# Technical Memorandum

# Technical Briefing Paper on Arsenic

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# 1 Introduction

Arsenic is often thought of as a toxic element, although natural low-level exposure is ubiquitous and without apparent health consequences. This technical memorandum presents a summary of background information of relevance for understanding exposure and risks to human health posed by arsenic in the environment. The focus of this summary is on potential exposures of relevance to the December 2008 failure of a coal ash containment dike at TVA's Kingston Fossil Plant in East Tennessee. This failure resulted in coal ash entering into two sloughs that flow into the Emory River upstream of its confluence with the Clinch River. Coal ash also was deposited above the waterline in the affected sloughs and in and along the banks of the Emory River. Recovery efforts by TVA have been ongoing to reduce migration of ash by river currents or by wind erosion, and to remove ash from the waterways and land. This briefing paper does not specifically quantify risks from arsenic in the coal ash released from this event. Rather, the purpose of this report is to summarize information on the exposure and toxicity of arsenic from the scientific literature and from regulatory agency reports within the available time and resources for this project. This information could be used, along with the site data resulting from ongoing investigations, to support assessment and communication of health risks.

The primary concerns for arsenic in the environment such as at this site are more related to human health rather than ecological issues. The reasons for the lower level of concern for ecological receptors, such as aquatic life, are briefly summarized.

The sections below review:

- Key factors and conditions that affect arsenic mobility and disposition in the environment, with particular focus on solid material such as coal fly ash deposited on land, water, and in sediments
- Exposure to arsenic in the environment via several different pathways of possible relevance to deposited coal ash
- Toxicity of arsenic via inhalation and oral routes of exposure, including the basis of regulatory toxicity criteria for risk assessment
- Perspective on arsenic exposure from naturally-occurring, low-level, background exposures and from biomonitoring data.

## 1.1 Transport and Fate of Arsenic in the Environment

Arsenic is a naturally-occurring element that exhibits complex behavior in the environment. Technically, arsenic is classified as a metalloid because it exhibits properties of metals and non-metals, but it is commonly, although incorrectly, referred to as a heavy metal. The chemical form of arsenic can change depending on pH, presence or absence of oxygen, and the concentration of other elements. Other changes in form are mediated by microorganisms. The forms of arsenic, the conditions that affect its transport and fate, and their typical concentrations in uncontaminated environments are briefly reviewed in this section.

Various sources have ranked arsenic's abundance from 20th to 50th out of 92 elements in the earth's crust (API 1998). Occurrences of pure elemental arsenic are uncommon. Common arsenic-bearing minerals include realgar ($As_4S_4$), orpiment ($As_2S_3$), and arsenolite ($As_2O_3$). Arsenic is also a common accessory element in other minerals, such as arsenopyrite (FeAsS). Igneous rocks are reported to contain from 0.2 to 13.8 mg/kg (or parts per million, ppm) arsenic and average 1.5 ppm (Taylor and McLennan 1985). Shales contain from 0.3 to 500 ppm arsenic and average 14.5 ppm (Kopp 2001).

### 1.1.1 Chemical Forms of Arsenic in the Environment

Natural weathering of parent rock releases arsenic to soil and surface waters. In aquatic systems, soluble inorganic arsenic occurs primarily in one of two oxidation states, generally referred to as arsenate, $As^V$, and arsenite, $As^{III}$. In oxygenated waters, the arsenate species, $H_3AsO_4$, $H_2AsO_4^-$, $HAsO_4^{2-}$, and $AsO_4^{3-}$ are stable, with the abundance of specific species controlled by pH. Under slightly reducing conditions, arsenous acid becomes more abundant, mainly as neutral $H_3AsO_3$ (Cullen and Reimer 1989). The reduction of $As^V$ to $As^{III}$, whether by bacterial mediation or chemical reduction, is relatively slow, so that both forms can be present in anoxic waters. Both forms can also be present in oxic waters as a result of bacterial reduction of $As^V$ and slow oxidation of $As^{III}$.

Arsenic in soil is relatively immobile under oxidizing conditions. Arsenate adsorbs to clay minerals; organic matter; iron, manganese, and aluminum oxides; and phosphate. Adsorption is strongest at neutral to mildly acidic pH. In general, arsenate adsorption decreases with increasing pH (ATSDR 2007). Kopp (2001) reported arsenate adsorption to soil under oxidizing conditions to be four to ten times as strong as that of arsenite. Adsorption of both species is diminished in reducing environments such as in flooded soils and sediments. In reducing environments, arsenate can be desorbed and reduced to arsenite.

Several forms of organic arsenic are present in soils, sediment, and water as the result of bacterially mediated reactions. Microorganisms can transform inorganic arsenic into various methylated organic compounds, some of which are volatile (trimethylarsinous acid [TMA]) (see Table 1). TMA is then rapidly converted to water soluble species, $As^V$ and trimethylarsine oxide (TMAO) (Turpeinen et al. 1999).

**Table 1. Organic arsenic species in the environment**

| Name | Abbreviation | Chemical formula |
|---|---|---|
| Monomethylarsonic acid | $MMA^V$ | $CH_3AsO(OH)_2$ |
| Monomethylarsonous acid | $MMA^{III}$ | $CH_3As(OH)_2$ |
| Dimethylarsinic acid | $DMA^V$ | $(CH_3)_2AsO(OH)$ |
| Dimethylarsinous acid | $DMA^{III}$ | $(CH_3)_2AsOH$ |
| Trimethylarsinous acid | TMA | $(CH_3)_3AsOH$ |
| Trimethylarsine oxide | TMAO | $(CH_3)_3AsO$ |

Plants and animals also metabolize inorganic arsenic species into methylated organic species (primarily MMA and DMA), as well as forming other more complex organic arsenic species. These other forms are described below under food chain uptake and bioaccumulation.

### 1.1.2 Arsenic Concentrations in Background Soil, Sediment, Water, and Air

Arsenic concentrations in soils are strongly influenced by the concentration of arsenic in the parent rock. Shacklette and Boerngen (1984) of the U.S. Geological Survey (USGS) reported arsenic concentrations in U.S. soils, based on 1,257 samples, to range from 0.1 to 97 ppm and average 7.2 ppm. Other summaries (USGS 2008) indicate maximum soil concentrations that exceed 100 ppm in some areas with considerable variation across the U.S. (Figure 1). Soils in areas that are geologically enriched with arsenic-bearing minerals can have arsenic concentrations that exceed the upper end of this range (ATSDR 2007). For Tennessee, a statistical summary by the Tennessee Division of Superfund reported arsenic concentrations in soils to range from 0.1 to 120 ppm based on 197 samples, and estimated a naturally occurring background level for arsenic of 10 ppm (Kopp 2001). Kopp (2001) also reported the results of a study that included analyses of arsenic concentrations in 120 uncontaminated soil samples collected near the Oak Ridge National Laboratory. The average arsenic concentration was 14.7 ppm with a standard deviation of 16.6 ppm.

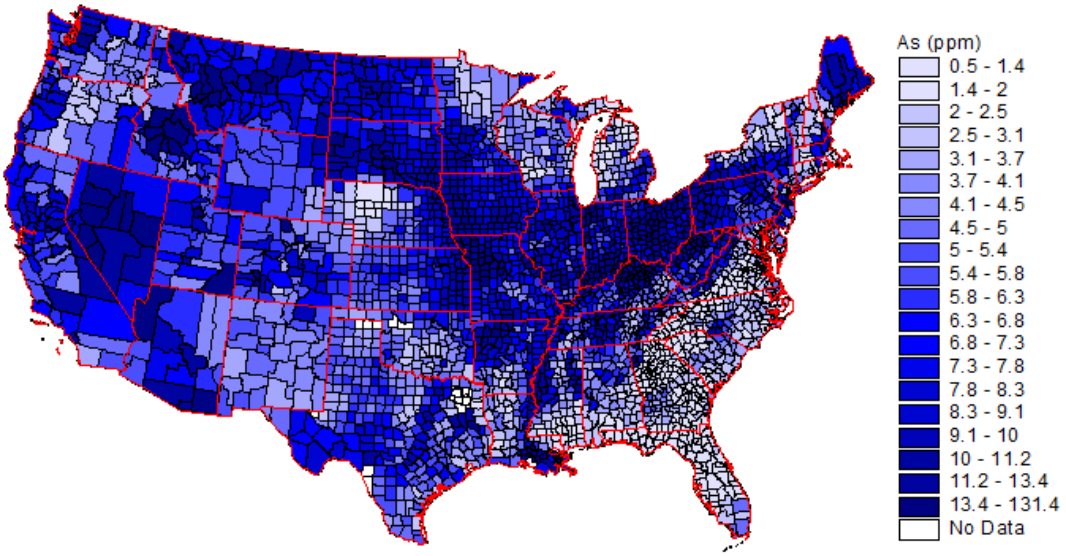


Figure 1. Arsenic concentrations in surface soils of the United States (USGS 2008)

Arsenic in anoxic sediments is usually present as arsenous sulfide or iron-arsenic sulfides (Moore et al. 1988). Woolson (1977) reported typical background arsenic concentrations in freshwater sediments to range from 3 to 11 ppm, similar to concentrations reported for deep sea sediments. Sediment arsenic concentrations are positively correlated with organic matter, clay content, extractable iron and aluminum concentrations, and decreasing particle size.

Total arsenic concentrations in natural surface waters are usually < 10 $\mu$g/L (ATSDR 2007). Arsenic concentrations measured in precipitation have been reported to range from 0.005 to 5 $\mu$g/L (API 1998). Groundwater levels of arsenic can be naturally elevated by bedrock and are typically higher than surface water concentrations. Several regions of the U.S. have elevated well water concentrations including parts of New England, many Western states, and the Midwest (ATSDR 2007). A review of arsenic concentrations in U.S. municipal drinking water supplies found that 33 counties in 11 states had estimated average arsenic concentrations of ≥10 $\mu$g/L, 11 counties had ≥20 $\mu$g/L, and 2 had ≥50 $\mu$g/L (Frost et al. 2003). These statistics do not include unregulated private well concentrations. Historical population exposures to drinking water arsenic concentrations up to 100 to 200 $\mu$g/L have been reported in several parts of the U.S. (summarized by Mink et al. 2008).

Arsenic in ambient air is usually a mixture of particulate arsenite and arsenate (ATSDR 2007). Concentrations of organic species are usually very low except in areas of substantial biotic activity. Mean levels in ambient air have been reported to range from <0.001 to 0.003 micrograms arsenic per cubic meter of air ($\mu g/m^3$) in remote areas and from 0.02 to 0.03 $\mu g/m^3$ in urban areas (ATSDR 2007).

