Arsenic Compounds

Hazard Summary

Arsenic, a naturally occurring element, is found throughout the environment. For most people, exposure to arsenic, including to inorganic arsenic compounds, occurs through their diet. Acute (short-term), high-level inhalation exposure to inorganic arsenic has resulted in respiratory effects (cough, dyspnea, chest pain), gastrointestinal effects (nausea, diarrhea, abdominal pain), and central and peripheral nervous system effects. Chronic (long-term) inhalation exposure to inorganic arsenic in humans is associated with skin, cardiovascular, and neurological effects. Acute oral exposure to inorganic arsenic has resulted in effects on the digestive tract, respiratory tract, central nervous system (CNS), cardiovascular system, liver, and blood and has resulted in death. Chronic oral exposure to elevated levels of inorganic arsenic has resulted in gastrointestinal effects, anemia, peripheral neuropathy, skin lesions, hyperpigmentation, and liver and kidney damage in humans. EPA has concluded that inorganic arsenic is a human carcinogen. Evidence from human studies suggests that exposure to inorganic arsenic by inhalation may result in lung cancer, while exposure by ingestion may result in nonmelanoma skin cancer and bladder, kidney, liver, and lung cancers.

Arsine is a gas consisting of arsenic and hydrogen. It is extremely toxic to humans and can result in general malaise, headaches, apprehension, giddiness, shivering, thirst, vomiting, and abdominal pains with vomiting within a few hours of exposure. Arsine can be fatal if inhaled in sufficient quantities. EPA has not classified arsine for carcinogenicity.

Please Note:

- This fact sheet has a particular focus on inorganic arsenic compounds, including the gaseous arsenic compound arsine. The main sources of toxicity information for this fact sheet are EPA's Integrated Risk Information System (IRIS), which contains information on the carcinogenic effects of inorganic arsenic, including the unit cancer risk for inhalation exposure, and on effects of arsine; as well as the Agency for Toxic Substances and Disease Registry's (ATSDR's) Toxicological Profile for Arsenic.

Uses

- Inorganic arsenic is primarily used as a preservative to make wood resistant to rot and decay, although the use for certain residential items, such as decks and picnic tables, has been phased out. Inorganic arsenic is still used for this purpose in industrial applications. (1)
- The use of arsenic in agricultural or commercial pesticide applications has been restricted and is most recently limited to organic arsenic compounds in a limited number of approved uses. (1)
- Arsenic and its compounds have been used as alloy additives; in electronic devices, such as smartphones; in veterinary medicines; in pigment production; in glass manufacturing; as bronzing or decolorizing agents; in textile printing; in tanning; and other uses. (1,2)
- Until the 1940s, inorganic arsenic was used as a therapeutic agent 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 is a gas that has much more limited usage than the other inorganic compounds. The use of arsine is primarily in electronics and semiconductor components manufacturing, organic syntheses, and lead-acid storage battery manufacturing. (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 commercial and industrial processes. (1)
- General population exposure occurs through ingestion of contaminated drinking water or food. For most people, diet is the largest source of arsenic exposure, with smaller intakes from drinking water and air. Grains, produce, fish, and shellfish are significant sources of arsenic exposure via food. High arsenic levels have been found in fish and shellfish; however, arsenic in fish and shellfish exists primarily as two forms of organic arsenic (i.e., "fish arsenic") that are essentially nontoxic. Inorganic arsenic compounds are the predominant forms to which people are exposed. (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 at metal smelting facilities 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 wood treated with an arsenical wood preservative or dermal contact with wood treated with arsenic. (1)
- Arsine is formed when arsenic comes in contact with an acid. Most exposures to arsine have occurred after unintentional formation of arsine in the workplace of chemical, smelting, and refining industries. (2,9)

Assessing Personal Exposure

- Arsenic can be measured in blood, urine, hair, and fingernails. Measurement of inorganic arsenic in the urine is the best way to determine recent exposure (within the previous 1 to 2 days), while measuring inorganic arsenic in hair or fingernails can detect high-level exposures that occurred over the prior 6 to 12 months. (1)

Health Hazard Information

Acute Effects:

- Inorganic Arsenic (other than arsine)
  - Workers inhaling very high levels of arsenic over a short period have experienced respiratory tract symptoms (cough, chest pain, dyspnea, pulmonary edema), gastrointestinal effects (nausea, diarrhea, abdominal pain), and central and peripheral nervous system effects (peripheral neuropathy, frank encephalopathy). (1,2)
  - Ingestion of high levels inorganic arsenic over a short period has resulted in death. Acute oral exposure to lower levels has resulted in effects on the digestive tract (constriction of the throat, dysphagia, nausea, vomiting, watery diarrhea), respiratory tract (respiratory distress, hemorrhagic bronchitis), CNS (encephalopathy, weakness, delirium), cardiovascular system (hypotension, shock), the liver (increased enzymes and size), and blood (anemia, leukopenia). (1,2)
- Arsine
  - Inhaling high levels of arsine over very short periods has resulted in death; a half-hour exposure to 25 to 50 parts per million (ppm) can be lethal. (2,3)
  - Acute arsine poisoning can cause pulmonary edema, massive hemolysis with subsequent hemolytic anemia, and can cause kidney, liver, and heart damage. (2)
  - The major effects from short-term exposure to lower levels of arsine include headaches, vomiting,

abdominal pains, and effects on the blood, including hemolytic anemia, hemoglobinuria, and jaundice; these effects can lead to kidney failure. (2,3)

