Human Health Risk Assessment to Support Site-Specific Soil Remediation Levels for Arsenic, Copper, and Lead at the United Verde Soil Program

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January 22, 2015

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ACRONYMS AND ABBREVIATIONS

A.A.C.	Arizona Administrative Code
ADHS	Arizona Department of Health Services
AIHC	American Industrial Health Council
ADEQ	Arizona Department of Environmental Quality
ATSDR	Agency for Toxic Substances and Disease Registry
BHP	BHP Copper Inc.
CalEPA	California Environmental Protection Agency
CFR	Code of Federal Regulations
CSF	cancer slope factor
UVSP	United Verde Soil Program
dl	deciliter
DRW	Douglas Reduction Works
DTSC	Department of Toxic Substances Control
FMC	Freeport Minerals Corporation
HI	Hazard Index
HQ	Hazard Quotient
IEUBK	Integrated Exposure Uptake Biokinetic Model
IRIS	Integrated Risk Information System
m^3/kg	cubic meters per kilogram
mg/cm^2	milligrams per square centimeter
mg/day	milligrams per day
mg/kg	milligrams per kilogram
mg/l	milligrams per liter
ODEQ	Oregon Department of Environmental Quality
PRA	probabilistic risk assessment
RBA	relative bioavailability
RfD	Reference Dose
SSRL	Site-Specific Soil Remediation Level
µg/dl	micrograms/deciliter
USEPA	United States Environmental Protection Agency
VRP	Voluntary Remediation Program

EXECUTIVE SUMMARY

Freeport Minerals Corporation (FMC) is undertaking a soil sampling and remediation program in the historical areas of Clarkdale, Arizona near the former United Verde copper smelter. A map of the project area is included as Figure 1. The smelter operated between 1913 and 1953 just northwest of historical Clarkdale. FMC will perform the sampling and remediation program under the Arizona Voluntary Remediation Program (VRP). As part of this remediation effort, residential use Site-Specific Remediation Levels (SSRLs) for arsenic, copper and lead of 30, 9000, and 425 mg/kg, respectively, in soil are proposed. These same SSRLs have been previously approved by the Arizona Department of Environmental Quality (ADEQ) for similar soil sampling and cleanup programs in Ajo, Bisbee and portions of Douglas, Arizona. In this report, probabilistic risk assessment (PRA) methods were used to verify that cumulative cancer risk and non-cancer hazards associated with these proposed Clarkdale project area SSRLs will be consistent with ADEQ health risk criteria, including a cumulative cancer risk less than or equal to 1E-05 and non-cancer hazards less than or equal to 1. Chemical exposure circumstances at the Clarkdale project area are virtually identical to those with the Ajo, Bisbee and Douglas projects. PRA methods are specifically allowed for site-specific health risk assessment under Arizona regulation (Arizona Administrative Code R18-7-206 (B)). The PRA analysis calculated cumulative cancer risks associated with the proposed SSRLs of 1E-05 (1 in a 100,000) and a maximum non-cancer Hazard Index of 1, consistent with ADEQ acceptable risk criteria.

1.0 INTRODUCTION

Corporate predecessors, subsidiaries, and divisions of FMC owned and operated historical mining and processing operations located in and near the towns of Jerome and Clarkdale, Yavapai County, Arizona. A former copper smelting site is located near Clarkdale. FMC now plans to implement a soil sampling and remediation program, referred to as the United Verde Soil Program (UVSP), at selected residential, publicly-owned, and commercial properties in and around the historical area of Clarkdale. The UVSP will be performed with oversight by the Arizona Department of Environmental Quality (ADEQ) under ADEQ's Voluntary Remediation Program (VRP). The objective of the UVSP is to identify and remediate any soils that may exceed applicable soil cleanup levels for lead, arsenic, and copper, the metals most associated with former mining and processing operations. The purposes of this risk assessment report are twofold: First, to propose residential use, Site-Specific Soil Remediation Levels (SSRLs) for lead, arsenic, and copper for use in implementing the UVSP, and second, to demonstrate that these cleanup levels meet human health risk criteria established by the ADEQ.

The remainder of this report is organized as follows:

- Background
- Exposure Assessment
- Toxicity Assessment
- Risk Characterization
- Uncertainty Analysis
- Summary and Conclusions

2.0 BACKGROUND

SSRLs for arsenic, copper, and lead of 30, 9000, and 425 milligrams/kilogram (mg/kg), respectively, were previously approved by the ADEQ for residential properties that have been sampled and remediated as part of VRPs being performed in the vicinity of FMC's Ajo and Bisbee smelter sites, hereinafter referred to as "Ajo/Bisbee". The same SSRLs were also recently approved by ADEQ for a similar soil sampling and remediation program in a portion of Douglas (ADEQ, 2013). The Ajo/Bisbee SSRLs were based on a site-specific risk assessment (URS, 2007a,b; Brown and Caldwell [BC], 2009).

FMC proposes to apply these previously approved SSRLs to the UVSP; however, FMC has requested Damian Applied Toxicology, LLC (DAT) to review the input parameters that were used in the Ajo/Bisbee and Douglas risk assessments to ensure that they remain applicable to the UVSP. The review, documentation, and risk results presented in this report have been prepared to respond to FMC's request. This report uses the same PRA methods that were used for the Ajo/Bisbee and Douglas risk assessments to assess cancer and non-cancer hazard associated with the SSRLs proposed for the UVSP.

Unlike deterministic risk assessment methods, PRA methods use exposure assumptions that are expressed as statistical distributions rather than as a single value (i.e. a constant or "point estimate"). So for example, instead of expressing arsenic bioavailability in soil as a single value, it may be expressed as a triangular statistical distribution specified by a minimum value, a most likely value, and a maximum value. The advantage of PRA methods is that they incorporate the likely range of uncertainty or variability in exposure parameters into the final risk estimates. ADEQ regulatory guidance specifically permits the use of PRA methods (Arizona Administrative Code [A.A.C.] R18-7-206(B)). The PRA methods used in this report are also consistent with United States Environmental Protection Agency (USEPA) guidance on PRA (*Volume III, Part A – Process for Conducting Probabilistic Risk Assessment* [USEPA, 2001a]).

This report presents information previously used to support the arsenic, lead, and copper SSRLs at the Ajo/ Bisbee and Douglas sites (BC, 2009 and 2013). Except for arsenic bioavailability, the information which served as a basis for development of input parameters for the Ajo/Bisbee assessment has not changed, and there is no basis to modify these input parameters for the UVSP risk assessment. Specifically, the circumstances of chemical exposure (i.e., the conceptual site model) at the UVSP site are fundamentally the same as at Ajo/Bisbee and Douglas. At all three sites, residential receptors are exposed to metals in soil, primarily arsenic, lead, and copper. Thus, the receptors (adult and child residents),

exposure pathways (soil ingestion, dermal contact with soil, and inhalation of resuspended soil), and chemicals of concern are the same. None of the sites involves chemical exposure via water bodies or water supplies (e.g., dermal contact, drinking water). Nonetheless, the discussion of the basis for the input parameters is presented in this report in its entirety to allow for a stand-alone UVSP risk assessment.

As noted above, except for arsenic bioavailability, there is no basis for revising any of the original risk assessment input parameters that were used at Ajo/Bisbee. However, arsenic bioavailability information was updated as part of the Douglas risk assessment and that updated information is also included here for completeness. As concluded in the Douglas risk assessment, the updated arsenic bioavailability information did not indicate, or support, any change to the original Ajo/Bisbee arsenic bioavailability assumptions.

The following section describes the exposure assumptions used to evaluate the health risks associated with the proposed residential use SSRLs.

3.0 EXPOSURE ASSESSMENT

As noted previously, the circumstances of potential chemical exposure at the UVSP are fundamentally the same as at the Ajo/Bisbee and Douglas programs. In all three cases the potentially impacted population (receptor population) is nearby residents. The chemicals of concern are three metals: arsenic, copper and lead. Exposure is via soil, not drinking water or surface water, so the relevant exposure pathways are limited to soil ingestion, dermal contact with soil, and inhalation of resuspended soil. Additional details and the basis for each exposure assumption used in this risk assessment are presented below.

3.1 Receptor Populations

For purposes of developing the SSRLs, residential use is assumed. This use results in the most conservative cleanup level, and will allow the widest variety of future uses once the relevant property areas have been remediated. The relevant receptor populations for a residential use risk assessment are an adult and child resident, where the child is assumed to be 0 to 6 years old (USEPA, 1989).

3.2 Exposure Pathways

Exposure to metals in soil may occur via ingestion, dermal contact and inhalation. Soil ingestion is assumed to occur when individuals incidentally transfer soil on the hands to the mouth. A portion of soil ingestion is assumed to consist of indoor dust ingestion (discussed in Section 3.3.3 below). Dermal absorption of metals from soil may also occur. However, the dermal absorption of metals from soil is very low, typically 1 percent or less (Department of Toxic Substances Control [DTSC], 1994). Inhalation exposure to metals in soil occurs entirely via resuspension and subsequent inhalation of airborne dust since arsenic, copper and lead are non-volatile at ambient temperatures.

3.3 Exposure Assumptions

Numerous assumptions are used to calculate potential chemical exposure. These assumptions, which may be specified as single point estimates (i.e., constants), or as statistical distributions, describe the physical/physiological characteristics of the receptors (e.g., body weight, skin surface area, inhalation rate, etc.), chemical-specific assumptions (e.g., oral bioavailability, dermal absorption efficiency) and receptor behavioral characteristics (e.g., length of time a person lives at their residence). The assumptions used in this risk assessment and their basis are described in detail below.

3.3.1 Body Weight

Body weights for the child (Table 1) and adult (Table 2) residents were expressed as custom statistical distributions obtained from the Oregon Department of Environmental Quality (ODEQ) for the child (ODEQ, 1998), and the American Industrial Health Council (AIHC) for the adult (AIHC, 1994). The AIHC distribution was used for adults because it is much clearer and more straightforward than the adult body weight distributions developed by the ODEQ. Specifically, the AIHC distribution addresses adults only, whereas the ODEQ body weight distribution includes all age groups (including children), and a separate distribution for adults specifically would have to be derived. In addition, the ODEQ uses separate body weight distributions for males and females, whereas the AIHC distribution combines adult males and females into a single distribution. Since this exposure assessment only differentiates exposure between adults and children, not males and females, the AIHC distribution is more appropriate. On the other hand, the ODEQ distribution is more relevant for the child receptor because, unlike the corresponding AIHC distribution for children, the ODEQ distribution allows close correlation of the body weight with the specific age range normally assumed in risk assessments for children (1 to 6 years). Both the ODEQ and AIHC distributions were developed from the second National Health and Nutrition Survey conducted from February 1976 to February 1980. Body weights were measured in 20,322 individuals ranging in age from 6 months to 74 years, representing women and men from a variety of ethnic backgrounds. For this risk assessment, the probability distribution of body weights of children (male and female averaged) from 0 to 6 years of age was used to represent children, and the distribution of average body weights for adults over 18 years was used to represent adults.

3.3.2 Exposure Duration and Frequency

Exposure duration is the number of years that an individual is assumed to live at one location. Exposure frequency is the number of days a person is assumed to spend at home during each of those years.

For children (Table 3), a custom probability distribution of the average exposure duration for children from 3 to 11 years was used with a maximum exposure duration of 6 years (ODEQ, 1998). This dataset is the closest approximation for the standard child age range assumed in risk assessment for children of 0 to 6 years (USEPA, 1989). For adults (Table 4), a custom distribution based on the age group from 12 to 20 years old was conservatively used because that is the group that spends the highest number of years in one location as compared to other age groups (ODEQ, 1998). Selection of the 12-20 year-old age group for adults was also based on the fact that the 99th percentile exposure duration of this group was 23 years, which closely matches the standard deterministic residential exposure duration of 24 years assumed for

adults (ADHS, 2003). This is also conservative since it represents the 99th percentile exposure duration. In other words, 99 percent of the exposed population is expected to have an exposure duration equal to or less than this value. The ODEQ distribution was truncated for adults at 24 years based on the deterministic risk assessment (point estimate) value of 24 years for the adult residential exposure duration parameter (ADHS, 2003), and therefore does not reflect longer durations by older adults. This is consistent with standard risk assessment methodology. The exposure duration for the child was modified in the same way with a truncation of the distribution at 6 years (the maximum exposure duration typically used in deterministic risk assessments) (Smith, 1994; ADHS, 2003).

The exposure frequency for a resident was specified as a triangular distribution with a minimum of 300 days a year, a maximum of 365 days a year, and most likely value of 345 days a year (Table 5) (BHP Copper Inc. [BHP], 2006; ADEQ, 2007). This distribution is considered a conservative representation of conditions at the UVSP. Use of this distribution assumes that children and adults spend several days away from home each year (e.g., on vacation or visiting relatives) and therefore some of the soil that they contact is not from the impacted area near their home.

3.3.3 Ingestion of Outdoor Soil and Indoor Dust

Adult and child residents are assumed to incidentally ingest some outdoor soil and indoor dust each day. Most of the studies on soil ingestion have focused on young children as the most exposed age group. The custom distributions used for these exposure parameters were obtained from ODEQ (1998). Children were assumed to ingest up to 399 milligrams of soil per day (mg/day), and adults were assumed to ingest up to 150 mg/day (Tables 6 and 7, respectively). Of the soil ingested each day, 45 percent was assumed to be as outdoor soil and 55 percent as indoor dust (USEPA, 2007). The contribution of arsenic and copper in indoor dust from the outside soil was specified as a triangular distribution with a minimum of 6 percent, a maximum of 70 percent, and a most likely value of 43 percent (USEPA, 1996, 2001b, 2007) (Table 5). Additional supporting documentation for each of these distribution parameters is provided in Appendices A, B and C, respectively.

3.3.4 Oral Bioavailability of Arsenic and Copper in Soil

When soil containing metals is incidentally ingested, for example, by inadvertent hand-to-mouth transfer, not all of the chemical is absorbed into the body due to partitioning or adsorption onto the soil. The fraction of the chemical that is absorbed into the body systemically is the “bioavailable” fraction. A triangular distribution (minimum - 18.3 percent, most likely – 40 percent, and maximum – 50 percent) of the relative bioavailability (RBA) of arsenic in soil was approved by ADEQ for the prior Ajo/Bisbee risk

assessment. The dataset used to arrive at that distribution consisted of reported *in vivo* studies on 35 samples from 15 separate sites, including mining and smelting sites.

The *in vivo* data included in the Ajo/Bisbee dataset had a minimum RBA of 3 percent, a mean of 26 percent, and a maximum of 61 percent. Approximately 39 percent of the reported RBA values were less than the 18.3 percent used in the Ajo/Bisbee arsenic RBA distribution and 12 percent of the values were higher than the maximum of 50 percent used in that distribution (BHP, 2006; ADEQ, 2007; BC, 2009).

To verify that the Ajo/Bisbee arsenic RBA distribution remains appropriate for use in this UVSP risk assessment, the published scientific literature was searched using the National Library of Medicine search engine PubMed to determine if there was additional available RBA information to that used in the Ajo/Bisbee analysis. In addition, a general Internet search was conducted to locate unpublished studies conducted or sponsored by regulatory agencies, in particular USEPA Region 8, which has been extensively involved in this type of work for many years. Based on this review, several additional studies were identified and reviewed to determine whether a modification to the Ajo/Bisbee arsenic RBA distribution was needed. These studies, as well as those included in the original Ajo/Bisbee risk assessment, are included in Appendix D. The results of that review are discussed below.

Of primary importance is a published USEPA review and compilation of *in vivo* arsenic bioavailability in 29 samples from 11 sites (including mine and smelter sites) using the swine model (USEPA, 2010). Young swine are commonly used for bioavailability studies because they are considered to be a good physiological model for the human gastrointestinal tract and are more practical and economical than primates (Juhasz et al., 2007; USEPA, 2010). Some of the data included in the USEPA review were also included in the Ajo/Bisbee dataset; however, the USEPA review included a re-analysis of the raw data from those studies. The data included in the USEPA review determined a minimum RBA of 8 percent and a maximum RBA of 61 percent. The mean RBA across 26 samples was 34 percent (three samples were discarded by the USEPA due to insufficient arsenic content). Of the studies evaluated, this review by USEPA presents the best initial basis for an assessment of the Ajo/Bisbee arsenic RBA distribution for several reasons. First, all the data were from *in vivo* studies using a species widely considered to be a good model for the human gastrointestinal tract. Second, all the results were obtained from the same laboratory using the same methods, so inter-laboratory method differences are eliminated. Third, USEPA performed a separate and uniform data reduction procedure on the raw data from the studies reviewed,

which allowed for consistent interpretation of the results. Fourth, the data included a wide diversity of sample types, including samples from numerous mine and smelter sites.

The literature review identified five studies that were not part of the Ajo/Bisbee RBA dataset. Juhasz et al. (2007) used a swine model to evaluate arsenic RBA in 12 contaminated soils collected from railway corridors, mine sites, gossan soils containing naturally high levels of arsenic, and livestock pesticide dip sites. These investigators reported a minimum arsenic RBA of 7 percent and a maximum of 75 percent. Using the monkey, Roberts et al. (2007) reported a minimum RBA of 5 percent and a lower maximum of 31 percent in 14 soil samples from 12 different sites, including mine sites. In addition, Bradham et al. (2011) reported a mean arsenic RBA of 33 percent in 11 soils using an *in vivo* mouse model. The Agency for Toxic Substances and Disease Registry (ATSDR) reported a bioavailability for arsenic of 15 percent for soils from a former foundry site in Palestine, Texas (ATSDR, 2006).

When the data from the additional studies and the USEPA review are considered with the original Ajo/Bisbee arsenic RBA, data there are a total of 73 separate arsenic RBA test results. Thirty-seven percent of these results are less than the minimum RBA of 18.3 percent used in the Ajo/Bisbee distribution and 11 percent are greater than the maximum in the RBA distribution, a very similar distribution to the data that served as the basis for development of the Ajo/Bisbee RBA distribution. There are two RBA results within the additional data that are higher than the 61 percent considered in the development of the Ajo/Bisbee arsenic RBA distribution. Those RBAs (75 percent and 67 percent) were reported by Juhasz et al. (2007) and are on samples of railroad corridor soil as opposed to a mining or smelting site soil. The mean arsenic RBA of the combined dataset is 27 percent, well below the most likely value of 40 percent used in the Ajo/Bisbee RBA distribution.

Most recently, Brattin and Casteel (2013) determined relative bioavailabilities in swine ranging from 18-42% in mine- or smelter-related soils. These values are consistent with the triangular distribution parameters assumed in this HRA (min=18%, most likely = 40%, max = 50%).

This updated review of additional arsenic RBA data demonstrates that the Ajo/Bisbee distribution is conservative and that there is not a compelling reason to revise the distribution for the UVSP risk assessment.

With respect to copper, the same triangular distribution used for the bioavailability of copper in soil and dust in the Ajo/Bisbee and Douglas risk assessments was used in this risk assessment (i.e., a minimum of 48 percent, a most likely value of 64 percent, and a maximum of 78 percent (Table 5)). These data are based on *in vitro* analysis of samples from a mining site (Golder Associates, 2002).

3.3.5 Dermal Exposure to Arsenic in Soil and Dust

The dermal absorption of metals through the skin is very limited. California state agencies for example, assume that dermal absorption is only 1 percent or less for most metals (DTSC, 1994). USEPA guidance lists a factor of 3 percent absorption of arsenic in soil or dust, and negligible dermal absorption of copper (USEPA, 2004). Dermal absorption of copper was therefore not considered further in this risk assessment.

A triangular distribution was assumed for the dermal absorption of arsenic, specified by a minimum of zero, a most likely value of 1 percent and maximum of 3 percent (BHP, 2006; ADEQ, 2007b) (Table 5). The value of 3 percent absorption used by USEPA is based on a study of soluble arsenic freshly added to soil that was placed in contact with the skin of monkeys for 24 hours (Wester et al., 1993). More recent studies on humans have shown that arsenic in water used for bathing and showering does not result in an increase in urinary arsenic (Knobeloch, 2002). Arsenic dissolved in water is more biologically available than arsenic in soil. In addition, studies of children exposed to arsenic in soil in Anaconda, Montana, showed that the arsenic in their urine could be predicted well from the ingestion of soil alone, thus indicating that dermal exposure is not an important route of exposure (Walker and Griffin, 1998). Another study of children in Bingham Creek, Utah, showed that there was no correlation between arsenic in soil on children's hands and urinary arsenic (University of Cincinnati, 1997). Nonetheless, dermal absorption of arsenic is included in this risk assessment as a complete exposure pathway to be conservative.

The custom distributions for the surface area of exposed skin on children (Table 8) and adults (Table 9) were obtained from USEPA guidance (USEPA, 1997). Note that these distributions are for total body surface area. An adjustment factor of 0.25 was used to approximate the proportion of total body surface area represented by the area of the hands, the feet, one-half of the arms (representing exposed forearms), and one-half of the legs (representing exposure up to the knee) (USEPA, 1997).

The amount of soil or dust assumed to adhere to the skin was specified as point estimates of 0.2 milligrams per square centimeter (mg/cm^2) for the child and 0.07 mg/cm^2 for the adult (ADHS, 2003;

USEPA, 2004). Point estimates were used for the soil adherence factor for two main reasons. First, ODEQ acknowledges that several key reviewers (including the CalEPA, USEPA, etc.) have concluded there is insufficient information to develop a distribution for this parameter as follows from ODEQ (1998):

> "…several investigators (CalEPA 1996; EPA 1996a; Kissel et al 1996b) currently suggest that insufficient data are available to develop a distribution or a probability function for soil loading."

Second, the ODEQ distribution does not separate children from adults, and the distribution is based primarily on data in children. But since children tend to have much higher skin soil loadings than adults the ODEQ distribution ignores the important differences in soil loading between adult and child receptors. On the other hand, the deterministic parameters most commonly used for this exposure parameter (0.07 mg/cm^2 for adults and 0.2 mg/cm^2 for children) do reflect this important difference in skin soil loading between the adult and child, and are therefore more appropriate in this case.

3.3.6 Inhalation Rate

The inhalation rate distributions assumed for children (Table 10) and adults (Table 11) were obtained directly from custom distributions shown in Table 3-26 from ODEQ (1998). The distribution for children was for ages up to 12 years and for adults ages greater than 12 years. The particulate emission factor is a point estimate of 1.396E9 m^3/kg of soil (ADHS, 2003).

3.3.7 Averaging Time

The averaging time is the period of the lifetime over which the exposure is averaged. Averaging time was assumed to be a point estimate and no distribution was assumed for this exposure parameter. For carcinogenic risk evaluation the standard averaging time is 70 years or 25,550 days (USEPA, 1989). This value is also consistent with Arizona risk guidance (ADHS, 2003). For non-cancer hazard evaluation the averaging time is equal to the exposure duration in years times the number of days per year (365). For the child resident the non-cancer averaging time is 6 years times 365 days per year, or 2190 days (ADHS, 2003).

3.3.8 Summary of Exposure Assumptions

All of the exposure parameters described above are listed in Table 12 for arsenic cancer risk, Table 13 for arsenic non-cancer hazard, and Table 14 for copper non-cancer hazard.

4.0 TOXICITY ASSESSMENT

The purpose of the Toxicity Assessment is to present the toxicity criteria used to calculate cancer and non-cancer health hazard, as well as present basic information about the potential health effects related to exposure to the chemicals of concern. Toxicity criteria include oral and inhalation route Reference Doses (RfDs) for the evaluation of non-cancer health hazard, and oral and inhalation route cancer slope factors (CSFs) to calculate cancer risks. Note that in the case of lead, a unique toxicity criterion is used to evaluate health risks instead of an RfD. Lead health risks are evaluated based on the predicted blood lead concentration in potentially exposed children. A potential lead exposure in soil is considered safe if the predicted blood lead concentration resulting from that exposure will result in no more than 5 percent of the exposed children having a blood lead greater than 10 micrograms/deciliter (µg/dl) (USEPA, 2007).

Toxicity criteria for arsenic and copper were treated as point estimates or constants in this risk assessment; statistical distributions were not used for these parameters. The specific toxicity criteria used for arsenic, copper and lead are described in detail below.

4.1 Arsenic

Arsenic is considered by USEPA and other government agencies to be carcinogenic via both oral and inhalation routes of exposure (USEPA, 2014). Therefore, oral and inhalation cancer slope factors for arsenic were obtained from the USEPA *Integrated Risk Information System* (IRIS) (USEPA, 2014) (Table 12). For non-cancer hazard assessment, oral and inhalation RfDs for arsenic were also obtained from IRIS and are shown in Table 13.

According to ATSDR, the most sensitive and characteristic non-cancer health effects of arsenic exposure via the ingestion route of exposure are dermal effects, including hyperkeratosis (thickening of the skin) and hyperpigmentation (excess pigmentation of the skin) (ATSDR, 2007a). At much higher exposure levels, gastrointestinal irritation, manifested as nausea, vomiting, diarrhea, and abdominal pain are typical. Other effects associated with ingestion exposure may include anemia, cardiovascular effects, and liver damage (ATSDR, 2007a). The most common non-cancer effect associated with inhalation exposure to arsenic is irritation of the respiratory tract.

4.2 Copper

Copper is not considered a carcinogen by USEPA (USEPA, 2014). The oral RfD for copper was obtained from IRIS and is shown in Table 14.

According to ATSDR, the most sensitive non-cancer health effect related to ingestion exposure is gastrointestinal irritation, primarily nausea and diarrhea. At higher levels of exposure kidney damage may occur (ATSDR, 2004). Inhalation exposure is primarily associated with irritation of the respiratory tract (ATSDR, 2004).

4.3 Lead

As noted previously, the health risks associated with lead exposure are not evaluated using an RfD as for virtually all other chemicals, instead, lead risks are evaluated using a unique pharmacokinetic model developed by USEPA called the *Integrated Exposure Uptake Biokinetic Model* (IEUBK) (USEPA, 2007). This model is used to determine the percentage of potentially exposed children who would have blood lead levels exceeding 10 µg/dl. If, based on this model, this percentage is 5 percent or less, lead risks are considered to be negligible. The primary and most sensitive non-cancer effect associated with lead exposure is neurologic impairment (ATSDR, 2007b).

The following section describes the calculation of cancer and non-cancer hazard estimates for the proposed SSRLs.

5.0 RISK CHARACTERIZATION

The health risks of a chemical are quantified in terms of non-cancer hazard as well as carcinogenic risks if the chemical is considered a carcinogen. Non-cancer health hazard refers to all other adverse health effects besides cancer. Carcinogenic chemicals may present non-cancer hazard in addition to cancer risks, therefore the potential for both types of effects must be evaluated for carcinogens.

This section discusses how cancer and non-cancer hazards were calculated (as appropriate) for the proposed SSRLS of 30, 9000, and 425 mg/kg for arsenic, copper and lead, respectively. Cancer risks are expressed simply as cancer risk, with a value of 1E-05 (one in a 100,000) consistent with acceptable ADEQ risk criteria. Non-cancer hazard is expressed as the Hazard Quotient (HQ), with a value of 1 or less being consistent with ADEQ non-cancer hazard criteria for any given chemical.

The cancer risk and HQ corresponding to each of the proposed SSRLs (as appropriate) were calculated using PRA methods and standard USEPA risk equations (USEPA, 2013). In this approach, the usual point estimates of the exposure parameters are replaced in some cases by statistical distributions in order to more accurately describe the uncertainty or variability in the parameter for the exposed population. In most cases where this approach is used only some of the exposure parameters are replaced by statistical distributions. Typically, statistical distributions are only used for those parameters where the uncertainty or variability is well defined and selection of the appropriate statistical distribution is clear. When using probabilistic risk assessment methods, ADEQ statutes require that the 95th percentile cancer risk be equal to 1E-05 or less and the 95th percentile Hazard Quotient (Hazard Index for multiple chemicals) be 1 or less. The Hazard Index (HI) is the sum of the HQs for each chemical.

The probabilistic modeling software *Crystal Ball* (Version 11.1.2.3.000, Oracle, Redwood City, CA) was used to perform the analysis based on standard USEPA equations for calculating cancer risk and the HQ for soil exposure. These equations are described in detail below.

5.1 Cancer Risks

Of the three chemicals of concern at the UVSP, only arsenic is evaluated as a carcinogen by USEPA (USEPA, 2014). Carcinogenic risks associated with the proposed SSRL for arsenic of 30 mg/kg were calculated using the USEPA equation shown in Figure 1 and the exposure assumptions listed in Table 12. The *Crystal Ball* analysis using this proposed arsenic soil SSRL resulted in a 95 percentile cancer risk based on residential exposure of 1E-05, which is considered acceptable under ADEQ statutes. The *Crystal*

Ball output showing the input parameter distributions and cancer risk percentiles are shown in Appendix E.

With respect to potential site remediation, based on the above analysis, if the concentrations of arsenic in a given defined use area are below this proposed SSRL (after sampling conducted in accordance with the sampling and analysis plan that will be provided to ADEQ for approval), that particular defined use area will be considered to be in compliance with respect to arsenic cancer risks.

5.2 Non-Cancer Hazard

Non-cancer hazard (expressed as the HQ) for arsenic and copper were calculated with *Crystal Ball* using the equations shown in Figures 2 and 3, respectively. Exposure parameters for these equations are listed in Tables 13 and 14 for arsenic and copper, respectively. The calculated 95th percentile HQ associated with an arsenic concentration of 30 mg/kg is 0.3, and the 95th percentile HQ associated with the proposed copper SSRL of 9,000 mg/kg is 1. These HQ values are the same as previous values approved by ADEQ at the Ajo/Bisbee and Douglas programs. The *Crystal Ball* output showing the input parameter distributions and HQ percentiles are shown in Appendix F for arsenic and Appendix G for copper.

With respect to potential site remediation, if the concentrations of arsenic and copper in a given defined use area are below these proposed SSRLs (after sampling conducted in accordance with the sampling and analysis plan that will be provided to ADEQ for approval), that particular defined use area will be considered to be in compliance with respect to arsenic and copper non-cancer hazard.

5.3 Lead Risks

A lead SSRL of 425 mg/kg was previously approved by ADEQ in 2008 and 2013. This SSRL was proposed in the URS reports, *Bisbee Smelter Risk Assessment Evaluation for the Site-Specific IEUBK Model* and *Bisbee Residential Soil Remediation-Interim Action Workplan* (URS, 2007a,b). It was also proposed in the Douglas risk assessment (BC, 2013). This value was obtained using the USEPA lead model for children, the *Integrated Exposure Uptake Biokinetic Model* (USEPA, 2007), and assuming all USEPA default values, except that the indoor dust lead concentration was assumed to be 273 mg/kg. This indoor dust lead concentration was derived based on a conversion factor developed by USEPA (USEPA, 2001b). To verify that the previously approved SSRL for lead of 425 mg/kg presents health risks related to lead in soil that the USEPA has determined to be protective, the IEUBK model was run using the same assumptions as specified above. This model run showed that the lead SSRL of 425 mg/kg will result in 4.4 percent of exposed children aged 0 to 7 years having a blood lead concentration greater than 10 µg/dl.

The IEUBK model output is included in Appendix H. USEPA considers lead health risks to be protective when less than 5 percent of exposed children are predicted to exceed a blood lead concentration of 10 µg/dl. Thus, the proposed lead SSRL will provide adequate protection of children with respect to potential lead exposure.

With respect to potential site remediation, if the concentrations of lead in a given defined use area are below the proposed lead SSRL (after sampling conducted in accordance with the sampling and analysis plan that will be provided to ADEQ for approval), that particular defined use are will be considered to be in compliance with respect to lead health risks.

5.4 Cumulative Health Risks

Consistent with USEPA and Arizona risk guidance (USEPA, 1989; ADHS, 2003), cumulative cancer risk is determined by adding the cancer risk from each carcinogenic chemical. Since copper and lead are not carcinogenic chemicals, there is no additional cancer risk to add to the arsenic cancer risk estimate and the total cumulative cancer risk associated with the proposed SSRLs is 1E-05 (at the 95th percentile). This level of cancer risk is consistent with ADEQ cancer risk criteria.

For non-cancer hazard, cumulative toxicity is accounted for by summing the HQs for all chemicals to obtain a HI (USEPA, 1989; ADHS, 2003). An HI of 1 is consistent with ADEQ cumulative non-cancer hazard criteria. Summing the HQs of 0.3 for arsenic and 1 for copper results in a HI of 1.3. Although this results in an acceptable HI of 1 (to one significant figure) this HI can be refined further using the "segregation of Hazard Indices" approach per USEPA risk guidance (USEPA, 1989). According to this method, only the HQs of chemicals which have a similar mechanism of toxicity, or which act on the same target organ, should be added to account for cumulative toxicity. For the proposed SSRLs the critical effects of arsenic (skin pigmentation and keratin changes, cancer risk) and copper (gastrointestinal irritation) at low doses do not affect the same target organ or act by a similar mechanism of toxicity, so it would not be appropriate to add the HQs related to these chemicals, and the highest final HQ of 1 (for copper) becomes the relevant HI. This maximum HI of 1 is consistent with ADEQ risk criteria for non-cancer hazard.

6.0 UNCERTAINTY ANALYSIS

A PRA approach was used to calculate cancer risks and non-cancer hazard associated with the proposed SSRLs for arsenic, copper and lead. This risk assessment method is specifically designed to take into account the uncertainty and variability represented by the various exposure parameters used to calculate health risks. The significant uncertainty and variability represented in a potentially exposed population is explicitly taken into account in the risk calculations by replacing simple point estimates of the exposure parameters with more realistic statistical distributions. This results in a more realistic analysis that better reflects the likely different exposures that may potentially be experienced by the various individuals in the exposed population.

The statistical distributions used, while still subject to some uncertainty, are the same distributions published and utilized by other governmental agencies. They have been peer-reviewed and so are well accepted. The point estimate parameters used, for example, the USEPA toxicity criteria, are designed to be conservative and to specifically take into account sensitive populations.

Consistent with ADEQ risk guidance, the 95th percentile cancer risk and HQ were calculated in this risk assessment. This means that 95 percent of the potentially exposed population would experience less health risk than the 95th percentile values at these proposed SSRLs. Thus, the 95th percentile cancer risk and HQ reflect conservative, upper-bound estimates of the health risk estimates. Cumulative risks, expressed as cumulative cancer risk and the maximum HI, were explicitly evaluated in this risk assessment and found to be acceptable and consistent with ADEQ health risk criteria.

Two specific sources of uncertainty in the present risk assessment are related to the lack of an inhalation RfD for copper and the use of an arsenic oral cancer slope factor that is based on drinking water exposure. The lack of an inhalation RfD for copper prevents the quantitative assessment of non-cancer hazard related to the inhalation of airborne copper. However, in our experience, metal exposure via the inhalation route of exposure is insignificant relative to the exposure occurring via incidental soil ingestion. Thus, the absence of an inhalation RfD for copper is not expected to result in a significant underestimate of non-cancer hazard.

The arsenic oral cancer slope factor is based on drinking water exposure not soil exposure (USEPA, 2014). The use of such a cancer slope factor for evaluating cancer risks related to arsenic in soil is likely

to overestimate cancer risks due to the reduced solubility and bioavailability of arsenic forms in soil (particularly smelter soils) relative to arsenic forms in drinking water (Davis et al., 1996).

7.0 SUMMARY AND CONCLUSIONS

A PRA was conducted to verify that health risks related to the soil SSRLs proposed for the UVSP are: 1) within the range that ADEQ and the USEPA have determined to be protective of human health and, 2) consistent with the health risk benchmarks that ADEQ has determined to be acceptable at other sites (i.e., Ajo/Bisbee, and Douglas). The Ajo/Bisbee and Douglas programs are very similar in exposure circumstances to the UVSP. The PRA used the same input parameters that were previously approved by ADEQ for use in the Ajo/Bisbee and Douglas risk assessments. Justification for the use of the Ajo/Bisbee arsenic RBA in the present risk assessment was performed by developing an even more comprehensive and up-to-date database of *in vivo* bioavailability data reported in the literature than that used for developing the RBA input for the Ajo/Bisbee risk assessment.

The PRA showed that the 95th percentile cancer risk for arsenic at 30 mg/kg was 1E-5, the same as for the Ajo/Bisbee and Douglas programs. Non-cancer hazards, expressed as the 95th percentile HQs for arsenic and copper at the proposed SSRLs, were 0.3 and 1, respectively. The maximum HI of 1, representing cumulative non-cancer health hazard, was acceptable based on a “segregation of Hazard Indices”. Lead health risks, evaluated using the USEPA IEUBK model, were also determined to be negligible at the proposed SSRL of 425 mg/kg.

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TABLES

TABLE 1

Child Body Weight Distribution (Both Sexes)

Percentile	Body Weight (kg)
Minimum	9.03
5	10.75
10	11.28
15	11.65
20	11.95
25	12.22
30	12.46
35	12.7
40	12.92
45	13.14
50	13.36
55	13.58
60	13.81
65	14.05
70	14.31
75	14.6
80	14.93
85	15.31
90	15.81
95	16.58
Maximum	19.73

Source: Derived from Tables 3-47 and 3-49 ODEQ (1998). See text.

TABLE 2

Adult Body Weight Distribution (Both Sexes)

Percentile	Body Weight (kg)
Min	44
5	52.3
15	57.6
50	68.7
85	84.4
95	97
Max	107

Source: Page 4.2 of AIHC (1994).

TABLE 3

Child Exposure Duration Distribution

Percentile	Exposure Duration (yr)
Minimum	0.01
5	0.59
10	1.18
15	1.77
20	2.36
25	2.96
30	3.37
35	3.76
40	4.16
45	4.56
50	4.95
55	5.37
60	5.78
Maximum	6

Source: From Table 3-38 of ODEQ (1998) and truncated at age 6.

TABLE 4

Adult Exposure Duration Distribution

Percentile	Exposure Duration (yr)
Minimum	0.01
5	0.98
10	1.94
15	2.97
20	3.91
25	4.91
30	5.73
35	6.53
40	7.33
45	8.13
50	8.9
55	9.5
60	10.08
65	10.66
70	11.22
75	11.81
80	13.03
85	14.38
90	15.75
95	17.57
Maximum	24

Source: From Table 3-38 of ODEQ (1998) and truncated at age 24.

TABLE 5

Triangular Distribution Parameters

Exposure Parameter	Units	Minimum	Most Likely	Maximum	Reference
Residential exposure frequency, EF_r	days/yr	300	345	365	BHP (2006)
Oral bioavailability of arsenic in soil, $BIO_{a/s}$	Unitless	0.183	0.4	0.5	BHP (2006)
Oral bioavailability of arsenic in dust, $BIO_{a/d}$	Unitless	0.183	0.4	0.5	BHP (2006)
Oral bioavailability of copper in soil, $BIO_{c/s}$	Unitless	0.48	0.64	0.78	Golder (2002)
Oral bioavailability of copper in dust, $BIO_{c/d}$	Unitless	0.48	0.64	0.78	Golder (2002)
Ratio of concentration of metal in dust to soil, $Ratio_{d/s}$	Unitless	0.06	0.43	0.7	USEPA (1996, 2001b, 2007)
Dermal absorption factor for arsenic, ABS	Unitless	0	0.01	0.03	BHP (2006)

TABLE 6

Child Soil Ingestion Rate Distribution

Percentile	Ingestion Rate (mg/day)
Minimum	0.52
5	5.52
10	8.34
15	11.04
20	13.78
25	16.67
30	19.81
35	23.21
40	26.95
45	31.17
50	35.94
55	41.39
60	47.83
65	55.44
70	64.66
75	76.34
80	91.54
85	112.85
90	145.1
95	205.24
Maximum	398.75

Source: From Table 3-2 of ODEQ (1998).

TABLE 7

Adult Soil Ingestion Rate Distribution

Percentile	Ingestion Rate (mg/day)
Minimum	16.57
5	32.78
10	36.7
15	39.6
20	42.07
25	44.33
30	46.43
35	48.48
40	50.5
45	52.53
50	54.61
55	56.79
60	59.12
65	61.59
70	64.29
75	67.37
80	70.92
85	75.43
90	81.33
95	91.03
Maximum	150.07

Source: From Table 3-2 of ODEQ (1998).

TABLE 8

Child Skin Surface Area Distribution

Percentile	Surface Area (cm^2/kg-day)
Minimum	421
5	470
10	507
25	563
50	617
75	719
90	784
95	846
Maximum	1,142

Source: From Table 6-9 of USEPA (1997).

TABLE 9

Adult Skin Surface Area Distribution

Percentile	Surface Area (cm^2/kg-day)
Minimum	200
5	238
10	244
25	270
50	286
75	302
90	316
95	329
Maximum	351

Source: From Table 6-9 of USEPA (1997).

TABLE 10

Child Inhalation Rate Distribution

Percentile	Inhalation Rate (m^3/kg-day)
Minimum	0.342
5	0.364
10	0.379
15	0.390
20	0.400
25	0.409
30	0.418
35	0.426
40	0.434
45	0.442
50	0.450
55	0.458
60	0.467
65	0.476
70	0.485
75	0.496
80	0.508
85	0.523
90	0.542
95	0.572
Maximum	0.741

Source: From Table 3-26 of ODEQ (1998).

TABLE 11

Adult Inhalation Rate Distribution

Percentile	Inhalation Rate (m^3/kg-day)
Minimum	0.113
5	0.140
10	0.153
15	0.163
20	0.172
25	0.180
30	0.187
35	0.195
40	0.202
45	0.210
50	0.217
55	0.225
60	0.233
65	0.242
70	0.251
75	0.262
80	0.275
85	0.290
90	0.311
95	0.344
Maximum	0.556

Source: From Table 3-26 of ODEQ (1998).

TABLE 12

Summary List of Exposure Assumptions Used to Calculate Cancer Risk for Arsenic in Residential Soil Based on Proposed Arsenic Site-Specific Remediation Level of 30 mg/kg

Exposure Parameter	Notation	Units	Distribution Type	Value(s)	Reference
Averaging time for cancer risk	AT_c	days	Point estimate	25,550	ADHS (2003)
Age-adjusted inhalation rate	IRA_{adj}	m^3-yr/kg-day	Point estimate	Calculated (see Figure 1)	USEPA (2013)
Age-adjusted skin surface area	SA_{adj}	mg-yr/kg-day	Point estimate	Calculated (see Figure 1)	USEPA (2013)
Age-adjusted soil ingestion rate	IRS_{adj}	mg-yr/kg-day	Point estimate	Calculated (see Figure 1)	USEPA (2013)
Body weight, adult	BW_a	kg	Custom	Table 2	AIHC (1994)
Body weight, child	BW_c	kg	Custom	Table 1	ODEQ (1998)
Cancer slope factor (inhalation)	CSF_i	$(mg/kg\text{-}day)^{-1}$	Point estimate	15	USEPA (2014)
Cancer slope factor (oral)	CSF_o	$(mg/kg\text{-}day)^{-1}$	Point estimate	1.5	USEPA (2014)
Conversion factor	CF	mg/kg	Point estimate	1.00E+06	
Dermal absorption	ABS	unitless	Triangular	Table 5	BHP (2006)
Dermal soil adherence factor, adult	AF_a	mg/cm^2	Point estimate	0.07	USEPA (2004)
Dermal soil adherence factor, child	AF_c	mg/cm^2	Point estimate	0.2	ADEQ (1997, 2007)
Exposure duration, adult	ED_a	yr	Custom	Table 4	ODEQ (1998)
Exposure duration, child	ED_c	yr	Custom	Table 3	ODEQ (1998)
Exposure frequency, residential	EF_r	days/yr	Triangular	Table 5	BHP (2006)
Fraction of dust ingested	FI_d	unitless	Point estimate	0.55	USEPA (2007)
Fraction of soil ingested	FI_s	unitless	Point estimate	0.45	USEPA (2007)
Inhalation rate, adult	IRA_a	m^3/kg-day	Custom	Table 11	ODEQ (1998)
Inhalation rate, child	IRA_c	m^3/kg-day	Custom	Table 10	ODEQ (1998)
Oral bioavailabilty of arsenic in dust	$BIO_{a/d}$	unitless	Triangular	Table 5	BHP (2006)
Oral bioavailabilty of arsenic in soil	$BIO_{a/s}$	unitless	Triangular	Table 5	BHP (2006)
Particulate emission factor	PEF	m^3/kg	Point estimate	1.396E+09	ADHS (2003)
Ratio of metal concentration in dust to soil	$Ratio_{d/s}$	unitless	Triangular	Table 5	USEPA (1996, 2001, 2007)
Skin surface area, adult	SA_a	cm^2/(kg-day)	Custom	Table 9	(USEPA, 1997)
Skin surface area, child	SA_c	cm^2/(kg-day)	Custom	Table 8	USEPA (1997)
Soil concentration (Site-Specific Remediation Level)	C_s	mg/kg	Point estimate	30	
Soil ingestion, adult	IRS_a	mg/day	Custom	Table 7	ODEQ (1998)
Soil ingestion, child	IRS_c	mg/day	Custom	Table 6	ODEQ (1998)
Target cancer risk	TR	unitless	NA	Calculated	ADHS (2003)

TABLE 13

Summary List of Exposure Assumptions Used to Calculate Non-Cancer Hazard (Hazard Quotient) for Arsenic in Residential Soil Based on Proposed Arsenic Site-Specific Remediation Level of 30 mg/kg

Exposure Parameter	Notation	Units	Distribution Type	Value(s)	Reference
Averaging time for non-cancer risk	AT_{nc}	days	Point estimate	2,190	ADHS (2003)
Body weight, child	BW_c	kg	Custom	Table 1	ODEQ (1998)
Conversion factor	CF	mg/kg	Point estimate	1.00E+06	
Dermal absorption	ABS	unitless	Triangular	Table 5	BHP (2006)
Dermal soil adherence factor, child	AF_c	mg/cm^2	Point estimate	0.2	ADEQ (1997, 2007)
Exposure duration, child	ED_c	yr	Custom	Table 3	ODEQ (1998)
Exposure frequency, residential	EF_r	days/yr	Triangular	Table 5	BHP (2006)
Fraction of dust ingested	FI_d	unitless	Point estimate	0.55	USEPA (2007)
Fraction of soil ingested	FI_s	unitless	Point estimate	0.45	USEPA (2007)
Hazard Quotient	HQ	unitless	NA	Calculated	
Inhalation rate, child	IRA_c	m^3/kg-day	Custom	Table 10	ODEQ (1998)
Oral bioavailabilty of arsenic in dust	$BIO_{a/d}$	unitless	Triangular	Table 5	BHP (2006)
Oral bioavailabilty of arsenic in soil	$BIO_{a/s}$	unitless	Triangular	Table 5	BHP (2006)
Particulate emission factor	PEF	m^3/kg	Point estimate	1.396E+09	ADHS (2003)
Ratio of metal concentration in dust to soil	$Ratio_{d/s}$	unitless	Triangular	Table 5	USEPA (1996, 2001, 2007)
Reference Dose, inhalation	RfD_i	mg/kg-day	Point estimate	8.57E-06	USEPA (2014)
Reference Dose, oral	RfD_o	mg/kg-day	Point estimate	3.00E-04	USEPA (2014)
Skin surface area, child	SA_c	cm^2/(kg-day)	Custom	Table 8	USEPA (1997)
Soil concentration (Site-Specific Remediation Level)	C_s	mg/kg	Point estimate	30	Proposed
Soil ingestion, child	IRS_c	mg/day	Custom	Table 6	ODEQ (1998)

TABLE 14

Summary List of Exposure Assumptions Used to Calculate Non-Cancer Hazard (Hazard Quotient) for Copper in Residential Soil Based on Proposed Copper Site-Specific Remediation Level of 9,000 mg/kg

Exposure Parameter	Notation	Units	Distribution Type	Value (s)	Reference
Averaging time for non-cancer risk	AT_{nc}	days	Point estimate	2,190	ADHS (2003)
Body weight, child	BW_c	kg	Custom	Table 14	ODEQ (1998)
Conversion factor	CF	mg/kg	Point estimate	1.00E+06	
Exposure duration, child	ED_c	yr	Custom	Table 3	ODEQ (1998)
Exposure frequency, residential	EF_r	days/yr	Triangular	Table 5	BHP (2006)
Fraction of dust ingested	FI_d	unitless	Point estimate	0.55	USEPA (2007)
Fraction of soil ingested	FI_s	unitless	Point estimate	0.45	USEPA (2007)
Hazard Quotient	HQ	unitless	NA	Calculated	
Oral bioavailabilty of copper in dust	$BIO_{c/d}$	unitless	Triangular	Table 5	Golder (2002)
Oral bioavailabilty of copper in soil	$BIO_{c/s}$	unitless	Triangular	Table 5	Golder (2002)
Ratio of metal concentration in dust to soil	$Ratio_{d/s}$	unitless	Triangular	Table 5	USEPA (1996, 2001b, 2007)
Reference Dose, oral	RfD_o	mg/kg-day	Point estimate	4.00E-02	USEPA (2014)
Soil concentration (Site-Specific Remediation Level)	C_s	mg/kg	Point estimate	9000	
Soil ingestion, child	IRS_c	mg/day	Custom	Table 6	ODEQ (1998)

FIGURES

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FIGURE 1

FIGURE 2

Equation Used to Calculate Cancer Risk Associated with the Proposed Site-Specific Remediation Level for Arsenic of 30 mg/kg

$$Target\ Risk = \frac{C_s \times EF_r \times \left(\left(\frac{\left(IRS_{adj} \times CSF_o \left(\left(FI_s \times BIO_{a/s} \right) + \left(Ratio_{d/s} \times FI_d \times BIO_{a/d} \right) \right) \right)}{CF} \right) + \left(\frac{SFS_{adj} \times ABS \times CSF_o}{CF} \right) + \left(\frac{IRA_{adj} \times CSF_i}{PEF} \right) \right)}{AT_c}$$

Where:

$$IRS_{adj} = \frac{ED_c \times IRS_c}{BW_c} + \frac{ED_a \times IRS_a}{BW_a}$$

$$SA_{adj} = (ED_c \times AF_c \times 0.25 \times SA_c) + (ED_a \times AF_a \times 0.25 \times SA_a)$$

$$IRA_{adj} = (ED_c \times IRA_c) + (ED_a \times IRA_a)$$

See Table 12 for definitions and values of all parameters.

FIGURE 3

Equation Used to Calculate the Non-Cancer Hazard (Hazard Quotient) Associated with the Proposed Site-Specific Remediation Level for Arsenic of 30 mg/kg

$$HQ = \frac{C_s \times EF_r \times ED_c \times \left(\left(\frac{\left(IRS_c \times \left(\left(FI_s \times BIO_{a/s} \right) + \left(Ratio_{d/s} \times FI_d \times BIO_{a/d} \right) \right) \right)}{BW_c \times RfD_o \times CF} \right) + \left(\frac{SA_c \times ABS \times AF_c}{RfD_o \times CF} \right) + \left(\frac{IRA_c}{PEF \times RfD_i} \right) \right)}{AT_{nc}}$$

See Table 13 for definitions and values of all parameters.

FIGURE 4

Equation Used to Calculate Non-Cancer Hazard (Hazard Quotient) Associated with the Proposed Site-Specific Remediation Level for Copper of 9,000 mg/kg

$$HQ = \frac{C_s \times EF_r \times ED_c \times \frac{IRS_c \times \left(\left(FI_s \times BIO_{c/s}\right) + \left(Ratio_{d/s} \times FI_d \times BIO_{c/d}\right)\right)}{BW_c \times RfD_o \times CF}}{AT_{nc}}$$

See Table 14 for definitions and values of all parameters.

APPENDICES

APPENDIX A

Documentation of Minimum Value for Indoor Dust/Outdoor Soil Concentration

2.6.2 Residential Dust Sampling

As discussed in greater detail in Section 3, one pathway by which residents may be exposed to contaminants in soil is by transport of outdoor soil into the house where it combines with other sources to form house dust. When data are absent, USEPA often assumes that the concentration of contaminants in house dust is the same as in yard soil. However, studies at other sites have shown that dust levels of metals are often lower in indoor dust than in outdoor soil. Therefore, USEPA Region VIII undertook a study to define the relationship between arsenic and lead levels in soil and dust at this site. The details of the sampling and analysis plan are presented in the Phase III Project Plan (USEPA 1999d). In brief, dust samples were collected from 74 properties. The locations of these properties were selected to span a range of arsenic and lead levels in soil, and to provide for spatial representativeness across the site. One composite sample was collected from each residence by vacuuming dust from 8-14 different living areas within the house, focusing on those areas judged to be most likely to be a source of dust exposure (e.g., bedroom, family room, kitchen, etc.). Samples were collected in October and November, 1999[1]. The results are shown in Figure 2-9. In the case of lead, two dust samples were excluded as outliers because they contained lead at concentration values (2,000 ppm and 9,900 ppm) that were much higher than that observed in yard soil (268 ppm and 320 ppm, respectively). The source of the high dust lead at these two locations is not known, but could be associated with releases from indoor leaded paint. Individuals living in these two homes were referred to the City and County of Denver's Department of Environmental Health to discuss the possible source of lead in the dust in their home, and the USEPA offered free blood lead testing to all family members.

As seen, there is only a weak correlation between the level of either arsenic or lead in paired soil and dust samples ($R^2 = 0.14$ to 0.18, respectively). Nevertheless, the slopes of both regression lines are statistically different from zero ($p < 0.01$), with best estimate parameter values as follows:

Arsenic: $C_{dust} = 0.06 \cdot C_{soil} + 11$

Lead: $C_{dust} = 0.34 \cdot C_{soil} + 150$

These slope values are somewhat higher than were observed in the Risk-Based sampling data (arsenic = -0.004 ppm per ppm, lead = -0.014 ppm per ppm) (see Section 2.3.2), perhaps because of the larger number of samples or perhaps because of differences in sampling and analysis methods for soil and dust. These slope values are within the range of values that have been observed at other sites investigated in Region VIII, as shown below:

---

[1] It is not known if dust concentrations at the site vary seasonally, but maximum impact from yard soil is suspected to occur in the late summer.

Paul Damian

BASELINE HUMAN HEALTH RISK ASSESSMENT VASQUEZ BOULEVARD AND I-70 SUPERFUND SITE DENVER, CO

August, 2001

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APPENDIX B

Documentation of Most Likely Value for Indoor Dust/Outdoor Soil Concentration

3.3.1.2 Dust

The dust data for arsenic were provided in the Bornschein (1992 and 1994) study. Interior dust samples were collected from homes in Anaconda and Opportunity. Three interior dust samples were commonly taken for each residence. Data from a single residence were averaged prior to calculation of exposure point concentrations. Statistical tests of dust arsenic concentrations suggest a lognormal distribution. Therefore, data were logtransformed and arsenic exposure point concentrations derived for each subarea by calculating the 95% UCL of the arithmetic mean (EPA 1992b) for the lognormalized data (Table 3-3).

Dust samples were not analyzed for lead. However, analysis of paired soil and interior dust measurements for arsenic suggest a transfer coefficient of 0.43 for movement from soil to dust (Bornschein 1994). That is, concentrations of arsenic in indoor dust are about 43 percent of arsenic concentrations in outdoor soil. This value is derived from multiple regression analyses performed by Bornschein (1994) on data collected during the Anaconda arsenic exposure study, and represents information from paired soil and dust samples from over 300 locations. If arsenic and lead in smelter wastes are assumed to move in similar fashion from soil into dust, then the arsenic coefficient can be used to estimate transfer of lead.

In addition to a transfer coefficient, it is expected that there will be a "background" level of lead in homes unrelated to outdoor soil. This background may be represented by the y-intercept of the soil/dust regression line. Since no dust lead measurements have been made in Anaconda, the y-intercept must be obtained indirectly, again using the arsenic data. If arsenic is used as a surrogate for lead, a constant term for lead can be calculated assuming that the ratio of the constant term for average soil lead to indoor dust lead is the same as the parallel ratio for arsenic.

