential for adverse health effects increases. (6)
- The RfD for hexachlorobenzene is 0.0008 mg/kg/d based on liver effects in rats. The RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious noncancer effects during a lifetime. (5)
- EPA has medium confidence in the study used as the basis for the RfD because it had an unusual dosing scheme making it difficult to determine the true doses received by each

experimental group; high confidence in the database due to the extensive number of quality research studies available; and consequently medium confidence in the RfD. (5)

Reproductive/Developmental Effects:

- One human study reported abnormal physical development in young children who ingested contaminated bread during a 4-year poisoning incident. (1)
- Hexachlorobenzene has been found to decrease the survival rates of newborn animals and to cross the placenta and accumulate in fetal tissue in several animal species. (3)
- Neurological, teratogenic, liver, and immune system effects have been reported in the offspring of animals orally exposed to hexachlorobenzene while they were pregnant. (1)

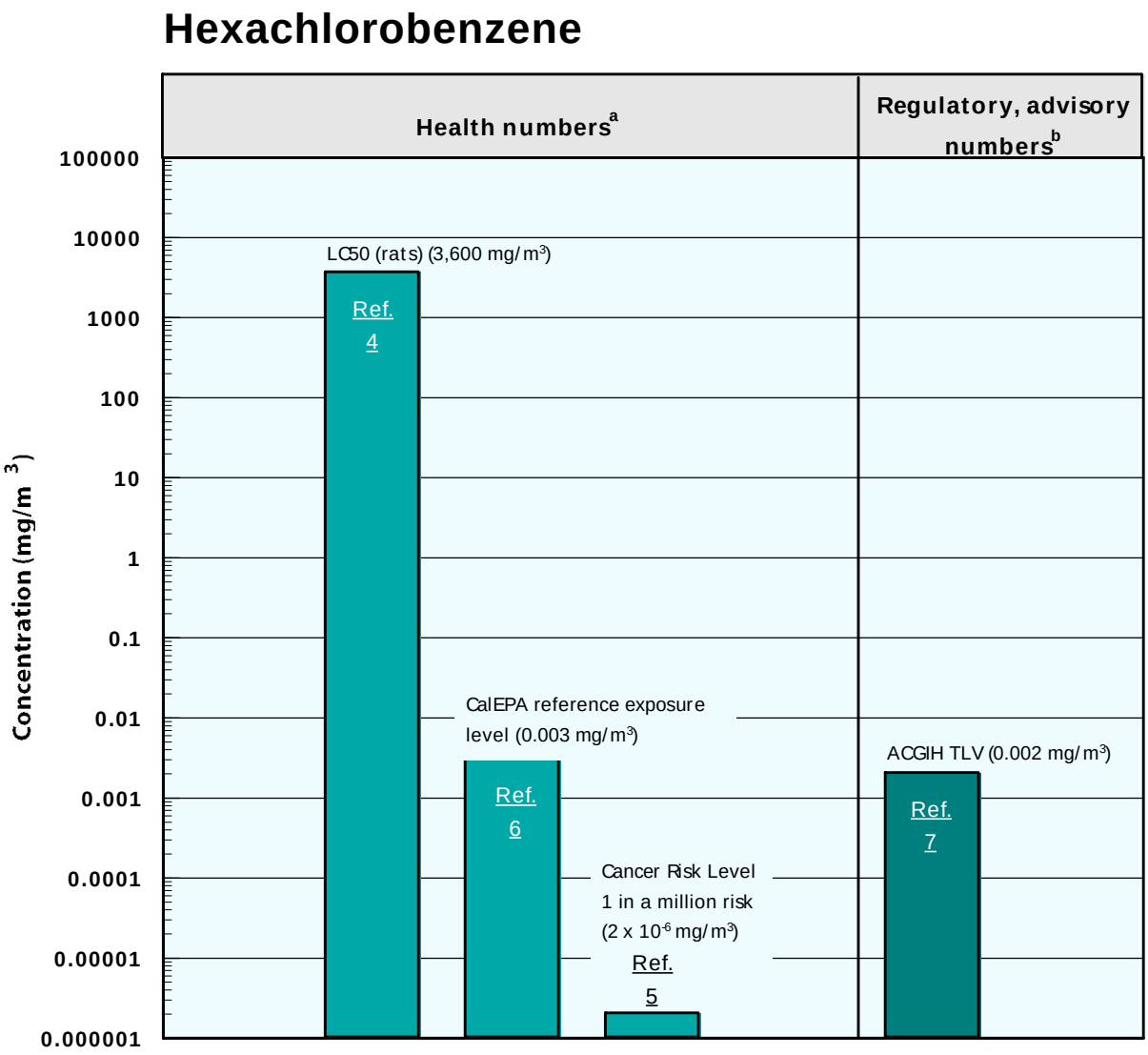
Cancer Risk:

- Human data regarding the carcinogenic effects of hexachlorobenzene are inadequate. (5)
- Hexachlorobenzene, when administered orally, has been shown to induce tumors of the liver, thyroid, and kidney in several animal species. (1,3,5)
- EPA has classified hexachlorobenzene as a Group B2, probable human carcinogen. (5)
- EPA uses mathematical models, based on human and animal studies to estimate the probability of a person developing cancer from breathing air containing a specified concentration of a chemical. EPA calculated an inhalation unit risk estimate of 4.6×10^{-4} $(\mu g/m^3)^{-1}$. EPA estimates that, if an individual were to continuously breathe air containing hexachlorobenzene at an average of 0.002 $\mu g/m^3$ (2.0×10^{-6} mg/m^3) over his or her entire lifetime, that person would theoretically have no more than a one-in-a-million increased chance of developing cancer as a direct result of breathing air containing this chemical. Similarly, EPA estimates that breathing air containing 0.02 $\mu g/m^3$ (2.0×10^{-5} mg/m^3) would result in not greater than a one-in-a-hundred thousand increased chance of developing cancer, and air containing 0.2 $\mu g/m^3$ (2.0×10^{-4} mg/m^3) would result in not greater than a one-in-ten thousand increased chance of developing cancer. For a detailed discussion of confidence in the potency estimates, please see IRIS. (5)
- EPA has calculated an oral cancer slope factor of 1.6 $(mg/kg/d)^{-1}$. (5)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45).
For hexachlorobenzene: 1 ppm = 11.6 mg/m^3.

Health Data from Inhalation Exposure



ACGIH TLV – American Conference of Governmental and Industrial Hygienists' threshold limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effects.
LC_{50} (Lethal Concentration$_{50}$) – A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.

[a] Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA.
[b] Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the Government or other groups as advice.

[c] These cancer risk estimates were derived from oral data and converted to provide the estimated inhalation risk.

References

1. Agency for Toxic Substances and Disease Registry (ATSDR). *Toxicological Profile for Hexachlorobenzene* (Update). Public Health Service, U.S. Department of Health and Human Services, Atlanta, GA. 1996.

2. U.S. Environmental Protection Agency (EPA). *Deposition of Air Pollutants to the Great Waters*. First Report to Congress. EPA-453/R-93-055. Office of Air Quality Planning and Standards, Research Triangle Park, NC. 1994.

3. U.S. Department of Health and Human Services. Hazardous Substances Data Bank (HSDB, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.

4. U.S. Department of Health and Human Services. Registry of Toxic Effects of Chemical Substances (RTECS, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.

5. U.S. Environmental Protection Agency (EPA). *Integrated Risk Information System (IRIS) on Hexachlorobenzene*. National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1999.

6. California Environmental Protection Agency (CalEPA). *Technical Support Document for the Determination of Noncancer Chronic Reference Exposure Levels.* Draft for Public Comment. Office of Environmental Health Hazard Assessment, Berkeley, CA. 1997.

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

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HYDRAZINE
302-01-2

Hazard Summary

Individuals may be exposed to hydrazine in the workplace or to small amounts in tobacco smoke. Symptoms of acute (short-term) exposure to high levels of hydrazine may include irritation of the eyes, nose, and throat, dizziness, headache, nausea, pulmonary edema, seizures, and coma in humans. Acute exposure can also damage the liver, kidneys, and central nervous system (CNS) in humans. The liquid is corrosive and may produce dermatitis from skin contact. Effects to the lungs, liver, spleen, and thyroid have been reported in animals chronically (long-term) exposed to hydrazine via inhalation. Exposure of rodents to hydrazine has resulted in fetotoxicity and damage to reproductive organs. Increased incidences of lung and liver tumors have been observed in mice exposed to hydrazine. Tumors in the nasal cavity were observed in rats and hamsters exposed by inhalation. The U.S. Environmental Protection Agency (EPA) has classified hydrazine as a Group B2, probable human carcinogen.

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

Physical Properties

- The chemical formula for hydrazine is H_4N_2, and its molecular weight is 32.05 g/mol. (6)
- Hydrazine occurs as a colorless, oily, flammable liquid that is miscible with water. (6,8)
- Hydrazine has a penetrating odor, resembling that of ammonia, with an odor threshold of 3.7 ppm. (8,9)
- The vapor pressure for hydrazine is 14.4 mm Hg at 25 EC, and its log octanol/water partition coefficient (log K_{ow}) is 0.08. (6)

Uses

- Hydrazine is used in agricultural chemicals (pesticides), chemical blowing agents, pharmaceutical intermediates, photography chemicals, boiler water treatment for corrosion protection, textile dyes, and as fuel for rockets and spacecraft. (4,6,8,10)

Sources and Potential Exposure

- Individuals may be occupationally exposed to hydrazine in the workplace. (1,2,10)
- Accidental discharge into water, air, and soil may occur during storage, handling, transport, and improper waste disposal. However, hydrazine rapidly degrades in the environment and is rarely encountered. (2,3)

- Small amounts of hydrazine have been detected in tobacco smoke. (2,10)

Assessing Personal Exposure

- Hydrazine may be detected in the blood of exposed individuals. (1,2)

Health Hazard Information

Acute Effects:

- Symptoms of acute exposure to high levels of hydrazine include irritation of the eyes, nose, and throat, temporary blindness, dizziness, headache, nausea, pulmonary edema, seizures, and coma in humans. Acute exposure can also damage the liver, kidneys, and the CNS in humans. (2-4)
- The liquid is corrosive and may produce chemical burns and severe dermatitis from skin contact. (1,4)
- Acute animal tests, such as the LC_{50} and LD_{50} tests in rats, mice, rabbits, and guinea pigs, have demonstrated hydrazine to have high acute toxicity from inhalation and ingestion and extreme acute toxicity from dermal exposure. (5)

Chronic Effects (Noncancer):

- Information is not available on the chronic effects of hydrazine in humans.
- In animals chronically exposed to hydrazine by inhalation, effects on the respiratory system, liver, spleen, and thyroid have been observed. (10)
- EPA has not established a reference concentration (RfC) or a reference dose (RfD) for hydrazine. (4)
- The California Environmental Protection Agency (CalEPA) has calculated a chronic inhalation reference exposure level of 0.0002 mg/m^3 based on liver and thyroid effects in hamsters. The CalEPA reference exposure level is a concentration at or below which adverse health effects are not likely to occur. It is not a direct estimator of risk but rather a reference point to gauge the potential effects. At lifetime exposures increasingly greater than the reference exposure level, the potential for adverse health effects increases. (11)
- ATSDR has calculated an intermediate inhalation minimal risk level (MRL) of 0.005 mg/m^3 (0.004 ppm) based on liver effects in mice. The MRL is an estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk of adverse noncancer health effects over a specified duration of exposure. (10)

Reproductive/Developmental Effects:

- Information is not available on the reproductive or developmental effects of hydrazine in humans.
- Data regarding developmental effects in animals are limited to a study in which hydrazine injected into pregnant rats resulted in fetotoxicity including increased fetal and neonatal mortality. (6,10)

- Inhalation of hydrazine for a year resulted in effects to the ovaries, endometrium, and uterus in female rats and to the testes in male hamsters. (10)

Cancer Risk:

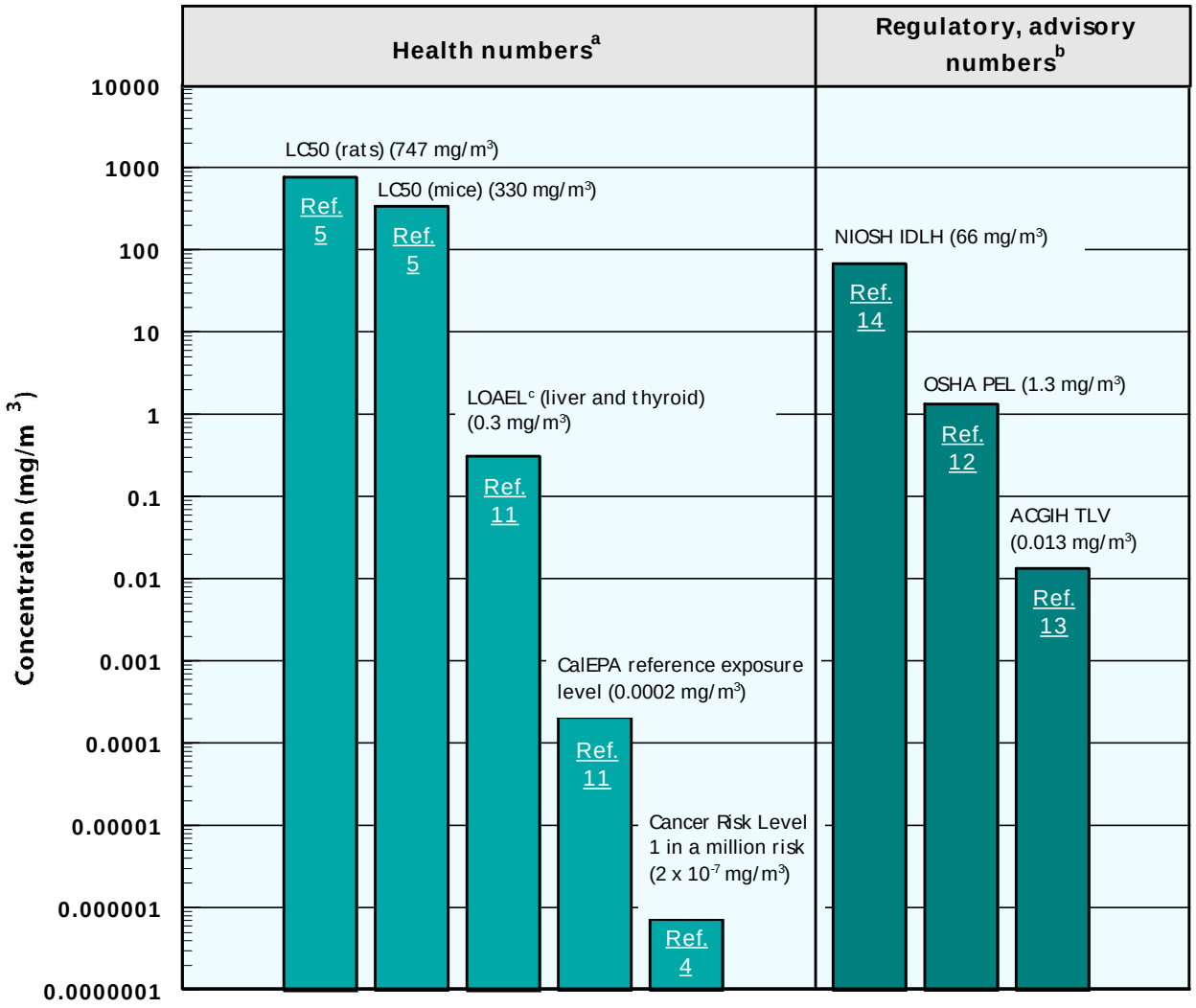
- Adequate information is not available on the carcinogenic effects of hydrazine in humans. (4)
- Increased incidences of lung and liver tumors have been observed in mice exposed to hydrazine by inhalation, in their drinking water, via gavage and injection. Tumors in the nasal cavity were observed in rats and hamsters exposed by inhalation. (4,6,7)
- EPA has classified hydrazine as a Group B2, probable human carcinogen. (4)
- EPA uses mathematical models, based on human and animal studies, to estimate the probability of a person developing cancer from breathing air containing a specified concentration of a chemical. EPA calculated an inhalation unit risk estimate of 4.9×10^{-3} $(\mu g/m^3)^{-1}$. EPA estimates that, if an individual were to continuously breathe air containing hydrazine at an average of 0.0002 $\mu g/m^3$ (2.0×10^{-7} mg/m^3) over his or her entire lifetime, that person would theoretically have no more than a one-in-a-million increased chance of developing cancer as a direct result of breathing air containing this chemical. Similarly, EPA estimates that breathing air containing 0.002 $\mu g/m^3$ (2.0×10^{-6} mg/m^3) would result in not greater than a one-in-a-hundred thousand increased chance of developing cancer, and air containing 0.02 $\mu g/m^3$ (2.0×10^{-5} mg/m^3) would result in not greater than a one-in-ten thousand increased chance of developing cancer. For a detailed discussion of confidence in the potency estimates, please see IRIS. (4)
- EPA has calculated an oral cancer slope factor of 3.0 $(mg/kg/d)^{-1}$. (4)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45). For hydrazine: 1 ppm = 1.31 mg/m^3.

Health Data from Inhalation Exposure

Hydrazine



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

LC_{50} (Lethal Concentration$_{50}$) – A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.

LOAEL – Lowest-observed-adverse-effect level

NIOSH IDLH – National Institute of Occupational Safety and Health's immediately dangerous to life or health limit; NIOSH recommended exposure limit to ensure that a worker can escape from an exposure condition that is likely to cause death or immediate or delayed permanent adverse health effects or prevent escape from the environment.

OSHA PEL – Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.

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

References

1. M. Sittig. *Handbook of Toxic and Hazardous Chemicals and Carcinogens*. 2nd ed. Noyes Publications, Park Ridge, NJ. 1985.

2. World Health Organization (WHO). *Environmental Health Criteria 68: Hydrazine*. Geneva, Switzerland. 1987.

3. U.S. Department of Health and Human Services. Hazardous Substances Data Bank (HSDB, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.

4. U.S. Environmental Protection Agency (EPA). *Integrated Risk Information System (IRIS) on Hydrazine/Hydrazine Sulfate*. National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1999.

5. U.S. Department of Health and Human Services. Registry of Toxic Effects of Chemical Substances (RTECS, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.

6. U.S. Environmental Protection Agency (EPA). *Health and Environmental Effects Profile for Hydrazine and Hydrazine Sulfate*. EPA/600/x-84/332. Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment, Office of Research and Development, Cincinnati, OH. 1984.

7. International Agency for Research on Cancer (IARC). *IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man: Some Aromatic Amines, Hydrazine and Related Substances, N-Nitroso Compounds and Miscellaneous Alkylating Agents*. Volume 4. World Health Organization, Lyon. 1974.

8. *The Merck Index. An Encyclopedia of Chemicals, Drugs, and Biologicals*. 11th ed. Ed. S. Budavari. Merck and Co. Inc., Rahway, NJ. 1989.

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

10. Agency for Toxic Substances and Disease Registry (ATSDR). *Toxicological Profile for Hydrazines.* Public Health Service, U.S. Department of Health and Human Services, Atlanta, GA. 1997.

11. California Environmental Protection Agency (CalEPA). *Technical Support Document for the Determination of Noncancer Chronic Reference Exposure Levels. Draft for Public Comment.* Office of Environmental Health Hazard Assessment, Berkeley, CA. 1997.

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

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

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

LEAD COMPOUNDS[1]

Hazard Summary

Lead is used in the manufacture of batteries, metal products, paints, and ceramic glazes. Exposure to lead can occur from breathing contaminated workplace air or dust or eating lead-based paint chips or contaminated dirt. Lead is a very toxic element, causing a variety of effects at low dose levels. Brain damage, kidney damage, and gastrointestinal distress are seen from acute (short-term) exposure to high levels of lead in humans. Chronic (long-term) exposure to lead in humans results in effects on the blood, central nervous system (CNS), blood pressure, kidneys, and Vitamin D metabolism. Children are particularly sensitive to the chronic effects of lead, with slowed cognitive development, reduced growth and other effects reported. Reproductive effects, such as decreased sperm count in men and spontaneous abortions in women, have been associated with lead exposure. The developing fetus is at particular risk from maternal lead exposure, with low birth weight and slowed postnatal neurobehavioral development noted. Human studies are inconclusive regarding lead exposure and cancer, while animal studies have reported an increase in kidney cancer from lead exposure by the oral route. The U.S. Environmental Protection Agency (EPA) considers lead to be a Group B2, probable human carcinogen.

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

Physical Properties

- Lead is a naturally occurring, bluish-gray metal that is found in small quantities in the earth's crust. (1,2)
- Lead is present in a variety of compounds such as lead acetate, lead chloride, lead chromate, lead nitrate, and lead oxide. (1,2)
- Pure lead is insoluble in water; however, the lead compounds vary in solubility from insoluble to water soluble. (1,2)
- The chemical symbol for lead is Pb, and the atomic weight is 207.2 g/mol. (1)
- The vapor pressure for lead is 1.0 mm Hg at 980 EC. (1)

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[1] Human exposure to lead occurs through a combination of inhalation and oral exposure, with inhalation generally contributing a greater proportion of the dose for occupationally exposed groups, and the oral route generally contributing a greater proportion of the dose for the general population. The effects of lead are the same regardless of the route of exposure (inhalation or oral) and are correlated with internal exposure as blood lead levels. For this reason, this fact sheet will not discuss the exposure in terms of route but will present it in terms of blood lead levels.