## 1.2 Arsenic in Coal Ash

### 1.2.1 General Characteristics Coal Combustion Ash

Two types of ash are generated during coal combustion: bottom ash or slag, which falls into the bottom of the combustor; and fly ash, which is vented along with the exhaust gases and collected with emission control devices such as electrostatic precipitators. Fly ash represents approximately 74 percent of the generated coal combustion products, bottom ash approximately 20 percent, with the remainder being boiler slag (U.S. EPA 2009a). Despite their similar origin, bottom and fly ash differ in their physical and chemical characteristics. Fly ash consists of small glassy, spherical particles (Gieré et al. 2003; Tishmack and Burns 2004) that may be hollow and empty, or hollow and packed with smaller spherical particles (Tishmack and Burns 2004). Bottom ash, on the other hand, consists primarily of random conglomerations of fused subangular and angular particles that are several orders of magnitude larger in diameter than fly ash particles (Tishmack and Burns 2004).

The chemical composition of fly and bottom ash varies with coal origin and rank. However, both ash types are mainly composed of oxides of silica, aluminum, iron, calcium, magnesium, and sulfur (Tishmack and Burns 2004). Ash from subbituminous and lignite coals contains greater amounts of calcium and magnesium oxides, which are basic minerals that form basic solutions when mixed with water. Bituminous coal ash, on the other hand, consists of higher amounts of pyritic iron than subbituminous or lignite coal ash, which results in acidic solutions when mixed with water (Tishmack and Burns 2004). The “natural pH” of bituminous and subbituminous ash ranges from 4.5 to 6.5 and from 10.6 to 12.3, respectively, when mixed with deionized water in a 1:10 ratio of solid to liquid (Wang 2007).

In addition to the major components, fly ash contains trace elements, including arsenic, whose concentrations are generally enriched relative to the original coal. Enrichment factors for trace elements in fly ash can range between 2 and 100 times (Gieré et al. 2003).

### 1.2.2 Arsenic Concentration in Coal Ash

Total arsenic concentrations in coal combustion ash from energy production utilities are summarized in a Technical Background Document for Report to Congress on Remaining Wastes from Fossil Fuel Combustion (U.S. EPA 1999). According to this report, arsenic concentrations in fly or bottom ashes vary widely. Total arsenic concentrations in coal fly ash were reported to range from 0.0003 to 391 ppm from different data sources (U.S. EPA 1999), although even higher arsenic concentrations, up to 1,385 ppm, have been reported (Tishmack and Burns 2004). Arsenic concentrations in bottom ash, on the other hand, were reported to range from 0.5 to 168 ppm (U.S. EPA 1999). The median arsenic concentrations in different data sources indicated that bottom ash contains somewhat less arsenic than fly ash (the median arsenic concentration in bottom ash was 4.5 to 4.7 ppm, while in fly ash the median was 25 to 57 ppm) (U.S. EPA 1999).

Arsenic concentrations in coal combustion products are dependent on the source of the coal. Arsenic concentrations in fly ash from bituminous coal are typically higher than in fly ash from subbituminous or lignite coals (Eary et al. 1990). Generally, arsenic is associated either with iron sulfide phases in coals, such as pyrite in bituminous coals, or the organic fraction (Eary et al. 1990 and references therein). In laboratory leaching studies, arsenic has been found to be bound to carbonates or to iron-magnesium oxides or in residual fraction (Narukawa et al. 2005).

Hicks (1993) reported on arsenic concentrations in fly ash samples and in air for maintenance workers of air pollution control devices at four different coal-fired power plants. The two plants burning Western subbituminous coal had the lowest concentrations in ash (mean arsenic levels for different work areas of approximately 10 to 70 ppm), the interior bituminous plant had intermediate levels (mean arsenic levels of 140 to 240 ppm), and the Eastern bituminous plant had the highest levels (mean of 170 to 940 ppm). These higher arsenic concentrations are considerably higher than reported for ash from the impoundment at the Kingston site (e.g., generally less than 120 ppm). Hicks (1993) reported that arsenic in the coal ash sampled was in the $As^{V}$, pentavalent form rather than the form emitted by smelters ($As^{III}$, trivalent form). Arsenic in Kingston coal ash is likewise predominantly in the pentavalent rather than trivalent oxidation state (U.S. AERDC 2009).

### 1.2.3 Leachability of Arsenic from Coal Ash

Leachability tests are conducted to assess degree of leaching under rigorous test conditions that provide some indication of the degree to which chemicals in ash might be mobilized in the environment. Leaching of arsenic from coal ash is dependent on several factors, including pH, oxidation-reduction potential, solid to liquid ratio, and the coal origin. Wang (2007) studied the effect of pH on arsenic leaching from a bituminous coal fly ash. Minimum arsenic release was observed at pH between 3 and 7. At pH below 3 and above 7, greater leaching occurred with

decreasing or increasing pH, respectively. Similar results were obtained by EPRI (2008). Arsenic leaching from subbituminous ash, on the other hand, was found to be much lower in the pH range of 6 to 12 than from bituminous ash (EPRI 2008). The high calcium content in subbituminous coal ash has been found to control the leaching of arsenic by formation of calcium precipitates.

Arsenic concentrations in laboratory water leaching tests of fly ash samples have ranged from 10 to 1,290 $\mu$g/L (Narukawa et al. 2005). In this study, the pH of the water used in the leaching experiments was not mentioned, although it was likely neutral. The pH of the fly ash leachates, determined in separate experiments, ranged from 4.1 to 11.8. Similar concentrations in leachates collected from coal combustion product management facilities have been reported. EPRI (2006) reported arsenic concentrations ranging from 1.4 to 1,380 $\mu$g/L with a median of 25 $\mu$g/L for 67 ash leachate samples collected from landfills or impoundments that manage coal combustion products.

$As^{V}$ has been identified as the dominant arsenic species in laboratory leachates (Narukawa et al. 2005; Wang 2007). Similar observations were reported by EPRI (2006) for leachate samples from coal ash landfills and impoundments, although $As^{III}$ was identified as the dominant arsenic species in 4 of 36 leachate samples from bituminous coal ash impoundments (EPRI 2006).

# 2 Exposure to Arsenic in the Environment

Humans and biota may be exposed to arsenic in coal ash released to the river and deposited in sediments and along the shoreline by several possible means under recreational or residential exposure scenarios (Figure 2). Specifically, pathways associated with recreational exposure might include: 1) incidental ingestion or skin contact with ash in nearshore sediments, particularly by those playing on the shoreline; 2) food chain transfer of arsenic in sediments or the water column to fish that are caught and ingested by fishermen; 3) ingestion of arsenic in water while swimming; 4) incidental ingestion of or dermal contact with ash in river bank soil; 5) drying of ash on the shoreline or in exposed sediments resulting in inhalation of windblown dust. In a residential scenario, exposure pathways include 1) possible leaching of arsenic in sediments or soil to groundwater and ingestion of and skin contact with well water, 2) incidental ingestion or skin contact with ash in soil, 3) uptake of arsenic from ash in soil by homegrown produce or watering gardens with arsenic-contaminated water, and 4) inhalation of windblown dust from ash on the shoreline. Overlap between the residential and recreational scenario is also possible for local residents who engage in recreational activities.

The relative importance of these pathways depends on the amount of potential exposure to arsenic and the form of arsenic to which the individual is exposed. As noted above, arsenic released into the environment may bind to various mineral and organic constituents or be transformed into different compounds and forms that differ in degree of absorption and relative toxicity in the body.

TVA has been conducting actions to limit these possible pathways of exposure (e.g., purchase of residential properties affected by ash, remediation of ash in the waterways, windblown dust mitigation) and continues to monitor the environment (e.g., air, surface water, groundwater, sediments, fish tissue) so that potential risks can be assessed and addressed. Monitoring has also been conducted by the Tennessee Department of Environment and Conservation (TDEC) and the U.S. Environmental Protection Agency (EPA).

## 2.1 Uptake and Transformation of Arsenic in Aquatic Life and Ingestion of Fish

Arsenic taken up by aquatic life and accumulated in the food chain primarily occurs in various organic forms, with a low percentage accumulated in the more toxic inorganic form. The fate and uptake of arsenic in aquatic environments has been more extensively studied for marine environments, although the processes are similar in freshwater systems. Arsenic in coal ash released on the shoreline or into water bodies may leach inorganic arsenic into surface water, although, as noted above, the amount is expected to be relatively small under aerobic conditions. Stagnant areas with anaerobic conditions may result in increased leaching, as has been observed for some ash landfills.

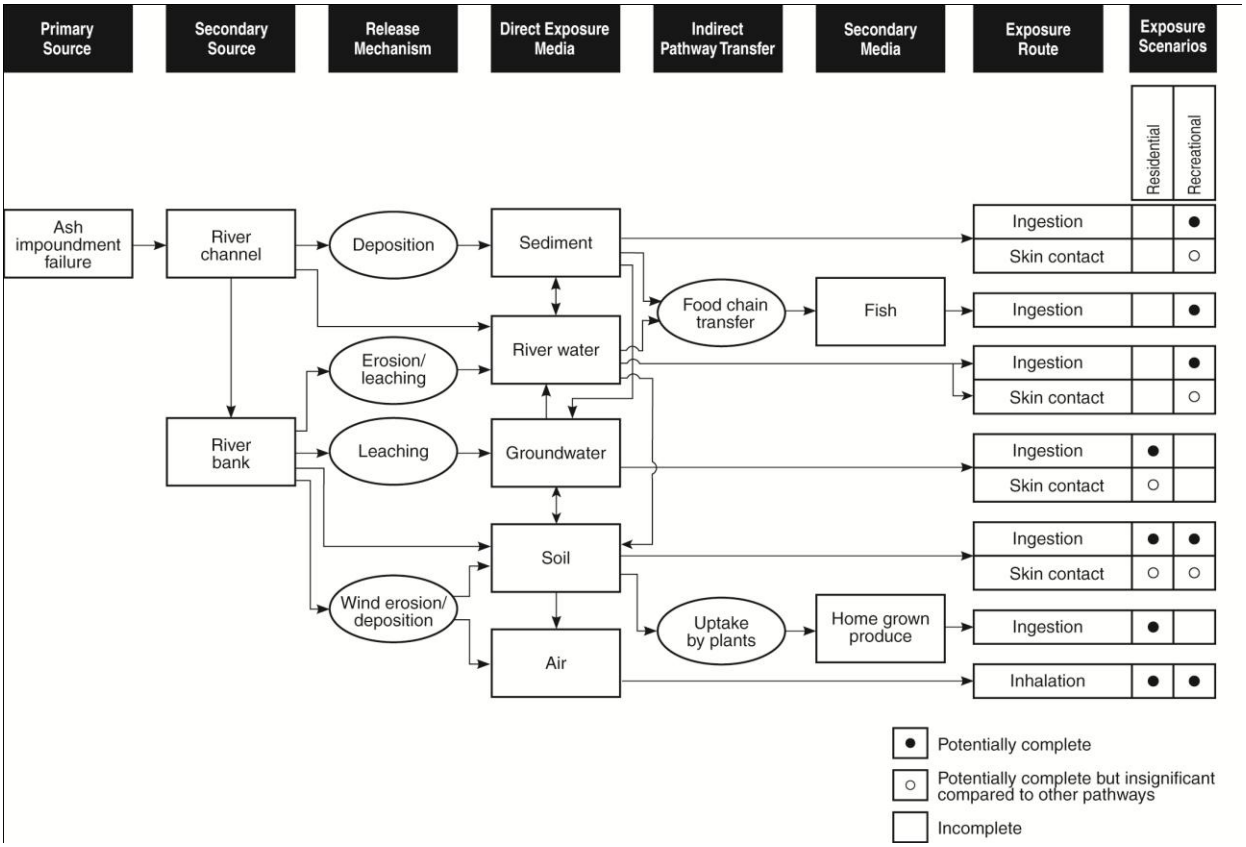


Figure 2. Exposure pathway diagram for the Kingston Fossil Plant Ash Spill

Uptake and transformation of arsenic in the aquatic food chain has been summarized by Borak and Hosgood (2007). According to this review, fish and other organisms take up relatively little inorganic arsenic from surface water compared to organic arsenic forms in their food. Bacteria in sediments, periphytic algae, and planktonic organisms in the water column are the first level in arsenic's metabolic transformation and transfer up the food chain. Phytoplankton and algae reduce and methylate arsenate to form arsenic-containing sugars (arsenosugars) and lesser amounts of DMA and MMA. Arsenic levels in algae can thus be many orders of magnitude greater than in water.