The approach used to estimate the above ratio for arsenic in this assessment follows that recommended by EPA (1995e). This guidance suggests that a "y-intercept", or constant term,

REMEDIAL PLANNING ACTIVITIES AT SELECTED UNCONTROLLED HAZARDOUS SUBSTANCES DISPOSAL SITES IN A ZONE FOR EPA REGIONS VI, VII, & VIII

FINAL

BASELINE HUMAN HEALTH RISK ASSESSMENT

ANACONDA SMELTER NPL SITE
ANACONDA, MONTANA

January 24, 1996

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APPENDIX C

Documentation of Maximum Value for Indoor Dust/Outdoor Soil Concentration

TABLE 3-1 (cont'd). DEFAULT VALUES FOR MODEL PARAMETERS

PARAMETER	DEFAULT VALUE	UNITS
DATA ENTRY FOR DUST (by year)		
Dust lead concentration		
1-2 years (12-23 mo)	0	μg/g
2-3 years (24-35 mo)	0	
3-4 years (36-47 mo)	0	
4-5 years (48-59 mo)	0	
5-6 years (60-71 mo)	0	
6-7 years (72-84 mo)	0	
DATA ENTRY FOR SOIL/DUST MULTIPLE SOURCE ANALYSIS (constant)		
Ratio of dust lead concentration to soil lead concentration	0.70	unitless
Ratio of dust lead concentration to outdoor air lead concentration	100	μg Pb/g dust per μg Pb/m^3 air
DATA ENTRY FOR SOIL/DUST MULTIPLE SOURCE ANALYSIS WITH ALTERNATIVE HOUSEHOLD DUST LEAD SOURCES (constant)		
Concentration		
household dust	150	μg/g
secondary occupational dust	1,200	
school dust	200	
daycare center dust	200	
second home	200	
interior lead-based paint	1,200	
Percentage		
household dust	100 minus all other	%
secondary occupational dust	0	
school dust	0	
daycare center dust	0	
second home	0	
interior lead-based paint	0	
BIOAVAILABILITY DATA ENTRY FOR ALL GUT ABSORPTION PATHWAYS		
Total lead absorption (at low intake)		
diet	50	%
drinking water	50	
soil	30	
dust	30	
alternate source	0	
Fraction of lead absorbed passively at high intake		
diet	0.2	unitless
drinking Water	0.2	
soil	0.2	
dust	0.2	
alternate source	0.2	

United States
Environmental Protection
Agency

Office of Emergency
and Remedial Response
Washington, DC 20460

Publication Number 9285.7-15-1
EPA/540/R-93/081
PB 93 - 963510
February 1994

Macro: IEUBK Paul Damian

EPA

GUIDANCE MANUAL FOR THE INTEGRATED EXPOSURE UPTAKE BIOKINETIC MODEL FOR LEAD IN CHILDREN

APPENDIX D

Arsenic Bioavailability Papers

EPA
OSWER Directive #9200.0-76
June 2010

RELATIVE BIOAVAILABILITY OF ARSENIC IN SOILS AT 11 HAZARDOUS WASTE SITES USING AN *IN VIVO* JUVENILE SWINE METHOD

Bioavailability Subcommittee of the Technical Review Workgroup

Office of Solid Waste and Emergency Response

U.S. Environmental Protection Agency

Washington, DC 20408

ACKNOWLEDGMENTS

The work described in this report is the product of a team effort involving a large number of people. In particular, the following individuals contributed significantly to the findings reported here:

Most of the *in vivo* studies described in this report were planned and sponsored by USEPA, Region 8. Technical and managerial direction for this project was provided mainly by Christopher P. Weis, PhD, DABT, and Gerry M. Henningsen, DVM, PhD, DABT/DABVT.

All of the *in vivo* studies described in this report were performed by Stan W. Casteel, DVM, PhD, DABVT, at the Veterinary Medical Diagnostic Laboratory, College of Veterinary Medicine, University of Missouri, Columbia, Missouri. Dr. Casteel was supported by Larry D. Brown, DVM, MPH, Ross P. Cowart, DVM, MS, DACVIM, James R. Turk, DVM, PhD, DACVP, John T. Payne, DVM, MS, DACVS, Steven L. Stockham, DVM, MS, DACVP, Margaret E. Dunsmore, BS, and Roberto E. Guzman, DVM, MS. Analysis of urine and other biological samples was performed by Dr. Edward Hindenberger, of L.E.T., Inc., Columbia, Missouri.

Technical support in planning and evaluating the animal studies was provided by staff from Roy F. Weston, Inc.; ISSI Consulting Group; and SRC.

Dr. Drexler, University of Colorado, Boulder, performed all of the electron microprobe and particle size analyses of the test materials evaluated in these studies.

Dr. Timothy Barry, USEPA National Center for Environmental Economics, provided on-going support in the development, testing, and evaluation of the statistical methods used in dose response curve fitting and data reduction.

Dr. William Brattin, SRC, provided assistance in the design of the swine bioassay and data reduction procedures, and authorship of this report.

EXECUTIVE SUMMARY

INTRODUCTION

Reliable analysis of the potential hazard to humans from ingestion of a chemical depends upon accurate information on a number of key parameters, including the concentration of the chemical in environmental media (e.g., soil, dust, water, food, air, paint), intake rates of each medium, and the rate and extent of absorption ("bioavailability") of the chemical by the body from each ingested medium. Knowledge of bioavailability is important because the amount of a chemical (e.g., arsenic) that actually enters the body from an ingested medium depends on the physical-chemical properties of the chemical and of the medium. Accurate assessment of the human health risks resulting from oral exposure to arsenic requires knowledge of the amount of arsenic absorbed from the gastrointestinal tract into the body. When reliable data are available on the relative bioavailability (RBA) of a chemical in a site medium (e.g., soil), this information can be used to improve the accuracy of exposure and risk calculations at that site. Available RBA data can be used to adjust default oral toxicity values (reference dose and slope factor) to account for differences in absorption between the chemical ingested in water and the chemical ingested in site media, assuming the toxicity factors are based on a readily soluble form of the chemical.

This document summarizes a number of *in vivo* studies that have been performed in young swine to investigate the RBA of arsenic in different environmental media.

METHODS

Basic In Vivo Experimental Design

All *in vivo* studies were performed using young swine. Swine were selected for use because available physiological data indicate that young swine are a good model for the human gastrointestinal system. Groups of animals (usually 5 per dose group) were exposed to test material or reference material for 12–15 days. Dosing was usually oral, although some groups were exposed to sodium arsenate by gavage or by intravenous injection.

Samples of urine were collected from each animal on several different days during the study (the exact days varied from study to study). Prior to analysis, samples of urine were digested using one of two alternative methods. Studies that used the first digestion method are referred to as Phase II, and studies that used the second digestion method are referred to as Phase III. After digestion, all samples were analyzed for arsenic using the hydride method.

Basic Method for Estimating RBA

Arsenic that is absorbed into the body from the gastrointestinal tract is excreted in the urine within 1–2 days (see Table 2-1). Based on this, the RBA of a test material may be estimated by measuring the urinary excretion fraction (UEF) of arsenic administered in test material and in reference material (sodium arsenate), and calculating the ratio of the two UEF values:

$$RBA(test\ material) = UEF(test\ material) / UEF(sodium\ arsenate)$$

The UEF for each material (test soil, sodium arsenate) is estimated by plotting the mass of arsenic excreted by each animal as a function of the dose administered, and then fitting the data for the two test materials to a simultaneous weighted regression model. The slopes estimated for each test material are direct estimates of the UEF. The RBA is estimated as the ratio of the slopes (slope test material/slope sodium arsenate); the regression model also provides estimates of the uncertainty in the slope estimates. A complete description of the regression model is included in Appendix A of the report.

RESULTS

In total, 29 test materials were investigated using the *in vivo* swine bioassay (two in duplicate). In three cases, the amount of arsenic administered was too low to allow reliable measurement of RBA, and the results for these samples are not considered to be meaningful. Values for the remaining all 29 test materials are shown below.

Summary of RBA Estimates for Phase II and Phase III Test Materials

Phase	Experiment	Sample	Arsenic Concentration[a] (ppm)	RBA ± SEM
Phase II	2	Bingham Creek Channel Soil	149	39% ± 8%
	4	Murray Smelter Slag	695	55% ± 10%
		Jasper County High Lead Mill[b]	16.4	327% ± 105%
	5	Aspen Berm[b]	66.9	100% ± 46%
		Aspen Residential[b]	16.7	128% ± 52%
	6	Butte Soil	234	9% ± 3%
		Midvale Slag	591	23% ± 4%
	7	California Gulch Phase I Residential Soil	203	8% ± 3%
		California Gulch Fe/Mn PbO	110	57% ± 12%
	8	California Gulch AV Slag	1050	13% ± 4%
	9	Palmerton Location 2	110	49% ± 10%
		Palmerton Location 4	134	61% ± 11%
	10	California Gulch AV Slag	1050	18% ± 2%
	11	Murray Smelter Soil	310	33% ± 5%
	15	Clark Fork Tailings	181	51% ± 6%

Summary of RBA Estimates for Phase II and Phase III Test Materials				
Phase	**Experiment**	**Sample**	**Arsenic Concentration[a] (ppm)**	**RBA ± SEM**
Phase III	1	VBI70 TM1	312	40% ± 4%
		VBI70 TM2	983	42% ± 4%
		VBI70 TM3	390	37% ± 3%
	2	VBI70 TM4	813	24% ± 2%
		VBI70 TM5	368	21% ± 2%
		VBI70 TM6	516	24% ± 3%
	3	Butte TM1	234	18% ± 3%
		Butte TM2	367	24% ± 2%
	4	Aberjona River TM1	676.3	38% ± 2%
		Aberjona River TM2	312.8	52% ± 2%
	5	El Paso TM1	74	44% ± 3%
		El Paso TM2	73	37% ± 3%
	6	ACC Utility Pole Soil	320	47% ± 3%
	7	ACC Dislodgeable Arsenic	3500	26% ± 1%

SEM = Standard error of the mean, an indicator of the relative uncertainty around the RBA estimate (see Appendix A)
[a]Same sample as evaluated in Phase II
[b]The amount of arsenic administered was too low to allow reliable measurement of RBA, and the results for these samples are not considered to be meaningful

As seen, using sodium arsenate as a relative frame of reference, estimated RBA values range from less than 10% to more than 60% (excluding the 3 values considered to be unreliable). This wide variability supports the conclusion that there can be important differences in RBA between different types of samples, and that use of a site-specific RBA value is likely to increase the accuracy of risk estimates for arsenic. This conclusion is also consistent with the similarity between the coefficient of variability of the dose-UEF slope for test materials (0.38) and the coefficient of variability of estimated RBAs for the same test materials (0.32).

Correlation of RBA with Arsenic Geochemistry

One objective of this project was to obtain preliminary information on which chemical forms or mineral associations of arsenic tend to have high bioavailability and which tend to have low bioavailability. Geochemical speciation data were obtained for 20 different test materials using electron microprobe analysis. A total of 28 different arsenic phases were represented in the test materials; some test materials contained more than one arsenic phase. In order to derive quantitative estimates of phase-specific RBA values, a multivariate linear regression approach was used. Because the total number of phases (28) was larger than the number of RBA measurements (20), the existing data are not sufficient to perform a robust regression analysis based on individual phases. A screening-level analysis was performed by grouping the 28 different phases into broader categories based on professional judgment

regarding the expected degree of similarity between members of a group. Only the arsenic mass in partially or entirely *liberated* particles (arsenic-bearing grains that are partially or entirely exposed on their outer surfaces) was included in this analysis. Based on this analysis, it is possible to assign tentative qualitative estimates of bioavailability, as follows:

Low Bioavailability	**Medium Bioavailability**	**High Bioavailability**
As_2O_3 Sulfosalts	As Phosphate FeAs Oxide PbAs Oxide MnAs Oxide Fe and Zn sulfates	FeAsO

CONCLUSION

The data from the investigations performed under this program support the following main conclusions:

1. Juvenile swine constitute a useful and stable animal model for measuring the relative bioavailability of arsenic in a variety of soil or soil-like test materials. The Phase III protocol described in this report is the recommended standard operating procedure (SOP) for the juvenile swine RBA assay.
2. There are clear differences in the *in vivo* RBA of arsenic between different types of test materials, ranging from less than 10% to more than 60%. Thus, knowledge of the RBA value for different types of test materials at a site can be important for improving arsenic risk assessments at a site.
3. Available data are not yet sufficient to allow reliable quantitative calculation of the RBA for a test material based only on knowledge of the relative amounts of arsenic mineral phases present. However, tentative qualitative estimates of low, medium, or high bioavailability have been made based on the major phase type of the arsenic containing waste material.
4. Additional extraction steps were identified and necessary to convert urinary organoarsenic metabolites to inorganic arsenic for analysis of total arsenic in urine.
5. Due to limitations in detection limits for measurement of arsenic in urine, a minimum arsenic dose of 25 µg/kg bw-day is recommended for the juvenile swine RBA assay, so that the amount of arsenic excreted in urine reaches a measurable quantity.

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APPENDIX C: TEST MATERIAL CHARACTERIZATION

APPENDIX D: DETAILED RAW DATA FILES (see electronic files on attached CD)

APPENDIX E: DETAILED DATA FITTING AND RBA CALCULATIONS

ACRONYMS AND ABBREVIATIONS

AAS	Atomic absorption spectrometer
ABA	Absolute bioavailability
AFo	Oral absorption fraction
bw	Body weight
°C	Degrees Celsius
CV	Coefficient of variation (SD/mean)
DMA	Dimethylarsinic acid
EDS	Energy dispersive spectrometer
EMPA	Electron Microprobe Analysis
ERA	Environmental Resource Associates
GLP	Good Laboratory Practices
HCl	Hydrochloric acid
HNO_3	Nitric acid
ICP-AES	Inductively Coupled Plasma-Atomic Emission Spectrometry
IRIS	Integrated Risk Information System
kg	Kilogram
KI	Potassium iodide
L	Liter
mg	Milligram
mL	Milliliter
MMA	Monomethylarsonic acid
NaAs	Sodium arsenate
NIST	National Institute of Standards and Testing
NRCC	National Resource Council Canada (Institute for National Measurement Standards)
ORD	USEPA Office of Research and Development
oRfD	Oral reference dose
oSF	Oral slope factor
PE	Performance Evaluation
ppm	Parts per million
QA	Quality assurance
RBA	Relative bioavailability
RME	Reasonable maximum exposure
SD	Standard deviation
SEM	Standard error of the mean
SOP	Standard operating procedure
TAL	Target Analyte List
UEF	Urinary excretion fraction
µg	Microgram
µm	Micrometer
U.S. EPA	U.S. Environmental Protection Agency
WDS	Wavelength dispersive spectrometers
XAS	X-ray absorption spectroscopy

1.0 INTRODUCTION

1.1 Overview

Accurate assessment of the human health risks resulting from oral exposure to arsenic requires knowledge of the amount of arsenic absorbed from the gastrointestinal tract into the body. This information on gastrointestinal absorption may be described either in absolute or relative terms:

Absolute Bioavailability (ABA) is the ratio of the amount of arsenic absorbed to the amount ingested:

$$ABA = (Absorbed\ Dose) / (Ingested\ Dose)$$

This ratio is also referred to as the oral absorption fraction (AFo).

Relative Bioavailability (RBA) is the ratio of the absolute bioavailability of arsenic present in some test material to the absolute bioavailability of arsenic in some appropriate reference material:

$$RBA = ABA(test) / ABA(reference)$$

Usually the form of arsenic used as the reference material is an arsenic compound dissolved in water or a readily soluble form (e.g., sodium arsenate) that is expected to completely dissolve when ingested.

For example, if 100 µg of arsenic dissolved in drinking water were ingested and a total of 90 µg were absorbed into the body, the ABA would be 0.90 (90%). Likewise, if 100 µg of arsenic contained in soil were ingested and 30 µg were absorbed into the body, the ABA for soil would be 0.30 (30%). If the arsenic dissolved in water was used as the frame of reference for describing the relative amount of arsenic absorbed from soil, the RBA would be 0.30/0.90, or 0.33 (33%).

When reliable data are available on the RBA of a chemical (e.g., arsenic) in a site medium (e.g., soil), this information can be used to improve the accuracy of exposure and risk calculations at that site. Available RBA data can be used to adjust default oral toxicity values (reference dose and slope factor) to account for differences in absorption between the chemical ingested in water and the chemical ingested in site media, assuming the toxicity factors are based on a readily soluble form of the chemical.

1.2 Using Relative Bioavailability Data to Improve Risk Calculations for Arsenic

The Risk Assessment Guidance for Superfund (RAGS) Part A (U.S. EPA, 1989) and Guidance for Evaluating the Bioavailability of Metals in Soils for Use in Human Health Risk Assessment (U.S. EPA, 2007) discuss making adjustments to exposure estimates in Superfund site-specific risk assessments when the medium of exposure in the exposure assessment differs from the medium of exposure assumed by the toxicity value (cancer slope factor, reference dose value, etc.) based upon site-specific

bioavailability data. When a reliable RBA value is available for a particular site medium (e.g., soil), the RBA can be used to adjust estimate of the daily intake (DI) as follows:

2.0 EXPERIMENTAL METHODS FOR ESTIMATING ARSENIC RBA BY *IN VIVO* STUDIES

All *in vivo* studies were performed according to the spirit and guidelines of Good Laboratory Practices (GLP: 40 CFR 792). Standard Operating Procedures (SOPs) that included detailed methods for all of the components of each study were prepared, approved, and distributed to all team members prior to all studies.

2.1 Basic Approach for Measuring RBA *In Vivo*

Summary of Arsenic Toxicokinetics

Available data from studies on the absorption and excretion of soluble arsenic compounds in humans and animals are summarized in Table 2-1. Based on the fecal excretion data, absorption of soluble arsenic compounds (sodium arsenate and sodium arsenite) typically appears to be at least 90% in both humans and animals.

Estimates of biliary excretion are available from studies in which soluble arsenic compounds have been given by intravenous injection. Results from studies by Johnson and Farmer (1991) and Freeman et al. (1994) indicate biliary excretion is probably about 4–8% of the absorbed dose. Correction of fecal excretion data by subtraction of 8% to account for biliary excretion suggests that absorption of soluble arsenic is probably close to 100% in most cases.

Figure 2-1 plots the urinary excretion data from Table 2-1. It is apparent that typical urinary recovery of soluble arsenic in humans (top panel) is dose-independent, and averages about 67% (range = 45 to 85%). Urinary recovery of arsenic in rodents (Figure 2-1, lower panel) is similar, with an average value of 70% (range = 36 to 94%). Often the sum of arsenic recovery in urine plus feces is slightly less than 100%. This could be partly due to experimental error, but is more likely due to retention of some arsenic in tissues such as skin and hair.

Conceptual Model

Based on the human and animal data above, it appears that both absorption and excretion are likely to be linear (i.e., dose independent) processes at dose levels well above those expected from

exposure to arsenic in soil (e.g., 1000 ppm × 100 mg/day = 100 µg/day). Figure 2-2 shows a conceptual model for the toxicokinetic fate of ingested arsenic that is based on concept that absorption and excretion are linear. Key points of the model are as follows:

- If 100% of all absorbed arsenic were excreted in the urine, the UEF would be equal to the oral absorption fraction or ABA. However, some absorbed arsenic is excreted in the feces via the bile and some absorbed arsenic enters tissue compartments (e.g., skin, hair) from which it is cleared very slowly or not at all. Thus, the urinary excretion fraction should not be equated with the absolute absorption fraction.

- The RBA of two orally administered materials (e.g., a test soil and sodium arsenate) can be calculated from the ratio of the urinary excretion fraction of the two materials. This calculation is independent of the extent of tissue binding or biliary excretion, because the fraction of absorbed arsenic that is excreted in urine (K_u), which does depend on tissue binding and biliary excretion, cancels in the calculation:

$$RBA(x\ vs.\ y) = \frac{UEF(x)}{UEF(y)} = \frac{AF_o(x) \cdot K_u}{AF_o(y) \cdot K_u} = \frac{AF_o(x)}{AF_o(y)}$$

where:

RBA(x vs. y) is the relative bioavailability of As in test material (*x*) vs. sodium arsenate (*y*);

UEF is the urinary excretion fraction of the dose excreted in urine;

AF_O is the absorption fraction, which is the fraction of the dose absorbed following oral administration; and

K_u is the fraction of the absorbed dose excreted in urine.

Thus, measurement of the urinary excretion fraction (µg/day excreted in urine per µg/day administered) of test material and reference material (sodium arsenate) is the key experimental goal in these arsenic RBA studies.

Estimation of UEF

The amount of arsenic excreted in urine (µg/day) is calculated as the product of urinary concentration (µg/L) and urinary volume (L/day). The UEF is the rate of As excreted in urine (mL/day) divided by the dose (mg/day). Conceptually, the UEF could be estimated for each animal on each day that data are collected, and the UEF estimates for a particular dose material could then be averaged across different animals, dose levels, and days. However, this approach does not account for baseline intake and excretion of arsenic in the control group (unexposed animals), and tends to overemphasize UEF values at

the low end of the dose range where the estimate of urinary excretion is most uncertain. A more robust approach, used in this evaluation, is to plot the mass excreted by each animal as a function of the dose administered to each animal, and then fit a linear regression line to the combined data. The slope of this line is a direct estimate of the UEF (µg/day excreted per µg/day ingested). This approach automatically accounts for baseline arsenic ingestion and excretion in control (unexposed) animals, and is not disproportionately influenced by measurement error at the low end of the dose curve.

The process of deriving the best fit linear regression lines through the data is complicated by the fact that the equations for each dose material in a study must have the same intercept, and because the variability in the data tend to increase as the dose increases (this is referred to as heteroscedasticity). In order to address these issues, the data from each study were fit using simultaneous weighted linear regression, as detailed in Appendix A.

2.2 Experimental Methods

2.2.1 Study Designs

Phase II Study Designs

Measurement of arsenic bioavailability in most Phase II studies was performed in parallel with studies designed to estimate lead bioavailability (U.S. EPA, 2007). Groups of animals (typically 4 or 5 per dose group) were given oral doses of a test material (e.g., soil, tailings, slag, sediment) twice daily for 15 days, and 24-hour urine samples were collected several times during the study (typically on days 7 and 14). Because the main focus of these studies was on lead RBA, these early studies did not include groups of animals that were exposed to an arsenic reference material. Thus, these studies, taken alone, were not sufficient to allow for an estimation of the arsenic RBA of the test materials.

In order to address this data gap and provide data on the urinary excretion fraction of a suitable reference material, two “pilot studies” (Phase II, Experiments 10 and 15) were performed to establish the urinary excretion fraction for sodium arsenate administered by three different routes: orally with a small amount of food, orally by gavage (no food), and by intravenous injection.

Appendix B1 provides the detailed study designs for each Phase II study, and Appendix B2 provides the detailed designs for the two pilot studies.

Phase III Study Designs

After the completion of the Phase II studies, a modified study design was developed that was specifically optimized for evaluation of arsenic RBA, rather than lead RBA. In this design, each study includes a set of animals exposed to the reference material (sodium arsenate) and one to three different

test materials, each at two or three different dose levels. In some cases, the doses of arsenic (expressed as µg/day) were held constant over time, rather than being adjusted to account for changing body weight. This is because the basic computational approach used to estimate RBA (described above) compares the mass of arsenic excreted in urine (µg/day) to the mass of arsenic ingested (µg/day), so body weight adjustments are not needed.

Appendix B3 provides the detailed study designs for each Phase III study.

2.2.2 Experimental Animals

Juvenile swine were selected for use in these studies because their gastrointestinal physiology is more similar to humans than most other animal models (Weis and LaVelle, 1991). All animals were young males of the Pig Improvement Corporation genetically defined Line 26, and were purchased from Chinn Farms, Clarence, MO. All studies used intact animals, except for one (the second VBI70 study), which used castrated animals. The number of animals purchased for each study was typically 6–8 more than required by the protocol. These animals were usually purchased at age 4–5 weeks (weaning occurs at age 3 weeks), and they were then held under quarantine for one week to observe their health before beginning exposure to test materials. Any animals that appeared to be in poor health during this quarantine period were excluded. To minimize weight variations between animals and groups, extra animals most different in body weight (either heavier or lighter) four days prior to exposure (day-4) were also excluded from the study. The remaining animals were assigned to dose groups at random. When exposure began (day zero), the animals were about 5–6 weeks old and weighed an average of about 7–12 kg.

All animals were housed in individual stainless steel cages. Each animal was examined by a certified veterinary clinician (swine specialist) prior to being placed on study, and all animals were examined daily by an attending veterinarian while on study. There were no instances where animals that became ill could not be promptly restored to good health by appropriate treatment, so no animals were removed from the studies.

2.2.3 Diet

Animals provided by the supplier were weaned onto standard pig chow purchased from MFA Inc., Columbia, MO. In order to minimize arsenic exposure from the diet, the animals were gradually transitioned from the MFA feed to a special feed (Zeigler Brothers, Inc., Gardners, PA) over the time interval from day -7 to day -3; this feed was then maintained for the duration of the study. The feed was nutritionally complete and met all requirements of the National Institutes of Health–National Research Council. The typical nutritional components and chemical analysis of the feed is presented in Table 2-2.

Each day every animal was given an amount of feed equal to 5% (4% in the Aberjona River study) of the mean body weight of all animals on study. Feed amounts were adjusted every three days, when pigs were weighed. Feed was administered in two equal portions of 2.5% (2% in the Aberjona River study) of the mean body weight at 11:00 AM and 5:00 PM daily. Periodic analysis of feed samples indicated that the arsenic level was generally below the detection limit (0.1 ppm), which corresponds to a dose contribution from food of less than 5 µg/kg-day (less than 50 µg/day for a 10 kg animal).

Drinking water was provided *ad libitum* via self-activated watering nozzles within each cage. Periodic analysis of samples from randomly selected drinking water nozzles indicated the arsenic concentration was less than the detection limit (about 1 µg/L). Assuming water intake of about 0.1 L/kg-day, this corresponds to a dose contribution from water of less than 0.1 µg/kg-day (1 µg/day for a 10 kg animal).

2.2.4 Dosing

Animals were exposed to sodium arsenate (abbreviated in this report as "NaAs") or a test material for 12–15 days, with the dose for each day being administered in two equal portions given at 9:00 AM and 3:00 PM (two hours before feeding). Animals were administered dose material when in a semi-fasted state (i.e., two hours before feeding) to avoid the presence of food in the stomach, which is known to reduce absorption of arsenic. In Phase II, doses were based on measured group mean body weights and were adjusted every three days to account for animal growth. In most Phase III studies, doses were held constant (independent of body weight).

Dose material was placed in the center of a small portion (about 5 grams) of moistened feed (referred to as a "doughball"), which was administered to the animals by hand. In cases where the mass of soil was too large to fit into one doughball, the test material was distributed among two or more doughballs. Occasionally, some animals did not consume some or the entire dose (usually because the dose dropped from their mouth while chewing). All missed doses were recorded and the time-weighted average dose calculation for each animal was adjusted downward accordingly.

2.2.5 Collection and Preservation of Urine

Samples of urine were collected from each animal on several different days during the study (the exact days varied from study to study). Collection began at about 8:00 AM and ended 24 hours later in the Phase II studies and 48 hours later in most Phase III studies. The urine was collected in a stainless steel pan placed beneath each cage, which drained into a plastic storage bottle. Each collection pan was fitted with a nylon screen to minimize contamination with feces or spilled food. At the end of each collection period, the urine volume was measured and two 60-mL portions were removed for analysis.

Each 60 mL sample was preserved by addition of 0.6 mL of concentrated nitric acid. These samples were refrigerated until sample analysis.

2.2.6 Arsenic Analysis

All samples were assigned random chain-of-custody tag numbers and submitted to the analytical laboratory in a blind fashion. Arsenic concentrations in urine were measured using a hydride generation approach. This method requires that all arsenic exist in the form of inorganic arsenic before hydride generation. Because arsenic in urine can exist in organic forms (monomethylarsonic acid [MMA] and dimethylarsinic acid [DMA]) as well as inorganic forms, digestion of the urine prior to analysis is required.

2.2.6.1 Sample Digestion

Two different methods of arsenic digestion prior to analysis were employed during this project. The first method was used during Phase II and a revised method was used for Phase III studies. As discussed in greater detail below (see *PE Samples and Blind Duplicates* in Section 2.2.7), this change in digestion method was adopted because recovery of total arsenic from urine and other biological samples using the first method was limited by incomplete conversion of organic metabolites of arsenic (MMA and DMA) to inorganic arsenic. The revised method produced improved recoveries of these metabolites and of total arsenic.

<u>Digestion Method 1</u>

A 25 mL aliquot of acidified urine was removed and placed in a clean 100 mL glass beaker. 20 mL of concentrated nitric acid and 2.5 mL of concentrated perchloric acid were then added. The beaker was covered with a watch glass and placed on a hot plate to reflux for 4–12 hours. After this period, the heat was increased to drive off the nitric acid and to cause the perchloric acid to fume. After about 10 minutes of fuming, the digestate was cooled slightly and diluted with 20 mL of distilled water. This was heated until clear, and then cooled and diluted to 50 mL.

<u>Digestion Method 2</u>

A 25 mL aliquot of acidified urine was removed and placed in a clean 100 mL beaker. 3.0 mL of methanol, 10.0 mL of 40% (w/v) magnesium nitrate hexahydrate, and 10.0 mL of concentrated trace metal grade nitric acid (HNO_3) were then added. The beaker was covered with a watch glass and placed on a hot plate to reflux for 8–12 hours at 70–80ºC. After this, the temperature was increased to 200°C, and the watch glass was moved back to allow faster evaporation. The sample was then heated to complete dryness (8–12 hours), covered with a watch glass, and allowed to cool. Dried samples were

transferred to a cool muffle furnace which was heated at a rate of 1 degree/minute to a temperature of 500ºC, and then held at 500ºC for 3 hours before cooling. Ashed samples were dissolved by adding 5 mL distilled water and 5 mL concentrated trace metal grade hydrochloric acid (HCl), and boiling gently until the white residue was completely dissolved. After cooling, the dissolved sample was diluted with distilled water to 50.0 mL and held until analysis.

2.2.6.2 Arsenic Analysis by Hydride Generation

Arsenic concentrations in urine were measured by hydride generation. Samples were prepared for hydride generation by dilution with a solution of 10% HCl, 10% potassium iodide (KI), and 5% ascorbic acid. The samples were diluted l/10 or 1/5 (v/v), depending on the detection limit desired. Samples were held in the diluting fluid at least 30 minutes before analysis, but overnight was preferred. Analysis was performed on a Perkin-Elmer 3100 atomic absorption spectrometer (AAS) equipped with a FIAS 200 flow injection system. Calibration standards were prepared in dilution fluid (10% HCl, 10% KI, 5% ascorbic acid) at concentrations of 0.0, 0.2, 1.0, 5.0, 10.0, and 15.0 µg/L.

The detection limit of the method was evaluated by performing 10 replicate analyses of a low standard (about 1 µg/L). The detection limit was defined as three times the standard deviation of these 10 analyses. A 1/10 dilution typically gave a detection limit of about 2 µg/L, while a dilution of 1/5 typically yielded a detection limit of about 1 µg/L. All responses below the detection limit were evaluated at one-half the detection limit.

2.2.7 Quality Assurance

A number of quality assurance (QA) steps were taken throughout the studies to assess and document the quality of the data that were collected. These steps are summarized below.

<u>Blanks</u>

Blank samples analyzed with each batch of samples never yielded a measurable level of arsenic, with all values being reported as less than 2.0 µg/L of arsenic.

<u>Spike Recovery</u>

Randomly selected samples were spiked with known amounts of inorganic arsenic (5–20 µg) and the recovery of the added arsenic was measured. In Phase II, recovery of arsenic from spiked samples typically ranged from 95 to 105%, with an average across all analyses of 99.8%. In Phase III, recovery of arsenic from spiked samples typically ranged from 83 to 120%, with an average across all analyses of 103%.

Laboratory Duplicates

Random urine samples were selected for duplicate analysis by the analyst. In Phase II, the average absolute difference across all pairs of duplicates samples was 2.4 µg/L (n = 58). In Phase III, the average absolute difference across all samples was 2.3 µg/L (n = 115).

Laboratory Control Standards

Samples of various reference materials were analyzed with each set up test samples. Results for these standards are summarized below:

Reference Material	Description	Certified Value	Measured Results		
			Mean (% Certified Value)	Standard Deviation	n
Phase II					
ERA Potable WatR™ #697 (Trace Metals, Lot 3413)	Plain water spiked with inorganic trace metals	68.8 µg/L	23.6 µg/L (34.3%)	10.2 µg/L	12
NIST 2670 Elevated	Normal human urine spiked with inorganic trace elements	480 ± 100 µg/L	451 µg/L (94%)	12.8 µg/L	26
Phase III					
ERA Waste WatR™ #500 (Trace Metals, Lot P081)	Plain water spiked with inorganic trace metals	366 µg/L	361 µg/L (98.6%)	7.2 µg/L	220
ERA Waste WatR #500™ (Trace Metals, Lot 99106)	Plain water spiked with inorganic trace metals	347 µg/L	328 µg/L (95%)	6.7 µg/L	38
ERA Waste WatR #500™ (Trace Metals, Lot 9978)	Plain water spiked with inorganic trace metals	92.9 µg/L	96 µg/L (103%)	1.7 µg/L	90
NIST 2670 Elevated	Normal human urine spiked with inorganic trace elements	480 ± 100 µg/L	544 µg/L (113%)	9.6 µg/L	7
NIST 1640	Natural water containing trace elements (not spiked)	0.0267 ± 0.0004 µg/g	0.027 µg/g (99.4%)	0.001 µg/g	2
NRCC Dolt-2	Dogfish liver (not spiked)	16.6 ± 1.1 µg/g dry wt	14.7 µg/g dry wt (88.6%)	0.8 µg/g dry wt	10
NRCC Tort-2	Lobster hepatopancreas (not spiked)	21.6 ± 1.8 µg/g dry wt	21.3 µg/g dry wt (98.8%)	1.2 µg/g dry wt	12
NIST 1566b	Oyster tissue (not spiked)	7.65 ± 0.65 µg/g dry wt	7.6 µg/g dry wt (99.9%)	0.5 µg/g dry wt	13

ERA: Environmental Resource Associates
NIST: National Institute of Standards and Technology
NRCC: National Resource Council Canada (Institute for National Measurement Standards)

As seen, results were good with the exception of one standard (ERA #697) in Phase II. The low recovery from these samples is not understood.

PE Samples and Blind Duplicates

In addition to these laboratory-based (non-blind) QA procedures, a series of blind Performance Evaluation (PE) samples (known concentrations of sodium arsenate in control urine) and blind duplicates were submitted to the laboratory in a random fashion, commingled with normal test samples.

The combined results for samples evaluated during the Phase II pilot studies are shown in Figure 2-3. As seen in Panel A, there was good accuracy on sodium arsenate PE samples (10, 30, and 1000 µg/L) throughout the duration of each study. As shown in Panel B, there was also good reproducibility between blind duplicate samples.

Initially, these QA results were interpreted to indicate that the analytical procedure was operating correctly. However, the low recovery of arsenic for the ERA standard, as well as the observation that the recovery of arsenic from the urine of animals administered sodium arsenate was lower than expected, suggested that a problem did exist. In order to investigate this, a series of PE samples were prepared by addition of three different concentrations of each of the four major urinary arsenic metabolites to control urine, and each was analyzed in triplicate. The results are summarized below:

Urinary Metabolite	**Average Recovery (Method 1)**
Arsenate	101±2%
Arsenite	93±2%
MMA	73±3%
DMA	15±4%

As seen, recovery of inorganic forms of arsenic were within reasonable bounds, but recovery of MMA was somewhat decreased and recovery of DMA was very poor. Based on the expectation that this low recovery was based on incomplete conversion of MMA and DMA to inorganic arsenic prior to hydride generation, a more vigorous digestion method was developed (see *Digestion Method 2* in Section 2.2.6). Recovery of each urinary metabolite using this new digestion method is summarized below:

Urinary Metabolite	Average Recovery (Method 2)
Arsenate	106±2%
Arsenite	106±7%
MMA	107±3%
DMA	113±3%

As seen, the revised digestion method yielded good recovery of all metabolites, including both MMA and DMA. On this basis, the revised digestion method was used on all arsenic RBA studies following the completion of Phase II.

The results for the Phase III PE samples are shown in Figure 2-4. As seen, the PE samples included several different concentrations each of four different types of arsenic (As^{+3}, As^{+5}, MMA, and DMA). With the exception of one unexplained outlier, there was good recovery of the arsenic from all four types of PE sample.

The results for the blind duplicates from Phase III are shown in Figure 2-5. As seen, there was good agreement between results for duplicate pairs, with an average absolute difference between pairs of about 6.0 µg/L and an average relative percent difference of about 1.5%.

Inter-laboratory Comparison

In two Phase III studies (Experiments 1 and 2), a series of samples was submitted to a second laboratory for inter-laboratory comparison of results. This included investigative samples (urine samples collected from study animals) as well as several PE samples. The results are shown in Figure 2-6. As seen, there is generally good agreement between the two laboratories, with somewhat better reproducibility for the Phase III studies.

Conclusion

Based on the results of all of the quality assurance samples and steps described above, it is concluded that the analytical results for samples of urine are generally of high quality and are suitable for derivation of reliable estimates of arsenic absorption from test materials. The only potential limitation is that recovery of organic arsenic (especially DMA) is low in Phase II studies, which will tend to result in an underestimate of UEF values. However, since RBA calculations are based on the ratio of two UEFs, if both UEFs are underestimated by the same amount, then the resultant RBA may still be reliable (see Section 2.3.2, below).

2.2.8 Test Material Characterization

Table 2-3 describes the test materials for which RBA was measured in this program and provides the analytical results for arsenic. Data on other Target Analyte List (TAL) metals, if available, are provided in Appendix C. As seen, 27 different test materials were investigated (two in duplicate). In all cases, these samples were sieved prior to analysis and dosing, and only materials which passed through a 60-mesh screen (corresponding to particles smaller than about 250 µm) were used. This is because it is believed that soil particles less than about 250 µm are most likely to adhere to the hands and be ingested by hand-to-mouth contact, especially in young children.

Many of the test materials[1] were characterized with regard to arsenic mineral phase, particle size distribution, and matrix association using electron microprobe analysis (EMPA). In this procedure, an electron microprobe with combined energy dispersive spectrometer (EDS) and multiple wavelength dispersive spectrometers (WDS) was used to evaluate the elemental composition of arsenic-bearing particles. A 1 to 2 gram split of dried sample was placed in a 2.5 cm plastic mold and impregnated with epoxy. Once the sample was hardened, it was polished and carbon coated for EMPA. The EMPA was operated at 15 kV accelerating voltage, with a 20 nA current and a 1 micron focused beam. Instrument response was calibrated using certified mineral or pure metal standards and counting times were chosen to provide 3-sigma detection limits of between 100–200 ppm. Elemental concentrations were corrected using ZAF factors and concentration errors were generally less than 5% relative. For a more detailed explanation of the EMPA method of analyses see Birks (1971) or Heinrich (1981).

Although the electron microprobe is capable of determining the precise stoichiometry of the elements in any given particle, this was not attempted in this project. This is mainly because investing time in obtaining precise stoichiometry decreases the number of different particles that can be examined. In addition, many arsenic-bearing particles are not composed of a pure mineral phase with an exact stoichiometry, but are characterized by arsenic that is either adsorbed onto other mineral particles, or is a mixture of phases that are undergoing transition from one phase to another. For this reason, particles were classified into “phases” that may not be purely stoichiometric and may contain a mixture of similar chemical phases. The first step used in the assignment of a phase designation was to determine if the

[1]Arsenic was not speciated in three Phase II samples (Aspen Berm, Aspen Residential, and Jasper County High Lead Mill) because the concentration of arsenic in each material was too low (17 ppm, 67 ppm, and 16 ppm, respectively) to allow reliable evaluation. In addition, speciation data were unavailable for four Phase III samples (El Paso TM1, El Paso TM2, ACC Utility Pole Soil, and ACC Dislodgeable Arsenic).

phase was an oxide, carbonate, sulfide, sulfate, or phosphate. Secondly, with the exception of the "phosphates," the major cation associated with the phase was identified. Therefore, phases such as Fe-sulfate, FeOOH, MnOOH, PbMO, AsMO, or $PbMSO_4$ were identified (where M represents "metal"). Some of these phases could represent a stoichiometric mineral form, but most are likely to be metastable and/or amorphous and have some quantity of arsenic sorbed to their surface.

The "phosphate" group is even more generic in that the only common dominant ion is PO_4. Although arsenic and phosphorous are both oxy-anions, a number of particles that contain both arsenic and phosphate have been identified. As above, these might include minerals that contain mixtures of phosphate and arsenate such as walentaite $(Ca,Mn,Fe)Fe_3(AsO_4,PO_4)_4\text{-}7H_2O$, morelandite $(Ba,Ca,Pb)_5Cl[AsO_4,PO_4]_3$, or turneaureite $Ca_5(Cl)[(AsO_4, PO_4)_3]$, but more likely represent arsenic adsorbed onto other phosphate-containing particles.

Detailed EMPA results are presented in Appendix C and the results, expressed as relative arsenic mass, are summarized in Table 2-4. The relative arsenic mass for a particular phase is the estimated percentage of the total arsenic in a sample that is present in that phase. Of the 28 different phases detected in one or more samples, 14 are relatively minor, with relative arsenic mass values less than 5%. However, the remaining 14 phases occur at concentrations that could contribute significantly to the bioavailability of the sample.

Table 2-5 summarizes data on the size distribution of arsenic-containing particles (measured as the longest dimension) in each sample. As seen, most samples contain a range of particle sizes, with the majority of particles being less than 50 µm in diameter.

Table 2-6 summarizes information on the degree to which arsenic-bearing grains in each sample are partially or entirely exposed on their outer surfaces (*liberated*), or are entirely enclosed within a larger particle of rock or slag (*included*). Data are presented both on a simple particle frequency basis and on the basis of relative arsenic mass. As seen, the majority of arsenic-bearing particles in all samples are partly or entirely *liberated*.

In interpreting the results of the particle speciation studies, it is important to understand that, on a mass basis, only a tiny fraction of the total sample is evaluated by electron microprobe and, hence, there is moderate uncertainty as to whether the results for the grains examined are truly representative of the sample as a whole.

It is also worth noting that other speciation methods are available to determine the chemical forms of metals in soil systems. Each method has distinct advantages and disadvantages; and some methods provide more robust data than others (see D'Amore et al. 2005). One such technique is X-ray

absorption spectroscopy (XAS) for which USEPA Office of Research and Development (ORD) has resident experts to conduct studies and the service is available to support Regional research efforts. XAS probes the sub-atomic structure of elements to distinguish specific bonding mechanisms which leads to precise determination of metal speciation. An example for As is differentiation of As sorbed to an iron oxide versus As present as the mineral scorodite ($FeAsO_4$) for which XAS can easily identify the different phases that have vastly different bioavailability behaviors whereas EMPA will identify both phases as containing As, Fe, and O.

2.3 Results

2.3.1 RBA Estimates

Detailed raw data for each study are provided in Appendix D. Results of simultaneous weighted linear regression fitting and RBA calculations are presented in Appendix E. The results are summarized below.

The upper portion of Table 2-7 summarizes the RBA results for all Phase II studies, and the lower portion summarizes the results for materials studied during Phase III. As seen, using sodium arsenate as a relative frame of reference, estimated RBA values range from 8% to more than 100%. This wide variability supports the conclusion that there can be important differences in RBA between different types of samples and that use of a site-specific RBA value is likely to increase the accuracy of risk estimates for arsenic. Available data do not include replicate estimates of RBA of the same test materials; therefore, there is no empirical basis for estimating variability in the RBA estimates that might be attributable to within-test material variability as opposed to between-test material variability. Although ABA of As is not estimated in the data reduction procedure for the swine assays, RBA is estimated as the ratio of the slopes of the dose-UEF relationships for sodium arsenate and the test material. Table 2-8 provides summary statistics for the dose-UEF slopes for sodium arsenate and all test materials assayed in the Region 8 Phase III studies. The coefficient of variation (SD/mean) for the sodium arsenate slopes is approximately 0.13 (N=7). This variability reflects an unknown combination of biological variability in As bioavailability and other assay variables that contribute to variability in the measurement of the dose-UEF slope. The coefficient of variability for the dose-UEF slopes for the test materials is 0.38 (N=14), and is greater than that for sodium arsenate by a factor of approximately 3. The difference in the two estimates reflects, at least in part, the additional variability introduced into the dose-UEF slope estimates contributed by differences in bioavailability of the test materials. This outcome suggests that test material characteristics contribute substantially to the observed variability in RBA estimates. This conclusion is also consistent with the similarity between the coefficient of variability of the dose-UEF slope for test materials (0.38) and the estimated RBAs for the same test materials (0.32).

Figure 2-7 shows that the uncertainty in the RBA value for a test material (as reflected by the difference between the upper bound and the lower bound) depends on the dose of arsenic administered in the study. As seen, three of the test materials (Aspen Berm, Aspen Residential, and Jasper County High Lead Mill) were administered only at low dose levels (less than 20 µg/kg bw-day) and have extremely wide uncertainty bounds around the RBA estimates. This is due mainly to the fact that the concentrations of arsenic in the urine were very low and, hence, were difficult to quantify with good accuracy and also difficult to distinguish from baseline. Because of the high uncertainty in these results, the data from these three test materials are not considered further. Thus, based on these results, a minimum daily As dose of 25 µg/kg-bw/day is recommended to ensure the amount if excreted in urine reaches a measurable quantity and, that is to minimize uncertainty in RBA estimates.

2.3.2 Effect of Low Analytical Recovery on Phase II RBA Values

As noted above, all of the calculations of arsenic RBA performed during Phase II are based on data obtained using an analytical method that had low recovery of organic metabolites of arsenic, which raises a concern over the accuracy of the results. However, the low recovery of arsenic is not necessarily a basis for complete distrust of the results. This is because the RBA is a ratio of two measured values, and if the degree of error (underestimation) is the same in both the numerator and denominator, then the error will cancel and the resulting ratio will be correct. However, the degree of error in each measurement depends on the relative concentration of the metabolites in the urine: if the level of MMA and DMA is low, the error will be smaller than if the levels of MMA and DMA are high. Thus, the key question is whether or not the ratio of the urinary metabolites tends to be relatively constant as a function of dose and dose material, at least over the range of exposures investigated in the Phase II studies.

The most direct approach for testing this question is to measure the relative concentration of each metabolite (As^{+3}, As^{+5}, MMA, DMA) in urine from a number of animals exposed to a series of different dose levels and dose materials. This approach was attempted, but the results for quality control samples indicated that the results were not reliable, presumably due to the technical difficulty of performing the separation and quantification of the individual metabolites. Therefore, this approach was not pursued further.

An alternative approach is to measure the UEF and RBA of several test materials using both analytical methods, and to compare the results. This approach was implemented for two different test materials (Butte TM1 and Butte TM2), and the results are shown below:

Substance Administered	Digestion Method 1		Digestion Method 2	
	UEF	RBA	UEF	RBA
Sodium Arsenate	0.238	[1.00]	0.890	[1.00]
Butte TM1	0.047	0.20	0.158	0.18
Butte TM2	0.056	0.23	0.210	0.24

As seen, the measured UEF for sodium arsenate based on Digestion Method 1 (24%) is much lower than the UEF based on Digestion Method 2 (89%). However, the UEF of each of two different soil test materials was also lower by approximately the same relative amount when measured by Digestion Method 1 compared to Digestion Method 2, so the ratio (the RBA) was approximately constant when calculated for each method. These results indicate that, even though the low recovery of arsenic in Phase II studies is a basis for uncertainty in the RBA estimates derived during Phase II, the error due to low recovery of organic metabolites of arsenic is likely to approximately cancel, and the final RBA estimates are likely to be approximately correct. For this reason, the Phase II data were included in the overall estimates of As RBA.

2.3.3 Effect of Food on Arsenic Absorption

In Phase II Pilot Study 2 (Experiment 15), some animals were dosed with NaAs *via* gavage in order to compare the results with NaAs given in orally in doughballs. These results are shown below:

Substance Administered	UEF		
	Slope	SEM	N
NaAs – Gavage	0.189	0.014	31
NaAs – Doughball	0.177	0.014	31

As seen, the UEF for sodium arsenate administered orally in a doughball is only slightly lower than the UEF for sodium arsenate administered by gavage, indicating that the amount of feed (about 5 grams) used to administer the arsenic doses does not significantly affect arsenic absorption.

2.4 Correlation of RBA with Arsenic Geochemistry

One objective of this project was to obtain preliminary information on which mineral and chemical forms of arsenic tend to have high bioavailability and which tend to have low bioavailability. As noted above, data on chemical form or mineral association were obtained using EMPA. Detailed data are presented in Appendix C and results are summarized in Section 2.2.8 and in Tables 2-4 to 2-6.

In order to derive quantitative estimates of phase-specific RBA values, a multivariate linear regression approach was used, employing the following basic model:

$$RBA = \sum (f_i \cdot RBA_i)$$

where:

fi = Fraction of total arsenic present in phase "*i*"

RBAi = Inherent RBA of phase "*i*"

However, because a total of 28 different phases were identified and reliable RBA results were obtained for only 20 different samples, it is clear that the existing data are not sufficient to perform a robust regression analysis. Instead, a screening-level analysis was performed, as follows. First, in order to reduce the number of independent variables, the 28 different phases were grouped into 9 categories as described in Table 2-9. These categories were based on professional judgment regarding the expected degree of similarity between members of a group, along with information on the relative abundance of each phase (see Table 2-4). Phases with low relative arsenic mass (maximum relative mass in any test material less than 15%) were grouped together under "Minor Constituents;" these phases included AsMO, $AsMSO_4$, Clays, Paint, Pb Solder, Pb-As Vanidate, PbAsMO, PbAsSbCuO, $PbCrO_4$, PbMO, PbMS, $PbMSO_4$, Pyrite, TiO_2, and $ZnSiO_4$. Next, the fraction of arsenic present in each group was calculated by summing the relative arsenic mass for each phase in the group. Based on the expectation that particles that are totally *included* (fully enclosed or encased in mineral or vitreous matrices) are not likely to contribute significantly to the observed RBA value of a sample, only the relative arsenic mass in partially or entirely *liberated* particles (partially or entirely exposed on their outer surfaces) was included in the sum. The results are shown in Table 2-10.

Group-specific RBA values were then estimated by fitting the grouped data to the model using minimization of square errors. Two different options were employed. In the first option, each fitting parameter (group-specific RBA) was fully constrained to be between zero and one, inclusive. In the second option, all parameters were unconstrained. Because the minor constituents do not contribute significantly to the total arsenic mass in any of the tested materials, a reasonable estimate of their specific RBA cannot be obtained. Therefore, an arbitrary coefficient of 0.5 was assumed for this group and the coefficient was not treated as a fitting parameter. The resulting estimates of the group-specific average RBA values for the remaining groups are shown in Table 2-11 (these values apply only to *liberated* particles).

As seen, there is a wide range of group-specific RBA values, with the precise values depending on the method used to constrain the parameters. It is important to stress that these group-specific RBA estimates are derived from a very limited data set, so the group-specific RBA estimates are inherently very uncertain. In addition, both the measured sample RBA values and the relative arsenic mass in each phase are subject to additional uncertainty. Therefore, the group-specific RBA estimates should not be considered to be highly precise, and calculation of a quantitative sample-specific RBA value from these estimates is not appropriate. Rather, it is more appropriate to consider the results of this study as sufficient to support only a qualitative classification of phase-specific RBA values, as follows:

Low Bioavailability	**Medium Bioavailability**	**High Bioavailability**
As_2O_3 Sulfosalts	As Phosphate FeAs Oxide PbAs Oxide MnAs Oxide Fe and Zn Sulfates	FeAsO

2.5 Discussion of *In Vivo* Results

The results of this investigation indicate that juvenile swine are a useful model for quantifying gastrointestinal absorption of arsenic from different test materials, using urinary arsenic excretion as the measurement endpoint. In addition, this experimental protocol can be used to estimate lead and arsenic RBA in the same animals. Because of the size of juvenile swine (about 10 kg at the beginning of the study), it is usually possible to administer doses of test soils that are relatively close to the range thought to be of concern to humans. For example, in Pilot Study 1 (Phase II, Experiment 10), the low dose of slag administered averaged about 260 mg/day, only slightly higher than the reasonable maximum exposure (RME) value of 200 mg/day assumed for human children (U.S. EPA, 1991). Thus, most measurements are obtained in a portion of the dose-response curve that is more relevant to humans than is achieved in most other animal models.

Most studies of arsenic absorption employ a single dose protocol and measure urinary excretion for 2–3 days. In contrast, these studies employed a repeated dosing protocol, with repeated 24- or 48-hour urine collections. An advantage of this protocol is that it reflects a more realistic human exposure scenario than does a single dose protocol. Further, multiple measurements can be made from the same animal on different days. In essence, data from different days allow multiple independent estimates of the UEF, and these data can be combined (once steady state has been achieved) to provide a robust estimate of the excretion fraction.

The RBA results for different test materials investigated strongly support the view that absorption of arsenic from soils and mine wastes is highly variable, and generally is not as well absorbed as soluble arsenic. The detailed chemical mechanism accounting for this variable and reduced bioavailability of arsenic in soil-like media is not known, but almost certainly is related to the chemical form of arsenic in the sample.

Because arsenic in most test materials is absorbed less-extensively than soluble forms of arsenic, and because soluble forms of arsenic are the basis of the oral RfD and oral slope factor for arsenic, the use of the unadjusted toxicity factors for assessing human health risk from soil ingestion will usually lead to an overestimate of risk. Consequently, measurement and application of site-specific RBA values to adjust the toxicity factors to account for the lower level of absorption is expected to increase the accuracy and decrease the uncertainty in human health risk assessments for arsenic in soil.

3.0 CONCLUSIONS

The data from the investigations performed under this program support the following main conclusions:

1. Juvenile swine constitute a useful and stable animal model for measuring the relative bioavailability of arsenic in a variety of soil or soil-like test materials. The Phase III protocol described in this report is the recommended SOP for the juvenile swine RBA assay.
2. There are clear differences in the *in vivo* RBA of arsenic between different test materials, ranging from less than 10% to more than 60%. Thus, knowledge of the RBA value for different materials at a site can be very important for improving arsenic risk assessments at a site.
3. Available data are not yet sufficient to allow reliable calculation of the RBA for a test material based only on knowledge of the relative amounts of the arsenic mineral phases present. However, tentative qualitative estimates of low, medium, or high bioavailability have been made based on the major phase type of the arsenic containing waste material.
4. For analysis of total arsenic in urine, additional extraction steps were identified and necessary to convert urinary organoarsenic metabolites to inorganic arsenic.
5. Due to limitations in detection limits for measurement of arsenic in urine, a minimum arsenic dose of 25 µg/kg bw-day is recommended for the juvenile swine RBA assay, so that the amount of arsenic excreted in urine reaches a measurable quantity.

