Inorganic Arsenic

TEACH Chemical Summary

U.S. EPA, Toxicity and Exposure Assessment for Children's Health

This TEACH Chemical Summary is a compilation of information derived primarily from U.S. EPA and ATSDR resources, and the TEACH Database. The TEACH Database contains summaries of research studies pertaining to developmental exposure and/or health effects for each chemical or chemical group. TEACH does not perform any evaluation of the validity or quality of these research studies. Research studies that are specific for adults are not included in the TEACH Database, and typically are not described in the TEACH Chemical Summary.

I. INTRODUCTION

Arsenic is a semi-metallic element found in soils, groundwater, surface water, air, and some foods (1). Arsenic occurs naturally in the earth's crust, with higher concentrations in some geographic areas, and in some types of rocks and minerals (1). In its pure form, arsenic is a gray-colored, odorless, and tasteless metal; arsenic is usually found combined with other elements (1). When combined with elements other than carbon, it is called "inorganic arsenic." Arsenic and inorganic arsenic compounds can be emitted into air and then deposited into water and soil during industrial operations such as ore mining and smelting, and during volcanic eruptions and forest fires (1-3). One form of inorganic arsenic, chromated copper arsenate (CCA), has been commonly used as a preservative in wood products to prevent rotting from insects and microbial agents (1, 4). CCA had previously been used in residential settings for decks, playsets, and playgrounds; but such uses have been voluntarily withdrawn by the industry (5). Inorganic arsenic is also found in some Asian folk remedies that claim to relieve constipation during pregnancy, facilitate delivery in women, and relieve asthma in adults and children (6, 7).

Organic (carbon-containing) forms of arsenic (e.g., monosodium methanearsonate and disodium methanearsonate) are used in pesticides for agricultural applications (1), and details pertaining to organic forms of arsenic will not be discussed in this Chemical Summary.

Children are most likely to be exposed to inorganic arsenic compounds from drinking water, or from ingesting contaminated foods or soil (predominantly via hand-to-mouth activity) (1, 4, 8). Ingested inorganic arsenic is metabolized to mono- and dimethylated arsenic compounds prior to excretion in urine. In general, dimethylated compounds are predominantly found in urine. Although methylation of inorganic arsenic is generally considered a detoxification mechanism, some methylated compounds (trivalent forms) are considered very toxic (1, 3).

Regarding human health effects, the primary target of inorganic arsenic exposure is dependent on the route of exposure. For ingestion and dermal (skin) routes of exposure, adverse effects are most often manifested in skin (skin discoloration and lesions) and in the gastrointestinal tract (nausea, diarrhea, and abdominal pain) (1). Ingestion exposure has also been linked to cancer of the skin, bladder, liver, and lung (1). Inhalation exposure has been linked to increased incidence of irritation of mucous membranes and lung cancer (1). Inorganic arsenic is classified as a known human carcinogen (cancer-causing agent) by the U.S. ATSDR (1), U.S. EPA (www.epa.gov/iris/subst/0278.htm) (9), and the IARC (http://monographs.iarc.fr/ENG/Monographs/vol23/volume23.pdf) (10).