Animals that ingest phytoplankton or algae, such as snails, bivalve filter feeders (e.g., mussels), and some fish, take up the arsenosugars and other arsenic compounds (e.g., MMA, DMA). Organisms may also take up arsenic compounds formed by algae that are released back into the environment with the death and decay of algae. Microorganisms in water or sediments or in the digestive tracts of animals that consume algal arsenic compounds may then transform some amounts of these organic arsenic compounds to more complex arsenic forms, most notably the water-soluble, tri-methylated pentavalent arsenic compound, arsenobetaine or its precursors such as arsenocholine. Fish may also metabolize inorganic arsenic to methylated arsenic compounds, although the predominant form of arsenic in fish tissues is arsenobetaine. Small amounts of trimethyl arsenicals (e.g., trimethyl arsine oxide) may also be formed by methylation

of ingested arsenate by the microbial intestinal flora of fish and by post-mortem bacterial breakdown of arsenobetaine.

Ingested arsenobetaine is excreted essentially unchanged by fish, crustaceans, and mammals, including humans, and thus is considered to be essentially nontoxic. Arsenocholine is of similar low toxicity and is transformed to arsenobetaine by fish and not degraded to MMA, DMA, and inorganic arsenic. Ingested arsenosugars in mollusks or algae are metabolized to DMA. Consumption of these aquatic foods by humans results in DMA excretion in urine (Le et al. 1999). $MMA^V$ and $DMA^V$ in biota are considered of lower toxicity compared to inorganic arsenic. Although small amounts of the more genotoxic forms, $MMA^{III}$ and $DMA^{III}$, may also be present, these unstable intermediate forms are metabolized to the pentavalent forms within the body (Cohen et al. 2006). Ingestion of $MMA^V$ does not result in back transformation to $MMA^{III}$ or inorganic arsenic. Rather, ingested $MMA^V$ is transformed to $DMA^{III}$ and then to $DMA^V$ (Cohen et al. 2006). $MMA^V$ has not been found to be carcinogenic in 2-year animal bioassays. Although $DMA^V$ has been associated with bladder tumors in rats (but not mice) when administered at high doses (e.g., 40,000 to 200,000 $\mu$g/L in drinking water), such effects are considered to occur by a mechanism that is relevant only at high sustained doses (Cohen et al. 2006). Consequently, EPA considers MMA and DMA to be threshold carcinogens with essentially no risk at low doses (U.S. EPA 2006).

Concentrations of various arsenic forms reported in fish have been summarized by Schoof and Yager (2007). Freshwater fish appear to have lower total arsenic concentrations (mean of 0.304 $\mu$g/g, range of 0.025–1.8 $\mu$g/g wet weight) than marine fish (mean of 3.6 $\mu$g/g, range of 0.156–44 $\mu$g/g wet weight) but generally higher percentage of inorganic arsenic (10 percent at the 75th percentile) compared to marine fish (1.6 percent at the 75th percentile). The average amounts of inorganic arsenic in freshwater and marine species are thus similar, despite the differences in concentrations of total arsenic in freshwater versus marine fish. Among the subset of 13 studies in fish reporting levels of the methylated arsenic compounds, MMA was rarely detected, whereas DMA levels were on average 0.01 $\mu$g/g in freshwater fish (four studies of 10 species) and somewhat higher at 0.08 $\mu$g/g in marine fish (12 studies of 17 species).

Following the release of a solid material such as coal ash to water, the amount of soluble inorganic arsenic available for exposure and potential toxic effects is limited by the rate of leaching processes combined with biotransformation of inorganic arsenic in solution to more complex organic compounds by sediment or surface water biota. Consequently, although soluble arsenic at sufficiently high concentrations can be toxic to aquatic life in spills or discharges of high concentration inorganic arsenic solutions, arsenic leaching from solid materials is typically not a major concern for aquatic effects compared to more cationic metals such as cadmium and copper, with considerably higher toxicity. For example, EPA's aquatic life criteria for protection against acute and chronic effects of arsenic are 340 $\mu$g/L and 150 $\mu$g/L, respectively, whereas acute and chronic criteria are much lower for cadmium at 2 $\mu$g/L and 0.25 $\mu$g/L, and for copper at 13 and 9 $\mu$g/L, respectively (U.S. EPA 2009b).

Arsenic and mercury are both transformed into and accumulated as organic compounds in biota; however, unlike mercury, transformation of arsenic in the environment results in accumulation of less toxic compounds. Thus, the potential for toxicity and bioaccumulation of inorganic

arsenic in aquatic organisms is reduced by limitations in migration of arsenic from solids to water in combination with transformation of much of the arsenic into less toxic organic forms. Assessments of health risks to fish consumers should accordingly focus on the small fraction of arsenic in fish tissue that is in the inorganic form, which typically is insufficient to result in exposures of concern for health effects.

## 2.2 Inhalation of Arsenic in Dust

Coal ash, particularly fly ash, is a fine grain material and thus is subject to wind dispersion when dry. As part of the recovery effort, TVA has been covering or stabilizing the surface of exposed ash and minimizing the potential for wind erosion of ash.

Hicks (1993) measured arsenic air levels in work areas of four coal-fired power plants. Among these plants, the Eastern bituminous plant had the highest arsenic concentrations in the fly ash (noted above) as well as the highest arsenic air concentrations, averaging 5–6 $\mu g/m^3$ during maintenance, with the highest concentration from a personal monitor of 380 $\mu g/m^3$. Despite these occasional peak levels, no acute arsenic symptoms from handling ash have been reported in the electric utility industry (Hicks 1993).

Passive re-entrainment of metals in soil into airborne dust results in far lower exposures than for workers handling ash in enclosed spaces within a plant or exposures for historical smelter workers. Moreover, EPA models used to develop soil screening guidance (U.S. EPA 1996) indicate that the level of exposure via particulate inhalation is much lower than by soil ingestion for most chemicals, particularly for metals such as arsenic. Other analyses of background exposures to arsenic in the U.S. concur that passive exposure to arsenic in soil via windblown dust is a minor source of exposure compared to incidental oral ingestion of arsenic in soil and ingestion of background levels of inorganic arsenic in food and water (Petito-Boyce et al. 2008; Meacher et al. 2002).

Air concentrations of arsenic in fine particulates ($PM_{2.5}$, $PM_{10}$) in and around the TVA plant site near areas of the ash spill have been undetectable in many samples, and overall have been similar to national background levels in remote areas[1]. As noted above, nationwide data for arsenic in ambient air summarized by ATSDR (2007) indicate mean air levels of <0.001 to 0.003 $\mu g/m^3$ in remote areas and from 0.02 to 0.03 $\mu g/m^3$ in urban areas.

## 2.3 Dermal Contact with Arsenic in Soil or Water

Dermal contact with soil or ash and subsequent absorption of arsenic through the skin is a lesser route of exposure. EPA guidance on dermal risk assessment of chemicals recognizes that non-lipophilic substances such as metals are only minimally absorbed (U.S. EPA 2004). U.S. EPA (2004) guidance provides dermal absorption information for only two metals, arsenic and cadmium, with dermal absorption fractions of 0.03 (3 percent) for arsenic that is based on a

[1] http://www.tva.gov/kingston/air/index.htm; http://www.state.tn.us/environment/kingston/air/

study in which soluble arsenic was freshly added to soil then held in place on the skin of monkeys for 24 hours (Wester et al. 1993). This study has been updated more recently by research conducted by the same laboratory using aged arsenic in soil from a contaminated site (Lowney et al. 2007). This new study showed undetectable arsenic absorption (<1 percent). As such, the contribution from dermal absorption likely has a minor effect on estimated exposures to arsenic or cadmium in soil. Even with the default of 3 percent, EPA regional screening level calculations for various routes of exposure indicate that arsenic exposure via dermal contact is 10-fold less than for ingestion of arsenic in soil[2]. EPA's soil screening guidance (U.S. EPA 1996) also notes that exposure via particulate inhalation and dermal contact is not considered to approach that of soil ingestion for most chemicals, particularly metals. Absorption via the dermal route must be greater than 10 percent to equal the dose from ingestion exposure (U.S. EPA 1996).

Accordingly, the policy of at least one EPA Region, Region 8, is to evaluate dermal exposure qualitatively and not quantify it in risk assessment. Risk assessments conducted in this region typically do not include this route of exposure (e.g., U.S. EPA and SRC 2001). Even when dermal exposure is calculated in risk assessments for sites, cleanup level decisions for arsenic are usually based on the soil ingestion route only.

Evidence of the negligible effect of dermal absorption is also available from biomonitoring studies at residential arsenic sites. Estimated exposure from soil ingestion and drinking water more than accounted for the measured arsenic exposure (urinary arsenic levels) of children at the Anaconda, Montana, smelter site (Hwang et al. 1997; Walker and Griffin et al. 1998).

Skin absorption of arsenic from water also appears to be low compared to the ingestion route of exposure. Urinary arsenic levels were elevated in residents of a community in Wisconsin with high arsenic levels in their well water; however, after switching to bottled water for drinking, their urinary arsenic levels were no longer elevated even though they continued to contact the well water while bathing, washing, and in other non-ingestion household purposes (Knobeloch 2002).