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Table 2-1. Summary of Arsenic Excretion Studies in Humans and Animals Exposed to Soluble Arsenic Compounds in Water

Species	Sex	N	Chemical Form	Dose µg/day	Days Exposed	Percent Recovered			Reference
						Urine	Feces	Days	
Human	M,F	4	NS	8520	1	NA	4	10	Bettley and O'Shea 1975
Human	M	3	$NaAsO_2$	500	1	45	NA	4	Buchet et al. 1981a
Human	M	1	$NaAsO_2$	125	5	54	NA	14	Buchet et al. 1981b
Human	M	1	$NaAsO_2$	250	5	73	NA	14	
Human	M	1	$NaAsO_2$	500	5	74	NA	14	
Human	M	1	$NaAsO_2$	1000	5	64	NA	14	
Human	NS	2	As_2O_3	1000	1	85	1.4	5	Coulson et al. 1935
Human	M	1	As_2O_3	760	5	70	NA	22	Mappes 1977
Human	M	1	Mixture	63	1	80	NA	3	Crecelius 1977
Human	M	1	Na_2HAsO_4	200	1	50	NA	3	
Human	M	6	Na_2HAsO_4	0.01	1	58	NA	6	Tam et al. 1979
Human	M	2	Na_2HAsO_4	220	1	67	NA	7	Johnson and Farmer 1991
Hamster	NS	4	$NaAsO_2$	2000	1	36	49	3	Marafante and Vahter 1987
Mouse	M	5	$NaAsO_2$	400	1	90	7	2	Vahter and Norin 1980
Mouse	M	5	$NaAsO_2$	4000	1	65	9	2	
Mouse	M	5	$NaAsO_2$	40	1	88	NA	2	Vahter 1981
Mouse	M	5	$NaAsO_2$	400	1	91	NA	2	
Mouse	M	5	$NaAsO_2$	2000	1	86	NA	2	
Mouse	M	5	$NaAsO_2$	4000	1	75	NA	2	
Monkey	F	4	As_2O_3	1000	1	73	NA	14	Charbonneau 1978
Monkey	M	5	Na_2HAsO_4	360	1	49	2	4	Roberts et al. 2002
Monkey	M	7	Na_2HAsO_4	50-200	1	40	42	4	Roberts et al. 2007
Hamster	M	5	As_2O_3	4500	1	49	11	5	Yamauchi and Yamamura 1985
Hamster	NS	4	Na_2HAsO_4	2000	1	74	12	3	Marafante and Vahter 1987
Mouse	M	5	Na_2HAsO_4	400	1	77	8	2	Vahter and Norin 1980
Mouse	M	5	Na_2HAsO_4	4000	1	89	6	2	
Mouse	M	5	Na_2HAsO_4	40	1	94	NA	2	Vahter 1981
Mouse	M	5	Na_2HAsO_4	400	1	93	NA	2	
Mouse	M	5	Na_2HAsO_4	2000	1	92	NA	2	
Mouse	M	5	Na_2HAsO_4	4000	1	85	NA	2	

Table 2-2. Typical Swine Feed Composition

Nutrient Name	Amount
Protein	20.10%
Arginine	1.21%
Lysine	1.47%
Methionine	0.84%
Met+Cys	0.59%
Tryptophan	0.28%
Histidine	0.56%
Leucine	1.82%
Isoleucine	1.13%
Phenylalanine	1.11%
Phe+Tyr	2.05%
Threonine	0.82%
Valine	1.19%
Fat	4.44%
Saturated Fat	0.56%
Unsaturated Fat	3.74%
Linoleic 18:2:6	1.94%
Linoleic 18:3:3	0.04%
Crude Fiber	3.80%
Ash	4.33%
Calcium	0.87%
Phos Total	0.77%
Available Phosphorous	0.70%
Sodium	0.24%
Potassium	0.37%

Nutrient Name	Amount
Chlorine	0.19%
Magnesium	0.05%
Sulfur	0.03%
Manganese	20.4719 ppm
Zinc	118.0608 ppm
Iron	135.3710 ppm
Copper	8.1062 ppm
Cobalt	0.0110 ppm
Iodine	0.2075 ppm
Selenium	0.3196 ppm
Nitrogen Free Extract	60.23%
Vitamin A	5.1892 kIU/kg
Vitamin D3	0.6486 kIU/kg
Vitamin E	87.2080 IU/kg
Vitamin K	0.9089 ppm
Thiamine	9.1681 ppm
Riboflavin	10.2290 ppm
Niacin	30.1147 ppm
Pantothenic Acid	19.1250 ppm
Choline	1019.8600 ppm
Pyridoxine	8.2302 ppm
Folacin	2.0476 ppm
Biotin	0.2038 ppm
Vitamin B12	23.4416 ppm

Feed obtained from and nutritional values provided by Zeigler Bros., Inc

Table 2-3. Description of Test Materials

Phase	Experiment	Sample Designation	Site	Sample Description	Arsenic Concentration[a] (ppm)	Lead Concentration[a] (ppm)
II	2	Bingham Creek Channel Soil	Kennecott NPL Site, Salt Lake City, Utah	Soil composite of samples containing 3000 ppm or greater of lead; collected from a residential area (Jordan View Estates) located along Bingham Creek in the community of West Jordan, Utah	149	6330
	4	Jasper County High Lead Mill	Jasper County, Missouri Superfund Site	Soil composite collected from an on-site location	16	6940
		Murray Smelter Slag	Murray Smelter Superfund Site	Composite of samples collected from areas where exposed slag existed on site	695	11,700
	5	Aspen Berm	Smuggler Mountain NPL Site, Aspen, Colorado	Composite of samples collected from the Racquet Club property (including a parking lot and a vacant lot)	67	14,200
		Aspen Residential	Smuggler Mountain NPL Site, Aspen, Colorado	Composite of samples collected from residential properties within the study area	17	3870
	6	Butte Soil	Silver Bow Creek/Butte Area NPL Site, Butte, Montana	Soil composite collected from waste rock dumps in Butte Priority Soils Operable Unit (BPSOU)	234	8530
		Midvale Slag	Midvale Slag NPL Site, Midvale, Utah	Composite of samples collected from a water-quenched slag pile in Midvale Slag Operable Unit 2	591	8170
	7	California Gulch Phase I Residential Soil	California Gulch NPL Site, Leadville, Colorado	Soil composite collected from residential properties within Leadville	203	7510
		California Gulch Fe/Mn PbO	California Gulch NPL Site, Leadville, Colorado	Soil composite collected from near the Lake Fork Trailer Park located southwest of Leadville near the Arkansas River	110	4320
	8 and 10 (Pilot 1)	California Gulch AV Slag	California Gulch NPL Site, Leadville, Colorado	Sample collected from a water-quenched slag pile on the property of the former Arkansas Valley (AV) Smelter, located just west of Leadville	1050	10,600

Table 2-3. Description of Test Materials

Phase	Experiment	Sample Designation	Site	Sample Description	Arsenic Concentration[a] (ppm)	Lead Concentration[a] (ppm)
	9	Palmerton Location 2	New Jersey Zinc NPL Site, Palmerton, Pennsylvania	Soil composite collected from on-site	110	3230
		Palmerton Location 4	New Jersey Zinc NPL Site, Palmerton, Pennsylvania	Soil composite collected from on-site	134	2150
	11	Murray Smelter Soil	Murray Smelter Superfund Site	Soil composite collected from on-site	310	3200
	15 (Pilot 2)	Clark Fork Tailings	Milltown Reservoir Sediments NPL Site, Milltown, Montana	Sample collected from a tailings deposit along the banks of the Clark Fork River on the property of the Grant-Kohrs Ranch near Deer Lodge, Montana	181	
III	1	VBI70 TM1	Vasquez Boulevard and I-70 NPL Site, Denver, Colorado	Soil composite from impacted residential property (Eastern Swansea/Elyria neighborhood)	312	733
		VBI70 TM2	Vasquez Boulevard and I-70 NPL Site, Denver, Colorado	Soil composite from impacted residential property (Western Swansea/Elyria neighborhood)	983	824
		VBI70 TM3	Vasquez Boulevard and I-70 NPL Site, Denver, Colorado	Soil composite from impacted residential property (Eastern Cole neighborhood)	390	236
	2	VBI70 TM4	Vasquez Boulevard and I-70 NPL Site, Denver, Colorado	Soil composite from impacted residential property (Western Cole neighborhood)	813	541
		VBI70 TM5	Vasquez Boulevard and I-70 NPL Site, Denver, Colorado	Soil composite from impacted residential property (Clayton neighborhood)	368	157
		VBI70 TM6	Vasquez Boulevard and I-70 NPL Site, Denver, Colorado	Clean site soil (from the Swansea/Elyria neighborhood) plus added PAX pesticide	516	264
	3	Butte TM1	Silver Bow Creek/Butte Area NPL Site, Butte, Montana	Soil composite collected from waste rock dumps in Butte Priority Soils Operable Unit (BPSOU)	234	7980

Table 2-3. Description of Test Materials

Phase	Experiment	Sample Designation	Site	Sample Description	Arsenic Concentration[a] (ppm)	Lead Concentration[a] (ppm)
		Butte TM2	Silver Bow Creek/Butte Area NPL Site, Butte, Montana	Soil composite collected from a residential property located adjacent to a railroad grade in Butte, Montana	367	492
	4	Aberjona River TM1	Wells G & H Superfund Site, Woburn, Massachusetts	Composite of sediment samples containing arsenic concentrations greater than 500 ppm, collected along the Aberjona River, Massachusetts	676	410
		Aberjona River TM2	Wells G & H Superfund Site, Woburn, Massachusetts	Composite of sediment samples containing arsenic concentrations from 180 to 460 ppm, collected along the Aberjona River, Massachusetts	313	350
	5	El Paso TM1	El Paso/Dona Ana County Metals Survey site, El Paso County, Texas, and Dona Ana County, New Mexico	Soil sample collected approximately 1.5 miles east of the American Canal in El Paso County, Texas	74	NM
		El Paso TM2	El Paso/Dona Ana County Metals Survey site, El Paso County, Texas, and Dona Ana County, New Mexico	Soil sample collected approximately 1.5 miles east of the American Canal in El Paso County, Texas	73	NM
	6	ACC Utility Pole Soil	– (Study sponsored by American Chemistry Council)	Soil affected by chromated copper arsenate (CCA)-treated wood utility poles from a test plot in Conley, Georgia (soil was affected by being adjacent to the poles for over ten years)	320	NM

Table 2-3. Description of Test Materials

Phase	Experiment	Sample Designation	Site	Sample Description	Arsenic Concentration[a] (ppm)	Lead Concentration[a] (ppm)
	7	ACC Dislodgeable Arsenic	– (Study sponsored by American Chemistry Council)	Dislodgeable material obtained from the surface of chromated copper arsenate (CCA)-treated wood (boards from in-service residential decks, aged outdoors for one to three years)	3500	NM

[a]Values are arithmetic means
All samples were analyzed by ICP/AES in accord with EPA Method 2007.
NM = Not Measured

Table 2-4. Relative Mass of Arsenic By Mineral Phase in Test Materials

Phase	Experiment	Sample	Number of Particles Counted	Phase																												
				As Phosphate	As_2O_3	AsMO	AsSbO	Pb-As Vanidate	PbAsMO	PbAsSbCuO	$AsMSO_4$	Barite	Clays	FeAs Oxide	FeAs Sulfate	$ZnSO_4$	FeAsO	MnAs Oxide	PbAs Oxide	PbMO	PbMS	$PbMSO_4$	Pyrite	Slag	Sulfosalts	AgAsS	Paint	Pb Solder	$PbCrO_4$	TiO_2	$ZnSiO_4$
I	2	Bingham Creek Channel Soil	430	8%								<1%		11%	46%			<1%	34%												
	4	Murray Smelter Slag	1108											27%	10%			<1%	49%	<1%				14%							
	6	Butte Soil[a]	636	8%								<1%		20%	53%			16%								2%					
		Midvale Slag	1847											<1%	<1%				87%					11%	1%						
	7	California Gulch Phase I Residential Soil	510	15%						5%		<1%		29%	11%			36%						4%							
		California Gulch Fe/Mn PbO	380	5%				<1%				<1%		23%	5%			66%													
	8	California Gulch AV Slag	1472			5%			<1%						<1%				84%	2%	3%	<1%		5%							
	9	Palmerton Location 2	111	27%								11%		21%	<1%			40%													
		Palmerton Location 4	105	<1%				4%				<1%		5%			38%	10%	42%												<1%
	11	Murray	355			2%								3%	6%				87%	<1%				2%							

Table 2-4. Relative Mass of Arsenic By Mineral Phase in Test Materials

Phase	Experiment	Sample	Number of Particles Counted	Phase																											
				As Phosphate	As_2O_3	AsMO	AsSbO	Pb-As Vanidate	PbAsMO	PbAsSbCuO	$AsMSO_4$	Barite	Clays	FeAs Oxide	FeAs Sulfate	$ZnSO_4$	FeAsO	MnAs Oxide	PbAs Oxide	PbMO	PbMS	$PbMSO_4$	Pyrite	Slag	Sulfosalts	AgAsS	Paint	Pb Solder	$PbCrO_4$	TiO_2	$ZnSiO_4$
		Smelter Soil																													
	15	Clark Fork Tailings	238	16%										40%	24%		2%	<1%						<1%	16%						
II	1	VBI70 TM1	261	8%	54%								<1%	3%	<1%			2%	32%	<1%								<1%		<1%	
		VBI70 TM2	128	4%	22%								<1%	3%	<1%			<1%	70%	<1%				<1%							
		VBI70 TM3	97	2%	80%								<1%	8%				5%	6%	<1%				<1%				<1%	<1%		
	2	VBI70 TM4	139	<1%	86%		<1%						<1%	2%	<1%			<1%	10%					<1%				<1%	<1%		
		VBI70 TM5	103		97%							<1%		3%	<1%			<1%		<1%				<1%			<1%	<1%			
		VBI70 TM6	124	<1%	80%	<1%	1%						<1%	<1%					18%				<1%	<1%				<1%	<1%		
	3	Butte TM2	137								<1%		<1%	39%	18%								<1%	<1%	42%						
	4	Aberjona River TM1	186											69%	29%	2%							<1%								
		Aberjona River TM2	123											16%	27%	55%							2%								

Table 2-4. Relative Mass of Arsenic By Mineral Phase in Test Materials

Phase	Experiment	Sample	Number of Particles Counted	Phase																												
				As Phosphate	As_2O_3	AsMO	AsSbO	Pb-As Vanidate	PbAsMO	PbAsSbCuO	$AsMSO_4$	Barite	Clays	FeAs Oxide	FeAs Sulfate	$ZnSO_4$	FeAsO	MnAs Oxide	PbAs Oxide	PbMO	PbMS	$PbMSO_4$	Pyrite	Slag	Sulfosalts	AgAsS	Paint	Pb Solder	$PbCrO_4$	TiO_2	$ZnSiO_4$

[a] Same sample as evaluated in Phase III Experiment 3 (Butte TM2).

Table 2-5. Size Distributions of Arsenic Particles

Phase	Experiment	Sample	Particle Size (µm)								
			0–5	6–10	11–20	21–50	51–100	101–150	151–200	201–250	>250
II	2	Bingham Creek Channel Soil	71%	14%	6%	6%	3%	<1%			
	4	Murray Smelter Slag	14%	15%	4%	15%	24%	23%	2%	3%	<1%
	6	Butte Soil[a]	21%	9%	16%	26%	17%	9%	1%	<1%	<1%
		Midvale Slag	3%	1%	2%	13%	19%	40%	6%	14%	<1%
	7	California Gulch Phase I Residential Soil	22%	16%	14%	22%	16%	6%	1%	1%	<1%
		California Gulch Fe/Mn PbO	35%	24%	13%	17%	9%	2%			
	8	California Gulch AV Slag	21%	9%	2%	11%	12%	18%	14%	7%	6%
	9	Palmerton Location 2	40%	26%	12%	15%	7%				
		Palmerton Location 4	21%	28%	18%	19%	13%	<1%			
	11	Murray Smelter Soil	18%	31%	17%	10%	12%	7%	3%	1%	<1%
	15	Clark Fork Tailings	34%	20%	17%	21%	7%	1%			
III	1	VBI70 TM1	81%	9%	7%	3%			<1%		
		VBI70 TM2	59%	20%	10%	9%	2%				
		VBI70 TM3	49%	21%	18%	11%	1%				
	2	VBI70 TM4	45%	32%	13%	9%	1%	<1%			
		VBI70 TM5	48%	18%	24%	10%					
		VBI70 TM6	63%	23%	6%	6%	2%				
	3	Butte TM2	18%	11%	20%	30%	18%	4%			
	4	Aberjona River TM1	33%	34%	6%	13%	6%	4%	<1%	2%	
		Aberjona River TM2	59%	9%	15%	9%	6%	2%			

[a] Same sample as evaluated in Phase III Experiment 3 (Butte TM2).

Table 2-6. Matrix Associations of Arsenic Particles

Phase	Experiment	Sample	Particle Frequency (Percent)	Relative Arsenic Mass (Percent)	
			Liberated	*Liberated*	*Included*
II	2	Bingham Creek Channel Soil	100%	100%	0%
	4	Murray Smelter Slag	99%	95%	5%
	6	Butte Soil[a]	92%	87%	13%
		Midvale Slag	96%	78%	22%
	7	California Gulch Phase I Residential Soil	88%	94%	6%
		California Gulch Fe/Mn PbO	98%	100%	0%
	8	California Gulch AV Slag	85%	73%	27%
	9	Palmerton Location 2	100%	100%	0%
		Palmerton Location 4	84%	58%	42%
	11	Murray Smelter Soil	92%	79%	21%
	15	Clark Fork Tailings	99%	96%	4%
III	1	VBI70 TM1	100%	100%	0%
		VBI70 TM2	99%	95%	5%
		VBI70 TM3	100%	100%	0%
	2	VBI70 TM4	100%	100%	0%
		VBI70 TM5	95%	100%	0%
		VBI70 TM6	100%	100%	0%
	3	Butte TM2	100%	100%	0%
	4	Aberjona River TM1	100%	99%	1%
		Aberjona River TM2	100%	100%	0%

[a] Same sample as evaluated in Phase III Experiment 3 (Butte TM2).

Table 2-7. RBA Estimates for Arsenic in Test Materials

Phase	Experiment	Sample	Site	Sample	Arsenic Concentration[a] (ppm)	RBA ± SEM
Phase II	2	Bingham Creek Channel Soil	Bingham Creek	Channel Soil	149	39% ± 8%
	4	Murray Smelter Slag	Murray Smelter	Slag Composite	695	55% ± 10%
		Jasper County High Lead Mill	Region VII Jasper County	High Lead Smelter	16.4	327% ± 105%
	5	Aspen Berm	Aspen	Berm	66.9	100% ± 46%
		Aspen Residential	Aspen	Residential Soil Composite	16.7	128% ± 52%
	6	Butte Soil	Butte	Soil 1	234	9% ± 3%
		Midvale Slag	Midvale	Slag Composite	591	23% ± 4%
	7	California Gulch Phase I Residential Soil	California Gulch	Phase I Residential Soil Composite	203	8% ± 3%
		California Gulch Fe/Mn PbO	California Gulch	FeMnPb Oxide Soil	110	57% ± 12%
	8	California Gulch AV Slag	California Gulch	AV Smelter Slag	1050	13% ± 4%
	9	Palmerton Location 2	Palmerton	Location 2	110	49% ± 10%
		Palmerton Location 4	Palmerton	Location 4	134	61% ± 11%
	10	California Gulch AV Slag	California Gulch	AV Smelter Slag (reproducibility)	1050	18% ± 2%
	11	Murray Smelter Soil	Murray Smelter	Soil Composite	310	33% ± 5%
	15	Clark Fork Tailings	Clark Fork	Grant Kohrs Tailings	181	51% ± 6%
Phase III	1	VBI70 TM1	VBI70	TM1	312	40% ± 4%
		VBI70 TM2	VBI70	TM2	983	42% ± 4%
		VBI70 TM3	VBI70	TM3	390	37% ± 3%
	2	VBI70 TM4	VBI70	TM4	813	24% ± 2%
		VBI70 TM5	VBI70	TM5	368	21% ± 2%
		VBI70 TM6	VBI70	TM6	516	24% ± 3%
	3	Butte TM1	Butte Arsenic	Soil 1[b]	234	18% ± 3%
		Butte TM2	Butte Arsenic	Soil 2	367	24% ± 2%
	4	Aberjona River TM1	Aberjona River	River Sediment – High Arsenic	676.3	38% ± 2%
		Aberjona River TM2	Aberjona River	River Sediment – Low Arsenic	312.8	52% ± 2%
	5	El Paso TM1	El Paso	Soil 1	74	44% ± 3%
		El Paso TM2	El Paso	Soil 2	73	37% ± 3%
	6	ACC Utility Pole Soil	ACC	Soil Affected by CCA-Treated Wood Utility Poles	320	47% ± 3%

Table 2-7. RBA Estimates for Arsenic in Test Materials

Phase	Experiment	Sample	Site	Sample	Arsenic Concentration[a] (ppm)	RBA ± SEM
	7	ACC Dislodgeable Arsenic	ACC	Dislodgeable Arsenic from Weathered CCA-Treated Wood	3500	26% ± 1%

[a]Values are arithmetic means
[b] Same sample as evaluated in Phase II
SEM = Standard error of the mean, an indicator of the relative uncertainty around the RBA estimate (see Appendix A)

Table 2-8. Summary Statistics for Dose-UEF Slopes and RBA Estimates for Phase III RBA Assays

Parameter	Sodium Arsenate Slope	Test Material Slope	Test Material RBA
N	7	14	14
Mean	0.78	0.26	0.34
SD	0.099	0.098	0.118
CV	0.13	0.38	0.32

CV, coefficient of variation (SD/mean); RBA, relative bioavailability; SD, standard deviation; UEF, urinary excretion fraction

Table 2-9. Consolidated Arsenic Phases

Phase Grouping	Phase	Other Abbreviations Used	Phase Description
As Phosphate	As Phosphate	Phos, Phosphate	Arsenic bearing phosphate: although naturally occurring forms are rare (arsenocrandallite-$CaAl_3AsPO_4$-OH_6), these may be metastable forms of phosphate with sorbed arsenic formed by secondary soil processes.
As_2O_3	As_2O_3	As	Arsenic trioxide: a common pyrometallurgical-formed phase that is common to arsenic kitchens or copper smelters. It can also be found as a product in old formulas for herbicides, pesticides, and rodenticides.
FeAs Oxide	FeAs Oxide	Fe, Fe Oxide, FeSi	Iron oxide (FeOOH) with sorbed arsenic and lead, probably from soil.
Fe & Zn Sulfates	FeAs Sulfate	Fe Sulfate, Sulf	Iron-rich sulfates: probably related to jarosite ($KFe_3(OH)_6(SO_4)_2$) or plumbojarosite ($PbFe_3(OH)_6(SO_4)_2$). Can form in oxide zone of hydrothermal deposits, but is also common to baghouse dust associated with copper-lead smelters.
	$ZnSO_4$	–	Zinc sulfates: recognized by an elemental composition dominated by zinc, sulfur, and oxygen with minor quantities of lead, arsenic, and/or cadmium. Generally found as inclusions in slag or in baghouse dust and sometimes used in commercial products.
FeAsO	FeAsO	FeAs	Iron oxide (FeOOH) that is highly enriched with arsenic; probably a flue dust.
MnAs Oxide	MnAs Oxide	Mn, Mn Oxide	Arsenic sorbed to the surface of manganese oxide-containing particles in soil. Formed by release of arsenic from soluble forms. Recognized by an elemental composition dominated by manganese, arsenic, and oxygen.
PbAs Oxide	PbAs Oxide	PbAsO	A product released from smelter flues and sometimes used in commercial products. Recognized by an elemental composition dominated by lead, arsenic, and oxygen.
Pyrite	Pyrite	Py	Iron sulfide (FeS_2): a gaunge mineral associated with base-metal ore deposits. Pyrite may contain small quantities of arsenic or have arsenic sorbed to its oxidized surface.
Sulfosalts	AgAsS	Ags	Silver arsenic sulfides: a mineral form related to mining activity (from a class of minerals referred to as sulfosalts). These ores of silver may be in the chemical form of proustite (Ag_3AsS_3), xanthoconite (Ag_3AsS_3), pearceite ($(AgCu)_2As_2S_{11}$), or polybasite ($(AgCu)_{16}(Sb,As)_2S_{11}$).
	Sulfosalts	–	A group consisting of more than 100 forms of unoxidized minerals composed of metal or semimetals and sulfur, distinct from a sulfide. These include numerous arsenic-bearing phases: tennantite ($Cu_{12}As_4S_{13}$) and enargite (Cu_3AsS_4) are perhaps the most common.
Minor Constituents	AsMO	–	Arsenic-metal oxides: these are arsenic-rich oxides formed from pyrometallurgical processes. Common associated elements (M) include lead, antimony, copper, zinc, and/or cadmium.
	$AsMSO_4$	–	Arsenic-antimony oxide: this is a common pyrometalurgically formed phase that is common to arsenic kitchens. Its occurrence is significant in “dirty” or “black” arsenic and is still found in trace quantities in “white” arsenic.

Table 2-9. Consolidated Arsenic Phases

Phase Grouping	Phase	Other Abbreviations Used	Phase Description
	AsSbO	–	Arsenic-antimony oxide: this is a common pyrometalurgically formed phase that is common to arsenic kitchens. Its occurrence is significant in "dirty" or "black" arsenic and is still found in trace quantities in "white" arsenic.
	Barite	–	Barium sulfate: common gaunge mineral with base metals. Will adsorb lead and arsenic during smelting.
	Clays	AlSi	Arsenic sorbed to the surface of soil-forming clays (hydrated, Al-Mg silicates).
	Paint	–	Arsenic may be present in some very old paint pigments or as a trace contaminant in lead, copper, and antimony pigments.
	Pb Solder	Pbsold	Lead solder with trace levels of arsenic. Recognized by an elemental composition dominated by lead and tin with minor base metals.
	Pb-As Vanidate	$PbAsVo_4$	A phase probably associated with mining or smelting of copper-rich ores, not used in commercial products. Recognized by an elemental composition dominated by lead, arsenic, vanadium, and oxygen.
	PbAsMO	–	Lead-arsenic metal oxides: these are lead-arsenic rich oxides formed from pyrometallurgical processes. Common associated elements (M) include antimony, copper, zinc, and/or cadmium.
	PbAsSbCuO	–	Lead-arsenic metal oxides: these are lead-arsenic rich oxides formed from pyrometallurgical processes.
	$PbCrO_4$	–	A common lead pigment in paint and a rare form of lead.
	PbMO	–	Lead-metal oxides: these are lead-rich oxides formed from pyrometallurgical processes. Common associated elements (M) include arsenic, antimony, copper, zinc, and/or cadmium.
	PbMS	–	Lead-metal sulfides: these are lead-rich oxides formed from pyrometallurgical processes. Common associated elements (M) include arsenic, antimony, copper, zinc, and/or cadmium.
	$PbMSO_4$	–	Lead-metal sulfates: these are lead-rich oxides formed from pyrometallurgical processes. Common associated elements (M) include arsenic, antimony, copper, zinc, and/or cadmium.
	Slag	–	A waste by-product of pyrometallurgical activity. Recognized by an elemental composition dominated by silica, calcium, iron, and oxygen with variable quantities of lead, arsenic, copper, and/or zinc.
	TiO_2	Ti	Rutile or anatase with surface sorbed arsenic in small quantities. Recognized by an elemental composition dominated by titanium and oxygen.
	$ZnSiO_4$	–	Zinc silicate, recognized by an elemental composition dominated by zinc, silica, and oxygen with minor quantities of lead, arsenic, and/or cadmium. Generally found as inclusions in slag or in baghouse dust and sometimes used in commercial products.

Table 2-10. Relative Arsenic Mass for Consolidated Phase Groupings

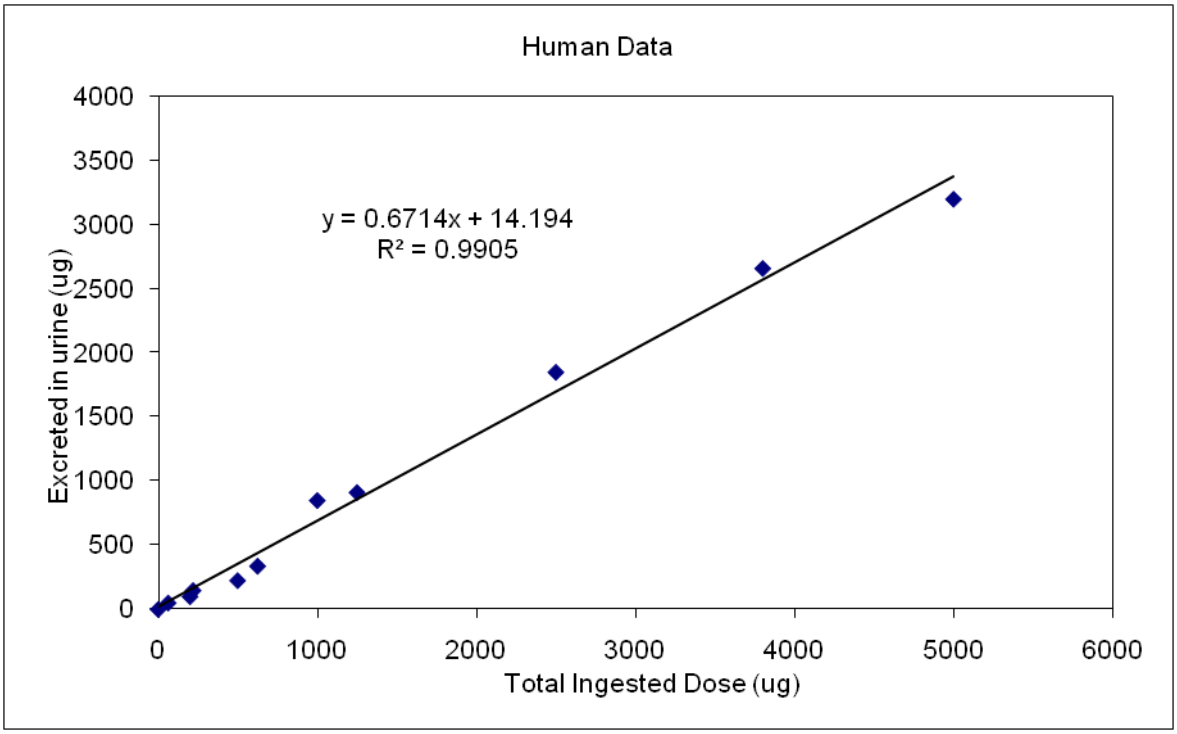
Phase	Experiment	Sample	RBA	Arsenic Conc. (ppm)	Number of Particles Counted	Phase (Liberated/Included)																	
						As Phosphate		As_2O_3		FeAs Oxide		Fe & Zn Sulfates		FeAsO		MnAs Oxide		PbAs Oxide		Sulfosalts		Minor Constits.	
II	2	Bingham Creek Channel Soil	39.3%	149	430	8%	<1%			11%	<1%	46%	<1%			<1%	<1%	34%	<1%			<1%	<1%
	4	Murray Smelter Slag	55.1%	695	1108					27%	<1%	10%	<1%			<1%	<1%	44%	5%			15%	<1%
	6	Butte Soil[a]	17.8%	234	636	<1%	7%			18%	2%	51%	3%			16%	<1%			2%	<1%	<1%	<1%
		Midvale Slag	22.9%	591	1847					<1%	<1%	<1%	<1%					65%	22%	1%	<1%	11%	<1%
	7	California Gulch Phase I Residential Soil	8.4%	203	510	14%	<1%			29%	<1%	11%	<1%			36%	<1%					5%	5%
		California Gulch Fe/Mn PbO	56.6%	110	380	5%	<1%			23%	<1%	5%	<1%			66%	<1%					<1%	<1%
	8	California Gulch AV Slag	12.9%	1050	1472							<1%	<1%					58%	26%			16%	<1%
	9	Palmerton Location 2	49.2%	110	111	27%	<1%			21%	<1%	<1%	<1%			40%	<1%					11%	<1%
		Palmerton Location 4	61.0%	134	105	<1%	<1%			5%	<1%			38%	<1%	10%	<1%	<1%	42%			5%	<1%
	11	Murray Smelter Soil	33.0%	310	355					3%	<1%	6%	<1%					66%	21%			4%	<1%
	15	Clark Fork Tailings	50.7%	181	238	16%	<1%			40%	<1%	24%	<1%	2%	<1%	<1%	<1%			13%	3%	<1%	<1%
III	1	VBI70 TM1	40.3%	312	261	8%	<1%	54%	<1%	3%	<1%	<1%	<1%			2%	<1%	32%	<1%			<1%	<1%
		VBI70 TM2	42.2%	983	128	4%	<1%	17%	5%	3%	<1%	<1%	<1%			<1%	<1%	70%	<1%			<1%	<1%
		VBI70 TM3	36.7%	390	97	2%	<1%	80%	<1%	8%	<1%					5%	<1%	6%	<1%			<1%	<1%
	2	VBI70 TM4	23.8%	813	139	<1%	<1%	86%	<1%	2%	<1%	<1%	<1%			<1%	<1%	10%	<1%			<1%	<1%
		VBI70 TM5	21.2%	368	103			97%	<1%	3%	<1%	<1%	<1%			<1%	<1%					<1%	<1%
		VBI70 TM6	23.5%	516	124	<1%	<1%	80%	<1%	<1%	<1%							18%	<1%			1%	<1%
	3	Butte TM2	23.6%	367	137					39%	<1%	18%	<1%							42%	<1%	<1%	<1%
	4	Aberjona River TM1	38.1%	676	186					69%	<1%	30%	1%									<1%	<1%
		Aberjona River TM2	52.4%	313	123					16%	<1%	82%	<1%									2%	<1%

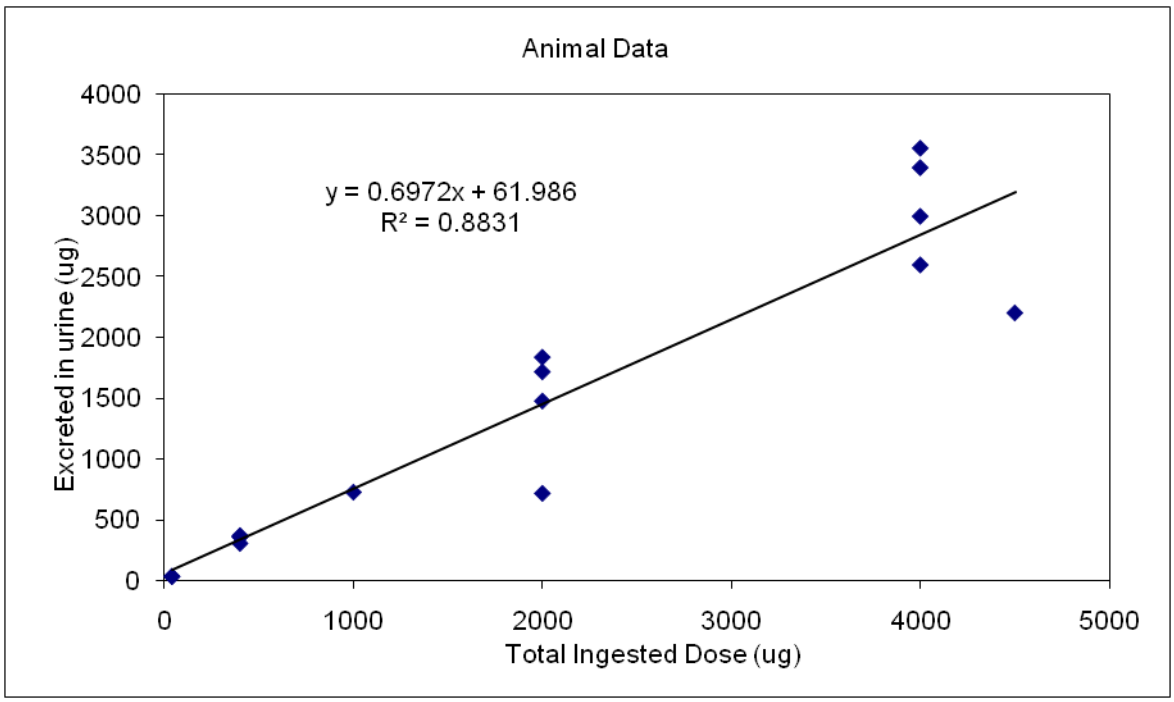
[a] Same sample as evaluated in Phase III Experiment 3 (Butte TM2).

Table 2-11. Estimated Group-Specific RBA Values for *Liberated* Particles

Group Name	Estimated Group-Specific RBA[1]		RBA Category[2]
	Method 1	Method 2	
FeAsO	1.00	1.42	High
As Phosphate	0.55	0.59	Medium
FeAs Oxide	0.45	0.44	Medium
Fe & Zn Sulfates	0.40	0.40	Medium
PbAs Oxide	0.38	0.38	Medium
MnAs Oxide	0.38	0.35	Medium
As_2O_3	0.25	0.25	Low
Sulfosalts	0.02	0.01	Low

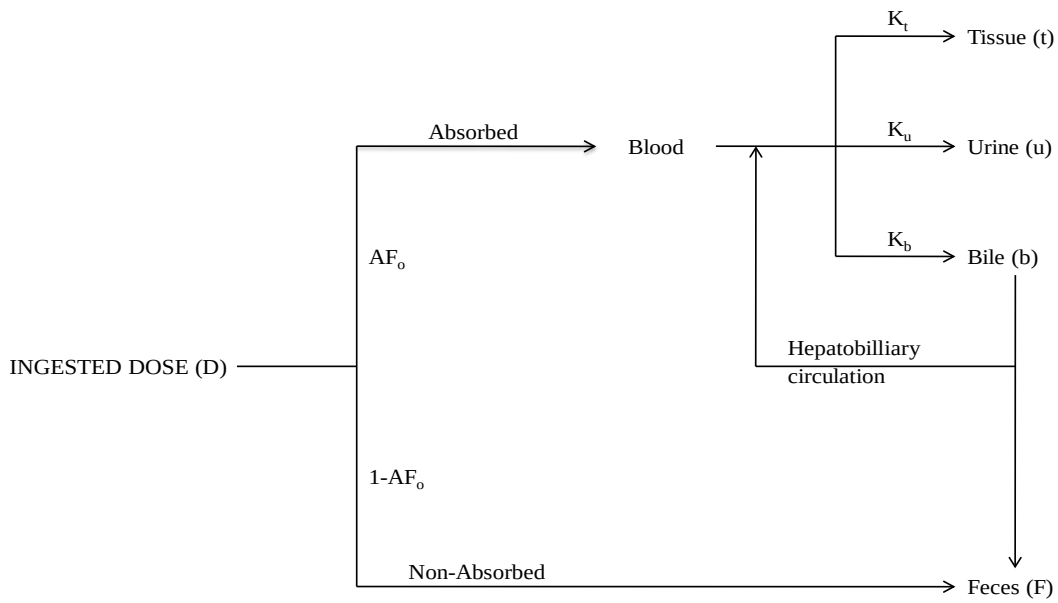
Figure 2-1. Excretion of Soluble As in Humans and Animals[a]





[a]See Table 2-1 for literature sources of RBA estimates.

Figure 2-2. Conceptual Model for Arsenic Absorption and Excretion



Where:

D = Ingested dose (µg)
AF_o = Oral Absorption Fraction
K_t = Fraction of absorbed arsenic which is retained in tissues
K_u = Fraction of absorbed arsenic which is excreted in urine
K_b = Fraction of absorbed arsenic which is excreted in the bile

BASIC EQUATIONS:

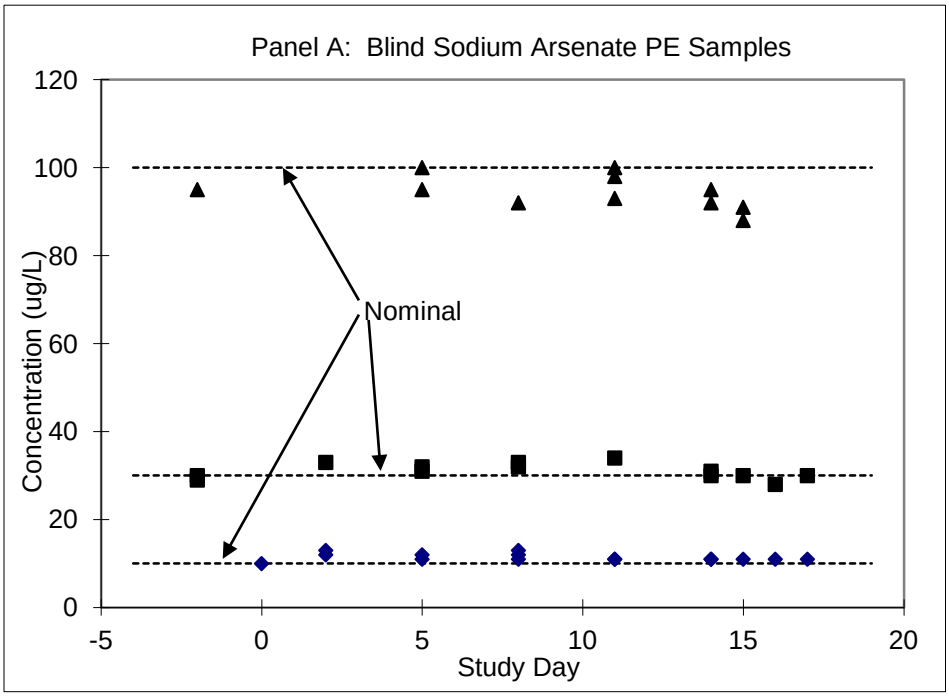
Amount Absorbed (µg) $= D \cdot AF_o$

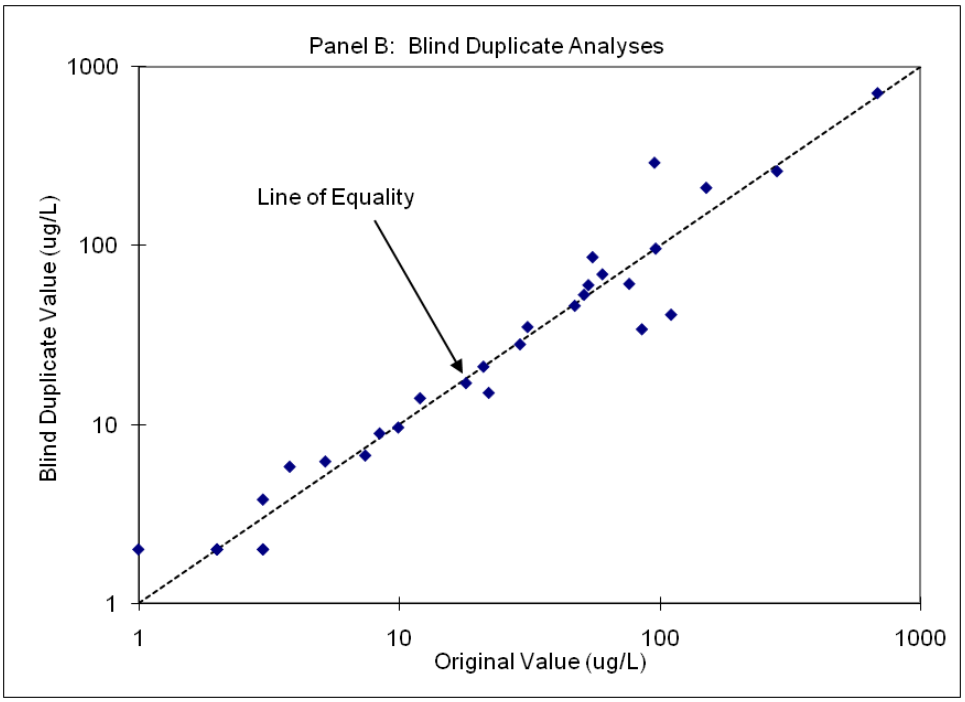
Amount Excreted in Urine (µg) $= \textit{Amount absorbed} \cdot K_u$
$= D \cdot AF_o \cdot K_u$

Urinary Excretion Fraction (UEF) $= \textit{Amount excreted / Amount Ingested}$
$= (D \cdot AF_o \cdot K_u) / D$
$= AF_o \cdot K_u$

Relative Bioavailability (x vs. y) $= UEF(x) / UEF(y)$
$= (AF_o(x) \cdot K_u) / (AF_o(y) \cdot K_u)$
$= AF_o(x) / AF_o(y)$

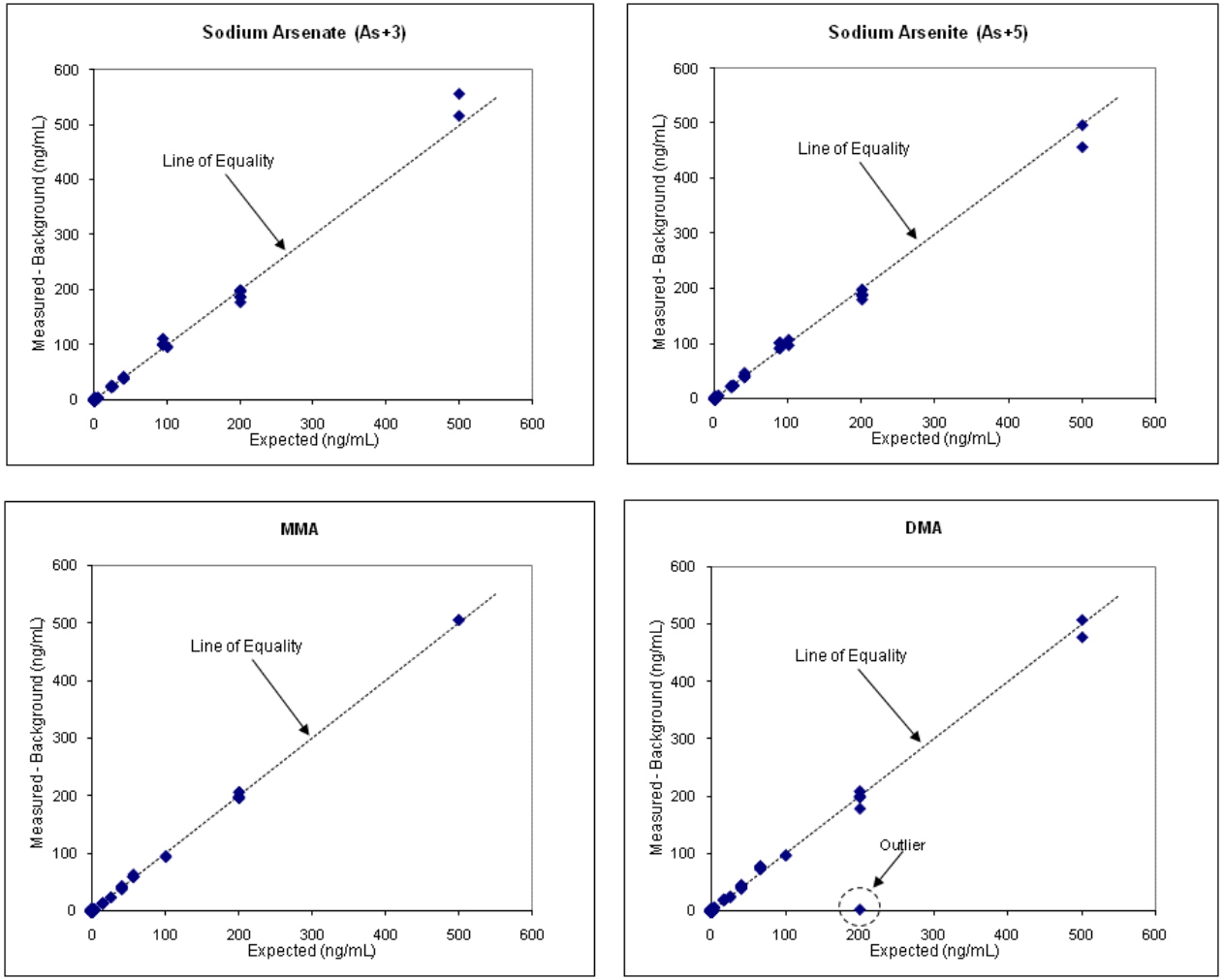
Figure 2-3. Quality Assurance Data from Phase II Pilot Studies[a]





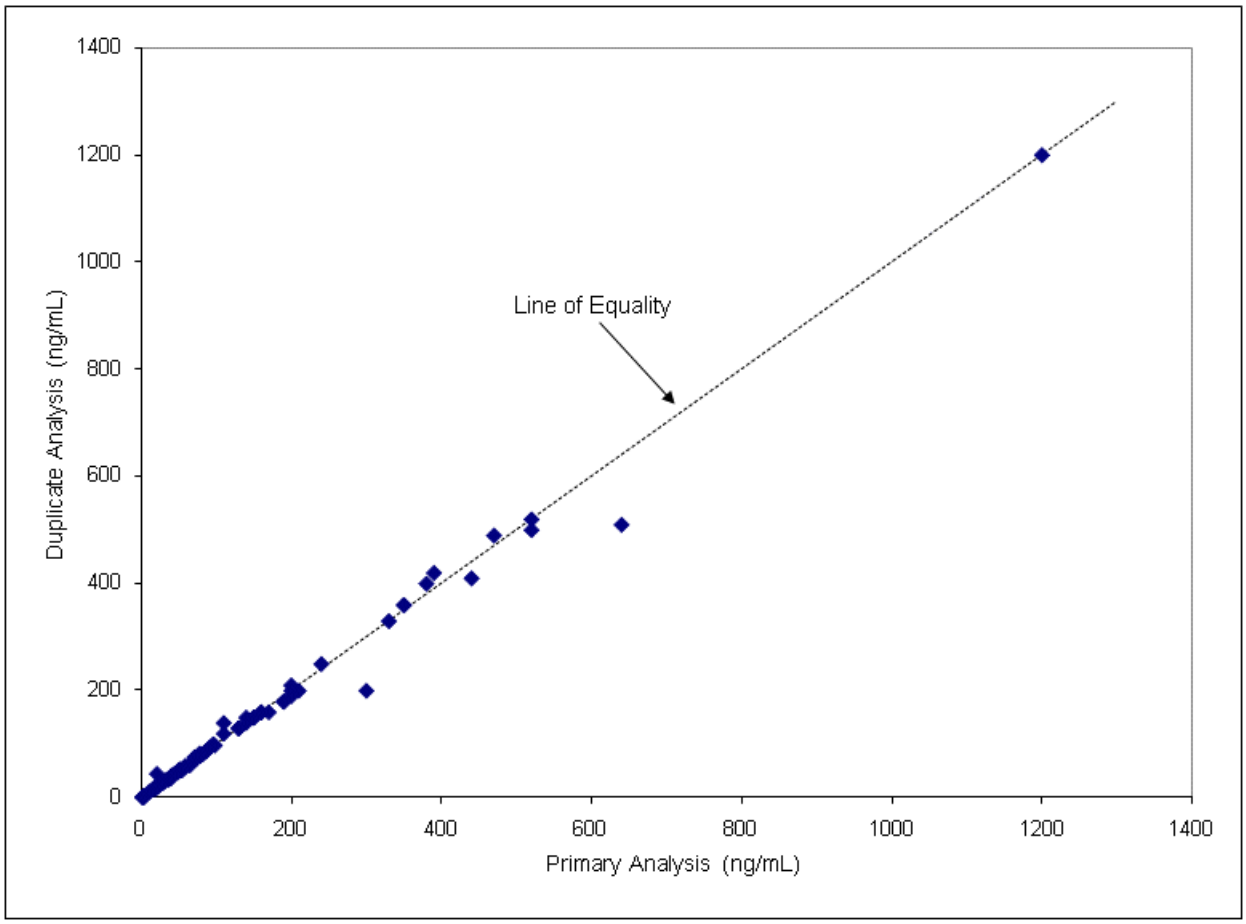
[a]Comparion of measured and actual (nominal) concentrations of performance evaluation (PE) samples for urine (panel A), and between duplicate measurements on the same urine sample (panel B), for Phase II studies. R^2 for blind duplicates was 0.91 (n=30).

Figure 2-4. Phase III Performance Evaluation Samples[a]



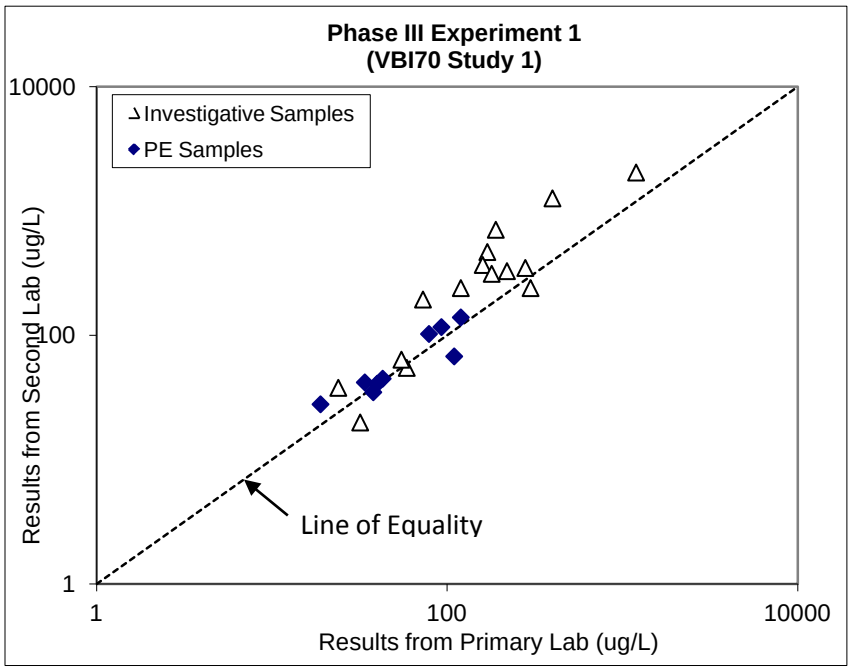
[a]Comparison of measured and actual concentrations of performance evaluation (PE) urine samples for Phase III studies. DMA, dimethylasinic acid; MMA, monomethylarsonic acid. R^2 values were <0.99 for the four analytes (N=35–37).

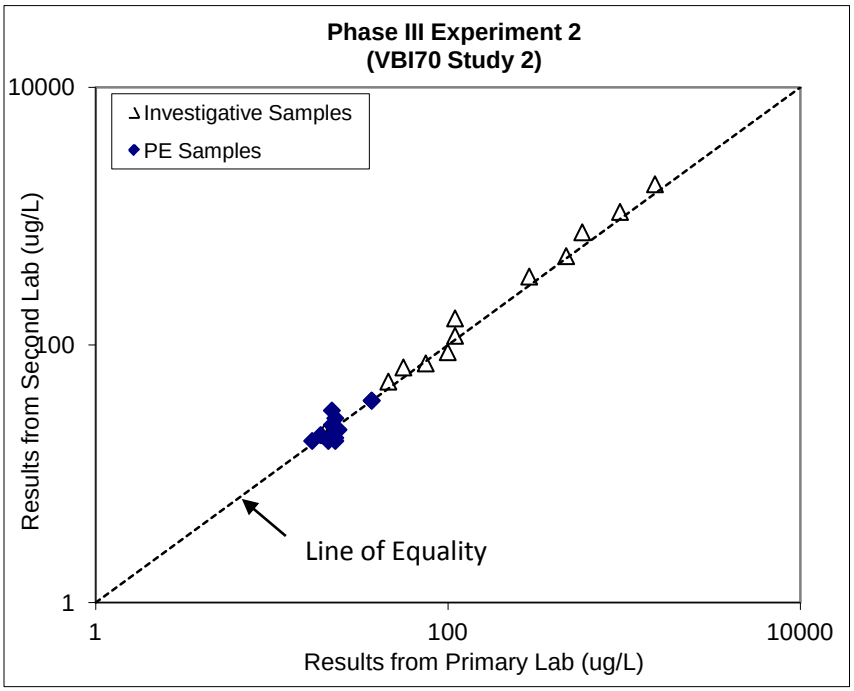
Figure 2-5. Phase III Blind Duplicate Samples [a]



[a]Comparion between duplicate measurements on the same urine sample for Phase III studies. The R^2 was 0.98 (n=72).

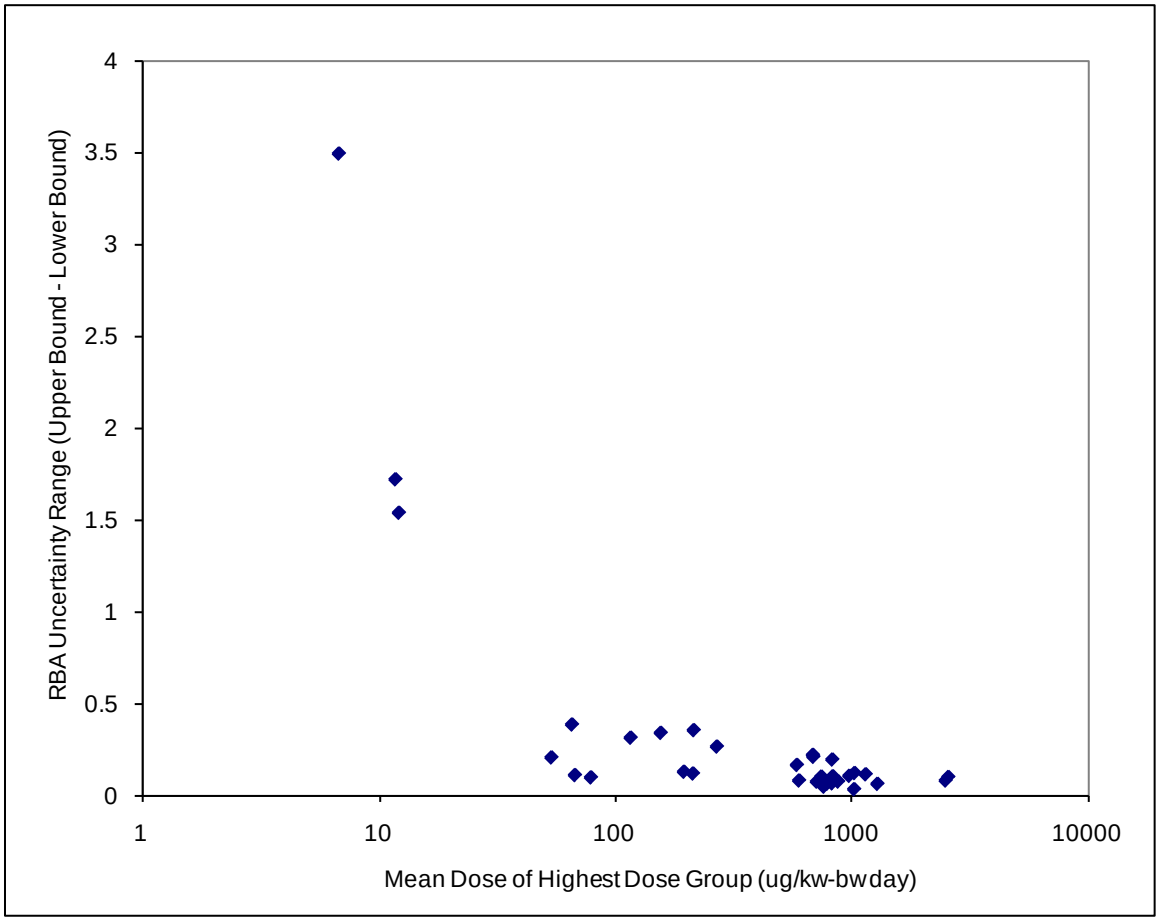
Figure 2-6. Phase III Inter-Laboratory Comparison[a]





[a]Comparison of interlaboratory results of analyses of arsenic in urine in two Phase III studies. Values for R^2 were 0.87 (n=24) for Experiment 1 and 1.0 (n=25) for Experiment 2. Samples included urines collected during the RBA assay (investigative samples) and performance evaluation samples (PE).