II. EXPOSURE MEDIA AND POTENTIAL FOR CHILDREN'S EXPOSURE[1]

Exposure Media	Relative Potential for Children's Exposure[2,3]	Basis[4]
Drinking Water	Higher	Children can be exposed to arsenic via ingestion of contaminated drinking water. Drinking water can be contaminated by natural sources of arsenic or by mining or smelting operations.
Groundwater	Higher	Groundwater can be contaminated with arsenic from natural sources of arsenic, or by mining and smelting operations. When contaminated groundwater serves as a source of drinking water, the drinking water is a concern.
Soil	Higher	Exposure to arsenic-contaminated soil can be a concern if chromated copper arsenate (CCA)-treated wood products are present (e.g., decks, playground equipment), or if there are industrial sources of arsenic (e.g., mines, smelters, production of some agricultural products) near residences or schools. Arsenic occurs naturally in soil, and background concentrations can vary in different regions of the U.S.
Sediment	Lower	In some areas, moderately elevated levels of arsenic are naturally occurring in sediment. The level of exposure from this route is not usually of concern.
Ambient Air	Lower	Arsenic in ambient air is generally of lower concern for most parts of the U.S. Arsenic can be a concern in some U.S. towns, cities, or regions, particularly near metal processing industries such as mining operations and smelters.
Indoor Air	Lower	Arsenic is not generally found in indoor air, although low levels of arsenic may be present from environmental tobacco smoke in homes with people who smoke cigarettes.
Diet	Lower	Arsenic (predominately organic arsenic) can be found naturally in many types of fish and shellfish. Inorganic arsenic has been detected in some foods, including some carrots and rice.

[1] For more information about child-specific exposure factors, please refer to the Child-Specific Exposure Factors Handbook (http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=55145).

[2] The Relative Potential for Children's Exposure category reflects a judgment by the TEACH Workgroup, U.S. EPA, that incorporates potential exposure pathways, frequency of exposure, level of exposure, and current state of knowledge. Site-specific conditions may vary and influence the relative potential for exposure. For more information on how these determinations were made, go to http://www.epa.gov/teach/teachprotocols_chemsumm.html.

[3] Childhood represents a lifestage rather than a subpopulation, the distinction being that a subpopulation refers to a portion of the population, whereas a lifestage is inclusive of the entire population.

[4] Information described in this column was derived from several resources (e.g., 1, 2) including studies listed in the TEACH Database (http://www.epa.gov/teach).

III. TOXICITY SUMMARY[5, 6]

Chronic inorganic arsenic exposure is known to be associated with adverse health effects on several systems of the body, but is most known for causing specific types of skin lesions (sores, hyperpigmentation, and other lesions) and increased risks of cancer of the lung and skin (1).

Other effects of chronic arsenic exposure reported for adults include kidney damage and failure, anemia, low blood pressure and shock, and central nervous system symptoms such as headaches, weakness, and delirium (1, 11). There also may be an increased risk of diabetes in chronically-exposed adults and children (1, 12). Chronic arsenic exposure of children and adults has been associated with adverse liver and respiratory effects, including irritation of mucous membranes (1, 13).

During development, chronic high level inorganic arsenic exposure in humans was associated with increased incidence of preterm delivery, miscarriage, stillbirths, low birth weight, and infant mortality (14-22). Inorganic arsenic exposure during childhood was associated with decreased performance in tests of intelligence (I.Q.) and long-term memory (23-26). Skin lesions associated with As exposure have been reported in children (19, 27, 28).

Acute exposure (14 days or less, including single exposure) of adults and children resulted in gastrointestinal effects, such as nausea, vomiting, abdominal pain, and diarrhea; and neurological effects (e.g., headaches, dizziness) on the central and peripheral nervous system (1, 29, 30). Acute one-time exposure of adults of approximately 22-600 μg/day has resulted in death (1). One case reported death of an infant exposed to approximately 3,430 mg of arsenic (31).

Experimental animal studies have reported teratogenic effects of arsenic, arsenate, or arsenite either alone or when combined with other stressors during fetal development (32-44); teratogenic effects included cleft palate, delayed bone hardening, and neural tube defects. Increased incidence of liver, lung, and other cancers in adult animals was reported following *in utero* exposure to arsenic (45, 46).

Carcinogenicity Weight-of-Evidence Classification[7]: Inorganic arsenic is classified by the U.S. EPA as a known human carcinogen, based on extensive population studies of lung cancers following inhalation exposure, and skin cancers following ingestion of contaminated drinking water in adults; arsenic exposure also may be associated with a higher incidence of bladder, liver, kidney, and prostate cancer. (www.epa.gov/iris/subst/0278.htm, II.A.1) (9). The World Health Organization International Agency for Research on Cancer (IARC) classifies arsenic as a known (Group 1) human carcinogen (http://monographs.iarc.fr/ENG/Monographs/vol23/volume23.pdf) (10).