## 2.4 Ingestion of Arsenic in Soil, Sediments, or Water

Direct ingestion of soils or sediments is the primary pathway of concern for inorganic arsenic originating from solid material such as coal ash that is introduced to soil or sediments. Leaching of arsenic from ash in sediments to surface water may also present exposure via inadvertent ingestion of water while swimming or wading in the river. If coal ash is buried and becomes anaerobic, thereby increasing the leaching rate, groundwater concentrations of arsenic may be elevated. Use of this groundwater for well water would result in ingestion of arsenic in water.

The water pathways of exposure at the Kingston site do not appear to increase arsenic exposure. Except for immediately after the initial spill event, or for brief events such as heavy rainfall or when sediments are highly disturbed (immediately downstream of dredging), arsenic

[2] http://www.epa.gov/region09/superfund/prg/

concentrations in the river have been below the EPA drinking water standard (i.e., 10 $\mu$g/L; U.S. AERDC 2009).[3] Arsenic concentrations at intake points on the river for local drinking water supplies and in finished water have also been below the drinking water standard.[4] The arsenic drinking water standard is intended to be protective of far greater exposure (i.e., consumption of 2 liters of water per day for a lifetime) than would occur during recreational use of the river. The direction of groundwater flow for all drinking water wells located near the Kingston site is from the wells toward the ash disposal area rather than from the ash disposal area toward the residential drinking water wells. Consequently, all drinking water wells near the site are upstream in the groundwater flow and would not be affected. Testing of more than 100 private wells by TDEC has not shown sample results for metals above primary drinking water standards.[5]

An important consideration for arsenic in solid media is the fraction that is available to be systemically absorbed by the body (i.e., bioavailable). Bioavailability describes the fraction of an ingested compound that enters the bloodstream from the gastrointestinal tract, compared to the total amount that is ingested. Because the toxicity of arsenic is based on ingestion of the highly absorbable form of arsenic dissolved in water, the relative difference in bioavailability between soil and water must be considered (U.S. EPA 2007). Considerable evidence from various sites with arsenic in soil indicates that arsenic in soil and dust is much less bioavailable than in water (Ruby et al. 1999; Roberts et al. 2002, 2007; U.S. EPA 2005b; ATSDR 2007). Therefore, arsenic exposure from incidental soil or dust ingestion should be adjusted by a relative bioavailability factor to account for the lower absorption of arsenic in soil and dust compared to arsenic in water.

In risk assessments of arsenic, EPA's default relative bioavailability for arsenic in soil is often 80 percent (e.g., SRC 2002). Lower relative bioavailability values have been considered for sites based on the available scientific evidence. *In vivo* (feeding studies in juvenile swine or monkeys) and *in vitro* (laboratory extraction tests) bioavailability testing results for arsenic in soil from various sites indicates ranges of approximately less than 3 to 62 percent, with few that exceed 50 percent (Ruby et al. 1999; Rodriguez et al. 1999; Roberts et al. 2002, 2007; U.S. EPA 2005b).

Although the more cost-effective *in vitro* bioaccessibility method has not been validated with *in vivo* results for arsenic in soil as it has for lead, validation research on *in vitro* methods for arsenic is ongoing as a partnership among U.S. EPA Region 8, the Department of Defense, and Exponent.

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[3] http://state.tn.us/environment/kingston/surface_water.shtml

[4] http://tn.gov/environment/kingston/pdf/comm_guid/factsheet012610.pdf

[5] http://tn.gov/environment/kingston/pdf/comm_guid/factsheet012610.pdf

## 2.5 Arsenic in Food and Homegrown Vegetables

As in the aquatic environment, the dominant types of arsenic in many U.S. market basket foods, both plant- and animal-based, are the less toxic, organic arsenic forms. Comprehensive surveys of background levels of inorganic arsenic in various food groups (Schoof et al. 1999; Mohri et al. 1990) indicate that the foods containing the highest total arsenic concentrations (i.e., seafood) have relatively little arsenic in the inorganic form (Schoof et al. 1999; Schoof and Yager 2007), and consequently, fish is not a significant contributor to dietary intake of inorganic arsenic for U.S. diets, (i.e., less than 0.1 percent in children ages 1–6 in Yost et al. 2004). Food groups contributing the most inorganic arsenic to the U.S. diet include grains such as rice and, secondarily, fruits (particularly grapes) (Yost et al. 2004; Tsuji et al. 2007). These contributions are a function of the amount consumed and the amount of inorganic arsenic in these foods.

Homegrown vegetables may take up arsenic from soil or soil pore water if coal ash is mixed with soil or if arsenic-contaminated water is used to irrigate gardens. The amount of exposure by these pathways will depend on the concentration of arsenic in the ash or water and the amount of ash mixed with soil or quantity of water applied. Uptake of arsenic varies by plant type and part (Schoof et al. 1999; Yost et al. 2004). Reduced plant growth from low organic matter and nutrients in ash limit the amount of ash in garden soil. Enrichment of arsenic in soil from irrigation with arsenic-contaminated water depends on the climate. Accumulation of dissolved substances in soil is highest for dry climates requiring frequent irrigation, with little dilution from rainfall and high evaporation of moisture from soil which leaves the dissolved substances in the water behind.

Overall, exposure to arsenic in soil via uptake by home-grown produce has been recognized as a lesser pathway of exposure relative to soil ingestion by EPA risk assessments of metals sites (e.g., U.S. EPA and SRC 2001; SRC 2002; Glass and SAIC 1992). Consequently, soil cleanup levels for arsenic that meet risk goals for soil ingestion are also considered protective of other related exposures.

Concentrations of metals in garden soil are typically lower than elsewhere in the yard because of amendment of gardens with compost, topsoil, manure, or other organic matter, which dilute metal concentrations and result in binding of arsenic to organic compounds. For example, at the Vasquez Blvd/I-70 Superfund site in Denver, the relationship between the concentration of arsenic in garden soil and soil elsewhere in the same yard was such that a yard with a soil concentration of 50 ppm would have a garden soil concentration of 18 ppm (U.S. EPA and SRC 2001). Uptake of arsenic by vegetables was low. The increase in arsenic concentration in home-grown produce with increasing concentrations in soil was small, resulting in a linear regression line that was nearly parallel to the x-axis, showing little change in vegetable arsenic concentration with increase in soil concentration (Figure 3; U.S. EPA and SRC 2001). Arsenic concentrations in home-grown produce therefore may not substantially differ from those of store-purchased vegetables.

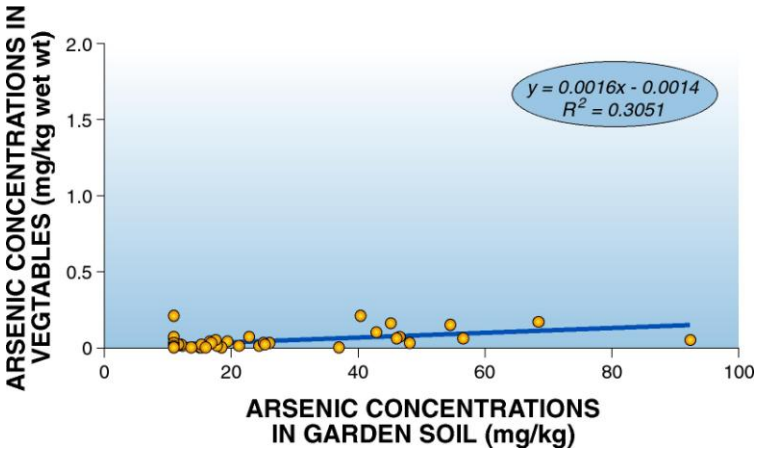


Figure 3. Relationship between arsenic in garden soil and arsenic in vegetables measured at the Vasquez Blvd./I-70 site (modified from U.S. EPA and SRC [2001]).

An experiment in which vegetables were grown in soil with different percentages of mine waste (from 0 to 100 percent) reported uptake of arsenic by lettuce and radishes but no translocation from roots to tomatoes or beans (Cobb et al. 2000). Arsenic concentrations in the test soils were variable and greatly above background soil concentrations. The average arsenic concentration in soil with 0, 25, 50, 75, and 100 percent mine waste was 23, 187, 196, 303, and 408 ppm, respectively, with wide variation within groups (e.g., 86 to 609 ppm for the 25 percent group). The average arsenic concentration in lettuce was 6 times as high at 100 percent mine waste compared to the control, whereas the average concentration in radish root grown in 100 percent mine waste was 12 times the average of the control. Most lettuce and radish plants survived even at the higher concentrations of mine waste, although they were stunted and chlorotic, and thus unlikely to be consumed. Tomato and bean plants showed phytotoxicity even at the 25 percent amendment level with reduced survival. Cobb et al. (2000) note that the nutrient-poor mine waste likely affected plant growth. Lack of organic matter may have also reduced arsenic binding and increased arsenic uptake. Thus, the conditions in this experiment are not representative of exposure to arsenic via garden vegetables in residential gardens that may have been affected by coal ash.

Biomonitoring data (i.e., urinary arsenic levels) of residents from multiple sites with elevated arsenic in their yard soils have indicated 1) no increased exposure by those who had a vegetable garden or consumed homegrown produce (Hwang et al. 1997; UCDEH 1997a,b; Polissar et al. 1990, Tsuji et al. 2005), and 2) that arsenic exposures calculated based on soil ingestion do not underestimate actual exposures in children (Walker and Griffin 1998). Thus, cleanup levels for arsenic calculated using soil ingestion equations are sufficiently protective to account for any additional pathways.

In summary, incidental ingestion of coal ash deposited in soils/sediments is the primary pathway with greatest potential for exposure to inorganic arsenic (most relevant form for health concerns) if such soils and sediments receive regular contact, such as in a residential situation.

Inhalation of windblown dust may also be possible if deposited ash dries and is not stabilized, although passive resuspended dust is considered a lesser pathway of exposure for residential exposure, as is dermal absorption and homegrown vegetable ingestion. Ingestion of arsenic in drinking water will depend on the disposition of coal ash, and whether environmental conditions promote leaching of arsenic into a groundwater source that is used for drinking water. Exposure to inorganic arsenic via fish ingestion is limited by the accumulation of primarily low toxicity organic arsenic forms in fish.

# 3 Arsenic Toxicity

Popular knowledge of the toxicity of arsenic stems from its infamy as a poison since ancient times, as portrayed in popular movies such as Arsenic and Old Lace[6]. Nevertheless, low-level exposure to arsenic is ubiquitous as a result of its natural occurrence, but without apparent adverse effects. Health concerns regarding arsenic exposure are consequently based on extrapolating from health effects reported at high exposures involving more readily absorbable, more toxic forms (e.g., soluble forms of inorganic arsenic, or arsenic trioxide fumes and dust in historical smelters). Thus, health risks from arsenic depend on the amount of exposure and the relationship between arsenic dose and risk of health effects.

## 3.1 Toxicity by Inhalation

Public health concerns for inhalation of inorganic arsenic include direct effects on the lungs as well as systemic effects from arsenic in dust that is swallowed and absorbed in the gastrointestinal tract. The latter route of entry would contribute to systemic arsenic exposure from oral ingestion, with similar health effects as described below for oral toxicity.