Figure 2-7. Uncertainty in RBA Values[a]



[a]Plot of uncertainty range (90% confidence interval) against administered dose. The dose axis is the group mean dose (µg/kg-day) for the highest dosing group in each study. The confidence interval increases substantially when the administered dose levels are less than 25 µg/kg-day.

Relative Bioavailability and Bioaccessibility and Speciation of Arsenic in Contaminated Soils

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Background: Assessment of soil arsenic (As) bioavailability may profoundly affect the extent of remediation required at contaminated sites by improving human exposure estimates. Because small adjustments in soil As bioavailability estimates can significantly alter risk assessments and remediation goals, convenient, rapid, reliable, and inexpensive tools are needed to determine soil As bioavailability.

Objectives: We evaluated inexpensive methods for assessing As bioavailability in soil as a means to improve human exposure estimates and potentially reduce remediation costs.

Methods: Nine soils from residential sites affected by mining or smelting activity and two National Institute of Standards and Technology standard reference materials were evaluated for As bioavailability, bioaccessibility, and speciation. Arsenic bioavailability was determined using an *in vivo* mouse model, and As bioaccessibility was determined using the Solubility/Bioavailability Research Consortium *in vitro* assay. Arsenic speciation in soil and selected soil physicochemical properties were also evaluated to determine whether these parameters could be used as predictors of As bioavailability and bioaccessibility.

Results: In the mouse assay, we compared bioavailabilities of As in soils with that for sodium arsenate. Relative bioavailabilities (RBAs) of soil As ranged from 11% to 53% (mean, 33%). *In vitro* soil As bioaccessibility values were strongly correlated with soil As RBAs (R^2 = 0.92). Among physicochemical properties, combined concentrations of iron and aluminum accounted for 80% and 62% of the variability in estimates of RBA and bioaccessibility, respectively.

Conclusion: The multifaceted approach described here yielded congruent estimates of As bioavailability and evidence of interrelations among physicochemical properties and bioavailability estimates.

Key words: arsenic, bioaccessibility, bioavailability, gastrointestinal, human health, human health risk assessment, metalloid, soil physicochemical properties, speciation. *Environ Health Perspect* 119:1629–1634 (2011). http://dx.doi.org/10.1289/ehp.1003352 [Online 13 July 2011]

The metalloid arsenic (As), a group 1 human carcinogen (International Agency for Research on Cancer 2004), is the second most common inorganic contaminant at Superfund sites [U.S. Environmental Protection Agency (EPA) 2001]. Hence, cancer risk associated with ingestion of As-contaminated soils (Calabrese et al. 1996; Davis et al. 1991; Dudka and Miller 1999) often drives risk assessments for human exposure to metal contaminants at Superfund sites (U.S. EPA 2007c). With increasing urbanization, exposure to As-contaminated soils grows more likely as residential areas extend into the vicinity or, in some cases, intrude onto Superfund sites (Scheckel et al. 2009). Reliable analysis of human health risks from ingestion of As-contaminated soil depends on estimating the bioavailability of As in the soil (U.S. EPA 1989). Current exposure estimates from ingestion of As-contaminated soils often do not consider differences between the bioavailability of As in water and soil (Ehlers and Luthy 2003). The use of default values that assume equivalent bioavailabilities for As in the two matrices can overestimate risk associated with ingestion of As-contaminated soil (Bradham and Wentsel 2010; U.S. EPA 2007b, 2007c). Speciation of As in soil, concentrations of other metals or metalloids, and other soil properties (e.g., pH and mineralogy) can affect the bioavailability of soil As and the amount available for systemic disposition [Kelly et al. 2002; National Research Council (NRC) 2003; U.S. EPA 2007b]. Because even small adjustments in soil As bioavailability estimates can significantly affect estimated risk and cleanup goals (U.S. EPA 2007c), methods are needed that quickly and inexpensively provide accurate and reliable data that can be applied to cleanups of As-contaminated sites worldwide.

Studies of soil As bioavailability have used species as diverse as rodents, swine, and monkeys (Casteel et al. 1997; Freeman et al. 1995; Lorenzana et al. 1996; Nagar et al. 2009; Ng et al. 1998; Pascoe et al. 1994; Rees et al. 2009; Roberts et al. 2002). Time and cost considerations may limit use of some species in bioavailability assays (U.S. EPA 2007a, 2007b). In the present study, we chose the mouse as the test species because of low purchase and husbandry costs, ease of handling, improved predictive value of data because of the feasibility of an increased sample size in assays, and the potential for widespread use of a mouse-based assay in many laboratories. Mice are well characterized physiologically and can be manipulated experimentally (e.g., altered dietary components, altered genotype) to determine the effects of biological variation on the gastrointestinal absorption of metals and metalloids. Extant data on gastrointestinal absorption of ingested arsenicals facilitate use of the mouse as a test species in assays of soil As bioavailability (Hughes et al. 2003, 2005, 2008). Although mice and humans differ in metabolism and disposition of arsenicals (Vahter 1999), similarities are sufficient to permit use of mouse data to create physiologically based pharmacokinetic models that can be scaled for humans (El-Masri and Kenyon 2008; Evans et al. 2008; Gentry et al. 2004a, 2004b; Hughes et al. 1999).

Use of complementary experimental approaches to assess bioavailability has been advocated as a strategy to develop models that reduce uncertainty in risk assessment (NRC 2003). In this study, we linked *in vivo* and *in vitro* assays with physicochemical characterization of soils in a unified approach to develop accurate and reliable methods for risk assessment of As-contaminated soils. Results for test soils and standard reference materials

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Supplemental Material is available online (http://dx.doi.org/10.1289/ehp.1003352).

We thank K. Herbin-Davis and B. Edwards for excellent technical assistance and the EPA Region 9 Superfund program for their support. Materials Research Collaborative Access Team operations at Argonne National Laboratory are supported by the U.S. Department of Energy and institutional members.

The U.S. Environmental Protection Agency through its Office of Research and Development partially funded and collaborated in this research.

The research described in this article has been subjected to agency review and approved for publication.

The authors declare they have no actual or potential competing financial interests.

Received 16 December 2010; accepted 13 July 2011.

(SRMs) suggest that concerted use of *in vivo* and *in vitro* methods combined with physicochemical characterization of soils provides a stronger scientific basis for the refinement of risk assessments for As-contaminated soils. In addition, correlations between physicochemical properties of soils and estimates of As bioavailability and bioaccessibility indicate that use of physicochemical properties could profitably inform the refinement of both animal-based and *in vitro* assays.

Materials and Methods

Soil origin, processing, and physicochemical characterization. For full description of soil origin, processing, and physicochemical characterization, see Supplemental Material (http://dx.doi.org/10.1289/ehp.1003352). Soils used in this study were collected from sites affected by mining and smelter activities. Physicochemical properties were determined in duplicate samples of each soil.

Arsenic speciation in soils was examined using the Materials Research Collaborative Access Team's beamline 10-ID (Sector 10, Advanced Photon Source, Argonne National Laboratory, Argonne, IL). A principal component analysis coupled with linear combination fitting was used to identify the major As species in the samples. Linear combination fits were performed using X-ray absorption spectroscopy k^2 space spectra from reference standards to As phases in the soil samples.

Arsenic concentrations in all soil and biological samples were determined by Instrumental Neutron Activation Analysis (INAA) at the Department of Nuclear Engineering, North Carolina State University (Raleigh, NC; mean As mass detection limit, 0.035 µg). All bioavailability and bioaccessibility calculations were based on INAA values.

Mouse bioavailability assay. The Institutional Animal Care and Use Committee of the U.S. EPA National Health and Environmental Effects Research Laboratory approved the protocol for mouse use, which assured humane treatment and alleviation of suffering. Female C57BL/6 mice 4–6 weeks of age (Charles River Laboratory, Raleigh, NC) were acclimated in groups of three in a 12/12-hr light/dark photocycle at 20–22°C. Mice had free access to rodent diet (TestDiet, Richmond, IN) and tap water that contained < 11 µg/L As (Kenyon et al. 2008). Composition of AIN-93G purified rodent diet (Reeves et al. 1993) obtained from Dyets (Bethlehem, PA) is given in Supplemental Material, Table 1 (http://dx.doi.org/10.1289/ehp.1003352). Soil-amended diets were prepared by thorough mixing of test soil with powdered AIN-93G purified rodent diet to a 1% (wt/wt) soil:diet ratio. Arsenate (As^V)-amended diet prepared by addition of sodium arsenate heptahydrate (Sigma, St. Louis, MO) to powdered AIN-93G purified rodent diet was used to determine the bioavailability of a freely soluble As salt. Diets were stored at 4°C until used.

At the start of an assay, three mice housed together during acclimation were transferred as a group to a metabolic cage that separated urine and feces (Nalgene, Rochester, NY). Twelve mice in four metabolic cages constituted an experimental run. Metabolic cages were maintained for 10 days under environmental conditions given above with unlimited access to test diet and drinking water. For sample collection and data analysis, the unit of observation was the cage and the standard assay for a soil had a sample size of four (except soil 9, which had a sample size of three). To examine assay variability and reproducibility, bioavailability of As in soils 4 and 10 were assayed two and three times, respectively, over a 2-year period.

Daily food consumption for each cage was calculated as the difference between the weight of the food hopper immediately after each morning's filling and before replenishment the next morning. Cumulative food consumption for each cage was the sum of daily food consumption. Urine and feces were collected each morning from each metabolic cage. Combined body weights of the three mice in each metabolic cage were determined immediately before initial transfer into the metabolic cage and at termination. Mice were euthanized by carbon dioxide (CO_2) anesthesia on day 10.

Daily urine or feces collections for each cage were stored at –20°C until processed to produce a single cumulative urine sample and single cumulative feces sample. After thorough mixing, multiple aliquots of the cumulative urine sample for each cage were taken for determination of As concentration by INAA. Cumulative urinary excretion of As was calculated as the product of As concentration in the cumulative urine sample and the volume of the cumulative urine sample. Cumulative feces samples were homogenized with a freezer/mill (model 6850; Spex CertiPrep, Metuchen, NJ). Multiple aliquots of cumulative feces sample were taken for determination of As concentration by INAA. Cumulative fecal excretion of As was calculated as the product of As concentration in the cumulative feces sample and the mass of the cumulative feces sample.

Absolute bioavailability (ABA) of As from ingestion of a soil- or As^V-amended diet was calculated as the ratio of cumulative excretion of As in urine and cumulative dietary intake

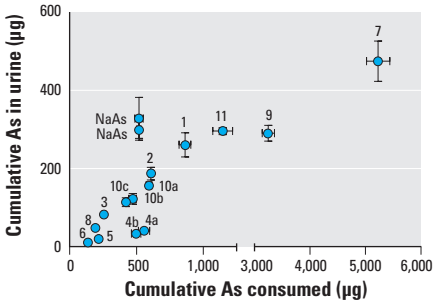

Figure 1. Relationship between cumulative As intake and cumulative urinary As excretion (mean ± SD). For soil numbers, see Table 1. Replicate assays are shown for soil 4 (4a, 4b) and soil 10 (10a, 10b, 10c). NaAs, sodium arsenate–amended diet.

Table 1. Description, elemental composition, and As speciation in test soils.[a]

		Soil properties					Arsenic speciation[b]				
							As^V		As^{III}		
Soil ID	Soil source[c]	As[d] (mg/kg)	Fe[e,f] (g/kg)	Mn[e,f] (g/kg)	Al[e,f] (g/kg)	pH[f]	Sorbed As^V (%)	Scorodite (%)	Realgar (%)	Arsenopyrite (%)	Reduced chi squared[g]
1	Urban residential	990	20.9	0.5	11.8	6.1	52.0	21.2	26.8	—	0.004
2	Urban residential	829	20.5	0.7	9.4	6.3	96.7	3.3	—	—	0.004
3	Urban residential	379	18.9	0.2	9.0	5.0	53.1	15.2	31.7	—	0.003
4	Smelter slag	837	294.4	2.7	13.2	7.2	18.7	1.6	47.7	32.1	0.001
5	Residential	244	46.0	0.8	21.7	7.3	96.2	3.8	—	—	0.002
6	Residential	173	63.4	0.7	20.9	6.6	66.8	33.2	—	—	0.002
7	Smelter slag	6,899	144.5	0.9	15.0	5.2	18.3	47.1	—	34.6	0.001
8	Residential	280	72.3	0.0	3.9	2.1	79.5	20.5	—	—	0.007
9	Smelter slag	4,495	120.1	0.4	12.3	2.6	67.6	32.4	—	—	0.011
10	NIST 2710	601	29.2	8.5	17.2	5.0	95.0	5.0	—	—	0.007
11	NIST 2710a	1,513	34.0	1.7	10.0	4.0	66.8	23.2	9.9	—	0.01

[a]The < 250 µm particle size fraction was used for all analyses. [b]Determined by linear combination of As X-ray absorption spectroscopy. [c]Source of As-contaminated soil. [d]Determined by INAA. [e]Extracted using U.S. EPA Method 3051A (U.S. EPA 2007d) and analyzed using U.S. EPA Method 6010C (U.S. EPA 2007e) by ICP-OES. [f]Data represent the mean of duplicate analyses. [g]Reduced chi-square values = $(\text{data} - \text{fit})^2/\text{data}^2$.

of As (NRC 2003; U.S. EPA 2007c). ABA is commonly calculated and expressed on a percentage basis:

$$\%ABA = (\text{cumulative As excreted in urine} \div \text{cumulative As consumed}) \times 100, \quad [1]$$

with As measured in micrograms. Relative bioavailability (RBA) was calculated as the ratio of the ABA for As in a specific soil-amended diet to the ABA for As in a diet containing sodium arsenate (NRC 2003; U.S. EPA 2007c). RBA is commonly expressed on a percentage basis:

$$\%RBA = (\text{ABA of As in a specific diet} \div \text{ABA of As in sodium arsenate}) \times 100. \quad [2]$$

Bioaccessibility assays. For a full description of bioaccessibility assays, see Supplemental Material (http://dx.doi.org/10.1289/ehp.1003352). Bioaccessible As was determined using an *in vitro* method developed by the Solubility/Bioavailability Research Consortium (SBRC) assay (Kelly et al. 2002). *In vitro* assays were performed in triplicate for each soil and included addition of 1 g test soil to 100 mL gastric fluid consisting of 0.4 M glycine at pH 1.5 in a 125-mL high-density polyethylene bottle and rotating end over end in a water bath at 37°C for 1 hr. All soils tested in the bioaccessibility protocol were identical to those administered to mice in the *in vivo* studies and used in the mineralogy studies described above. All *in vitro* extraction solutions were refrigerated at 4°C for preservation and subsequent analysis by Inductively Coupled Plasma–Optical Emission Spectroscopy (ICP-OES) (U.S. EPA 2007e).

In vitro bioaccessibility (IVBA) was calculated and expressed on a percentage basis:

$$\%IVBA = (\textit{in vitro}\ \text{extractable mg As/kg soil} \div \text{total contaminant mg As/kg soil}) \times 100. \quad [3]$$

Statistical analysis. Simple linear regression was used to evaluate the relationship between *in vivo* As RBA data and IVBA data and to examine the effect of selected soil physicochemical properties on As RBA and bioaccessibility. All analyses were performed using R software (version 2.9.1; R Development Core Team, Vienna, Austria), and figures were created using GraphPad Prism (version 5.0; GraphPad, San Diego, CA).

Results

Soil characterization. Table 1 summarizes selected characteristics of test soils. Total As concentration in test soils ranged from 173 to 6,899 /mg/kg. Arsenic speciation by oxidation state varied among soils [see Supplemental Material, Figure 1 (http://dx.doi.org/10.1289/ehp.1003352)]. Soils 1, 3, 4, 7, and 11 had varying ratios of arsenite (As^{III}) to As^{V} species; soils 2, 5, 6, 8, 9, and 10 contained only As^{V}. We identified realgar in soils 1, 3, 4, and 11 and arsenopyrite in soils 4 and 7. Sorbed As^{V} and scorodite are common As species in soil environments and often result from the oxidation of As ore materials such as realgar or arsenopyrite. Concentration ranges of iron (Fe), manganese (Mn), and aluminum (Al) in soils were 18.9–294.4 g/kg, 0–8.5 g/kg, and 3.9–21.7 g/kg, respectively. Soil pH ranged from 2.1 to 7.3.

Mouse bioavailability assay. The gross clinical condition of mice was unaffected by ingestion of any of the amended diets; amendment of diet with soil or sodium arsenate did not significantly affect cumulative diet consumption (data not shown). Thus, amendment of AIN-93G rodent diet with 1% (wt/wt) soil or As^{V} did not affect diet palatability for mice. Mean cumulative consumption of As strongly correlated with the concentration of As in the diet [see Supplemental Material, Figure 2 (http://dx.doi.org/10.1289/ehp.1003352)]. We evaluated mouse assay performance by determining the percentage of cumulative As intake recovered in cumulative urine and feces collections. Arsenic recoveries in excreta averaged 83.7% (range, 67–96%) for sodium arsenate–amended or soil-amended diets. For all dietary additives, percentage recovery and dietary As concentration were not correlated (R^2 = 0.227; p = 0.398, Pearson product moment correlation).

Increasing cumulative ingestion of As from amended diets was associated with increasing cumulative urinary excretion of As (Figure 1). Figure 2A shows As ABA estimates from diets amended with As^{V}, test soils, or SRMs. Duplicate assays with As^{V}-amended diet yielded an As ABA of approximately 60%. Arsenic ABA estimates for test soils ranged widely from approximately 7% to approximately 33%. Duplicate assays with diets amended with soil 4 (4a, 4b) yielded As ABA estimates of 6.7% and 7.1%. Triplicate assays with diets amended with National Institute of Standards and Technology's NIST-2710, Montana Soil SRM (soils 10a, 10b, 10c), yielded As ABA estimates ranging from 25.9% to 27.2%. For comparison, NIST-2710a SRM-amended diets (soil 11) dosed at multiple levels yielded an As ABA of approximately 26% for each dose level [see Supplemental Material, Figure 2 (http://dx.doi.org/10.1289/ehp.1003352)]. Figure 2B shows As RBA estimates for test soils and SRMs. Relative to As^{V} bioavailability, As RBA estimates for test soils ranged from 11% to 53%. Arsenic RBA estimates for NIST 2710–amended diet (soil 10) and NIST 2710a–amended diet (soil 11) were approximately 44%. Supplemental Material, Table 2, summarizes data from mouse assays.

Correlations among estimates of bioaccessibility and bioavailability and physicochemical properties. IVBA values ranged from 6.8% to 67% (SD were 0–3%). We extracted NIST SRMs (soils 10 and 11) multiple times over the course of the study in accordance with the SBRC assay (SDs were 4.1 and 1.7, respectively). We used linear regression to assess predictability of As RBAs from bioaccessibility values derived from the SBRC assay. The derived regression model accounted for 92% of the variability in As bioavailability observed in the mouse assay (R^2 = 0.92; Pearson correlation = 0.96; Figure 3).

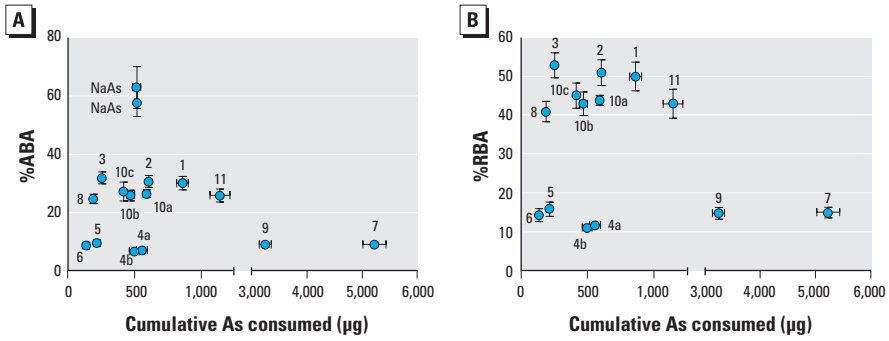

Figure 2. %ABA (*A*) and %RBA (*B*) of As from amended diets as a function of cumulative As intake (mean ± SD). Replicate assays are shown for soil 4 (4a, 4b) and soil 10 (10a, 10b, 10c); NaAs, sodium arsenate–amended diet.

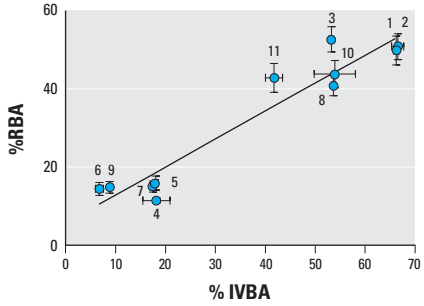

Figure 3. Correlation between estimates of As bioaccessibility and bioavailability (mean ± SD). %RBA = 0.72(%IVBA) + 5.64 (R^2 = 0.92).

We examined predictability of As bioavailability or bioaccessibility from the physicochemical properties and speciation of As in soils by simple linear regression (Table 2). Physicochemical properties of soil that were significant predictors ($p < 0.10$) of As RBA estimates were also significant predictors of IVBA estimates, with the exception of percent arsenopyrite. Among predictors, sums of concentrations of extractable soil Fe and Al (Fe+Al) accounted for the largest amount of variation in RBA and IVBA estimates ($R^2 = 0.58$ and 0.40, respectively). Log(Fe+Al) improved the predictive value of this term ($R^2 = 0.80$ and 0.62 for RBA and IVBA, respectively). Although multivariable linear regression analysis has been used to estimate As bioavailability (Yang et al. 2002), application of this method in the present study did not materially improve predictions of As RBA or IVBA.

Discussion

The concordance of RBA and bioaccessibility estimates obtained in mouse and *in vitro* assays with common physicochemical characteristics of soils suggested that these approaches could be used in a complementary manner to reduce uncertainty in assessment of risk associated with exposure to As-contaminated soils.

The mouse assay proved adaptable for use with soils with a wide range of As concentrations and physicochemical properties. Amended diets were palatable, and as anticipated from earlier studies (Xie et al. 2004), mice remained in apparent good health throughout the experimental period. In this study, calculation of the As ABA used results from the mouse assay for a diet amended with 7 ppm As as sodium arsenate. This amendment produced As dose levels of 8.9 and 9.2 mg/kg in duplicate studies [see Supplemental Material, Tables 1 and 2 (http://dx.doi.org/10.1289/ehp.1003352)]. The dose levels for As^V-amended diets exceeded those for contaminated soils 3, 5, 6, 8, and 10b; approximately equaled (i.e., with overlapping standard deviations) those for soils 4a, 4b, 10a, and 10c; and was lower than those for soils 1, 2, 7, 9, and 11. Hence, for most soils tested, the concentration of As^V added to the diet equaled or exceeded that present in diet after soil amendment. Although additional studies with As^V-amended diets are needed to confirm that estimates of bioavailability of As^V or As in soil are unaffected by As concentration in amended diets, studies in As^V-treated laboratory mice suggest that dose level does not affect the rate of urinary clearance of As (Hughes and Thompson 1996; Hughes et al. 1994; Kenyon et al. 2008). Similarities in the pattern and extent of urinary clearance of As in mice that have received sodium arsenate over a wide range of dose levels suggest that dose level does not influence uptake of As^V across the gastrointestinal barrier or its clearance into urine. In the absence of a change in the rate of urinary clearance of As over a wide dose range, it is likely that mice ingesting diets amended with As^V or As-containing soils will reach whole-body steady-state body burden during the experimental period used in this study (Hughes et al. 2003).

Similar estimates of As bioavailability obtained for soils 4 and 10 in assays over a 2-year period indicated that assay performance was stable (Figure 2A,B). In adult female mice receiving repeated daily oral doses of sodium arsenate, the body burden of As reaches steady state after 8 or 9 days of dosing (Hughes et al. 2003, 2010). Under steady-state conditions, concentrations of As in tissues and outputs of As in urine and feces will reach plateau values that will remain unchanged throughout the dosing interval. Although concentrations of As in urine and feces are both good indicators of current exposure, the predominance of urine as the route for As clearance after oral administration of inorganic As (Hughes et al. 2003) makes it ideal for estimating the extent of absorption of dietary As. Summing amounts of As excreted in urine and feces during the experimental period can be used to approximate recovery of As in the mouse assay. For the materials evaluated in the mouse assay, recoveries of ingested As in excreta ranged from 67% to 96%. However, these values should be regarded as minimal estimates because they do not include As that is retained in tissues of mice.

The mouse assay can be further refined by examining the role of dietary composition on the estimates of soil As bioavailability obtained with this model. Compared with AIN-93 purified diets, the human diet common in developed countries derives more calories from fat, contains less fiber, and may not be optimal in terms of mineral and vitamin composition. These differences in dietary composition could affect the bioavailability of As in two ways. First, the elemental composition of the diet can affect As uptake across the gastrointestinal barrier. For example, an increasing concentration of phosphate reduces *in vitro* uptake of As^V by Caco-2 intestinal cells derived from human colonic adenocarcinoma cells (Calatayud et al. 2010) and gastrointestinal uptake of As in rats dosed orally with As^V (Gonzalez et al. 1995). Second, in humanized gnotobiotic mice the microbiota of the gastrointestinal tract is quickly altered by consumption of a diet with a high fat and high sugar content (Turnbaugh et al. 2009). Alteration of the microbiota of the gastrointestinal tract produced by changes in dietary composition could alter gastrointestinal uptake of ingested As^V. Recent studies show that the anaerobic microbiota from the mouse cecum extensively metabolize As^V to produce inorganic thioarsenicals and methylated oxy- and thioarsenicals (Pinyayev et al. 2011). The mouse model can readily be adapted to examine effects of dietary composition of diets on the bioavailability of As in soils.

Soil As RBA estimates obtained in juvenile swine and monkeys have ranged from 0% to 52% (Casteel et al. 1997; Freeman et al. 1995; Lorenzana et al. 1996; Rees et al. 2009; Roberts et al. 2002; Rodriguez et al. 1999). Comparisons of As RBA data obtained in mice and juvenile swine are problematic because of differences in experimental design and dosing levels. However, four soils have been evaluated in both species. For three soils (soils 9, 10, and 11 in this study), As RBA estimates from mouse and juvenile swine differed by 4%, 0%, and 1%, respectively (U.S. EPA 2009). For the fourth soil (soil 8 in this study), As RBA estimates differed by 19.1% (with estimates of 40.9% for mouse and 60% for juvenile swine. Differences in As RBAs for mouse and juvenile swine may reflect physiological differences between species. Additional soils should be evaluated in both species to identify possible sources of variability and permit a detailed comparison of the assays.

Table 2. Results of linear regression analyses to explore the influence of select soil properties on As RBA and IVBA.

	RBA			IVBA		
Predictor	Equation	R^2	*p*-Value	Equation	R^2	*p*-Value
Sorbed As^V (%)	$0.2x + 17.1$	0.14	0.26	$0.3x + 18.4$	0.11	0.31
Scorodite (%)	$-0.4x + 38.9$	0.10	0.35	$-0.7x + 50.9$	0.16	0.22
Realgar (%)	$0.1x + 31.1$	0.01	0.80	$0.2x + 36.1$	0.01	0.73
Arsenopyrite (%)	$-0.7x + 36.2$	0.28	0.09*	$-0.7x + 42.5$	0.16	0.23
AsV (%)	$0.2x + 19.0$	0.05	0.50	$0.1x + 26.9$	0.02	0.70
As^{III} (%)	$-0.2x + 34.7$	0.05	0.50	$-0.1x + 40.2$	0.02	0.70
As (mg/kg)	$x + 37.3$	0.17	0.21	$x + 45.2$	0.15	0.23
Fe (g/kg)	$-0.1x + 43.5$	0.48	0.02**	$-0.2x + 51.4$	0.32	0.07*
Al (g/kg)	$-1.9x + 57.3$	0.34	0.06*	$-2.7x + 73.3$	0.32	0.07*
Mn (g/kg)	$0.7x + 31.0$	0.01	0.77	$1.1x + 36.3$	0.01	0.76
pH	$-2.2x + 43.3$	0.05	0.52	$-1.2x + 44.0$	0.01	0.82
Fe+Al (mol/kg)	$-8.8x + 48.7$	0.58	0.01#	$-10.5x + 57.9$	0.40	0.04**
Log(Fe+Al) (mol/kg)	$-53.1x + 41.6$	0.80	0.00#	$-67.5x + 50.1$	0.62	0.00#

*$p \le 0.10$, **$p \le 0.05$, and #$p \le 0.01$.

A recent NRC report has recommended development and validation of *in vitro* assays that can replace *in vivo* assays and can provide reliable and accurate data that reduce uncertainty in risk assessment (NRC 2007). This recommendation prompted development of bioaccessibility assays that reflect processes that control As bioavailability in the human gastrointestinal tract (Basta et al. 2007; Juhasz et al. 2007; Kelly et al. 2002; Rodriguez et al. 1999; Ruby et al. 1999). High correlation (R^2 = 0.92, Pearson correlation = 0.96) between the As bioaccessibility data from the SBRC assay and As RBA estimates from the mouse assay is consistent with the high correlation of estimates of As RBA from juvenile swine with As bioaccessibility estimates from the SBRC assay (R^2 = 0.75, Pearson correlation = 0.87) (Juhasz et al. 2009). The correlation of findings from the SBRC assay and the mouse assay suggests that the bioaccessibility assay provides useful information about the characteristics of As-containing soils that influence As RBA as measured in the mouse assay. In addition, strong agreement of estimates from the SBRC *in vitro* assay and the mouse assay suggest that the mouse assay can be used to validate performance of bioaccessibility assays.

Metal speciation and the concentrations of Fe, Al, and Mn are known to affect solubilities and bioavailabilities of metals in soils (Bradham et al. 2006; Kelly et al. 2002; NRC 2003; Scheckel et al. 2009). In this study, we evaluated the effects of As speciation and metal concentrations on estimates of soil As RBA and bioaccessibility obtained in the mouse assay and SBRC assay by linear regression analyses. We found significant inverse correlations between concentrations of extractable Fe and Al in soils and estimates of soil As RBA and bioaccessibility. For example, the log-transformed sum of Fe+Al accounted for 80% and 62% of the variability in estimates of As RBA and bioaccessibility, respectively. The high predictive value of log(Fe+Al) suggests that sorption of As to Fe and Al oxides reduces As solubilization and thereby reduces As RBA and bioaccessibility. Beak et al. (2006a, 2006b) found similar results for As bioaccessibility using a modified Rodriguez et al. (1999) *in vitro* method, which investigated As sorption on ferrihydrite [$Fe^{3+}{}_5O_3(OH)_9$] and corundum (Al_2O_3). Thus, determination of the concentrations and forms of Fe and Al in soils may be useful in assessing As bioavailability. Several clay minerals contain ferrous and ferric iron that, upon release via weathering, will form iron oxides and hydroxides in soil environments (Bowell 1994). Similar processes are also identified for aluminum and manganese oxides in soils (Jenne 1968; McKeague et al. 1971). Lower As RBA estimates for soils containing sulfide forms of As (realgar or arsenopyrite) may reflect slow dissolution kinetics of these mineral species. Although arsenopyrite was present in only two of the test soils, its presence significantly reduced As bioavailability estimates ($p < 0.10$). This finding is consistent with reports showing that As in arsenopyrite is bound tightly; therefore, As bioavailability is likely to be low (Roberts et al. 2007). Additional studies would be useful to identify other metals and metalloids in soils that are potential modifiers of As bioavailability and bioaccessibility and to determine concentration dependencies of these interactions.

Conclusions

A multifaceted approach combining *in vivo* assays, *in vitro* assays, and physicochemical characterization of soils yielded comparable estimates of As bioavailability and provided evidence of interrelations among physicochemical properties and estimates of As bioavailability. The range of As RBA estimates in this study (11–53%) implies that use of a default value of 100% for As bioavailability in human health risk assessments may overestimate risk associated with exposure to As-contaminated soils. Further studies with the mouse assay and the *in vitro* assay coordinated with physiochemical characterization of test soils can confirm and extend the results obtained in this study and identify refinements in experimental design and data analysis that can improve the accuracy and reliability of estimates of bioaccessibility and bioavailability.

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Chemosphere 69 (2007) 961–966
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Comparison of *in vivo* and *in vitro* methodologies for the assessment of arsenic bioavailability in contaminated soils

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Received 8 February 2007; received in revised form 27 April 2007; accepted 8 May 2007
Available online 21 June 2007

Abstract

An *in vivo* swine assay was utilised for the determination of arsenic (As) bioavailability in contaminated soils. Arsenic bioavailability was assessed using pharmacokinetic analysis encompassing area under the blood plasma–As concentration time curve following zero correction and dose normalisation. In contaminated soil studies, As uptake into systemic circulation was compared to an arsenate oral dose and expressed as relative As bioavailability. Arsenic bioavailability ranged from $6.9 \pm 5.0\%$ to $74.7 \pm 11.2\%$ in 12 contaminated soils collected from former railway corridors, dip sites, mine sites and naturally elevated gossan soils. Arsenic bioavailability was generally low in the gossan soils and highest in the railway soils, ranging from $12.1 \pm 8.5\%$ to $16.4 \pm 9.1\%$ and $11.2 \pm 4.7\%$ to $74.7 \pm 11.2\%$, respectively. Comparison of *in vivo* and *in vitro* (Simplified Bioaccessibility Extraction Test [SBET]) data from the 12 contaminated soils and bioavailability data collected from an As spiked soil study demonstrated that As bioavailability and As bioaccessibility were linearly correlated (*in vivo* As bioavailability (mg kg^{-1}) = $14.19 + 0.93 \cdot$ SBET As bioaccessibility (mg kg^{-1}); $r^2 = 0.92$). The correlation between the two methods indicates that As bioavailability (*in vivo*) may be estimated using the less expensive, rapid *in vitro* chemical extraction method (SBET) to predict As exposure in human health risk assessment.
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Keywords: Arsenic; Bioavailability; Bioaccessibility; *In vivo*; SBET; Swine

1. Introduction

In order to reduce the uncertainty in estimating risk associated with incidental ingestion of As-contaminated soil, an understanding of As bioavailability is essential. A variety of animal assays have been developed in order to determine As bioavailability in contaminated soils for human health risk assessment. Rodents (Ng et al., 1998), rabbits (Freeman et al., 1993), dogs (Groen et al., 1994), primates (Freeman et al., 1995; Roberts et al., 2002) and swine (Casteel et al., 1997; Rodriguez et al., 1999; Juhasz et al., Submitted for publication) have been utilised to quantify the amount of As that enters systemic circulation following administration of contaminated soil.

Although primates are the first choice for bioavailability studies due to their close relatedness to man, few studies have been undertaken with this animal model due to the prohibitive costs. Immature swine are considered remarkably similar to humans in terms of their metabolism of As, nutritional requirements, bone development and mineral metabolism. In addition, their body size, weight and bone to weight ratio is similar to young children, the age

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doi:10.1016/j.chemosphere.2007.05.018

group at greatest risk of As absorption due to incidental ingestion of soil (Weis and LaVelle, 1991; Casteel et al., 1997). As a result, the swine model has been used for assessing As bioavailability in soils impacted by mining activities. Casteel et al. (1997) determined that As bioavailability ranged from 0% to 52% in contaminated soils, tailing and slag while swine assays conducted by Rodriguez et al. (1999) reported that As bioavailability in mining and smelting material ranged from 4% to 43%.

While few studies have assessed As bioavailability in contaminated soils using the swine models (due to time and expense limitations), numerous researchers have employed *in vitro* assays to estimate the contaminant fraction that is potentially available for absorption (bioaccessible fraction) (Ruby et al., 1996; Williams et al., 1998; Rodriguez et al., 1999; Basta et al., 2001; Oomen et al., 2003; Sarkar and Datta, 2003; Sarkar et al., 2006). *In vitro* assays overcome the time and expense limitations of *in vivo* studies thereby providing a surrogate measurement of bioavailability that is quick and inexpensive compared to animal models (Ruby et al., 1996; Basta et al., 2001). However, to date, limited studies utilizing only a handful of soils have been performed in order to validate the relationship between *in vitro* As bioaccessibility and *in vivo* As bioavailability (Rodriguez et al., 1999). Before *in vitro* assays can act as a surrogate measurement of As bioavailability, further evaluation of the relationship between As bioaccessibility and As bioavailability in a variety of soil types is required.

In a previous study, As bioaccessibility in contaminated soils was assessed using the simplified bioaccessibility extraction test (SBET) (Juhasz et al., in press). Arsenic bioaccessibility varied greatly in railway corridor, dip site, mine site and gossan soils (1–89%) and was dependent on As mineralogy and soil properties. The objective of this study was to assess As bioavailability using the swine model to determine the suitability of *in vitro* bioaccessibility assays (SBET) for predicting As bioavailability in a variety of As-contaminated soils.

2. Materials and methods

2.1. Arsenic-contaminated soil

Soils used in this study were collected from four regional areas where the soil type, mode of As input and As residence time varied. Soils were collected from railway corridors (South Australia), cattle tick dip sites (North-eastern New South Wales), mine sites (Victoria) and locations in South Australia containing naturally elevated concentrations of As (gossans). In a previous study (Juhasz et al., in press), As-contaminated soils were characterised and SBET extractable As determined. Table 1 outlines soils properties (pH, total As, Al, Fe, P, free Fe) and As bioaccessibility values for soils used in this study.

2.2. Assessment of As bioavailability – in vivo swine assays

Female Large White swine, weighing 20–25 kg, were used for *in vivo* bioavailability assays. Following acclimation for 12 days to animal house conditions, swine were fasted for 24 h prior to surgery for the insertion of jugular

Table 1
Selected properties of soils used in this study

Sample no.	Soil properties					
	Total As (mg kg^{-1})[a]	Total Al (g kg^{-1})[a]	Total Fe (g kg^{-1})[a]	Total P (mg kg^{-1})[a]	pH[a]	% Bioaccessible As[b,c]
Railway corridors						
2	267	22.2	17.6 (10.6)	234	8.8	89
4	42	18.3	13.7 (8.5)	385	8.4	43
5	1114	16.3	68.3 (16.6)	874	7.8	32
10	257	27.8	25.8 (9.9)	242	6.4	23
16	751	10.8	14.5 (11.4)	422	8.3	43
18	91	5.1	10.0 (3.2)	130	7.5	59
Dip sites						
24	713	94.7	98.6 (48.6)	3144	5.7	25
27	228	22.4	17.9 (12.5)	2941	5.2	89
Mine sites						
33	807	10.9	23.5 (7.1)	546	7.6	35
34	577	17.6	24.6 (12.5)	468	6.6	5
Gossans						
44	190	8.3	21.0 (15.6)	200	8.6	22
45	88	9.6	21.0 (13.2)	370	8.1	14

The <250 μm particle size fraction was used for all analyses.
Values in parenthesis represent dithionite citrate bicarbonate extractable Fe (Free Fe).
[a] Data represent the mean of duplicate analysis. Values varied by less than 5%.
[b] Data represent the mean of triplicate analysis. Values varied by less than 2%.
[c] As bioaccessibility determined using the SBET method.

catheters using the method of Bain et al. (1991). During bioavailability assays, animals were housed in metabolic cages. Swine were fed twice daily (500 g of low As pig pellets), 2 and 10 h following As dosage while water was supplied *ad libitum*. Prior to As dosage, blood samples were taken to determine baseline blood As concentrations. Arsenic-contaminated soils (<250 μm particle size fraction) were administered as soil slurries via gavage (10–25 g of soil in 150 ml of As free water) while sodium arsenate (100 μg As kg^{-1}) was administered as the reference dose. Intravenous As dosages (As^{III} and As^{V}: 20 μg As kg^{-1}) were administered using a catheter separate from the blood sampling catheter. Blood samples were routinely taken over a 26 h period following dosage and collected in 7.5 ml heparinised collection tubes. Plasma was separated from red blood cells by centrifugation (4000 rpm for 10 min) then stored at −20 °C prior to As analysis. For each *in vivo* treatment (As^{III}/As^{V} intravenous dose, As^{III}/As^{V} oral dose or As-contaminated soil dose), three separate animals were used.

As bioavailability was assessed using pharmacokinetic analysis encompassing areas under the blood plasma-concentration (AUC) time curves following zero correction and dose normalisation. Absolute and relative As bioavailability were calculated according to Eqs. (1) and (2) respectively. When calculating relative As bioavailability, the AUC for the sodium arsenate oral treatment was used for comparison.

$$\text{Absolute As bioavailability, } \% = \left(\frac{AUC_{Oral\text{-}As}}{AUC_{IV\text{-}As}} * \frac{DR_{IV\text{-}As}}{DR_{Oral\text{-}As}}\right) * 100 \quad (1)$$

where, $AUC_{Oral\text{-}As}$ is the area under the As blood plasma concentration versus time curve for an Oral-As dose; $AUC_{IV\text{-}As}$ is the area under the As blood plasma concentration versus time curve for an intravenous As dose; $DR_{IV\text{-}As}$ is the dose of intravenously administered As (mg kg^{-1}); $DR_{Oral\text{-}As}$ is the dose of orally administered As (mg kg^{-1}).

$$\text{Relative As bioavailability, } \% = \left(\frac{AUC_{Oral\text{-}Soil}}{AUC_{Oral\text{-}AsV}} * \frac{DR_{Oral\text{-}AsV}}{DR_{Oral\text{-}Soil}}\right) * 100 \quad (2)$$

where, $AUC_{Oral\text{-}Soil}$ is the area under the As blood plasma concentration versus time curve for an Oral-As-contaminated soil dose; $AUC_{Oral\text{-}AsV}$ is the area under the As blood plasma concentration versus time curve for an oral dose of sodium arsenate; $DR_{Oral\text{-}Soil}$ is the dose of orally administered soil (mg kg^{-1}); $DR_{Oral\text{-}AsV}$ is the dose of orally administered sodium arsenate (mg kg^{-1}).

2.3. Arsenic determination in blood plasma

Two methods were used for the determination of As in blood plasma. Samples (3 ml) were digested with nitric acid (2 ml; 70%) and H_2O_2 (1 ml; 30%) using USEPA method 3015A (USEPA, 1998). Following digestion, samples were diluted with Milli-Q water to reduce the acid content to 10%. Alternatively, blood serum was diluted 10-fold in diluent solution containing 1-butanol (2% w/v), EDTA (0.05% w/v), Triton X-100 (0.05% w/v) and ammonium hydroxide (1% w/v) in Milli-Q water (Agilent Technologies, 2006) prior to analysis. All samples were analysed by ICP-MS with the appropriate number of duplicate samples, duplicate analysis, spiked sample recoveries and check values included for quality assurance and quality control purposes.

3. Results and discussion

3.1. Arsenic bioavailability

In order to determine As bioavailability in contaminated soils (railway corridors, dip sites, mine sites and gossan soils), *in vivo* swine experiments were performed. Arsenic doses were administered to fasting animals to represent a 'worst-case scenario' for As exposure. As food ingestion increases gastric pH conditions, which in turn influences As dissolution (Ruby et al., 1996), feed was administered to swine 2 h following As dosage to ensure the lowest gastric pH conditions in the animals at the time of As exposure. Initially pharmacokinetic studies were performed with As^{III} and As^{V} to determine the absolute bioavailability of these As species. Only the bioavailability of inorganic As species was assessed as these species are reported to be the dominant forms present in soil extracts (Bissen and Frimmel, 2000; Montperrus et al., 2002). The absolute As bioavailability was determined by comparing AUCs for oral and intravenous routes of administration (Fig. 1). For both As^{III} and As^{V}, the absolute bioavailability was approximately 100% although some variability was observed between animal treatment. For As^{III} and As^{V}, 103.9 ± 25.8% and 92.5 ± 22.3% of the administered oral dose was absorbed from the gastrointestinal tract and entered systemic circulation respectively.

Following pharmacokinetic studies, feeding trials were conducted with selected As-contaminated soils. Arsenic uptake in these soils was compared to an As^{V} oral dose and expressed as relative As bioavailability (Eq. (2)). Mean relative As bioavailability varied significantly between contaminated soils. In railway corridor soils ($n = 6$), As bioavailability ranged from 11.2 ± 4.7% to 74.7 ± 11.2% while in dip site soils As bioavailability was 33.0 ± 17.0% and 49.9 ± 11.0% in the two soils studied. In mine site soils ($n = 2$), As bioavailability was 6.9 ± 5.0% and 40.8 ± 7.4% while As bioavailability was generally low in gossan soils (16.4 ± 9.1% and 12.1 ± 8.5%). Previous *in vivo* studies with mining impacted soils, slags and dust have reported that As bioavailability ranged from 10% to 52% (Casteel et al., 1997; Freeman et al., 1993; Freeman et al., 1995). In a study by Roberts et al. (2002), As bioavailability in soils ($n = 5$) collected from an electrical substation, a wood preservation site, a dip site and two pesticide sites ranged from 11% to 25%. Juhasz et al. (Submitted for publication)

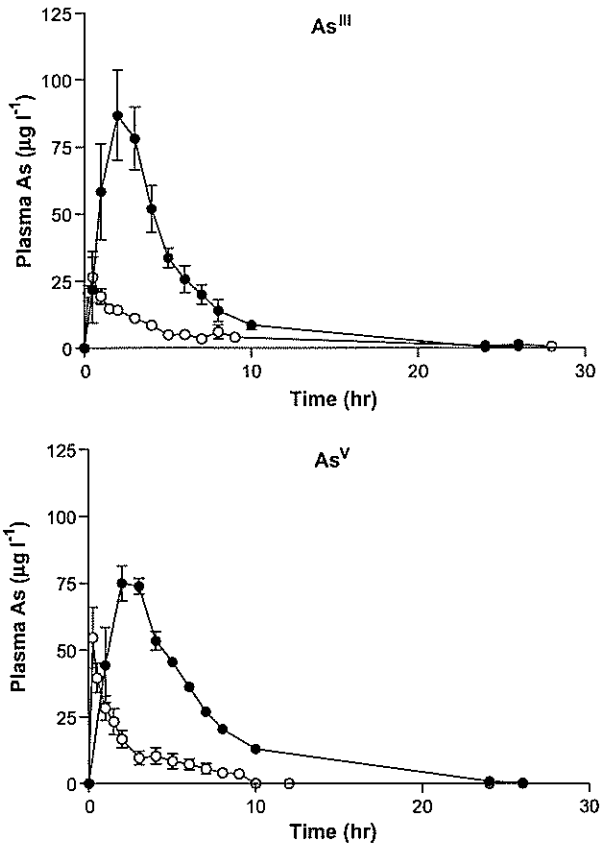

Fig. 1. Arsenic concentration in blood plasma following oral (●) or intravenous (○) administration of As^{III} or As^{V}. Each swine received a single administration of 20 μg As kg^{-1} or 80 to 100 μg As kg^{-1} for intravenous and oral doses respectively. Data points represent the mean and standard deviation of three separate *in vivo* assays.

utilised the swine model for the determination of As bioavailability in spiked soils aged over a 12 month period. Juhasz et al. (Submitted for publication) reported that after the addition of As^{V} (1000 mg kg^{-1}) to a Red Ferrosol (pH: 5.8; Fe content: 99.6 g kg^{-1}; % clay: 24), As bioavailability was reduced to 25% after 12 months of aging. In contrast, there was no reduction in As bioavailability observed following the addition of 1000 mg As kg^{-1} to a Brown Chromosol (pH: 7.8; Fe content: 8.0 g kg^{-1}; % clay: 7.5) soil and subsequent aging.

The determination of As bioavailability using *in vivo* assays is time consuming laborious and expensive. However, *in vitro* assays that simulate human gastric conditions, such as the SBET, may provide a surrogate assay for predicting As bioavailability that is rapid and inexpensive. While numerous researchers have reported the use of *in vitro* assays for determining As bioaccessibility, a dearth of information is available regarding the relationship between As bioaccessibility (*in vitro*) and As bioavailability (*in vivo*). In a previous study with railway corridor, dip site, mine site and gossan soils, Juhasz et al. (in press) determined As bioaccessibility using the SBET method. SBET data was collected from the same soils and the same ageing time-frame from which the present *in vivo* study was conducted. Using data from these studies, the Pearson correlation method was used to calculate the relationship between As bioaccessibility as measured by the SBET method and As bioavailability as measured by the *in vivo* method (Fig. 2). As the spiked soil study of Juhasz et al. (Submitted for publication) utilised the SBET method, and *in vivo* experiments were conducted under the same condition as the present study, this data was also included in Pearson calculations. Comparison of *in vitro* and *in vivo* results indicate that the correlation between As bioaccessibility and As bioavailability was significant ($p = 0.01$; $n = 49$), with SBET assessment of contaminated soils providing a good prediction of *in vivo* As bioavailability (*in vivo* As bioavailability (mg kg^{-1}) = 14.19 + 0.93 · [SBET As bioaccessibility (mg kg^{-1})]; $r^2 = 0.92$). While some variability was observed in the data collected during *in vivo* studies, this may be attributable to physiological intra-species variability including genetic factors, disparity in stomach clearance times, stomach pH and rates of As absorption. The same variability was not evident in the *in vitro* assay with the data being extremely reproducible under laboratory conditions.

Although data on As bioavailability is accumulating in the literature, few studies have correlated As bioavailability with As bioaccessibility as determined by *in vitro* assays. This is surprising given that *in vitro* assays are used as surrogates for estimating As bioavailability for incorporation into human health risk models. To the best of our knowledge, the work described in Rodriguez et al. (1999) is the only other study where *in vivo* and *in vitro* As bioavailability/bioaccessibility were compared. In the study of Rodriguez et al. (1999), there was no statistical difference in the relative availability of As in mining and smelting material when measured by *in vitro* (IVG method) or

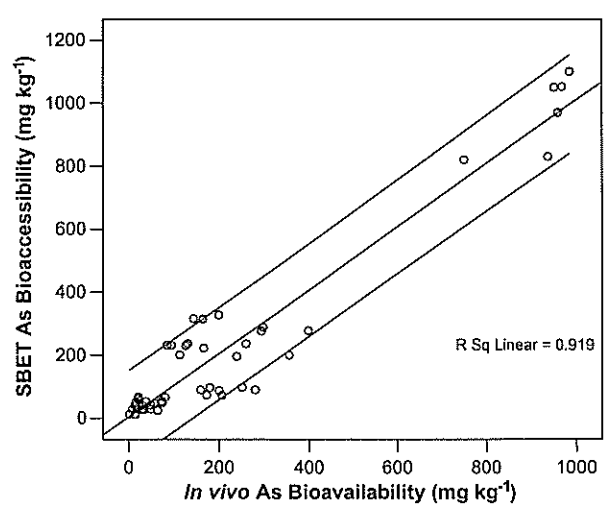

Fig. 2. Correlation between As bioaccessibility (*in vitro* SBET assay) and As bioavailability (*in vivo* swine assay) for railway corridor, dip site, mine site, gossan (this study) and As-spiked soils (Juhasz et al., in press) ($n = 49$). 95% confidence limits are also shown.

in vivo (swine feeding trials) methods. However, the calcine samples analysed by the *in vitro* methods were not statistically equivalent to the *in vivo* method as As bioavailability was underestimated by the *in vitro* method. In this study, no calcinated materials were tested, however, a much wider range of As-contaminated soil types were evaluated compared to the study of Rodriguez et al. (1999). From the soils used in this study, it can be concluded that the assessment of As bioaccessibility using the SBET method will yield a reproducible value with a low standard deviation that can be used to predict *in vivo* As bioavailability.

3.2. Predicting As bioavailability using soil properties

In order to develop a model to predict As bioavailability in contaminated soils, linear and multivariate regression analysis was performed to describe *in vivo* As bioavailability as a function of soil properties. Soil properties that were included in the analysis were pH, total As, Fe, Al and P concentrations (Table 2). The selection of these soil properties was based on previous studies that have been identified these parameters as being important factors in controlling As bioavailability in spiked soils (Yang et al., 2002). Regression analysis identified that total As and Fe concentrations were the variables that best described the variation in *in vivo* As bioavailability. Results from the regression model summary produced the following model:

In vivo As bioavailability (mg kg^{-1}) = 11.310 + 0.678 · Total As (mg kg^{-1}) − 4.368 · Total Fe (g kg^{-1}) $r^2 = 0.72$.

Although a workable model appears to adequately describe As bioavailability using total As and Fe, there is some discrepancy in the predicted data (Fig. 3). Statistical analysis of the residuals indicates that the model developed is not highly significant. This is evident from a high residual in relation to the regression model, as well as the model producing a Durbin–Watson factor of 0.585. Durbin–Watson values near zero indicate positive autocorrelation of the random error while a value of 2 indicates no correlation. No correlation is necessary for regression models to be deemed reliable. While the importance of Fe and pH in controlling As sorption has been demonstrated by a number of researchers (Smith et al., 1998; Goldberg, 2002; Yang et al., 2002), it is evident that other variables, such as As speciation, mineralogy, As-soil contact time etc. will impact on As bioavailability. These variables will also influence the prediction of As bioaccessibility (based on soil properties) as exemplified by the research of Juhasz et al. (in press).

Table 2
Pearson correlation data for *in vivo* As bioavailability (swine assays) and soil properties

Soil parameter	Correlation coefficient	*p*-Value
Total arsenic (mg kg^{-1})	0.694	0.000
pH	0.078	0.296
Total iron (g kg^{-1})	−0.162	0.133
Total aluminium (g kg^{-1})	−0.048	0.373
Total phosphorous (mg kg^{-1})	−0.147	0.157

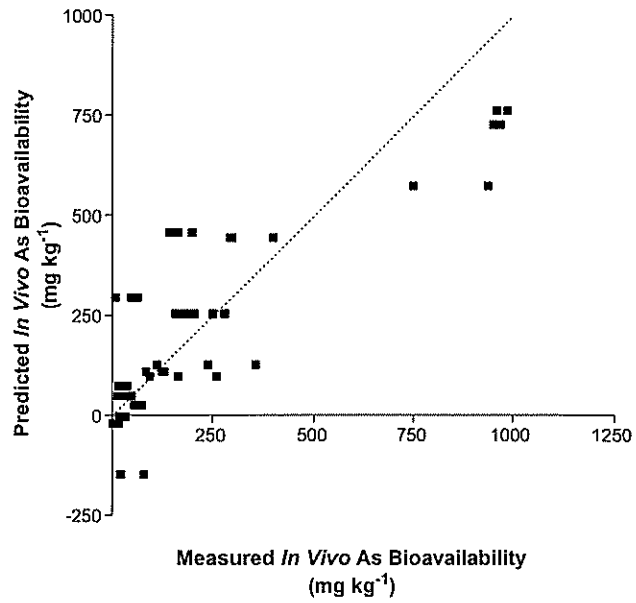

Fig. 3. Comparison of As bioavailability values for railway corridor, dip site, mine site, gossan and As-spiked soils as determined by *in vivo* assays or predicted using a linear regression model based on soil properties.

4. Conclusion

The bioavailability of As in contaminated soil was determined by monitoring blood As concentrations in swine following oral administration of contaminated soil. Arsenic bioavailability varied considerably between soils ranging from 6.9 ± 5.0% to 74.7 ± 11.2% of the total As concentration. When *in vivo* As bioavailability data was compared to As bioaccessibility data obtained SBET analysis, the rapid, inexpensive *in vitro* assay could accurately predict *in vivo* As bioavailability. This suggests that the *in vitro* chemical extraction method may be used as a surrogate assay for the assessment of As bioavailability.

Acknowledgements

This research was funded through the Australian Research Council Linkage Grant Scheme with the generous support of IPOH Pacific Ltd. (Grant number LP0347301). *In vivo* assays were approved and conducted according to application 1702 of the Institute for Medical and Veterinary Science Animal Ethic Committee. The authors would like to acknowledge the support of the Centre for Environmental Risk Assessment and Remediation (University of South Australia), Centre for Pharmaceutical Studies (University

of South Australia) and the Institute of Medical and Veterinary Science for this research.

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Health Consultation

Palestine Bioavailability Study

Arsenic and Vanadium Soil Action Levels

Palestine, Anderson County, Texas

EPA No. TXN000605670

May 24, 2006

Prepared by

Texas Department of State Health Services
Under a Cooperative Agreement with the
Agency for Toxic Substances and Disease Registry

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Purpose and Statement of Issues

In response to recommendations made in previous health consultations, the U.S. Environmental Protection Agency Region 6 (EPA-6) contracted with the College of Veterinary Medicine at the University of Missouri, Columbia (CVMUM) to assess the relative bioavailability of arsenic and vanadium in soil from the Palestine area. Using data from this study, scientists from EPA-6 proposed residential soil action levels of 155 mg/kg for arsenic and 975 mg/kg for vanadium. The EPA has asked the Texas Department of State Health Services (DSHS) and the Agency for Toxic Substances and Disease Registry (ATSDR) for an independent assessment to evaluate whether the proposed residential surface soil action levels for arsenic and vanadium would be protective of public health (Note: Appendix A lists abbreviations and acronyms used in this report).

Background

Site Description and History

The area in question, a mixed industrial/residential area, is located in the southeastern portion of Palestine, Anderson County, Texas. Although the exact source and extent of the contamination have not been determined, historically, two major industrial facilities operated in the area: the Palestine Light, Heat, and Power Company and the former George M. Dilley and Son, Founders and Machinists Shop (also known as the Palestine Foundry).