Uses

- The primary use of lead is in the manufacture of batteries. (1)
- Lead is also used in the production of metal products, such as sheet lead, solder (but no longer in food cans), and pipes, and in ceramic glazes, paint, ammunition, cable covering, and other products. (1)
- Tetraethyl lead was used in gasoline to increase the octane rating until lead additives were phased out and eventually banned from use in gasoline by the EPA beginning in 1973. (1)

Sources and Potential Exposure

- The largest source of lead in the atmosphere has been from leaded gasoline combustion, but with the phase down of lead in gasoline, air lead levels have decreased considerably. Other airborne sources include combustion of solid waste, coal, and oils, emissions from iron and steel production and lead smelters, and tobacco smoke. (1,2)
- Exposure to lead can also occur from food and soil. Children are at particular risk to lead exposure since they commonly put hands, toys, and other items in their mouths, which may come in contact with lead-containing dust and dirt. (1,2)
- Lead-based paints were commonly used for many years and flaking paint, paint chips, and weathered paint powder may be a major source of lead exposure, particularly for children. (1,2)
- Lead in drinking water is due primarily to the presence of lead in certain pipes, solder, and fixtures. (1,2)
- Exposure to lead may also occur in the workplace, such as lead smelting and refining industries, steel and iron factories, gasoline stations, and battery manufacturing plants. (1,2)
- Lead has been listed as a pollutant of concern to EPA's Great Waters Program due to its persistence in the environment, potential to bioaccumulate, and toxicity to humans and the environment. (3)

Assessing Personal Exposure

- The amount of lead in the blood can be measured to determine if exposure to lead has occurred. (1,2)
- The level of lead in the blood is measured in µg/dL.
- The Centers for Disease Control concluded in 1993 that blood lead concentrations at or around 10 µg/dL present a public health risk to sensitive populations.
- Exposure to lead can also be evaluated by measuring erythrocyte protoporphyrin (EP), a component of red blood cells known to increase when the amount of lead in the blood is high. This method was commonly used to screen children for potential lead poisoning. (1,2)
- Methods to measure lead in teeth or bones by X-ray fluorescence techniques are not widely available. (1)

Health Hazard Information

Acute Effects:

- Death from lead poisoning may occur in children who have blood lead levels greater than 125 µg/dL, and brain and kidney damage have been reported at blood lead levels of approximately 100 µg/dL in adults and 80 µg/dL in children. (1,2)
- Gastrointestinal symptoms, such as colic, have also been noted in acute exposures at blood lead levels of approximately 60 µg/dL in adults and children. (1,2)
- Short-term (acute) animal tests, such as the LC_{50} test in rats, have shown lead to have moderate to high acute toxicity. (4)

Chronic Effects (Noncancer):

- Chronic exposure to lead in humans can affect the blood. Anemia has been reported in adults at blood lead levels of 50 to 80 µg/dL, and in children at blood lead levels of 40 to 70 µg/dL. (1,2)
- Lead also affects the nervous system. Neurological symptoms have been reported in workers with blood lead levels of 40 to 60 µg/dL, and slowed nerve conduction in peripheral nerves in adults occurs at blood lead levels of 30 to 40 µg/dL. (1,2)
- Children are particularly sensitive to the neurotoxic effects of lead. A greatly expanded body of research has shown that even low levels of lead exposure can result in neurobehavioral changes, such as lowered IQ, in developing children. There is evidence that blood lead levels of 10 to 30 µg/dL, or lower, may affect the hearing threshold and growth in children. (1,2)
- Other effects from chronic lead exposure in humans include effects on blood pressure and kidney function, and interference with vitamin D metabolism. (1,2,5)
- Animal studies have reported effects similar to those found in humans, with effects on the blood, kidneys, and nervous, immune, and cardiovascular systems noted. (1,2,5)
- EPA has not established a reference concentration (RfC) or a reference dose (RfD) for elemental lead or inorganic lead compounds. (6)
- EPA has established an RfD for tetraethyl lead (an organometallic form of lead) of 1 x 10^{-7} mg/kg/d based on effects in the liver and thymus of rats. The RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious noncancer effects during a lifetime. It is not a direct estimator of risk, but rather a reference point to gauge the potential effects. At exposures increasingly greater than the RfD, the potential for adverse health effects increases. Lifetime exposure above the RfD does not imply that an adverse health effect would necessarily occur. (7)
- EPA has medium to low confidence in the RfD due to: medium to low confidence in the study on which the RfD for tetraethyl lead was based because, although only a few animals per sex per dose level were tested, a good histopathologic exam was conducted and a dose-severity was observed; and medium to low confidence in the database because some supporting information was available. (7)

- The EPA has set a national ambient air quality standard (NAAQS) for lead at 1.5 µg/m3 as a quarterly average concentration. The NAAQS was set on the basis of evidence that numerous health effects were associated with lead exposure, including impairment of heme synthesis, and in recognition that young children (age 1-5 years) were a particularly sensitive group to lead effects. (11,12)

Reproductive/Developmental Effects:

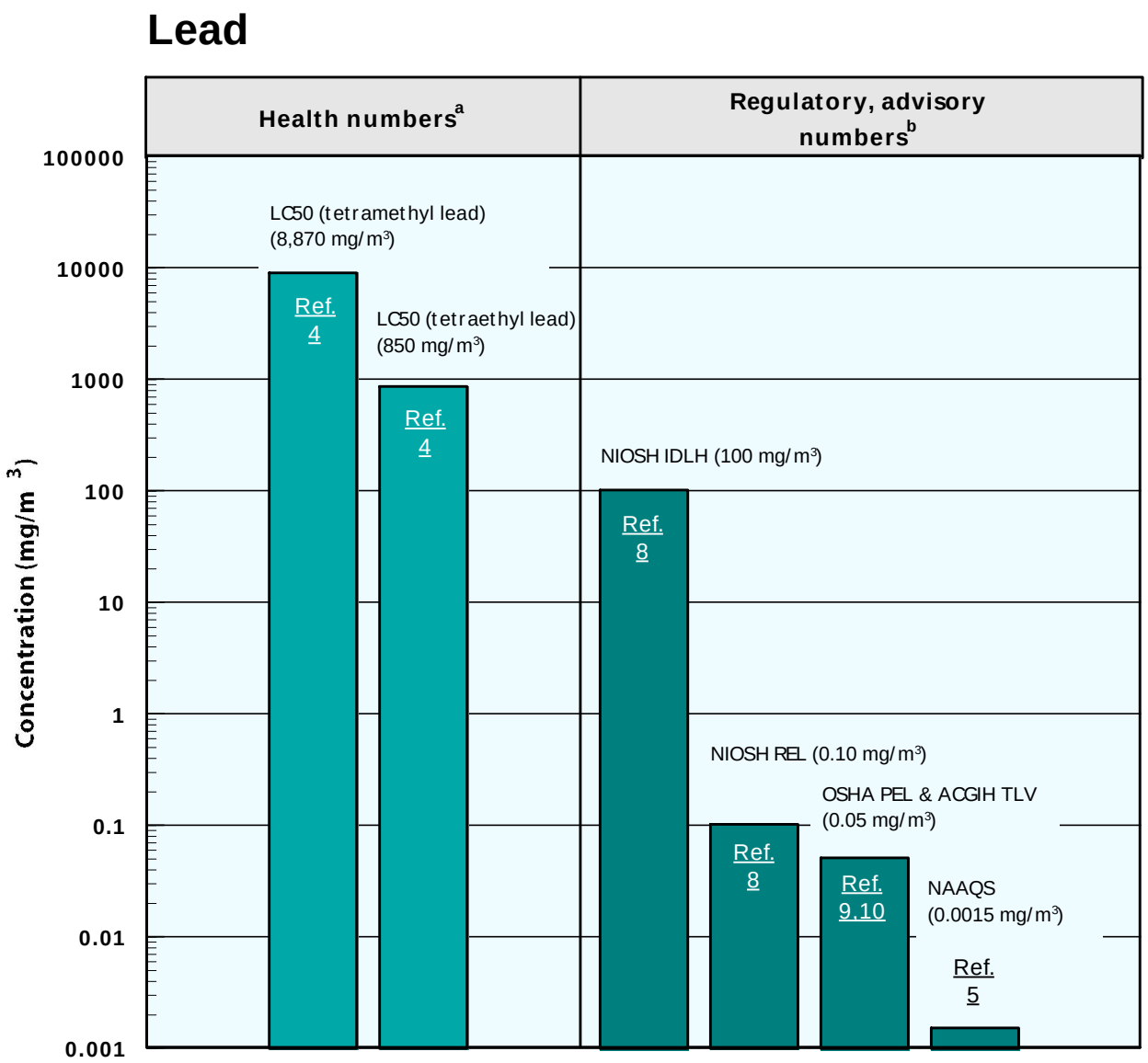
- Studies on male lead workers have reported severe depression of sperm count and decreased function of the prostate and/or seminal vesicles at blood lead levels of 40 to 50 µg/dL. These effects may be seen from acute as well as chronic exposures. (1,5)
- Occupational exposure to high levels of lead has been associated with a high likelihood of spontaneous abortion in pregnant women. However, the lowest blood lead levels at which this occurs has not been established. These effects may be seen from acute as well as chronic exposures. (1,5)
- Exposure to lead during pregnancy produces toxic effects on the human fetus, including increased risk of preterm delivery, low birth weight, and impaired mental development. These effects have been noted at maternal blood lead levels of 10 to 15 µg/dL, and possibly lower. Decreased IQ scores have been noted in children at blood lead levels of approximately 10 to 50 µg/dL. (1,2)
- Human studies are inconclusive regarding the association between lead exposure and other birth defects, while animal studies have shown a relationship between high lead exposure and birth defects. (1,5)

Cancer Risk:

- Human studies are inconclusive regarding lead exposure and an increased cancer risk. Four major human studies of workers exposed to lead have been carried out; two studies did not find an association between lead exposure and cancer, one study found an increased incidence of respiratory tract and kidney cancers, and the fourth study found excesses for lung and stomach cancers. However, all of these studies are limited in usefulness because the route(s) of exposure and levels of lead to which the workers were exposed were not reported. In addition, exposure to other chemicals probably occurred. (1,2,6)
- Animal studies have reported kidney tumors in rats and mice exposed to lead via the oral route. (1,2,5,6)
- EPA considers lead to be a Group B2, probable human carcinogen. (6)

Conversion Factors:
To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45).
For lead: 1 ppm = 8.5 mg/m^3.

Health Data from Inhalation Exposure



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

LC_{50} (Lethal Concentration$_{50}$) – A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.

NIOSH REL – National Institute of Occupational Safety and Health's recommended exposure limit; NIOSH-recommended exposure limit for an 8- or 10-h time-weighted-average exposure and/or ceiling.

NIOSH IDLH – NIOSH's immediately dangerous to life or health concentration; NIOSH

recommended exposure limit to ensure that a worker can escape from an exposure condition that is likely to cause death or immediate or delayed permanent adverse health effects or prevent escape from the environment.
NAAQS – National Ambient Air Quality Standard. NAAQS set by EPA for pollutants that are considered to be harmful to public health and the environment; the NAAQS for lead is 1.5 $\mu g/m^3$, maximum arithmetic mean averaged over a calendar quarter.
OSHA PEL – Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.

[a] Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA.
[b] Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the Government or other groups as advice.

References

1. Agency for Toxic Substances and Disease Registry (ATSDR). *Toxicological Profile for Lead (Update).* Draft for Public Comment. Public Health Service, U.S. Department of Health and Human Services, Atlanta, GA. 1997.

2. Agency for Toxic Substances and Disease Registry (ATSDR). *Case Studies in Environmental Medicine, Lead Toxicity*. Public Health Service, U.S. Department of Health and Human Services, Atlanta, GA. 1992.

3. U.S. Environmental Protection Agency (EPA). *Deposition of Air Pollutants to the Great Waters*. *First Report to Congress*. EPA-453/R-93-055. Office of Air Quality Planning and Standards, Research Triangle Park, NC. 1994.

4. U.S. Department of Health and Human Services. Registry of Toxic Effects of Chemical Substances (RTECS, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.

5. U.S. Department of Health and Human Services. Hazardous Substances Data Bank (HSDB, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.

6. U.S. Environmental Protection Agency (EPA). *Integrated Risk Information System (IRIS) on Lead and Compounds (Inorganic)*. National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1999.

7. U.S. Environmental Protection Agency (EPA). *Integrated Risk Information System (IRIS) on Tetraethyl Lead*. National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1999.

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

9. Occupational Safety and Health Administration (OSHA). Occupational Safety and Health Standards, Toxic and Hazardous Substances. *Code of Federal Regulations* 29 CFR 1910.1025. 1998.

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

11. U.S. Environmental Protection Agency (EPA). National Ambient Air Quality Standard for Lead. 43 FR 46246, October 5, 1978.

12. U.S. Environmental Protection Agency (EPA). Review of the National Ambient Air Quality Standards for Lead: Assessment of Scientific and Technical Information. Office of Air Quality Planning and Standards, Research Triangle Park, NC 27711. EPA-450/2-89-022. December 1990.

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MANGANESE COMPOUNDS

Hazard Summary

Manganese is naturally ubiquitous in the environment. Manganese is essential for normal physiologic functioning in humans and animals. Health effects in humans have been associated with both deficiencies and excess intakes of manganese. Chronic (long-term) exposure to low levels of manganese in the diet is considered to be nutritionally essential in humans, with a recommended daily allowance of 2 to 5 mg/d. Chronic exposure to high levels of manganese by inhalation in humans results primarily in central nervous system (CNS) effects. Visual reaction time, hand steadiness, and eye-hand coordination were affected in chronically-exposed workers. A syndrome named manganism may result from chronic exposure to higher levels; manganism is characterized by feelings of weakness and lethargy, tremors, a mask-like face, and psychological disturbances. Respiratory effects have also been noted in workers chronically exposed by inhalation. Impotence and loss of libido have been noted in male workers afflicted with manganism attributed to high-level inhalation exposures to manganese. No studies are available regarding the carcinogenic effects of manganese in humans, and animal studies are inadequate. The U.S. Environmental Protection Agency (EPA) has classified manganese as a Group D, not classifiable as to carcinogenicity in humans.

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

Physical Properties

- Manganese is a silver-colored metal that forms compounds in the environment with chemicals such as oxygen, sulfur, and chlorine. (1)
- Manganese compounds are solids that do not evaporate; however, small dust particles can become suspended in air. (1)
- Manganese can dissolve in water. (1)
- The chemical symbol for manganese is Mn, and elemental manganese has an atomic weight of 54.94 g/mol. (1)
- Some manganese compounds are: manganese dioxide (MnO_2), manganese tetraoxide (Mn_3O_4), manganese salts (chloride, sulfate, carbonate, and nitrate), manganese silicate, and potassium permanganate ($KMnO_4$).

Uses

- Metallic manganese is used primarily in steel production to improve hardness, stiffness, and strength. It is also used in carbon steel, stainless steel, and high-temperature steel, along with cast iron and superalloys. (1)

- Manganese compounds have a variety of uses. Manganese dioxide is used in the production of dry-cell batteries, matches, fireworks, and the production of other manganese compounds. (1)
- Manganese chloride is used as a catalyst in the chlorination of organic compounds, in animal feed, and in dry-cell batteries, while manganese sulfate is used as a fertilizer, livestock nutritional supplement, in glazes and varnishes, and in ceramics. (1)
- Potassium permanganate is used for water purification purposes in water and waste-treatment plants. (1)

Sources and Potential Exposure

- Manganese is a naturally occurring substance found in many types of rock and soil; it is ubiquitous in the environment and found in low levels in water air, soil, and food. (1)
- Manganese can also be released into the air by iron and steel production plants, power plants, and coke ovens. (1)
- The average manganese levels in various media are as follows: levels in drinking water are approximately 0.004 ppm; average air levels are approximately 0.02 $\mu g/m^3$; levels in soil range from 40 to 900 ppm; the average daily intake from food ranges from 1 to 5 mg/d. (1)
- People who work in factories where manganese metal is produced from manganese ore or where manganese compounds are used to make steel or other products are most likely to be exposed through inhalation to higher than normal levels of manganese. (1)

Assessing Personal Exposure

- Several tests are available for measuring manganese in blood, urine, hair, or feces. As manganese is naturally present in the body, some manganese is always found in these materials. In addition, excess manganese is usually removed from the body within a few days, making it difficult to measure past exposure to manganese. (1)

Health Hazard Information

Acute Effects:

- No reports of effects in humans following acute (short-term) effects of exposure to manganese are available.
- Effects to the lung have been reported following acute exposure of rats to manganese via inhalation. (1)
- Manganese is considered to have moderate acute toxicity based on short-term tests, such as the LD_{50} test given by gavage in rats. However, other animal tests in which manganese has been given orally have indicated that manganese has low acute oral toxicity. (1)

Chronic Effects (Noncancer):

- Chronic exposure to manganese at low levels is nutritionally essential in humans. The recommended daily intake of manganese is 2 to 5 mg/d for adults and adolescents. (1)
- No cases of manganese deficiency have been observed in the general population. However, manganese deficiency in animals has been associated with impaired growth, skeletal abnormalities, impaired reproductive function in females, and testicular degeneration in males. (1)
- Chronic inhalation exposure of humans to manganese results primarily in effects on the nervous system. Slower visual reaction time, poorer hand steadiness, and impaired eye-hand coordination were reported in several studies of workers occupationally exposed to manganese dust in air. (1,3)
- Chronic inhalation exposure of humans to high levels may result in a syndrome called manganism and typically begins with feelings of weakness and lethargy and progresses to other symptoms such as gait disturbances, clumsiness, tremors, speech disturbances, a mask-like facial expression, and psychological disturbances. (1,3)
- Other chronic effects reported in humans from inhalation exposure to manganese are respiratory effects such as an increased incidence of cough, bronchitis, dyspnea during exercise, and an increased susceptibility to infectious lung disease. (1,3)
- The RfC for manganese is 0.00005 mg/m^3 based on impairment of neurobehavioral function in humans. The RfC is an estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious noncancer effects during a lifetime. It is not a direct estimator of risk but rather a reference point to gauge the potential effects. At exposures increasingly greater than the RfC, the potential for adverse health effects increases. Lifetime exposure above the RfC does not imply that an adverse health effect would necessarily occur. (3)
- EPA has medium confidence in the RfC due to medium confidence in the principal studies on which the RfC was based and medium confidence in the database. Neither of the principal studies identified a no-observed-adverse-effect level (NOAEL) for neurobehavioral effects, nor did either study directly measure particle size or provide information on the particle size distribution. These limitations of the studies are mitigated by the fact that the principal studies found similar indications of neurobehavioral dysfunction, and these findings were consistent with the results of other human studies. EPA has medium confidence in the database because the duration of exposure was relatively limited in the principal and supporting studies, the majority of studies did not specify the species of manganese, and the reproductive and developmental effects have not been adequately studied. (3)
- EPA has established a RfD for manganese of 0.14 mg/kg/d based on CNS effects in humans. The RfD is estimated to be an intake for the general population that is not associated with adverse health effects; this is not meant to imply that intakes above the RfD are necessarily associated with toxicity. Some individuals may, in fact, consume a diet that contributes more than 10 mg Mn/day without any cause for concern. When assessing risk from manganese in drinking water or soil, a modified RfD of 0.05 mg/kg/d is recommended. (3)

- EPA has medium confidence in the RfD due to medium confidence in the studies on which the RfD for manganese was based; and medium confidence in the database. (3)

Reproductive/Developmental Effects:

- Reproductive effects, such as impotence and loss of libido, have been noted in male workers afflicted with manganism attributed to occupational exposure to high levels of manganese by inhalation. No information is available on developmental effects of manganese in humans. (1,3)
- Animal studies have reported degenerative changes in the seminiferous tubules leading to sterility from intratracheal instillation of high doses of manganese (experimentally delivering the manganese directly to the trachea). In young animals exposed to manganese orally, decreased testosterone production and retarded growth of the testes were reported. (1)
- Decreased activity levels and a decrease in average pup weight have been noted in the offspring of mice exposed to manganese by inhalation. (1)

Cancer Risk:

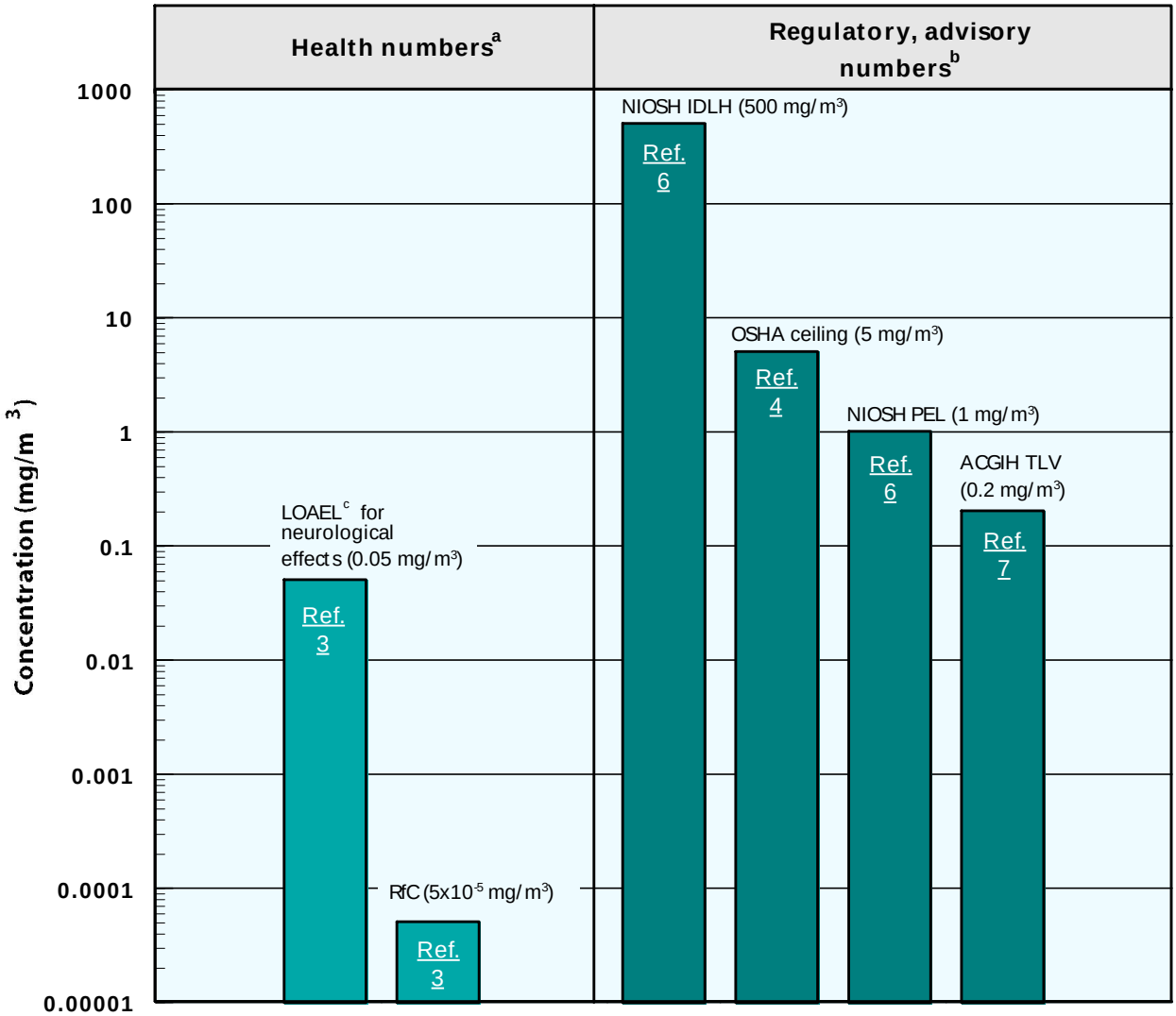
- No studies are available regarding carcinogenic effects in humans or animals from inhalation exposure to manganese. (1,3)
- No studies are available regarding cancer in humans from oral exposure to manganese. Oral animal studies on manganese sulfate are inadequate, with several studies reporting negative results, one study reporting an increased incidence of thyroid gland follicular cell adenomas and hyperplasia, and one study noting an increased incidence of pancreatic tumors. (1,3)
- EPA has classified manganese as a Group D, not classifiable as to carcinogenicity in humans. (3)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45).
For manganese: 1 ppm = 2.25 mg/m^3.
To convert from µg/m^3 to mg/m^3: mg/m^3 = (µg/m^3) x (1 mg/1,000 µg).

Health Data from Inhalation Exposure

Manganese



ACGIH TLV – American Conference of Governmental and Industrial Hygienists' threshold limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effects.
LOAEL – Lowest-observed-adverse-effect level.
NIOSH REL – National Institute of Occupational Safety and Health's recommended exposure limit; NIOSH-recommended exposure limit for an 8- or 10-h time-weighted-average exposure and/or ceiling.
NIOSH IDLH – NIOSH's immediately dangerous to life or health concentration; NIOSH recommended exposure limit to ensure that a worker can escape from an exposure condition that is likely to cause death or immediate or delayed permanent adverse health effects or prevent escape from the environment.

OSHA PEL – Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.
OSHA ceiling – OSHA's short-term exposure limit ceiling; an exposure that should not be exceeded at any time during a workday even if the 8-h time-weighted-average is within the threshold limit value.