The critical effect of concern for public health regulation of airborne arsenic exposure is risk of lung cancer based on observed associations at much higher exposure levels (e.g., time-weighted average air concentrations from 213 to 1,487 $\mu g/m^3$ for low to high exposure groups) experienced by historical smelter or chemical workers with years of exposure (U.S. EPA 1998; ATSDR 2007). Workers were exposed to high levels of arsenic in fumes and dust, along with sulfur dioxide, other carcinogenic metals, and carcinogenic by-products of combustion before the advent of modern industrial hygiene protocols, equipment, or air pollution devices. The smelter worker studies also typically compared the mortality rate from lung cancer to that of the general white male population without correction for the higher rates of smoking in the smelter worker population. In considering this issue, U.S. EPA (1998) acknowledged smoking as an important confounder, but noted that a study of limited smoking data for one of the cohorts indicated that this difference would not have a major effect on the study outcome. However, exposures to other carcinogenic or co-carcinogenic substances and lack of correction for smoking likely increased the apparent risk of lung cancer attributed solely to arsenic.

Based on the epidemiological studies of historical smelter workers in Tacoma, Washington, and Anaconda, Montana, EPA derived an inhalation unit risk factor for inorganic arsenic as a risk of $4.3 \times 10^{-3}$ per $\mu g/m^3$. This relationship is used for evaluating carcinogenic risks associated with inhalation of arsenic for the purposes of public health protection. The unit risk is the upper-bound excess lifetime cancer risk estimated to result from continuous exposure to an

[6] Actually, arsenic was probably not the constituent added to the poisoned wine that dispatched the old gentlemen so efficiently. The old ladies added twice as much arsenic as strychnine, but strychnine is more than twice as acutely toxic as arsenic and the effects of strychnine would have more swiftly and neatly eliminated the gentlemen. The wine also contained a “dash” of cyanide but this compound also is less toxic than strychnine. “Strychnine and Old Lace”, however, doesn’t have the same appeal.

agent at a concentration of 1 $\mu g/m^3$ in air. This model assumes a linear relationship between arsenic in air and risk of lung cancer such that no dose is without some risk of cancer. Risk management decisions are typically based on a comparison of a calculated risk to a specific risk goal within a target risk range (e.g., 1 in a million to 1 in 10,000; U.S. EPA 1991).

Elevated rates of cancer or other diseases related to arsenic for coal fly ash workers within power plants have not been reported in authoritative reviews of the arsenic toxicity literature (e.g., ATSDR 2007). Several factors may account for this difference. Arsenic air levels in the electric utility industry are lower than in historical smelters. The form of inhaled arsenic related to lung cancer in smelter workers is the trivalent form arsenic trioxide, whereas the form of arsenic in coal fly ash samples reported by Hicks (1993) is pentavalent arsenic, which is generally considered a less toxic form of arsenic at higher doses.

At lower exposure levels than in smelters (but still elevated compared to modern exposures), communities near these historical industrial facilities have generally not shown increases in lung or other cancers examined related to arsenic. These facilities typically had a long history of operation pre-dating air pollution controls and would also have emitted other potential lung carcinogens or co-carcinogenic substances (e.g., combustion by-products, polycyclic aromatic hydrocarbons, other carcinogenic metals, sulfur dioxide).

The Tacoma, Washington, community near a former copper smelter (1912 to 1986) is one of the best-studied of such communities. Community residents were studied in numerous health monitoring and epidemiological studies conducted by local and state health departments and the University of Washington (summarized in part by Glass and SAIC 1992). The best conducted studies included: 1) a case control study of lung cancer mortality between 1935 and 1969 in women who lived near the smelter (Frost et al. 1987); 2) a cohort mortality study of lung cancer in individuals who lived near the smelter as children for at least 2 years between 1907 and 1932 (WSDH and ATSDR 1994); and 3) a retrospective cohort study of a number of types of cancer and other causes of death in the same group studied by WSDH and ATSDR (1994) (Tollestrup et al. 2003). Overall, these studies do not indicate an increase in risk of lung or other cancers related to arsenic exposure in this population.

Historical exposures to arsenic near the Tacoma smelter would have been considerably higher than arsenic levels in the community measured after the advent of modern air pollution control regulations and devices. Even in the late 1970s and early 1980s with air pollution controls, air levels in the nearby community averaged 0.8 $\mu g/m^3$ with an occasional elevation to 10 $\mu g/m^3$ (Frost et al. 1987; Milham 1988). Elevated exposures were also apparent in the residential population. Speciated urinary arsenic levels (sum of inorganic arsenic, MMA, and DMA resulting from metabolism of inorganic arsenic) in children during the time of smelter shutdown and shortly afterward in the early 1980s averaged 52 $\mu g/L$ (Polissar et al. 1987) compared to about 7 $\mu g/L$ for the remote population of the Anaconda smelter site measured long after that smelter had shut down (Hwang et al. 1997).

In addition to health studies in Washington, studies have been conducted at other communities near smelting and mining sites, the majority of which have focused on lung cancer (Lyon et al. 1977; Greaves et al. 1981; Rom et al. 1982; CDPHE 1995; Marsh et al. 1997, 1998), although

one study examined skin cancer (Wong et al. 1992). These studies likewise do not indicate an increase in health risks associated with arsenic exposure.

Studies reporting an increased risk in offsite populations involved two smelters in Sweden (Pershagen 1985) and Canada (Cordier et al. 1983), an arsenical pesticide plant in Baltimore, Maryland (Matanoski et al. 1981), and a smelting and mining area in Montana (Newman et al. 1976). Three of these studies (except Newman et al. 1976) found increased risks of lung cancers only in men (Pershagen 1985 evaluated only men). Newman et al. (1976) also reported an elevated rate of lung cancer mortality in women, although this study was of weaker study design and compared lung cancer rates for people living in one area with rates in a reference area without mining and smelting industries. This study had no information on individual exposures, nor much correction for potential confounding factors.

Thus, considering the number of studies conducted on communities living near historical arsenic emitting sources, the overall evidence does not indicate increased cancer risk at low-level arsenic exposures. Airborne arsenic exposures experienced by these populations (e.g., 0.8 $\mu g/m^3$ as an average for Tacoma, Washington) were considerably higher than has been measured at the TVA Kingston site (e.g., <0.005 $\mu g/m^3$).

## 3.2 Toxicity by Ingestion

Knowledge of arsenic health effects from oral exposure is primarily based on high dose exposures from medicinal uses of arsenic, naturally-occurring elevated levels of arsenic in well water used for drinking water, and poisoning case studies. The primary health effects, sensitive effects at lower doses, and associated federal regulatory values for ingested arsenic are presented for noncancer and cancer effects. Because few health effects have been reported for dermal absorption, assumed doses by the dermal route are assessed based on systemic effects associated with the oral route of exposure.

### 3.2.1 Noncancer Effects

Noncancer health effects of inorganic arsenic are summarized below from ATSDR (2007), Tsuji et al. (2004a,b), and Schoof et al. (2004). Short-term exposures to high doses (e.g., >0.05 mg/kg-day) from elevated well water exposure (typically in foreign countries), poisoning cases, or medicinal use result in gastrointestinal upset, swelling of the eyes, facial edema, peripheral neurological changes, liver effects, or cardiac effects (e.g., changes in heart rhythm such as QT prolongation have been observed with injection of arsenic trioxide to treat specific types of leukemia). These symptoms that appear acutely can be reversible even with continued exposure. Peripheral neuropathy may appear or progress after exposure ceases or resolve without sequelae, as reported for use of arsenic trioxide in treating leukemia patients. These effects are not relevant for much lower exposures associated with levels of arsenic in solid media such as soil or coal ash.

The most prevalent effects reported with subchronic or chronic exposure (typically in foreign populations exposed to arsenic in well water and often having inadequate nutrition) involve skin

pigmentation changes (hyper- or hypopigmentation) and wart-like structures in the skin (hyperkeratosis; Tsuji et al. 2004a). Pigmentation changes have generally been reported at lower doses than keratoses in children (age 0–9; Mazumder et al. 1998; Cebrían et al. 1983), and adults exposed chronically (Tseng et al. 1968). Young children do not appear to be more sensitive than adults to the health effects of arsenic on a dose per body weight basis (Tsuji et al. 2004a). The literature indicates that lower doses require longer exposure durations for skin changes and other health effects to appear. Skin lesions appear to be a sensitive effect in populations exposed to elevated arsenic levels, although this finding may reflect the relative ease of identifying skin effects compared with internal effects. However, other effects such as on the cardiovascular or nervous system, when present in populations, are also accompanied by increased occurrence of arsenical skin effects, although not necessarily in the same person. Other effects may include gastrointestinal and liver effects, as well as hematological changes.

Evidence of cardiovascular effects of arsenic is primarily from high-dose exposures associated with contaminated drinking water in foreign countries such as the arsenic-endemic area of Southwest Taiwan or Bangladesh, medicinal arsenic use, or historical industrial emissions of arsenic. Specifically, a unique vascular disease resulting in gangrene of the lower extremities (blackfoot disease) has been observed in Southwest Taiwan but not in other highly exposed populations. Other vascular disorders have been reported for some highly exposed populations in foreign countries. Evidence at lower doses associated with elevated environmental arsenic exposures in U.S. populations is mixed and inconsistent within and among studies. Epidemiological risk ratios for adverse health endpoints are relatively low (typically less than 2.0) and even in studies that find some significant results, other related effects are not significant (e.g., Engel and Smith 1994; Tollestrup et al. 1995; Navas-Acien et al. 2005). Tollestrup et al. (1995), for example, examined coronary heart disease, other heart disease, and stroke in males and females of three categories related to degree of exposure to arsenic from pesticide sprays in orchards. Only one exposure category and effect had a significant hazard ratio: coronary heart disease in males for intermediate exposure. All other categories and cardiovascular diseases were not significant. In the study of people who lived as children near the Tacoma smelter in the early 1900s, ischemic heart disease was found to be significantly increased in the highest exposure category for males only (Tollestrup et al. 2003). However, no increase in atherosclerosis, other heart conditions, or diabetes was found to be related to exposure in males or females. Thus, compared to other factors such as smoking, diet, lifestyle, and BMI, any effect of arsenic on these diseases is likely weak if even present at low exposures.