The Palestine Light, Heat, and Power Company site is a one-acre site that was formerly a town coal gas operation. The site consists of several waste piles (railroad ties, concrete blocks, and rock piles) from the adjacent railroad system on the east side of the property. The Palestine Foundry site is north of the Palestine Light, Heat, and Power Company and east of the railroad tracks on South May Street. It was the first large industry in Palestine and operated from 1873 to 1949. Historically, several buildings and a smoke stack may have existed on the property; only two buildings currently remain and the site is heavily vegetated [1].

Both properties are accessible to children as well as adults. Residential homes are located across South May Street from the Palestine Foundry. The fence along the road does not prevent access to the foundry property. The foundry office building is dilapidated and thereby poses a physical hazard.

In previous consults [2, 3], it was determined that there may be human exposure to elevated levels of arsenic, vanadium, and lead in the soil and that selected residences and daycare facilities warranted further attention [3].

Discussion

In determining the health risks that may be associated with contaminants found in various media, the concentration of each contaminant is compared to its health-based assessment comparison (HAC) value for non-cancer and cancer endpoints. These values are guidelines that specify

levels of chemicals in specific environmental media (soil, air, and water) that are considered safe for human contact with respect to identified human endpoints. Non-cancer screening values are generally based on ATSDR's minimal risk levels (MRLs)[1] and EPA's reference doses (RfDs)[2]. Both of these are based on the assumption that there is an identifiable exposure threshold (both for the individual and for populations) below which there are no observable adverse effects. Thus, MRLs and RfDs are estimates of daily exposures to contaminants that are unlikely to cause adverse non-cancer health effects even if exposure occurs for a lifetime. The cancer risk comparison values used in this consultation are based on EPA's chemical-specific cancer slope factors (CSFs)[3].

Knowing how much of the contaminant is actually absorbed into the body (bioavailability) is important in determining the potential risks associated with the contaminant [4]. The bioavailability of any contaminant is both soil- and contaminant-specific; thus, it is not possible to predict bioavailability without considering these factors. In the absence of bioavailability data, and in order to be protective of public health, it is customary to assume that a contaminant is 100% bioavailable; all the contaminant that enters the body is absorbed into the blood. In reality the rate and extent of absorption of a chemical from an ingested media such as soil is much less than 100%.

CVMUM determined the bioavailability of the contaminants at this site by feeding site specific soil to juvenile swine. Swine were given oral doses of sodium arsenate, vanadyl sulfate, or the Palestine soil; and the relative bioavailability of arsenic and vanadium was assessed by comparing the absorption of arsenic or vanadium from the reference material to that of the test soil [4]. Results of this study indicated that the relative bioavailability of arsenic and vanadium in Palestine soil was approximately 15% and 8%, respectively [4].

Using the results of the CVMUM bioavailability study, EPA revised the action levels for arsenic and vanadium in Palestine soil to 155 and 975 mg/kg, respectively [5]. DSHS was asked to conduct an independent assessment to evaluate whether these revised action levels for residential soil would be protective of public health.

Arsenic

Arsenic is a naturally occurring element that is widely distributed throughout the earth's crust and may be found in air, water, and soil [6]. Arsenic exists as inorganic arsenic, organic arsenic, and arsine gas. Generally, organic arsenic is less toxic than inorganic arsenic, with some forms of organic arsenic being virtually non-toxic. Inorganic arsenic occurs naturally in soil, and children may be exposed to arsenic by eating soil or by direct skin contact with soil or water

[1] An MRL is a contaminant specific exposure dose below which adverse health effects in the people most sensitive to chemical-induced effects would not be expected. MRLs generally are based on the most sensitive chemical-induced end point considered to be of relevance to humans.

[2] An RfD is an estimate (with a level of uncertainty from 10 to 1000 times below the level of harmful effects) of a daily exposure to the human population (including sensitive groups) that is likely to be without appreciable risk of deleterious effects during a lifetime.

[3] A CSF is an estimate of excess lifetime risk of one cancer in one million (1×10^{-6}) people exposed over a lifetime (70 years).

containing arsenic [6]. Children and adults normally take in small amounts of arsenic through inhalation of air and ingestion of food and water, with food being the largest source of arsenic. Fish and seafood contain the highest concentrations of arsenic; however, most of this is in the less toxic organic form of arsenic [6].

A chronic oral MRL of 0.0003 mg/kg/day for inorganic arsenic was derived by dividing the identified chronic No Observable Adverse Effect Levels (NOAEL) of 0.0008 mg/kg/day (obtained from human epidemiologic studies) by an uncertainty factor of three to account for the lack of data on reproductive toxicity and to account for some uncertainty as to whether the NOAEL accounts for all sensitive individuals [6]. The Lowest Observed Adverse Effect Levels (LOAEL) associated with these epidemiologic studies was 0.014 mg/kg/day, where exposure to arsenic above this level resulted in hyperpigmentation of the skin, keratosis (patches of hardened skin), and possible vascular complications [6]. The chronic oral MRL was used to evaluate the potential public health significance of exposure to arsenic.

A provisional acute oral MRL of 0.005 mg/kg/day for inorganic arsenic was derived by dividing the LOAEL of 0.05 mg/kg/day (based upon gastrointestinal effects and facial edema in humans) by an uncertainty factor of 10 for extrapolation from a LOAEL to a NOAEL [6]. The acute oral MRL was used to evaluate the potential public health significance of acute exposure to arsenic due to pica behavior.

Inorganic arsenic is a known carcinogen [6]. The most characteristic effect of long-term exposure to inorganic arsenic is a pattern of skin changes including darkening of the skin and the appearance of small “corns” or “warts” on the palms, soles, and torso. A small number of these corns may ultimately develop into skin cancer. Liver, bladder, kidney, and lung cancer also have been associated with exposure to arsenic [6]. While there are certainly both cases of and deaths due to these types of cancer in Palestine, Texas, it would be impossible to determine if any one of these cancers was caused by exposure to arsenic b[0]ecause there is nothing that indisputably links these cancers to arsenic exposure and there are other causes of cancer. The incidence and mortality of these cancer types in Palestine are similar to what would be expected based on state rates [2].

Vanadium

Vanadium is a naturally occurring element in the earth that may be released to air, groundwater, surface water, or soil when rocks or soil containing vanadium are broken down by wind or water erosion [7]. People are exposed to vanadium daily in food, water, and air, with food being the largest source of vanadium. Determining the public health implications of vanadium in soil is difficult. The toxic effects of vanadium are greater when vanadium is inhaled as compared to when it is taken orally [7]. Protein and other trace elements in the diet may have an affect on vanadium toxicity and the toxic effects also may vary by species. Humans who have been exposed to relatively large doses for up to five months only reported minor complaints at the higher doses; whereas, in animals numerous effects such as weight loss, dehydration, depressed growth, cardiac irregularities, and loss of renal function have been reported [7]. Whether vanadium is essential to the diet is controversial. There is *in vivo* evidence that vanadium may be

needed for normal iodine and/or thyroid function and other evidence that it may have some effect on glucose metabolism. Although a variety of inconsistent deficiency symptoms have been reported in animals, no specific function for vanadium has been identified for humans [7].

An intermediate oral MRL of 0.003 mg/kg/day for vanadium was derived by dividing the NOAEL of 0.3 mg/kg/day (based upon renal effects in rats) by uncertainty factors of 10 for human variability and 10 for interspecies variability [7]. The intermediate oral MRL was used to evaluate the potential public health significance of exposure to vanadium.

Although no acute oral MRL has been derived for vanadium, an acute LOAEL of 8.4 mg/kg/day based upon developmental effects in rats is available [7]. As no other advisories are available, this acute LOAEL was used to evaluate the potential public health significance of acute exposure to vanadium due to pica behavior.

No human studies are available regarding the carcinogenicity of vanadium [7]. However, no increase in tumor frequency was noted in rats and mice chronically exposed to 0.5 to 4.1 mg-vanadium/kg-body weight as vanadyl sulfate in drinking water [8]. Currently, vanadium is not classified as a human carcinogen.

Non-Carcinogenic Effects

We used the proposed actions level of 155 mg/kg and 975 mg/kg for arsenic and vanadium, respectively, to evaluate the exposure that children might receive from incidental ingestion of surface soil. Children were considered because they constitute the sub-population most likely to experience the highest levels of exposure to contaminants in soil (due to play activities and normal hand-to-mouth exposure) and because their dose relative to body weight is higher than that of adults.

We applied the bioavailability factors reported by CVMUM to the proposed action levels and used standard assumptions for body weight (16 kg, child) and incidental soil ingestion (200 mg per day, child) to estimate exposure. Other assumptions that were used are listed in Tables 1-8. For non-cancer endpoints, wherever possible, we compared estimated exposures either to known effect levels in humans or to documented NOAEL and/or LOAEL in humans or animals.

In addition to incidental ingestion of small quantities of soil, a sizable portion of the child population periodically may ingest more than 1.0 g[4] of soil per day (pica behavior) [9]. While an individual child may exhibit pica behavior infrequently it has been estimated that about 62% of children will ingest >1.0 g of soil on 1-2 days/year. Additionally, 42% of children will ingest >5 g of soil and 33% will ingest >10 g of soil on 1-2 days per year. Since ingesting large amounts of soil potentially could result in acute intoxication we also evaluated the proposed action levels with respect to periodic pica behavior [9].

[4] 1 g is equal to 1,000 mg (about the same size as a pack of artificial sweetener)

Assuming a maximum soil arsenic concentration of 155 mg/kg, the estimated daily dose that a child would receive from the ingestion of soil (0.0003 mg/kg/day, Tables 1-2) is equal to the chronic oral MRL of 0.0003 mg/kg/day. Therefore, with respect to non-carcinogenic health effects, the proposed action level of 155 mg/kg for arsenic in soil is adequate to protect children.

Assuming a maximum soil vanadium concentration of 975 mg/kg, the estimated daily dose that a child would receive from the ingestion of soil (0.0009 mg/kg/day, Tables 3-4) is below the intermediate oral MRL of 0.003 mg/kg/day. Therefore, with respect to non-carcinogenic health effects, the proposed action level of 975 mg/kg for vanadium in soil is adequate to protect children.

Short-Term or Sporadic Pica Behavior

To explore the potential public health significance of pica behavior at this site, we considered the scenario of a 16 kg child ingesting 5,000 mg of soil per day for 14 days. At a soil arsenic concentration of 155 mg/kg and a bioavailability factor of 15%, the daily dose of absorbed arsenic during pica events would be approximately 0.007 mg/kg/day (Table 5). This estimated exposure dose is slightly higher than the acute oral MRL for arsenic which would indicate some degree of risk; however, as it is seven times lower that the dose reported to cause gastrointestinal effects in humans the likelihood that it would result in adverse health effects is low. At a soil vanadium concentration of 975 mg/kg and a bioavailability factor of 8%, the daily dose of absorbed vanadium during pica events would be approximately 0.02 mg/kg/day (Table 6), 420 times below the acute LOAEL for less serious effects in animals. We would not expect to see children exhibiting signs or symptoms of acute toxicity either from arsenic or vanadium as a result of short-term, sporadic pica behavior.

Carcinogenic Effects

Arsenic is a known carcinogen, and oral cancer slope factor and inhalation unit risk factors have been developed by EPA to estimate the excess lifetime risk for developing cancer. Vanadium has not been classified as a human carcinogen, and thus no slope factors or risk factors have been developed for vanadium.

Using EPA's cancer slope factor for arsenic, based on an 30 year exposure scenario (a 70 kg adult ingesting 100 mg of soil per day) we estimated the excess lifetime risk of developing cancer from the incidental ingestion of soil to be 2.0×10^{-5} (Tables 7-8). Qualitatively, we would interpret this as no apparent increased lifetime risk for developing cancer.

There is evidence that suggests some carcinogens, especially ones with a mutagenic mode of action, exhibit a greater effect in early-life versus later-life exposures [10]. The EPA has developed guidance on assessing the potential for early-life exposure to contribute to the appearance of cancer later in life. In this, cancer risks are calculated by combining age-dependent adjustment factors and exposure estimates [10]. The lifetime risk of developing cancer is based upon the risk during three time periods: risk during the first two years of life (10-fold adjustment representing to toxicokinetic and toxicodynamic differences between

children and adults), risk for ages 2 through <16 (3-fold adjustment to account for developmental changes occurring prior to middle adolescence), and risk for ages 16 until 70 years (average life expectancy, no adjustment factor for adult exposures) [10].

The risk for cancer due to exposure to arsenic over a lifetime was calculated using EPA methodology [10]. Body weight (10 kg infant, 40 kg child/middle adolescent, and 70 kg adult), soil intake rate (200 mg/day infant, 150 mg/day child/middle adolescent, and 100 mg/day adult), and age-dependent adjustment factors were used to calculate cancer risk over a lifetime of exposure (4.8×10^{-5}). Qualitatively, we would interpret this as no apparent increased lifetime risk for developing cancer.

Public Health Implications

Based on the above assumptions we would not expect the proposed action levels to pose an appreciable risk either to children or adults. However, in this consultation, we only evaluated the potential health effects associated with ingestion of soil. In some communities, backyard vegetable gardens are common and may provide an additional source of exposure, particularly during the growing season. In such situations it would be prudent to also consider the ingestion of home-grown vegetables and the incidental inhalation of dust while people are working in their gardens when proposing an action level. Thus, if there is reason to believe that vegetable gardening is occurring in Palestine, the proposed action level for arsenic may need to be revised. Using default exposure assumptions for inhalation of dust and ingestion of home-grown vegetables (Tables 1-8) we estimate that a soil arsenic concentration of 131 mg/kg would be a suitable action level. For vanadium the proposed action level of 975 mg/kg would still be adequate even when considering other sources of exposure. The estimated daily dose of vanadium from all sources is 0.001 mg/kg/day, well below the intermediate oral MRL for vanadium. The absorption of either arsenic or vanadium through the skin via dermal contact with soil was too low to consider[5].

Based on data presented in previous health consultations [2, 3], the maximum arsenic and vanadium concentrations detected in surface soils (0-1 inch) in Palestine (85.4 mg/kg and 325 mg/kg, respectively) were well below proposed action levels.

Child Health Considerations

In communities faced with air, water, or food contamination, children could be at greater risk than are adults from certain kinds of exposure to hazardous substances. A child's lower body weight and higher intake rate results in a greater dose of hazardous substance per unit of body weight. Sufficient exposure levels during critical growth stages can sustain permanent damage to the developing body systems of children. Children are dependent on adults for access to housing,

[5] Cadavers were used to assess the uptake of arsenic from soil via dermal absorption. Following 24 hours of exposure to soil containing arsenic, only 0.43% of the arsenic passed through the skin and 0.33% of the arsenic remained in the skin after washing [6].

for access to medical care, and for risk identification. Thus adults need as much information as possible to make informed decisions regarding their children's health.

In this consult, we evaluated the exposure children might receive from accidental ingestion of soil to evaluate whether the proposed residential surface soil action levels for arsenic and vanadium would be protective of public health. We used children because they constitute the sub-population most likely to experience the highest levels of arsenic and vanadium in soil and because their dose of arsenic and vanadium relative to body weight is higher than that of adults.

Conclusions

Based on available information we have concluded that:

1. Considering exposure to arsenic and vanadium via accidental ingestion of surface soil, the proposed soil action levels would pose no apparent public health hazard.

2. The soil action level of 131 mg/kg may be more appropriate for yards where vegetable gardening occurs; however, based on available data all the levels measured in Palestine were well below this level.

Recommendations

Not applicable

Public Health Action Plan

Not applicable

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15. Justification for the Approach Used to Calculate the Above and Belowground Vegetable Ingestion Rate for TRRP.

Certification

This public health consultation was prepared by the Texas Department of State Health Services (DSHS) under a cooperative agreement with the Agency for Toxic Substances and Disease Registry (ATSDR). It is in accordance with approved methodology and procedures existing at the time the public health consultation was initiated. Editorial review was completed by the Cooperative Agreement partner.

Technical Project Officer, SPS, SSAB, DHAC, ATSDR

The Division of Health Assessment and Consultation, ATSDR, has reviewed this public health consultation and concurs with its findings.

Team Lead, CAT, SPAB, DHAC, ATSDR

Appendix A: Acronyms and Abbreviations

ATSDR	Agency for Toxic Substances and Disease Registry
CSF	Cancer Slope Factor
CVMUM	College of Veterinary Medicine at the University of Missouri, Columbia
DSHS	Texas Department of State Health Services
EFH	Exposure Factors Handbook
EPA	U.S. Environmental Protection Agency
EPA-6	U.S. Environmental Protection Agency Region 6
g	gram
HAC	health-based assessment comparison
kg	kilogram
kg/m^3	kilogram per cubic meter
LOAEL	Lowest Observable Adverse Effect Level
m^3/day	cubic meter per day
mg	milligram
mg/day	milligram per day
mg/kg	milligram per kilogram
mg/kg/day	milligram per kilogram per day
MRL	Minimal Risk Level
NOAEL	No Observable Adverse Effect Level
PHAGM	Public Health Assessment Guidance Manual
RAGS	Risk Assessment Guidance for Superfund
RfD	Reference Dose
TAC	Texas Administrative Code
TRRP	Texas Risk Reduction Program

Appendix B: Tables

Table 1. Summary of non-carcinogenic estimated daily doses for children exposed to arsenic via various pathways. Refer to Table 2 for calculations of estimated exposure doses.

Exposure Pathway	Estimated Daily Dose (mg/kg/day)
Soil Ingestion Exposure Dose	**0.0003**
Inhalation Exposure Dose	0.00000002
Aboveground Vegetables Exposure Dose	0.00006
Belowground Vegetables Exposure Dose	0.00002
Total Daily Dose from all Pathways	**0.0004**

Table 2. Non-carcinogenic estimated daily doses for children exposed to arsenic via various pathways.

Exposure Factor	**EF=(F*ED)/AT**
EF=exposure factor (unitless)	0.95890411
F=frequency of exposure (day/year)	350 [a]
ED=exposure duration (year)	6 [b]
AT=averaging time (ED*365 day/year)	2190
Soil Ingestion Exposure Dose	**D=(C*RBAF*IR*EF*CF)/BW**
D=exposure dose (mg/kg/day)	0.0003
C=contaminant concentration (mg/kg)	155 [c]
RBAF=relative bioavailability factor (unitless)	15% [d]
IR=intake rate of soil (mg/day)	200 [b]
EF=exposure factor (unitless)	0.95890411
CF=conversion factor (10^{-6} kg soil/mg soil)	0.000001
BW=body weight (kg)	16 [b]
Inhalation Exposure Dose	**D=(C*SPL*IR*EF)/BW**
D=exposure dose (mg/kg/day)	0.00000002
C=contaminant concentration (mg/kg)	155 [c]
SPL=suspended particulate level (kg/m^3)	2.16E-10 [e]
IR=intake rate (m^3/day)	8.08 [f]
EF=exposure factor (unitless)	0.95890411
BW=body weight (kg)	16 [b]
Aboveground Vegetables	**D=(C*CF*PC*CF*IR*EF*PH)/BW**
D=exposure dose (mg/kg/day)	0.00006
C=contaminant concentration (mg/kg)	155 [c]
CF=conversion factor (10^{-3} kg soil/g soil)	0.001
PC=partition coefficient soil to vegetable (g soil/g dry weight)	0.01 [g]
CF=conversion factor (g dry weight/g as consumed)	17.4% [h]
IR=intake rate (g as consumed/day)	41.87
EF=exposure factor (unitless)	0.95890411
PH=% of food homegrown (%)	8.2% [i]
BW=body weight (kg)	16 [b]
Belowground Vegetables	**D=(C*CF*PC*CF*IR*EF*PH)/BW**
D=exposure dose (mg/kg/day)	0.00002
C=contaminant concentration (mg/kg)	155 [c]
CF=conversion factor (10^{-3} kg soil/g soil)	0.001
PC=partition coefficient soil to vegetable (g soil/g dry weight)	0.008 [g]
CF=conversion factor (g dry weight/g as consumed)	22.2% [h]
IR=intake rate (g as consumed/day)	29.36
EF=exposure factor (unitless)	0.95890411
PH=% of food homegrown (%)	4.3% [i]
BW=body weight (kg)	16 [b]

[a] TRRP standard default, 30 TAC 350.74(a) [11]
[b] PHAGM standard default, child 1-6 years old [12]
[c] proposed action level [5]
[d] site-specific study [4]
[e] 1/Particulate Emission Factor, EPA RAGS [13]
[f] EFH Table 5-23, weighted average, child 1-6 years old [14]
[g] TRRP standard default, 30 TAC 350.73(e) [10]
[h] [15]
[i] EFH Table 13-71, total population [14]

Table 3. Summary of non-carcinogenic estimated daily doses for children exposed to vanadium via various pathways. Refer to Table 4 for calculations of estimated exposure doses.

Exposure Pathway	Estimated Daily Dose (mg/kg/day)
Soil Ingestion Exposure Dose	**0.0009**
Inhalation Exposure Dose	0.0000001
Aboveground Vegetables Exposure Dose	0.0001
Belowground Vegetables Exposure Dose	0.00005
Total Daily Dose from all Pathways	**0.001**

Table 4. Non-carcinogenic estimated daily doses for children exposed to vanadium via various pathways.

Exposure Factor	**EF=(F*ED)/AT**
EF=exposure factor (unitless)	0.95890411
F=frequency of exposure (day/year)	350 [a]
ED=exposure duration (year)	6 [b]
AT=averaging time (ED*365 day/year)	2190
Soil Ingestion Exposure Dose	**D=(C*RBAF*IR*EF*CF)/BW**
D=exposure dose (mg/kg/day)	0.0009
C=contaminant concentration (mg/kg)	975 [c]
RBAF=relative bioavailability factor (unitless)	8% [d]
IR=intake rate of soil (mg/day)	200 [b]
EF=exposure factor (unitless)	0.95890411
CF=conversion factor (10^{-6} kg soil/mg soil)	0.000001
BW=body weight (kg)	16 [b]
Inhalation Exposure Dose	**D=(C*SPL*IR*EF)/BW**
D=exposure dose (mg/kg/day)	0.0000001
C=contaminant concentration (mg/kg)	975 [c]
SPL=suspended particulate level (kg/m^3)	2.16E-10 [e]
IR=intake rate (m^3/day)	8.08 [f]
EF=exposure factor (unitless)	0.95890411
BW=body weight (kg)	16 [b]
Aboveground Vegetables	**D=(C*CF*PC*CF*IR*EF*PH)/BW**
D=exposure dose (mg/kg/day)	0.0001
C=contaminant concentration (mg/kg)	975 [c]
CF=conversion factor (10^{-3} kg soil/g soil)	0.001
PC=partition coefficient soil to vegetable (g soil/g dry weight)	0.0036 [g]
CF=conversion factor (g as consumed/g dry weight)	17.4% [h]
IR=intake rate (g as consumed/day)	41.87
EF=exposure factor (unitless)	0.95890411
PH=% of food homegrown (%)	8.2% [i]
BW=body weight (kg)	16 [b]
Belowground Vegetables	**D=(C*CF*PC*CF*IR*EF*PH)/BW**
D=exposure dose (mg/kg/day)	0.00005
C=contaminant concentration (mg/kg)	975 [c]
CF=conversion factor (10^{-3} kg soil/g soil)	0.001
PC=partition coefficient soil to vegetable (g soil/g dry weight)	0.003 [g]
CF=conversion factor (g dry weight/g as consumed)	22.2% [h]
IR=intake rate (g as consumed/day)	29.36
EF=exposure factor (unitless)	0.95890411
PH=% of food homegrown (%)	4.3% [i]
BW=body weight (kg)	16 [b]

[a] TRRP standard default, 30 TAC 350.74(a) [11]
[b] PHAGM standard default, child 1-6 years old [12]
[c] proposed action level [5]
[d] site-specific study [4]
[e] 1/Particulate Emission Factor, EPA RAGS [13]
[f] EFH Table 5-23, weighted average, child 1-6 years old [14]
[g] TRRP standard default, 30 TAC 350.73(e) [11]
[h] [15]
[i] EFH Table 13-71, total population [14]

Table 5. Non-carcinogenic estimated daily doses of arsenic resulting from short-term or sporadic pica behavior in children.

2 days out of 365 days	
Exposure Factor	**EF=(F*ED)/AT**
EF=exposure factor (unitless)	0.005479452
F=frequency of exposure (day/year)	2
ED=exposure duration (year)	1
AT=averaging time (ED*365 day/year)	365
Soil Ingestion Exposure Dose	**D=(C*RBAF*IR*EF*CF)/BW**
D=exposure dose (mg/kg/day)	0.00004
C=contaminant concentration (mg/kg)	155 [c]
RBAF=relative bioavailability factor (unitless)	15% [d]
IR=intake rate of soil (mg/day)	5000 [j]
EF=exposure factor (unitless)	0.005479452
CF=conversion factor (10^{-6} kg soil/mg soil)	0.000001
BW=body weight (kg)	16 [b]

2 days out of 14 days	
Exposure Factor	**EF=(F*ED)/AT**
EF=exposure factor (unitless)	0.142857143
F=frequency of exposure (day/year)	2
ED=exposure duration (year)	1
AT=averaging time (day)	14
Soil Ingestion Exposure Dose	**D=(C*RBAF*IR*EF*CF)/BW**
D=exposure dose (mg/kg/day)	0.001
C=contaminant concentration (mg/kg)	155 [c]
RBAF=relative bioavailability factor (unitless)	15% [d]
IR=intake rate of soil (mg/day)	5000 [j]
EF=exposure factor (unitless)	0.142857143
CF=conversion factor (10^{-6} kg soil/mg soil)	0.000001
BW=body weight (kg)	16 [b]

14 days out of 14 days	
Exposure Factor	**EF=(F*ED)/AT**
EF=exposure factor (unitless)	1
F=frequency of exposure (day/year)	14
ED=exposure duration (year)	1
AT=averaging time (day)	14
Soil Ingestion Exposure Dose	**D=(C*RBAF*IR*EF*CF)/BW**
D=exposure dose (mg/kg/day)	0.007
C=contaminant concentration (mg/kg)	155 [c]
RBAF=relative bioavailability factor (unitless)	15% [d]
IR=intake rate of soil (mg/day)	5000 [j]
EF=exposure factor (unitless)	1
CF=conversion factor (10^{-6} kg soil/mg soil)	0.000001
BW=body weight (kg)	16 [b]

[b] PHAGM standard default, child 1-6 years old [12]
[c] proposed action level [5]
[d] site-specific study [4]
[j] PHAGM standard default, pica child, acute exposure situations [12]

Table 6. Non-carcinogenic estimated daily doses of vanadium resulting from short-term or sporadic pica behavior in children.

2 days out of 365 days	
Exposure Factor	**EF=(F*ED)/AT**
EF=exposure factor (unitless)	0.005479452
F=frequency of exposure (day/year)	2
ED=exposure duration (year)	1
AT=averaging time (ED*365 day/year)	365
Soil Ingestion Exposure Dose	**D=(C*RBAF*IR*EF*CF)/BW**
D=exposure dose (mg/kg/day)	0.0001
C=contaminant concentration (mg/kg)	975 [c]
RBAF=relative bioavailability factor (unitless)	8% [d]
IR=intake rate of soil (mg/day)	5000 [j]
EF=exposure factor (unitless)	0.005479452
CF=conversion factor (10^{-6} kg soil/mg soil)	0.000001
BW=body weight (kg)	16 [b]

2 days out of 14 days	
Exposure Factor	**EF=(F*ED)/AT**
EF=exposure factor (unitless)	0.142857143
F=frequency of exposure (day/year)	2
ED=exposure duration (year)	1
AT=averaging time (day)	14
Soil Ingestion Exposure Dose	**D=(C*RBAF*IR*EF*CF)/BW**
D=exposure dose (mg/kg/day)	0.003
C=contaminant concentration (mg/kg)	975 [c]
RBAF=relative bioavailability factor (unitless)	8% [d]
IR=intake rate of soil (mg/day)	5000 [j]
EF=exposure factor (unitless)	0.142857143
CF=conversion factor (10^{-6} kg soil/mg soil)	0.000001
BW=body weight (kg)	16 [b]

14 days out of 14 days	
Exposure Factor	**EF=(F*ED)/AT**
EF=exposure factor (unitless)	1
F=frequency of exposure (day/year)	14
ED=exposure duration (year)	1
AT=averaging time (day)	14
Soil Ingestion Exposure Dose	**D=(C*RBAF*IR*EF*CF)/BW**
D=exposure dose (mg/kg/day)	0.02
C=contaminant concentration (mg/kg)	975 [c]
RBAF=relative bioavailability factor (unitless)	8% [d]
IR=intake rate of soil (mg/day)	5000 [j]
EF=exposure factor (unitless)	1
CF=conversion factor (10^{-6} kg soil/mg soil)	0.000001
BW=body weight (kg)	16 [b]

[b] PHAGM standard default, child 1-6 years old [12]
[c] proposed action level [5]
[d] site-specific study [4]
[j] PHAGM standard default, pica child, acute exposure situations [12]

Table 7. Summary of estimated lifetime excess cancer risk from exposure to arsenic via various pathways. Refer to Table 8 for calculations of cancer risk.

Exposure Pathway	Estimated Cancer Risk
Soil Ingestion Cancer Risk	**2.0E-05**
Inhalation Cancer Risk	5.9E-08
Aboveground Vegetables Cancer Risk	2.1E-05
Belowground Vegetables Cancer Risk	7.8E-06
Total Cancer Risk from all pathways	**5.0E-05**

Table 8. Estimated lifetime excess cancer risk from exposure to arsenic via various pathways.

Exposure Factor	**EF=(F*ED)/AT**
EF=exposure factor (unitless)	0.410958904
F=frequency of exposure (day/year)	350 [k]
ED=exposure duration (year)	30 [k]
AT=averaging time (ED*365 day/year)	25550
Soil Ingestion Cancer Risk	**CR=((C*RBAF*IR*EF*CF)/BW)*CSF**
CR=excess lifetime cancer risk (unitless)	2.0E-05
C=contaminant concentration (mg/kg)	155 [c]
RBAF=relative bioavailability factor (unitless)	15% [d]
IR=intake rate of soil (mg/day)	100 [l]
EF=exposure factor (unitless)	0.410958904
CF=conversion factor (10^{-6} kg soil/mg soil)	0.000001
BW=body weight (kg)	70 [l]
CSF=cancer slope factor $(mg/kg/day)^{-1}$	1.5
Inhalation Cancer Risk	**CR=(C*SPL*IUR*CF*EF)**
CR=excess lifetime cancer risk (unitless)	5.9E-08
C=contaminant concentration (mg/kg)	155 [c]
SPL=suspended particulate level (kg/m^3)	2.16E-10 [e]
IUR=inhalation unit risk $(ug/m3)^{-1}$	0.0043
CF=conversion factor (10^3 ug arsenic/mg arsenic)	1000
EF=exposure factor (unitless)	0.410958904
Aboveground Vegetables	**CR=((C*CF*PC*CF*IR*EF*PH)/BW)*CSF**
CR=excess lifetime cancer risk (unitless)	2.1E-05
C=contaminant concentration (mg/kg)	155 [c]
CF=conversion factor (10^{-3} kg soil/g soil)	0.001
PC=partition coefficient soil to vegetable (g soil/g dry weight)	0.01 [g]
CF=conversion factor (g dry weight/g as consumed)	17.4% [h]
IR=intake rate (g as consumed/day)	109.32
EF=exposure factor (unitless)	0.410958904
PH=% of food homegrown (%)	8.2% [i]
BW=body weight (kg)	70 [l]
CSF=cancer slope factor $(mg/kg/day)^{-1}$	1.5
Belowground Vegetables	**CR=((C*CF*PC*CF*IR*EF*PH)/BW)*CSF**
CR=excess lifetime cancer risk (unitless)	7.8E-06
C=contaminant concentration (mg/kg)	155 [c]
CF=conversion factor (10^{-3} kg soil/g soil)	0.001
PC=partition coefficient soil to vegetable (g soil/g dry weight)	0.008 [g]
CF=conversion factor (g dry weight/g as consumed)	22.2% [h]
IR=intake rate (g as consumed/day)	74.7
EF=exposure factor (unitless)	0.410958904
PH=% of food homegrown (%)	4.3% [i]
BW=body weight (kg)	70 [l]
CSF=cancer slope factor $(mg/kg/day)^{-1}$	1.5

[c] proposed action level [5]
[d] site-specific study [4]
[e] 1/Particulate Emission Factor, EPA RAGS [13]
[g] TRRP standard default, 30 TAC 350.73(e) [11]
[h] [15]
[i] EFH Table 13-71, total population [14]
[k] PHAGM standard default, cancer risk [12]
[l] PHAGM standard default, adult [12]

TOXICOLOGICAL SCIENCES 67, 303–310 (2002)
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Measurement of Arsenic Bioavailability in Soil Using a Primate Model

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Received September 28, 2001; accepted January 17, 2002

Several studies have shown limited absorption of arsenic from soils. This has led to increased interest in including measurements of arsenic relative bioavailability from soils in the calculation of risks to human health posed by arsenic-contaminated sites. Most of the information in the literature regarding arsenic bioavailability from soils comes from studies of mining and smelter sites in the western United States. It is unclear whether these observations are relevant to other types of arsenic-contaminated sites. In order to obtain information regarding arsenic bioavailability for other types of sites, relative bioavailability of arsenic from selected soil samples was measured in a primate model. Sodium arsenate was administered to five male *Cebus apella* monkeys by the intravenous and oral routes, and blood, urine, and feces were collected. Pharmacokinetic behavior of arsenic after intravenous administration and the fractions of dose excreted in urine and feces after both intravenous and oral doses were consistent with previous observations in humans. Soil samples from five waste sites in Florida (one from an electrical substation, one from a wood preservative treatment site, two from pesticide sites, and one from a cattle-dip vat site) were dried and sieved. Soil doses were prepared from these samples and administered orally to the monkeys. Relative bioavailability was assessed based on urinary excretion of arsenic following the soil dose compared with excretion following an oral dose of arsenic in solution. Differences in bioavailability were observed for different sites, with relative bioavailability ranging from 10.7 ± 4.9% (mean ± standard deviation) to 24.7 ± 3.2% for the five soil samples. These observations, coupled with data in the literature, suggest limited oral bioavailability of arsenic in soils from a variety of types of arsenic-contaminated sites.

Key Words: arsenic; bioavailability; intestinal absorption; primate model; soil; urinary excretion.

Arsenic is both a naturally occurring substance and a common contaminant at hazardous waste sites in the United States. Mining and manufacturing activities, as well as the use of arsenic-containing pesticides, have resulted in a wide array of types of contaminated sites, including mine tailings, smelter facilities, cattle dip sites, electric substations, wood treatment (chromated copper arsenate) sites, pesticide treatment areas, railroad rights-of-way, golf courses, and dumps. Collectively, these sites number in the tens of thousands or more, and the management of these sites is a significant public health and economic problem.

Arsenic is classified by the U.S. Environmental Protection Agency (U.S. EPA) as a Group A carcinogen; that is, it is known to produce cancer in humans. Workers exposed to arsenic by inhalation have been found to be at increased risk of lung cancer, and a number of studies have indicated that ingestion of inorganic arsenic is associated with increased risk of cancer of the skin, bladder, and lung (Morales *et al.*, 2000; NAS, 1999). The risk of cancer from arsenic is calculated using an estimate of arsenic exposure and an arsenic cancer slope factor. The cancer slope factor for arsenic ingestion developed by the U.S. EPA is based on a study of Taiwanese who were exposed to elevated arsenic concentrations in drinking water (Tseng *et al.*, 1968, 1977). This cancer slope factor is used to estimate cancer risk from arsenic ingestion, not only from drinking water, but also from other environmental media including soils. The cancer risk that results from arsenic ingestion is dependent upon the dose of arsenic that is absorbed. Arsenic in drinking water is in a water-soluble form, and its absorption from the gastrointestinal tract is thought to be extensive. Arsenic contaminants in soils, however, may be incompletely absorbed because they are present in water-insoluble forms or because they interact with other soil constituents. Logically, the diminished absorption of arsenic from soil relative to water should be taken into consideration when evaluating the cancer risk posed by arsenic exposure. The problem lies in determining, for a given situation, the degree of reduction of arsenic absorption.

A number of studies have attempted to measure the relative bioavailability of arsenic from soils compared with water using animal models (Table 1). An important limitation of these studies, from the perspective of regulating arsenic-contaminated sites throughout the United States, is that most involve soil samples from mining and smelter sites. Although the data indicate diminished bioavailability from these soils, generalizing these results to other types of contaminated sites is questionable, as there is reason to suspect that differences in the type of arsenic contamination, as well as perhaps soil type, may influence arsenic bioavailability.

The need for arsenic soil bioavailability information for a broader array of contaminated sites prompted this study. A primate model was used to measure arsenic bioavailability in

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TABLE 1
Literature Reports of Arsenic Relative Bioavailability in Soils

Study	Animal	Soil type	Relative bioavailability
Freeman *et al.*, 1993	Rabbit	Smelter area soils	48%[a]
Lorenzana *et al.*, 1996	Swine	Mining area soil	78%
		Mining area slag	42%
Battelle, 1996	Swine	Mining area slag	ND
Casteel *et al.*, 1997	Swine	Soils and mining area wastes	0–50%[b]
Casteel *et al.*, 2001	Swine	Residential soils	18–45%[c]
Freeman *et al.*, 1995	Monkey	Mining area soils	20%[d]
		Mining area dusts	28%[d]

Note. A few reports in the literature have developed estimates of absolute bioavailability of arsenic from soils (e.g., Ellickson *et al.*, 2001; Groen *et al.*, 1994; Ng *et al.*, 1998). The relative bioavailability of arsenic was not measured in these studies and cannot be reliably inferred from the data. These studies are not included in this table. For all studies listed, relative bioavailability was assessed through comparison with absorption of a dose of sodium arsenate; ND = not detectable.

[a]Average of six observations using differing doses (mg soil/kg body weight) of the soil sample in male and female rabbits.

[b]Two soil samples had relative bioavailability > 90%. The arsenic concentrations in soil in these samples were low, and the authors considered these measurements to be unreliable.

[c]Values shown are best estimates from six soil samples. The 90% confidence intervals for the soil samples with the lowest and highest relative bioavailability values were 15–21% and 38–52%, respectively.

[d]Determined from urinary excretion data.

soil samples from sites with differing sources of arsenic contamination. The *Cebus* monkey was selected for this study because of our extensive experience with this species for gastrointestinal absorption studies and its demonstrated value as a model for humans in preclinical pharmacokinetic studies (Bergeron *et al.*, 1990, 1999, 2000). Since the *Cebus* monkey has not been used previously for arsenic absorption studies, initial experiments were directed to characterizing absorption and excretion of sodium arsenate. The objective of these experiments was to ensure that the absorption and excretion of arsenic in the *Cebus* monkey is sufficiently similar to humans that these monkeys can serve as an effective model for bioavailability studies. Subsequent experiments used urinary excretion data to measure the oral bioavailability of arsenic in five soil samples relative to sodium arsenate in water.

MATERIALS AND METHODS

Animals and animal care. Five adult male *Cebus* (*Cebus apella*) monkeys, 2.5–3.0 kg body weight, were purchased from Osage Regional Primates, Inc. (Osage Beach, MO). Between experiments, they were housed individually in metal cages in a climate-controlled room with a population of other monkeys. During these periods, the animals were fed standard monkey chow. During the experimental period, the animals were transferred to nonmetal metabolic cages in another environmentally controlled room. While in the metabolic cages, the monkeys were fed a low-arsenic liquid diet. The diet consisted of casein, 180 g; sucrose, 194 g; dextrin, 194 g; dextrose, 194 g; fiber (cellulose), 90 g; vitamin mix, 5 g; methionine, 5 g; banana flavor, 2 g; choline chloride, 2 g; cholesterol, 1 g; corn oil, 45 g; coconut oil, 45 g; soy lecithin, 20 g; manganese sulfate, 0.1 g; calcium carbonate, 25.4 g; potassium hydrogen phosphate, 35.8 g; magnesium sulfate, 5.2 g; and deionized water, 1350 ml. Solids and oils for the liquid diet were obtained from Bio-Serv (Frenchtown, NJ); minerals (manganese sulfate, calcium carbonate, potassium dihydrogen phosphate, and magnesium sulfate) were obtained from Fisher Scientific (Norcross, GA). The liquid diet presented to the animals was replaced daily from stocks kept refrigerated for up to 7 days after preparation. The arsenic concentration of each batch of liquid diet was measured as described below and confirmed to be below detection limits (< 1 ppb). The housing conditions, environmental enrichment program, and all procedures involving the animals were approved by the Institutional Animal Care and Use Committee.

Drugs and chemicals. Sodium arsenate heptahydrate was purchased from Sigma Chemical Co. (St. Louis, MO). Telazol was purchased from Fort Dodge Animal Health (Fort Dodge, IA). Atropine for injection (Fugisawa USA, Deerfield, IL), Zofran (GlaxoWellcome, Inc., Research Triangle Park, NC), ketamine (Elkins Simm, Inc., Cherry Hill, NJ), and isoflurane (Abbott Labs, Abbott Park, IL) were obtained through the University of Florida Animal Resources Stores.

Soil samples. Surface soil samples from selected contaminated sites were collected and provided by the Florida Department of Environmental Protection (FDEP). The top six inches of ground were excavated from areas known through previous sampling to contain substantial arsenic contamination (i.e., > 100 mg As/kg soil). Soil samples were either shipped to the laboratory at the University of Florida by commercial carrier or delivered directly by FDEP personnel. They were delivered in 5 × 5 gallon buckets and stored in an air-conditioned room until processing. For processing, the soils were dried for at least 3 days at 30–38°C, sieved through a 2-mm screen, and then thoroughly mixed. A 250-ml aliquot of this soil was retained for future reference, and the remainder was sieved to 250 μm or less using a number 6 screen and pan sieve shaker apparatus (Meinzer Sieve Shaker, Fisher Scientific, Norcross, GA). The 250-μm sieved soil was stored in sealed containers at room temperature until utilized. The total arsenic concentration in an aliquot of the 250-μm sieved soil was measured by the Central Chemistry Laboratory, Florida Department of Environmental Protection (Tallahassee, FL) using EPA Method 6010.

Animal dosing and sampling. At the beginning of each experiment, monkeys were sedated with ketamine (10 mg/kg, im) combined with atropine (0.01 mg/kg, im) and weighed, and a blood sample was taken for standard health assessment. The animals were then transferred to metal-free metabolic cages and fed a low-arsenic liquid diet beginning 48 h prior to the arsenic dose. Each monkey was fasted overnight before dosing, but the liquid diet was restored 6 h after the animal was dosed and returned to its metabolic cage. Feces produced during the 24 h prior to the dose were collected and designated as baseline samples.

For experiments involving oral dosing, the animal was first pretreated with the antiemetic Zofran (0.15 mg/kg, im) and then 30 min later given a dose of the short-term anesthetic Telazol (2 mg/kg, im). While the monkey was sedated, a bladder catheter was inserted, and the contents of the bladder were collected, including a 5-ml rinse with sterile saline. This was designated as the baseline (or "0 time") urine sample. Additionally, a baseline blood sample (2 ml) was taken from the saphenous vein. Blood samples were collected in a 2-ml Vacutainer tube containing 0.2 ml buffered citrate (Becton Dickinson and Company, Rutherford, NJ). A gastric tube was placed, and a measured dose of sodium arsenate solution or soil was introduced into the stomach. Soil doses were administered as a slurry in metal-free, deionized water. Sodium arsenate was administered as a 1.0 mg As/ml solution in deionized water, and the volume was adjusted to provide a dose of 1.0 mg As/kg body weight. The gastric tube was flushed with metal-free, deionized water to ensure complete transfer of the dose to the stomach. Both the gastric tube and bladder catheters were then removed, and the animal was returned to its metabolic cage for 1 h. During this period, the animal was allowed to recover from the sedative. Any urine or feces produced during this period were collected from the metabolic

cage. After removal of urine and feces from the metabolic cage, urine collection surfaces of the cage were rinsed with metal-free water to remove any residual excreted arsenic. Cage rinsate was recovered and analyzed separately from urine and feces. For purposes of assessing arsenic excretion, the arsenic present in cage rinsate was considered to have come from urine produced during the collection interval.

One hour after the oral dose, the animal was again sedated with Telazol and intubated. Anesthesia was maintained using isoflurane gas at 1.5%. An intravenous line was placed in the lower leg, and 100 ml of sterile saline was introduced by slow infusion for hydration. A bladder catheter was placed, again by standard technique, and urine samples were collected initially and every hour for the next 5 h. Blood samples (2 ml in Vacutainers with 0.2 ml buffered citrate) were collected 1, 1.5, 2, 2.5, 3, 4, 5, and 6 h after the dose. While anesthetized, supplemental heat was provided in the form of warm water blankets, and body temperature was closely monitored. At 6 h after the dose, the animal was allowed to regain consciousness and was returned to its metabolic cage, where urine and feces were collected daily over the next 4 days. As part of the collection procedure, the cage was rinsed with metal-free water as described above to ensure complete recovery of arsenic excreted in urine. At the end of the collection period, the monkey was returned to its home cage for a minimum of 2 weeks before another dosing experiment was conducted.

Initially, an experiment was conducted in which the monkeys were administered a single intravenous dose of arsenic (1 mg As [as sodium arsenate] per kg body weight in sterile saline). For this experiment, each monkey was sedated with Telazol and placed under isoflurane anesthesia as described above. Intravenous and urinary catheters were then placed. The bladder was rinsed prior to administration of the intravenous dose. The arsenic dose was introduced through the intravenous line over a period of about 5 min. Blood and urine samples were taken at 30 min and 1, 1.5, 2, and 2.5 h. Two milliliters of blood were taken at each time point, and all urine produced was collected via catheter. After 6 h, the anesthetic was withdrawn, intravenous and bladder catheters were removed, and the animals were returned to their metabolic cages after regaining consciousness. Urine and feces were then collected for 4 days.

Sample preparation. Urine samples were collected in 1-l polycarbonate bottles containing 10 ml of 65% nitric acid and then stored in smaller, sealed polycarbonate bottles at room temperature until processed for analysis. A 1.0-ml aliquot of urine was added to 1.0 ml 65% nitric acid in a 15-ml pressure tube. The tube was sealed, placed in a 140°C oil bath for 3 h to digest, and then allowed to cool. Hydrogen peroxide (0.75 ml of a 30% solution) was then added to the tube, which was placed in a 100°C oil bath for 45–60 min while loosely capped. After cooling, the contents of the tube and five successive washes with metal-free water were transferred to a 5-ml volumetric flask for analysis.

Feces were collected and weighed. Nitric acid (65%) was then added in an amount equal to 10% of the fecal weight, and the samples were homogenized. A 3-g sample of homogenate (actual weight was recorded to the nearest 0.01 g) was added to 20 ml of 65% nitric acid. The mixture was refluxed at 100°C in an extractor for 24–48 h until the entire sample was dissolved. The sample was allowed to cool and 5 ml of hydrogen peroxide (30%) was added. Heat was reapplied, and the mixture was allowed to reflux for 1 h. After cooling, the contents of the flask and five successive washes with metal-free water were transferred to a 50-ml volumetric flask for analysis. Samples of each batch of liquid diet were processed using the same procedure as for feces.

Whole blood was centrifuged just after collection to separate plasma. The plasma layer was stored at −80°C until analyzed. A 0.25-ml aliquot of plasma was added to 1.0 ml of 65% nitric acid in a 15-ml pressure tube. As with the urine assay described above, the sample was digested in a 140°C oil bath for 3 h and allowed to cool. Hydrogen peroxide (0.75 ml) was then added to the acidified plasma, and the mixture was heated at 100°C for 45–60 min. The contents of the tube and five successive washes with metal-free water were transferred to a 5-ml volumetric flask for analysis.

Quantification of arsenic in plasma, urine, and feces. All samples were analyzed with a Perkin-Elmer Model 5000 atomic absorption spectrophotometer using a modification of Method 7060A, Revision A, September 1994. The instrument used was a graphite furnace unit with Zeeman background correction. A sample was placed into the L'vov platform of a graphite tube via an auto sampler. Matrix modifiers and diluents were placed into the graphite tube. For urine samples, the following additions were made to the tube: 20 μl of sample/standard, 5 μl of diluent (6.5% HNO_3), and 10 μl of palladium nitrate working solution (500 ppm). For fecal samples, the additions were as follows: 20 μl of sample/standard, 5 μl of diluent, 10 μl of palladium nitrate working solution, and 5 μl of magnesium nitrate/ascorbic acid solution (0.5%/1.0%). All samples were ashed at 1200–1300°C and atomized at 2200–2300°C. Feces/liquid diet samples required preinjection of the matrix modifiers and ashing to 1200°C. Blanks, duplicates, spikes, and lab control samples were run at a rate of 5%, or minimally one, per batch. The blank was run with all components minus the sample matrix. Metal-free water was added at the same volume as the sample matrix. Spikes were added at 10 ppb for urine and plasma samples and at 20 ppb for feces or food samples. Laboratory control samples were prepared in plasma, urine, or feces samples collected prior to dosing (T_0 time point). Plasma and urine samples had 5 ppb arsenic added; feces samples had 25 ppb added. Spikes and lab control samples were prepared using commercially obtained arsenic standards (SPEX CertiPrep, Inc, Metuchen, NJ).

Standard curves were run at the start of each analytical batch. At least five standards from 2.5 μg/l to 100 μg/l were analyzed for the calibration, requiring a minimal correlation coefficient of 0.995. Samples outside the range were diluted and rerun. The mean detection limit (MDL) for each matrix was determined as the lowest concentration that falls within 2–5 times the calculated MDL (3.14 × standard deviation, $n = 7$).

Derivation of descriptive pharmacokinetic parameters. Nonlinear regression (PCNONLIN, V4.2, Pharsight, Mountain View, CA) was used to estimate the terminal elimination rate constant (β) for disappearance of arsenic from plasma over time. The elimination half-life ($t_{1/2\beta}$) was calculated from $0.693/\beta$. The area under the plasma concentration-versus-time curve (AUC) between time 0 and the last data point was derived using the linear trapezoidal rule. In order to estimate the AUC from time 0 to infinity, the area beyond the last time point in the study was estimated by dividing the last measurable plasma concentration by β. Mean residence time (MRT) was calculated by dividing the first moment of the plasma concentration versus time profile (AUMC) by the AUC. The volume of distribution at steady state (Vd_{ss}) was calculated as Dose × AUMC/$(AUC)^2$. Clearance (Cl) was derived from the Dose/AUC.

Urinary excretion data following intravenous and oral administration of sodium arsenate were used to calculate the absolute bioavailability (F_A) of the oral dose using the following relationship:

$$F_A = \frac{U_{As,oral} \times D_{As,iv}}{U_{As,iv} \times D_{As,oral}}$$

where U refers to the amount of arsenic excreted in urine over the observation period, and D is the dose of arsenic. Urinary excretion data were also used to calculate the relative bioavailability of orally administered arsenic in soil versus sodium arsenate in solution. Relative bioavailability (F_R) was calculated as follows:

$$F_R = \frac{U_{As,soil} \times D_{As,water}}{U_{As,water} \times D_{As,soil}}$$

Statistical analyses. An analysis of variance was used to analyze the relationship between soil sample, animal, and relative bioavailability. Main effects for soil sample and animal were included in the model. Statistical significance was determined if p values were < 0.05. In the case of multiple comparisons for differences in relative bioavailability, 10 comparisons were calculated. Ten comparisons were also calculated for animal effect. To preserve the overall Type I error rate for the entire comparison, the Bonferroni

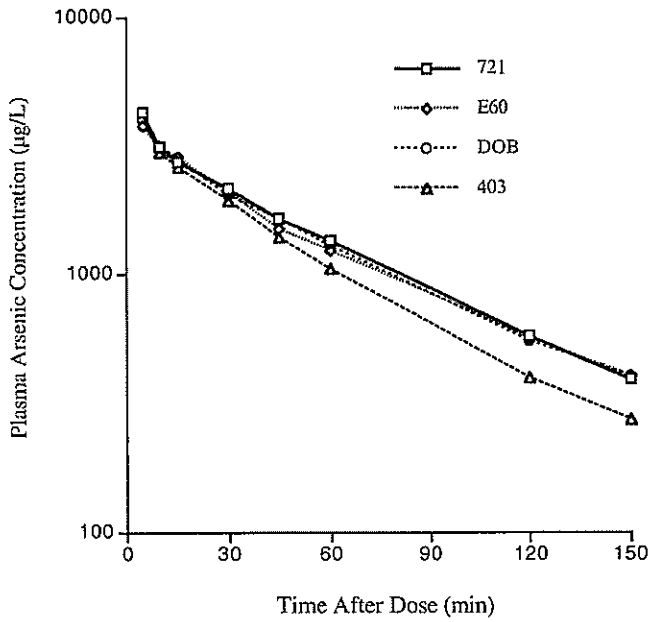

FIG. 1. Plasma concentrations over time after a single intravenous dose of sodium arsenate. Each monkey received a single intravenous dose of sodium arsenate (1 mg As/kg body weight). Plasma concentrations for each animal are shown. Descriptive pharmacokinetic parameters derived from these data are presented in Table 2.

adjustment was used and significance was determined for p values < 0.0005 (resulting in an overall Type I error rate of 0.05).

RESULTS

Blood samples were collected following intravenous administration of arsenic, permitting pharmacokinetic analysis. Intravenous dose data were available for four monkeys.[2] Figure 1 shows the disappearance of arsenic from plasma following the 1 mg As/kg body weight dose. Plasma concentrations were remarkably consistent among the animals, with almost superimposable plasma concentration versus time profiles. Descriptive pharmacokinetic parameters were derived from the plasma concentration data for each monkey and are shown in Table 2. Mean values are also presented.

Urinary and fecal excretion were also measured after the intravenous arsenic dose. Urinary excretion of arsenic was rapid, with nearly half of the arsenic dose appearing in the urine within a few hours after the dose (time course not shown). Collection of urine over 4 days recovered, on average, 66.8% ± 6.5% (± standard deviation) of the arsenic dose. As expected, only a very small fraction of the intravenous arsenic dose appeared in feces over 4 days of collection (0.5–0.6%), indicating little biliary excretion.

Following oral (intragastric) administration of the same dose of sodium arsenate to five monkeys, 48.8 ± 2.3% (mean ± standard deviation) of the dose was recovered in urine within the 4-day collection period. Most of the dose was recovered within the first 24 h after the dose (time course not shown). Consistent with extensive gastrointestinal absorption of sodium arsenate in solution, fecal excretion was low—only 1.9 ± 1.3% of the dose appeared in the feces over the 4-day recovery period. Fecal excretion was, however, generally higher than that observed with intravenous administration, indicating that absorption was not complete. An estimate of the absolute oral bioavailability of sodium arsenate solution in the monkey can be obtained by comparing the urinary excretion (cumulative percent of dose excreted over the collection period) following the oral dose with that obtained in the same animal following administration of the same dose intravenously. From such comparisons, the absolute bioavailability of sodium arsenate solution was found to be 74.4 ± 4.8% (mean ± standard deviation; $n = 4$). Absolute bioavailability could not be calculated for one animal because data for urinary recovery after intravenous administration were not obtained.

Funding was available for measurement of arsenic bioavailability from five soil samples. Each soil sample included in the study was obtained from a different arsenic-contaminated site, and the arsenic concentrations in the samples ranged from 101 to 743 mg/kg. For purposes of assessing relative bioavailability, an attempt was made to use an arsenic dose in soil as close as possible to the comparison dose of sodium arsenate in solution (1 mg As/kg body weight). However, it was also considered important to use soil doses that were not excessive in volume. In order to keep the dose of soil itself to 12 g or less,

TABLE 2
Descriptive Pharmacokinetics after Intravenous Administration of Sodium Arsenate

	Animal ID				
Parameters*	403	721	E60	DOB	Mean
AUC (µg/L-h)	3260	3926	3247	3943	3594
AUMC (µg /L-h²)	3541	4703	5068	5175	4622
Vd_{ss} (L/kg)	0.333	0.305	0.481	0.333	0.363
MRT (h)	1.086	1.198	1.313	1.313	1.228
$t_{1/2\beta}$ (h)	0.935	0.906	1.042	1.071	0.989
Cl (L/kg-hr)	0.307	0.255	0.308	0.254	0.278

Note. A single intravenous dose of sodium arsenate (1 mg As/kg body weight) was administered and blood samples were collected over time. AUC is the area under the plasma concentration versus time curve; AUMC is the first moment of the plasma concentration-time profile; Vd_{ss} is the volume of distribution at steady state; MRT is the mean residence time; $t_{1/2\beta}$ is the terminal elimination half-life; and Cl is the clearance.

[2] One of the original five monkeys purchased for the project was not in good health, and was therefore not included in the study. By the time a replacement animal was obtained, the intravenous dosing portion of the study was completed. Since obtaining intravenous data from each animal was not essential to the objectives of the study, an intravenous-dose experiment was not conducted using this animal.