[5] Please refer to research article summaries listed in the TEACH Database for details about study design considerations (e.g., dose, sample size, exposure measurements).

[6] This toxicity summary is likely to include information from workplace or other studies of mature (adult) humans or experimental animals if child-specific information is lacking for the chemical of interest. Summaries of articles focusing solely on adults are not listed in the TEACH Database because the TEACH Database contains summaries of articles pertaining to developing organisms.

[7] For recent information pertaining to carcinogen risk assessment during development, consult Guidelines for Carcinogen Risk Assessment and Supplemental Guidance on Risks from Early Life Exposure at *http://www.epa.gov/cancerguidelines*.

IV. EXPOSURE AND TOXICITY STUDIES FROM THE TEACH DATABASE

This section provides a brief description of human and animal studies listed in the TEACH Database. For more details about study design parameters, e.g., doses and exposure information, please refer to article summaries in the TEACH Database. Any consideration should include an understanding that exposure levels in animal studies, in many cases, are greater than exposure levels normally encountered by humans.

A. *HUMAN EXPOSURE AND EFFECTS*

- Many studies discussed in the bullets below involved large populations of people living in regions of India and Bangladesh who were exposed to arsenic in drinking water from tube-wells at concentrations over 300 μg/L (47, 48). Numerous studies have been published based on these regional arsenic exposures, providing information on exposures of children (48-52) and health effects in children following ingestion exposure (19, 21, 25, 28, 48, 53-58).
- Studies have shown that arsenic can cross the placenta to the fetus. Arsenic has been detected in placenta (59-61) and cord blood (59, 60). Arsenic concentrations in cord blood correlated with arsenic concentrations in maternal blood (60). In one study, arsenic was not detected in analyses of fetal waste products (62).
- Urine arsenic concentrations are indicative of arsenic exposure within 24 hours with a half life of 4 days of exposure (1, 8), and have been measured in several studies that included children (52, 63-74). The urine excretion rates of arsenic in infants and children were higher than in adults (52, 63). Urine arsenic concentrations in children were significantly associated with residence distance from copper smelters or mines in some studies (64-66, 75), but not others (67, 76). In another study, concentrations of arsenic in children's urine did not correlate with concentrations of arsenic in air (68). Urine arsenic concentrations in children have been measured in large populations (69, 70). Urine concentrations of several arsenic metabolites have also been measured in pregnant women (77) and in children (52, 71-73, 78).
- In addition to urine, arsenic concentrations in blood, hair, and fingernails have also been measured in children (48, 79-90). While the presence of arsenic in urine is an indication of recent exposure (approximately within days), arsenic in hair or fingernails is an indication of exposure within 3-6 months (1). A recent study reported new arsenic reference blood and urine concentrations for German children (90).
- Children's exposure to arsenic from chromated copper arsenate (CCA)-treated wood has been studied (1, 4, 91-97). Arsenic was detected in soil under CCA-treated wood play structures (93, 97), and on hands of children after playing on such wood structures (91, 92, 94-96). See "Considerations for Decision-Makers" section in this Chemical Summary for more information about U.S. EPA risk assessments pertaining to CCA exposure.
- Arsenic has been measured in breast milk (98-101). Arsenic concentrations were generally low in breast milk and within reference ranges in these studies, and did not accumulate in or partition strongly to breast milk, even when arsenic concentrations in maternal blood were high (10 μg/dL) (98). The studies measured total arsenic (99, 101), or inorganic and organic arsenic (98, 100).

