Arsenic Compounds

ARSENIC COMPOUN DS(A)

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 of humans is associated with irritation of the skin and mucous membranes and effects in the brain and nervous system. Chronic oral exposure to elevated levels of inorganic arsenic has resulted in gastrointestinal effects, anemia, peripheral neuropathy, skin lesions, hyperpigmentation, and liver or kidney damage in humans. Inorganic arsenic exposure of humans, by the inhalation route, has been shown to be strongly associated with lung cancer, while ingestion of inorganic arsenic by humans has been linked to a form of skin cancer and also to bladder, liver, and lung cancer. EPA has classified inorganic arsenic as 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. 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) (7), which contains information on 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. (1)

Uses

- The major use for inorganic arsenic has been in wood preservation, although its use for preservation of wood used for residential purposes has been phased out. Although reduced from in the past, arsenic, primarily in organic forms, is also used in a range of agricultural products. Arsine is used in the microelectronics industry and in semiconductor manufacture. (1)
- Until the 1940s, inorganic arsenic was used as therapeutic agents in the treatment of various diseases, such as leukemia, psoriasis and chronic bronchial asthma. Inorganic arsenic may still be used in homeopathic or folk remedies in the United States and other countries, and its use has reemerged in an FDA-approved treatment for a specific type of leukemia. (1)
- Arsine has much more limited usage, primarily in the semiconductor industry and in the synthesis of organoarsenic compounds. (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)

- For most people, diet is the largest source of arsenic exposure, with usually smaller intakes from drinking water and air. Among foods, some of the highest levels are found in fish and shelfish; however, this arsenic exists primarily as organic compounds, which are essentially nontoxic. Inorganic arsenic compounds are the predominant forms in drinking water. (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. (1,2)
- Other sources of inorganic arsenic exposure include burning plywood treated with an arsenical wood preservative or dermal contact with wood treated with arsenic. (1)
- Most arsenic poisoning incidents in industry have involved the production of arsine, a short-lived, extremely toxic gas. (3)

Assessing Personal Exp osure

- 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 such exposures to inorganic arsenic have also resulted in central and peripheral nervous system disorders. (1,2)
- Acute oral exposure to inorganic arsenic, at doses of approximately 600 micrograms per kilogram body weight per day (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)

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 parts per million (ppm) can be lethal. (3)
- 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. (3)

Chronic Effects (Noncancer):

Inorganic arsenic

- Chronic inhalation exposure to elevated levels of 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 elevated levels of 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) Some recent studies have reported an association between elevated arsenic levels in drinking water and neurocognitive or behavioral test results in school age children. (1)
- No chronic inhalation exposure studies have been performed in animals for any inorganic arsenic compound. (1)
- Some animal studies have suggested that inorganic arsenic is an essential dietary nutrient; no comparable data are available for humans. (4)
- EPA has not established a Reference Concentration (RfC) for inorganic arsenic. (5)
- The California Environmental Protection Agency (CalEPA) has established a chronic inhalation reference level (REL) of 0.000015 milligrams per cubic meter (0.000015 mg/m3) estimated from a study indicating decreased intellectual function in 10 year old children exposed to elevated arsenic in drinking water. 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 Reference Dose (RfD) for inorganic arsenic is 0.0003 milligrams per kilogram body weight per day (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. (5)
- 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. (5)

Arsine

- No information is available on the chronic effects of arsine in humans.
- 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. (3)
- EPA has medium confidence in the RfC based on: (1) 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 (2) medium confidence in the database because while there were three inhalation animal studies and a developmental/reproductive study, there were no data available on human exposure. (3)

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 birthweights. 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. (3)

Cancer Risk:

Inorganic arsenic

- Human, inhalation studies have reported inorganic arsenic exposure to be strongly associated with lung cancer. (1,2)
- 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. (1,5)
- 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)
- The International Agency for Research on Cancer has classified inorganic arsenic in their Group 1 of substances that are carcinogenic to humans. (7)
- EPA has classified inorganic arsenic as a Group A, human carcinogen. (5)
- EPA used a mathematical model, using data from an occupational study of arsenic-exposed copper smelter workers, to estimate the probability of a person developing cancer from continuously breathing air containing a specified concentration of inorganic arsenic. 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. (5)
- EPA has calculated an oral cancer slope factor of 1.5 $(mg/kg/d)^{-1}$ for inorganic arsenic. (5)

Arsine

- No cancer inhalation studies in humans or animals are available for arsine. (1)
- EPA has not classified arsine for carcinogenicity. (3)