Peripheral neurological effects of arsenic have been reported in populations experiencing elevated doses, such as in foreign populations consuming arsenic in drinking water (ATSDR 2007). A few studies have also examined effects of arsenic exposure on neurobehavioral development in children. Small decrements in test scores have been noted in children from some populations with elevated arsenic exposures and other health effects related to arsenic poisoning. For example, a study of children in West Bengal reported small decrements in intellectual function tests that were associated with urinary arsenic levels but not long-term well water arsenic concentrations (Von Ehrenstein et al. 2007). Exposures were high (i.e., lifetime average water concentrations ranged from 1 to 870 $\mu$g/L with peak concentrations up to 2,480 $\mu$g/L) and other arsenic-related health effects were noted in this population, many of whom also suffered from nutritional deficiency (Von Ehrenstein et al. 2007). In a more

comprehensive study of a population in Bangladesh, no significant effects of arsenic exposure during pregnancy (urinary arsenic levels of mothers) were found on cognitive or motor development of infants at 7 months of age (Tofail et al. 2009). This study also reported that arsenic exposure was related to many indicators of poor socioeconomic conditions and that these conditions affected child development measures. Not controlling for these indicators, therefore, would have falsely indicated that arsenic exposure affected child development.

Arsenic has also been associated with type II diabetes in highly-exposed populations from Taiwan, Bangladesh, and Mexico (Navas-Acien et al. 2008). An evaluation of U.S. population survey data from the 2003–2004 National Health and Nutritional Examination Survey (NHANES) reported that participants with type II diabetes had a 26 percent higher total arsenic level in urine (corrected for other risk factors for diabetes and the seafood arsenic compound arsenobetaine). Correlations with speciated urinary arsenic forms (i.e., inorganic arsenic and its metabolites) were not examined because of frequent lack of detection for some of the compounds. Nevertheless, it is unclear if type II diabetes at these low arsenic levels is related to arsenic exposure or if diabetes or other related factors affect arsenic metabolism and excretion, or if some other confounding factor may be responsible. The authors note that prospective studies are needed to further evaluate whether this relationship is causal.

For assessing the noncancer hazards of arsenic, EPA has developed a chronic reference dose for skin lesions of 0.0003 mg/kg-day based on the population in the arsenic-exposed area of Southwest Taiwan (U.S. EPA 1993). The lowest observed adverse effect level for skin lesions and possible vascular complications in this population was identified at an arsenic drinking water concentration of 170 $\mu$g/L (equivalent to a daily dose of 0.014 mg/kg-day). The no observed adverse effect level (NOAEL) was set at 9 $\mu$g/L and converted to a daily dose of 0.0008 mg/kg-day. In calculating the reference dose, this NOAEL dose was divided by a factor of 3 to account for database uncertainties. The chronic reference dose is considered protective for up to lifetime exposure even for sensitive individuals.

The EPA toxicity criteria for arsenic are inclusive of *in utero* and early childhood exposure compared to toxicity factors for most chemicals in risk assessment. The population that forms the basis for these values were exposed *in utero*, in infancy and childhood, and all other lifestages. *In utero* exposure in a population exposed to a substance by drinking water would also be much higher than in a population exposed to a substance in soil, because soil ingestion is primarily by young children with comparatively little ingested by adults.

Possible environmental exposures to arsenic in coal ash would result in doses that are well below those at which health effects from arsenic have been observed in exposed populations. For example, to reach the lowest arsenic dose that EPA estimated caused observable effects in the population in Southwest Taiwan, one would have to eat approximately a tablespoon of coal ash every day for 20 years or longer.[7]

[7] Assumes average arsenic concentration in ash of 66 ppm, 2.3 g/cm$^3$ ash density, 70 kg average lifetime body weight, and 50 percent absorption of arsenic in the gastrointestinal tract, which is relatively high for this amount of material ingested.

### 3.2.2 Carcinogenic Effects

A number of epidemiological studies of foreign populations and case reports have associated ingestion of high concentrations of arsenic in well water or historical medicinal uses of arsenic with certain cancers, most notably of the skin, lung, and bladder (ATSDR 2007). Other internal cancers such as of the liver, kidney, and prostate are sometimes mentioned in some studies but less consistently, and may have other confounding risk factors such as endemic hepatitis for liver cancer in parts of Asia.

EPA has derived an oral cancer slope factor (CSF) for assessing risks associated with ingested arsenic exposure. The EPA oral CSF (risk per unit arsenic dose of 1.5 per mg/kg-day) extrapolates cancer risk from high to low doses based on an assumed linear relationship at low doses between arsenic dose and cancer risk, such that no dose is without an assumed risk of cancer. The current oral CSF is based on an ecological study of skin cancer in a large population (>40,000 people) in Southwest Taiwan with lifetime exposure to well water containing elevated levels of arsenic (grouped into low, medium, and high village well water concentrations of <300, 300–600, and 600–1,820 $\mu$g/L; 70 percent of wells had arsenic levels $\geq$ 400 $\mu$g /L; Tseng et al. 1968; Tseng 1977; U.S. EPA 1984, 1998). As an ecological study, this analysis lacked information on individual exposures and had to assign exposures to skin cancer incidence based on median village water concentration before further grouping into the three concentration categories for dose-response assessment.

EPA is currently revising the CSF that will be listed in their Integrated Risk Information System (IRIS) database for use in risk assessment for site remediation. Two EPA assessments have used a higher arsenic slope factor of 3.67 per mg/kg-day (U.S. EPA 2006, 2008). Ranges including even higher values, on the order of 25 per mg/kg-day, have been proposed in draft EPA documents associated with a Science Advisory Board review (U.S. EPA 2005a; U.S. EPA SAB 2007)[8] and in a subsequent draft Toxicological Review document released in February 2010 for a 60-day public comment period (U.S. EPA 2010; 75 CFR 7477–7479). The revised values have been based on studies of lung and bladder cancer in the Southwest Taiwanese population (Morales et al. 2000; 40 CFR 6976-7066; NRC 2001). Analysis of bladder and lung cancer in this population was the basis of the revision of the arsenic maximum contaminant for drinking water from 50 to 10 $\mu$g/L (40 CFR 6976-7066).

The recent re-analyses have evaluated bladder and lung cancer mortality in relation to median well water concentrations of 42 villages (Chen et al. 1985, 1992; Wu et al. 1989). EPA's approach has generally followed that of NRC (2001), assuming a linear relationship between arsenic exposure and lung or bladder cancer with no threshold for negligible risk at low doses (U.S. EPA 2010). The approach also uses a comparison population to "anchor" the lower end of the dose-response curve through one point, which helps produce a linear relationship between dose and risk (Figure 4). Numerous technical comments have been submitted on this approach

[8] http://www.epa.gov/sab/panels/arsenic_review_panel.htm

as noted in the next section[9]. EPA is scheduled to finalize their revised CSF in the fourth quarter of 2010.[10]

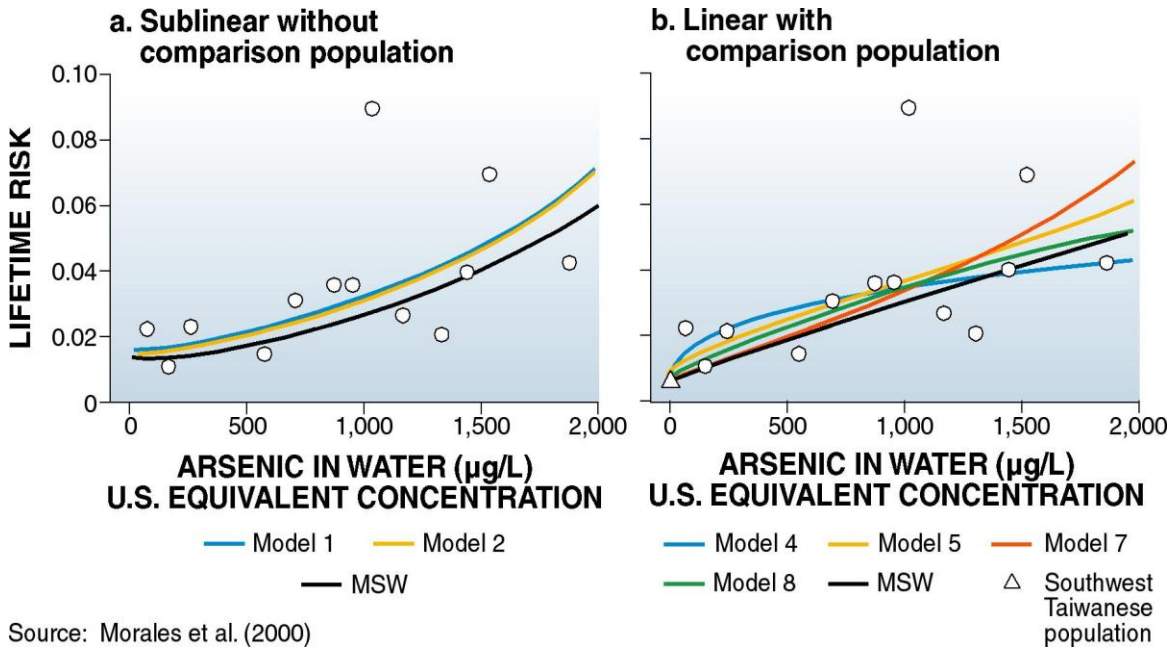


Figure 4. Dose-response relationship for arsenic in well water with male bladder cancer risk for Southwest Taiwan with and without comparison population. Points summarize data for villages grouped by 50 $\mu$g/L increments, i.e., 0–50, 50–100 $\mu$g/L, etc. Modeling was conducted on the full data set (MSW=multistage-Weibull model).

## 3.3 Limitations in the Southwest Taiwanese Database for U.S. Populations

### 3.3.1 Uncertainty in Exposure

Despite the large population size, cancer risks are compared to the median arsenic well concentrations on a village level, thereby incorporating considerable uncertainty in arsenic exposure for individuals, and an inability to attribute individual cancer risks to specific doses (Brown and Ross 2002; Brown 2007). Of the 42 villages, 20 had only one well test and the others had multiple well results. Within some villages, concentrations in different wells varied widely. For example, one village with a median of 30 $\mu$g/L had well water concentrations of 10, 10, 30, 259, and 770 $\mu$g/L (Brown 2007). The cancer incidence of this village attributed to 30 $\mu$g/L was likely increased by exposures to the two higher well water concentrations.

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9 See also technical comments submitted to the EPA Science Advisory Board (SAB) (http://www.epa.gov/sab/panels/arsenic_review_panel.htm)

10 http://cfpub.epa.gov/ncea/iristrac/

### 3.3.2 Effect of Nutritional Deficiency

The extreme nutritional deficiency in the Southwest Taiwanese population and others (e.g., Bangladesh, Inner Mongolia, West Bengal, India) has been shown to increase the toxicity of arsenic (Chen et al. 2001; Milton et al. 2004; Mitra et al. 2004; Gamble et al. 2005, 2007; Spallholtz et al. 2004; Yang et al. 2002; Miyazaki et al. 2005). Although populations with more sufficient diets in South America also show elevated lung and bladder cancer rates when exposed to high doses of arsenic in drinking water (ATSDR 2007), the effect of extreme nutritional deficiency on the shape of the dose-response curve, particularly at low to moderate doses, has not been evaluated sufficiently.