- Specific forms or species of arsenic and arsenic metabolites in blood or urine have been measured (52, 73, 89). For example, hair concentrations of As(III) correlated more strongly with duration of exposure to arsenic and age of individual, than hair concentrations of As(V) or total arsenic (89). In urine, methylarsonite (MAs(III)) concentrations were significantly associated with presence of skin lesions (73).
- Concentrations of total arsenic in a broad array of foods have been measured in studies that included consideration of children's diet (8, 102-108). Three studies measured arsenic in baby foods (105-107). The U.S. FDA has measured total arsenic in a wide variety of commercially-available foods in the U.S. as part of the "Total Diet Study" (105, 106). Inorganic arsenic has been detected in some foods that children eat (e.g., carrots and rice) (109, 110). Arsenic was also detected in house dust and soil near homes (111).
- Arsenic was present in products stored in the home that have been reported to be accidentally ingested by children (e.g., rodenticides, or rat poisons) (112). Accidental ingestion of arsenic also occurred when an arsenic-containing herbicide had been transferred to a bottle that was previously used for drinking water, and was mistaken for drinking water (31). Arsenic has been shown to leach from some crayons and some art paints when exposed to acidic solutions that mimic saliva (113).
- Increased rates of pre-term births, stillbirths, spontaneous abortions, and infant mortality have been associated with maternal exposure to arsenic in drinking water (14, 15, 17-22, 50) or to arsenic in air (16). Significantly decreased birthweight was associated with increased arsenic in drinking water (mean arsenic concentration 42 μg/L as compared to <1 μg/L for controls) in a study in Chile (17) but not in a study in Taiwan (maximum concentration 3.6 μg/L) (20).
- Arsenic acid, arsenic pentoxide, and sodium arsenate are known human carcinogens (cancer-causing agents) in adults (1, 114); however, little childhood-specific information is available regarding cancer effects of inorganic arsenic exposure during development. In adults, exposures to these chemicals have correlated with skin cancer and lung cancer (1). Arsenic exposure *in utero* was associated with increased risk of lung cancer in adulthood (115). In children, one study found no significant association between incidence of bone cancers, testicular cancers, soft tissue cancers, and lymphomas with arsenic concentrations (up to 92 μg/L) in drinking water (116). Two studies found no significant association between incidence of leukemia and arsenic concentration in drinking water (116, 117). Another study reported increased expression of genes associated with carcinogenesis (118).
- Indicators of DNA damage and repair have been shown to be increased in children and adults who were chronically exposed to arsenic in drinking water (119-122). For example, chromosomal and DNA damage was increased in lymphocytes from exposed children and adults in India (120, 122).

- Chronic high level exposure to arsenic in drinking water (up to over 500 μg/L) was associated with a increased incidence of skin lesions in children, including hyperpigmentation (dark colorations) and keratosis (a local overgrowth of skin, like a callous) (19, 21, 27, 28, 50, 53-57, 73, 86, 123-127). Studies of skin lesions and exposure to arsenic performed in India and Bangladesh suggested that a possible confounder in these studies was malnutrition of the children (54, 55), and arsenic exposure may be a factor in malnutrition as well (128). However, another study in Chile demonstrated that the incidence of skin lesions was associated with arsenic exposure regardless of nutritional state of the children (123). Two other studies in the U.S. found no arsenic-associated skin lesions in children associated with concentrations of arsenic in drinking water up to 90 μg/L (129, 130).
- Arsenic exposure was associated with impaired neuropsychological development in children (23-26). One study found that higher levels of arsenic in hair of children correlated with lower Intelligence Quotients, or I.Q. (24). Another study in Bangladesh found that lower neurobehavioral test scores in 9-10 year old children were significantly associated with arsenic exposure (25).
- Studies have reported an association between arsenic exposure and peripheral neuropathy (adverse effects in nerves in limbs and fingers) in children in India (28, 58, 131). Increased risk of autism spectrum disorders was associated with the highest 25% of arsenic air concentrations in the San Francisco Bay area (132).