Chronic Effects (Noncancer):

- Inorganic Arsenic (other than arsine)
  - Chronic inhalation exposure of humans to elevated levels of inorganic arsenic has been associated with effects on the cardiovascular system and skin (including dermatitis, conjunctivitis, pharyngitis and rhinitis) and with nerve damage. (1,2,4)
  - EPA has not established a reference concentration (RfC) for inhalation exposure to inorganic arsenic. (4)
  - The California Environmental Protection Agency (CalEPA) has established a chronic inhalation reference exposure level (REL) of 0.000015 milligrams per cubic meter (0.000015 mg/m^3) estimated from an epidemiologic study indicating decreased intellectual function in 10-year-old children exposed to elevated arsenic in drinking water and assumptions for exposure and risk from inhalation exposure. The CalEPA REL 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 REL, the potential for adverse health effects increases. (4)
  - Chronic oral exposure of humans to elevated levels of inorganic arsenic has been associated with effects on the gastrointestinal system, blood, skin, eyes, lungs, heart, CNS, liver, and kidneys. Such effects include anemia, peripheral neuropathy, skin lesions, hyperpigmentation, gangrene of the extremities, vascular lesions, and liver or kidney damage. (1,4).
  - Some studies have reported an association between elevated arsenic levels in drinking water and neurocognitive or behavioral test results of school age children. (1)
  - Animal studies have reported effects on the blood, liver, and kidneys from oral exposure to inorganic arsenic. (1,4)
  - The EPA reference dose (RfD) for inorganic arsenic is 0.0003 milligrams per kilogram body weight per day (mg/kg/d) based on effects on the skin (hyperpigmentation and keratosis) and possible vascular effects reported in epidemiologic studies of exposure to contaminated drinking water . 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 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. While extensive, the supporting human toxicity database is somewhat flawed; therefore, EPA has assigned medium confidence to the RfD. (4)

- Arsine
  - Long-term occupational exposure to arsine can damage skin and nerves and can affect the circulatory and hematopoietic systems and result in hemolytic anemia. At higher exposures, it may damage the spleen and kidney. (2, 3)
  - The EPA RfC for arsine is 0.00005 mg/m^3 based on effects on the blood and spleen, including hemolysis, abnormal red blood cell morphology, and increased spleen weight in rats, mice, and hamsters. (3)
  - EPA has assigned medium confidence to the RfC based on medium confidence in the database. While there were three inhalation animal studies and a developmental/reproductive study, there were no data available on human exposure. However, EPA has high confidence in the animal studies on which the RfC is 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. (3)

Reproductive/Developmental Effects:

- Inorganic Arsenic
  - Studies have reported an association between maternal exposure to elevated arsenic levels in drinking water and low birth weights, neonatal death, and infant mortality. (1)
  - Ingested inorganic arsenic can cross the placenta in humans, exposing the fetus to the chemical. (1)
  - Oral animal studies have reported inorganic arsenic to produce developmental effects in offspring, including birth defects and neurobehavioral deficits. (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)
  - A National Toxicology Program (NTP) study found no adverse developmental effects in offspring of pregnant rats and mice exposed to arsine. (6)

Cancer Risk:

- Inorganic Arsenic
  - Human occupational studies have shown that inhalation exposure to inorganic arsenic increases the risk of lung cancer. (1,4)
  - Ingestion of inorganic arsenic in humans has been associated with an increased risk of nonmelanoma skin cancer and an increased risk of bladder, liver, kidney and lung cancers. (1,4)
  - No animal inhalation studies reporting cancer effects from inorganic arsenic exposure were identified. Most oral animal studies have not shown an association between inorganic arsenic exposure and cancer; however, a study in mice involving exposure to inorganic arsenic in drinking water reported an increased risk of lung tumors. (1)
  - EPA has concluded that inorganic arsenic is a human carcinogen. (4)
  - EPA used a mathematical model with 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} per $\mu g/m^3$. 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 their entire lifetime, the person would theoretically have no more than a one-in-a-million increased chance of developing cancer as a direct result. 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. (4)
  - EPA has calculated an oral cancer slope factor of 1.5 per mg/kg/d for inorganic arsenic. The oral cancer slope factor is an estimate of the increased cancer risk from ingestion of 1 mg inorganic arsenic per kg body weight per day over a lifetime. (4)

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

Physical Properties

- Inorganic arsenic is a naturally occurring element in the earth's crust. (1)

- Pure inorganic arsenic is a gray-colored metal. Arsenic combined with elements such as oxygen, chlorine, and sulfur forms inorganic arsenic; inorganic arsenic compounds include arsenic pentoxide, arsenic trioxide, and arsenic acid. (1)
- The chemical symbol for arsenic is As, and it has a molecular weight of 74.92 g/mol. (2)
- The chemical formula for arsine is AsH_3, and it has a molecular weight of 77.95g/mol. (2)
- Arsine is an extremely flammable, colorless gas with a slight garlic-like odor. (2)
- Arsenic combined with carbon and hydrogen forms organic arsenic; organic arsenic compounds include arsanilic acid, arsenobetaine, and dimethylarsinic acid. (1)

Conversion Factors:

To convert concentrations in air (at 25 °C) from ppm to mg/m³:

mg/m³ = (ppm) × (molecular weight of the compound) / (24.45).