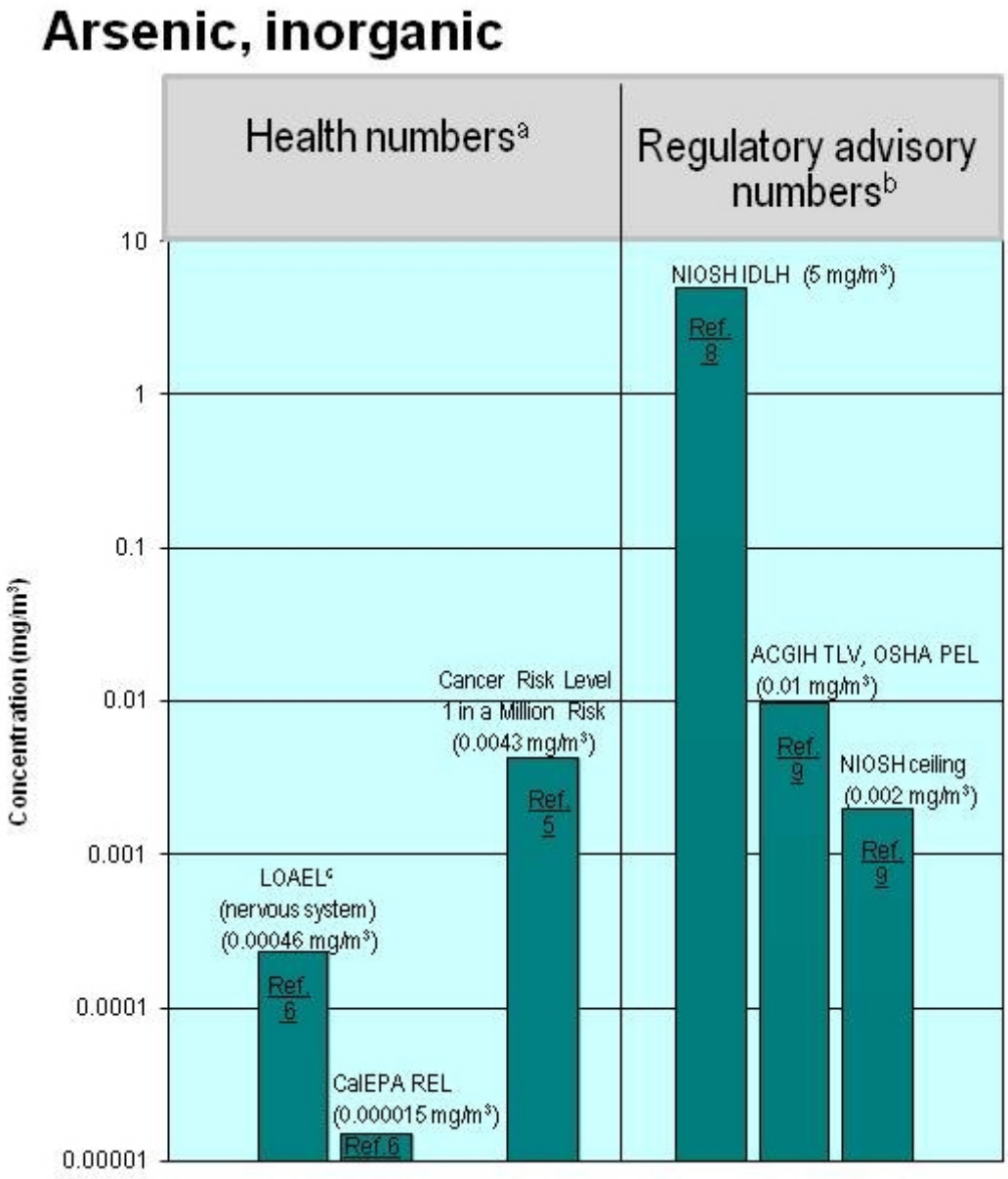
Physical Properties

- 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. (1)
- The chemical formula for arsine is AsH_3, and it has a molecular weight of 77.95 g/mol. (3)
- Arsine is a colorless gas with a disagreeable garlic odor. (3)
- 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)

Conversion Factors (only for the gaseous form):
To convert concentrations in air (at 25°C) from ppm to mg/m^3: mg/m^3 = (ppm) × (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 concentrations in air from $\mu g/m^3$ to mg/m^3: mg/m^3 = ($\mu g/m^3$) × (1 mg/1,000 µg).

Health Data for 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.
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 value--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.

The health and regulatory values cited in this factsheet were obtained in August 2012.
[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. OSHA numbers are regulatory, whereas NIOSH and ACGIH numbers are advisory.
[c] The concentration presented here is the inhalation exposure concentration estimated by California EPA to be associated with a similar chronic arsenic intake as the drinking water concentration selected to represent a LOAEL using information from study identified as the basis for the CalEPA chronic reference exposure level.

Summary created in April 1992, updated in January 2000

References

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4. Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc. Food and Nutrition Board, Institute of Medicine. National Academy Press, Washington, D.C. 2001
5. U.S. Environmental Protection Agency. Integrated Risk Information System (IRIS) on Arsenic. National Center for Environmental Assessment, Office of Research and Development, Washington, DC. 1998.
6. California Environmental Protection Agency (CalEPA). Technical Support Document for the Determination of Noncancer Chronic Reference Exposure Levels. . Office of Environmental Health Hazard Assessment, Berkeley, CA. 2008.
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8. American Conference of Governmental Industrial Hygienists (ACGIH). 2009 Guide to Occupational Exposure Values. ACGIH, Cincinnati, OH. 2009.
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. 2007.

A. *This fact sheet addresses the toxicity of the inorganic arsenic compounds as well as the toxicity of the gaseous arsenic trihydride: arsine.