B. *EXPERIMENTAL ANIMAL EXPOSURE AND EFFECTS*

- Arsenic has been shown to cross the placenta in hamsters and mice (133-136). Exposure of pregnant mouse dams by intraperitoneal injection resulted in more arsenic reaching the fetus than when exposure to arsenic occurred via tube feeding (135).
- Experimental animal studies of effects of prenatal arsenic exposure on the development of offspring have been performed. Prenatal exposure of rats to arsenic trioxide via maternal inhalation (41) or maternal gavage (feeding tube) (42) resulted in no observed gross malformations or increased fetal mortality, even at maternally-toxic doses. Similar results were obtained in studies of arsenic-exposed mice and rabbits (43). Inhibition of methylation at the time of arsenic exposure of pregnant rats also significantly increased the incidence of fetal mortality and deformities in their offspring (44).
- Exposure of pregnant animals to arsenic, combined with another stressor, has resulted in an increased incidence of teratogenic effects in their offspring as compared to arsenic exposure alone. For example, prenatal arsenate exposure of hamsters (via continuous maternal injection by an osmostic pump) combined with heat-induced stress, resulted in an increased incidence of fetal malformations as compared to fetuses exposed to arsenic alone (32). Prenatal arsenate exposure (via maternal gavage in mice) combined with restraint-induced stress resulted in a longer delay in eye opening and delayed pivoting behavior in exposed offspring as compared to treatment with arsenate alone (33). Also, a protein-deficient diet combined with arsenic exposure (via single maternal injection) during pregnancy has also resulted in increased incidence of teratogenic effects, e.g., exencephaly (growth of brain outside of skull) and skeletal defects such as fused ribs (34).

- Prenatal exposure to arsenic concurrently with other chemicals showed increased teratogenicity (induction of fetal malformations) of the chemicals in some studies but not others. For example, prenatal exposure to arsenate via maternal intraperitoneal injection, concurrently with dichromate and copper sulfate, was highly teratogenic at doses that were not teratogenic when any compound was administered alone (35). In other studies, concurrent exposure to arsenic, lead, and methylmercury resulted in fetal malformations (e.g., cleft palate and delayed bone ossification, or hardening) that were additive for each chemical alone (36), or were attributed primarily to methylmercury exposure (37).
- Neurodevelopmental defects have been reported following prenatal exposure to arsenic. For example, neural tube defects, exencephaly (growth of brain outside of the skull), and disturbed neurulation (the process of formation of the neural tube during fetal development) were observed following prenatal exposure to arsenate via maternal injection (38, 39, 137). Results in two of these studies suggested that genetic differences in different strains of mice may contribute to greater susceptibility to neurological effects following arsenate exposure (38, 137). Neurobehavioral changes were also observed in adult rats who were exposed to arsenite beginning *in utero* via maternal ingestion of arsenite in drinking water, and continuing throughout lactation and into adulthood (40).
- Increased incidence of liver, lung, adrenal, and ovarian cancer was observed in adult offspring following prenatal exposure to sodium arsenite via maternal drinking water in mice (45, 46, 138, 139). Exposure of mice to arsenic and diethylstilbesterol (DES), or arsenic and Tamoxifen increased the incidence of tumors above that seen with any of the compounds alone (138, 139).

V. CONSIDERATIONS FOR DECISION-MAKERS

This section contains information that may be useful to risk assessors, parents, caregivers, physicians, and other decision-makers who are interested in reducing the exposure and adverse health effects in children for this particular chemical. Information in this section focuses on ways to reduce exposure, assess possible exposure, and, for some chemicals, administer treatment.

- Arsenic can exist in different oxidation states (e.g., arsenite - As^{III} and arsenate - As^{V}) (1). Arsenic compounds can be metabolized (broken down) and methylated in the body following to form monomethylarsonic acid (MMA^{V}), dimethylarsinic acid (DMA^{V}), MMA^{III}, and DMA^{III} (1). The toxicity and excretion rates of different arsenic compounds and metabolites may depend in part on the oxidation state and degree of methylation (1).
- Detailed compilations and analyses of information pertaining to exposure and health effects of arsenic are available in the U.S. ATSDR Toxicological Profile for Arsenic (1). Additional summaries of exposure and health risks for arsenic are available from the U.S. EPA (3, 11). The U.S. EPA cancer assessment is in review for an updated IRIS Chemical Assessment for Arsenic (140).