TABLE 3
Urinary and Fecal Excretion of Arsenic Dose after Oral Administration of Contaminated Soil

Site type	Arsenic conc.	Arsenic dose	Excretion (% of dose)			Relative bioavailability (%)
			Urine	Feces	Total	
Electrical substation	312	0.5	7.1 ± 2.6	51.8 ± 13.0	58.9 ± 11.3	14.6 ± 5.1
Cattle dip site	189	0.5	12.1 ± 1.7	63.8 ± 9.3	75.8 ± 10.4	24.7 ± 3.2
Pesticide site #1	743	1.0	5.2 ± 2.5	72.7 ± 8.5	77.9 ± 8.8	10.7 ± 4.9
Wood treatment site	101	0.3	8.1 ± 2.8	71.9 ± 16.7	80.0 ± 16.8	16.3 ± 6.5
Pesticide site #2	329	0.5	8.4 ± 5.2	68.5 ± 16.0	76.9 ± 14.5	17.0 ± 10.0

Note. Data represent the percent of the arsenic dose in soil recovered in urine and feces over a 4-day period, and are presented as the mean ± standard deviation (n = 5). Relative bioavailability is based on the urinary excretion data. Arsenic conc., mg As/kg soil; arsenic dose, mg As/kg bw.

the arsenic in the soil doses ranged from 0.3 to 1.0 mg As/kg body weight (see Table 3 for the arsenic dose for each soil sample).

Only a small fraction of the dose, generally less than 15%, was recovered in urine when arsenic was administered in soil (Table 3). Consistent with incomplete gastrointestinal absorption, the vast majority of the dose in nearly all cases was eliminated with the feces. The urinary excretion of arsenic from soil was compared with excretion following an oral dose of sodium arsenate in solution to generate relative bioavailability estimates for each soil sample in each animal (Table 3). Mean relative bioavailability values for the five soil samples ranged from 10.7 ± 4.9% (mean ± standard deviation) to 24.7 ± 3.2%. As expected, some variability in relative bioavailability was observed among subjects within each soil-treatment group, and the average coefficient of variation was about 39%. Although the results suggested that some of the animal subjects tended to have higher arsenic bioavailability from soils than others, differences among animals were not statistically significant, as determined through an analysis of variance. Relative bioavailabilities from the highest sample (from the cattle-dip site) and lowest sample (from pesticide site #1) were significantly different from each other. No statistically significant differences in relative bioavailability were detected between other samples.

Few of the blood samples collected after administration of arsenic in soil had concentrations above the minimum quantitation limit. Arsenic could be quantified in only one or two samples per soil per animal (data not shown), making it impossible to calculate a meaningful AUC for bioavailability measurement. Consequently, relative bioavailability was assessed based on urinary excretion only.

DISCUSSION

In developing bioavailability information relevant to human health risk assessment, it is important to assess, to the extent possible, the degree to which absorption and elimination behavior in animal models resembles that in humans. Arsenic administered intravenously to the *Cebus* monkey disappeared rapidly from blood, with an apparent half-life of about 1 h (Fig. 1). This is consistent with the initial, very rapid disappearance of arsenic from blood observed in four human subjects administered an intravenous dose of As^{74} (Mealey *et al.*, 1959). By using a radiolabeled arsenic dose, plasma arsenic concentrations in the human subjects could be followed for 10 days, revealing a much slower rate of disappearance after the first few hours. The terminal elimination rate, which appeared after about 7 days, corresponded to a half-life of approximately 86 h. Collection of urine from these subjects over 9 days recovered 57–90% of the intravenous dose. The urinary recovery of intravenous arsenic in the *Cebus* monkey (66.8% on average) falls within this range. Ducoff *et al.* (1948) administered sodium arsenite intravenously to two subjects and collected urine and feces over the next 7 days. Their recovery of 65.7 and 59.1% of the dose in urine for the two subjects, and 0.9 and 0.5% of the dose from feces, matches quite closely the urinary and fecal recoveries of arsenic in the *Cebus* monkeys (66.8 ± 6.5% of the dose in urine and 0.6 ± 0.1% of the dose in feces). Urinary and fecal recoveries were also consistent with previous observations in other nonhuman primates. Vahter *et al.* (1995) administered arsenic intravenously to two chimps and recovered 52 and 63% of the dose in urine and 1.2% and 1.4% of the dose in feces over 4 days. Another 5.1 and 5.4% of the dose was recovered in cage wash and was presumed to reflect primarily urinary excretion. Freeman *et al.* (1995) administered arsenic intravenously to three cynomolgus monkeys, and recovered 76.5 ± 2.5% of the dose in urine and 3.2 ± 1.9% in feces.

Urinary and fecal excretion of sodium arsenate after oral administration in the *Cebus* monkey was also consistent with previous observations in humans and other primates (Bettley and O'Shea, 1975; Buchet *et al.*, 1981; Crecelius, 1977; Mappes, 1977; Pomroy *et al.*, 1980; Tam *et al.*, 1979). The studies by Bettley and O'Shea (1975) and Pomroy *et al.* (1980) are among the few to present data for both urinary and fecal excretion of arsenic after oral administration in human volunteers. The results for three volunteers reported by Bettley and

O'Shea (52% of the dose excreted in urine and ≤ 3.5% excreted in feces) are nearly identical to those observed here with the *Cebus* monkey. Dose recovery from six subjects was slightly greater in the study of Pomroy *et al.* (1980), with 62.3 ± 4.0% of the dose excreted in urine and 6.1 ± 2.8% of the dose eliminated in feces.

Humans methylate inorganic arsenic to monomethylarsonic acid (MMA) and dimethylarsinic acid (DMA) metabolites, which are excreted in the urine along with unmetabolized inorganic arsenic (Buchet *et al.*, 1981; Crecelius, 1977; Vahter, 1986)). Chimpanzees and marmoset monkeys do not appear to methylate arsenic, although MMA and DMA are formed from hepatic metabolism of arsenate in cynomolgus and rhesus monkeys, both Old World species (Vahter *et al.*, 1995; Zakharyan *et al.*, 1996). The metabolism of arsenic has not been examined in the *Cebus* monkey, which like the marmoset is a New World species. It is possible that the hepatic metabolism of arsenic may be different in *Cebus* monkeys than humans. This would be an important consideration in a metabolism study and also in a study of the toxicity of arsenic. However, the focus of this study is arsenic bioavailability. Given the way in which the relative bioavailability of arsenic is operationally defined and measured, differences in arsenic metabolism, even if they exist, would not be a confounding factor. The bioavailability of arsenic, for risk assessment purposes, is evaluated in terms of total arsenic rather than the appearance in the systemic circulation of any particular form. Bioavailability is consequently independent of metabolism in this situation. To the extent that urinary and fecal excretion of total arsenic are used as means to measure bioavailability, metabolism could affect bioavailability measurement indirectly by influencing excretion. The most straightforward means of assessing this is through comparisons of total arsenic excretion behavior among species. The studies of urinary and fecal excretion of arsenic following intravenous and oral administration of sodium arsenate, described above, strongly suggest that the fundamental absorption and excretion of arsenic are the same in the *Cebus* monkey and humans.

The incomplete recovery of the arsenic dose in urine and feces during the experiment indicated that a substantial fraction of the dose was being retained in the body. Under such circumstances, care must be taken that the chemical does not accumulate to toxic levels with repeated dosing, and that residual chemical in the body does not affect interpretation of absorption data from a subsequent dose. With a 2-week minimum washout period between doses, we did not observe significant residual arsenic in blood, urine, or feces. That is, despite the fact that each monkey had received over time several doses of arsenic, baseline blood, urine, and fecal measurements taken before dosing were consistently below detection levels. This is not surprising. Assuming that the terminal elimination rate in the monkeys is similar to that observed in humans (ca. 86 h, as discussed above), the 3-week minimum collection and washout period allowed six elimination half-lives to pass between doses. Typically, the dosing interval was 1 month or more, corresponding to eight or more half-lives. Under these circumstances, significant accumulation would not be expected.

To minimize stress to the animal subjects, it was necessary to anesthetize them during the period of most frequent blood and urine sample collection. It was also considered important to include in the experimental protocol a period without anesthesia immediately after the dose to allow normal gastric emptying. Extensive preliminary experimentation (not presented in Results) established 1 h as the optimum interval between the dose and the beginning of sampling. When sampling was initiated more than 1 h after the dose, peak blood concentrations and urinary excretion rate were missed, and shorter intervals resulted in reduced recovery of arsenic dose, perhaps due to interference by the anesthetic with normal gastric contractions and emptying. A half-life for gastric emptying of 30 min has been reported for fasted male Red Patas monkeys (Franklin, 1977). If this emptying rate is applicable also to the *Cebus* monkeys in this study, it would suggest that most of the oral dose was emptied from the stomach before induction of anesthesia with the 1-h interval protocol. Perhaps the best argument for the acceptability of this protocol is empirical; that is, that the absorption and excretion of arsenic appear to match closely that observed in unanesthetized human volunteers, as discussed above.

Relative oral bioavailability can be measured using either blood concentration or urinary excretion data, and it was the original intent of this study to use both approaches. However, with the analytical methods employed, it was very difficult to develop an accurate characterization of the blood concentration versus time profile after oral dosing, particularly for arsenic in soils. The amount absorbed was simply too small to produce blood concentrations that could be measured at more than one or two time points. A previous study of arsenic bioavailability from soil in cynomolgus monkeys also measured arsenic in blood and urine, and reported estimates of relative bioavailability based on both approaches (Freeman *et al.*, 1995). However, as we observed with *Cebus* monkeys, blood arsenic concentrations after the soil doses were only marginally above quantitation limits at a few time points. In this situation, the ability to capture the complete arsenic blood concentration versus time profile from the soil dose is compromised, resulting in an underestimation of absorption. This would explain why these investigators obtained a relative bioavailability estimate from blood data that was only about one-half that based on urinary excretion data. For the purposes of assessing arsenic bioavailability from soils, the use of urinary excretion data would appear to be much more reliable, at least in nonhuman primates.

The objective of this study was to begin to generate data on bioavailability of arsenic from soils covering a broader range of types of arsenic-contaminated sites than currently exists in the literature. This study offers some of the first measurements of the relative bioavailability of arsenic in soil at cattle dip,

wood treatment, electrical substation, and pesticide sites. The limitations in generalizing these results are obvious. It would be inappropriate, for example, to use the single value reported here from a wood treatment facility as representative of all wood-treatment sites. There are a variety of factors (e.g., soil characteristics, arsenic formulation, manner of release of arsenic to the soil) that could conceivably affect arsenic soil bioavailability from site to site, and even different areas within a site. This is illustrated well by the recent report (Casteel *et al.*, 2001) of the relative bioavailability of arsenic from five samples of soil contaminated with the arsenical herbicide PAX. All five samples were taken from residential yards at the Vasquez Boulevard and I-70 Superfund site and all were presumably contaminated with arsenic from the same product. The relative arsenic bioavailability among the five samples, as measured in a swine model, ranged from 18 to 45%.

Despite the expectation of some variability in arsenic bioavailability from specific types of sites, the results of this study are nonetheless consistent with the concept that arsenic bioavailability from soils is generally reduced compared with that from water. For the sites included in this study, the extent of reduction ranged from 4- to 10-fold (based on relative bioavailabilities ranging, on average, from about 25 to 10%). Typically, when evaluating risks from arsenic-contaminated soils, the predominant route of arsenic intake is assumed to be through incidental ingestion of soil, and the relative bioavailability of arsenic is assumed to be 100%. That is, the bioavailability of arsenic from soil is assumed to be equivalent to the bioavailability of soluble arsenic in water. Because incidental ingestion is the dominant route of exposure, any adjustment in the oral relative bioavailability from the default 100% assumption will have an essentially proportional effect on the overall dose (and risk) estimate. For example, a relative bioavailability adjustment of 4-fold (i.e., incorporation of a relative bioavailability of 0.25) reduces the estimated risk for a given concentration of arsenic in soil 4-fold. At some sites, a correction of this magnitude in the risk estimate to improve accuracy can have important economic consequences in terms of the resources required for cleanup. Consequently, even though the reduction in relative bioavailability measured in this study and others is not large, usually an order of magnitude or less, its recognition can be of enormous practical value in some situations.

There are uncertainties in the measurement of bioavailability as conducted in this and similar studies that should be acknowledged. One such uncertainty is whether the animal model used in the study serves as a sufficiently valid predictor of human response. We attempted to address this by comparing pharmacokinetic and excretion behavior of sodium arsenate in the *Cebus* monkey with previous studies in human volunteers. Although the results were quite similar, it is always possible that there could be species differences when arsenic is present in a soil matrix. Unfortunately, there are no reliable measurements of arsenic bioavailability from soil samples in human subjects to serve as a basis for comparison, making true validation of animal models difficult. A second uncertainty relates to the possible effect of arsenic concentration in soil on bioavailability. Existing measurements of relative bioavailability of arsenic from soils, including those presented here, use soil samples with arsenic concentrations in the hundreds of ppm. These concentrations are needed to present to the experimental animal an arsenic dose sufficient for detection in a reasonable soil volume. This raises the question of whether bioavailability measurements at these concentrations are predictive of the bioavailability in lesser-contaminated soils (i.e., with arsenic concentrations < 100 ppm.). Conceivably, arsenic bioavailability from soils could be influenced by concentration if critical interactions with soil constituents are capacity-limited, but this issue has not been well studied. In the present study, there was no significant relationship between soil arsenic concentration and bioavailability, but the range of concentrations tested (ca. 100 to 750 mg/kg) was not particularly large. Another area of uncertainty pertains to the feeding status of the animals during bioavailability measurement. In this study, monkeys received a soil dose after an overnight fast. The previous bioavailability study using monkeys (Freeman *et al.*, 1995) and two studies using swine (Battelle, 1996; Lorenzana *et al.*, 1996) also fasted the animals overnight before the dose. Other studies using the swine model (Casteel *et al.*, 1997, 2001) did not fast the animals *per se*, but timed the presentation of food to the animals such that the dose was always given on an empty stomach. Administering the dose on an empty stomach no doubt aids in reducing variability associated with the bioavailability measurements, but probably does not mimic well the circumstances under which humans ingest soil. If the presence of food diminishes the bioavailability of arsenic from soil, as might be expected, then the measurements as conducted in these studies are upper-bound estimates and therefore useful for regulatory purposes. However, this is speculation, and basic information on the effects of food on bioavailability from soils is lacking.

The results presented here extend considerably the types of arsenic-contaminated sites for which quantitative soil bioavailability data are available. As with soils from other types of sites, those investigated in this study showed substantially diminished arsenic bioavailability. The consistency of this observation highlights the importance of explicit, quantitative consideration of bioavailability when assessing the risks from arsenic-contaminated soils.

ACKNOWLEDGMENT

This study was funded by a contract with the Florida Department of Environmental Protection.

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TOXICOLOGICAL SCIENCES 95(1), 281–288 (2007)
doi:10.1093/toxsci/kfl117
Advance Access publication September 27, 2006

Relative Oral Bioavailability of Arsenic from Contaminated Soils Measured in the Cynomolgus Monkey

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Received July 6, 2006; accepted September 18, 2006

A number of studies have found that gastrointestinal absorption of arsenic from soil is limited, indicating that a relative oral bioavailability (RBA) adjustment is warranted when calculating risks from exposure to arsenic-contaminated soil. However, few studies of arsenic bioavailability from soil have been conducted in animal models with phylogenetic similarity to humans, such as nonhuman primates. We report here the results of a study in which the RBA of arsenic in soil from a variety of types of contaminated sites was measured in male cynomolgus monkeys. A single oral dose of each contaminated soil was administered to five adult male cynomolgus monkeys by gavage, and the extent of oral absorption was evaluated through measurement of arsenic recovery in urine and feces. Urinary recovery of arsenic following doses of contaminated soil was compared with urinary recovery following oral administration of sodium arsenate in water in order to determine the RBA of each soil. RBA of arsenic in 14 soil samples from 12 different sites ranged from 0.05 to 0.31 (5–31%), with most RBA values in the 0.1–0.2 (10–20%) range. The RBA values were found to be inversely related to the amount of arsenic present with iron sulfate. No other significant correlations were observed between RBA and arsenic mineralogic phases in the test soils. The lack of clear relationships between arsenic mineralogy and RBA measured *in vivo* suggests that gastrointestinal absorption of arsenic from soil may be more complex than originally thought, and subject to factors other than simple dissolution behavior.

Key Words: arsenic; oral bioavailability; contaminated soil; nonhuman primates.

The use of arsenic as an herbicide and an insecticide, as well as its occurrence naturally in mineral deposits subject to mining, has led to the creation of numerous arsenic-contaminated sites in the United States. When assessing potential risks from arsenic contamination in soil, contemporary models and assumptions generally regard incidental soil ingestion as the dominant route of exposure. The process of estimating arsenic doses resulting from incidental soil ingestion requires an assumption on the extent to which arsenic in soil is absorbed from the gastrointestinal tract. The default assumption typically used in risk assessments is that the extent of gastrointestinal absorption of arsenic from soil is equivalent to its absorption under the conditions in which the toxicity value was derived (NRC, 2003), which in the case of arsenic is from water. Absorption from water is the relevant comparison for arsenic because the cancer slope factor used to estimate excess cancer risks was developed from studies of individuals exposed to arsenic in drinking water. Assuming equivalent absorption is the same as stating that the relative oral bioavailability (RBA) of arsenic from soil (compared to water) is 1.0, or 100%.

A variety of animal models have been used to assess arsenic bioavailability from soil, including rats and rabbits (e.g., Freeman *et al.*, 1993, Ng *et al.*, 1998). However, the principal animal models used to measure arsenic bioavailability from soils are swine and monkeys. The swine model has been used in studies of soils at a variety of contaminated sites in the western United States, principally in mining areas (Casteel *et al.*, 1997, 2001; Lorenzana *et al.*, 1996). The monkey model has been used to measure arsenic bioavailability in soils from a variety of types of sites, including soils from a mining area, electrical substation, cattle dip vat site, a wood treatment site, and pesticide sites (Freeman *et al.*, 1995; Roberts *et al.*, 2002). In general, RBA values for arsenic in soils range from 0 to about 50% in these two models (Roberts *et al.*, 2002; Ruby *et al.*, 1999).

Although the principle of reduced bioavailability of arsenic from soils is well established, understanding of the factors that dictate bioavailability is limited. One of the obstacles in conducting research on factors influencing arsenic bioavailability is the limited number of soil samples available for which bioavailability has been measured. Many of the soil samples for which bioavailability data have been published are no longer available or are inaccessible for research for other reasons. Consequently, there is a need for characterization of additional soils in terms of arsenic bioavailability, not only to support additional research on this topic but also to better define the range of arsenic bioavailabilities that may exist in contaminated soils. For this project, arsenic RBA values for 14 soil samples obtained from 12 different contaminated sites were measured in

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cynomolgus monkeys, expanding considerably the range of sites from which arsenic bioavailability has been measured. Correlations between the RBA of arsenic in soil and soil mineralogy were obtained to provide a preliminary evaluation of potential soil characteristics influencing bioavailability.

MATERIALS AND METHODS

Animals and animal care. Seven young adult male cynomolgus (*Macacus cynomolgus*) monkeys, 4–5 kg bw, were purchased from Primate Products, Inc (Miami, FL). Between experiments, the monkeys were housed individually in metal cages in a climate-controlled room with a population of other monkeys. During these periods, the animals were fed standard monkey chow. The animals were observed daily for normal appearance and behavior, and comprehensive health assessments by a veterinarian were completed every 6 months. During the experimental period, the animals were transferred to nonmetal metabolic cages in another environmentally controlled room. While in the metabolic cages, the monkeys were fed a low-arsenic pelletized diet (Bio-Serv, Frenchtown, NJ). This diet consisted of (g/kg basis): cornstarch, 361 g; casein, 266 g; dextrin, 155 g; oils (corn, olive, and safflower) 96 g; fiber, 52 g; mineral mix, 40 g; vitamin mix, 20 g; DL-methionine, 1.2 g; L-cystine, 2.0 g; choline chloride, 2 g; and banana flavor, 4.0 g. All procedures involving the animals were approved by the Institutional Animal Care and Use Committee.

Drugs and chemicals. Sodium arsenate heptahydrate was purchased from Sigma Chemical Co. (St Louis, MO). Atropine for injection (Fujisawa USA, Deerfield, IL) and ketamine (Elkins Simm, Inc, Cherry Hill, NJ) were purchased from Webster Veterinary Supply (Alachua, FL).

Soil samples. Soil samples were obtained from selected arsenic-contaminated sites. Samples were sought from sites that varied in arsenic contamination source (e.g., wood treatment, herbicide use, mining) and in geographic region. Only samples with arsenic concentration of at least 100 mg As/kg soil were accepted for study. Each soil sample was dried and sieved to 250 μm. This was selected as the particle size fraction believed to adhere to skin and to result in incidental ingestion exposures (U.S. EPA, 2000). Use of this particle size fraction is also consistent with other research regarding the RBA of metals from soils (Casteel *et al.*, 2001; Ruby *et al.*, 2002; Schroder *et al.*, 2003), and existing and proposed guidance (Kelly *et al.*, 2002; U.S. EPA, 2004). The 250-μm sieved soil was stored in sealed containers at room temperature until utilized. The total arsenic concentration in an aliquot of the 250-μm sieved soil was measured using EPA Method 6010.

Animal dosing and sampling. At the beginning of each experiment, monkeys were fed a low-arsenic diet beginning 5 days prior to the arsenic dose. Three days after initiating the diet, the animals were sedated with ketamine (10 mg/kg bw, im) combined with atropine (0.01 mg/kg bw, im), a health assessment was performed, and the animals were weighed. (Note that atropine was administered to reduce intraoral secretions produced by ketamine. Although atropine can suppress gastrointestinal motility, its potential impact on measurement of arsenic absorption was considered negligible because it was administered 2 days before the arsenic dose.) The animals were then transferred to metal-free metabolic cages where urine was collected for baseline arsenic levels prior to dose. Each monkey was fasted overnight before dosing, but the low-arsenic diet was restored 4 h after the animal was dosed and continued while the animal remained in the metabolism cage.

Dosing was accomplished by transferring the animal with the use of a pole and collar arrangement to a chair designed to comfortably restrain the animal so that its hands could not contact its mouth. A gastric tube consisting of a 40 cm length of 3/16″ ID × ¼″ OD Tygon tubing was placed, and a measured dose of sodium arsenate solution or soil was introduced into the stomach. Soil doses were administered as a slurry in metal-free, deionized water from a 60 ml irrigating syringe attached to the gastric tube. The mass of soil administered did not exceed 1 g per kg bw. Sodium arsenate was administered from a 1.0 mg As/ml stock solution in deionized water, and the volume was adjusted to provide a dose no greater than 1.0 mg As/kg bw. The syringe and gastric tube were flushed twice with metal-free, deionized water to ensure complete transfer of the dose to the stomach. After dosing, the tube was removed, and the animal allowed to ingest a few drops of flavored Gatorade to overcome any unpleasant taste from the gastric intubation. The animal was then walked via pole and collar back to its metabolism cage. Urine and feces were subsequently collected for 4 days. After collection of urine and feces was complete, each animal was returned to its home cage for a period of at least 3 weeks before the next dosing period. This "wash out" period allowed urinary and fecal arsenic concentrations to return to baseline levels. Evaluation of predosing urine samples collected over the course of the study confirmed no carryover of arsenic from one dose to the next under these conditions. Typical baseline concentrations of arsenic in urine were about 6 μg/l.

In one experiment, each animal was administered iv a single dose of sodium arsenate (1 mg As, as sodium arsenate, per kg bw in sterile saline). Animals were placed in a metal-free metabolism cage and fed a low-arsenic diet as detailed above. At the time of dosing, an iv line was placed in the leg via the saphenous vein. The arsenic dose was introduced through the iv line over a period of about 5 min. The animal was returned to the metabolism cage where urine and feces were collected as described for the gavage experiments.

Sample preparation. Urine samples were collected in 1-l polycarbonate bottles containing 10 ml of 65% nitric acid and then stored at room temperature until processing for analysis. For collection of urine, the metabolic cage was brushed and rinsed with 800 ml of deionized water. Preliminary studies were conducted in which monkeys were placed in the metabolism cage and arsenic-spiked blank urine was added beneath the animal. All conditions were the same as a standard experiment except no arsenic dose was administered. The cage-rinsing procedure was found to recover 87.2 ± 2.3% (mean ± SD, $n = 3$) of arsenic added to the cage. Feces samples were collected in tared 7 × 7 cm polypropylene cups (Nalge Co., Rochester, NY). Nitric acid (65%) was added at 30% of the feces weight, and the feces were homogenized. One gram of sample (urine or feces) was placed in a digestion vessel, and 5 ml of concentrated nitric acid was added. The sample was then heated on a digestion block for at least 2 h at 100°C. If the sample was still dark in color after 2 h, the sample was heated for an additional 30 min. One milliliter of 30% hydrogen peroxide was added, and the sample was heated for 30 min. The samples were clear and completely dissolved. The digested samples were then diluted to 100 ml with deionized water.

Quantification of arsenic in urine and feces. Baseline urine samples were analyzed by inductively coupled plasma-mass spectrometry by the Battelle Pacific Northwest Laboratory (Richland, WA). The limit of quantification for arsenic in urine was 0.3 μg/l. Urine samples collected after the dose, and all fecal samples, were analyzed by inductively coupled plasma-atomic emission spectrometry by ABC Laboratories (Gainesville, FL). The limits of quantification for urine and feces using this method were 2.3 μg/l and 0.5 μg/g, respectively.

Calculation of bioavailability. RBA of arsenic from each test soil was measured in five individual animals using urinary excretion data. Each animal received, on separate occasions, three doses of sodium arsenate by gavage—0.25, 0.5, and 1.0 mg As/kg bw (as arsenic). Measurement of arsenic in urine over 2 days prior to the dose was used to establish the baseline arsenic excretion rate due to diet for each subject in each experiment. The baseline excretion rate (in μg/day) was used to calculate the contribution of dietary arsenic to total excretion after a sodium arsenate or soil dose, and this was subtracted in order to obtain the amount excreted in urine attributable to the dose (U_{As}). The percent of arsenic dose recovered in urine ($U_{As,arsenate}/Dose_{As,arsenate}$) following each of the sodium arsenate doses was averaged for each animal. This average recovery, as a percent of dose, was used as the reference value for comparison with urinary recovery following administration of arsenic in soil.

The use of urinary recovery of arsenic as a means of comparing absorption of arsenic under different conditions (in this case, administered in water vs. soil) is valid only if the urinary excretion kinetics are identical or the urinary excretion of dose is substantially complete within the collection period.

In a previous study using Cebus monkeys (Roberts *et al.*, 2002), urinary excretion was evaluated during discrete intervals over a 4-day period after administration of sodium arsenate in water or arsenic-contaminated soil. Nearly half of the administered dose appeared in the urine within a few hours, and most of the recovered dose was collected in the first 24 h. An arsenic study in cynomolgus monkeys (Freeman *et al.*, 1995) similarly found peak excretion of arsenic within the first 24 h regardless of whether the arsenic was in water or soil. In view of these observations, a single 4-day collection of urine was considered adequate to provide comparable and essentially complete recovery of absorbed arsenic from both water and soil in this study.

For each soil sample, five animals were randomly selected, and a dose of the test soil was administered by gavage. An RBA was calculated for each subject by dividing the percent of arsenic dose in soil recovered in urine ($U_{As,soil}/Dose_{As,soil}$) by the sodium arsenate reference value for that animal. Thus, an RBA measurement was available for each of the five subjects for all the soil samples tested. Occasionally, the total arsenic recovery was less than 70% after a soil dose in a subject. When this occurred, the RBA value was flagged and the soil sample was re-administered. In all such instances, total recovery from the subsequent dose was greater than 70%, and the resultant RBA replaced the original, low-recovery value.

Soil mineralogy. Arsenic speciation on a subsample of all substrates dosed to the monkeys was evaluated by Dr John Drexler at the Laboratory for Environmental and Geological Studies at the University of Colorado, Boulder. Speciation was conducted as described previously (Davis *et al.*, 1993) using standard procedures (Drexler, 2006). The chemistry of individual arsenic-bearing grains in the sample was determined using an electron microprobe (JEOL 8600). Individual grains were evaluated until a representative number had been analyzed (generally 100–200), and the distribution of arsenic among the different arsenic forms in the soil was established.

Statistical analysis. The percentages of arsenic dose recovered in urine and feces after differing doses of sodium arsenate were compared by both parametric and nonparametric tests. A randomized complete block design ANOVA-based *F*-test was conducted, along with a test for linear trend in dose and checking the residuals for normality (Neterm *et al.*, 1989). Data were also evaluated using a nonparametric, distribution-free test for ordered alternative in a randomized complete block design (Page, 1963).

Mineralogy data were evaluated to determine whether they were useful in predicting oral RBA as measured in the cynomolgus monkey. Both backward and forward stepwise analysis evaluated the best fitting model of each size, i.e., including one variable up to including all 10 variables, based on the smallest residual sum of squares. The 10 variables used in the analysis were iron oxides, number of particles counted, arsenic concentration, iron sulfate, lead arsenate, manganese oxides, arsenic (metals) oxide, iron arsenic oxides, lead (metal) oxide, and phosphate. Analysis of the stepwise models resulted in a final model that included only variables significant at a 0.05 level.

RESULTS

To provide perspective on the recovery of arsenic in urine and feces expected following systemic absorption, each monkey in the study population was administered a single iv dose of sodium arsenate (1.0 mg As/kg bw). Urine and feces were collected over a 4-day period following the dose. Among the seven animals, urinary recovery of arsenic ranged from approximately 80 to 90%, with the exception of one subject from which only 53% was recovered (Table 1). Recovery of dose from feces was uniformly low (0.6% or less). Because of the striking difference in urinary recovery of arsenic in one animal, the iv dose was repeated in this subject. The second experiment yielded almost identical results—urinary recovery of 59% and fecal recovery of 0.5%.

TABLE 1
Urinary and Fecal Recovery of Arsenic after an iv Dose

Subject	% dose in urine	% dose in feces	% total recovery
7490	83.8	0.6	84.4
7630	84.9	0.4	85.3
7773	90.1	0.5	90.6
7597	86.4	0.1	86.5
7516	53.4[a]	0.3[a]	53.7
7499	80.4	0.5	81.0
7515	78.9	0.1	79.0
Mean ± SD	80.5 ± 10.2	0.4 ± 0.2	80.9 ± 10.2

Note. Each animal received a single iv dose of sodium arsenate (1 mg As/kg bw). The results reflect cumulative excretion in urine and feces over 4 days, expressed as a percent of administered dose.

[a]Months later a second dose was administered iv to this subject. Recovery was 58.9% of the dose in urine and 0.5% of the dose in feces.

Each monkey also received, on separate occasions, three differing doses of sodium arsenate in water by gavage. The arsenic doses were 0.25, 0.50, and 1.0 mg As/kg bw, spanning the range of doses anticipated to occur during dosing of the soil samples. The percent of arsenic dose recovered in urine was substantially lower after gavage administration than after iv injection (Table 2), indicating incomplete oral absorption of arsenic from the oral dose in water. Excretion of arsenic in feces in gavage-treated animals was correspondingly higher, and the total arsenic recovery (urine and feces combined) was essentially equivalent for the oral and iv routes. Although there was a tendency for the percent of arsenic recovered in urine to increase with increasing dose (Table 2), the differences in recovery among doses and the trend were not statistically significant. Consequently, the urinary recovery was treated as being unrelated to dose, and the recoveries from the three doses for each animal were averaged. To preserve for analysis potential differences in bioavailability among different experiment subjects, separate recoveries from sodium arsenate were calculated for each animal.

TABLE 2
Urinary and Fecal Recovery of Arsenic after a Gavage Dose of Sodium Arsenate

	Sodium arsenate dose (as As)			
	0.25 mg As/kg bw	0.50 mg As/kg bw	1.0 mg As/kg bw	Mean ± SD
% dose in urine	35.6 ± 8.6	40.9 ± 6.0	45.3 ± 16.7	40.6 ± 10.1
% dose in feces	45.9 ± 12.3	40.0 ± 9.2	40.5 ± 8.9	42.1 ± 9.1
% total recovery	79.5 ± 5.1	80.9 ± 9.0	81.5 ± 6.2	80.7 ± 4.2

Note. Each animal ($n = 7$) received, on separate experimental days, single doses of 0.25, 0.50, and 1.0 mg As/kg bw by gavage. The results reflect cumulative excretion in urine and feces over 4 days after the dose. There was no significant difference in the % of dose recovered in urine from the three sodium arsenate doses, nor was there a significant trend.

TABLE 3
Soil Arsenic Mineralogy Data—Arsenic Mass Distribution (%)

	MTSS	WISS	FLCDV	CAMT	WAOS	NYOS	COSCS	CORS	COSS	FLCPS	NYPF1	NYPF2	NYPF3	HIVS
As bromide	—	—	—	—	—	—	35.8	—	—	—	—	—	—	—
Arsenopyrite	—	—	—	70.4	—	—	—	—	—	—	—	—	—	—
Arsenic oxide (As_2O_3)	—	—	—	—	—	—	—	87.3	—	—	—	—	—	—
As (metals) oxide	6.4	—	—	—	—	—	30.0	0.2	—	—	—	—	—	—
As (metals) sulfate	—	7.5	—	—	—	—	—	—	—	—	—	—	—	—
Calcium arsenate ($CaAsO_4$)	—	—	—	—	—	—	—	—	—	—	—	—	1.7	—
Clay	—	—	85.5	—	—	—	—	—	—	—	—	—	—	—
Iron aluminum silicate	—	—	—	—	—	—	—	—	—	—	—	—	—	71.8
Fe As oxides (AsFeOOH)	12.3	10.6	—	—	—	—	3.0	—	—	—	—	—	54.5	
Iron oxides (FeOOH)	55.9	3.5	14.4	27.2	1.3	6.9	1.5	1.7	22.2	35.2	100	99.9 (37.5)	32.1	22.9
Iron sulfate ($FeSO_4$)	23.1	9.3	—	2.3	—	—	1.4	0.1	76.7	64.8	—	—	0.5	—
Lead arsenate ($PbAsO_4$)	—	66.4	—	—	98.6	37.2	24.7	10.3	—	—	—	—	8.1	2.3
Lead (metal) oxide	—	2.5	—	—	—	1.4	3.3	—	—	—	—	—	—	—
Manganese oxides (MnOOH)	0.4	—	—	—	0.04	54.5	—	0.3	—	—	—	0.1 (8.8)	3.0	3.0
Phosphate	—	0.02	—	—	—	—	—	0.2	—	—	—	—	0.1	—
Pyrite	—	0.3	—	—	—	—	—	—	—	—	—	—	—	—
Slag	1.9	—	—	—	—	—	—	—	—	—	—	—	—	—
Zinc (metal) oxide	—	0.1	—	—	—	—	—	—	—	—	—	—	—	—
No. of particles counted	130	130	147	109	215	112	105	163	183	153	88	104	118	132
Arsenic concentration (mg As/kg soil)	650	1412	189	300	301	125	394	1230	1492	268	339	546	1000	724

Note. Soil ID: CAMT, California mine tailings; WAOS, Washington orchard soil; NYOS, New York orchard soil; COSCS, Colorado smelter composite soil; COSS, Colorado smelter soil; FLCPS, Florida chemical plant soil; NYPF, New York Pesticide Facility soil; HIVS, Hawaiian volcanic soil.

From these, a measurement of RBA for each soil sample in each experimental subject could be made.

Samples of arsenic-contaminated soil were obtained from 12 different sites. As described in the "Materials and Methods" section, all soils were sieved to remove constituents greater than 250 μm. Total arsenic content was measured for each sample, and concentrations ranged from 125 to 1492 mg As/kg soil (Table 3). Each soil sample was administered to five randomly selected experimental subjects by gavage, and urine and feces were collected for 4 days (Table 4). For 11 out of 14 soil samples, the arsenic dose administered to the monkeys was within the range of doses used to establish absorption of sodium arsenate in water (i.e., 0.25–1.0 mg As/kg bw). For two soil samples with the lowest arsenic content, arsenic doses of 0.18 and 0.12 mg As/kg bw were administered in order to keep the total mass of the soil dose within protocol limits of ≤ 1 g soil/kg bw. The administered arsenic dose for the soil sample with the highest arsenic concentration was 1.33 mg As/kg bw. The percentages of the arsenic dose excreted in urine from soil doses were generally much less than observed after gavage doses of sodium arsenate in water, while recovery of the dose in feces was higher. This is consistent with reduced gastrointestinal absorption of the arsenic from soil relative to water. Total recovery of arsenic following the soil doses was similar to, and some instances higher than, total recovery of arsenic after gavage with sodium arsenate in water (Tables 2 and 4).

The RBA of arsenic in the soil sample was calculated for each subject. Mean (± SD) values obtained for each soil are presented in Table 4. The mean RBA values for the 14 soil samples varied from 0.05 to 0.31 (i.e., 5–31%). The coefficients of variation (COVs) were less than about 50%, except for the soil with the lowest RBA, which had a COV of 81% (Note that the RBA for this soil sample ranged from 0 to 11%). Results were calculated with and without inclusion of Subject #7516, which had unusually low-arsenic excretion after an iv dose (Table 1). Surprisingly, there was no apparent difference in the excretion of arsenic in urine between this subject and others after oral doses of sodium arsenate in water- or arsenic-contaminated soil. Consequently, data from this subject were included when calculating the RBA estimates for soils.

Because the RBA values for the various soil samples tested were all relatively low, an additional experiment was conducted to verify that the monkey model is in fact capable of measuring oral bioavailability over a wide range. For this experiment, a high bioavailability soil was created artificially by spiking a naturally low arsenic–content soil (3.6 mg As/kg soil) with sodium arsenate 3 h before the dose. The spiked soil was administered to seven animals by gavage in the same manner as the test soils. For the opposite extreme in bioavailability, six subjects were given a dose of soil spiked with arsenopyrite. In arsenopyrite, the arsenic is bound tightly and oral bioavailability is expected to be very low (Ruby *et al.*, 1999). RBA measurements from both types of spiked soil samples are shown in

TABLE 4
Relative Bioavailability (RBA) of Arsenic from Contaminated Soils

Soil sample	Arsenic dose (mg As/kg bw)	% dose in urine	% dose in feces	% total recovery	RBA
MTSS	0.65	5.2 ± 1.6	89.9 ± 11.6	95.1 ± 11.1	0.13 ± 0.05
WISS	1.33	5.1 ± 3.2	81.3 ± 5.5	86.3 ± 3.0	0.13 ± 0.07
FLCDV	0.18	12.4 ± 1.0	64.6 ± 15.6	77.0 ± 15.5	0.31 ± 0.04
CAMT	0.30	7.9 ± 2.0	84.7 ± 9.7	92.7 ± 11.5	0.19 ± 0.02
WAOS	0.30	9.3 ± 2.2	77.1 ± 8.5	86.4 ± 9.5	0.24 ± 0.09
NYOS	0.12	5.8 ± 2.6	76.7 ± 12.5	82.6 ± 13.4	0.15 ± 0.08
COSCS	0.40	6.9 ± 2.7	70.1 ± 9.4	77.0 ± 11.8	0.18 ± 0.06
CORS	1.0	6.5 ± 2.4	71.6 ± 12.4	78.1 ± 11.1	0.17 ± 0.08
COSS	1.0	1.8 ± 1.4	85.9 ± 4.3	87.7 ± 3.7	0.05 ± 0.04
FLCPS	0.34	2.9 ± 1.2	92.9 ± 4.3	95.8 ± 4.5	0.07 ± 0.03
NYPF1	0.99	7.6 ± 2.3	80.9 ± 6.8	88.5 ± 5.0	0.19 ± 0.05
NYPF2	0.30	10.1 ± 2.9	83.1 ± 10.0	93.2 ± 8.7	0.28 ± 0.10
NYPF3	0.49	7.3 ± 2.8	85.1 ± 6.7	92.3 ± 6.7	0.20 ± 0.10
HIVS	0.73	2.0 ± 0.6	73.7 ± 5.3	75.7 ± 5.1	0.05 ± 0.01

Note. Each soil sample was administered by gavage. The results reflect cumulative excretion in urine and feces over 4 days after the dose, and are expressed as the mean ± SD for five animals. The arsenic dose is based on the arsenic concentration in the soil and the soil mass administered. Soil ID: CAMT, California mine tailings; WAOS, Washington orchard soil; NYOS, New York orchard soil; COSCS, Colorado smelter composite soil; COSS, Colorado smelter soil; FLCPS, Florida chemical plant soil; NYPF, New York pesticide facility soil; HIVS, Hawaii volcanic soil.

Table 5. For sodium arsenate–spiked soil, the average RBA was 0.94, while the RBA for arsenopyrite was 0.01 in one subject and < 0.01 in the other animals. These observations suggest that the model is capable of measuring arsenic RBA over the full range of potential values.

Arsenic mass distribution across 18 mineralogic phases was evaluated for each soil fed to the monkeys (Table 3). The results indicated significant heterogeneity in the arsenic phases reflected in the soils. Some soils were dominated by arsenic in a single phase, while for other soils, arsenic was distributed across many mineralogic phases. Stepwise linear regression was used to evaluate the apparent relationship between each of the mineralogic

TABLE 5
Arsenic Recovery and RBA from Spiked Soil Samples

Spiked sample	% dose in urine	% dose in feces	% total recovery	RBA
Sodium arsenate	38.1 ± 7.2	47.01 ± 11.7	85.1 ± 15.4	0.94 ± 0.05
Arsenopyrite	0.08 ± 0.13	101 ± 30.7	101 ± 32.8	0.002 ± 0.003

Note. Each animal received a single gavage dose of soil spiked with sodium arsenate (0.5 mg As in water per kg bw; $n = 7$) or arsenopyrite (1.0 mg As per kg bw; $n = 6$) 3 h before the dose. The results reflect cumulative excretion in urine and feces over 4 days, expressed as a percent of administered dose.

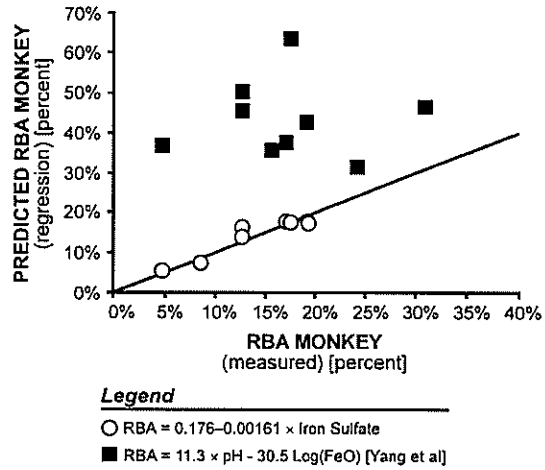

FIG. 1. Relationship between predicted and measured RBA values in cynomolgus monkeys. Open circles represent RBA values predicted based on content of arsenic in iron sulfate as described by the relationship shown. Closed square present RBA values predicted based on soil pH and iron oxide content as per Yang *et al.* (2005).

phases and RBA. In the eight samples for which arsenic was found to be present in iron sulfate, this mineral phase was the best single linear predictor of arsenic RBA ($p < 0.0005$, $R^2 = 0.883$), with RBA inversely related to arsenic present in the iron sulfate phase (Fig. 1). When all 14 samples were included in the regression analysis, the fit of the relationship was reduced ($p < 0.019$, $R^2 = 0.381$), but iron sulfate remained the best single linear predictor of RBA among the mineralogy parameters evaluated. There was no better fitting model using multiple mineralogy variables. Regression against metals, total organic carbon content, and particle size indicated no clear correlation with measured RBA.

DISCUSSION

Several species have been used as experimental models for measurement of arsenic bioavailability from soil. Among these species, the monkey is phylogenetically most similar to humans. The value of the monkey model in predicting gastrointestinal absorption in humans has been clearly demonstrated in pharmaceutical research (Ikegami *et al.*, 2003). For example, Chiou and Buehler (2002) compared the absorbed fraction of an oral dose for 43 drugs evaluated in both monkeys and humans and found excellent correlation with a slope near unity (Fig. 2). Less information is available specific to the comparative absorption of metals or metalloids in nonhuman primates, although O'Flaherty *et al.* (1996) reported that the fractional absorption of lead by cynomolgus monkeys is similar to that in fasted humans. Specifically, they found the rate of 35% absorption of lead in fasted humans (as reported in Rabinowitz *et al.*, 1980) to be comparable to the 22–44% absorption they observed in fasted monkeys.

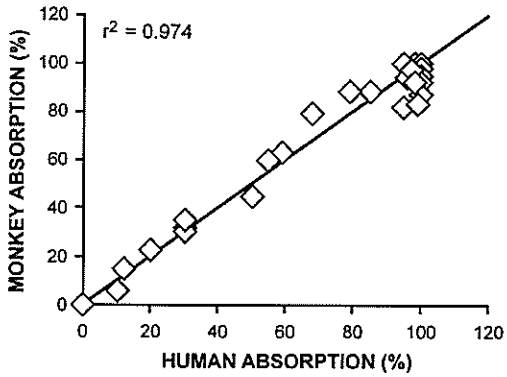

FIG. 2. Correlation of percentage oral dose absorbed between humans and monkeys for 43 drugs with a regression of equation of $F_{aM} = 0.96F_{aH} + 2.8$; $r^2 = 0.974$. Complete absorption demonstrated by 27 drugs in both species. The depicted line has a slope of unity. From Chiou and Buehler (2002).

Two previous studies have used primates to evaluate the RBA of arsenic from soil. A Battelle study measured arsenic RBA from one soil and one house dust sample collected near a Montana smelter site (Freeman *et al.*, 1995). Three female cynomolgus monkeys were used for this study. Another study (Roberts *et al.*, 2002) used five male Cebus monkeys to measure the RBA of arsenic from five soil samples collected from contaminated sites in Florida. Both previous studies measured urinary and fecal excretion of arsenic after iv and oral doses of sodium arsenate. The urinary and fecal recovery of iv administered arsenic in female cynomolgus monkeys in the Battelle study matched closely the recoveries observed in male cynomolgus monkeys reported here. In the Battelle study, 76.5 ± 2.5% (mean ± SD) of the arsenic dose was recovered in urine and 3.2 ± 1.9% was recovered in feces. Similarly, Cebus monkeys in the Florida study excreted 66.8 ± 6.5% of the iv dose in the urine and a very small percentage (0.5–0.6%) in feces.

The percent of arsenic dose recovered in urine following a gavage dose of sodium arsenate was about 40% in cynomolgus monkeys in this study, compared with about 50% in Cebus monkeys in the Florida study and almost 70% on average for cynomolgus monkeys in the Battelle study (Freeman *et al.*, 1995; Roberts *et al.*, 2002). The reason for the substantial difference in urinary excretion following oral sodium arsenate doses, particularly between studies using the same monkey species, is unclear. Total arsenic recoveries were also different, although the margin was smaller (about 80% in this study vs. 95% in the Battelle study), suggesting that at least part of the difference lies in lower gastrointestinal absorption of arsenic in water in monkeys in this study. The difference cannot be explained by dose—the Battelle study used a gavage dose (0.62 mg As/kg bw) in the middle of the range of doses in the study reported here (0.25–1.0 mg As/kg bw). It is also difficult to explain based on experimental protocol. Both studies administered the sodium arsenate dose by gavage tube without anesthesia, followed by recovery of urine and feces in metabolism cages for similar lengths of time (5 days in the Battelle study and 4 days in this study). Cage washes recovered nearly 90% of arsenic in urine (see the "Materials and Methods" section), so underrecovery of arsenic from the metabolism cages can be ruled out. The differences might be due to gender (females in the Battelle study and males in this study). Unfortunately, there are no studies of arsenic bioavailability that have included animals of both sexes to examine this possibility. It is also possible that different cynomolgus monkey strains were used in the two studies with differing gastrointestinal absorption characteristics.

Even though urinary arsenic recoveries following ingestion of sodium arsenate in water vary among studies, each serves as a valid basis for comparison within study for determination of RBA. Among the 14 soil samples tested in this study, the mean RBA values ranged from 0.05 to 0.31 (5–31%). The RBA values obtained from different subjects were variable, and the COV was near 50% for about half of the soil samples. This variability is not surprising. Gastric residence time is likely to be important in extracting arsenic from soil matrices in the low-pH intragastric environment, and gastric-emptying rates can vary substantially from one individual to another. As an example, a recent study found that the gastric half-emptying time in 10 unfed cynomolgus monkeys given a 60-ml liquid dose of acetaminophen (as a gastric-emptying marker) ranged from about 10 min to 4 h (Kondo *et al.*, 2003). Although gastric-emptying times following oral soil doses have not been reported, there is no obvious reason to expect that variability would be substantially less. Based on variability in recoveries following gavage treatment with sodium arsenate doses (Table 2), much of the variability may be intrasubject; that is, reflecting differences in absorption of arsenic on different experimental days. However, it is interesting to note that variability among subjects was small for the cattle dip vat soil (Florida cattle dip vat soil [FLCDV]), and that when previously tested in Cebus monkeys (Roberts *et al.*, 2002), this soil sample also produced relatively low intrasubject variability. This suggests that some attribute of the soil may also influence variability in RBA results among different experimental subjects.

Four soil samples tested in this study were from sites where soil arsenic RBA has been measured using different species or models. As mentioned above, the FLCDV soil sample was also evaluated in a previous study using the Cebus monkey (Roberts *et al.*, 2002) with similar results (RBA of 0.25 ± 0.03 in the Cebus vs. 0.31 ± 0.04 in the cynomolgus monkey here). Three other soil samples (namely, Montana smelter soil [MTSS], Colorado residential soil [CORS], and Western iron slag soil [WISS]) were from sites where arsenic soil bioavailability had been evaluated, but were not the same specific soil samples measured by others. MTSS (RBA 0.13 ± 0.05) was taken from a Montana smelter site where an RBA of 0.20 was measured, also using cynomolgus monkeys (Freeman *et al.*, 1995). CORS came from a site for which arsenic bioavailability had been previously measured in five soil samples using a swine model (Casteel *et al.*, 2001). The RBA values for these five samples ranged from 0.18 to 0.45 (best estimates). The RBA for arsenic in the CORS sample measured here in the monkey was at the

bottom end of this range (0.17 ± 0.08). Arsenic RBA from an iron slag site soil sample (WISS) measured in the cynomolgus monkey (0.13 ± 0.7) was lower than the value reported for another soil sample from the site measured in the swine model (0.29; Rodriguez *et al.*, 1999).

These limited comparisons suggest that the swine model might yield higher estimates of oral bioavailability than the monkey, but definitive conclusions are impossible without data from splits of the same soil sample measured in both models. The swine model uses a somewhat different protocol involving multiple doses of arsenic in soil, but there is no reason to suspect *a priori* that this would lead to higher bioavailability estimates. One important difference between the monkey and swine protocols is the volume of soil administered relative to body weight, with larger volumes administered to the monkey. To test whether this soil volume might interfere with arsenic absorption leading to underestimates of RBA, spiked soil samples were tested in the monkey model. These spiked samples showed high bioavailability from sodium arsenate (Table 5), as would be expected, suggesting that the higher soil volume in the monkey model is not an impediment to arsenic absorption.

Arsenic mineralogy data from the test soils were evaluated to determine whether they might serve as a predictor of RBA measured in the cynomolgus monkey. Arsenic is known to occur in soil as a complex mixture of mineral phases, coprecipitated and sorbed species and dissolved species, and the distribution of arsenic among these phases can control dissolution properties (Davis *et al.*, 1996; Ruby *et al.*, 1999). The distribution of arsenic among these phases may reflect the arsenic source or be altered substantially by weathering, such as association of arsenic with iron oxides within the soil (Cances *et al.*, 2005, Ruby *et al.*, 1999). Measurement of arsenic mass distribution across 18 mineralogic phases revealed significant heterogeneity among the 14 soil samples included in this study. A stepwise linear regression found arsenic present in iron sulfate was the best single linear predictor of arsenic RBA, which is consistent with proposed models of arsenic bioavailability (Ruby *et al.*, 1999). However, this result is the opposite of observations comparing soil mineralogy data with RBA measured in swine reported previously (Basta *et al.*, 2000). In that study, arsenic RBA in four samples (including two different types) of mine-waste soils increased as the percent of total arsenic in the iron sulfate fraction increased.

A number of recent studies have examined the impact of soil chemistry on the dissolution and bioavailability of arsenic. Several of these studies reported that the solubility of arsenic under physiologic conditions is inversely correlated with the soil content of other metals such as iron and aluminum (Fendorf *et al.*, 2004; Sarkar and Datta, 2004; Yang *et al.*, 2002, 2005) and/or directly related to the organic carbon content (Pouschat and Zagury, 2006; Sarkar *et al.*, 2005). With the exception of the importance of arsenic in iron sulfate, RBA measurements in the cynomolgus monkey do not support these findings. For example, Yang *et al.* (2005) have proposed a model for arsenic bioavailability from soil based on pH and extractable iron oxide content. As shown in Figure 1, this model markedly overpredicts RBA in the soils examined here, and was noted in the original report to overpredict RBA values measured previously in Cebus monkeys. Although not consistently biased in one direction, predicted arsenic bioavailability also did not correspond particularly well with RBA values measured for several soils in the swine model (Yang *et al.*, 2005).

There are several potential explanations for the apparent discrepancy between the soil chemistry studies cited above and RBA measured *in vivo*. These include the number of soils studied, soil provenance, the source of arsenic contamination, and the extraction methods used in the soil chemistry studies to approximate bioavailability. Of the six studies, four based their evaluations on two, three, or four discrete soil samples. Pouschat and Zagury evaluated 12 soils, but all were from the same source of contamination—chromated copper arsenate (CCA). Only Yang *et al.* (2002, 2005) evaluated a large diversity of soils. All but one study used soils that had been spiked with arsenic (arsenate or arsenite) and subjected to different aging or weathering regimes. Only the study of Pouschat and Zagury evaluated environmentally contaminated soils and, as noted above, this study was limited to soils affected by CCA. Finally, although some studies purported to correlate soil characteristics with "bioavailability," all the models and proposed relationships in these studies were based on data from *in vitro* extraction methods rather than actual RBA measurements *in vivo*. This suggests that information from contemporary *in vitro* "bioaccessibility" models, even those based on simulated physiological conditions, may not adequately address all the processes that affect absorption of arsenic from soils *in vivo*.

The results reported here expand considerably the number and types of soils for which arsenic bioavailability has been measured using a primate model. This study demonstrates that while the model is capable of measuring RBA values from < 10 to > 90%, results from a variety of types of contaminated sites are consistently low, i.e., about 30% or less. Recognition of the limited bioavailability of arsenic from soils is important in the evaluation of human health risks from arsenic-contaminated sites. RBA values are an important component of risk calculation and the development of risk-based cleanup goals. RBA values from *in vivo* bioavailability studies remain the "gold standard," but there is strong interest in developing more rapid, less expensive means of obtaining RBA information. Previous attempts to develop *in vitro* tools to predict arsenic RBA have met with limited success, and there are no existing *in vitro* models that predict well the RBA observations reported here for an expanded set of arsenic-contaminated soils. In order to develop a satisfactory *in vitro* model, a better understanding of factors that control gastrointestinal absorption of arsenic from soil matrices will be required.

ACKNOWLEDGMENTS

This research was supported in part by a grant from the Strategic Environmental Research and Development Program, U.S. Department of Defense

awarded to Exponent, Inc, Boulder, CO and from the Solubility/Bioavailability Research Consortium. The authors are indebted to Dr Eric Crecelius for measurement of arsenic in baseline urine samples and to Dr John Drexler, University of Colorado, Boulder, CO, for characterization of the mineralogy of soil samples.

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Advances in Evaluating the Oral Bioavailability of Inorganics in Soil for Use in Human Health Risk Assessment

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Cleanup goals for sites affected by inorganic contaminants often are established on the basis of risk assessments, and these assessments rely on the estimated oral toxicity of the substances of concern. These toxicity estimates typically are based on historical studies in which a soluble salt of the metal was dissolved in water or mixed in food and then ingested by an animal or human. However, these toxicity studies do not account for the characteristics of a metal in soil or the limitations that these characteristics place on enteric absorption of that metal. Therefore, a more accurate risk assessment must account for the bioavailability of the metal in site-specific soil, relative to the bioavailability of the metal in the form administered in the toxicity study (i.e., the relative bioavailability of the element in soil). Historically, relative bioavailability estimates for metals in soil have been based on in vivo studies in laboratory animals. Given the costs and time constraints associated with such studies, it is clear that a more efficient alternative is desirable. The most promising option involves the development and validation of in vitro extraction tests that are predictive of oral metals bioavailability from soil. Such tests would provide a rapid and inexpensive method for developing more accurate exposure estimates for use in human health risk assessments. This paper reviews the site-specific in vivo studies that have been conducted to estimate the relative bioavailability of arsenic and lead in soil, discusses the soil and mineralogical factors that influence the bioavailability of these elements, and reviews the research to date on the development of bioavailability-predictive extraction tests for metals in soil. Finally, this paper outlines an ongoing collaborative research project to formally validate an in vitro extraction test for use in estimating the oral bioavailability of arsenic and lead in soil.