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

References

1. Agency for Toxic Substances and Disease Registry (ATSDR). *Toxicological Profile for Manganese (Update).* Draft for Public Comment. U.S. Public Health Service, U.S. Department of Health and Human Services, Altanta, GA. 1997.

2. National Academy of Sciences (NAS). *Drinking Water and Health. Volume 3*. National Academy Press, Washington, DC. 1989.

3. U.S. Environmental Protection Agency (EPA). *Integrated Risk Information System (IRIS) on Manganese*. National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1999.

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

5. E.J. Calabrese and E.M. Kenyon. *Air Toxics and Risk Assessment*. Lewis Publishers, Chelsea, MI. 1991.

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

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

MERCURY COMPOUNDS

Hazard Summary

Mercury exists in three forms: elemental mercury, inorganic mercury compounds (primarily mercuric chloride), and organic mercury compounds (primarily methyl mercury). All forms of mercury are quite toxic, and each form exhibits different health effects.

Acute (short-term) exposure to high levels of elemental mercury in humans results in central nervous system (CNS) effects such as tremors, mood changes, and slowed sensory and motor nerve function. High inhalation exposures can also cause kidney damage. Effects on the gastrointestinal tract and respiratory system have also been noted in humans from acute inhalation exposure. Chronic (long-term) exposure to elemental mercury in humans also affects the CNS, with effects such as erethism (increased excitability), irritability, excessive shyness, and tremors. Human studies are inconclusive regarding elemental mercury and cancer. The U.S. Environmental Protection Agency (EPA) has classified elemental mercury as a Group D, not classifiable as to human carcinogenicity.

Acute exposure to inorganic mercury by the oral route may result in effects such as nausea, vomiting, and severe abdominal pain. The major effect from chronic exposure to inorganic mercury is kidney damage. Animal studies have reported effects such as alterations in testicular tissue, increased resorption rates, and abnormalities of development. Mercuric chloride (an inorganic mercury compound) exposure has been shown to result in forestomach, thyroid, and renal tumors in experimental animals. EPA has classified inorganic mercury as Group C, possible human carcinogen.

Acute exposure of humans to very high levels of methyl mercury results in CNS effects such as blindness, deafness, and impaired level of consciousness. Chronic exposure to methyl mercury in humans also affects the CNS with symptoms such as paresthesia (a sensation of pricking on the skin), blurred vision, malaise, speech difficulties, and constriction of the visual field. Methyl mercury exposure, via the oral route, has led to significant developmental effects. Infants born to women who ingested high levels of methyl mercury exhibited mental retardation, ataxia, constriction of the visual field, blindness, and cerebral palsy. No human studies are available on the carcinogenic effects of methyl mercury, and one animal study reported renal tumors in mice. EPA has classified methyl mercury as Group C, possible human carcinogen.

Please Note: The main sources of information for this fact sheet are EPA's Integrated Risk Information System (IRIS), which contains information on inhalation chronic toxicity and the reference concentration (RfC) for elemental mercury, oral chronic toxicity and the reference dose (RfD) for inorganic and methyl mercury, EPA's *Mercury Study Report to Congress*, and the Agency for Toxic Substances and Disease Registry's (ATSDR's)

Toxicological Profile for Mercury. Other secondary sources include the World Health Organization's *Environmental Health Criteria Documents on Methyl Mercury and Inorganic Mercury*.

Physical Properties

- Elemental mercury is a silver-white metal with an atomic weight of 200.59 g/mol. (1)
- Mercury is a liquid at room temperature and has a vapor pressure of 0.002 mm Hg at 25 EC. (1)
- Mercury can exist in three oxidation states — elemental, mercurous, and mercuric — and it can be part of both inorganic and organic compounds. (1)
- Inorganic mercury compounds include mercuric chloride, mercuric sulfide, mercurous chloride. Organic mercury compounds include mercuric acetate, methylmercuric chloride, dimethyl mercury, and phenylmercuric acetate. (1)

Uses

Elemental Mercury

- Elemental mercury is used in thermometers, barometers, and pressure-sensing devices. It is also used in batteries, lamps, industrial processes, refining, lubrication oils, and dental amalgams. (1)

Inorganic Mercury

- Inorganic mercury was used in the past in laxatives, skin-lightening creams and soaps, and in latex paint. In 1990, EPA canceled registration for all interior paints that contained mercury. Mercury use in exterior paint was discontinued after 1991. (1)

Methyl Mercury

- Methyl mercury has no industrial uses; it is formed in the environment from the methylation of the inorganic mercurial ion. (1)

Sources and Potential Exposure

Elemental Mercury

- A major source of exposure for elemental mercury is through inhalation in occupational settings. (1,3,4)
- Another source of exposure to low levels of elemental mercury in the general population is elemental mercury released in the mouth from dental amalgam fillings. (3-5)

Inorganic Mercury

- The general population is usually not exposed to inorganic mercury compounds to any significant extent today, as most products containing these compounds have now been banned. Limited exposure could occur through the use of old cans of latex paint, which until 1990, could contain mercury compounds to prevent bacterial and fungal growth. (1,4)

Methyl Mercury

- The most important organic mercury compound, in terms of human exposure, is methyl mercury. Methyl mercury exposure occurs primarily through the diet, with fish and fish products as the dominant source. Sources of past exposure to methyl mercury include fungicide-treated grains and meat from animals fed such grain. However, fungicides containing mercury are banned in the U.S. today, and this source of exposure is now negligible. (1)
- Mercury has been listed as a pollutant of concern to EPA's Great Waters Program due to its persistence in the environment, potential to bioaccumulate, and toxicity to humans and the environment. (6)

Assessing Personal Exposure

- Laboratory tests can detect mercury in blood, urine, and hair samples. (1)

Health Hazard Information

Acute Effects:

Elemental Mercury

- The major systems impacted by human inhalation of elemental mercury are the kidneys and CNS. Acute exposure to high levels of elemental mercury in humans results in CNS effects, such as tremors, irritability, insomnia, memory loss, neuromuscular changes, headaches, slowed sensory and motor nerve function, and reduction in cognitive function. (1,2)
- Acute inhalation exposure of humans to high concentrations has resulted in kidney effects ranging from mild transient proteinuria to acute renal failure. (1,2)
- Gastrointestinal effects and respiratory effects, such as chest pains, dyspnea, cough, pulmonary function impairment, and interstitial pneumonitis have also been noted from human inhalation exposure to elemental mercury. (1,2)

Inorganic Mercury

- Symptoms noted after acute oral exposure to inorganic mercury compounds include a metallic taste in the mouth, nausea, vomiting, and severe abdominal pain. (1,2,7)

- The acute lethal dose for most inorganic mercury compounds for an adult is 1 to 4 g or 14 to 57 mg/kg for a 70-kg person. (1,7)

Methyl Mercury

- Acute inhalation exposure to high levels of methyl mercury, which is extremely rare, has resulted in severe CNS effects, including blindness, deafness, impaired level of consciousness, and death. (8)
- It has been estimated that the minimum lethal dose of methyl mercury for a 70-kg person ranges from 20 to 60 mg/kg. (8)

Chronic Effects (Noncancer):

Elemental Mercury

- The CNS is the major target organ for elemental mercury toxicity in humans. Effects noted include erethism (increased excitability), irritability, excessive shyness, insomnia, severe salivation, gingivitis, and tremors. (1,2,9)
- Chronic exposure to elemental mercury also affects the kidney in humans, with the development of proteinuria. (1,2,9)
- Acrodynia is a rare syndrome found in children exposed to elemental mercury compounds. It is characterized by severe leg cramps, irritability, paresthesia (a sensation of prickling on the skin), and painful pink fingers and peeling hands, feet, and nose. (1,2)
- EPA has not established an RfD for elemental mercury. (11)
- The RfC for elemental mercury is 0.0003 mg/m^3 based on CNS effects in humans. The RfC is an estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious noncancer effects during a lifetime. It is not a direct estimator of risk but rather a reference point to gauge the potential effects. At exposures increasingly greater than the RfC, the potential for adverse health effects increases. Lifetime exposure above the RfC does not imply that an adverse health effect would necessarily occur. (11)
- EPA has medium confidence in the RfC due to: medium confidence in the studies on which the RfC was based because there were sufficient number of human subjects, inclusion of appropriate control groups, and exposure levels in a number of the studies had to be extrapolated from blood mercury levels; and medium confidence in the database due to a lack of human or multispecies reproductive/developmental studies. (11)

Inorganic Mercury

- The primary effect from chronic exposure to inorganic mercury is kidney damage, primarily due to mercury-induced autoimmune glomerulonephritis (induction of an immune response to the body's kidney tissue). (1,2,9,10)
- Acrodynia may also occur from exposure to inorganic mercury compounds. (1,2,9,10)

- The RfD for inorganic mercury (mercuric chloride) is 0.0003 mg/kg/d based on autoimmune effects in rats. (12)
- EPA has high confidence in the RfD based on the weight of evidence from the studies using Brown-Norway rats and the entirety of the mercuric chloride database. (12)
- EPA has not established an RfC for inorganic mercury. (12)

Methyl Mercury

- The primary effect from chronic exposure to methyl mercury in humans is damage to the CNS. The earliest effects are symptoms such as paresthesia, blurred vision, and malaise. Effects at higher doses include deafness, speech difficulties, and constriction of the visual field. (1,2,8)
- The RfD for methyl mercury is 0.0001 mg/kg/d based on CNS effects in humans. (13)
- EPA has medium confidence in the RfD due to: (1) medium confidence in the studies on which the RfD was based because the benchmark dose approach allowed use of the entire dose-response assessment, and the results of laboratory studies with nonhuman primates support the quantitative estimate of the no-observed-adverse-effect level (NOAEL)/ lowest-observed-adverse-effect level (LOAEL) range of the benchmark dose that was indicated by the human studies; and (2) medium confidence in the database. (13)
- EPA has not established an RfC for methyl mercury. (13)

Reproductive/Developmental Effects:

Elemental Mercury

- Studies on the reproductive and developmental effects of elemental mercury in humans have shown mixed results. One study did not see an association between mercury exposure and miscarriages, while another revealed an increase in the rate of spontaneous abortions. Another study showed a higher than expected frequency of birth defects, which was not confirmed in a fourth study. (1,9)

Inorganic Mercury

- No information is available on the reproductive or developmental effects of inorganic mercury in humans.
- Animal studies have reported effects including alterations in testicular tissue, increased resorption rates, and abnormalities of development. (1,7,9)

Methyl Mercury

- A large number of human studies on the systemic effects of methyl mercury have been carried out. This is the result of two large scale poisoning incidents in Japan and Iraq and several epidemiologic studies investigating populations that consume large quantities of fish. (1,2)

- Oral exposure to methyl mercury has been observed to produce significant developmental effects in humans. Infants born to women who ingested high concentrations of methyl mercury exhibited CNS effects, such as mental retardation, ataxia, deafness, constriction of the visual field, blindness, and cerebral palsy. At lower methyl mercury concentrations, developmental delays and abnormal reflexes were noted. (1,2,8)
- Considerable new data on the health effects of methyl mercury are becoming available. Large studies of fish and marine mammal consuming populations in Seychelles and Faroe Islands are being carried out. Smaller scale studies also describe effects around the U.S. Great Lakes. (1,2)

Cancer Risk:

Elemental Mercury

- Several studies have been carried out regarding elemental mercury and cancer in humans. These studies are inconclusive due to lack of valid exposure data and confounding factors. (1,2,9)
- EPA has classified elemental mercury as a Group D, not classifiable as to human carcinogenicity. (12)

Inorganic Mercury

- No studies are available on the carcinogenic effects of inorganic mercury in humans.
- A chronic study on mercuric chloride in rats and mice reported an increased incidence of forestomach and thyroid tumors in rats, and an increased incidence of renal tumors in mice. (14)
- EPA has classified inorganic mercury as Group C, possible human carcinogen. (12)

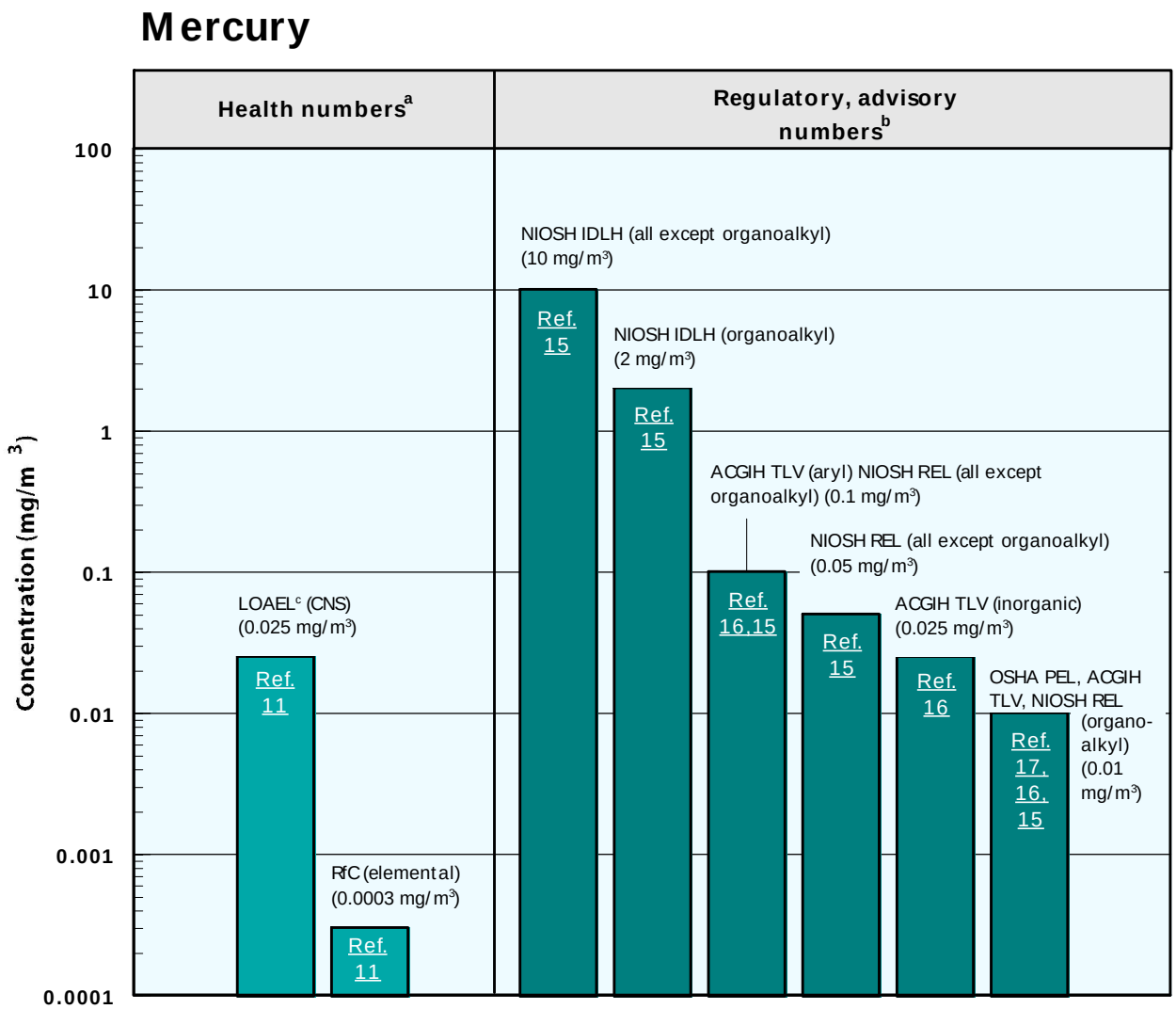
Methyl Mercury

- No studies are available on the carcinogenic effects of methyl mercury in humans, and the one available animal study reported renal tumors in mice. (1,2,13)
- EPA has classified methyl mercury as Group C, possible human carcinogen. (13)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45). For elemental mercury: 1 ppm = 8.2 mg/m^3. For mercuric chloride: 1 ppm = 11.1 mg/m^3. For methyl mercuric chloride: 1 ppm = 10.3 mg/m^3.

Health Data from Inhalation Exposure



ACGIH TLV – American Conference of Governmental and Industrial Hygienists' threshold limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect.
NIOSH IDLH – National Institute of Occupational Safety and Health's immediately dangerous to life or health value; the maximum environmental concentration of a contaminant from which one could escape within 30 min without any escape-impairing symptoms or irreversible health

effects.
NIOSH REL – National Institute of Occupational Safety and Health's recommended exposure limit; NIOSH-recommended exposure limit for an 8- or 10-h time-weighted-average exposure and/or ceiling.
OSHA PEL – Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.

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

References

1. Agency for Toxic Substances and Disease Registry (ATSDR). *Toxicological Profile for Mercury*. Public Health Service, U.S. Department of Health and Human Services, Atlanta, GA. 1999.

2. U.S. Environmental Protection Agency (EPA). *Mercury Study Report to Congress. Volume V: Health Effects of Mercury and Mercury Compounds.* Office of Air Quality Planning and Standards, Office of Research and Development. 1997

3. U.S. Environmental Protection Agency (EPA). *Locating and Estimating Air Emissions from Sources of Mercury and Mercury Compounds*. EPA-453/R-93-023. Office of Air Quality Planning and Standards, Research Triangle Park, NC. 1993.

4. U.S. Environmental Protection Agency (EPA). *National Emissions Inventory of Mercury and Mercury Compounds: Interim Final Report*. EPA-453/R-93-048. Office of Air Quality Planning and Standards, Research Triangle Park, NC. 1993.

5. U.S. Public Health Service. *Dental Amalgams: A Public Health Service Strategy for Research, Education, and Regulation*. Final Report. Committee to Coordinate Environmental Health and Related Programs, Washington, DC. 1993.

6. U.S. Environmental Protection Agency (EPA). *Deposition of Air Pollutants to the Great Waters*. *First Report to Congress*. EPA-453/R-93-055. Office of Air Quality Planning and Standards, Research Triangle Park, NC. 1994.

7. U.S. Environmental Protection Agency (EPA). *Summary Review of Health Effects Associated with Mercuric Chloride: Health Issue Assessment*. EPA/600/R-92/199. Office of Health and Environmental Assessment, Washington, DC. 1994.

8. World Health Organization (WHO). *Methyl Mercury. Volume 101*. Distribution and Sales Service, International Programme on Chemical Safety, Geneva, Switzerland. 1990.

9. World Health Organization (WHO). *Inorganic Mercury. Volume 118*. Distribution and Sales Service, International Programme on Chemical Safety, Geneva, Switzerland. 1991.

10. U.S. Environmental Protection Agency (EPA). *Drinking Water Criteria Document for Inorganic Mercury.* (Final). PB 89-19A 2207. Environmental Criteria and Assessment Office, Cincinnati, OH. 1988.

11. U.S. Environmental Protection Agency (EPA). *Integrated Risk Information System (IRIS) on Elemental Mercury*. National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1999.

12. U.S. Environmental Protection Agency (EPA). *Integrated Risk Information System (IRIS) on Mercuric chloride*. National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1999.

13. U.S. Environmental Protection Agency (EPA). *Integrated Risk Information System (IRIS) on Methyl mercury*. National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1999.

14. National Toxicology Program (NTP). *Toxicology and Carcinogenesis Studies of Mercuric Chloride in F344 Rats and B6C3F1 Mice (Gavage Studies)*. U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health, Bethesda, MD. 1991.

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

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

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

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METHYLENE CHLORIDE

75-09-2

Hazard Summary

Methylene chloride is predominantly used as a solvent. The acute (short-term) effects of methylene chloride inhalation in humans consist mainly of nervous system effects including decreased visual, auditory, and motor functions, but these effects are reversible once exposure ceases. The effects of chronic (long-term) exposure to methylene chloride suggest that the central nervous system (CNS) is a potential target in humans and animals. Limited animal studies have reported developmental effects. Human data are inconclusive regarding methylene chloride and cancer. Animal studies have shown increases in liver and lung cancer and benign mammary gland tumors following the inhalation of methylene chloride. The U.S. Environmental Protection Agency (EPA) has classified methylene chloride as a Group B2, probable human carcinogen.