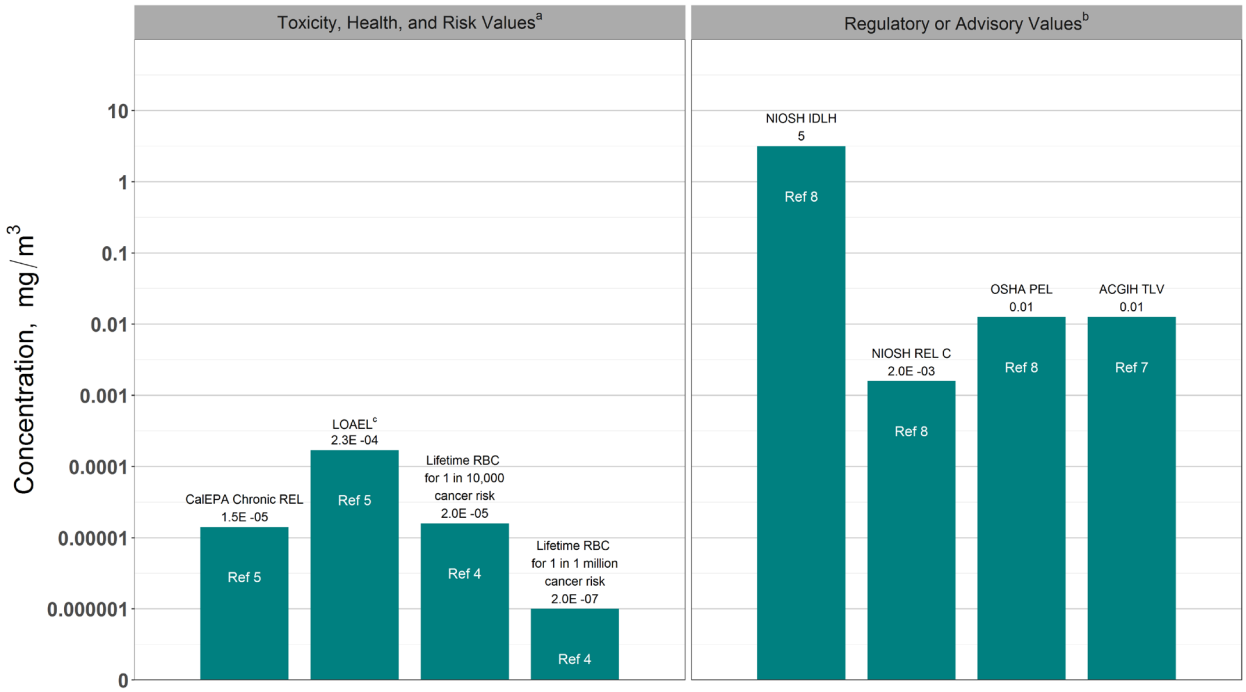
For inorganic arsenic: 1 ppm = 3.06 mg/m³.

For arsine: 1 ppm = 3.19 mg/m³

To convert concentrations in air from µg/m³ to mg/m³:

mg/m³ = (µg/m³) x (1 mg/1,000 µg)

Health Data from Inhalation Exposure (Inorganic Arsenic)



ACGIH TLV — American Conference of Governmental 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) — The lowest dose or concentration at which there was an observed toxic or adverse effect of a target organism distinguished from a normal or untreated organism of the same species.
CalEPA Chronic REL — California EPA Office of Environmental Health Hazard Assessment (OEHHA) chronic reference exposure level (REL) is the concentration at or below which no adverse health effect is anticipated for a lifetime exposure.
NIOSH IDLH — National Institute for Occupational Safety and Health's immediately dangerous to life or health concentration; IDLH values are established (1) to ensure that a worker can escape from a given contaminated environment in the event of failure of the respiratory protection equipment and (2) to indicate a maximum level

above which only a highly reliable breathing apparatus, providing maximum worker protection, is permitted.
NIOSH REL C (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-hour workday or a 40-hour workweek.
RBC (cancer risk-based concentration) — A calculated concentration of a chemical in air to which continuous exposure over a lifetime is estimated to be associated with a risk of contracting cancer not greater than the specified probability (e.g., 1-in-1 million).

[a]Toxicity, Health, and Risk numbers are toxicological values 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 Government or other groups as advice. OSHA numbers are regulatory, whereas NIOSH, ACGIH, and AIHA numbers are advisory.
[c]The concentration presented here is the LOAEL (calculated from the oral level) from the critical study used as the basis for the CalEPA chronic REL.

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