- Wood products treated with chromated copper arsenate (CCA) are a media of concern for potential exposure of children to arsenic. In December, 2003, the U.S. EPA released a draft document entitled, "A Probabilistic Risk Assessment for Children Who Contact CCA-Treated Playsets and Decks" (4). Arsenic has been detected in soil under decks and near playground equipment that used CCA-treated wood (4, 93, 141) and on hands of children after playing on CCA-treated wood playsets (91, 92, 94-96). A recent U.S. EPA Scientific Advisory Panel recommended the use of coatings on existing playground equipment as a mitigative measure to prevent exposure to CCA (5). As of January 1, 2004, the U.S. EPA recommended cessation of use of CCA to treat wood intended for residential uses, such as playsets and decks (5).
- Drinking water arsenic concentrations have been assessed in several regions as part of the U.S. EPA National Human Exposure Assessment Survey (NHEXAS), which evaluated human exposure to several chemicals on a regional scale (142-144). The U.S. EPA also collected data on arsenic in ground and surface water samples (as sources of drinking water) across the U.S. (3). The U.S. Geological Society also provides information on arsenic concentrations in groundwater samples collected across the U.S. (145).
- In view of the U.S. EPA Maximum Contaminant Level (MCL) of 10 μg/L for arsenic (see Toxicity Summary and Reference Values in this Chemical Summary), caregivers may consider an alternate water supply, e.g. bottled water, where drinking water arsenic concentrations exceed 10 μg/L (or 10 ppb).
- The U.S. EPA reported assessments of air concentrations of arsenic compounds on a regional scale based on 1999 emissions data, and included risk assessments for the air toxics based on chronic exposure; arsenic is one of 177 air pollutants included in this assessment (146). Ranges of concentrations of arsenic in ambient air for regions of the U.S. are available at this Web site (146).
- For physicians, information is available from the U.S. EPA that describes medical diagnosis and treatments for arsenic exposure, and for inorganic and organic arsenic exposure, in "Recognition and Management of Pesticide Poisonings" (147).
- Arsenic is the highest priority chemical listed on the 2005 Priority List of Hazardous Substances for the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) section 104 (i), as amended by the Superfund Amendments and Reauthorization Act (SARA). This is a prioritized list of chemicals of concern, ranking chemicals commonly found at sites listed on the National Priorities list (NPL); there are currently 275 substances on this list (148). The priority of concern is determined by considering the frequency of occurrence at NPL sites, the potential hazard to human health, and the potential for human exposure. Inorganic arsenic was found at 784 of 1,662 U.S. EPA NPL sites (149, 150).
- Consult "Child-Specific Exposure Factors Handbook," EPA-600-P-00-002B, for factors to assess children's drinking water consumption and inhalation rates; a 2006 draft version is also available (151, 152).

VI. TOXICITY REFERENCE VALUES

Inorganic Arsenic

A. Oral/Ingestion

U.S. EPA Reference Dose (RfD) for Chronic Oral Exposure: 3E-4 (or 0.0003) mg/kg-day, based on hyperpigmentation, keratosis, and possible vascular complications in adults (www.epa.gov/iris/subst/0278.htm, I.A.1) (9). Last Workgroup Verification Date 11/15/90.

U.S. EPA Cancer Oral Slope Factor: 1.5E+0 (or 1.5) per (mg/kg)/day; based on skin cancer from drinking water exposure in adults (www.epa.gov/iris/subst/0278.htm, II.B.1) (9). Last Workgroup Verification Date 2/3/94.