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

Physical Properties

- A common synonym for methylene chloride is dichloroethane. (1,4)
- Methylene chloride is a colorless liquid with a sweetish odor. (1,6)
- The chemical formula for methylene chloride is CH_2Cl_2, and the molecular weight is 84.93 g/mol. (1)
- The vapor pressure for methylene chloride is 349 mm Hg at 20 EC, and it has an octanol/water coefficient (log K_{ow}) of 1.30. (1)
- Methylene chloride has an odor threshold of 250 ppm. (7)
- Methylene chloride is slightly soluble in water and is nonflammable. (1,6)

Uses

- Methylene chloride is predominantly used as a solvent in paint strippers and removers; as a process solvent in the manufacture of drugs, pharmaceuticals, and film coatings; as a metal cleaning and finishing solvent in electronics manufacturing; and as an agent in urethane foam blowing. (1)
- Methylene chloride is also used as a propellant in aerosols for products such as paints, automotive products, and insect sprays. (1)
- It is used as an extraction solvent for spice oleoresins, hops, and for the removal of caffeine from coffee. However, due to concern over residual solvent, most decaffeinators no longer use methylene chloride. (1)

- Methylene chloride is also approved for use as a postharvest fumigant for grains and strawberries and as a degreening agent for citrus fruit. (1)

Sources and Potential Exposure

- The principal route of human exposure to methylene chloride is inhalation of ambient air. (1)
- Occupational and consumer exposure to methylene chloride in indoor air may be much higher, especially from spray painting or other aerosol uses. People who work in these places can breathe in the chemical or it may come in contact with the skin. (1)
- Methylene chloride has been detected in both surface water and groundwater samples taken at hazardous waste sites and in drinking water at very low concentrations. (1)

Assessing Personal Exposure

- Several tests exist for determining exposure to methylene chloride. These tests include measurement of methylene chloride in the breath, blood, and urine. It is noted that smoking and exposure to other chemicals may affect the results of these tests. (1)

Health Hazard Information

Acute Effects:

- Case studies of methylene chloride poisoning during paint stripping operations have demonstrated that inhalation exposure to extremely high levels can be fatal to humans. (1,2)
- Acute inhalation exposure to high levels of methylene chloride in humans has resulted in effects on the CNS including decreased visual, auditory, and psychomotor functions, but these effects are reversible once exposure ceases. Methylene chloride also irritates the nose and throat at high concentrations. (1,2)
- Tests involving acute exposure of animals, such as the LD_{50} and LC_{50} tests in rats, have shown methylene chloride to have moderate acute toxicity from oral and inhalation exposure. (3)

Chronic Effects (Noncancer):

- The major effects from chronic inhalation exposure to methylene chloride in humans are effects on the CNS, such as headaches, dizziness, nausea, and memory loss. (1,2)
- Animal studies indicate that the inhalation of methylene chloride causes effects on the liver, kidney, CNS, and cardiovascular system. (1,2)
- EPA has calculated a provisional reference concentration (RfC) of 3 mg/m^3 based on liver effects in rats. The RfC is an estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious noncancer effects during a lifetime. It is not a direct estimator of risk but rather a reference point to

gauge the potential effects. At exposures increasingly greater than the RfC, the potential for adverse health effects increases. Lifetime exposure above the RfC does not imply that an adverse health effect would necessarily occur. (5)

- The RfD for methylene chloride is 0.06 mg/kg/d based on liver toxicity in rats. (4)
- EPA has medium confidence in the RfD based on: high confidence in the study on which the RfD is based because a large number of animals of both sexes were tested in four dose groups, with a large number of controls, many effects were monitored, and a dose-related increase in severity was observed; and medium to low confidence in the database because only a few studies support the no-observed-adverse-effect level (NOAEL). (4)

Reproductive/Developmental Effects:

- No studies were located regarding developmental or reproductive effects in humans from inhalation or oral exposure. (1,2)
- Animal studies have demonstrated that methylene chloride crosses the placental barrier, and minor skeletal variations and lowered fetal body weights have been noted. (1,2)

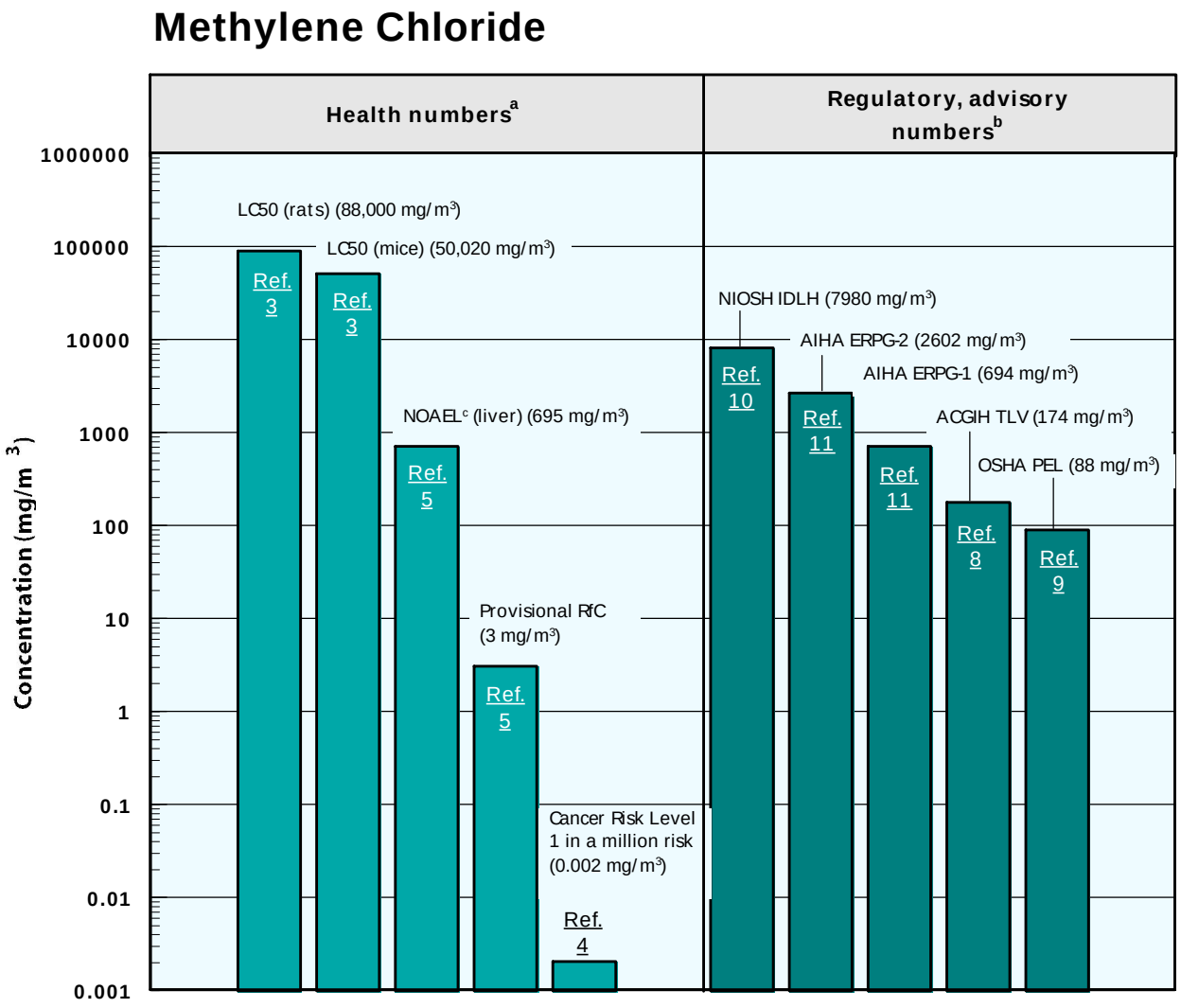
Cancer Risk:

- Several studies did not report a statistically significant increase in deaths from cancer among workers exposed to methylene chloride. (1,2)
- Animal studies have shown an increase in liver and lung cancer and benign mammary gland tumors following inhalation exposure to methylene chloride. (1,2,4)
- EPA has classified methylene chloride as a Group B2, probable human carcinogen. (4)
- EPA uses mathematical models, based on human and animal studies, to estimate the probability of a person developing cancer from breathing air containing a specified concentration of a chemical. EPA calculated an inhalation unit risk estimate of 4.7×10^{-7} $(\mu g/m^3)^{-1}$. EPA estimates that, if an individual were to continuously breathe air containing methylene chloride at an average of 2.0 $\mu g/m^3$ (0.002 mg/m^3) over his or her entire lifetime, that person would theoretically have no more than a one-in-a-million increased chance of developing cancer as a direct result of breathing air containing this chemical. Similarly, EPA estimates that breathing air containing 20 $\mu g/m^3$ (0.02 mg/m^3) would result in not greater than a one-in-a-hundred thousand increased chance of developing cancer, and air containing 200 $\mu g/m^3$ (0.2 mg/m^3) would result in not greater than a one-in-ten thousand increased chance of developing cancer. For a detailed discussion of confidence in the potency estimates, please see IRIS. (4)
- EPA calculated an oral cancer slope factor of 7.5×10^{-3} $(mg/kg/d)^{-1}$. (4)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45). For methylene chloride: 1 ppm = 3.5 mg/m^3. To convert from $\mu g/m^3$ to mg/m^3: mg/m^3 = ($\mu g/m^3$) x (1 mg/1,000 μg).

Health Data from Inhalation Exposure



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

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

LC_{50} (Lethal Concentration$_{50}$)--A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.

NIOSH IDLH – National Institute of Occupational Safety and Health's immediately dangerous to life or health concentration; NIOSH recommended exposure limit to ensure that a worker can escape from an exposure condition that is likely to cause death or immediate or delayed permanent adverse health effects or prevent escape from the environment.
NOAEL – No-observed-adverse-effects level.
OSHA PEL – Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average: the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.

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

References

1. Agency for Toxic Substances and Disease Registry (ATSDR). *Toxicological Profile for Methylene Chloride (Update).* Draft for Public Comment. Public Health Service, U.S. Department of Health and Human Services, Atlanta, GA. 1998.

2. U.S. Department of Health and Human Services. Hazardous Substances Data Bank (HSDB, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.

3. U.S. Department of Health and Human Services. Registry of Toxic Effects of Chemical Substances (RTECS, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.

4. U.S. Environmental Protection Agency (EPA). *Integrated Risk Information System (IRIS) on Methylene Chloride*. National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1999.

5. U.S. Environmental Protection Agency (EPA). *Health Effects Assessment Summary Tables. FY 1997 Update.* Solid Waste and Emergency Response, Office of Emergency and Remedial Response, Cincinnati, OH. EPA/540/R-97-036. 1997.

6. *The Merck Index. An Encyclopedia of Chemicals, Drugs, and Biologicals*. 11th ed. Ed. S. Budavari. Merck and Co. Inc., Rahway, NJ. 1989.

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

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

9. Occupational Safety and Health Administration (OSHA). Occupational Safety and Health Standards, Toxic and Hazardous Substances. *Code of Federal Regulations* 29 CFR 1910.1052. 1998.

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

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

NICKEL COMPOUNDS

Hazard Summary

Nickel occurs naturally in the environment at low levels. Nickel is an essential element in some animal species, and it has been suggested it may be essential for human nutrition. Nickel dermatitis, consisting of itching of the fingers, hands, and forearms, is the most common effect in humans from chronic (long-term) skin contact with nickel. Respiratory effects have also been reported in humans from inhalation exposure to nickel. No information is available regarding the reproductive or developmental effects of nickel in humans, but animal studies have reported reproductive and developmental effects. The U.S. Environmental Protection Agency (EPA) has not evaluated soluble salts of nickel as a class of compounds for potential human carcinogenicity. Human and animal studies have reported an increased risk of lung and nasal cancers from exposure to nickel refinery dusts and nickel subsulfide. EPA has classified nickel refinery dust and nickel subsulfide as Group A, human carcinogens. Animal studies of soluble nickel compounds (i.e., nickel carbonyl) have reported lung tumors. EPA has classified nickel carbonyl as a Group B2, probable human carcinogen.

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

Physical Properties

- Nickel is a silvery-white metal that is found in nature as a component of silicate, sulfide, or arsenide ores. (1)
- In the environment, nickel is found primarily combined with oxygen or sulfur as oxides or sulfides. (1)
- Each form of nickel exhibits different physical properties. (1,6)
- Soluble nickel salts include nickel chloride, nickel sulfate, and nickel nitrate. (6)
- Nickel carbonyl, a highly unstable form, is not found naturally and decomposes rapidly. (1)
- The chemical symbol for nickel is Ni, and it has an atomic weight of 58.71 g/mol. (1)

Uses

- Nickel is used for nickel alloys, electroplating, batteries, coins, industrial plumbing, spark plugs, machinery parts, stainless-steel, nickel-chrome resistance wires, and catalysts. (1,6)
- Nickel carbonyl has severely limited use in nickel refining. (1)

Sources and Potential Exposure

- Nickel is a natural element of the earth's crust; therefore, small amounts are found in food, water, soil, and air. (6)
- Food is the major source of nickel exposure, with an average intake for adults estimated to be approximately 100 to 300 µg/d. (1,6)
- Individuals also may be exposed to nickel in occupations involved in its production, processing, and use, or through contact with everyday items such as nickel-containing jewelry and stainless steel cooking and eating utensils, and by smoking tobacco. (1)
- Nickel is found in ambient air at very low levels as a result of releases from oil and coal combustion, nickel metal refining, sewage sludge incineration, manufacturing facilities, and other sources. (2,6)
- Given its high instability, nickel carbonyl exposure is extremely rare.

Assessing Personal Exposure

- Laboratory tests can detect nickel in blood, urine, feces, and hair samples. (1,6)

Health Hazard Information

Acute Effects:

- One person exposed to an extremely high level of nickel by inhalation suffered severe damage to the lungs and kidneys. (6)
- Gastrointestinal distress (e.g., nausea, vomiting, diarrhea) and neurological effects were reported in workers who drank water on one shift that was contaminated with nickel as nickel sulfate and nickel chloride. (1,6)
- Pulmonary fibrosis and renal edema were reported in humans and animals following acute (short-term) exposure to nickel carbonyl. (1)
- Acute animal tests, such as the LD_{50} test in rats, have shown nickel compounds to exhibit acute toxicity values ranging from low to high. The soluble compounds, such as nickel acetate, were the most toxic, and the insoluble forms, such as nickel powder, were the least toxic. (6)

Chronic Effects (Noncancer):

- Dermatitis is the most common effect in humans from chronic dermal exposure to nickel. Cases of nickel dermatitis have been reported following occupational and non-occupational exposure, with symptoms of eczema (rash, itching) of the fingers, hands, wrists, and forearms. (1,2,6,7)
- Chronic inhalation exposure to nickel in humans also results in respiratory effects, including a type of asthma specific to nickel, decreased lung function, and bronchitis. (6,7)

- Animal studies have reported effect on the lungs and immune system from inhalation exposure to soluble and insoluble nickel compounds (nickel oxide, subsulfide, sulfate heptahydrate). (1,6)
- Soluble nickel compounds are more toxic to the respiratory tract than less soluble compounds. (6)
- EPA has not established a reference concentration (RfC) for nickel. (2-5)
- The RfD for nickel (soluble salts) is 0.02 mg/kg/d based on decreased body and organ weights in rats. The RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious noncancer effects during a lifetime. It is not a direct estimator of risk, but rather a reference point to gauge the potential effects. At exposures increasingly greater than the RfD, the potential for adverse health effects increases. Lifetime exposure above the RfD does not imply that an adverse health effect would necessarily occur. (5)
- EPA has medium confidence in the RfD due to: low confidence in the study on which the RfD for nickel (soluble salts) was based because, although it was properly designed and provided adequate toxicological endpoints, high mortality occurred in the controls; and medium confidence in the database because it provided adequate supporting subchronic studies, one by gavage and the other in drinking water, but inadequacies in the remaining reproductive data. (5)
- Nickel is an essential nutrient for some mammalian species and has been suggested to be essential for human nutrition. By extrapolation from animal data, it is estimated that a 70-kg person would have a daily requirement of 50 µg per kg diet of nickel. (6)
- The California Environmental Protection Agency (CalEPA) has calculated a chronic inhalation reference exposure level of 0.00005 mg/m^3 for nickel based on respiratory and immune system effects reported in rats exposed to a soluble nickel salt. The CalEPA reference exposure level is a concentration at or below which adverse health effects are not likely to occur. (7)
- ATSDR has calculated a chronic-duration inhalation minimal risk level (MRL) of 0.0002 mg/m^3 for nickel based on respiratory effects reported in rats exposed to a soluble nickel salt. The MRL is an estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk of adverse noncancer health effects over a specified duration of exposure. (6)

Reproductive/Developmental Effects:

- No information is available regarding the reproductive or developmental effects of nickel in humans. (6)
- Animal studies have reported reproductive and developmental effects, such as a decreased number of live pups per litter, increased pup mortality, and reduction in fetal body weight, and effects to the female from oral exposure to soluble salts of nickel. (5,6)
- Sperm abnormalities and decreased sperm count have been reported in animals exposed to nickel nitrate orally and nickel oxide by inhalation, respectively. (6)

Cancer Risk:

Nickel Salts

- Nickel sulfate via inhalation and nickel acetate in drinking water were not carcinogenic in either rats or mice. (6)
- EPA has not evaluated soluble salts of nickel as a class of compounds for potential human carcinogenicity. (5)

Nickel Refinery Dust and Nickel Subsulfide

- Human studies have reported an increased risk of lung and nasal cancers among nickel refinery workers exposed to nickel refinery dust. Nickel refinery dust is a mixture of many nickel compounds, with nickel subsulfide being the major constituent. (3,4,6)
- Animal studies have also reported lung tumors from inhalation exposure to nickel refinery dusts and to nickel subsulfide. (3,4)
- EPA has classified nickel refinery dust and nickel subsulfide as Group A, human carcinogens. (3,4)
- EPA uses mathematical models, based on human and animal studies, to estimate the probability of a person developing cancer from breathing air containing a specified concentration of a chemical. EPA calculated an inhalation unit risk estimate of 2.4×10^{-4} $(\mu g/m^3)^{-1}$ for nickel refinery dusts. EPA estimates that, if an individual were to continuously breathe air containing nickel refinery dusts at an average of 0.004 $\mu g/m^3$ (4×10^{-6} mg/m^3) over his or her entire lifetime, that person would theoretically have no more than a one-in-a-million increased chance of developing cancer as a direct result of breathing air containing this chemical. Similarly, EPA estimates that continuously breathing air containing 0.04 $\mu g/m^3$ would result in not greater than a one-in-a-hundred thousand increased chance of developing cancer, and air containing 0.4 $\mu g/m^3$ would result in not greater than a one-in-ten thousand increased chance of developing cancer. For a detailed discussion of confidence in the potency estimates, please see IRIS. (3)
- For nickel subsulfide, EPA calculated an inhalation unit risk estimate of 4.8×10^{-4} $(\mu g/m^3)^{-1}$. EPA estimates that, if an individual were to continuously breathe air containing this nickel compound at an average of 0.002 $\mu g/m^3$ (2×10^{-6} mg/m^3) over his or her entire lifetime, that person would theoretically have no more than a one-in-a-million increased chance of developing cancer as a direct result of breathing air containing this chemical. Similarly, EPA estimates that continuously breathing air containing 0.02 $\mu g/m^3$ would result in not greater than a one-in-a-hundred thousand increased chance of developing cancer, and air containing 0.2 $\mu g/m^3$ would result in not greater than a one-in-ten thousand increased chance of developing cancer. (4)

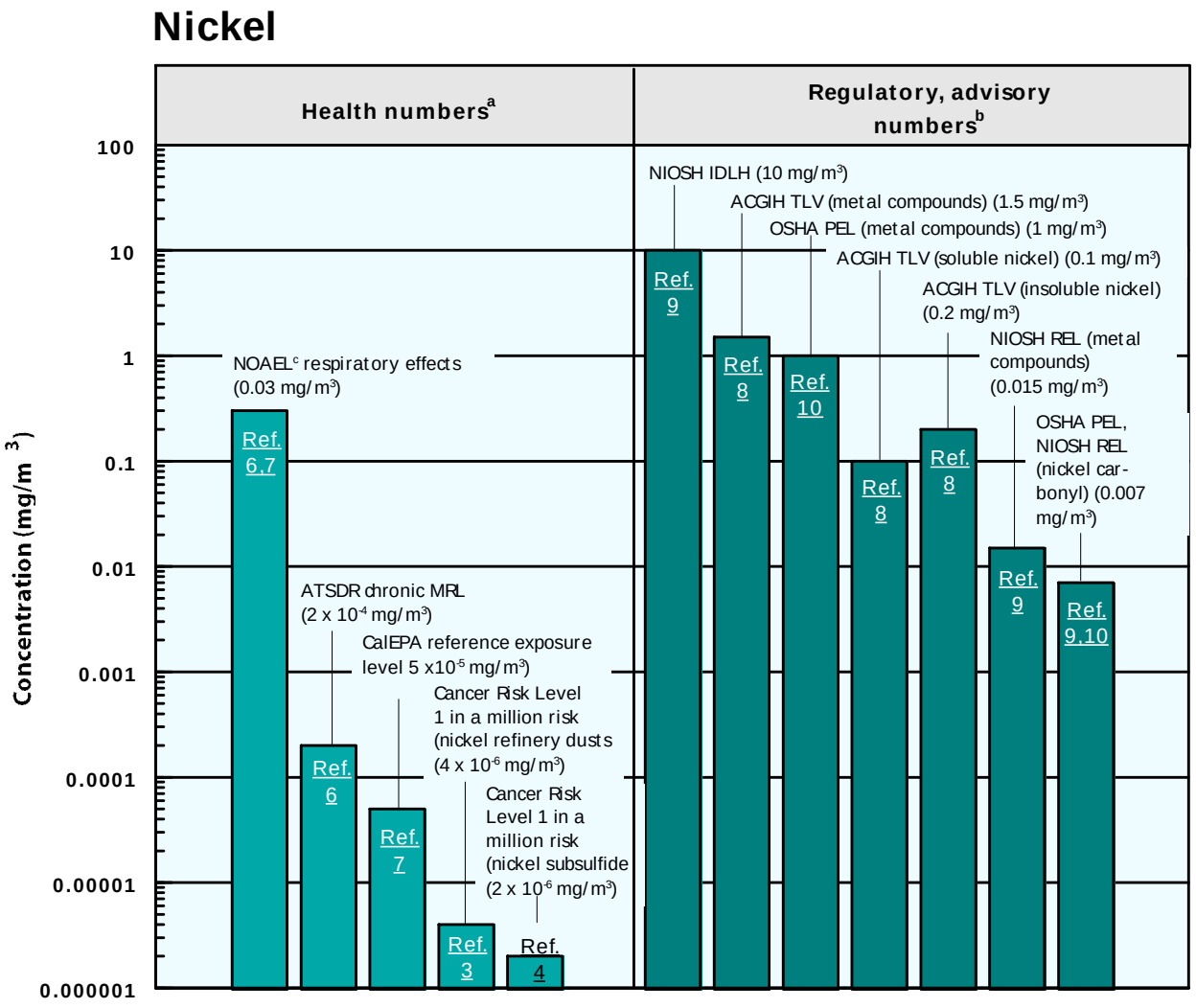
Nickel Carbonyl

- Nickel carbonyl has been reported to produce lung tumors in rats exposed via inhalation. (2)
- EPA has classified nickel carbonyl as a Group B2, probable human carcinogen. (2)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45).
For nickel: 1 ppm = 2.4 mg/m^3.
To convert from µg/m^3 to mg/m^3: mg/m^3 = (µg/m^3) x (1 mg/1,000 µg).

Health Data from Inhalation Exposure



ACGIH TLV – American Conference of Governmental and Industrial Hygienists' threshold limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effects.
NIOSH REL – National Institute of Occupational Safety and Health's recommended exposure limit; NIOSH-recommended exposure limit for an 8- or 10-h time-weighted-average exposure and/or ceiling.

NIOSH IDLH – NIOSH's immediately dangerous to life or health concentration; NIOSH recommended exposure limit to ensure that a worker can escape from an exposure condition that is likely to cause death or immediate or delayed permanent adverse health effects or prevent escape from the environment.
NOAEL – No-observed-adverse-effect level.
OSHA PEL – Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.

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

References

1. U.S. Environmental Protection Agency (EPA). *Health Assessment Document for Nickel*. EPA/600/8-83/012F. National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1986.

2. U.S. Environmental Protection Agency (EPA). *Integrated Risk Information System (IRIS) on Nickel Carbonyl*. National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1999.

3. U.S. Environmental Protection Agency (EPA). *Integrated Risk Information System (IRIS) on Nickel Refinery Dust*. National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1999.

4. U.S. Environmental Protection Agency (EPA). *Integrated Risk Information System (IRIS) on Nickel Subsulfide*. National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1999.

5. U.S. Environmental Protection Agency (EPA). *Integrated Risk Information System (IRIS) on Nickel, Soluble Salts*. National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1999.

6. Agency for Toxic Substances and Disease Registry (ATSDR). *Toxicological Profile for Nickel (Update)*. Public Health Service, U.S. Department of Health and Human Services, Altanta, GA. 1997.

7. California Environmental Protection Agency (CalEPA). *Technical Support Document for the Determination of Noncancer Chronic Reference Exposure Levels.* Draft for Public Comment. Office of Environmental Health Hazard Assessment, Berkeley, CA. 1997.

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

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

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

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POLYCHLORINATED BIPHENYLS (PCBs)

1336-36-3

Hazard Summary

PCBs are a group of chemicals that contain 209 individual compounds (known as congeners) with varying harmful effects. Information on specific congener toxicity is very limited. Most toxicity testing has been done on specific commercial mixtures; however, PCB mixtures found in the environment will differ in composition from the commercial mixtures because of biotransformation and bioaccumulation. The U.S. Environmental Protection Agency (EPA) treats all PCBs as being potentially hazardous based on results from some formulations. However, this can have large uncertainty for any given mixture situation.

PCBs are no longer produced or used in the U.S. today; the major source of exposure to PCBs today is the redistribution of PCBs already present in soil and water. No information is available on the acute (short-term) effects of PCBs in humans, and animal studies have reported effects on the liver, kidney, and central nervous system (CNS) from oral exposure to PCBs. Chronic (long-term) exposure to some PCB formulations by inhalation in humans results in respiratory tract symptoms, gastrointestinal effects, mild liver effects, and effects on the skin and eyes such as chloracne, skin rashes, and eye irritation. Epidemiological studies suggest an association between dietary PCB exposures and developmental effects; human reproductive studies are inconclusive. Human studies provide inconclusive, yet suggestive, evidence of an association between PCBs exposure and liver cancer. Animal studies have reported an increase in liver tumors in rats and mice exposed orally to some PCB formulations. EPA has classified PCBs as a Group B2, probable human carcinogen.