Introduction

In this paper, we discuss ongoing research to develop and validate simple extraction tests to estimate the oral bioavailability of metals from soil. Much of our current understanding on this topic derives from in vivo estimates of arsenic and lead bioavailability (i.e., studies in animal models), which have been developed for predicting human exposures to these elements in soil. Given the expense and time constraints associated with in vivo testing, development of accurate and inexpensive extraction tests that are predictive of relative bioavailability provides an opportunity to improve the accuracy of risk assessments in a cost-effective manner. Such tests could be used both for site assessment and for developing and evaluating remedial technologies, like soil washing or soil amendments, that may have an impact on metals bioavailability. Because the extraction tests that have been developed to date can be conducted for a small fraction of the cost of in vivo studies, a sufficient number of samples can be evaluated to fully characterize soils at a site. In the long run, it would be ideal to have simple, bioavailability-predictive extraction tests for all metals of human health concern, so that risk from metals in soil could be assessed based on the site-specific fraction of bioavailable metals.

The focus of this paper is on relative bioavailability after oral exposure, because this route is typically assumed to provide the greatest exposure for metals in soil, and because

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10.1021/es990479z CCC $18.00
Published on Web 09/23/1999
1999 American Chemical Society

this is the exposure route that has been studied most extensively to date. [Although arsenic is technically a metalloid, the term "metal" is used in this paper to refer to the elements arsenic and lead collectively.] The oral toxicity of metals is typically determined on the basis of studies in which a soluble salt of the metal was dissolved in water or mixed with food. If the toxicity values used in risk assessments of metals in soil are based on studies using soluble forms of the metals, the impacts of soil exposures may be overestimated. For metals, reduced absorption from soil may be due to a combination of factors, including the presence of less soluble species of the metal as well as interactions of dissolved metals with soil constituents (e.g., sorption and precipitation reactions). These factors may limit metal dissolution from soil during passage through the gastrointestinal tract. Absorption would then be reduced, because the primary mechanism of absorption for most metals is via passage of dissolved species across the small-intestinal epithelium (*1*). To account for limited dissolution of metals from soil, it may be important to determine the bioavailability of the element in soil, relative to its bioavailability when it is solubilized in water, to derive more accurate exposure estimates.

Because this document addresses issues related to the bioavailability of metals in soil in human health risk assessment, the definition of bioavailability used throughout is the definition commonly used by mammalian toxicologists.

Definitions

Bioavailability. Oral bioavailability is defined as the fraction of an administered dose that reaches the central (blood) compartment from the gastrointestinal tract. Bioavailability defined in this manner is commonly referred to as "absolute bioavailability", and is equal to the oral absorption fraction.

Relative Bioavailability. Relative bioavailability refers to comparative bioavailabilities of different forms of a substance or for different exposure media containing the substance (e.g., bioavailability of a metal from soil relative to its bioavailability from water), expressed in this document as a relative absorption factor (RAF).

Relative Absorption Factor. The RAF describes the ratio of the absorbed fraction of a substance from a particular exposure medium relative to the fraction absorbed from the dosing vehicle used in the toxicity study for that substance (the term relative bioavailability adjustment [RBA] is also used to describe this factor).

Bioaccessibility. The oral bioaccessibility of a substance is the fraction that is soluble in the gastrointestinal environment and is available for absorption. The bioaccessible fraction is not necessarily equal to the RAF (or RBA) but depends on the relation between results from a particular in vitro test system and an appropriate in vivo model.

The following sections (1) discuss the mineralogy and soil factors that influence the extent of lead and arsenic bioavailability, (2) present an overview of the in vivo studies that have been conducted for lead and arsenic in soil, (3) review the in vitro research that has been conducted to date, and (4) discuss some of the ongoing research on validation of in vitro extraction tests for estimating the oral bioavailability of arsenic and lead. This review is limited to arsenic and lead because relative bioavailability studies (e.g., in vivo studies) have been almost exclusively limited to these two elements. However, many of the issues discussed herein are pertinent to other inorganic elements of human health concern (e.g., beryllium, cadmium, chromium, mercury, and nickel), particularly those that exhibit similar geochemical behaviors to arsenic and lead.

Mineralogic and Soil Factors that Control Bioavailability

Lead and arsenic occur in soil as a complex mixture of solid-phase chemical compounds of varying particle size and morphology. These compounds include discrete mineral phases, coprecipitated and sorbed species associated with soil minerals or organic matter, and dissolved species that may be complexed by a variety of organic and inorganic ligands. The occurrence and relative distribution of an element among these various phases, and the physical relation between the phases and the soil, will control an element's dissolution properties and, hence, its bioavailability. The spatial heterogeneity of these complex mixtures in soil will be reflected by variable metal bioavailability from soil at a site.

Changes in the distribution of an element among these various phases over time resulting from physical and chemical weathering, biological processes, the infiltration of water, and anthropogenic disturbances may change the bioavailability of that element. The importance of these changes for human health risk assessment depends on the relative rate and magnitude of the changes in bioavailability. Factors to consider include the relative stability of the compound released to soil, the potential for chemical or physical alteration of this compound, the likely reaction products (based on soil chemistry), and the likelihood of disturbances that may alter soil chemistry. For example, if highly soluble lead acetate is released to soil, lead will rapidly become incorporated in soil minerals, and its bioavailability will decrease over time. In contrast, little change would be expected in the bioavailability of lead dispersed in high-silica smelter slag (due to its relative insolubility), even after this mining waste had remained in the environment for decades. Therefore, the identity of and potential change in elemental speciation (and thus bioavailability) must be considered in predicting human health risk.

Lead. Lead concentrations in naturally occurring surficial soils range from less than 10 to 700 mg/kg (*2*), with an arithmetic mean of 19 mg/kg for soils in the conterminous United States ($n = 1319$ (*3*)). Lead may occur in soils as native pure mineral phases, such as lead sulfide (PbS), lead sulfate ($PbSO_4$), or lead carbonate ($PbCO_3$). Lead sulfide occurs primarily at mining, milling, smelting, and ore-handling sites. At mining and smelting sites, lead minerals may be encapsulated within other soil mineral grains, such as quartz, which limit its bioavailability. In addition, lead minerals are often present within the matrix of smelter slags and other pyrometallurgical waste materials. Lead sulfate and lead carbonate are commonly found as mineral phases in soils; they can occur through inefficient pyrometallurgical processes, but more commonly, they result from precipitation reactions in soils. Formation of lead sulfate is favored in acidic soils, while lead carbonate is favored in alkaline soils (*4*).

All of the lead forms discussed herein exhibit different rates of lead dissolution, depending on their chemistry and particle size distribution, the mechanism by which they dissolve (e.g., surface reaction or transport-controlled dissolution kinetics), and the geochemistry of the soils in which they are present. Figure 1 provides a schematic of the processes that are believed to control the bioavailability of lead in soil. Soil chemistry—including the presence of anionic species that form complexes with lead (e.g., organic acids, soil organic matter [SOM], phosphate, carbonate, sulfides, chloride, and hydroxide), iron and manganese concentrations, soil pH, cation exchange capacity, and redox conditions—determines the extent to which various dissolution, precipitation, complexation, and adsorption reactions occur for lead in a particular soil.

Lead may also be coprecipitated with, or sorbed to, various mineral phases that result from soil weathering. These

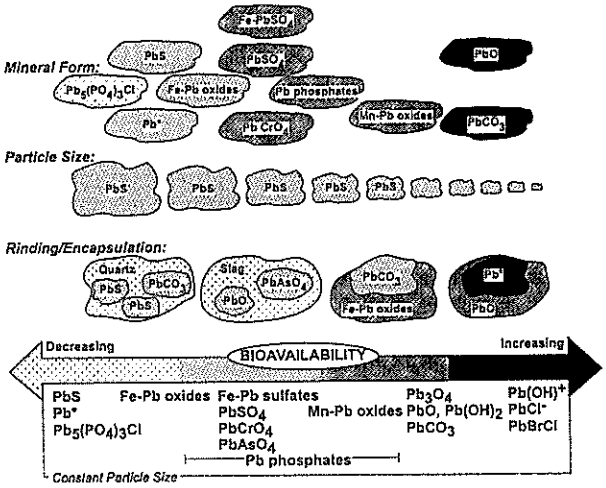

FIGURE 1. Schematic of how different lead species, particle sizes, and morphologies affect lead bioavailability.

minerals—including iron and manganese oxides, iron sulfates, and phosphate minerals—tend to have variable lead compositions and may be found either as discrete mineral particles or as rinds on other soil particles (Figure 1). Mineral phases that form under acidic conditions (e.g., lead sulfate, iron–lead sulfate) will tend to be more stable in the acidic conditions of the stomach and hence less bioaccessible. Mineral phases that form under alkaline conditions (e.g., lead carbonate, lead oxide) will be less stable in the acidic conditions of the stomach and more bioaccessible (Figure 1). The phosphate minerals, in particular, have highly variable compositions (*5*), which result in a wide range of bioaccessibility values. In addition, lead may be present bound to sulfhydryl and carboxyl ligands on SOM, sorbed to clay and other metal oxide (Fe, Al, Mn) mineral surfaces, and as dissolved, complexed ionic species, such as Pb^{2+}, $Pb(OH)^+$, $PbCl^+$, $PbHCO_3^+$, or $Pb(CO_3)_2^{2-}$. Each of these lead species may have a different bioaccessibility, depending on the manner in which it is bound or complexed.

Dissolution rate-controlling processes also are important in determining oral lead bioavailability, because lead must dissolve during the limited transit time in the gastrointestinal tract to become bioaccessible (*6*). Smaller particles have greater ratios of surface area to volume and, hence, are more rapidly solubilized, resulting in greater bioaccessibility and ultimately greater bioavailability (*6–9*). In general, less soluble lead minerals (e.g., lead in calcium phosphates) dissolve by surface-reaction-controlled kinetics, which are limited by surface detachment of ions (*9*). More soluble lead minerals (e.g., lead oxide) dissolve by transport-controlled kinetics, where dissolution ions are detached very rapidly and accumulate to form a saturated solution adjacent to the mineral surface. The dissolution rate thus becomes controlled by the rate of transport of ions away from this saturated layer. The rate-limiting step for dissolution of lead minerals of intermediate solubility (e.g., lead sulfate) is mixed or partial surface-reaction-controlled kinetics (*9*), which contain elements of both the above mechanisms. An understanding of lead mineral dissolution kinetics is important in determining which lead species will contribute to bioavailable lead; the bioavailability of minerals that dissolve through the transport-controlled mechanism is sensitive to the extent of mixing and agitation in the gastrointestinal tract, while the bioavailability of minerals that dissolve through surface-reaction control is sensitive only to transit time.

Soil lead from anthropogenic activities also includes that from paint, gasoline additives, and other commercial products (e.g., lead acid batteries, cable coverings, ammunition, and solder). The most common forms of lead in paint are red lead (Pb_3O_4), which historically was used primarily on painted steel, white lead (also known as basic lead carbonate [$2PbCO_3 \cdot Pb(OH)_2$]), basic lead sulfate ($PbO_2 \cdot PbSO_4$), and lead chromate ($PbCrO_4$ (*10*)). Lead paints were manufactured by drying the lead pigments in sheets, stamping out small (approximately 1–10 μm) particles of the material, and then mixing these particles in a binder material. As a result, as paints weather in soil, they release small particles of lead, which are likely to be highly bioavailable (due to the solubility of lead oxide and carbonate species and the small particle size).

Lead from gasoline used in internal combustion engines (primarily tetraethyl lead) is present as lead halides (e.g., PbBrCl) in fresh exhaust but alters to lead carbonates, oxides, and sulfates due to photochemically induced reactions during atmospheric transport (*11*). As a result, lead from combustion of leaded gasoline is deposited in soils as a mixture of lead halides, carbonates, oxides, and sulfates, which subsequently weather in soil (*11*). When organic lead forms (primarily tetraethyl and tetramethyl lead) are deposited in soils due to gasoline spills, they degrade to inorganic lead with the degradation of the gasoline hydrocarbons (*12*). The resulting lead ions (Pb^{2+}) participate in the soil reactions discussed above.

The lead species present in other commercial products include elemental (native) lead (lead acid batteries, cable coverings, and ammunition), lead sulfate (also present in lead acid batteries), and tin–lead alloys (solder). Elemental lead particles that are deposited in soils quickly form coatings of highly bioavailable lead oxide.

Given the complex and dynamic nature of the soil lead cycle, it is clear that a simple test for estimating lead bioavailability would be useful for quantifying both the extent and rate of change in the bioavailability of lead from soils.

Arsenic. The manner in which arsenic occurs in soils can also be viewed as a complex and evolving mixture. Arsenic concentrations in undisturbed soils range from 0.1 to 97 mg/kg (*2*), with an arithmetic mean concentration of 7.2 mg/kg for surficial soils in the conterminous United States (n = 1257 (*3*)). Arsenic is substantially different from lead, in that it occurs in natural environments in two valence states: arsenic(III) and arsenic(V). Typically, arsenic(III) is present in anoxic conditions, while arsenic(V) is the dominant form of arsenic in oxic soils. Arsenic(III) may occur as uncharged $As(OH)_3$ in acidic soils and as an anion (AsO_3^{3-}) in alkaline soils (*13*). Arsenic(V) is present as an anion ($H_2AsO_4^-$ or $HAsO_4^{2-}$) in the natural pH range of soils (pH 4–8) (*14*). The presence of arsenic as anionic species causes it to be quite mobile in soils when it occurs in a soluble form.

The primary anthropogenic sources of arsenic in the United States include releases from mining and smelting operations, agricultural uses (e.g., pesticides, insecticides, defoliants, feed additives, and livestock dips), tanning operations, wood treatment/preservation operations, and releases as a byproduct of burning coal.

Arsenic, like lead, may occur as sulfide minerals (e.g., arsenopyrite [FeAsS] and enargite [Cu_3AsS_4]) at mining and milling sites. The particle size distribution of the arsenic species discussed herein, in combination with their chemical composition, controls their bioavailability (Figure 2). Arsenic dissolution appears to be particularly sensitive to particle size, especially for certain arsenic mineral phases. In soils, arsenic may be present as the anthropogenic form in which it was deposited (lead and calcium arsenates from pesticides, arsenic pentoxide from herbicides and fungicides, copper-chrome arsenate from wood treating, or arsenic disulfide from tanning operations) or as various soil alteration phases of variable composition, such as arsenic in iron and manganese oxides and in phosphate minerals (arsenate replaces phosphate in the mineral lattice; Figure 2). Arsenic

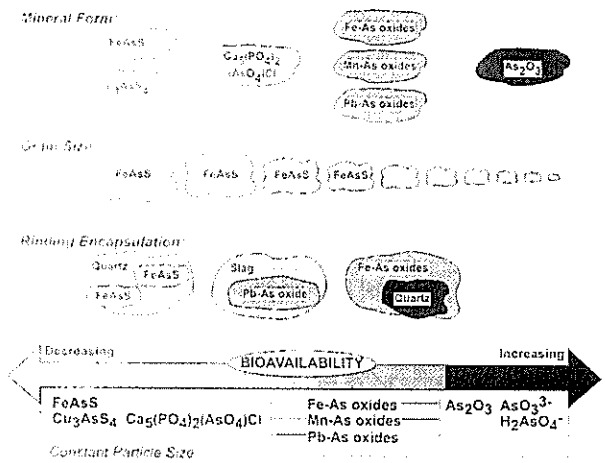

FIGURE 2. Schematic of how different arsenic species, particle sizes, and morphologies affect arsenic bioavailability.

displays a propensity to coprecipitate with iron to form iron–arsenic oxides, the most common soil alteration phase for arsenic (*15*). Arsenic commonly co-occurs with lead in many soil alteration phases, and the same range and complexity of soil lead reactions also take place for arsenic. The in vivo and in vitro studies conducted to date (discussed below) suggest that for a constant particle size, soil arsenic phases such as arsenic sulfides (arsenopyrite [FeAsS] and enargite [Cu_3AsS_4]) and arsenic dispersed in slag have lower relative bioavailability than iron–arsenic oxides, manganese–arsenic oxides, and lead–arsenic oxide (Figure 2).

Further information concerning the effect of arsenic mineralogy on the oral bioavailability of arsenic can be gleaned from the Anaconda monkey study (discussed below). Arsenic mineralogy in fecal material from the monkeys indicated a mineral assemblage similar to that of the preingested soil (*15*). These data suggest that bioavailable arsenic from this soil originates primarily from dissolution of either the surface-bound arsenic fraction or the exterior portion of individual arsenic-bearing grains, rather than through complete dissolution of any discrete arsenic mineral phase. Thus, the data provide mechanistic evidence for the limited bioavailability of arsenic from this soil sample.

Review of in Vivo Database

This section provides a brief review of the in vivo studies that have been conducted to determine the relative bioavailability of lead and arsenic from soil. The test substrates from the soil studies described below constitute the validation samples for ongoing attempts to validate in vitro extraction tests. The following review is not intended to provide a discussion of in vivo study design nor an exhaustive list of all the in vivo studies that have been conducted to date.

In Vivo Database for Lead. Gastrointestinal absorption of lead in humans varies with the age, diet, and nutritional status of the subject as well as with the chemical species and the particle size of lead that is administered. Age is a well-established determinant of lead absorption; adults typically absorb 7–15% of lead ingested from dietary sources, while estimates of lead absorption from dietary sources in infants and children range from 40 to 53% (*16–18*). For the purpose of modeling exposure to lead in soil, the U.S. EPA currently assumes that the absolute bioavailability of lead in diet and water is 50% and that the absolute bioavailability of lead in soil is 30% for children (*19*). This corresponds to a soil RAF of 0.60 (60%) for the bioavailability of soil lead relative to lead in water (i.e., RAF = 0.3/0.5).

In the studies described below, lead absorption from ingested soil was compared to absorption of soluble lead in rats and swine, and the data were used to determine the relative bioavailability of soil lead (results are summarized in Table 1). Soil samples from all of these in vivo studies are available for testing and form the basis for validation of in vitro extraction tests.

EPA Region VIII has developed an oral lead bioavailability assay in a young swine model and has used this model to evaluate relative lead bioavailability in 19 substrates from eight hazardous waste sites. In the young swine model, groups of five swine (5–6 weeks of age) were dosed for 15 days with varying concentrations of lead in soil (<250-μm size fraction) or lead acetate. The swine were dosed twice daily, with the first dose delivered after an overnight fast, and the second dose was delivered in the afternoon after a 4-h fast. The swine were fed 2 h after each dosing. Serial blood samples were collected during the study and analyzed for lead concentration. At the completion of the study, samples of blood, bone (femur), liver, and kidney were collected and analyzed for lead concentration. The resulting data were used to estimate relative lead bioavailability from the test substrates. A more detailed discussion of this model is found in Casteel et al. (*20*).

To date, final study reports have been released for eight sites ((*21–27, 64*) Table 1). Relative bioavailability estimates have also been developed for lead in unweathered, galena-enriched soil and for paint mixed with soil (*28, 29*). RAFs for the 19 substrates range from less than 0.01 to 0.90, based on measurement of lead in blood, bone, liver, and kidney (values cited in Table 1 are recommended point estimates based on a combination of these data, with blood data weighted most heavily). In general, the samples that produced the least lead uptake were derived from tailings, smelter slags, and soil from mining sites, while soils from the vicinity of smelters generally yielded higher RAFs. An exception to this observation occurs for carbonate rich soils at mining areas (such as Jasper, MO), where lead carbonates, which yield high lead bioavailability, tend to predominate in the lead mineral assemblage.

Several studies of relative lead bioavailability from soil at mining and smelting sites have been conducted in a weanling rat model (*30–34*). These studies involved dosing groups of five weanling rats for 30 days with varying concentrations of lead-bearing soil (<250-μm size fraction used in all studies, except Dieter et al. who used <38-μm material) or lead acetate in the diet. At the end of the studies, lead concentrations were measured in blood and bone (femur) and various soft tissues (liver, kidney, and brain), depending on the study. RAFs developed from these studies ranged from 0.087 to 0.41 (Table 1), depending on the origin of the various materials studied. As with the swine studies, the lead forms in the samples tested reflect their origin. The sites that produced the lowest lead absorption were mining and tailings sites (primarily lead sulfide and lead sulfate), and those that produced the greatest proportion of bioavailable lead were soils from the vicinity of historical lead and zinc smelters (lead forms present include common soil alteration phases: iron–lead oxides, manganese–lead oxides, lead phosphates, and lead carbonate).

Over the last several years, considerable effort has been applied to developing chemical amendments that would reduce the bioavailability of lead in soils by changing the mineral species of the lead (*5, 35–38*). These amendments have generally been phosphate based, and they rely on the formation of pyromorphite [$(Pb_5(PO_4)_3X$, X = Cl or OH]-type minerals, which are quite insoluble, to reduce the oral bioavailability of lead. If they are determined to provide long-term reductions in lead bioavailability, these amendments could provide a cost-effective remedial option for lead-contaminated soils. The young swine model discussed above has been used to evaluate the relative bioavailability of lead

TABLE 1: Validation Study Substrates

site/study	test material	lead concn (mg/kg)	arsenic concn (mg/kg)	lead RAF[a,h]	arsenic RAF[a,h]	pH (s.u.)	TOC[i] (%)	ref
	NIST SRM 2711	1162	105	*j*	*j*	7.8	1.25	*55*
		Swine Studies (EPA Region VIII)						
Aspen	soil (berm)	14 200	66.9	0.60	0.62 ± 0.55[b]	*j*	*j*	*24, 45*
Aspen	soil (residential)	3870	16.7	0.61	0.98 ± 0.86[b]	*j*	*j*	*24, 45*
Bingham Creek	tailings (residential soil)	1590	51.2	0.31	*j*	*j*	*j*	*64*
Bingham Creek	tailings (channel)	6330	149	0.28	0.37 ± 0.19[b]	*j*	*j*	*45, 64*
Butte	soil	8585	239	0.19	0.10 ± 0.05[b]	*j*	*j*	*27, 45*
Jasper	soil (HL smelter)	10 800	25.1	0.58	*j*	*j*	*j*	*23*
Jasper	soil (LL yard)	4050	10.7	0.80	*j*	*j*	*j*	*23*
Jasper	soil (HL mill)	6940	16.4	0.79	*j*	*j*	*j*	*23*
Leadville	soil (residential)	7510	203	0.74	−0.08 ± 0.09[b]	*j*	*j*	*25, 45*
Leadville	soil (Fe−Mn lead oxide)	4320	110	0.90	0.28 ± 0.15[b]	*j*	*j*	*25, 45*
Leadville	slag (AV)	10 600	1050	0.18	0.15 ± 0.01[b]	*j*	*j*	*25, 45*
Leadville	tailings (Oregon gulch)	1270	1290	0.06	*j*	*j*	*j*	*25*
Midvale	slag	7895	591	0.17	0.18 ± 0.04[b]	*j*	*j*	*26, 45*
Murray Smelter	slag	11 500	695	0.53	0.51 ± 0.09[b]	*j*	*j*	*21, 45*
Murray Smelter	soil	3200	310	0.71	0.34 ± 0.03[b]	*j*	*j*	*21, 45*
Palmerton	soil (location 2)	3230	110	0.67	0.39 ± 0.09[b]	*j*	*j*	*22, 45*
Palmerton	soil (location 4)	2150	134	0.54	0.52 ± 0.15[b]	*j*	*j*	*22, 45*
NA	NIST paint std + soil	8350	4.8	0.80	*j*	*j*	*j*	*29*
NA	Galena + soil	11 200	4.9	0.01	*j*	*j*	*j*	*28*
Clark Fork	tailings (GK)	152	181	*j*	0.49 ± 0.05[b]	*j*	*j*	*45*
		Swine Studies (Missouri DNR/EPA Region VII)[d]						
Joplin	no. 1—bench control	4300	*j*	0.59	*j*	7.5	4.6	*39*
Joplin	no. 2—bench/1% P, 70 day	4270	*j*	0.38	*j*	8	4.2	*39*
Joplin	no. 6—bench/0.5% P, 1 yr	4610	*j*	0.69	*j*	6.6	3.4	*41*
Joplin	no. 3—field control, 3 mo	5100	*j*	0.67	*j*	3	5.8	*40*
Joplin	no. 4—field/0.5% P, 3 mo	2890	*j*	0.49	*j*	8	6.1	*40*
Joplin	no. 5—field/1% P, 3 mo	4890	*j*	0.45	*j*	5	5.8	*40*
Joplin	no. 7—field/1% P, 1% Fe, 3 mo	4500	*j*	0.82	*j*	3	4.9	*41*
Joplin	no. 8—field control, 18 mo	5200	*j*	0.63	*j*	7.5	5.5	*63*
Joplin	no. 9—field/1% P, 18 mo	4240	*j*	0.39	*j*	6.6	5.5	*63*
		Rat Studies						
Butte	mine waste	3908	*j*	0.093	*j*	3.7	4.1	*48*
Butte	mine waste	3940	*j*	0.225	*j*	3.6	2.61	*48*
Bartlesville	soil	1388	*j*	0.35	*j*	7.0	12.8	*34*
Murray	soil	2090	*j*	0.41	*j*	7.5	4.8	*33*
Copperton	tailings	7220	*j*	0.147	*j*	2.4	0.56	*49*
Copperton	tailings	6890	*j*	0.087	*j*	2.8	1.78	*49*
Bingham Creek	tailings (channel)	10 230	*j*	0.36	*j*	4.9	2.86	*49*
Skagway	ore concentrate	611 000	*j*	0.10[f]	*j*	*j*	*j*	*30*
Skagway	Galena (PbS)	866 000	*j*	0.10[f,g]	*j*	*j*	*j*	*30*
		Swine Studies (U. of Missouri)[e]						
Oklahoma	calcine/soil 1	11 070	11 300	*j*	0.027 ± 0.027[c]	2.6	0.36	*47*
Oklahoma	calcine/soil 2	12 100	17 500	*j*	0.033 ± 0.020[c]	2.6	0.22	*47*
Oklahoma	calcine/soil 3	10 980	13 500	*j*	0.083 ± 0.020[c]	3.1	0.58	*47*
Oklahoma	calcine/soil 4	8430	11 500	*j*	0.221 ± 0.032[c]	3.1	0.41	*47*
Oklahoma	calcine/soil 5	5530	6250	*j*	0.301 ± 0.147[c]	5.7	0.61	*47*
Oklahoma	iron slag 3	3510	1180	*j*	0.287 ± 0.130[c]	7.1	1.58	*47*
Oklahoma	iron slag 4	12 600	5020	*j*	0.30 ± 0.075[c]	7.4	3.38	*47*
Oklahoma	iron slag 5	11 530	4650	*j*	0.164 ± 0.035[c]	7.4	3.22	*47*
		Rabbit Study						
Anaconda	soil	*j*	3900	*j*	0.48	6.6	7.4	*48*
		Monkey Study						
Anaconda	soil (residential)	*j*	410	*j*	0.20	7.8	12	*49*
Anaconda	house dust	*j*	170	*j*	0.28	7.6	42	*49*

[a] All swine-based RBA estimates are recommended point estimates based on blood and tissue data from EPA Region VIII reports. All rat-based RBA estimates are based on measurements of blood lead. [b] Standard deviation from Monte Carlo simulation. [c] Standard deviation across set of swine (n = 5) for each substrate. [d] Joplin samples collected and characterized by Missouri DNR. In vivo swine studies conducted at U. of Missouri and funded by EPA Region VII. [e] Oklahoma samples collected and characterized by Nick Basta (Oklahoma State U.). In vivo studies by Stan Casteel (U. of Missouri). [f] Calculated from data in cited reference. [g] No statistical difference was noted between blood and tissue lead based RBA estimates for Skagway ore concentration and PbS. [h] RAF = relative adsorption factor. [i] TOC = total organic carbon. [j] No analysis performed.

from phosphate-amended soils at a site in Joplin, MO. Both the Missouri Department of Natural Resources and EPA Region VII are participants in this project, which is being conducted under the auspices of the U. S. EPA Remedial Technology Development Forum (RTDF). A description of the amendment studies can be obtained from the RTDF Web site at http://www.rtdf.org/iinert.htm.

Control and chemically amended soils evaluated in the swine model to date include (all of the phosphate amendments used phosphoric acid, unless otherwise noted) the following: (1) laboratory control and laboratory-amended soils (1% phosphate in soil at field-capacity moisture content

incubated for 70 days, and 0.5% phosphate incubated at 55 °C for 1 year and subjected to wet/dry cycles every 2–3 weeks); (2) field control and amended soils (0.5 and 1.0% phosphate after 3 months of field weathering, and 1% phosphate as Triple Super Phosphate plus 1% iron as amorphous ferric hydroxide after 3 months of field weathering); and (3) field control and amended soil (1.0% phosphate, 18 months of field weathering).

Results from these animal studies (Table 1 (*39–41, 63*)) suggest that phosphate-based amendments may be effective at reducing lead bioavailability from Joplin soils by 25–40%.

In Vivo Database for Arsenic. Both the cancer slope factor (CSF) and reference dose (RfD) used to assess the cancer risks and other adverse health effects, respectively, that might be associated with oral exposure to arsenic (*42*) were derived from an epidemiological study that characterized health effects in a population of Taiwanese who consumed drinking water containing arsenic (*43, 44*). After ingestion, water-soluble forms of inorganic arsenic are absorbed extensively from the gastrointestinal tract of humans and most laboratory animals. Because most absorbed arsenic is excreted rapidly in urine, urinary arsenic measurements provide a lower limit on the estimate of oral bioavailability. In the studies described below, arsenic absorption from ingested soil was compared to absorption of soluble arsenic in swine, monkeys, and rabbits, and the data were used to calculate the relative bioavailability of soil arsenic.

The bioavailability of soil arsenic has been evaluated in the young swine assay that was designed initially by EPA Region VIII to estimate lead bioavailability. During the lead studies, EPA also evaluated 14 samples for relative arsenic bioavailability. In the young swine model, groups of five swine (5–6 weeks of age) were dosed twice daily for 15 days (as described above) with varying concentrations of arsenic in soil or slag or with sodium arsenate. Urinary arsenic data for the 14 substrates indicate that relative arsenic uptake in these studies varied from near 0 to 50% (Table 1), with the exception of two samples from Aspen, CO that contained arsenic concentrations that were too low (less than 100 mg/kg) to produce reliable RAF values (*45*). Arsenic bioavailability depended on the form of arsenic present in the sample (Table 1 (*45*)). Soil samples containing only smelter waste or tailings in stream sediments contained the greatest amount of bioavailable arsenic (RAFs ranged from 0.34 to 0.52), while samples containing smelter slag produced intermediate values (RAFs ranged from 0.15 to 0.51; Table 1). Soil samples containing only mining waste (Butte), or a mixture of mining waste and smelting waste (two Leadville soil samples), contained the least bioavailable arsenic (RAFs range from −0.08 to 0.28). This finding is not unexpected, because arsenic in mining waste may be present in larger particle sizes and less soluble forms (e.g., sulfides) (*46*).

During the EPA Region VIII swine studies for arsenic bioavailability, arsenic mass recovery was quite low (23 and 36%, respectively, for sodium arsenate and Grant-Kohrs [GK] tailings (*45*)). The reason for this is not clear. Because the basis for this low recovery is unknown, its significance is also unclear. If the mechanism leading to this low recovery is systemic and applies equally to all dosing materials, then the RAFs are expected to be correct. Only if the mechanism affects arsenic recovery differently for different treatment groups would the RAFs be incorrect. This difficulty with the swine model causes considerable uncertainty regarding the accuracy of the RAFs derived from this model. However, at this time, the most comprehensive assessment of relative arsenic bioavailability from a variety of different environmental substrates is based on the young swine model.

The University of Missouri used the same swine protocol to determine relative arsenic bioavailability from eight mineral processing waste samples from Oklahoma. Arsenic mass balance was not evaluated during these studies. The Oklahoma samples are either a calcine material (low pH and TOC) mixed with soils or an iron slag (neutral pH and higher TOC; Table 1). These eight samples produced arsenic RAFs ranging from 0.027 to 0.30 (Table 1 (*47*)).

In one of the first studies of the relative bioavailability of arsenic in weathered soil, New Zealand White rabbits were used to study the oral absorption of arsenic in a soil sample from Anaconda, Montana that had been affected primarily by emissions from a copper smelter (*48*). Mineral speciation results indicated that arsenic in the soil was present primarily as copper–lead–arsenic oxides and iron–arsenic oxides, with minor contributions from enargite (copper–arsenic sulfide), slag, arsenic phosphates, and copper–lead–arsenic silicates. The rabbits were dosed with arsenic in soil as well as receiving soluble sodium arsenate by gavage and by intravenous injection. Based on urinary arsenic data, the RAF was estimated to be 0.48.

Relative arsenic bioavailability from a composite residential soil from the Anaconda smelter site was determined in a second animal model, the monkey (*49*). Although collected from a different area of the site, the mineralogy of the composite soil sample used in the monkey bioavailability study was nearly identical to that of the soil used in the rabbit study. Three female *Cynomolgus* monkeys were administered single oral doses of soil, house dust, or soluble sodium arsenate by gavage or intravenous injection, using a round-robin study design. Based on urinary arsenic data, the RAFs were estimated to be 0.20 for arsenic in soil and 0.28 for house dust. Based on the above studies, it is clear that considerable evidence exists for the reduced bioavailability of arsenic from soil relative to soluble arsenic. However, the available arsenic in vivo database is not as comprehensive or well resolved as that for lead. In addition, the model that has been used most extensively for arsenic, young swine, may have limitations associated with it (e.g., low arsenic mass recovery for unknown reasons), the importance of which remains to be determined.

In Vitro Extraction Tests

Simple extraction tests have been used for several years to assess the degree of metals dissolution in a simulated gastrointestinal-tract environment (*50–52*). The predecessor of these systems was developed originally to assess the bioavailability of iron from food, for studies of nutrition (*53, 54*). In these systems, various metal salts or soils containing metals are incubated in a low-pH solution for a period intended to mimic residence time in the stomach. The pH is then increased to near neutral, and incubation continues for a period intended to mimic residence time in the small intestine. Enzymes and organic acids are added to simulate gastric and small-intestinal fluids. The fraction of lead, arsenic, or other metals that dissolve during the stomach and small-intestinal incubations represents the fraction that is bioaccessible (i.e., is soluble and available for absorption). For example, the European Standard for Safety of Toys (*55*) provides for an extraction test to evaluate the bioaccessibility of eight metals (including arsenic and lead) from children's toys. The European method involves extraction of the particular metal (toy material reduced to <500 μm in size, at a liquid-to-solid ratio of 50:1) in pH 1.5 (HCl) fluid at 37 ± 2 °C for 2 h. This method has been in use since 1994 by the 18 member countries of the Comite European de Normalization (CEN) to regulate the safety of toys.

Variation in the bioaccessibility of arsenic, chromium, nickel, cadmium, and lead, as a function of liquid-to-solid ratio, was evaluated by Hamel et al. (*56*). These authors determined that bioaccessibility in synthetic gastric juice was affected only slightly by changes in the liquid-to-solid ratios in the range of 100:1 to 5000:1 (mL/g). Ruby et al. (*52*)

demonstrated that for a set of seven soils that had been evaluated for relative lead bioavailability in a weanling rat model, the stomach phase of the in vitro test at a pH value of either 1.3 or 2.5 correlated with RAFs from the in vivo model ($r^2 = 0.93$ at both pH values, $p < 0.01$). More recently, a revised version of the extraction test (different test cell and stirring method) developed in the laboratory of Dr. John Drexler, at the University of Colorado at Boulder, has indicated that data from the stomach phase of the test correlates well with in vivo data for samples used in a series of young swine studies conducted by EPA Region VIII and the University of Missouri ($r^2 = 0.85$, $n = 15$ (*57*)). These results indicate that the extent of lead dissolution in the acidic stomach environment of the extraction test is predictive of relative lead bioavailability in two animal models (weanling rats and young swine). Finally, concentrations of lead, extracted from house dust by the method of Ruby et al. at pH 3.0 (stomach phase only), correlated with blood lead values for children living in the homes from which the particular house dust was collected ($r^2 = 0.79$, $n = 7$ (*58*)).

Further research by Dr. Drexler has resulted in a streamlined extraction test for estimating relative lead bioavailability: 1-h extraction (mixing by end-over-end rotation at 37 °C) of 1 g of soil (<250-μm size fraction) in 100 mL of buffered (HCl and glycine) pH 1.5 solution. Preliminary results for this test appear to correlate well with relative lead bioavailability values from the EPA Region VIII swine studies (*59*). A formal validation of this extraction test in three independent laboratories is currently being conducted (described below).

For arsenic, the correlation between in vitro and in vivo estimates of relative arsenic bioavailability is less clear, primarily due to a less comprehensive and reliable in vivo database (discussed above). Recent research in the laboratory of Dr. Nick Basta (Oklahoma State University) indicates that results from both stomach-phase (pH 1.8, 60 min in a stirred flask at 37 °C) and small-intestinal-phase (pH 5.5, bile acids, pancreatic enzymes, 60 min in a stirred flask at 37 °C) extractions correlated equally well with RAFs from the EPA Region VIII young swine model for 13 mining-related samples ($r^2 = 0.69$ and 0.67, respectively, $p < 0.01$ (*47*)). As with lead, these data suggest that the extent of arsenic dissolution during an acidic gastric-like extraction is predictive of RAFs in the young swine model.

The Solubility/Bioavailability Research Consortium (SBRC)

To further the development and acceptance of in vitro methods for estimating metals bioavailability from soil, a stakeholder group was formed in January 1997, titled the Solubility/Bioavailability Research Consortium (SBRC). The SBRC is a collaborative effort among scientists from academia, government agencies, consulting firms, and industry. It was convened to develop and validate in vitro methods for estimating the relative bioavailability of metals in contaminated soils. Funding for the SBRC has been provided primarily by the industrial members of the group. The New Jersey Department of Environmental Protection (DEP) and the Massachusetts DEP have participated by providing input to this research effort.

The initial goal of the SBRC is to develop and validate an extraction test that correlates with in vivo measurements of relative lead bioavailability from soil in an immature swine model (discussed above). Once this has been accomplished, the extraction test will be available for use in deriving site-specific human exposure estimates. Data have been collected simultaneously for arsenic and used to evaluate the applicability of the test for arsenic bioavailability determination. Every effort is being made to develop tests that are simple, convenient, and reproducible and to disseminate these test protocols for general use in risk assessment.

The SBRC's ongoing research includes an in vitro method validation study for lead and arsenic in three independent laboratories (each extracting blind triplicates of each in vivo tested material), ongoing laboratory research to elucidate the factors that control arsenic bioaccessibility under simulated gastric and small-intestinal conditions, and efforts to develop a more comprehensive in vivo database for relative arsenic bioavailability from soil. Future work will most likely involve application of the existing in vitro test, or development of alternative tests, to other inorganic elements of human health concern (e.g., beryllium, cadmium, chromium, mercury, and nickel).

Discussion

One of the thorny issues facing the SBRC is the question of what constitutes "validation" of a bioaccessibility test for developing site-specific exposure values for use in human health risk assessment. The polar viewpoints appear to advocate either that such a test must be "validated" extensively against appropriate animal models for each new element or that—given our current understanding of the mechanisms that control metals bioavailability from soil—the existing bioaccessibility tests are more appropriate than animal studies and do not require "validation" at all. Between these viewpoints are more moderate perspectives, which might include "validation" against animal models for specific elements, or classes of elements (e.g., cations versus anions when dissolved in solution), rather then rigorous "validation" studies for every element. Validation efforts for lead and arsenic have depended on large in vivo databases developed over the past decade. Similar databases are not available for other metals, requiring that alternative approaches be considered.

All of the animal models currently in use for bioavailability assessment, with the possible exception of monkeys, have substantial anatomical and physiological differences from humans (*60, 61*), and none of these models has been validated against estimates of metal absorption in either children or adults (only one soil sample has ever been studied for oral metals bioavailability in humans [lead only (*62*)], although rough oral absorption estimates can be derived from site-specific exposure studies that have been conducted in human populations). Thus, it is possible that the animal models used most extensively to date (rats and swine) may produce relative bioavailability estimates that are not equal to those in humans.

The research to date indicates that the extent of lead and arsenic dissolution in the acidic environment of the stomach is predictive of relative oral bioavailability of these elements in animal models. Although lead and arsenic are absorbed through the intestinal epithelium, these results suggest that the rate-controlling step in oral lead and arsenic absorption is dissolution in the stomach rather than absorption across the intestinal epithelium. As a result, the extraction test required to simulate the rate-controlling process is quite simple. Given this simplicity, the test is likely to be more reproducible (i.e., have smaller discrepancy between replicate measurements) and sensitive (i.e., capable of being used at lower soil lead and arsenic concentrations) than a well-designed in vivo study for the same soil. Based on the apparent feasibility of developing extraction tests for bioavailability assessment, the observed range of relative lead and arsenic bioavailability, and the great difference in cost between in vivo and in vitro models (a factor of 500–1000), the development of such tests appears to be a worthwhile goal.

Acknowledgments

The authors wish to thank Dr. Chris Weis and Mr. Stanley Christensen, both of U.S. EPA Region VIII, and Dr. John Drexler of the University of Colorado at Boulder for their contributions to this research effort. Although personnel from New Jersey DEP, Massachusetts DEP, and Missouri DNR participated in the preparation of this paper, it has not been subjected to peer or policy review within either agency; it does not necessarily reflect the views of either agency, and no official endorsement should be inferred. The authors also wish to thank three anonymous reviewers for their helpful comments.

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Received for review April 26, 1999. Revised manuscript received July 12, 1999. Accepted July 22, 1999.

ES990479Z

Environ. Sci. Technol. **1999**, *33*, 642–649

An In Vitro Gastrointestinal Method To Estimate Bioavailable Arsenic in Contaminated Soils and Solid Media

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A method was developed to simulate the human gastrointestinal environment and to estimate bioavailability of arsenic in contaminated soil and solid media. In this in vitro gastrointestinal (IVG) method, arsenic is sequentially extracted from contaminated soil with simulated gastric and intestinal solutions. A modified IVG-AB method, where iron hydroxide gel is used to simulate the absorption of arsenic, was also evaluated. Fifteen contaminated soils collected from mining/smelter sites ranging from 401 to 17 460 mg As kg^{-1} were analyzed. In vitro results were compared with in vivo relative bioavailable arsenic (RBA) determined from dosing trials using immature swine which ranged from 2.7 to 42.8% RBA. Arsenic extracted by the IVG and IVG-AB methods was not statistically different than RBA arsenic measured by the in vivo method. Arsenic extracted by the IVG stomach and intestinal phases was linearly correlated ($r = 0.83$ and 0.82, respectively) with in vivo arsenic ($P < 0.01$). Similarly, the IVG-AB method was linearly correlated ($r = 0.79$) with in vivo bioavailable arsenic ($P < 0.05$). All IVG methods extracted similar amounts of arsenic and provided estimates of bioavailable As in contaminated media. The IVG method may aid in the design and cost-effectiveness of remedial strategies of arsenic-contaminated sites.

Introduction

Arsenic is ubiquitous in soils with natural background concentrations ranging from 0.1 to 40 mg kg^{-1} (*1*). Arsenic contamination of soil may result from mining, milling, and smelting of copper, lead, and zinc sulfide ores (*2, 3*); raw and spent oil shale (*4*); and coal fly ash (*5, 6*). Chronic exposure to arsenic may result in skin and internal organ cancers, impaired nerve function, kidney and liver damage, and skin lesions (*7*). Arsenic has been found at high levels (10 000–20 000 mg kg^{-1}) that present risk to human health from the incidental ingestion of soil (*8, 9*). Incidental soil ingestion by children is an important pathway in assessing public health risks associated with exposure to arsenic-contaminated soils. Incidental ingestion of soil results from normal hand-to-mouth activities and represents the principal direct pathway for exposure to nondietary sources of arsenic in contaminated areas. Soil ingestion by children as a health issue fully illustrates the importance of this pathway in terms of subsequent chemical exposure (*10–14*).

Most risk from arsenic is associated with the forms of arsenic that are biologically available for absorption into systemic circulation or "bioavailable" to humans. Presently, methods are not available to quantify the percentage of bioavailable arsenic in soils or to estimate risk from incidental ingestion of arsenic-contaminated materials. Some baseline risk assessments developed for contaminated sites have used the conservative assumption that all (i.e., 100%) of the arsenic present in soils and wastes is bioavailable. However, arsenic may exist in many geochemical forms (e.g., oxides, sulfides) and physical forms (e.g., flue dust, slag, tailings, calcine, waste ore) at hazardous waste sites contaminated by mining and smelter wastes. These waste forms vary in their solubilities and geochemical stabilities to the extent that many are not likely to be very bioavailable and therefore may pose only minimal risks to humans.

The bioavailability of metals, especially lead and arsenic, in some mining wastes have been assessed by conducting expensive and lengthy dosing trials using animal models. The animal model of choice for investigating the enteric bioavailability of arsenic in children requires selection based on similar age and anatomical and physiological characteristics. Pigs are remarkably similar to humans with respect to their digestive tract, nutritional requirements, bone development, and mineral metabolism (*15*). Also, pigs, like humans, tend to ingest food intermittently allowing the stomach to evacuate periodically. This physiology is consistent with the way children most likely ingest arsenic-contaminated materials, between meals when the gastric pH is lowest. Immature pigs have therefore been used successfully as a model for the gastrointestinal function of children (*16, 17*).

To overcome some of the difficulties and expenses associated with animal dosing trials used to assess bioavailability of lead in soils, a research effort has been directed toward development of in vitro chemical methods that simulate the gastrointestinal environment. One such method is the physiologically based extraction test (PBET) (*18*). The PBET method is a good predictor of lead bioavailability. However, PBET research with arsenic-contaminated materials has been limited to only a small number of materials, and the ability of PBET to predict arsenic bioavailability is not known.

The gastrointestinal digestive processes are quite complicated and difficult to simulate in vitro. Several studies in the area of human nutrition have reported in vitro methods to assess bioavailable iron in foodstuffs (*19–22*). Many of these procedural steps are based upon the medical and biochemical scientific literature to gain an understanding of the digestive process, especially in terms of digestive solution volumes produced in response to food intake volume, pH conditions during digestive phases, and quantities of digestive juices and enzymes produced such as pepsin, bile acids, pancreatin, etc. (*23, 24*).

There are two predominant mechanisms involved during digestion of metals-contaminated soil: the solubility of the metal from the soil matrix and the uptake (absorption) of the metal across the intestinal membrane. Previous in vitro type studies have looked at the solubility of metals under gastrointestinal conditions as an indicator of potential

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10.1021/es980631h CCC: $18.00 © 1999 American Chemical Society
Published on Web 01/05/1999

TABLE 1. Chemical Element Content and Select Properties of Soils and Solid Media

properties	Soils and Solid Media 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
pH[a]	2.6	2.6	3.1	3.1	5.7	7.4	7.7	7.1	7.4	7.4	3.9	4.6	7.5	7.3	7.6
TOC (%)[b]	0.36	0.22	0.58	0.41	0.61	0.89	3.13	1.58	3.38	3.22	0.81	1.52	2.28	0.23	4.58
% <2 μm[c]	5.7	10.1	13.4	9.8	7.4	6.5	18.4	8.4	7.3	7.5					
% <50 μm[c]	51.6	49.8	57.4	45.5	49.4	30.2	59.1	36.5	45.1	45.6					
Soluble Anions[d] mg kg^{-1}															
chloride	2550	2950	1240	1080	1710	944	1170	2200	976	1130	4220	9870	912	2450	14200
sulfate	158300	83120	23400	224300	219800	1310	3290	10510	2900	2530	221100	347180	2480	1360	9450
nitrate	103	160	100	49.4	297	147	942	507	552	628	324	2470	53.8	77.5	876
Major Elements[e] %															
Si	17.4	17.0	18.0	18.0	22.7	16.8	21.3	23.0	20.1	20.5	22.6	28.8	16.7	12.8	26.5
Al	1.19	1.17	1.60	1.80	3.02	2.43	3.62	3.20	2.64	2.74	7.56	4.64	1.73	2.48	3.56
Ca	1.20	0.68	0.41	2.90	2.86	12.1	9.64	8.57	7.50	6.07	2.43	3.98	12.1	14.0	8.43
Fe	29.7	31.7	28.5	25.0	16.6	20.9	11.7	16.6	17.2	18.3	7.07	2.01	20.4	22.5	6.17
Trace Elements[f] mg kg^{-1}															
Pb	11070	12100	10980	8430	5530	8740	6840	3510	12600	11530	9200	214	11800	12060	3680
Zn	1600	1610	1650	1660	4740	3850	1560	2510	4045	3400	11200	5650	4400	6290	10770
Cu	385	318	384	524	997	1810	1610	2210	4230	4010	975	8240	2210	2550	954
Ni	39.1	35.9	31.4	32.2	37.4	24.5	24.4	31.9	35.3	34.0	14.8	17.3	36.7	24.5	24.3

[a] 1:1, soil:0.01 M$CaCl_2$ (*29*). [b] Total organic carbon (*30*). [c] Pipette method (*31*). [d] 1 g soil:10 mL of H_2O, shake 1 h, filter 0.45 μm. [e] X-ray diffraction (*32*). [f] SW 846, method 3050 (*33*).

bioavailability (*18, 25*), but in vitro gastrointestinal methods that simulate the mechanism of absorption have not been reported. Arsenate and the chemically similar phosphate have been shown to have a high affinity for amorphous iron hydroxide gel (*26–28*). Incorporation of iron hydroxide gel in an in vitro procedure to simulate intestinal absorption is also evaluated in this study.

The primary objective of our study is to develop a method to measure the bioavailable fraction of arsenic in soil and waste which is correlated with the bioavailable arsenic, as measured in vivo (per pig dosing trials). A second objective is to compare results from our in vitro methods with those from the PBET method.

Experimental Methods

Contaminated Soils and Solid Media. Two matrices were collected for this study from a typical mining/smelter site in the western U.S. where wastes were deposited between 20 and 50 years ago. These aged and weathered wastes included a calcine material (a waste product which results from the roasting and smelting of arsenopyrite ore for the extraction of arsenic) and an iron slag material (a waste product that results from the smelting of ores for lead which is also high in iron). Five calcine (soils and solid media 1–5) and five iron slag (soils and solid media 6–10) samples are fairly consistent in their respective chemical and physical properties for each matrix (Table 1); however, they differ in their total arsenic concentrations (Table 2), ranging from 401 to 17 456 mg kg^{-1}. Mineralogical composition of one calcine (soil 4) and one slag (soil 9) was determined by microprobe analysis for the various and arsenic-bearing solid phases. Soil 4 contained 38% of total arsenic as an arsenic jarosite analogue and 60% arsenic associated with Fe and Mn oxides. Soil 9 contained 17% of total arsenic as an arsenic jarosite analogue, 53% associated with Fe and Mn oxides, and 30% of total arsenic associated with lead oxide.

Approximately 20 kg of each soil was collected, air-dried under ambient conditions, and sieved to collect the particle size fraction <250 μm which adheres to fingers and is thus available for incidental ingestion. Soils were thoroughly homogenized/mixed prior to use and stored in secured, air-tight containers. Five more contaminated materials (soils and solid media, soils 11–15) were included in the study to test the in vitro method over a broader range of matrices. These materials, consisting of soils and slags, had been archived from previous studies involving chemical analyses and pig dosing trials.

Immature Pig Dosing Trial. Standard operating procedures developed by Dr. Stan Casteel of the University of Missouri—Columbia Veterinary Medical Diagnostic Laboratory, approved by the U.S. Environmental Protection Agency (EPA) Region 8 (*34*), were utilized in the immature pig trials. Intact male pigs weighing 10–12 kg were randomly assigned to treatment groups consisting of a calcine dosing group, slag dosing group, negative control group (no soil), and positive control group (oral Na_2AsO_4). Five pigs were used per treatment group, with the exception of three pigs per negative control group. All pigs were individually housed in arsenic-free cages and fed water and a grower ration formulated by the University of Missouri feed mill. After a three-day acclimation period, the pigs were exposed to soil/treatment doses. Pigs were dosed with 6.25 mg of soil per kg body weight per day with one-half of the dose administered 2 h before feeding in the morning and the remaining half given 2 h before the afternoon feeding. Soil doses were placed in the center of a 5 g portion of moistened low-arsenic/low-lead diet material (Ziegler Bros., Inc., Gardners, PA) and hand administered to each animal. The soil mass per dose

TABLE 2. Chemical Content and Bioavailability of Arsenic in Soils and Solid Media

arsenic	soils and solid media														
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
total (mg kg^{-1})[a]	11300	17500	13500	11500	6250	405	450	1180	5020	4650	331	233	799	1460	401
TCLP (mg L^{-1})[b]	2.97	3.01	3.03	2.94	3.00	2.96	2.78	2.91	3.17	2.93	2.65	2.75	2.61	2.73	2.95
TCLP (mg kg^{-1})[b]	59.4	60.3	60.5	58.8	60.0	59.2	55.6	58.1	63.4	58.6	53.0	55.1	52.2	54.5	59.0
bioavailable (%)[c]	2.7	3.3	8.3	22.1	30.1	bdl[d]	bdl[d]	28.7	30.1	16.4	6.2	42.8	29.1	18.7	36.5

[a] SW 846, method 3050 (*33*). [b] SW 846 method 1311 (*33*). [c] Relative bioavailable arsenic from in vivo swine study. [d] Below detection limit.

varied from 23 to 30 mg initially and was adjusted every 3 days to account for growth of the pigs. Soil masses delivered during the final 3 days of the dosing trial ranged from 41 to 45 mg. Every 3 days thereafter, for five collection periods, 24-h excretions of urine were collected from each pig. The urine samples were filtered (Whatman 2), placed into plastic bottles, and preserved to pH 2 with concentrated HCl. Urinary samples were packed securely in coolers on ice and shipped by overnight carrier under chain-of-custody procedures to Oklahoma State University (OSU) for arsenic analysis. Following an additional filtering through 0.45 μm filters, arsenic analysis was performed by a Thermo-Jarell Ash Inductively Coupled Plasma (ICP) (Maxim) utilizing Hydride Generation (HG). To prepare the urine samples for hydride generation, 10.0 mL aliquot of urine was placed into a test tube and mixed with 3.3 mL of concentrated HCl and 4.0 mL of a solution containing 10% potassium iodide and 1% ascorbic acid. After a reaction period of at least 1 h, arsenic was determined by ICP-HG. Adequate blanks, duplicates, and matrix spikes were analyzed to meet quality assurance and quality control requirements.

In Vitro Procedures. Bioavailable arsenic was estimated in our study by two separate in vitro methods and compared to the in vivo study results (Figure 1). An additional comparison of our in vitro results was made with another previously published in vitro procedure (*18, 35*). Canning jars (1 L) were used as reactor vessels because of their wide-mouth and heavy glass composition. All in vitro procedures were conducted in a water bath at body temperature (37 °C), anaerobic conditions were maintained by constantly diffusing argon gas through the solution, and the pH of the in vitro solutions was monitored constantly and adjusted as necessary throughout the procedure. Constant mixing was maintained throughout the procedures (to simulate gastric mixing) by use of individual paddle stirrers at a speed of approximately 100 rpm. A schematic diagram depicting the in vitro reactor design is illustrated in Figure 2.

The in vitro methods were conducted in two sequential phases: (1) gastric phase, low pH by adjustment with trace metal grade HCl, followed by (2) intestinal phase, pH raised by adjustment with a saturated solution of $NaHCO_3$. Throughout the gastric and intestinal phases, a small amount of antifoam agent was added (e.g., decanol) to control excessive foaming due to constant argon gas diffusing through the solutions. A 40 mL sample was collected using a new Luer-lock syringe at the end of each phase (1 h). Samples were centrifuged at 10 000 rpm for 15 min; and the supernatant was filtered through a 0.45 μm filter, acidified to pH 2 with concentrated HCl, and analyzed for arsenic by ICP-HG (following preparation for hydride generation as described above for urine). All in vitro tests were performed in triplicate for each contaminated material. The three in vitro methods studied are presented below. Adequate blanks, duplicates, and matrix spikes were analyzed to meet quality assurance and quality control requirements. The experimental parameters for each of the in vitro methods along with their respective literature references are presented in Table 3.

(1) In Vitro Gastrointestinal Method (IVG). Gastric phase solution was 0.15 M NaCl and 1% porcine pepsin (Sigma Chemical Co., St. Louis, MO. Soil (4 g) was added to 600 mL of gastric solution. An equivalent amount of the dosing vehicle (200 g dough) was added to the gastric solution to mimic the in vivo dosing of 100 mg of soil to 5 g of dough. Gastric solution pH was adjusted to 1.8 following the addition of soil. The gastric phase solution was modified to the intestinal phase solution by adjusting the pH to 5.5 with a saturated solution of $NaHCO_3$ followed by addition of porcine bile extract (2.10 g; Sigma Chemical Co., St. Louis, MO, cat. no. B8631) and porcine pancreatin (0.21 g; cat. no. P1500).