U.S. EPA Cancer Drinking Water Unit Risk: 5E-5 (or 0.00005) per (μg/L), calculated using the extrapolation method with time and dose-related formulation of the dose-related model (www.epa.gov/iris/subst/0278.htm, II.B.1) (9). Last Workgroup Verification Date 2/3/94.

U.S. EPA Drinking Water Concentrations at Specified Risk Levels: 1E-4 (or 1 in 10,000), 2E+0 (or 2) μg/L; 1E-5 (or 1 in 100,000), 2E-1 (or 0.2) μg/L; 1E-6 (or 1 in 1,000,000), 2E-2 (or 0.02) μg/L (www.epa.gov/iris/subst/0278.htm, II.B.1) (9). Last Workgroup Verification Date 2/3/94.

U.S. EPA Maximum Contaminant Level (MCL) for Drinking Water: 0.010 mg/L (or 10 μg/L or 10 ppb) total arsenic, based on potential health effects of skin damage, problems with the circulatory system, and possible increased cancer risk (http://www.epa.gov/safewater/arsenic/regulations.html) (153). Standard issued 1/22/01 was effective 1/23/06.

U.S. EPA Maximum Contaminant Level Goal (MCLG): 0. Last revised 1/23/06.

U.S. ATSDR Minimal Risk Level (MRL): 0.0003 mg/kg/day (chronic oral), based on dermatological effects; 0.005 mg/kg/day (acute oral), based on gastrointestinal effects (http://www.atsdr.cdc.gov/mrls/index.html) (154). Last revised 12/2006**.**

B. Inhalation

U.S. EPA Carcinogenic Risk from Inhalation Exposure Air Unit Risk: 4.3E-3 (or 0.0043) $\mu g/m^3$ based on lung cancer in adults. Derived using absolute-risk linear model; IRIS states that unit risk should not be used if air concentration is greater than 2 $\mu g/m^3$ (http://www.epa.gov/iris/subst/0278.htm, II.C.1) (9). Last Agency Verification Date 2/3/94.

U.S. EPA Air Concentrations at Specified Risk Levels: 1E-4 (or 1 in 10,000), 2E-2 (or 0.02) $\mu g/m^3$; 1E-5 (or 1 in 100,000), 2E-3 (or 0.002) $\mu g/m^3$; 1E-6 (or 1 in 1,000,000), 2E-4 (or 0.0002) $\mu g/m^3$; based on lung cancer in adults. (http://www.epa.gov/iris/subst/0278.htm, II.C.1) (9). Last Agency Verification Date 2/3/94.

VII. U.S. FEDERAL REGULATORY INFORMATION

- In January 2001, the U.S. EPA issued a new drinking water standard (Maximum Contaminant Level, or MCL) for total arsenic of 0.01 mg/L (or 10 µg/L). Compliance with the new standard must have been achieved by January 2006 (155).
- The U.S. EPA regulates CCA, arsenic acid, and arsenic pentoxide as Restricted Use Pesticides (RUPs), meaning that only licensed professionals can have access to and apply products containing these chemicals (RUP site) as specified in the RUP report (156); nonresidential uses of CCA are included in the RUP classification.
- In 2002, the U.S. EPA announced that industry had voluntarily decided to discontinue use of arsenic-containing preservatives in pressure-treated lumber products by December 31, 2003. The transition away from use of chromated copper arsenate (CCA) affected virtually all residential uses including play-structures, decks, picnic tables, landscaping timbers, residential fencing, patios, and walkways/ boardwalks. As of January 1, 2004, the U.S. EPA discourage CCA use to treat wood intended for any of these residential uses (5).
- The U.S. EPA requires reporting of quantities of certain chemicals that exceed a defined reportable quantity, and that quantity varies for different chemicals (157). Under the Emergency Planning and Community Right-to-Know Act (EPCRA) Section 313 "Toxic Chemicals," quantities of arsenic pentoxide, arsenic disulfide, arsenic trisulfide, and other inorganic arsenic compounds greater than 25,000 pounds manufactured or processed, or greater than 10,000 pounds otherwise used, is required; under the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA), reporting releases of any quantity of arsenic pentoxide, arsenic disulfide, or arsenic trisulfide exceeding 1 pound is required (157); there are 17 arsenic-containing chemicals for which there are reportable quantities ranging from 1-10,000 pounds (157).
- Arsenic is one of 188 hazardous air pollutants (HAPs) listed under section 112(b) of the 1990 Clean Air Act Amendments and regulated from more than 170 industrial source categories (158).