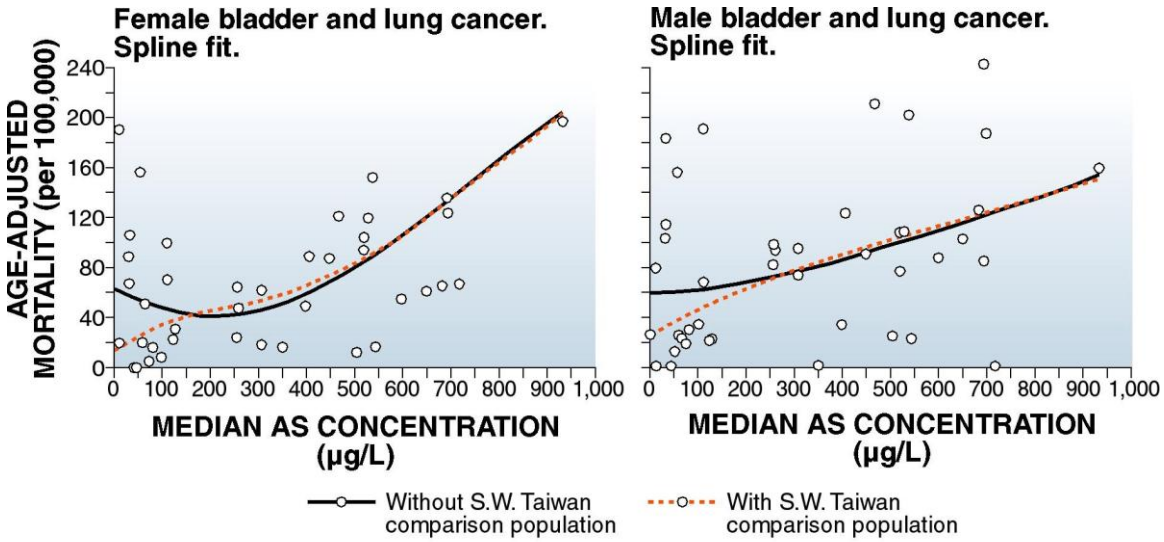
### 3.3.3 Confounding Factors

The Southwest Taiwanese population appears to have an elevated rate of bladder and lung cancers at very low arsenic exposure concentrations, along with increased cancer risks that depend on well type (e.g., artesian versus non-artesian) and possibly other confounding factors or carcinogenic substances contributing to cancer risks, particularly at low doses (Lamm et al. 2003, 2006, 2007; Lamm and Kruse 2005). As shown in Figure 4, at the low end of the exposure concentration range, several villages within the arseniasis-endemic region have much higher rates of cancer than the comparison population used by EPA even at the same arsenic well water concentrations. Lamm et al. (2006) note that certain townships had elevated cancer risks at low and high doses with no significant dose-response relationship between village cancer risk and arsenic well water level; the rest of the townships displayed a dose-response relationship with an estimated lower threshold for risk at about 150 $\mu$g/L.

### 3.3.4 Use of a Comparison Population in Dose-Response Modeling

In their low-dose linear modeling, EPA used a comparison population to represent the unexposed bladder and lung cancer rates in the population. A single data point based on either Taiwan-wide or the Southwest Taiwan region was used to anchor the lower end of the dose-response relationship. As shown by Morales et al. (2000), fixing the lower end of the relationship at this point resulted in linear or supralinear curves rather than the sublinear to threshold shape of the Southwest Taiwanese data (Figure 4). The comparison population approach, however, ignores the wide variation in cancer risk at very low arsenic water concentrations in the Southwest Taiwanese population, which implies that other confounding factors may be present that elevate background cancer risk for some of the villages. Fixing the low end of the relationship at the very low background cancer rate for the comparison population therefore seems inappropriate (Lamm et al. 2006, 2007; Brown 2007). Figures 4a,b and Figure 5 demonstrate the effect of a comparison population on the modeled shape of dose-response relationship between arsenic well water exposure and bladder and lung cancer risk in Southwest Taiwan. Whether or not a comparison population is used by itself does not necessarily have a large effect on EPA's calculated CSF, as long as a linear model is forced through the data (Figures 4 and 5). Similarly, use of a linear or non-linear model does not affect the CSF appreciably if the lower end of the relationship is anchored by the comparison population. The best fit through the actual data without the comparison population, however, is

clearly non-linear with little change in risk at low doses (Figures 4a, 5). This approach indicates a very different relationship between dose and cancer risk at low doses than specified by the linear model using a comparison population.




Source: Brown (2007)

Figure 5. Southwest Taiwan cancer mortality for bladder and lung cancer combined with and without a comparison population

## 3.4 Evidence at Low Doses

Several lines of evidence support much lower risks at low doses (than assumed by a linear model with a comparison population) for the U.S. population. This evidence includes the results of epidemiological studies of low-level arsenic exposure and mechanistic studies of arsenic's mode of action for toxicity and carcinogenicity

### 3.4.1 Epidemiological Studies of Low Level Exposures

The weight of evidence from studies of people with sufficient nutrition in the U.S. and other countries exposed to low doses of arsenic (e.g., water concentrations largely <100 $\mu$g/L) does not indicate a significant increase in bladder cancer risk associated with arsenic exposure (Lewis et al. 1999; Steinmaus et al. 2003; Karagas et al. 2004; Lamm et al. 2004; Kurttio et al. 1999; Michaud et al. 2004; Bates et al. 1995, 2004; Baastrup et al. 2008; Mink et al. 2008; Meliker et al. 2010). A study by Heck et al. (2009) of populations in New Hampshire and Vermont, likewise indicated no significant increased risk for lung cancer and toenail arsenic concentration, although when restricted to a much smaller subset of cases with small cell and squamous cell carcinoma, imprecise but significantly increased risks (i.e., odds ratios with very wide confidence intervals that excluded 1.0) were reported for the second and fourth (highest) of

four toenail concentration groups versus the first or lowest concentration group, with little evidence of a monotonic increase in odds ratio with increasing exposure.

The data from the Southwest Taiwanese population likewise show a sublinear or little to no increase in risk in bladder or lung cancer at lower arsenic doses (Figures 4a, 5; Brown 2007). The point of departure for significant risk in the Southwest Taiwanese population (around 150 $\mu$g/L; Lamm et al. 2006) shows consistency in several analyses of this population (Guo 2007), with Northeast Taiwan (Chiou et al. 2001; Chen et al. 2009, 2010), with the whole population of Taiwan (Guo 2007), and with analyses of data from the U.S. and other countries (Mink et al. 2008; Petito Boyce et al. 2008). Recent updates of lung and bladder cancer cohort studies in Northeast Taiwan by Chen et al. (2009, 2010) reported significantly increased hazard ratios at well water arsenic levels above 100 $\mu$g/L, but not in lower exposure categories in comparison to the reference group (<10 $\mu$g/L). A statistically significant trend in increasing risk was noted over the designated exposure categories; however, the corresponding hazard ratios did not always increase in a monotonic pattern. Furthermore, consistent patterns of increasing risk were not observed for younger age groups when study subjects started drinking water with arsenic levels >10 $\mu$g/L, or for older age groups when subjects stopped drinking water with arsenic levels >10 $\mu$g/L.

A case-control study of lung cancer in Bangladesh found no evidence of increased risk with arsenic water concentrations from $\leq$10 $\mu$g/L to 400 $\mu$g/L in nonsmokers, but a significant increase in risk for smokers in the highest exposure group (101 to 400 $\mu$g/L) (Mostafa et al. 2008).

A criticism of low-level arsenic exposure studies is that they did not involve 40,000 people, as did ecological studies of the Southwest Taiwanese population, and are subject to exposure misclassification which can reduce the statistical power for finding a significantly increased risk (U.S. EPA 2010). To help address the issue of low power of individual studies, a meta-analysis was conducted of eight studies with stronger study designs (e.g., case-control, cohort), involving low-level arsenic exposure (e.g., < 100 $\mu$g/L) and bladder cancer in nutritionally sufficient populations (Mink et al. 2008). Stronger study designs with individual cancer status and exposure information do not require as large a population size as ecological studies for which exposure and cancer rates and average exposures are assigned to groups of people with no knowledge of individual exposures. The meta-analysis concluded that at low exposure levels, arsenic alone was not a significant independent risk factor for arsenic-related bladder cancer observed at high doses (Mink et al. 2008). Moreover, for non-smokers, a consistent but non-significant relative risk estimate less than 1.0 indicated that non-differential exposure misclassification causing regression to the null (i.e., toward 1.0) could not explain the lack of a significant relative risk greater than 1.0. Some evidence indicated that smoking may act as a modifying factor in increasing cancer risk associated with arsenic, but this increase was not significant and more detailed studies are needed to quantify the effect of smoking on arsenic bladder cancer risk. Two more recent case-control studies that examined this issue did not find evidence of a synergistic effect of smoking on the association between arsenic exposure and lung or bladder cancer risk (Heck et al. 2009; Meliker et al. 2010).

Several other low level studies (many from the U.S.) were not included in the meta-analysis by Mink et al. (2008) because they were ecological studies, which have limited ability to evaluate causal associations, studied other endpoints than bladder cancer, or did not report sufficient quantitative detail to be included. These studies reported similar conclusions to those included in the meta-analysis for multiple cancer types (Berg and Burbank 1972), skin cancer (Morton et al. 1976; Wong et al. 1992), leukemia (Infante-Rivard et al. 2001; Moore et al. 2002; Rubin et al. 2007), and bladder cancer (Lamm et al. 2004; Baastrup et al. 2008).

Based on the EPA extrapolation of risk to lower doses, populations near historically high arsenic-emitting facilities would be expected to be at greater risk for lung cancer. Airborne emissions from these smelters resulted in greatly elevated soil arsenic concentrations (≥1,000 ppm in some cases; Glass and SAIC 1992; Hwang et al. 1997). Thus, communities residing near smelters would be exposed by the inhalation route as well as by incidental oral ingestion of dust deposited on surfaces and soil. Both inhalation and oral routes of exposure to arsenic have been associated with lung cancer. Nevertheless, as noted above for inhalation toxicity, the weight of evidence does not indicate increased risk of lung cancer or other arsenic-related cancers (when studied) in these populations. In addition to the above mentioned studies, Wong et al. (1992) conducted an ecological study of skin cancer in four Montana counties including a smelter county (Deer Lodge containing the Anaconda smelter), a mining county (Silver Bow containing a mining area), and two reference counties. Skin cancer rates were higher in the reference counties than the smelting or mining counties, but within rates reported elsewhere in the U.S. Thus, the overall evidence does not indicate increased rates of cancer in communities with historical exposure to these arsenic emitting facilities.