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

Physical Properties

- PCBs are a class of industrial chemicals that contain 209 individual compounds or congeners. (1)
- PCBs made in the U.S. were marketed under the trade name Aroclor and are identified by a four-digit numbering code in which the first two digits indicate that the parent molecule is a biphenyl and for the 1200 series Aroclors the last two digits indicate the chlorine content by weight. For example, Aroclor 1260 has 60 percent chlorine. (1)
- Commercial trade names for PCBs not manufactured in the U.S. include Kanechlor, Clophen, Fenclor, and Phenoclor. (1)
- PCBs are either oily liquids or solids and are colorless to light yellow in color with no known smell or taste. (1)

- The molecular weight for one particular PCB (Aroclor 1260) is 375.7 g/mol; the vapor pressure is 4.05 x 10^{-5} mm Hg at 25 EC; the octanol/water partition coefficient (log K_{ow}) is 6.8. (1)
- PCB mixtures found in environmental media (air, water, sediment, foods) will differ in composition from the commercial mixtures due to differential biotransformation and bioaccumulation among the individual compounds. (1)

Uses

- Before 1974, PCBs were used in capacitors, transformers, plasticizers, surface coatings, inks, adhesives, pesticide extenders, and carbonless duplicating paper. After 1974, use of PCBs was restricted to the production of capacitors and transformers, and after 1979 PCBs were no longer used in the production of capacitors and transformers. (1)

Sources and Potential Exposure

- PCBs are no longer produced in the U.S. and are no longer used in the manufacture of new products; the major source of air exposure to PCBs today is the redistribution of PCBs already present in soil and water. Smaller amounts of PCBs may be released to the air from disposal sites containing transformers, capacitors, and other PCB wastes, incineration of PCB-containing wastes, and improper disposal of the compounds to open areas. (1)
- PCBs have been detected in indoor air at concentrations of an order of magnitude greater than ambient air. It has been suggested that certain electrical appliances and devices, such as fluorescent lighting ballasts, which have PCB-containing components, may emit PCBs to the indoor air. (1)
- In the past, PCBs were released to wastewater from its industrial uses. Today, PCBs are still detected in water due to the environmental recycling of the compound. Most of the PCBs in water are bound to the soil and sediments and may be released to the water slowly over a long period of time. (1)
- PCBs have been detected in food; they bioaccumulate through the food chain, with some of the highest concentrations found in fish. (1)
- PCBs have been listed as a pollutant of concern to EPA's Great Waters Program due to their persistence in the environment, potential to bioaccumulate, and toxicity to humans and the environment. (3)

Assessing Personal Exposure

- Laboratory analyses can detect PCBs in blood, body fat, and breast milk. (1)

Health Hazard Information

Acute Effects:

- No reports of effects in humans following acute exposure to PCBs are available. (1)

- Animal studies have reported acute effects on the liver, kidney, and CNS from oral exposure to PCBs. (1)
- Acute animal tests, such as the LD_{50} test in rats, have shown PCBs to have moderate acute toxicity from oral exposure. (1,4)

Chronic Effects (Noncancer):

- Chronic inhalation exposure of workers to PCBs has been reported to result in respiratory tract symptoms, such as cough and tightness of the chest, gastrointestinal effects including anorexia, weight loss, nausea, vomiting, and abdominal pain, mild liver effects, and effects on the skin and eyes, such as chloracne, skin rashes, and eye irritation. (1,5)
- EPA has not established a reference concentration (RfC) or a reference dose (RfD) for all PCB mixtures. (6)
- The RfD for Aroclor 1016 is 0.00007 mg/kg/d based on reduced birth weights in monkeys. The RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious noncancer effects during a lifetime. It is not a direct estimator of risk, but rather a reference point to gauge the potential effects. At exposures increasingly greater than the RfD, the potential for adverse health effects increases. Lifetime exposure above the RfD does not imply that an adverse health effect would necessarily occur. (7)
- EPA has medium confidence in the RfD based on: medium confidence in the study on which the RfD was based because this was a well-conducted study, but only one group of monkeys was examined; and medium confidence in the database because an extensive amount of data are available but mixtures of PCBs in the environment do not match the pattern of congeners found in Aroclor 1016. (7)
- The RfD for Aroclor 1254 is 0.00002 mg/kg/d based on immunological effects in monkeys. (8)
- EPA has medium confidence in the RfD based on: (1) medium confidence in the study on which the RfD was based because groups of monkeys were tested at four dose levels and a lowest-observed-adverse-effect level (LOAEL) was established; and (2) medium confidence in the database because an extensive number of laboratory animal and human studies were available for review, but human data are available for PCB mixtures in general but not specifically for Aroclor 1254. (8)
- EPA has not established an RfC for Aroclor 1016 or Aroclor 1254. (7,8)

Reproductive/Developmental Effects:

- An epidemiological study of women occupationally exposed to high levels of PCBs suggested a relationship between PCB exposure and reduced birth weight and shortened gestational age of their babies; however, limitations of the study limit the strength of the conclusion. (1)
- Two human studies that investigated exposure to PCBs through the consumption of contaminated fish suggest that exposure to PCBs may cause developmental effects in humans. Both studies reported an association between consumption of fish with high

PCB levels by pregnant women and an increased incidence of neurodevelopmental effects, such as motor deficits at birth, impaired psychomotor index, impaired visual recognition, and deficits in short-term memory in infants. (1)

- Human studies are not conclusive on the reproductive effects of PCBs. One study of men who were occupationally exposed to PCBs showed no fertility abnormalities, while another study of men with low sperm counts found elevated levels of PCBs in the blood and an association between certain PCB compounds in semen and decreased sperm motility. (1)
- Animal studies have reported developmental effects, such as learning deficits, impaired immune functions, focal liver necrosis, and cellular alterations of the thyroid, in the offspring of animals exposed orally to PCBs. Reproductive effects, such as decreased fertility, decreased conception, and prolonged menstruation have also been noted in animal studies of dietary PCB exposures. (1)

Cancer Risk:

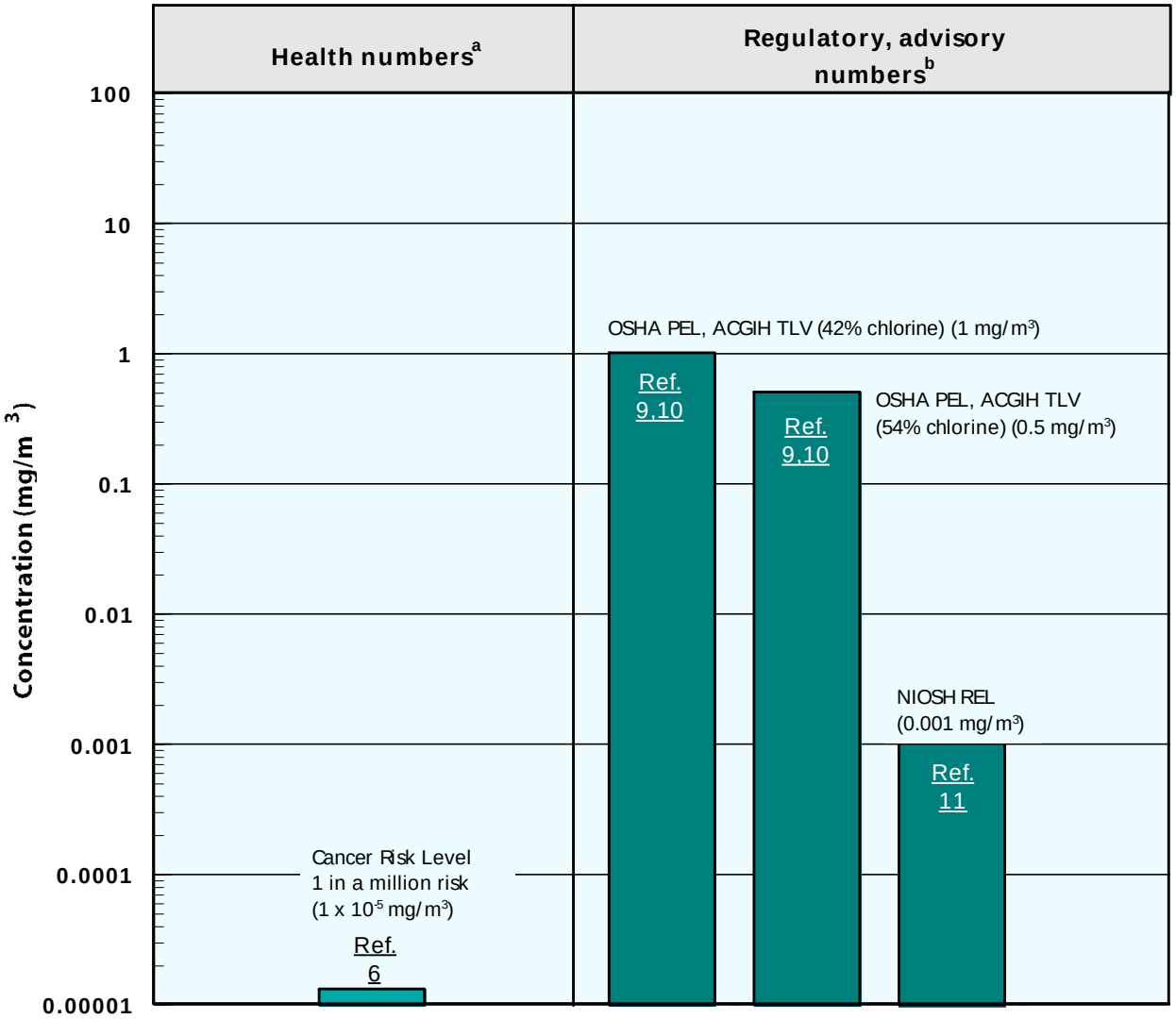
- Human studies provide inconclusive, yet suggestive evidence of an association between PCBs' exposure and liver cancer. Several studies have reported an increase in liver cancer among persons occupationally exposed to some PCB formulations. However, the studies are inconclusive due to confounding exposures and lack of exposure quantification. (1,6)
- Oral exposure studies in animals show an increase in liver tumors in rats and mice exposed to several commercial mixtures of PCBs and to several specific congeners. (1,6)
- No animal inhalation studies are available on PCBs. (1)
- EPA has classified PCBs as a Group B2, probable human carcinogen. (6)
- EPA uses mathematical models, based on human and animal studies, to estimate the probability of a person developing cancer from ingesting water containing a specified concentration of a chemical. EPA calculated an upper bound inhalation unit cancer risk estimate of 1.0×10^{-4} $(\mu g/m^3)^{-1}$ for inhalation of evaporated PCB congeners. EPA estimates that, if an individual were to continuously breathe air containing PCBs at an average of 0.01 $\mu g/m^3$ (1×10^{-5} mg/m^3) over his or her entire lifetime, that person would theoretically have no more than a one-in-a-million increased chance of developing cancer as a direct result of breathing air containing this chemical. Similarly, EPA estimates that breathing air containing 0.1 $\mu g/m^3$ (1×10^{-4} mg/m^3) would result in not greater than a one-in-a-hundred thousand increased chance of developing cancer, and air containing 1.0 $\mu g/m^3$ (1×10^{-3} mg/m^3) would result in not greater than a one-in-ten thousand increased chance of developing cancer. For a detailed discussion of confidence in the potency estimates, please see IRIS. (6)
- EPA has calculated an upperbound oral cancer slope factor of 0.4 $(mg/kg/d)^{-1}$ for ingestion of water soluble congeners, an upperbound oral cancer slope factor of 2.0 $(mg/kg/d)^{-1}$ for food chain exposure, and an upperbound oral cancer slope factor of 0.07 $(mg/kg/d)^{-1}$ for PCB exposures where congeners with more than 4 chlorines comprise less than 5 percent of the total. (6)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45). For Aroclor 1260: 1 ppm = 15.4 mg/m^3. To convert from µg/m^3 to mg/m^3: mg/m^3 = (µg/m^3) x (1 mg/1,000 µg).

Health Data from Inhalation Exposure

Polychlorinated biphenyls



ACGIH TLV – American Conference of Governmental and Industrial Hygienists' threshold limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effects.
NIOSH REL – National Institute of Occupational Safety and Health's recommended exposure limit; NIOSH-recommended exposure limit for an 8- or 10-h time-weighted-average exposure and/or ceiling.
OSHA PEL – Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.

[a] Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA.
[b] Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the Government or other groups as advice.

References

1. Agency for Toxic Substances and Disease Registry (ATSDR). *Toxicological Profile for Polychlorinated Biphenyls*. Public Health Service, U.S. Department of Health and Human Services, Atlanta, GA. 1997.

2. U.S. Environmental Protection Agency (EPA). *Workshop Report on Toxicity Equivalence for PCB Congeners*. EPA/625/3-91/020. 1991.

3. U.S. Environmental Protection Agency (EPA). *Deposition of Air Pollutants to the Great Waters*. *First Report to Congress*. EPA-453/R-93-055. Office of Air Quality Planning and Standards, Research Triangle Park, NC. 1994.

4. U.S. Department of Health and Human Services. Registry of Toxic Effects of Chemical Substances (RTECS, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.

5. U.S. Department of Health and Human Services. Hazardous Substances Data Bank (HSDB, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.

6. U.S. Environmental Protection Agency (EPA). *Integrated Risk Information System (IRIS) on PCBs*. National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1999.

7. U.S. Environmental Protection Agency (EPA). *Integrated Risk Information System (IRIS) on Aroclor 1016*. National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1999.

8. U.S. Environmental Protection Agency (EPA). *Integrated Risk Information System (IRIS) on Aroclor 1254*. National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1999.

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

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

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

POLYCYCLIC ORGANIC MATTER (POM)[1]

Hazard Summary

The term POM defines a broad class of compounds that includes the polycyclic aromatic hydrocarbon compounds (PAHs), of which benzo[a]pyrene is a member. POM compounds are formed primarily from combustion and are present in the atmosphere predominantly in particulate form with a smaller amount as vapor. Sources of air emissions are diverse and include cigarette smoke, vehicle exhaust, home heating, laying tar, and grilling meat. Skin exposures to mixtures of carcinogenic PAHs cause skin disorders in humans and animals. No information is available on the reproductive or developmental effects of POM in humans, while animal studies have reported that benzo[a]pyrene, via oral exposure, causes reproductive and developmental effects. Cancer is the major concern from exposure to POM. Epidemiologic studies have reported an increase in lung cancer in humans exposed to coke oven emissions, roofing tar emissions, and cigarette smoke; all of these mixtures contain POM compounds. Animal studies have reported respiratory tract tumors from inhalation exposure to benzo[a]pyrene and forestomach tumors, leukemia, and lung tumors from oral exposure to benzo[a]pyrene. The U.S. Environmental Protection Agency (EPA) has classified seven PAHs (benzo[*a*]pyrene, benz[a]anthracene, chrysene, benzo[b]fluoranthene, benzo[k]fluoranthene, dibenz[a,h]anthracene, and indeno[1,2,3-cd]pyrene) as Group B2, probable human carcinogens.

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

Physical Properties

- The term POM generally defines a broad class of compounds that includes all organic structures having two or more fused aromatic rings (i.e., rings that share a common border), and that have a boiling point greater than or equal to 212 EF (100 EC). The 1990 Amendments to the Clean Air Act describes POM as including “organic compounds with more than one benzene ring, and which have a boiling point greater than or equal to 100 degrees C.” (11)
- POM has been identified with up to seven fused rings and, theoretically, millions of POM compounds could be formed; however, only about 100 species have been identified and studied. (11)

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[1] Polycyclic organic matter consists of polycyclic aromatic hydrocarbons (PAHs), including benzo(*a*)pyrene (CAS#50-32-8), their nitrogen analogs, and a small number of oxygen-containing polycyclic organic matter compounds.

- Eight major categories of compounds have been defined by the EPA to constitute the class known as POM. The most common category is the polycyclic aromatic hydrocarbons (PAHs), also known as polynuclear aromatics, which include benzo[a]pyrene. (11)
- Most POM compounds are solids with high melting and boiling points, and are extremely insoluble in water. The PAHs are primarily planar, nonpolar compounds with melting points considerably over 212 EF (100 EC). Phenanthrene, with a melting point of 214 EF (101 EC), and benzo[c]phenanthrene, with a melting point of 154 EF (68 EC), are two exceptions. (11)
- POM is present in the atmosphere predominantly in the particulate form with a smaller amount in the vapor phase. (11)
- The chemical formula for benzo[a]pyrene is $C_{20}H_{12}$, and the molecular weight is 252.3 g/mol. (1)
- The vapor pressures of POM compounds vary, depending upon the ring size and molecular weight, from 6.8×10^{-4} mm Hg for phenanthrene, to 1.5×10^{-12} for coronene. The vapor pressure for benzo[a]pyrene is 5.6×10^{-9} mm Hg at 25 EC, and it has a log octanol/water partition coefficient (log K_{ow}) of 6.06. (1,11)

Uses

- The majority of the polycyclic organic compounds have no commercial uses. (11)
- Solutions containing mixtures of some PAHs are used to treat some skin disorders in humans. (1)

Sources and Potential Exposure

- The primary source of POM is formation during combustion. A less significant formation mechanism is the volatilization of lightweight POM compounds, which occurs in the production and use of naphthalene. (11)
- Polycyclic organic compounds have been detected in ambient air from sources including cigarette smoke, vehicle exhausts, asphalt road paving, coal burning, application of coal tar, agricultural burning, residential wood burning, and hazardous waste sites. The compounds present in POM and their relative amounts differ among different sources (e.g, POM from diesel exhaust is chemically different than POM from wood burning). (1,2)
- Benzo[a]pyrene, one of the more commonly monitored PAHs, has been detected in urban air at levels approximately twice as high as those in rural areas (e.g., 0.6 ng/m^3 versus 0.3 ng/m^3). Seasonal variations have also been observed from monitoring in the Northeast U.S. during the early 1980's, with mean benzo[a]pyrene concentrations during the winter more than an order of magnitude greater than during the summer. (11)
- PAHs have been found in some drinking water supplies. (1)
- Cooking meat or other foods at high temperatures increases the amount of PAHs in the food. (1)
- Occupational exposure to PAHs may occur in coal tar production plants, coking plants, coal-gasification sites, smokehouses, municipal trash incinerators, and other facilities. (1)

- POM has been listed as a pollutant of concern in EPA's Great Waters Program due to its persistence in the environment, potential to bioaccumulate, and toxicity to humans and the environment (2).

Assessing Personal Exposure

- PAHs or their breakdown products can be measured in urine, blood, or body tissues. (1)

Health Hazard Information

Acute Effects:

- No reports of effects to humans following acute (short-term) exposure to POM are available.
- Acute animal tests, such as the LD_{50} test in rats, have shown benzo[a]pyrene to have high acute toxicity from oral exposure. (3)

Chronic Effects (Noncancer):

- Skin exposures to mixtures of carcinogenic PAHs cause skin disorders in humans and animals, and adverse skin effects have been noted in humans and animals following application of solutions containing benzo[a]pyrene. (1)
- An epidemiological study of workers exposed by inhalation to benzo[a]pyrene and other particulate matter reported some respiratory effects. The role of benzo[a]pyrene in this association, however, is unclear. (1)
- Animal studies have reported effects on the blood and liver from oral exposure to benzo[a]pyrene and a slight hypersensitivity response from dermal exposure to benzo[a]pyrene. (1)
- EPA has not established a reference concentration (RfC) or a reference dose (RfD) for POM or for benzo[a]pyrene. (4,5)

Reproductive/Developmental Effects:

- No information is available on the reproductive or developmental effects of POM in humans.
- Animal studies have indicated that benzo[a]pyrene, via oral exposure, induces reproductive toxicity, including a reduced incidence of pregnancy and decreased fertility. Developmental effects, such as a reduced viability of litters and reduced mean pup weight, have also been noted from oral exposure to benzo[a]pyrene in animals. (1,6)

Cancer Risk:

- Epidemiologic studies have reported an increase in lung cancer in humans exposed to coke oven emission, roofing tar emissions, and cigarette smoke. Each of these mixtures contains a number of POM compounds (e.g., certain PAHs). (1,6)

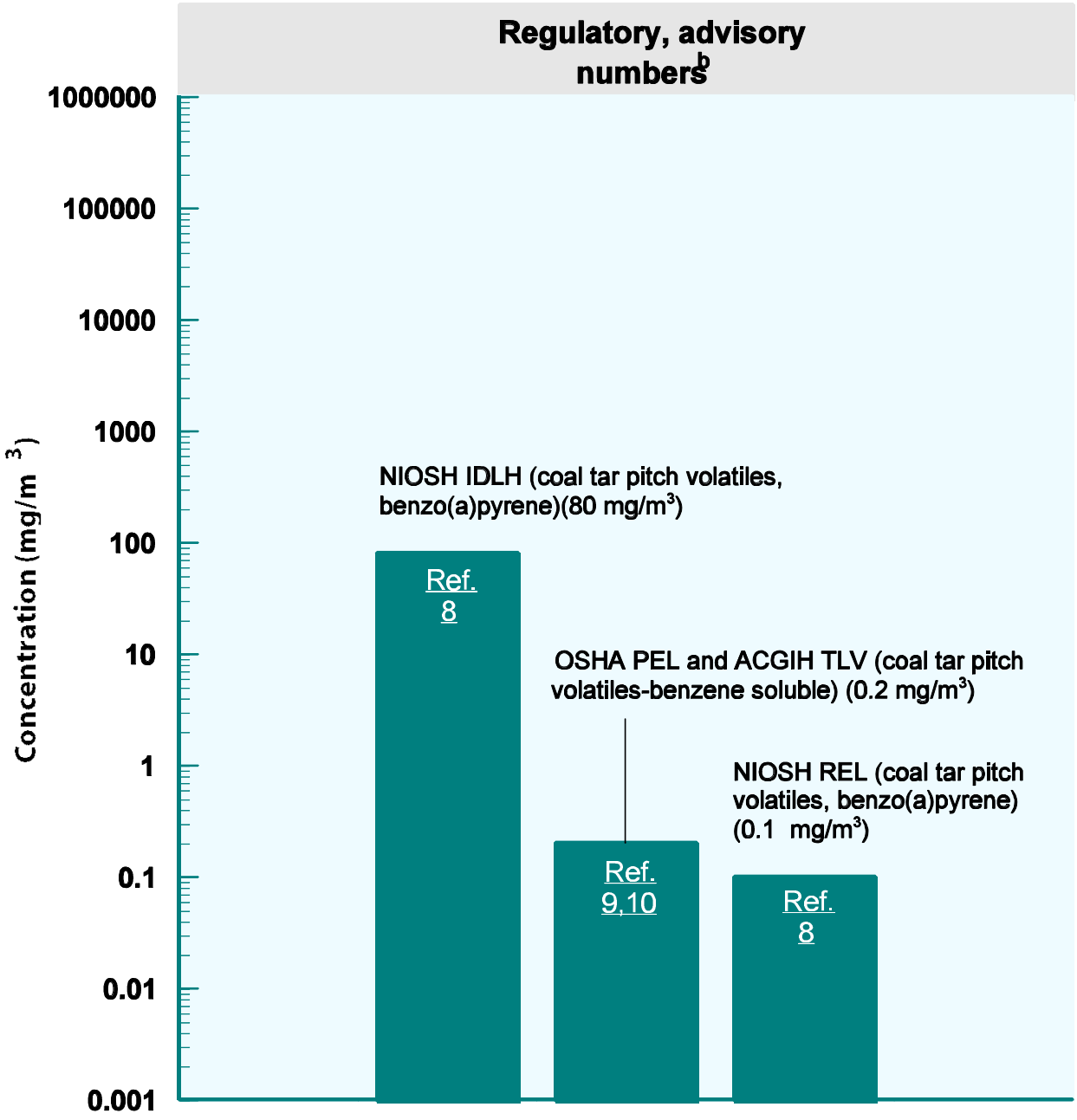
- Animal studies have reported respiratory tract tumors from inhalation exposure to benzo(*a*)pyrene and forestomach tumors, leukemia, and lung tumors from oral exposure to benzo[a]pyrene. (1,5,7)
- EPA has classified seven PAHs (benzo[*a*]pyrene, benz[a]anthracene, chrysene, benzo[b]fluoranthene, benzo[k]fluoranthene, dibenz[a,h]anthracene, and indeno[1,2,3-cd]pyrene) as Group B2, probable human carcinogens. (4,5,12-17)
- EPA uses mathematical models, based on human and animal studies, to estimate the probability of a person developing cancer from ingesting water containing a specified concentration of a chemical. Although a quantitative cancer risk estimate for the mixture of POM has not been derived, EPA has calculated an oral cancer slope factor of 7.3 $(mg/kg/d)^{-1}$ for benzo[a]pyrene, one of the many constituents of POM. For a detailed discussion of the confidence in the potency estimates, please see IRIS. (5)
- The California Environmental Protection Agency (CalEPA) has calculated an inhalation unit risk estimate of 1.1×10^{-3} $(\mu g/m^3)^{-1}$ for benzo[a]pyrene, one of the many constituents of POM. (7)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45).
For benzo(a)pyrene: 1 ppm = 10.3 mg/m^3.
To convert from $\mu g/m^3$ to mg/m^3: mg/m^3 = ($\mu g/m^3$) x (1 mg/1,000 μg).