VIII. BACKGROUND ON CHEMICAL

A. CAS Number: 7440-38-2 (arsenic).

B. Physicochemical Properties: Arsenic is a shiny gray element which occurs naturally in the earth's crust and in industrial processes, and occurs most commonly as metal arsenides. Arsenic can be found in inorganic and organic compounds. Arsenic can exist in different speciations and oxidation states (e.g., arsenite (As^{III}), arsenate (As^{V}), monomethylarsonic acid (MMA^{V}), dimethylarsinic acid (DMA^{V}), MMA^{III}, DMA^{III}) (1). The atomic abbreviation for arsenic is As. Search for arsenic, arsenic acid, arsenic pentoxide, sodium arsenate, chromated copper arsenate, or arsine at *http://chem.sis.nlm.nih.gov/chemidplus*.

C. Production: Arsenic is a naturally occurring element, comprising an average concentration of approximately 0.0002% of the Earth's crust. Arsenic is concentrated in certain minerals such as pyrite, which contains 5-10% arsenic by weight. Arsenic can be released during industrial processes, particularly metal processing (1, 159). Arsine is a short-lived, highly toxic gas produced during some industrial processes, and is the most common form of arsenic in industrial poisoning incidents of adults (1), but is unlikely to be of concern for exposure of children.

D. Uses: The majority (90%) of total inorganic arsenic use in the U.S. had been in the wood industry prior to 2002, where it is used as a preservative called chromated copper arsenate (CCA) (1), though currently use is discouraged in wood products designated for residential uses. It is also used in paints, drugs, dyes, soaps, metals, semi-conductors, agricultural products, and in mining and smelting operations (1, 159). In 2005, total TRI-reported disposals and releases of arsenic were over 1.2 million pounds, and of arsenic compounds were nearly 200 million pounds (160). These estimates of releases should be considered a minimum estimate because they do not include releases from agricultural applications, and from some mining, industrial, and electrical utility uses (160).

E. Environmental Fate: Arsenic does not break down as an element, but it can change form. A variety of natural processes affect its fate and transport in soil and water, including chemical reactions (e.g., oxidation-reduction reactions), ligand exchange reactions, and biotransformations (metabolism by living organisms) (1). The oxidation state of arsenic (arsenate in the +5 state, or arsenite in the +3 state) affects how easily the arsenic is removed from drinking water using treatment systems, with arsenate more easily removed. The solubility of inorganic arsenic compounds vary depending on the compound and the pH of the water (1, 3). Inorganic arsenic has been shown to readily migrate through soil to groundwater (1, 159), and arsenite, being charged, does not migrate as readily (1). Inorganic arsenic has been shown to persist in soil over 45 years (161). Arsenic disperses in the air but will settle out and deposit in soils (1).

F. Synonyms and Trade Names: arsenic, inorganic arsenic, gray-arsenic, arsenicals, arsenate, arsine, and others (for a more complete list, go to (1), page 238).

Additional information on arsenic is available in the TEACH Database for arsenic, and at the following Web sites:

http://www.epa.gov/oppad001/reregistration/cca/
http://www.epa.gov/oscpmont/sap/tools/subject/wood.htm
http://www.epa.gov/safewater/arsenic/index.html
http://www.atsdr.cdc.gov/tfacts2.html
http://www.epa.gov/ttn/atw/nata/

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