### 3.4.2 Cancer Mode of Action at Low Doses

Considerable knowledge has accumulated from *in vivo* and *in vitro* toxicological studies regarding the various modes of action of arsenic, all of which would indicate a sublinear dose-response relationship with a threshold dose for significant cancer risk at low doses (Schoen et al. 2004; Snow et al. 2005; Kenyon et al. 2008; Wang et al. 2009; Suzuki et al. 2008, 2010; Gentry et al. 2010). Efforts are also ongoing to develop biologically-based models of the kinetics and dynamics of arsenic in the body to more realistically evaluate the effects of arsenic and its metabolites at low doses (Kenyon et al. 2008; Kitchin and Conolly 2010). The U.S. EPA (2005c) cancer risk guidance allows the use of alternative dose-response models for substances with non-linear modes of action. Alternative methods such as margin of exposure analyses indicate that predicted risks associated with background exposures would be negligible, as indicated by the low-level epidemiological data (Petito-Boyce et al. 2008). However, in re-evaluating the arsenic CSF, EPA interpreted their 2005 cancer risk guidance as specifying use of a default linear model if uncertainty exists concerning the mode of action, and that uncertainty is associated with the multiple modes of action for inorganic arsenic and its metabolites (U.S. EPA 2005a; 2010). The SAB concurred with EPA's use of a linear model but also recommended that EPA evaluate non-linear models as well (U.S. EPA SAB 2007). U.S. EPA (2010) stated that use of non-linear models does not change the estimated risk by much; however, if a comparison population is being used to anchor the dose-response curve, the resulting relationship will still be close to the linear dose-response relationship (see Figures 4b, 5).

## 3.5 Implications of Revised Oral Cancer Slope Factor

With the current CSF, estimated risks for drinking water and diet are already slightly above EPA's target risk range of 1 in a million to 1 in 10,000 (Figure 6; Tsuji et al. 2007). Application of a 17 times higher CSF of 25.7 per mg/kg-day would suggest that typical water, soil, and dietary intakes at unavoidable background levels would all be well above acceptable risk levels. EPA's current preliminary remediation goal for arsenic in soil of 0.43 ppm is already below natural background levels in most of the U.S. (based on a 1-in-a million target risk).

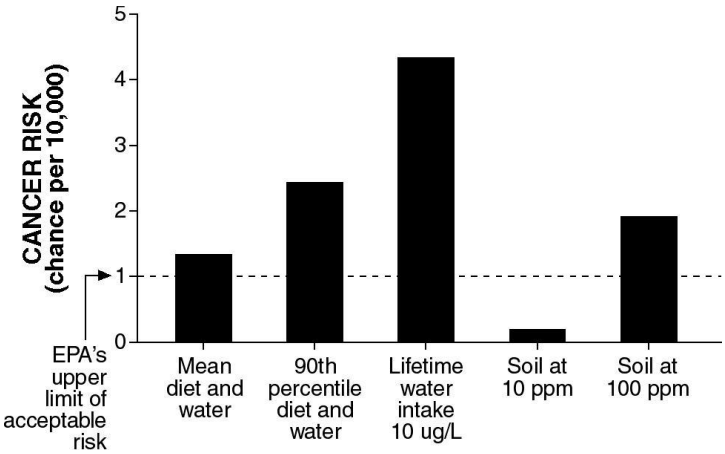



Figure 6. Comparison of hypothetical cancer risk for different exposures based on the current EPA arsenic CSF (modified from Tsuji et al. [2007]). Soil exposures are based on U.S. EPA default assumptions for reasonable maximum exposure (see Tsuji et al. [2007]).

# 4 Perspective from Background Inorganic Arsenic Exposure and Biomonitoring Data

Regardless of the magnitude of calculated risks for environmental arsenic exposures based on current or proposed changes to regulatory guidelines, background exposures to arsenic provide some perspective on the nature of such exposures at low doses. The primary source of exposure to arsenic in the U.S. is ingestion of water and food, rather than soil or air (Meacher et al. 2002; Petito-Boyce et al. 2008). Even for an arsenic soil concentration of 100 ppm, daily intake of arsenic from water at the revised arsenic water standard of 10 $\mu$g/L would result in far greater exposure than from inadvertent ingestion of soil based on default EPA reasonable maximum exposure assumptions (Figure 6; Tsuji et al. 2007). Exposure to soil at 100 ppm, based on conservative EPA default assumptions, is also within background variation in inorganic arsenic exposure from the diet and water.

Biomarker studies of inorganic arsenic metabolites in urine provide additional evidence that even exposure to somewhat elevated arsenic levels in soil is indistinguishable from background inorganic arsenic exposure such as from diet and water. Unlike exposures to arsenic in drinking water (e.g., Valentine 1994; Hinwood et al. 2003), biomonitoring studies of arsenic exposure in children at sites with arsenic in soil have generally not found significant correlations between soil arsenic concentrations and the most reliable biomarker of recent arsenic exposure, urinary arsenic level (specifically, "speciated" arsenic, which is the sum of arsenic forms in urine that result from ingestion of inorganic arsenic in soil) (UCDEH 1997a; Tsuji et al. 2005). Correlations, when significant, are from sites with much higher soil arsenic levels (more than 300 ppm at the Anaconda smelter site), and even for these sites, correlations are weak, and the impact of soil arsenic on increasing arsenic exposure is relatively small (Hinwood et al. 2004; Hwang et al. 1997).

An exposure study was conducted at the Bingham Creek site in Utah (UCDEH 1997a) that involved nearly 700 children who were exposed to arsenic in soil from alluvial deposition of tailings (geometric mean of 27 ppm, 95th percentile of 75 ppm, maximum of 623 ppm). No significant relationship was reported between soil arsenic level and speciated arsenic levels in urine. Geometric mean urinary arsenic levels for subareas ranged from about 3 to 7.7 $\mu$g/L (ppb) and geometric mean soil concentrations ranged from 22 to 52 ppm. Urinary arsenic levels were related to arsenic concentration in tap water (arsenic levels in water were relatively low; 95 percent <8.3 $\mu$g/L). The investigators surmised that the lack of correlation of urinary arsenic with soil arsenic was a result of greater variation in exposure to inorganic arsenic from background diet and water than from soil at the site (UCDEH 1997a).

A study of a community with arsenic in soil from former pesticide manufacturing investigated approximately half the population of children younger than 7 years old and included almost a quarter of the total population (439 participants) (Tsuji et al. 2005). Speciated urinary arsenic levels were low (mean 3.9 $\mu$g/L, range 0.89 to 19.9 $\mu$g/L) and similar to unexposed populations, despite average soil arsenic concentrations on properties of up to 340 ppm (geometric mean of about 20 ppm, with most properties <100 ppm). No significant correlations were found between

speciated urinary arsenic levels and soil arsenic levels for the subset of participants with soil data, although correlations were noted for certain staple food items that typically have more inorganic arsenic.

In the residential community near the Anaconda Smelter site (geometric mean soil arsenic level of 286 ppm), significant but relatively weak correlations (r = 0.12 to 0.25) were reported between speciated urinary arsenic in young children (approximately 300) and measures of arsenic in soil (Hwang et al. 1997). The predicted increase in urinary arsenic level resulting from arsenic in soil was small (0.85 $\mu$g/L increase for a change in soil arsenic from 10 to 100 ppm).

A weak association (Spearman correlation coefficient of 0.39) was reported for arsenic concentration in soil and inorganic arsenic in urine for 55 people (all ages combined) in Australia, living in areas with arsenic soil concentrations ranging from 9 to 9,900 ppm (Hinwood et al. 2004). When the data were stratified into soil concentration categories, increases in urinary inorganic arsenic concentration were apparent only for soil concentration categories greater than 600 ppm.

Based on the above studies, the actual contribution of arsenic in soil to urinary arsenic is small compared to the natural variation in urinary arsenic levels as a result of diet and water, the primary sources of inorganic arsenic exposure for the general population (Schoof et al. 1999; Meacher et al. 2002; Yost et al. 2004; Meliker et al. 2006; Pellizzari and Clayton 2006; Georgopoulos et al. 2008; Tsuji et al. 2007).

As reviewed by Tsuji et al. (2007), normal background dietary arsenic exposures have not been reported to cause arsenical health effects or risks of cancer, although comprehensive studies have not been performed. Lung and bladder cancer rates were not found to be elevated in populations (e.g., Japan versus U.S. or Asians versus other ethnic groups in San Francisco or Los Angeles) with likely higher dietary arsenic exposures because of greater intakes of staple food items that tend to have higher inorganic arsenic concentrations (e.g., rice) (reviewed by Tsuji et al. 2007).

# 5 Conclusions

The primary pathway of exposure to arsenic in solid material like coal ash that is released to the environment is direct ingestion of soil/sediments, if deposited in areas frequently contacted by people. By comparison, lesser pathways of exposure include inhalation of resuspended dust from soil, dermal contact, or ingestion of homegrown vegetables. Because the majority of arsenic forms accumulated in fish are relatively non-toxic, assessments of this pathway must consider the smaller fraction in the inorganic form. Inorganic arsenic is not readily mobile under aerobic conditions in surface soil or sediments, but anaerobic conditions in landfills or possibly in buried sediments may result in arsenic becoming more mobile and migrating to groundwater. Water exposures would depend on the extent of such leaching and whether the affected groundwater is being used for drinking water.

Exposure to arsenic in solid media is reduced by the binding of arsenic to other minerals or organic matter. As a result, bioavailability of arsenic in soil relative to water must be considered when assessing risks based on toxicity associated with more soluble/absorbable arsenic forms.

Health risks are assessed for arsenic based on observations of health effects observed with high exposure to the more toxic inorganic arsenic form. Endpoints typically assessed include the risk of lung cancer by inhalation and skin cancer by oral ingestion. Toxicity criteria for calculating cancer risks for inhalation or oral exposure to inorganic arsenic assume that risks observed at high doses can be extrapolated to low doses, but substantial evidence indicates that such extrapolation may greatly overestimate risk at low exposures. EPA is currently revising the oral cancer slope factor for arsenic based on bladder and lung cancer rates observed in the same population assessed earlier for skin cancer (Southwest Taiwan). This revised value could result in the arsenic drinking water standard and normal background levels of arsenic in diet and water exceeding acceptable regulatory risk levels. A number of uncertainties are associated with extrapolating risks observed at high exposures to more relevant lower exposures. Evidence from low-level epidemiological studies and arsenic's mode of action for toxicity and carcinogenicity provide additional support of lower risks than predicted at lower exposure levels.

Regardless of the change in regulatory criteria, normal background exposures to arsenic in diet and water help provide perspective on exposures to arsenic in soil. Biomonitoring studies of residential communities living on arsenic-contaminated soils indicate little relationship between arsenic in soil and measured biomarkers of exposure, except when arsenic soil concentrations are high (e.g., 300 ppm). A lack of measurable increase in arsenic exposure from soil is consistent with such exposures being only a fraction of the normal ranges from background inorganic arsenic in diet and water.

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