Health Data from Inhalation Exposure

Coal Tar Pitch Volatiles[a]



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

NIOSH REL – National Institute of Occupational Safety and Health's recommended exposure limit; NIOSH-recommended exposure limit for an 8- or 10-h time-weighted-average exposure and/or ceiling.

NIOSH IDLH – NIOSH's recommended exposure limit; NIOSH-recommended immediately dangerous to health level.
OSHA PEL – Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effects averaged over a normal 8-h workday or a 40-h workweek.

[a] These chemicals, a subset of POM, are emitted from the application of hot coal tar pitch.
[b] Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the Government or other groups as advice.

References

1. Agency for Toxic Substances and Disease Registry (ATSDR). *Toxicological Profile for Polycyclic Aromatic Hydrocarbons (PAHs)*. Public Health Service, U.S. Department of Health and Human Services, Atlanta, GA. 1995.

2. U.S. Environmental Protection Agency (EPA). *Deposition of Air Pollutants to the Great Waters*. *First Report to Congress*. EPA-453/R-93-055. Office of Air Quality Planning and Standards, Research Triangle Park, NC. 1994.

3. U.S. Department of Health and Human Services. Registry of Toxic Effects of Chemical Substances (RTECS, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.

4. U.S. Environmental Protection Agency (EPA). *Integrated Risk Information System (IRIS) on Polycyclic Organic Matter*. National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1999.

5. U.S. Environmental Protection Agency (EPA). *Integrated Risk Information System (IRIS) on Benzo(a)pyrene*. National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1999.

6. U.S. Department of Health and Human Services. Hazardous Substances Data Bank (HSDB, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.

7. California Environmental Protection Agency (CalEPA). *Air Toxics Hot Spots Program Risk Assessment Guidelines: Technical Support Document for Determining Cancer Potency Factors.* Draft for Public Comment. Office of Environmental Health Hazard Assessment, Berkeley, CA. 1997

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

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

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

11. U.S. Environmental Protection Agency (EPA). *Locating and Estimating Air Emissions from Sources of Polycyclic Organic Matter*. EPA-454/R-98-014. Office of Air Quality Planning and Standards, Research Triangle Park, NC. 1998.

12. U.S. Environmental Protection Agency (EPA). *Integrated Risk Information System (IRIS) on Benz[a]anthracene.* National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1999.

13. U.S. Environmental Protection Agency (EPA). *Integrated Risk Information System (IRIS) on Benzo[b]fluoranthene.* National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1999.

14. U.S. Environmental Protection Agency (EPA). *Integrated Risk Information System (IRIS) on Benzo[k]fluoranthene.* National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1999.

15. U.S. Environmental Protection Agency (EPA). *Integrated Risk Information System (IRIS) on Chrysene.* National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1999.

16. U.S. Environmental Protection Agency (EPA). *Integrated Risk Information System (IRIS) on Dibenz[a,h]anthracene.* National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1999.

17. U.S. Environmental Protection Agency (EPA). *Integrated Risk Information System (IRIS) on Indeno[1,2,3-cd]pyrene.* National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1999.

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QUINOLINE
91-22-5

Hazard Summary

Quinoline is used mainly as an intermediate in the manufacture of other products. Potential exposure to quinoline may occur from the inhalation of cigarette smoke and, to a much lesser extent, ambient air contaminated by emissions from the petroleum and coal industries. Acute (short-term) inhalation exposure to quinoline vapors irritates the eyes, nose, and throat and may cause headaches, dizziness, and nausea in humans. Information on the chronic (long-term), reproductive, developmental, or carcinogenic effects of quinoline in humans is not available. Liver damage has been observed in rats chronically exposed to quinoline by ingestion. An increased incidence of liver vascular tumors has been observed in rats and mice orally exposed to quinoline. The U.S. Environmental Protection Agency (EPA) has provisionally classified quinoline as a Group C, possible human carcinogen.

Please Note: The main source of information for this fact sheet is EPA's *Health and Environmental Effects Profile for Quinoline*. Other secondary sources include the Hazardous Substances Data Bank (HSDB), a database of summaries of peer-reviewed literature, and the Registry of Toxic Effects of Chemical Substances (RTECS), a database of toxic effects that are not peer reviewed.

Physical Properties

- The chemical formula for quinoline is C_9H_7N, and it has a molecular weight of 129.15 g/mol. (7)
- Quinoline occurs as a colorless, hygroscopic liquid that darkens with age and is sparingly soluble in water but is more easily soluble in hot water. (3,7)
- Quinoline has a penetrating, pungent odor. (3,7)
- The vapor pressure of quinoline is 0.0091 mm Hg at 25 EC and its log octanol/water partition coefficient (log K_{ow}) is 2.03. (3)

Uses

- Quinoline is used mainly as an intermediate in the manufacture of other products. (3)
- Quinoline is also used as a catalyst, a corrosion inhibitor, in metallurgical processes, in the manufacture of dyes, as a preservative for anatomical specimens, in polymers and agricultural chemicals, and as a solvent for resins and terpenes. It is also used as an antimalarial medicine. (2,3,7)

Sources and Potential Exposure

- Workers in certain industries may be occupationally exposed to quinoline by inhalation, ingestion of particulates, or dermal contact. (1,2)

- A potential source of very low exposure to quinoline includes the inhalation of ambient air contaminated by emissions from petroleum refining, coal mining, quenching and coking, and release in shale oil, synthetic coal conversion wastewaters, and wood preservative wastewaters. Levels of 2-7 $\mu g/m^3$ have been measured in ambient air. (1,3)
- Quinoline is found at higher levels in cigarette smoke (1-20 µg/cigarette). (1,3)
- Underground coal gasification has been a source of quinoline contamination of groundwater. Individuals may be exposed by consumption of contaminated water. (1)

Assessing Personal Exposure

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

Health Hazard Information

Acute Effects:

- Acute inhalation exposure to quinoline vapor irritates the eyes, nose, and throat, and may cause headaches, dizziness, and nausea, and, at high concentrations, coma in humans. (3)
- Tests involving acute exposure of animals, such as the LD_{50} test in rats and rabbits, have demonstrated quinoline to have high acute toxicity by oral or dermal exposure. (4)

Chronic Effects (Noncancer):

- Information on the chronic effects of quinoline in humans is not available. (3)
- Liver damage has been observed in rats chronically exposed to quinoline by ingestion. (3)
- EPA has not established a reference concentration (RfC) or reference dose (RfD) for quinoline. (5)

Reproductive/Developmental Effects:

- No information is available on the reproductive or developmental effects of quinoline in humans or animals. (3)

Cancer Risk:

- No human studies are available on the carcinogenicity of quinoline. (3)
- An increased incidence of liver hemangioendotheliomas (liver vascular tumors) has been observed in rats and mice orally exposed to quinoline. (3)
- EPA has provisionally classified quinoline as a Group C, possible human carcinogen. (3,6)
- EPA has calculated a provisional oral cancer slope factor of 12 $(mg/kg/d)^{-1}$. A provisional value is one which has not received Agency-wide review. (6)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45). For quinoline: 1 ppm = 5.3 mg/m^3.

Note: There are very few health numbers or regulatory/advisory numbers for quinoline; thus, a graph has not been prepared for this compound.

References

1. U.S. Department of Health and Human Services. Hazardous Substances Data Bank (HSDB, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.

2. G.D. Clayton and F.E. Clayton, Eds. *Patty's Industrial Hygiene and Toxicology*. Volume IIA, 3rd revised ed. John Wiley & Sons, New York. 1981.

3. U.S. Environmental Protection Agency (EPA). *Health and Environmental Effects Profile for Quinoline*. EPA/600/x-85/355. Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment, Office of Research and Development, Cincinnati, OH. 1985.

4. U.S. Department of Health and Human Services. Registry of Toxic Effects of Chemical Substances (RTECS, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.

5. U.S. Environmental Protection Agency (EPA). *Integrated Risk Information System (IRIS)*. National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1999.

6. U.S. Environmental Protection Agency (EPA). *Health Effects Assessment Summary Tables. FY 1997 Update.* Office of Research and Development, Office of Emergency and Remedial Response, Washington, DC. EPA/540/R-97-036. 1997.

7. *The Merck Index. An Encyclopedia of Chemicals, Drugs, and Biologicals*. 11th ed. Ed. S. Budavari. Merck and Co. Inc., Rahway, NJ. 1989.

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2,3,7,8-TETRACHLORODIBENZO-p-DIOXIN (2,3,7,8-TCDD)

1746-01-6

Hazard Summary

2,3,7,8-Tetrachlorodibenzo-p-dioxin (2,3,7,8-TCDD) is formed as an unintentional by-product of incomplete combustion. It may be released to the environment during the combustion of fossil fuels and wood, and during the incineration of municipal and industrial wastes. It causes chloracne in humans, a severe acne-like condition, and has been shown to be very toxic in animals studies. It is known to be a developmental toxicant in animals, causing skeletal deformities, kidney defects, and weakened immune responses in the offspring of animals exposed to 2,3,7,8-TCDD during pregnancy. Human studies have shown an association between 2,3,7,8-TCDD and soft-tissue sarcomas, lymphomas, and stomach carcinomas. The U.S. Environmental Protection Agency (EPA) has classified 2,3,7,8- TCDD as a Group B2, probable human carcinogen.

Please Note: The main source of information for this fact sheet is the Agency for Toxic Substances and Disease Registry's (ATSDR's) *Toxicological Profile for Chlorinated Dibenzo-p-Dioxins*.

Physical Properties

- 2,3,7,8-TCDD is a colorless solid with no distinguishable odor. (1)
- The chemical formula for 2,3,7,8-TCDD is $C_{12}H_4Cl_4O_2$, and the molecular weight is 322 g/mol. (1)
- The vapor pressure for 2,3,7,8-TCDD is 7.4 $x10^{-10}$ at 25 EC, and it has an octanol/water partition coefficient (log K_{ow}) of 6.8 - 7.58. (1)

Uses

- 2,3,7,8-TCDD is not intentionally produced by industry. It can be inadvertently produced in very small amounts as an impurity during the incineration of municipal and industrial wastes and during the manufacture of certain chemicals. (1)
- The only present use for 2,3,7,8-TCDD is in chemical research. (1)

Sources and Potential Exposure

- 2,3,7,8-TCDD may be formed during the chlorine bleaching process used by pulp and paper mills, and as a by-product from the manufacture of certain chlorinated organic chemicals, such as chlorinated phenols. (1)
- 2,3,7,8-TCDD is primarily released to the environment during the combustion of fossil fuels (including motor vehicles) and wood, and during incineration processes. (1)
- Very low levels of 2,3,7,8-TCDD are found throughout the environment, including air, food, and soil. (1)

- Most of the exposure of the general population to 2,3,7,8-TCDD is from food, mainly meat, dairy products, and fish. (1)

Assessing Personal Exposure

- Body fat, blood, and breast milk may be analyzed for 2,3,7,8-TCDD. (1)

Health Hazard Information

Acute Effects:

- The major acute (short-term) effect from exposure of humans to high levels of 2,3,7,8-TCDD in air is chloracne, a severe acne-like condition that can develop within months of first exposure. (1,2)
- Acute animal tests, such as the LD_{50} test in dogs, monkeys, and guinea pigs, have shown 2,3,7,8-TCDD to have extreme toxicity from oral exposure. (1)

Chronic Effects (Noncancer):

- Chloracne is also the major effect seen from chronic (long-term) exposure to 2,3,7,8-TCDD. (1)
- Animal studies have reported hair loss, loss of body weight, and a weakened immune system from oral exposure to 2,3,7,8-TCDD. (1)
- EPA has not established a reference concentration (RfC) or a reference dose (RfD) for 2,3,7,8-TCDD.
- ATSDR has calculated a chronic oral minimal risk level (MRL) of 1×10^{-9} mg/kg/d based on neurological effects in monkeys. The MRL is an estimate of daily exposure to a dose of a chemical that is likely to be without appreciable risk of adverse noncancerous effects over a specified duration of exposure. Exposure to a level above the MRL does not mean that adverse effects will occur. The MRL is used by public health professionals as a screening tool. (1)

Reproductive/Developmental Effects:

- The results of available reproductive and developmental studies in humans are inconclusive. (1)
- Animal studies have reported developmental effects, such as skeletal deformities, kidney defects, and weakened immune responses in the offspring of animals exposed to 2,3,7,8-TCDD during pregnancy. (1)
- Reproductive effects, including altered levels of sex hormones, reduced production of sperm, and increased rates of miscarriages, have been seen in animals exposed to 2,3,7,8-TCDD. (1)

Cancer Risk:

- Human studies, primarily of workers occupationally exposed to 2,3,7,8-TCDD by inhalation, have found an association between 2,3,7,8-TCDD and lung cancer, soft-tissue sarcomas, lymphomas, and stomach carcinomas, although for malignant lymphomas, the increase in risk is not consistent. (1)
- No information is available on the carcinogenic effects of 2,3,7,8-TCDD in animals following inhalation exposure. (1)
- Animal studies have reported tumors of the liver, lung, tongue, thyroid, and nasal turbinates from oral exposure to 2,3,7,8-TCDD. (1)
- EPA has classified 2,3,7,8-TCDD as a Group B2, probable human carcinogen. (2,3)
- EPA has calculated a provisional inhalation cancer slope factor of 1.5×10^5 $(mg/kg/d)^{-1}$ and an inhalation unit risk estimate of 3.3×10^{-5} $(pg/m^3)^{-1}$ for 2,3,7,8-TCDD. The provisional slope factor is a value that has had some form of Agency review, but it does not appear on IRIS. (2,3)
- EPA has calculated a provisional oral cancer slope factor of 1.5×10^5 $(mg/kg/d)^{-1}$ and an oral unit risk factor of 4.5 $(\mu g/L)^{-1}$ for 2,3,7,8-TCDD. (2,3)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45). For 2,3,7,8-TCDD: 1 ppm = 13.2 mg/m^3.

Note: There are very few health numbers or regulatory/advisory numbers for 2,3,7,8-TCDD; thus, a graph has not been prepared for this compound.

References

1. Agency for Toxic Substances and Disease Registry (ATSDR). *Toxicological Profile for Chlorinated Dibenzo-p-Dioxins*. Public Health Service, U.S. Department of Health and Human Services, Atlanta, GA. 1998.

2. U.S. Environmental Protection Agency (EPA). *Health Effects Assessment Summary Tables. FY 1997 Update.* Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment, Office of Research and Development, Cincinnati, OH. 1997.

3. U.S. Environmental Protection Agency (EPA). *Health Assessment Document for Polychlorinated Dibenzo-p-Dioxin.* Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment, Office of Research and Development, Cincinnati, OH. EPA 600/8-84-014F. 1985.

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1,1,2,2-TETRACHLOROETHANE
79-34-5

Hazard Summary

As 1,1,2,2-tetrachloroethane is no longer used much in the U.S., current air emissions predominantly result from its use as a chemical intermediate during the manufacture of other chemicals. Low levels have been detected in air. The main effects of 1,1,2,2-tetrachloroethane are liver and neurological effects. Acute (short-term) inhalation exposure to very high levels of 1,1,2,2-tetrachloroethane has resulted in effects on the liver and respiratory, central nervous, and gastrointestinal systems in humans. Chronic (long-term) inhalation exposure to 1,1,2,2-tetrachloroethane in humans results in jaundice and an enlarged liver, headaches, tremors, dizziness, numbness, and drowsiness. Animal studies have shown a significantly increased incidence of liver tumors in mice orally exposed to 1,1,2,2-tetrachloroethane. The U.S. Environmental Protection Agency (EPA) has classified 1,1,2,2-tetrachloroethane as a Group C possible human carcinogen.

Please Note: The main sources of information for this fact sheet are EPA's Integrated Risk Information System (IRIS), which contains information on the carcinogenic effects of 1,1,2,2-tetrachloroethane, and the Agency for Toxic Substances and Disease Registry's (ATSDR's) *Toxicological Profile for 1,1,2,2-Tetrachloroethane*.

Physical Properties

- 1,1,2,2-Tetrachloroethane is a colorless, dense liquid that has a sweet, chloroform like odor. (1,6)
- The odor threshold for 1,1,2,2-tetrachloroethane is 1.5 ppm. (6)
- The chemical formula for 1,1,2,2-tetrachloroethane is $C_2H_2Cl_4$, and the molecular weight is 167.85 g/mol. (1,2)
- The vapor pressure for 1,1,2,2-tetrachloroethane is 5.95 mm Hg at 25 EC, and it has a log octanol/water partition coefficient (log K_{ow}) of 2.39. (1)
- The half-life in air is about 60 days. (1)

Uses

- The production of 1,1,2,2-tetrachloroethane has decreased significantly in the U.S. (1)
- In the past, 1,1,2,2-tetrachloroethane was used in large amounts to produce trichloroethylene, tetrachloroethylene, and 1,2,-dichloroethylene. (1)
- It was also used as a solvent, in cleaning and degreasing metals, in paint removers, varnishes and lacquers, in photographic films, as an extractant for oils and fats, and in pesticides. (1)

Sources and Potential Exposure

- As it is no longer used much in the U.S., present sources of 1,1,2,2-tetrachloroethane are chemical production activities in which it is an intermediate product. (1)
- Low levels of 1,1,2,2-tetrachloroethane can be present in both indoor and outdoor air. In the early 1980s, average ambient air concentrations were around 0.005 ppb, and average concentrations in the indoor air of several homes measured 1.8 ppb. (1)
- 1,1,2,2-Tetrachloroethane has been found, in trace amounts, in adhesives, oils, greases, and lubricants; these household products may contaminate indoor air. (1)
- Limited occupational exposure to 1,1,2,2-tetrachloroethane may occur through inhalation of the vapors or through skin contact due to spills or accidents in the workplace. (1)
- 1,1,2,2-Tetrachloroethane has been detected in surface water and groundwater; however, a nationwide survey of drinking water supplies in the 1980s did not find any supplies containing 1,1,2,2-tetrachloroethane. (1)

Assessing Personal Exposure

- No specific medical tests are available to determine exposure to 1,1,2,2-tetrachloroethane. (1)

Health Hazard Information

Acute Effects:

- Acute exposure to very high levels of 1,1,2,2-tetrachloroethane has caused death in humans; the autopsies revealed severe liver destruction. (1,2)
- Respiratory and eye irritation, dizziness, nausea, and vomiting have been noted in humans exposed to fumes in the workplace. (1)
- Animal studies have reported effects on the liver, eyes, and central nervous system (CNS) from acute inhalation exposure to 1,1,2,2,-tetrachloroethane. (1)
- Tests involving acute exposure of animals, such as the LC_{50} and LD_{50} tests in rats and mice, have shown 1,1,2,2-tetrachloroethane to have moderate acute toxicity. (3)

Chronic Effects (Noncancer)*:*

- Chronic exposure of humans to high levels of 1,1,2,2-tetrachloroethane results in effects on the liver (jaundice and an enlarged liver), central and peripheral nervous system (headaches, tremors, dizziness, and drowsiness), and gastrointestinal effects (pain, nausea, vomiting, and loss of appetite). (1)
- Liver effects have also been observed in animals exposed via inhalation. (1)
- EPA has not established a reference concentration (RfC) or reference dose (RfD) for 1,1,2,2-tetrachloroethane. (4)
- ATSDR has calculated an intermediate-duration inhalation minimal risk level (MRL) of 0.4 ppm (3 mg/m^3) for 1,1,2,2-tetrachloroethane based on liver effects in rats. The MRL is an estimate of the daily human exposure to a hazardous substance that is likely to be

without appreciable risk of adverse noncancer health effects over a specified duration of exposure. Exposure to a level above the MRL does not mean that adverse health effects will occur. The MRL is intended to serve as a screening tool. (1)

Reproductive/Developmental Effects:

- No studies are available regarding developmental or reproductive effects in humans from inhalation or oral exposure to 1,1,2,2-tetrachloroethane. (1)
- Animal studies have not reported reproductive effects from inhalation exposure to 1,1,2,2-tetrachloroethane, while an oral study in rats reported histopathological changes in the testes. (1)
- No effects to the offspring of male rats exposed to 1,1,2,2-tetrachloroethane via inhalation were reported. (1)

Cancer Risk:

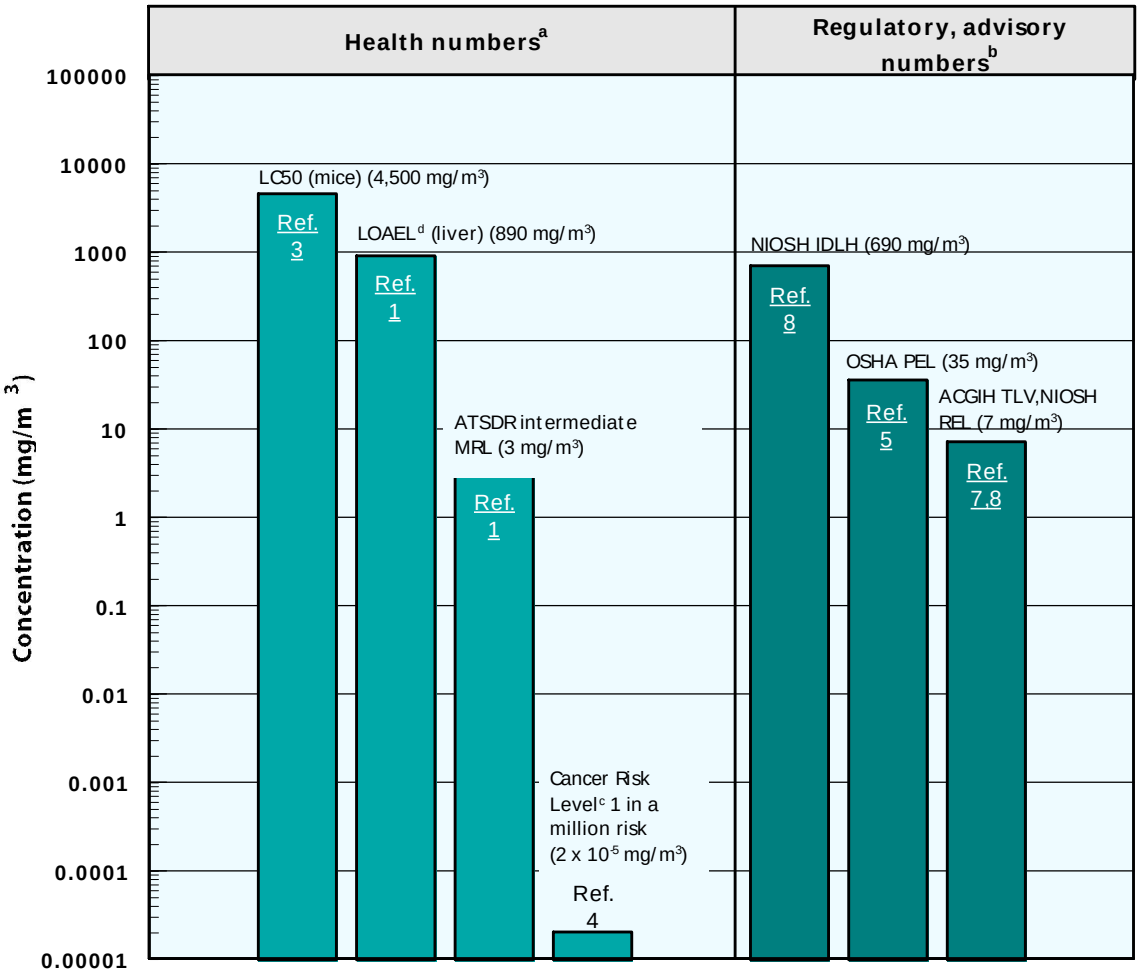
- Oral exposure to 1,1,2,2-tetrachloroethane in mice resulted in an increased incidence of hepatocellular carcinomas, while no increase in tumors was reported in rats. (1,4)
- EPA has classified 1,1,2,2-tetrachloroethane as a Group C, possible human carcinogen. (4)
- EPA uses mathematical models, based on human and animal studies, to estimate the probability of a person developing cancer from breathing air containing a specified concentration of a chemical. EPA has calculated an inhalation unit risk estimate of 5.8×10^{-5} $(\mu g/m^3)^{-1}$. EPA estimates that, if an individual were to continuously breathe air containing 1,1,2,2-tetrachloroethane at an average of 0.02 $\mu g/m^3$ (2.0×10^{-5} mg/m^3) over his or her entire lifetime, that person would theoretically have no more than a one-in-a-million increased chance of developing cancer as a direct result of breathing air containing this chemical. Similarly, EPA estimates that continuously breathing air containing 0.2 $\mu g/m^3$ (2.0×10^{-4} mg/m^3) would result in not greater than a one-in-a-hundred thousand increased chance of developing cancer over a lifetime, and air containing 2.0 $\mu g/m^3$ (2.0×10^{-3} mg/m^3) would result in not greater than a one-in-ten thousand increased chance of developing cancer. For a detailed discussion of confidence in the potency estimates, please see IRIS. (4)
- EPA has also calculated an oral cancer slope factor of 0.2 $(mg/kg/d)^{-1}$. (4)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45).
For 1,1,2,2-tetrachloroethane: 1 ppm = 6.86 mg/m^3.
To convert from $\mu g/m^3$ to mg/m^3: mg/m^3 = ($\mu g/m^3$) x (1 mg/1,000 μg).

Health Data from Inhalation Exposure

1,1,2,2-Tetrachloroethane



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

LC_{50} (Lethal Concentration$_{50}$) – A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.

LOAEL – Lowest-observed-no-adverse-affect level.

NIOSH REL – National Institute of Occupational Safety and Health's recommended exposure limit; NIOSH-recommended exposure limit for an 8- or 10-h time-weighted-average exposure and/or ceiling.

NIOSH IDLH – NIOSH's immediately dangerous to life or health concentration; NIOSH recommended exposure limit to ensure that a worker can escape from an exposure condition that is likely to cause death or immediate or delayed permanent adverse health effects or prevent escape from the environment.

OSHA PEL – Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average: the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.

[a] Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA.
[b] Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the Government or other groups as advice.
[c] These cancer risk estimates were derived from oral data and converted to provide the estimated inhalation risk.
[d] The LOAEL is from the critical study used as the basis for the ATSDR intermediate MRL.

References

1. Agency for Toxic Substances and Disease Registry (ATSDR). *Toxicological Profile for 1,1,2,2-Tetrachloroethane (Update)*. U.S. Public Health Service, U.S. Department of Health and Human Services, Atlanta, GA. 1996.

2. U.S. Department of Health and Human Services. Hazardous Substances Data Bank (HSDB, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.

3. U.S. Department of Health and Human Services. Registry of Toxic Effects of Chemical Substances (RTECS, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.

4. U.S. Environmental Protection Agency (EPA). *Integrated Risk Information System (IRIS) on 1,1,2,2-Tetrachloroethane*. National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1999.

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

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

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

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

TETRACHLOROETHYLENE (PERCHLOROETHYLENE)

127-18-4

Hazard Summary

Tetrachloroethylene is widely used for dry-cleaning fabrics and metal degreasing operations. The main effects of tetrachloroethylene in humans are neurological, liver, and kidney effects following acute (short-term) and chronic (long-term) inhalation exposure. Dizziness, sleepiness, and impaired coordination have been reported. Some adverse reproductive effects, such as menstrual disorders and spontaneous abortions, have been reported from occupational exposure to tetrachloroethylene; however, no definite conclusions can be made because of the limitations of the studies. Results from epidemiological studies of tetrachloroethylene and cancer incidence have been mixed; some studies reported an increased incidence of a variety of tumors, while other studies did not report any carcinogenic effects. Animal studies have reported an increased incidence of liver cancer in mice, via inhalation and gavage, and kidney and mononuclear cell leukemia in rats. The U.S. Environmental Protection Agency (EPA) considers trichloroethylene as intermediate between a probable and possible human carcinogen (Group B/C). The Agency is currently reassessing its potential carcinogenicity.

Please Note: The main sources of information for this fact sheet are EPA's Integrated Risk Information System (IRIS), which contains information on oral chronic toxicity and the reference dose (RfD), and the Agency for Toxic Substances and Disease Registry's (ATSDR's) *Toxicological Profile for Tetrachloroethylene*. Another secondary source is EPA's *Health Effects Assessment for Tetrachloroethylene*.

Physical Properties

- Tetrachloroethylene is a nonflammable colorless liquid with a sharp sweet odor; the odor threshold is 1 ppm. (1)
- The chemical formula for tetrachloroethylene is C_2Cl_4, and the molecular weight is 165.83 g/mol. (1)
- The vapor pressure for tetrachloroethylene is 18.47 mm Hg at 25 EC, and it has a log octanol/water partition coefficient (log K_{ow}) of 3.40. (1)

Uses

- Tetrachloroethylene is used for dry cleaning and textile processing, as a chemical intermediate, and for vapor degreasing in metal-cleaning operations. (1)

Sources and Potential Exposure

- Prior to 1981, tetrachloroethylene was detected in ambient air at average levels of 0.16 ppb in rural and remote areas, 0.79 ppb in urban and suburban areas, and 1.3 ppb in areas near emission sources. (1)

- Tetrachloroethylene has also been detected in drinking water; one survey prior to 1984 of water supplies from groundwater sources reported a median concentration of 0.75 ppb for the samples in which tetrachloroethylene was detected, with a maximum level of 69 ppb. (1)
- Occupational exposure to tetrachloroethylene may occur, primarily in dry cleaning establishments and at industries manufacturing or using the chemical. (1)

Assessing Personal Exposure

- Tetrachloroethylene can be measured in the breath, and breakdown products of tetrachloroethylene can be measured in the blood and urine. (1)

Health Hazard Information

Acute Effects:

- Acute exposure to very high levels of tetrachloroethylene in humans has caused death. Effects noted from short-term, inhalation exposure to tetrachloroethylene vapors include irritation of the upper respiratory tract and eyes, kidney dysfunction, and at lower concentrations, neurological effects, such as reversible mood and behavioral changes, impairment of coordination, dizziness, headache, sleepiness, and unconsciousness. (1)
- Animal studies have reported effects on the liver, kidney, and central nervous system (CNS) from acute inhalation exposure to tetrachloroethylene. (1)
- Acute animal tests, such as the LC_{50} and LD_{50} tests in mice have shown tetrachloroethylene to have low toxicity from inhalation and oral exposure. (1)

Chronic Effects (Noncancer):

- The major effects from chronic inhalation exposure to tetrachloroethylene in humans are neurological effects, including headaches, and impairment of memory, concentration, and intellectual function. Other effects noted in humans include cardiac arrhythmia, liver damage, and possible kidney effects. (1,5)
- Animal studies have reported effects on the liver, kidney, and CNS from chronic inhalation exposure to tetrachloroethylene. (1,5)
- EPA has not established a reference concentration (RfC) for tetrachloroethylene. (4)
- The RfD for tetrachloroethylene is 0.01 mg/kg/d based on hepatotoxicity in mice and weight gain in rats. The RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of deleterious noncancer effects during a lifetime. It is not a direct estimator of risk, but rather a reference point to gauge the potential effects. At exposures increasingly greater than the RfD, the potential for adverse health effects increases. Lifetime exposure above the RfD does not imply that an adverse health effect would necessarily occur. (4)
- EPA has medium confidence in the RfD based on low confidence in the study on which the RfD was based due to the lack of complete histopathological examination at the

no-observed-adverse-effect level (NOAEL) in the mouse; and medium confidence in the database because it is relatively complete but lacks studies of reproductive and teratology endpoints subsequent to oral exposure. (4)

- ATSDR has calculated a chronic-duration inhalation minimal risk level (MRL) of 0.04 ppm (0.3 mg/m^3) for tetrachloroethylene based on neurological effects in humans. The MRL is an estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk of adverse noncancer health effects over a specified duration of exposure. (1)
- Repeated skin contact may cause irritation. (1)

Reproductive/Developmental Effects:

- Some adverse reproductive effects, such as menstrual disorders and spontaneous abortions, have been reported in women occupationally exposed to tetrachloroethylene. However, no definitive conclusions can be made because of the limitations of the studies. (1)
- In a study of residents exposed to drinking water contaminated with solvents, including tetrachloroethylene, there was a suggestion that birth defects were associated with exposure. However, no firm conclusions can be drawn from this study due to multiple chemical exposures and problems with the analysis. (1)
- Increased fetal resorptions and effects to the fetus have been reported in animals exposed to high levels of tetrachloroethylene by inhalation. (1)

Cancer Risk:

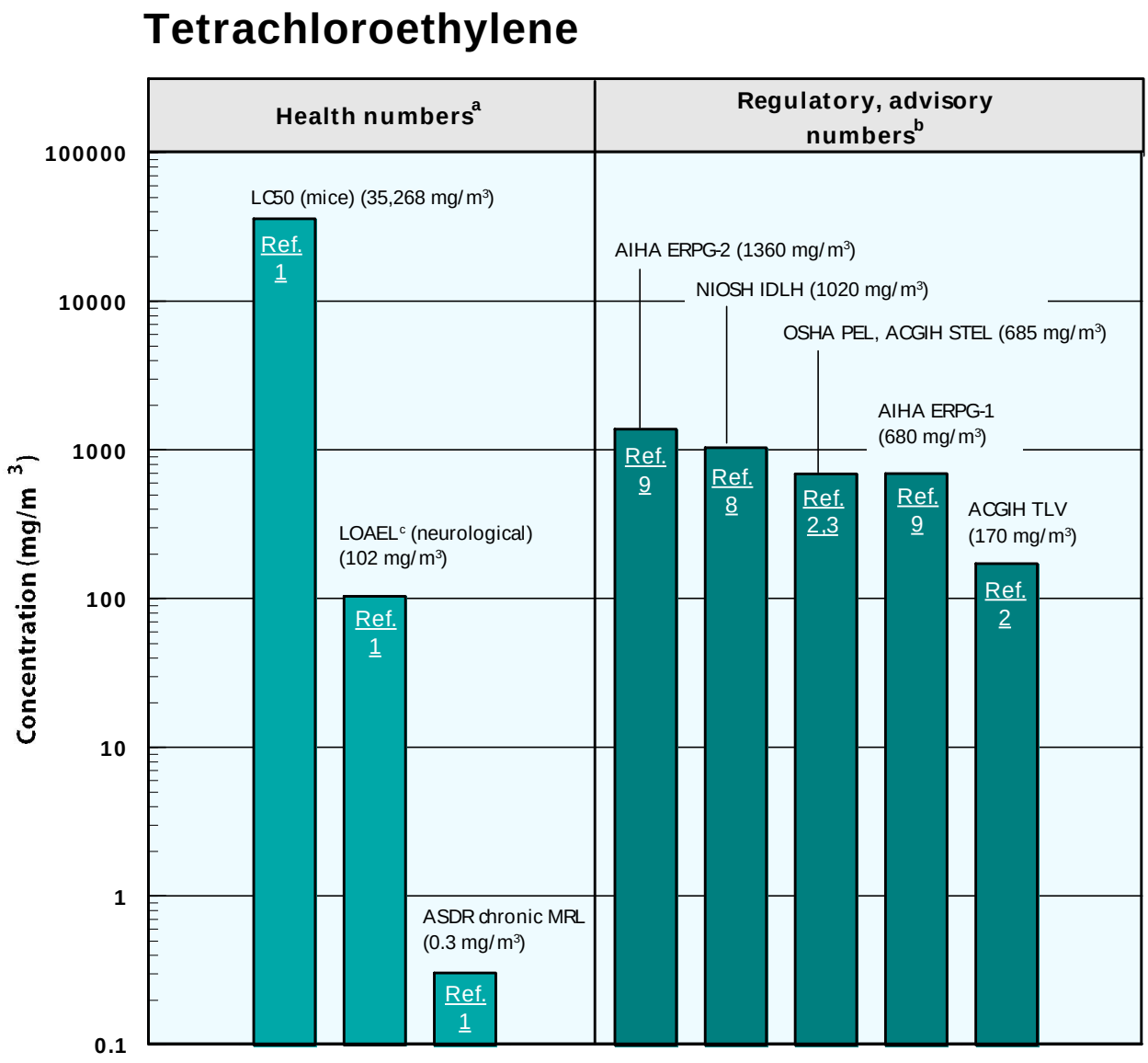
- Epidemiological studies of dry cleaning workers exposed to tetrachloroethylene and other solvents have shown mixed results; some studies reported an increased incidence of a variety of tumors, while other studies did not show any carcinogenic effects. All of these studies are complicated by potential exposure to numerous chemicals. (1,5,6)
- One human study reported that there was a potential association between drinking water contaminated with tetrachloroethylene and other chemicals and an increased risk of childhood leukemia. Other studies reexamined the data and did not agree with the association because the people were exposed to multiple chemicals and the statistical significance of the incidence of leukemia has not been resolved. (1)
- Animal studies have reported an increased incidence of liver tumors in mice, from inhalation and gavage exposure, and kidney and mononuclear cell leukemias in rats, via inhalation exposure. (1,5,6)
- Regardless of exposure route, less than 5 percent of absorbed tetrachloroethylene is metabolized by humans to trichloroacetic acid (TCA), with the remainder being exhaled unchanged. Trichloroacetic acid is classified as a Group C, possible human carcinogen based on limited evidence of liver tumors in mice (but not rats). (4,7)
- EPA considers trichloroethylene as intermediate between a probable and possible human carcinogen (Group B/C). The Agency is currently reassessing its potential carcinogenicity. (10)

- EPA uses mathematical models, based on animal studies, to estimate the probability of a person developing cancer from breathing air containing a specified concentration of a chemical. EPA has calculated a provisional inhalation unit risk estimate of 5.8×10^{-7} $(\mu g/m^3)^{-1}$. A provisional value is one which has not received Agency-wide review. (7)
- EPA has calculated a provisional oral cancer slope factor of 0.051 $(mg/kg/d)^{-1}$. (5)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45).
For tetrachloroethylene: 1 ppm = 6.78 mg/m^3.
To convert from $\mu g/m^3$ to mg/m^3: $mg/m^3 = (\mu g/m^3) \times (1\ mg/1{,}000\ \mu g)$.

Health Data from Inhalation Exposure



AIHA ERPG – American Industrial Hygiene Association's emergency response planning guidelines. ERPG 1 is the maximum airborne concentration below which it is believed nearly all individuals could be exposed up to one hour without experiencing other than mild transient adverse health effects or perceiving a clearly defined objectionable odor; ERPG 2 is the maximum airborne concentration below which it is believed nearly all individuals could be exposed up to one hour without experiencing or developing irreversible or other serious health effects that could impair their abilities to take protective action.
ACGIH STEL – American Conference of Governmental and Industrial Hygienists' short-term exposure limit; 15-min time-weighted-average exposure that should not be exceeded at any time during a workday even if the 8-h time-weighted-average is within the threshold limit value.
ACGIH TLV – American Conference of Governmental and Industrial Hygienists' threshold

limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effects.
LC_{50} (Lethal Concentration$_{50}$) – A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.
LOAEL – Lowest-observed-no-adverse-affect level.
NIOSH IDLH – National Institute of Occupational Safety and Health's immediately dangerous to life or health concentration; NIOSH recommended exposure limit to ensure that a worker can escape from an exposure condition that is likely to cause death or immediate or delayed permanent adverse health effects or prevent escape from the environment.
OSHA PEL – Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.

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

References

1. Agency for Toxic Substances and Disease Registry (ATSDR). *Toxicological Profile for Tetrachloroethylene (Update)*. U.S. Public Health Service, U.S. Department of Health and Human Services, Atlanta, GA. 1997.

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

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

4. U.S. Environmental Protection Agency (EPA). *Integrated Risk Information System (IRIS) on Tetrachloroethylene*. National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1999.

5. U.S. Environmental Protection Agency (EPA). *Health Effects Assessment for Tetrachloroethylene*. EPA/600/8-89-096. Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment, Office of Research and Development, Cincinnati, OH. 1988.

6. U.S. Environmental Protection Agency (EPA). *Updated Health Assessment Document for Tetrachloroethylene*. EPA/600/8-82/005B. Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment, Office of Research and Development, Cincinnati, OH. 1988.

7. U.S. Environmental Protection Agency (EPA). *Risk Assessment Issue Paper for Carcinogenicity Information for Tetrachloroethylene (Perchloroethylene, PERC) (CASRN 127-18-4).* Superfund Technical Support Center, National Center for Environmental Assessment, Cincinnati, OH. nd.

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

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

10. U.S. Environmental Protection Agency (EPA). National Emission Standards for Hazardous Air Pollutants: Wood Furniture Manufacturing Operations. *Federal Register* 63 FR 34336-346. June 24, 1998.

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TRICHLOROETHYLENE
79-01-6

Hazard Summary

Most of the trichloroethylene (TCE) used in the U.S. is released into the atmosphere from industrial degreasing operations. Acute (short-term) and chronic (long-term) inhalation exposure to trichloroethylene can affect the human central nervous system (CNS), with symptoms such as dizziness, headaches, confusion, euphoria, facial numbness, and weakness. High, short-term exposures of humans by inhalation also have been associated with effects on the liver, kidneys, gastrointestinal system, and skin. Although several epidemiological studies have investigated a possible link between trichloroethylene exposure and reproductive or developmental effects, no conclusive evidence has been identified. Similarly, the existence of a relationship between trichloroethylene exposure and cancer is also not clear from the epidemiological studies that have been performed. Animal studies have reported increases in lung, liver, and testicular tumors, via inhalation exposure. The U.S. Environmental Protection Agency (EPA) considers trichloroethylene as intermediate between a probable and possible human carcinogen (Group B/C). The Agency is currently reassessing its potential carcinogenicity.

Please Note: The main source of information for this fact sheet is the Agency for Toxic Substances and Disease Registry's (ATSDR's) *Toxicological Profile for Trichloroethylene*. Another secondary source used is EPA's *Health Assessment Document for Trichloroethylene*.

Physical Properties

- Trichloroethylene is a nonflammable colorless liquid with a sweet odor similar to ether or chloroform. (1)
- The odor threshold for trichloroethylene is 28 ppm. (6)
- The chemical formula for trichloroethylene is C_2HCl_3, and the molecular weight is 131.40 g/mol. (1)
- The vapor pressure for trichloroethylene is 74 mm Hg at 25 EC, and it has a log octanol/water partition coefficient (log K_{ow}) of 2.42. (1)
- Trichloroethylene is not a persistent chemical in the atmosphere; its half-life in air is about 7 days. (1)

Uses

- The main use of trichloroethylene is in the vapor degreasing of metal parts. (1)
- Trichloroethylene is also used as an extraction solvent for greases, oils, fats, waxes, and tars, a chemical intermediate in the production of other chemicals, and as a refrigerant. (1)
- Trichloroethylene is used in consumer products such as typewriter correction fluids, paint removers/strippers, adhesives, spot removers, and rug-cleaning fluids. (1)
- Trichloroethylene was used in the past as a general anesthetic. (1)

Sources and Potential Exposure

- Trichloroethylene has been detected in ambient air at levels less than 1 ppb. (1)
- Drinking water supplies relying on contaminated groundwater sources may contain trichloroethylene. A monitoring study in the early 1980s of drinking water systems relying groundwater sources detected TCE in 10 percent of the systems sampled. The median level among the systems where detected was 1 ppb. (1)
- Workers may be exposed to trichloroethylene in the factories where it is manufactured or used. In addition, persons breathing air around these factories may be exposed to trichloroethylene. (1)
- Persons may also be exposed to trichloroethylene through the use of products containing the chemical and from evaporation and leaching from waste disposal sites. (1)

Assessing Personal Exposure

- Trichloroethylene can be measured in the breath, and breakdown products of trichloroethylene can be measured in urine or blood. (1)

Health Hazard Information

Acute Effects:

- Acute exposure to extremely high levels of trichloroethylene (approximately 10,000 ppm) in humans has caused death. A few of these reports have cited cardiac arrhythmias as the cause of death, and one report noted massive liver damage. (1)
- CNS effects are the primary effects noted from acute inhalation exposure to trichloroethylene in humans, with symptoms including sleepiness, fatigue, headache, confusion, and feelings of euphoria. Effects on the liver, kidneys, gastrointestinal system, and skin have also been noted. (1)
- Neurological, lung, kidney, and heart effects have been reported in animals acutely exposed to trichloroethylene. (1)
- Tests involving acute exposure of animals, such as the LC_{50} and LD_{50} tests in rats and mice, have shown trichloroethylene to have low toxicity from inhalation exposure and moderate toxicity from oral exposure. (1,2)

Chronic Effects (Noncancer)*:*

- As with acute exposure, chronic exposure to trichloroethylene by inhalation also affects the human CNS. Case reports of intermediate and chronic occupational exposures included effects such as dizziness, headache, sleepiness, nausea, confusion, blurred vision, facial numbness, and weakness. (1)
- Studies have shown that simultaneous alcohol consumption and trichloroethylene inhalation increases the toxicity of trichloroethylene in humans. (1)
- Neurological, liver, and kidney effects were reported in chronically-exposed animals. (1)

- EPA has not calculated a reference concentration (RfC) or reference dose (RfD) for trichloroethylene. (3)
- ATSDR has calculated an intermediate-duration inhalation minimal risk level (MRL) of 0.1 ppm (0.5 mg/m^3) for trichloroethylene based on neurological effects in rats. The MRL is an estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk of adverse noncancer health effects over a specified duration of exposure. Exposure to a level above the MRL does not mean that adverse health effects will occur. The MRL is intended to serve as a screening tool. (1)
- The California Environmental Protection Agency (CalEPA) has calculated a chronic inhalation reference exposure level of 0.6 mg/m^3 based on neurological effects in humans. The CalEPA reference exposure level is a concentration at or below which adverse health effects are not likely to occur. (5)

Reproductive/Developmental Effects:

- A study of nurses occupationally exposed by inhalation to trichloroethylene along with other chemicals in operating rooms, and another epidemiological study of women exposed occupationally or nonoccupationally to trichloroethylene and other solvents, have reported increases in the incidence of miscarriages. The presence of other chemicals, however, limits the ability to draw conclusions specific to trichloroethylene. (1)
- An epidemiological study of 2,000 male and female workers exposed to trichloroethylene via inhalation found no increase in malformations in babies born following exposure. (1)
- Several studies have evaluated and not found an association between adverse reproductive effects in humans and exposure to trichloroethylene in contaminated drinking water. An association was found between the occurrence of congenital heart disease in children and a drinking water supply contaminated with trichloroethylene and other similar chemicals; however, no causal relationship with trichloroethylene could be concluded. (1)
- In one animal study, an increase in abnormal sperm morphology was observed following very high inhalation exposures of mice; however, other animal studies have not reported reproductive or developmental effects from either inhalation or ingestion exposures. (1,4)

Cancer Risk:

- Several human studies have investigated the relationship between inhalation exposure to trichloroethylene and cancer, some finding weak relationships and others finding none; however, each has limitations that restrict its usefulness. None of the studies found strong evidence of an association between trichloroethylene exposure and cancer incidence. (1,4)
- The existence of a relationship between oral exposure to trichloroethylene and cancer incidence is also not clear. One human study reported that there was a potential association between drinking water contaminated with trichloroethylene and an increased risk of childhood leukemia. Other studies reexamined the data and did not agree with the association because the people were exposed to chemicals other than trichloroethylene, and the statistical significance of the incidence of leukemia has not been resolved. (1)

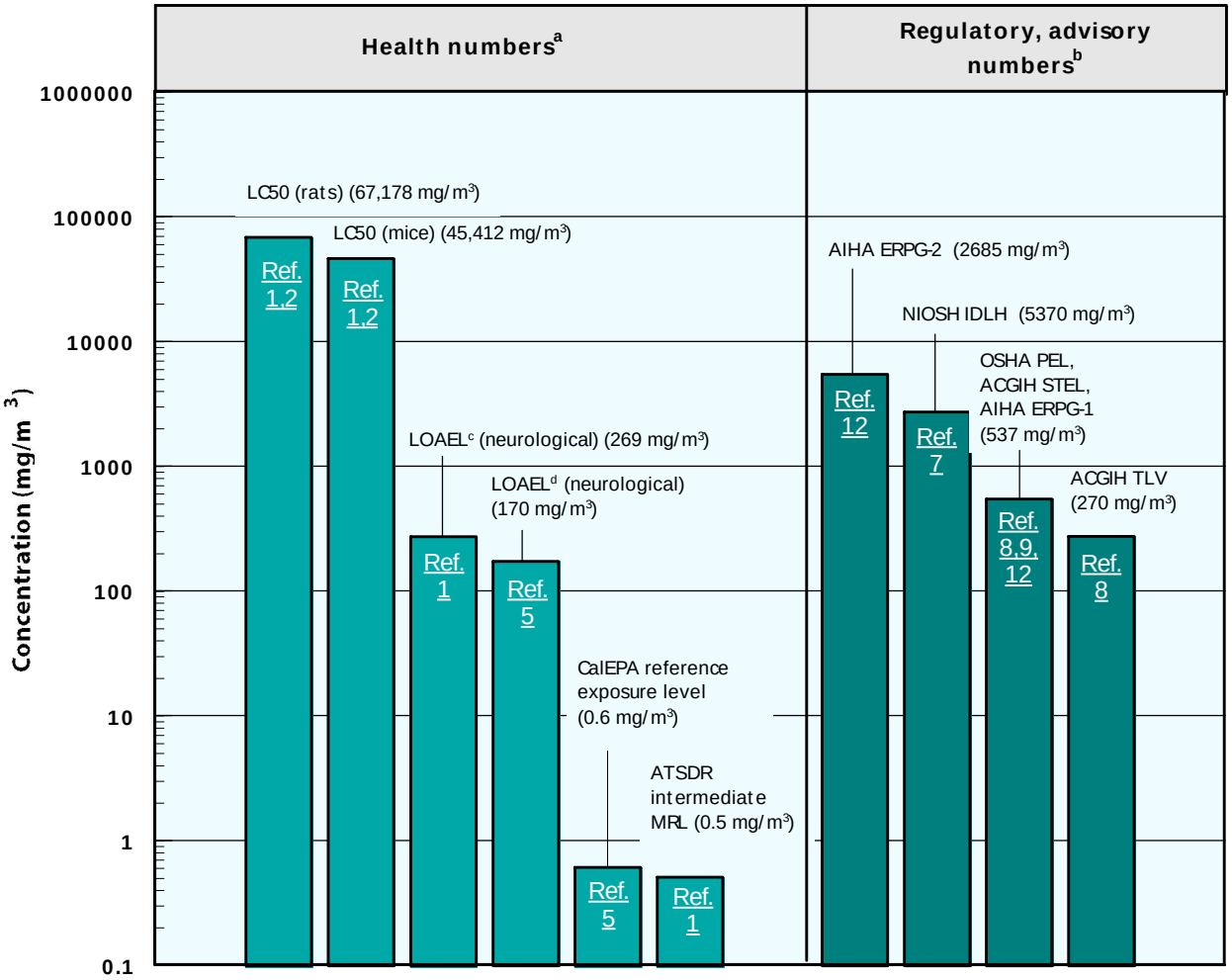
- Animal studies, via inhalation exposure, have reported increases in lung, liver, and testicular tumors and increases in liver tumors via gavage. (1,4)
- EPA considers trichloroethylene as intermediate between a probable and possible human carcinogen (Group B/C). The Agency is currently reassessing its potential carcinogenicity. (11)
- EPA uses mathematical models, based on animal studies, to estimate the probability of a person developing cancer from continuously breathing air containing a specified concentration of a chemical. EPA has calculated a provisional inhalation unit risk estimate of 1.7 x 10-6 $(\mu g/m^3)^{-1}$. A provisional value is one which has not received Agency-wide review. (10)
- EPA has also calculated a provisional oral cancer slope factor of 0.011 $(mg/kg/d)^{-1}$. (10)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45). For trichloroethylene: 1 ppm = 5.37 mg/m^3. To convert from $\mu g/m^3$ to mg/m^3: mg/m^3 = ($\mu g/m^3$) x (1 mg/1,000 µg).

Health Data from Inhalation Exposure

Trichloroethylene



ACGIH STEL – American Conference of Governmental and Industrial Hygienists' short-term exposure limit; 15-min time-weighted-average exposure that should not be exceeded at any time during a workday even if the 8-h time-weighted-average is within the threshold limit value.
ACGIH TLV – ACGIH's threshold limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effects.
AIHA ERPG – American Industrial Hygiene Association's emergency response planning guidelines. ERPG 1 is the maximum airborne concentration below which it is believed nearly all individuals could be exposed up to one hour without experiencing other than mild transient adverse health effects or perceiving a clearly defined objectionable odor; ERPG 2 is the maximum airborne concentration below which it is believed nearly all individuals could be exposed up to one hour without experiencing or developing irreversible or other serious health effects that could impair their abilities to take protective action.
LC_{50} (Lethal Concentration$_{50}$) – A calculated concentration of a chemical in air to which

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

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

References

1. Agency for Toxic Substances and Disease Registry (ATSDR). *Toxicological Profile for Trichloroethylene (Update).* U.S. Public Health Service, U.S. Department of Health and Human Services, Atlanta, GA. 1997.

2. U.S. Department of Health and Human Services. Registry of Toxic Effects of Chemical Substances (RTECS, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.

3. U.S. Environmental Protection Agency (EPA). *Integrated Risk Information System (IRIS) on Trichloroethylene*. National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1999.

4. U.S. Environmental Protection Agency (EPA). *Health Assessment Document for Trichloroethylene*. EPA/600/8-82/006F. Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment, Office of Research and Development. 1985.

5. California Environmental Protection Agency (CalEPA). *Technical Support Document for the Determination of Noncancer Chronic Reference Exposure Levels. Draft for Public Comment.* Office of Environmental Health Hazard Assessment, Berkeley, CA. 1997.

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

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

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

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

10. U.S. Environmental Protection Agency (EPA). *Risk Assessment Issue Paper for Carcinogenicity Information for Trichloroethylene (TCE) (CASRN 79-01-6).* Superfund Technical Support Center, National Center for Environmental Assessment, Cincinnati, OH. nd.

11. U.S. Environmental Protection Agency (EPA). National Emission Standards for Hazardous Air Pollutants: Wood Furniture Manufacturing Operations. *Federal Register* 63 FR 34336-346. June 24, 1998.

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

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VINYL CHLORIDE
75-01-4

Hazard Summary

Most vinyl chloride is used to make polyvinyl chloride (PVC) plastic and vinyl products. Acute (short-term) exposure to high levels of vinyl chloride in air has resulted in central nervous system(CNS) effects, such as dizziness, drowsiness, and headaches in humans. Chronic (long-term) exposure to vinyl chloride through inhalation and oral exposure in humans has resulted in liver damage. There are positive human and animal studies showing adverse effects which raise a concern about potential reproductive and developmental hazards to humans from exposure to vinyl chloride. Cancer is a major concern from exposure to vinyl chloride via inhalation, as vinyl chloride exposure has been shown to increase the risk of a rare form of liver cancer in humans. The U.S. Environmental Protection Agency (EPA) has classified vinyl chloride as a Group A, human carcinogen.

Please Note: The main sources of information for this fact sheet are the Agency for Toxic Substances and Disease Registry's (ATSDR's) *Toxicological Profile for Vinyl Chloride* and *Case Studies in Environmental Medicine. Vinyl Chloride Toxicity*.

Physical Properties

- Vinyl chloride is a colorless gas with a mild, sweet odor. (1)
- The odor threshold for vinyl chloride is 3,000 ppm. (5)
- Vinyl chloride is slightly soluble in water and is quite flammable. (1)
- The chemical formula for vinyl chloride is C_2H_3Cl, and the molecular weight is 62.5 g/mol. (1)
- The vapor pressure for vinyl chloride is 2,600 mm Hg at 25 EC, and it has a log octanol/water partition coefficient (log K_{ow}) of 1.36. (1)
- The half-life of vinyl chloride in air is a few hours. (1)

Uses

- Most of the vinyl chloride produced in the U.S. is used to make polyvinyl chloride (PVC), a material used to manufacture a variety of plastic and vinyl products including pipes, wire and cable coatings, and packaging materials. (1)
- Smaller amounts of vinyl chloride are used in furniture and automobile upholstery, wall coverings, housewares, and automotive parts. (1)
- Vinyl chloride has been used in the past as a refrigerant. (1)

Sources and Potential Exposure

- Ambient air concentrations of vinyl chloride are generally quite low, with exposure occurring from the discharge of exhaust gases from factories that manufacture or process vinyl chloride, or evaporation from areas where chemical wastes are stored. (1,2)
- Air inside new cars may contain vinyl chloride at higher levels than detected in ambient air because vinyl chloride may outgas into the air from the new plastic parts. (1,2)
- Drinking water may contain vinyl chloride released from contact with polyvinyl pipes. (1,2)
- Vinyl chloride is a microbial degradation product of trichloroethylene in groundwater, and thus can be found in groundwater affected by trichloroethylene contamination. (3)
- Occupational exposure to vinyl chloride may occur in those workers concerned with the production, use, transport, storage, and disposal of the chemical. (1,2)

Assessing Personal Exposure

- Vinyl chloride can be detected in urine and body tissues, but the tests are not reliable indicators of total exposure. (1,2)

Health Hazard Information

Acute Effects:

- Acute exposure of humans to high levels of vinyl chloride via inhalation in humans has resulted in effects on the CNS, such as dizziness, drowsiness, headaches, and giddiness. (1,2)
- Vinyl chloride is reported to be slightly irritating to the eyes and respiratory tract in humans. (1,2)
- Acute exposure to extremely high levels of vinyl chloride has caused loss of consciousness, lung and kidney irritation, and inhibition of blood clotting in humans and cardiac arrhythmias in animals. (1)
- Tests involving acute exposure of animals, such as the LC_{50} test in mice, have shown vinyl chloride to have high acute toxicity from inhalation exposure. (5)

Chronic Effects (Noncancer):

- Liver damage may result in humans from chronic exposure to vinyl chloride, through both inhalation and oral exposure. (1,2)
- A small percentage of individuals occupationally exposed to high levels of vinyl chloride in air have developed a set of symptoms termed "vinyl chloride disease," which is characterized by Raynaud's phenomenon (fingers blanch and numbness and discomfort are experienced upon exposure to the cold), changes in the bones at the end of the fingers, joint and muscle pain, and scleroderma-like skin changes (thickening of the skin, decreased elasticity, and slight edema). (1,2)

- CNS effects (including dizziness, drowsiness, fatigue, headache, visual and/or hearing disturbances, memory loss, and sleep disturbances) as well as peripheral nervous system symptoms (peripheral neuropathy, tingling, numbness, weakness, and pain in fingers) have also been reported in workers exposed to vinyl chloride. (1)
- Animal studies have reported effects on the liver, kidney, and CNS from chronic exposure to vinyl chloride. (1,6)
- EPA has not established a reference concentration (RfC) or a reference dose (RfD) for vinyl chloride. (8)
- ATSDR has calculated an intermediate-duration inhalation minimal risk level (MRL) of 0.03 ppm (0.08 mg/m^3) for vinyl chloride based on liver effects in rats. The MRL is an estimate of the daily human exposure to a hazardous substance that is likely to be without appreciable risk of adverse noncancer health effects over a specified duration of exposure. Exposure to a level above the MRL does not mean that adverse health effects will occur. The MRL is intended to serve as a screening tool. (1)
- The California Environmental Protection Agency (CalEPA) has calculated a chronic inhalation reference exposure level of 0.005 mg/m^3 based on liver effects in humans. The CalEPA reference exposure level is a concentration at or below which adverse health effects are not likely to occur. (15)

Reproductive/Developmental Effects:

- Several case reports suggest that male sexual performance may be affected by vinyl chloride. However, these studies are limited by lack of quantitative exposure information and possible co-occurring exposure to other chemicals. (1)
- Several epidemiological studies have reported an association between vinyl chloride exposure in pregnant women and an increased incidence of birth defects, while other studies have not reported similar findings. (1,2)
- Epidemiological studies have suggested an association between men occupationally exposed to vinyl chloride and miscarriages in their wives' pregnancies although other studies have not supported these findings. (1,2)
- Testicular damage and decreased male fertility have been reported in rats exposed to low levels for up to 12 months. (1)
- Animal studies have reported decreased fetal weight and birth defects at levels that are also toxic to maternal animals in the offspring of rats exposed to vinyl chloride through inhalation. (1)

Cancer Risk:

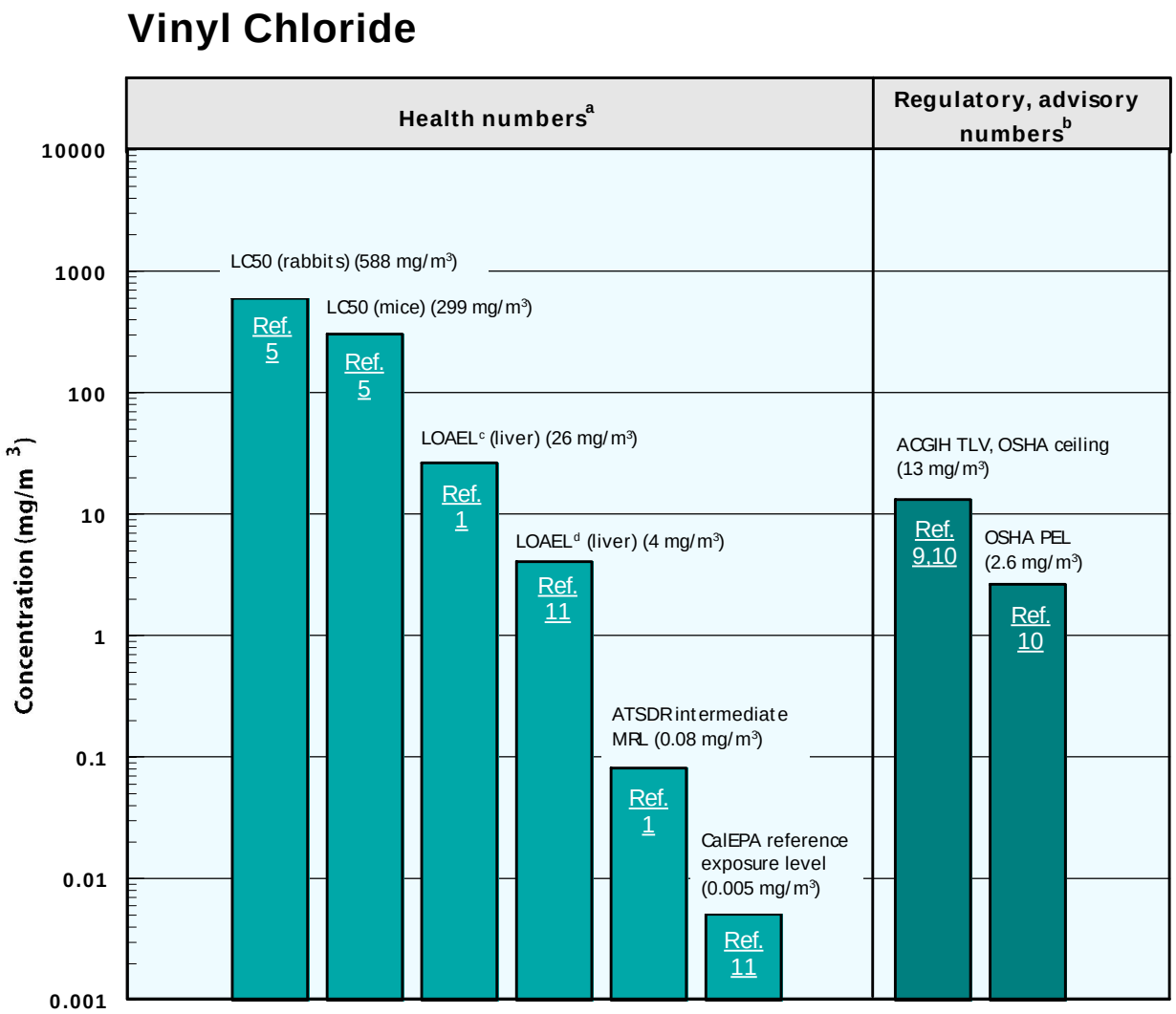
- Inhaled vinyl chloride has been shown to increase the risk of a rare form of liver cancer (angiosarcoma of the liver) in humans. (1,2,6)
- Vinyl chloride exposure, through inhalation, has also been associated with cancer of the brain, CNS, lung, respiratory tract, and the lymphatic/hematopoietic system in humans. (1,2)
- Animal studies have shown that vinyl chloride, via inhalation, increases the incidence of angiosarcoma of the liver and cancer of the liver and brain. (1,2,6)

- Several rat studies show a pronounced early-life susceptibility to the carcinogenic effect of vinyl chloride, i.e., early exposures are associated with higher cancer incidence than much longer exposures that occur after maturity. (1)
- EPA has classified vinyl chloride as a Group A, human carcinogen. (8)
- EPA uses mathematical models, based on human and animal studies, to estimate the probability of a person developing cancer from breathing air containing a specified concentration of a chemical. EPA has calculated a provisional inhalation unit risk estimate of 8.4×10^{-5} $(\mu g/m^3)^{-1}$ for vinyl chloride. A provisional value is one which has not received Agency-wide review. (8)
- EPA has calculated a provisional oral cancer slope factor of 1.9 $(mg/kg/d)^{-1}$ for vinyl chloride. (8)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) x (molecular weight of the compound)/(24.45).
For vinyl chloride: 1 ppm = 2.6 mg/m^3.
To convert from $\mu g/m^3$ to mg/m^3: mg/m^3 = ($\mu g/m^3$) x (1 mg/1,000 μg).

Health Data from Inhalation Exposure



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

LC_{50} (Lethal Concentration$_{50}$) – A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.

LOAEL – Lowest-observed-no-adverse-affect level.

OSHA PEL – Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average: the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.

OSHA PEL ceiling value – OSHA's permissible exposure limit ceiling value; the concentration of a substance that should not be exceeded at any time.

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

References

1. Agency for Toxic Substances and Disease Registry (ATSDR). *Toxicological Profile for Vinyl Chloride (Update)*. Public Health Service, U.S. Department of Health and Human Services, Atlanta, GA. 1997.

2. Agency for Toxic Substances and Disease Registry (ATSDR). *Case Studies in Environmental Medicine. Vinyl Chloride Toxicity.* Public Health Service, U.S. Department of Health and Human Services, Atlanta, GA. 1990.

3. Agency for Toxic Substances and Disease Registry (ATSDR). *Toxicological Profile for Trichloroethylene*. Public Health Service, U.S. Department of Health and Human Services, Atlanta, GA. 1992.

4. U.S. Department of Health and Human Services. Registry of Toxic Effects of Chemical Substances (RTECS, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.

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

6. U.S. Department of Health and Human Services. Hazardous Substances Data Bank (HSDB, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.

7. U.S. Environmental Protection Agency (EPA). *Integrated Risk Information System (IRIS)*. National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1999.

8. U.S. Environmental Protection Agency (EPA). *Health Effects Assessment Summary Tables. FY1997 Update*. Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment, Office of Research and Development, Cincinnati, OH. 1997.

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

10. Occupational Safety and Health Administration (OSHA). Occupational Safety and Health Standards, Toxic and Hazardous Substances. *Code of Federal Regulations* 29 CFR 1910.1017. 1998.

11. California Environmental Protection Agency (CalEPA). *Technical Support Document for the Determination of Noncancer Chronic Reference Exposure Levels. Draft for Public Comment.* Office of Environmental Health Hazard Assessment, Berkeley, CA. 1997.

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