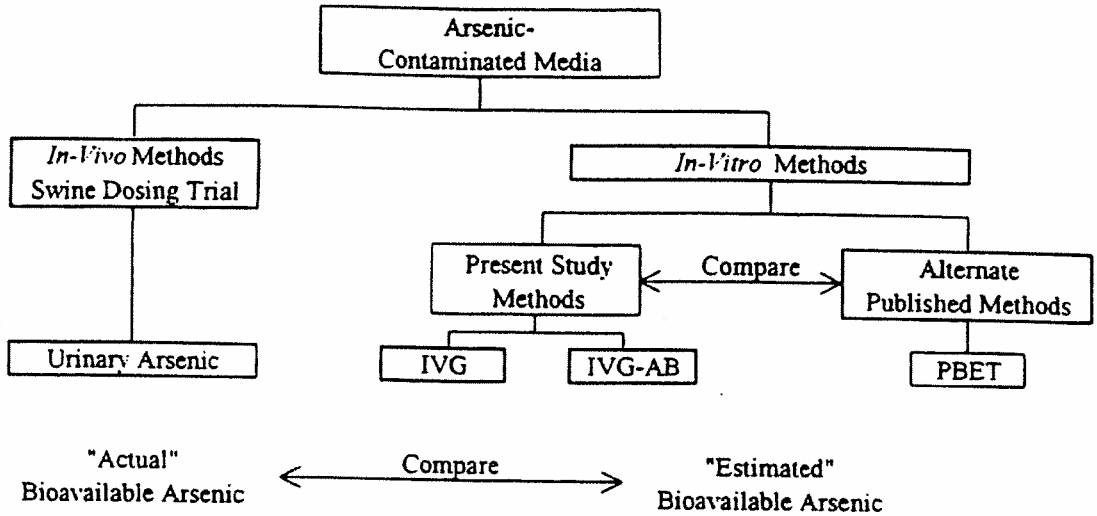

FIGURE 1. Conceptual approach to the in vitro method evaluation.

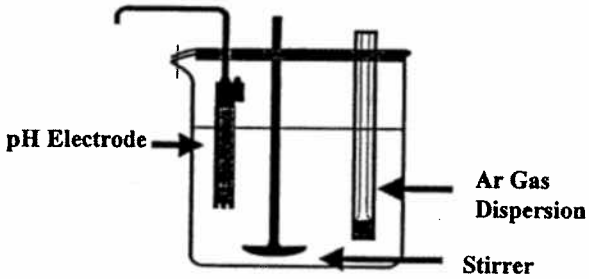

FIGURE 2. In vitro reactor design.

TABLE 3. In Vitro Experimental Parameters and Literature References

parameter	IVG method	IVG reference	IVG-AB method	IVG-AB reference	PBET[a]
Gastric Solution					
pH	1.8	24	1.8	24	2
NaCl	0.15 M	22	0.15 M	22	none
pepsin	1.0%	22	1.0%	22	0.10%
citrate	none		none		0.05%
malate	none		none		0.05%
lactic acid	none		none		0.5%
acetic acid	none		none		0.50%
soil:solution ratio	1:150	24	1:150	24	1:100
food added	yes	33	yes	33	no
Intestinal Solution					
pH	5.5	24	5.5	24	7.0
pancreatin	0.35%	22	0.35%	22	0.018%
bile extract	0.035%	22	0.035%	22	0.05%
adsorbent (iron gel)	no		yes		no

[a] Reference *18*.

(2) In Vitro Gastrointestinal Method with Adsorption (IVG-AB). A second in vitro procedure was performed to determine if an intestinal absorption step could be simulated. This procedure is the same as the IVG method described above with the exception of adding freshly prepared amorphous iron hydroxide gel during the intestinal phase as an adsorbent. Iron hydroxide gel is prepared by making a 0.65 M $FeCl_3$ solution and then slowly adding a solution of 2.7 M NH_4OH until the pH is approximately 6 (*28*). The amorphous iron hydroxide gel is collected by centrifuging the solution at 10000 rpm for 15 min and then carefully pouring off the supernatant. Iron hydroxide (10 g) is placed onto a square (161 cm^2) of 8 μm nylon membrane filter. The nylon filter is tied with nylon string, similar to a tea bag, which is then allowed to suspend freely in the reactor vessel throughout the entire intestinal phase. At the end of the intestinal phase, the iron hydroxide bag is removed and placed into a 250-mL Erlenmeyer flask. Arsenate is desorbed by adding 200 mL of 0.2 M H_2SO_4 to the flask and shaking on a reciprocal shaker for 1 h. The resulting solution is filtered through a 0.45 μm pore size filter and analyzed for arsenic by ICP-HG.

(3) Physiologically Based Extraction Test (PBET). The PBET procedure was performed (*18, 35*) with the following exceptions. To maintain anaerobic conditions, argon gas was diffused through the in vitro solutions continuously rather than utilizing closed reactor vessels, and the pH of the gastric solution was raised to 7.0 (to perform the intestinal phase step) by addition of a $NaHCO_3$ solution rather than using dialysis tubing packed with $NaHCO_3$ powder. The $NaHCO_3$ solution reacted much quicker (1.5–2 h faster) than using the $NaHCO_3$-packed dialysis tubing, which was subject to breaking by inadvertent contact with the mixing blade.

In Vivo Bioavailability Calculations. The amount of arsenic absorbed through the gastrointestinal tract (bioavailable arsenic) may be described in absolute or relative terms. Absolute bioavailability (ABA) is the ratio of the amount of arsenic absorbed compared to the amount ingested:

$$\text{ABA} = \frac{\text{absorbed dose}}{\text{ingested dose}} \quad (1)$$

Relative bioavailability (RBA) is the ratio of the absolute bioavailability of arsenic present in test material (study soil) compared to the absolute bioavailability of arsenic in an appropriate reference material:

$$\text{RBA} = \frac{\text{ABA (study soil)}}{\text{ABA (reference material)}} \quad (2)$$

In our study, we selected the $Na_2AsO_4 \cdot 7H_2O$ reference material as the control because it is a readily soluble form of arsenic that is easily absorbed. Arsenic excretion in urine was found to be a linear function of the administered dose and was approximately independent of time after 5 days of exposure during dosing trials. In most animals, including pigs, absorbed arsenic is excreted primarily in urine. Thus, the urinary excretion fraction (UEF), defined as the amount excreted in the urine divided by the amount dosed, is a reasonable approximation of the oral absorption fraction or ABA. However, this ratio will underestimate total absorption,

TABLE 4. Comparison of Methods Used To Measure Bioavailable Arsenic in Contaminated Soils and Solid Media[a]

samples	bioavailable arsenic method						
	IVG			PBET			
	stomach	intestinal	IVG-AB intestinal	stomach	intestine	in vivo	critical value[b]
all media (n = 13)	16.7 ab	14.8 b	15.3 b	11.8 bc	8.26 c	21.0 a	5.3
CV (%)[c]	75.2	74.6	73.0	95.2	76.4	65.6	
calcine (n = 5)	3.66 b	3.52 b	4.00 b	1.44 b	1.47 b	13.5 a	5.1
CV (%)	74.0	75.9	77.2	77.4	47.3	88.8	
iron slag (n = 3)	24.8 a	22.7 a	24.1 a	13.9 b	12.0 b	25.4 a	7.4
CV (%)	27.4	28.9	26.6	61.0	33.6	41.6	
all media except calcine (n = 8)	24.8 a	21.9 ab	23.0 ab	18.3 bc	12.5 c	25.9 a	6.6
CV (%)	41.3	42.4	38.7	58.9	40.7	49.1	

[a] Values reported are mean percent relative bioavailable arsenic for that group. Mean separation statistics were generated using Duncan's Multiple Range Test (*36*). Multiple comparison of mean values are made between bioavailable arsenic method (horizontally). Mean values with the same letter designation indicate no difference between groups at $P < 0.05$. [b] Quantitative difference between means necessary for methods significantly different at $P < 0.05$. [c] Coefficient of variation.

because some absorbed arsenic is excreted in the feces via the bile and some enters tissue compartments (e.g., liver, kidney, skin, hair, etc.) from which it is cleared very slowly or not at all. Thus, the urinary excretion fraction is not equated with the ABA. The UEF can be used, however, to compute the RBA as follows:

$$\text{RBA} = \frac{\text{UEF (study soil)}}{\text{UEF (reference material)}} \quad (3)$$

All in vivo bioavailabilities in this study are reported as RBAs.

In Vitro Bioavailability Calculations. The standard analysis for soil metal content, including arsenic, during the investigation of the nature and extent of contamination sites is by hot digestion with HNO_3 and H_2O_2, USEPA SW 846, Method 3050 (*33*). The resulting total metal concentration is then used for estimating risks to human health. The realization that probably not all (100%) of the total metal measured by complete digestion is bioavailable has led risk assessors to use a fraction (percentage) of total metal that better represents the bioavailable in the risk calculation. For our in vitro results, bioavailable arsenic is calculated by dividing the arsenic concentration measured in the in vitro stomach phase or the in vitro intestinal phase solutions by the total soil arsenic as described by the following equation:

$$\text{in vitro bioavailable As, \%} = \left[\frac{\text{in vitro As}}{\text{total As}}\right] \times 100 \quad (4)$$

For the in vitro method utilizing iron hydroxide adsorbing gel (IVG-AB), the intestinal phase solution arsenic and the arsenic dissolved from the iron hydroxide gel are summed to represent the total intestinal phase arsenic.

Statistical Methods. Analysis of variance using a randomized complete block design and subsequent separation of means by Duncan's Multiple Range Test (*36*) was used to compare results between in vitro chemical and in vivo methods. Linear regression was used to determine agreement between in vitro chemical and in vivo results. Linear regression parameters (slope equal to one and intercept equal to zero) were evaluated using t-tests to determine agreement between methods.

Results and Discussion

The length of time to perform the stomach phase and intestinal phase (reaction time) was not clearly described in the literature. Hence, an experiment was conducted using the PBET method (*18, 35*) (on one calcine and one slag sample) to determine the dissolution of arsenic over time for each of the phases. The soluble concentration of arsenic remained relatively constant during the stomach phase with samples collected every 20 min. Likewise, samples were collected every 60 min over a 3-h intestinal phase, and, again, arsenic concentration in solution remained relatively constant. A 1-h duration was selected for reaction time of each phase.

Other studies have shown the type of food incorporated into the in vitro method can affect lead bioavailability (*35*). To replicate conditions of the in vivo experiment as closely as possible, an experiment was conducted to evaluate food added (using the soil dosing vehicle) versus without food added. An equivalent volume of soil dosing vehicle (which represented 200 g of vehicle) was added to the reactor vessel. One calcine sample and one slag sample were tested with and without food. For the slag sample, there was no difference in the soluble arsenic measured in either the stomach or intestinal phases of the vessels with-food as compared to the vessels without-food (21.1 mg kg^{-1} stomach phase and 24.4 mg kg^{-1} intestinal phase, without-food conditions versus 19.7 mg kg^{-1} stomach phase and 24.3 mg kg^{-1} intestinal phase, with-food conditions). However, for the calcine sample, more arsenic was solubilized in the with-food treatment as compared to the without-food treatment (2.65 mg kg^{-1} stomach phase and 6.92 mg kg^{-1} intestinal phase, without-food conditions versus 7.86 mg kg^{-1} stomach phase and 10.3 mg kg^{-1} intestinal phase, with-food conditions). Apparently, adding food would not inhibit arsenic solubilization and, in some cases, may increase arsenic solubilization. For the IVG and the IVG-AB in vitro experiments, 200 g of dough, used as the pig dosing vehicle, was added to represent the addition of food. Presence of food in the digestive tract can affect bioavailability of heavy metal (*37*). For example, milk may lower Pb bioavailability by coprecipitation of Pb with calcium phosphate (*38*). The effect of food on Pb bioavailabity in gastrointestinal in vitro tests affects Pb bioavailability in some contaminated media (*35*). However, the effect on Pb bioavailability was found to depend on type of contaminated material and food included in the in vitro test. Inclusion of food affected dissolution of arsenic in our in vitro method but the exact mechanism is unclear.

Comparison of bioavailable arsenic estimated by in vitro methods with in vivo arsenic in contaminated media was accomplished using mean separation by Duncan's Multiple Range Test following analysis of variance (*36*) (Table 4). Only the IVG stomach phase method was equivalent with the in vivo method ($P < 0.05$) across all media. Evaluating the media separately, the iron slag material tested by the IVG stomach phase method was statistically equivalent to the in vivo method, yet the calcine materials were different (at $P < 0.05$). Arsenic extracted by in vitro methods (% RBA) was much lower than in vivo arsenic RBA. When only the slags and soils were evaluated (all media except the calcines), the agreement

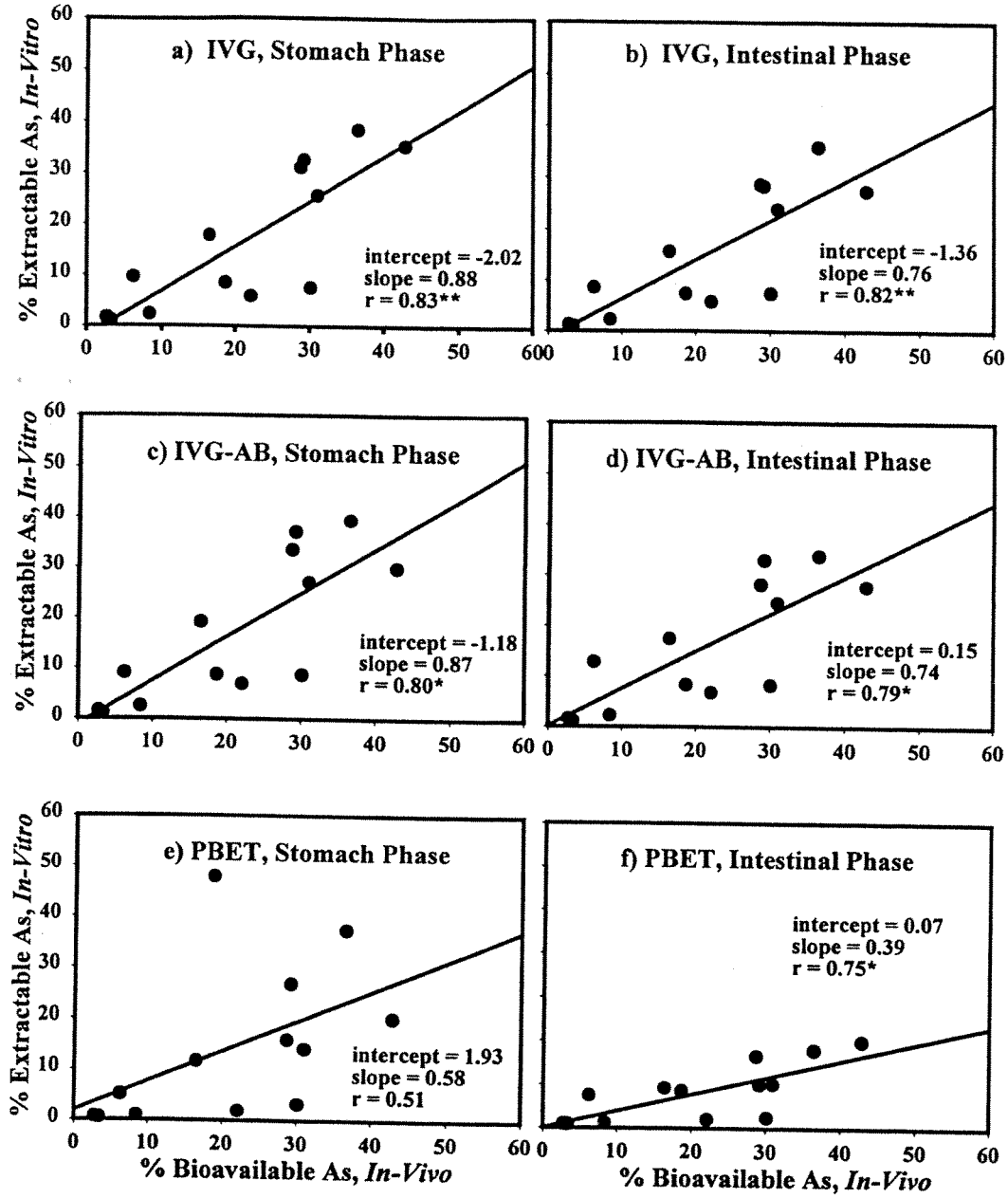

FIGURE 3. Comparisons of gastrointestinal in vitro stomach and intestinal phase bioavailable arsenic with in vivo bioavailable arsenic: (a) IVG, stomach phase; (b) IVG, intestinal phase; (c) IVG-AB, stomach phase; (d) IVG-AB, intestinal phase; (e) PBET, stomach phase; (f) PBET, intestinal phase. **Statistically significant at $P < 0.01$, *statistically significant at $P < 0.05$.

between percent RBA of the IVG stomach phase and in vivo methods improved. Similar results were demonstrated for the IVG-AB intestinal phase method. When only the slags and soils were evaluated, the IVG-AB intestinal method was statistically equivalent with the in vivo method (at $P < 0.05$). The calcine samples, as analyzed by any of the in vitro methods, were not statistically equivalent with the in vivo method.

Few statistical differences between the IVG stomach phase, IVG intestinal phase, and IVG-AB intestinal phase were found for most groups of material (Table 4). In other words, extending the in vitro method beyond the gastric phase did not improve the ability of the method to measure bioavailable As. To simulate absorption across the intestinal membrane, iron hyroxide gel was added to the IVG-AB intestinal phase solution. Intestinal absorption is a different process than adsorption of arsenic to iron hydroxide gel. However, both processes are sinks that remove arsenic from solution. To determine the quantity of iron hydroxide gel to use, an experiment was conducted using iron hydroxide gel to adsorb arsenic from the intestinal phase solution. Ten grams of Fe gel adsorbent in the IVG-AB method adsorbed 60 mg of arsenic from simulated gastric and intestinal solutions that contained 100 mg L^{-1} arsenic as sodium arsenate and 10 000 mg L^{-1} of sulfate. Arsenic concentrations in gastric and intestinal solutions of the IVG method for contaminated media ranged from 0.38 to 12.1 mg L^{-1} with a median value of 1.90 mg L^{-1}. Dissolved sulfate up to 3470 mg L^{-1} occurred in the in vitro solutions of contaminated media, which is below the sulfate concentration of the simulated IVG method solution. Therefore, the 10 g of Fe gel adsorbent was capable of adsorbing all of the arsenic from the gastric and intestinal solutions of the IVG method for contaminated media. However, the simulated absorption step of the IVG-AB did

not increase arsenic extracted from contaminated media compared to the IVG method (without adsorbent). Dissolution of arsenic solid phases of contaminated media by simulated gastrointestinal solutions appears to be the rate-limiting step rather than the subsequent Fe gel adsorption step in controlling dissolved arsenic in the IVG method.

Also of note is that neither the PBET stomach phase nor PBET intestinal phase in vitro methods were found to be statistically equivalent with the in vivo method for any group of contaminated materials tested (Table 4).

Coefficients of variation (CV) values, used to describe variability in bioavailability measurements, for in vivo and in vitro methods were determined (Table 4). The CV values for the IVG and IVG-AB methods for all media were similar ranging from 73.0 to 75.2%. The IVG and IVG-AB methods had a slightly lower degree of precision than the in vivo method (CV of 65.6%). The degree of precision for bioavailability measurements varied with test material. Determination of bioavailable arsenic by all methods for calcine was less precise than noncalcine materials (Table 4). The degree of precision of in vivo and in vitro methods for all media except calcine was very similar, with CV values ranging from 40.7 to 58.9%.

Linear regressions of percent RBA arsenic measured by in vitro tests with the swine in vivo method are presented in Figure 3. Although 15 soils were tested throughout all in vitro experiments, only 13 points are presented on each plot. Samples 5 and 6 (Table 2) had very low arsenic concentrations and were below in vivo bioavailability detection limits. Results of the IVG stomach phase were linearly correlated ($r = 0.83$) with in vivo bioavailable arsenic ($P < 0.01$) (Figure 3a). Statistical analysis of linear regression parameters showed the slope of 0.88 was not different than one, and the intercept of −2.02 was not different than zero; IVG stomach phase results were statistically the same as in vivo results. The IVG intestinal phase was also linearly correlated with in vivo arsenic with an r of 0.82 ($P < 0.05$) (Figure 3b). Statistical analysis of linear regression parameters showed the slope of 0.76 was not different than one, and intercept of −1.36 was not different than zero; IVG intestinal phase results were statistically the same as in vivo results. Comparison of stomach and intestinal phase results of the IVG methods (Table 4, Figure 3a,b) suggests arsenic bioavailability measured by the IVG method is controlled by dissolution of arsenic in gastric phase.

Figure 3c presents the results of the IVG-AB stomach phase. Because the IVG-AB stomach phase is the same procedure as the IVG stomach phase, the gastric solution arsenic for both methods is the same (Figure 3a,c). Slight differences were found between the IVG and the IVG-AB intestinal phases (Figure 3b,d). However, adding the adsorbing Fe gel to the in vitro solution of the IVG-AB method had little effect on the r values of the linear regressions of IVG methods vs in vivo (Figure 3b,d). Statistical analysis of linear regression parameters showed the slope of 0.79 was not different than one, and intercept of 0.15 was not different than zero (Figure 3d); IVG-AB intestinal phase results were statistically the same as in vivo results. Similar results between IVG or IVG-AB and in vivo methods were expected because the simulated absorption step of the IVG-AB did not increase arsenic extracted from contaminated media (Table 4).

Results from the PBET in vitro methods are shown in Figure 3e,f. The PBET stomach phase results are not linearly correlated with in vivo arsenic, while the intestinal phase is correlated with an r of 0.75 ($P < 0.05$). Slopes of the PBET vs in vivo method were different than one but intercepts were equivalent to zero (Figure 3e,f); results from the PBET method were not the same as in vivo results. The PBET method underestimated arsenic bioavailability in calcine materials (Table 4). Excluding calcine-derived contaminated media improved the PBET gastric phase vs in vivo linear regression. The PBET gastric phase arsenic was correlated ($r = 0.70$, $P < 0.10$) with in vivo arsenic when calcine was excluded producing a slope of 0.59 which was equivalant to one. Although both the PBET and IVG methods underestimated bioavailable arsenic for calcine materials (Table 4), parameters in the IVG method improved extraction of arsenic from contaminated media. One difference between the PBET and IVG methods is that the PBET method does not incorporate any type of food into the gastric solution. Food has been shown to have an affect on bioavailability (*35*). Another difference between these methods is the amount of pepsin used in the in vitro solutions. The PBET solution contains one-tenth the pepsin concentration of the IVG solutions. We selected the IVG pepsin concentrations from the human nutrition and medical literature (*22, 24*). Pepsin is one of the most important of the digestive enzymes; it hydrolyzes peptide bonds in proteins and polypeptides with a low degree of specificity. Perhaps hydrolyzed products are enhancing arsenic solubilization.

It is unlikely that an in vitro method can be developed which will replicate in vivo bioavailability. The human digestive system is too complex and dynamic to simulate in the laboratory. A more reasonable approach may be to develop in vitro methods that are based upon human gastrophysiology and correlate well with in vivo method results. From this correlation, mathematical relationships can be developed that will be useful in making risk estimates. The discipline of soil science has used this concept successfully when early work was performed to find suitable chemical extractants to measure plant-available nutrients. Chemical extractants cannot extract plant nutrients in the same manner as a living plant under the conditions of the plant root environment. However, good correlation between soil extractants and plant uptake has allowed soil scientists to use that relationship to make reasonable predictions of plant available nutrients in soil and fertilizer recommendations (*39*). Similar relationships between in vitro and in vivo methods may lead to the development of mathematical relationships from which predictions can be made to derive bioavailable As concentrations in soils for risk estimates that have a lower degree of uncertainty and aid in the design and cost-effectiveness of remedial strategies at contaminated sites.

Acknowledgments

The authors thank Dr. Gary Sayler and the three anonymous reviewers for their suggestions that led to an improved manuscript. The research in this manuscript has been funded by the U.S. Environmental Protection Agency, Office of Research and Development. Although the research described in this paper has been funded by U.S. EPA through Grant R825410-91-0 to Dr. Nick Basta, Dr. Stan Casteel, and Dr. Robin Rdoriguez, it has not been subjected to the Agency's required peer and policy review and therefore does not necessarily reflect the views of the Agency and no official endorsement should be inferred. Published with approval of the Director, Oklahoma Agricultural Experiment Station.

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Received for review June 19, 1998. Revised manuscript received November 11, 1998. Accepted November 11, 1998.

ES980631H

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FINAL

BASELINE HUMAN HEALTH RISK ASSESSMENT

ANACONDA SMELTER NPL SITE
ANACONDA, MONTANA

January 24, 1996

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January 24, 1996

Work Assignment No: 037-8P18
Document Control No.: 7760-037-RA-DMCG

Prepared for:

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January 24, 1996

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ABBREVIATIONS, ACRONYMS, AND INITIALISMS

AA	atomic absorption
ADLC	Anaconda-Deer Lodge County
AIC	acceptable intake for chronic exposure
AOC	Administrative Order on Consent
ARCO	Atlantic Richfield Company
As	arsenic
AT	averaging time (days)
ATSDR	Agency for Toxic Substances and Disease Registry
AUC	area under the curve
AWQC	Ambient Water Quality Criteria
BAF	bioavailability factor for COPC in soil or dust (unitless)
BW	body weight (kg)
CDI	Chronic Daily Intake (mg/kg-day)
CDM Federal	CDM Federal Programs Corporation
CERCLA	Comprehensive Environmental Response, Compensation, and Liability Act of 1980
CF	conversion factor (10^{-6} kg/mg)
CFR	Code of Federal Regulations
CLP	Contract Laboratory Program
cm	centimeter(s)
COPC	chemical of potential concern
CRAVE	Cancer Review and Validation Effort (EPA)
CS	chemical concentration in soil or dust (mg/kg)
CSF	cancer slope factor
CTE	central tendency exposure
DMA	dimethyl arsenic acid
DPS	Development Permit System

ABBREVIATIONS, ACRONYMS, AND INITIALISMS (continued)

ED	exposure duration (years)
EE/CA	Engineering Evaluation/Cost Analysis
EF	exposure frequency (days/year)
EPA	U.S. Environmental Protection Agency
°F	degrees Fahrenheit
FI	fraction ingested from contaminated source (unitless)
HEAST	Health Effects Assessment Summary Tables (EPA)
HHRA	human health risk assessment
HI	Hazard Index
HQ	Hazard Quotient
ICP-MS	inductively coupled plasma-mass spectroscopy
IEUBK	Integrated Exposure Uptake Biokinetic
IQ	intelligence quotient
IR	ingestion rate (mg/day)
IRIS	Integrated Risk Information System
L/day	liters per day
LOAEL	lowest-observable-adverse-effect level
LOEL	lowest-observed-effect-level
MCL	maximum contaminant level
MCLG	maximum contaminant level goal
mg/day	milligrams per day
mg/kg	milligram(s) per kilogram
mg/kg-day	milligram(s) per kilogram per day
mg/L	milligram(s) per liter
MMA	monomethyl arsenic acid
mph	miles per hour
NCDC	National Climatic Data Center
NCP	National Contingency Plan

NCV	nerve conduction velocities
NHANES II	National Health and Nutrition Examination Survey
NOAEL	no-observable-adverse-effect level
NPL	National Priorities List
OU	Operable Unit
OW/EADA	Old Works/East Anaconda Development Area (operable unit)
Pb	lead
pH	negative log of the hydrogen ion concentration
ppm	parts per million
PRP	potentially responsible party
QA/QC	quality assurance/quality control
RfC	reference concentration
RfD	reference dose
RI/FS	Remedial Investigation/Feasibility Study
RME	reasonable maximum exposure
ROD	Record of Decision
RPM	regional project manager (EPA)
SCEM	site conceptual exposure model
SQL	sample quantitative limit
SST	Streamside Tailings
TCRA	time-critical removal action
UCL	upper confidence limit
XRF	X-ray fluorescence
%	percent
µg/L	microgram(s) per liter

EXECUTIVE SUMMARY

CDM Federal Programs Corporation (CDM Federal) has been tasked by the U.S. Environmental Protection Agency (EPA), Region VIII to evaluate the potential for adverse human health effects to occur as the result of exposure to chemicals from ongoing and historic releases from the Anaconda Smelter National Priorities List (NPL) Site.

Risk assessments were previously performed by EPA for the Old Works/East Anaconda Development Area (OW/EADA) Operable Unit (OU), the Flue Dust OU, and the Mill Creek OU. EPA also prepared an endangerment assessment, in which the health effects associated with exposure to chemicals transported by air from the Anaconda Smelter NPL Site were evaluated. The Atlantic Richfield Company (ARCO), the primary potentially responsible party (PRP), has contributed to the characterization of environmental contamination and human exposure at the Anaconda Smelter NPL Site. Their efforts include environmental sampling throughout the site and site-specific studies of urinary arsenic, soil ingestion, and arsenic bioavailability. This human health risk assessment (HHRA) completes the risk assessment process for the Anaconda Smelter NPL Site by addressing risks in areas of the site that were not addressed under an OU-specific risk assessment.

CHEMICALS OF POTENTIAL CONCERN

Chemicals of potential concern (COPCs) have been identified for OUs of the Anaconda Smelter NPL Site, and for other sites in the upper Clark Fork Basin. Arsenic, cadmium, and lead are ubiquitous in the area and elevated concentrations are generally associated with mining, milling, and smelting activities. In some instances, elevated concentrations of copper and zinc are also site-related and potentially hazardous. COPCs for the remaining areas of the Anaconda Smelter NPL Site are expected to be similar to those for OUs within the site and for sites in the region. Selection of COPCs is limited, therefore, to a determination of which of the above metals should be included in the quantitative assessment.

Data are available describing concentrations of arsenic, cadmium, copper, lead, and zinc in soil and groundwater. Data describing arsenic dust concentrations are also available. Soil concentrations of cadmium, copper, and zinc are below health-based screening levels; therefore, these chemicals will not be considered further in the risk assessment. Of the groundwater data available in areas where it is presently used for human consumption, only arsenic is present in concentrations indicating a potential health hazard. COPCs for the site are, therefore, arsenic and lead in soil and dust and arsenic in groundwater.

CHEMICAL CONCENTRATIONS IN SITE MEDIA

Data for this HHRA were provided by soil investigations conducted by PTI (1992 and 1993) and an arsenic exposure study conducted by Dr. Bornschein, University of Cincinnati (1992 and 1994). There were initial concerns that soil arsenic concentrations from the two studies were not comparable. Therefore, the data from both studies were used in a statistical comparison to determine if significant differences exist between arsenic concentrations found in surface soil samples collected for these two studies in Anaconda and nearby communities on an area-by-area basis. The Bornschein study divided the site into subareas, labeled A through K. Results of the statistical tests indicate that PTI (1992 and 1993) data and Bornschein (1992 and 1994) data are not significantly different for eight of nine areas compared. It is concluded that using either data set or a combination of the data will result in similar characterization of arsenic in surface soils for Anaconda and nearby communities. However, the Bornschein data are about eight times more numerous in Anaconda for subareas A through F than the PTI data, and samples were collected from yards where actual exposure to children may occur. The Bornschein data also included collocated interior dust samples. The PTI (1992 and 1993) soil samples were collected both from yards and pasture or idle land. Based on the above, EPA decided to use only the Bornschein data to develop exposure point concentrations of arsenic and lead in soil.

In addition, only the Bornschein study sampled water from the town of Anaconda. Bornschein (1992 and 1994) collected tapwater samples from homes using groundwater wells as their source of drinking water. These were located in subarea A. Samples were also collected from the public water supply. Tapwater samples were analyzed only for arsenic. The public water supply of the town of Anaconda is from an area considered uncontaminated and arsenic was not detected in samples collected from the public water supply. Therefore, for Anaconda subareas other than subarea A, which obtain drinking water from the public water supply, risks were calculated using an arsenic concentration of non-detect.

Groundwater investigations in the town of Opportunity were conducted by Bornschein (1992 and 1994) and CDM Federal (1994a). The water source for Opportunity is private domestic wells. The samples collected by Bornschein were analyzed only for arsenic. Samples collected by CDM Federal (1994a) were analyzed for metals and metalloids. Only arsenic was detected in concentrations presenting a potential health hazard. Due to the relatively small number of samples available, domestic groundwater data from both the CDM Federal (1994a) and Bornschein (1992 and 1994) studies will be used to develop exposure point concentrations for arsenic in groundwater in the town of Opportunity.

Bornschein (1992 and 1994) collected interior dust samples from the areas of Anaconda, Opportunity, Lost Creek, and Fairmont. These samples were analyzed for arsenic, which was present in concentrations indicating a potential health risk. Both arsenic and lead were retained as COPCs in soil; therefore, lead was also assumed to be a COPC in dust. Lead dust concentrations were estimated using a soil-to-dust ratio developed using arsenic soil-to-dust concentrations.

RECEPTORS AND EXPOSURE PATHWAYS

Based on current and future land uses, the following populations are considered most likely to be exposed to COPCs at the Anaconda Smelter NPL Site:

- Current and future residents
- Agricultural workers
- Recreational users
- Commercial workers

Exposure pathways of concern for these populations are:

Exposure Pathways for Residents (Adults and Children Ages 0 - 6):

- Ingestion of surface soils
- Ingestion of interior dust
- Ingestion of groundwater

Agricultural Workers (Adults):

- Ingestion of surface soils
- Inhalation of dust

Recreational Users (Dirt Bike Riders):

- Ingestion of surface soils
- Inhalation of dust

Recreational Visitors (Swimmers):

- Ingestion of surface water
- Dermal exposure to surface water

Commercial Workers (Adults):

- Ingestion of surface soils
- Ingestion of interior dust

COPC concentrations in soil and groundwater outside of the towns of Anaconda and Opportunity are not adequately characterized due to the relatively small number of samples collected. Therefore, only risks to current residents of Anaconda and Opportunity are assessed quantitatively in this HHRA. Risk-based screening levels are developed for other receptors to be used in risk characterization when data are available.

EXPOSURE ASSUMPTIONS

Arsenic chronic daily intake (CDI) was estimated for each residential exposure pathway based on estimates regarding the extent, frequency, and duration of exposures and the exposure point concentrations. Site-specific exposure assumptions were used when available; these include estimates of arsenic bioavailability in dust, soil, and water. EPA has used available data to derive site-specific arsenic bioavailability estimates for ingested soil and dust (EPA 1994a, 1995a). The following are the bioavailability values used in the HHRA:

- 25.8 percent (%) bioavailability for dust
- 18.3% bioavailability for soil
- 100% bioavailability for water

Findings in the Anaconda soil ingestion study support the Superfund Program's usual approach of assuming ingestion of 100 milligrams (mg) soil and dust per day as a central tendency exposure (CTE) assumption and 200 mg soil and dust per day as a reasonable maximum exposure (RME) assumption for ingestion rates of children 0-6 years old. Though default assumptions are used for soil and dust ingestion rates for children, these assumptions are clearly consistent with available site-specific data.

Predictions of exposure obtained from calculations of CDIs were compared to measured exposures of urine arsenic concentrations for children living in Anaconda. The arithmetic and geometric means of predicted and measured urinary arsenic concentrations for these children were compared to evaluate the appropriateness of the exposure assumptions used. The Kruskal-Wallis one-way analysis of variance demonstrated that measured and predicted urinary arsenic are not statistically different. However, EPA exposure calculations underpredict urinary arsenic concentrations where measured levels are greater than 10 micrograms per liter (µg/L). Overall, the results of the comparison support the use of the described exposure calculations in risk assessment for the Anaconda Smelter NPL Site.

RISK-BASED SCREENING LEVELS

Risk-based screening levels were developed for arsenic based on residential, agricultural and commercial worker and recreational swimmer and dirt biker exposure scenarios. Screening levels for the different exposure scenarios have been developed for a carcinogenic risk range of 10^{-7} to 10^{-3} and a noncarcinogenic hazard index (HI) of 1, and are provided in Table ES-1.

HUMAN HEALTH RISK CHARACTERIZATION

Toxicity values for arsenic were combined with CDI to estimate quantitative health risk estimates for exposure to arsenic. Lead toxicity was assessed using the EPA Integrated Exposure Uptake Biokinetic (IEUBK) Lead Model, Version 0.99. Children (aged 0-6) were considered the sensitive subpopulation at risk for adverse effects due to exposure to lead in environmental media. Risks to adults from lead exposure were not evaluated.

Noncarcinogenic risks were calculated by dividing the CDI of arsenic for each pathway by the arsenic-specific oral reference dose (RfD). The total noncancer risks for all pathways for each subarea is less than unity, indicating there is little potential for adverse noncarcinogenic effects (Table ES-2).

Carcinogenic risks were calculated by multiplying estimates of arsenic CDI by the arsenic-specific oral slope factor (SF). The total cancer risks for all pathways for each subarea fall within the range considered acceptable by EPA (Table ES-3).

Results of the IEUBK model indicate that 5% of children in subarea E may have blood-lead levels in excess of 10 micrograms per deciliter (µg/dL).

TABLE ES-1

Risk-Based Screening Levels for Arsenic for the Anaconda Smelter Site

Medium	Soil								Surface Water	
Screening Level Based on Carcinogenic Risk	Residential Scenario (mg/kg)		Agricultural Scenario (mg/kg)		Commercial Worker Scenario (mg/kg)		Recreational Dirt Biker Scenario (mg/kg)		Recreational Youth/ Swimmer Scenario (mg/L)	
Carcinogenic Risk	RME	CTE	RME	CTE	RME	CTE	RME	CTE	RME	CTE
1×10^{-7}	0.30	1.85	1.00	10.04	1.33	10.15	2.32	53.55	0.002	0.008
1×10^{-6}	2.97	18.5	10.03	100.4	13.3	101.5	23.2	535.5	0.020	0.081
1×10^{-5}	29.7	185.2	100.3	1,003	133	1,015	232.3	5,355	0.20	0.81
1×10^{-4}	297	1,852	1,003	10,038	1331	10,155	2,323	53,551	2.0	8.1
1×10^{-3}	2,970	18,516	10,033	100,385	13,307	101,546	23,231	535,517	20.2	81.0
Screening Level Based on Noncarcinogenic Effects (HI = 1)	573	1,071	NC	NC	2,139	4,570	NC	NC	1.04	4.16

NC = Not calculated. Risk-based screening levels for these exposure scenarios are based on inhalation and ingestion exposures. A RfC for inhalation is not available; screening levels based on noncarcinogenic effects can, therefore, not be calculated for these exposure scenarios.

TABLE ES-2
NONCANCER RISKS
INGESTION OF ARSENIC IN GROUNDWATER, SOIL, AND DUST
RME AND CTE RESIDENTIAL SCENARIO
ANACONDA SMELTER SITE
(mg/kg-day)

SUBAREA	RME SCENARIO Total Arsenic Risk	CTE SCENARIO Total Arsenic Risk
Subarea A	5.48E-01	2.46E-01
Subarea B	2.79E-01	1.49E-01
Subarea C	3.60E-01	1.93E-01
Subarea D	5.70E-01	3.05E-01
Subarea E	3.80E-01	2.03E-01
Subarea F1	5.24E-01	2.80E-01
Subarea F2	4.48E-01	2.40E-01
Subarea I	3.45E-01	1.84E-01
Subarea J	3.32E-01	1.77E-01
Opportunity	6.03E-01	2.83E-01

TABLE ES-3
CANCER RISKS
INGESTION OF ARSENIC IN GROUNDWATER, SOIL, AND DUST
RME AND CTE RESIDENTIAL SCENARIO
ANACONDA SMELTER SITE
(mg/kg-day)

SUBAREA	RME SCENARIO Total Arsenic Cancer Risk	CTE SCENARIO Total Arsenic Cancer Risk
Subarea A	5.30E-05	6.38E-06
Subarea B	2.05E-05	3.23E-06
Subarea C	2.64E-05	4.17E-06
Subarea D	4.18E-05	6.59E-06
Subarea E	2.79E-05	4.40E-06
Subarea F1	3.84E-05	6.06E-06
Subarea F2	3.29E-05	5.19E-06
Subarea I	2.53E-05	3.98E-06
Subarea J	2.43E-05	3.83E-06
Opportunity	5.51E-05	7.01E-06

1.0 INTRODUCTION

1.1 OVERVIEW OF RISK ASSESSMENT

The U.S. Environmental Protection Agency (EPA) began initial investigations of the upper Clark Fork River Basin in 1982. These investigations prompted EPA to place the Anaconda Smelter on the National Priorities List (NPL) in 1983. Subsequent and ongoing remediation at this site has successfully addressed many of the waste sources, including flue dust, tailings, slag, and beryllium wastes associated with previous operations. However, chemicals released during smelter operations are still present in the environment near the former smelter. Fallout from past smelter emissions and transport of contaminants via wind and water, from existing tailings ponds, slag ponds, and other waste piles still present a potential risk to human health. EPA has initiated this baseline human health risk assessment (HHRA) to evaluate the potential for adverse effects to occur from exposure to chemicals from ongoing and historic releases to areas near the former smelter that have not been included in previous risk assessments.

Risk assessments were previously performed by EPA for the Old Works/East Anaconda Development Area (OW/EADA) Operable Unit (OU), the Flue Dust OU, and the Mill Creek OU. EPA also prepared an endangerment assessment in which the health effects associated with exposure to chemicals transported by air from the Anaconda Smelter NPL Site were evaluated.

Most data used to complete risk assessments for the Anaconda Smelter NPL Site have been gathered by the Atlantic Richfield Company (ARCO), which is the primary potentially responsible party (PRP). These data gathering efforts have contributed significantly to the characterization of environmental contamination and human exposure at the site. ARCO's efforts include environmental sampling throughout the site and site-specific studies of human arsenic exposure, soil ingestion, and arsenic bioavailability in experimental animals.

1.2 SITE BACKGROUND INFORMATION

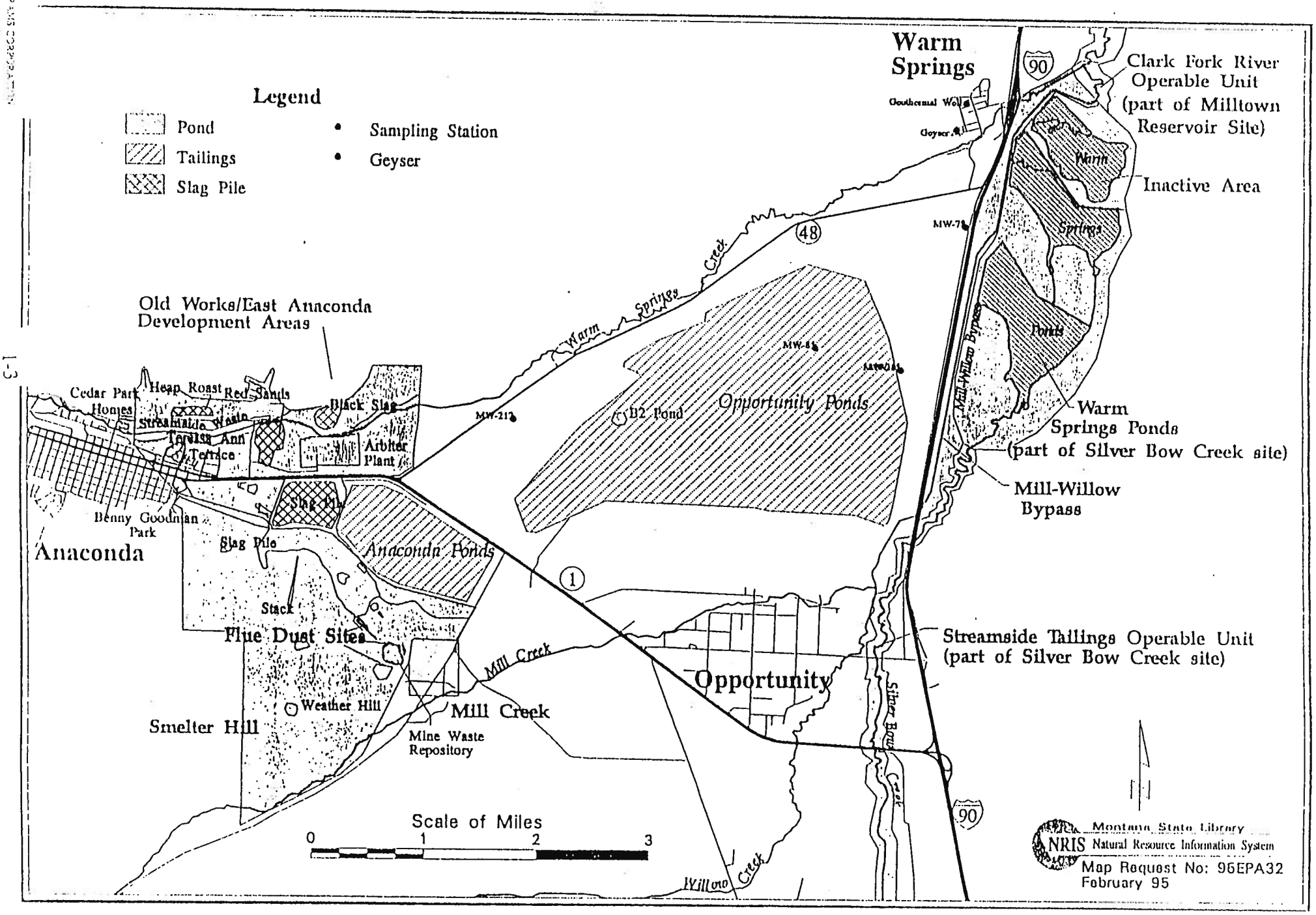
The Anaconda Smelter NPL Site is located in southwestern Montana, at the southern end of Deer Lodge Valley, approximately 25 miles northwest of the city of Butte (Figure 1-1). There are five communities located within the Anaconda Smelter NPL Site: Anaconda, Fairmont, Galen, Opportunity, and Warm Springs.

Around 1884, large copper concentrating and smelting operations commenced at the area presently known as the Old Works. The Old Works are located on the north side of Warm Springs Creek, east of Anaconda, and were operated until about 1901. In about 1902, ore processing and smelting operations began at the Anaconda Smelter (also called the Washoe Reduction Works, the Washoe Smelter, the New Works, and the Anaconda Reduction Works) on Smelter Hill south of Warm Springs Creek across from the Old Works. Operations at the Anaconda Smelter ceased in 1980, and the smelter facilities were dismantled soon thereafter. The only substantial feature remaining from the facility is the large brick smelter stack on Smelter Hill.

Activities at the Old Works and Anaconda Smelters and related facilities resulted in large volumes of waste materials, which were disposed of on the ground and in surface waters in and around the Anaconda Smelter NPL Site. Smelting activities also resulted in widespread, aerial deposition of contaminants released from stacks and from waste piles in the vicinity of the smelter, including the community of Anaconda. The history of significant releases of heavy metals to the environment at the Anaconda Smelter led to listing the site on the NPL in September 1983, under the authority of the Comprehensive Environmental Response, Compensation, and Liability Act of 1980 (CERCLA). On April 12, 1984, ARCO entered into an Administrative Order on Consent (AOC) with EPA to conduct demolition of the Smelter Hill facilities. In October 1984, ARCO entered into an AOC to conduct remedial investigations (RIs) for several OUs within the Anaconda Smelter NPL Site. Early draft

FIGURE 1-1

Anaconda Smelter NPL Site Map



reports based on initial investigations indicated wide-scale contamination and a need for more in-depth study.

In the initial stages of the Anaconda area investigations, it became apparent that the community of Mill Creek, located two miles east of Anaconda, was severely impacted by contamination. Children in Mill Creek had elevated urinary arsenic levels indicating an excess exposure to arsenic in their environment. EPA redirected the sequencing of the RIs for the site to focus on Mill Creek. Young children, the population determined to have the greatest exposure, were temporarily relocated from the community in May 1986. At this time, flue dust, the most concentrated arsenic and heavy metal contaminant source on the site, was sprayed with surfactant. In addition, contaminated road dust in the community was treated to reduce inhalation exposures. Following temporary relocation and the above remedial activities, none of the children from the Mill Creek area had levels of urinary arsenic above background.

In July 1986, EPA entered into an AOC with ARCO to conduct an expedited Remedial Investigation/Feasibility Study (RI/FS) for Mill Creek. The Record of Decision (ROD) for Mill Creek was completed by EPA in October 1987. The selected remedy was permanent relocation of Mill Creek residents. This remedy was chosen in part because of the potential for recontamination of the area from several nearby waste sources. EPA negotiated a Consent Decree with ARCO concerning the implementation of the relocation remedy for Mill Creek residents on January 7, 1988. The permanent relocation of residents was completed in the fall of 1988.

The generation and airborne transport of smokestack particulate and fugitive dust emissions during smelter operations also resulted in contamination of soils and household dust by arsenic, lead, cadmium, copper, and zinc in the neighborhoods of Teressa Ann Terrace, Elkhorn Apartments, Cedar Park Homes, and other areas surrounding the smelter. In

addition, contaminated material from the Old Works and/or Anaconda Smelter facilities was used as fill material around homes in the three Anaconda neighborhoods mentioned above.

On September 28, 1988, ARCO entered into an AOC with EPA to conduct an Engineering Evaluation/Cost Analysis (EE/CA) study and investigation for the Old Works and Community Soils OUs of the Anaconda Smelter NPL Site. Results of sampling conducted by ARCO in 1988–1989 in the areas of Teressa Ann Terrace, Elkhorn Apartments, and Cedar Park Homes indicated the presence of elevated heavy metal concentrations at or near the soil surface. Sampling conducted by ARCO in 1990 confirmed the presence of elevated concentrations of heavy metals in several yards, gardens, and common areas of the three neighborhoods.

In October 1988, EPA entered into an AOC with ARCO to conduct additional remedial and removal activities at the Anaconda Smelter NPL Site. Remedial investigations for the Flue Dust and Smelter Hill OUs were initiated at the same time as a removal analysis for the Old Works and Community Soils OUs. In March 1990, EPA and ARCO amended the October 1988 AOC to conduct an additional removal analysis at the Arbiter and Beryllium OUs. Further, EPA and ARCO agreed to conduct a siting analysis for a waste repository on the Anaconda Smelter NPL Site, and a site on Smelter Hill was eventually selected.

In 1990, ARCO entered into an AOC to conduct separate Old Works and Anaconda Community Soils investigations, and to conduct additional sampling in yards, gardens, and common areas of Teressa Ann Terrace, Elkhorn Apartments, and Cedar Park Homes neighborhoods. Sample analysis results confirmed that several yards and common areas contained elevated heavy metal concentrations at or near the soil surface. Arsenic concentrations ranged between 5 and 1,570 parts per million (ppm), cadmium ranged between 0.4 to 59.4 ppm, and lead ranged from 4.8 to 1,230 ppm.

A September 17, 1991, Enforcement/Action Memorandum (with a concurrent AOC) required ARCO to conduct a Time-Critical Removal Action (TCRA) by excavating and removing

contaminated soils in areas of Teressa Ann Terrace, Elkhorn Apartments, and Cedar Park Homes where arsenic concentrations exceeded 250 milligrams per kilogram (mg/kg). The proximity of these residential areas to the former Old Works smelting facilities may have contributed to the high levels of arsenic found. The primary objective of the action was mitigation of any direct contact threat to residents by removing the contaminated soil and replacing or capping the area with uncontaminated soil.

Under the TCRA, removal of arsenic-contaminated soils and replacement of topsoil and grass began in late 1991 and was completed in September 1992. The removed soils were disposed of in the Red Sands area of the OW/EADA OU. Removal occurred on about 8 acres of undeveloped lots and 19 front or back yards in Teressa Ann Terrace, 32 yards around the Elkhorn apartments, and 14 yards around Cedar Park Homes. Clean replacement soil was obtained from an area near Lost Creek.

From July through December 1992, material from two ponds east of the Arbiter Plant, four concrete bunkers behind the plant, and tailings from the Old Works Tailings Pond were excavated and taken to Smelter Hill for disposal in the Arbiter repository. Also during this time period, beryllium-contaminated tailings and other materials were removed and taken to a special repository constructed for these wastes.

In December 1992, EPA and ARCO entered into the Flue Dust Consent Decree, which resulted in the removal, stabilization, and placement in a repository of flue dust materials on Smelter Hill. This work was initiated in late 1992 and completed in 1994. In 1992, EPA and ARCO entered into an AOC to conduct the OW/EADA OU investigations. A March 1994 ROD selected a combination of engineering and institutional controls as the remedy. Remediation of recreational and commercial/industrial areas were conducted where waste and soils exceeded arsenic levels of 1,000 and 500 ppm, respectively. In early 1994, EPA began the scoping process for the final HHRA, culminating in the preparation of this report.

1.3 SCOPE OF THE BASELINE HUMAN HEALTH RISK ASSESSMENT

Risk assessments were previously performed by EPA for the OW/EADA OU, the Flue Dust OU, and the Mill Creek OU. This HHRA will complete the risk assessment process for the Anaconda Smelter NPL Site by addressing risks in areas of the site that were not addressed under an OU-specific risk assessment. The HHRA is based on information developed during the RIs, including the exposure and bioavailability studies sponsored by ARCO.

This HHRA quantitatively evaluates potential human health risks associated with site chemicals of potential concern (COPCs) found in soil, dust, and groundwater in areas of the Anaconda Smelter NPL Site not previously addressed in a risk assessment. The assessment is a baseline evaluation and assumes no further remedial action at the site. The no-action alternative is evaluated in accordance with Section 330.430(d) of the National Contingency Plan (NCP). The format and procedures used to develop this HHRA are based on the most recent EPA guidance for performing human health and evaluations at Superfund Sites (EPA 1989a, b; 1991a, b, c; 1992a, b, c; 1993a, b, c; 1994b, c).

A site conceptual exposure model (SCEM) for the Anaconda Smelter NPL Site is presented in this report. The SCEM includes potential current and future exposure pathways, and is presented in the form of an iterative flow chart, which depicts specific site characteristics including: (1) contaminant sources; (2) release mechanisms; (3) transport routes; (4) exposure routes; and (5) receptors. Exposure pathways identified in the SCEM for potential application to the site are individually evaluated for potential contribution to site-related exposure. Only those pathways that could present a significant risk to human health are evaluated quantitatively in this HHRA. For each such pathway, a complete description of receptors and exposure parameters are provided. Exposure parameters that deviate from defaults provided in EPA guidance documents are justified and referenced.

Toxicity profiles are provided for arsenic and lead, the only COPCs for this assessment. Each profile describes basic toxic properties and toxicokinetics and, where appropriate, provides EPA toxicity criteria. Toxicity criteria are not available for lead, since assessment of lead risks is now carried out using a physiologically-based, pharmacokinetic model.

Finally, carcinogenic and noncarcinogenic risks resulting from exposure to arsenic are estimated by combining estimates for arsenic exposure and toxicity criteria for arsenic. Risks from exposure to lead are estimated through use of the EPA Integrated Exposure Uptake Biokinetic (IEUBK) Lead Model Version 0.99. Uncertainties in all exposure and risk estimates are a critical part of risk characterization and are presented along with risk estimates to provide the risk manager with the appropriate perspective for applying risk information to remedial decisions.

2.0 IDENTIFICATION OF CHEMICALS OF POTENTIAL CONCERN

COPCs are chemicals that are potentially site-related and for which data are of sufficient quality for use in quantitative risk assessment (EPA 1989a). Selection of COPCs requires an evaluation of available data for useability in risk assessments, and a formal process for identifying site-related chemicals that might pose unacceptable risks at a site. COPCs have been previously identified for the Anaconda Smelter NPL Site and for other sites in the upper Clark Fork Basin. Arsenic, cadmium, and lead are ubiquitous in the area and elevated concentrations are generally associated with mining, milling, and smelting activities. In some instances, elevated concentrations of copper and zinc are also site-related and potentially hazardous. Based on this experience at other sites, the majority of sampling and analytical efforts at the Anaconda Smelter NPL Site focused specifically on these five chemicals, which are considered to be the primary COPCs at this site. Although some studies did collect data on other metals that might conceivably contribute to risk (e.g., antimony, barium, beryllium, manganese, and mercury), the relative contribution of these other chemicals to total risk is believed to be sufficiently small compared to the risks from the primary COPCs that they are not considered further. Selection of COPCs is limited, therefore, to a determination of which of the above metals should be included in the quantitative assessment.

2.1 SITE-SPECIFIC DATA CONSIDERATIONS

A large quantity of environmental data has been collected in the community of Anaconda and other areas addressed in this HHRA. In addition, site-specific studies of human exposure to arsenic and bioavailability of arsenic in experimental animals have been undertaken to support risk assessment at the site. In this section, available data are identified and evaluated for usefulness in quantitative risk assessment.

2.1.1 AVAILABLE DATA

Numerous investigations have been performed to provide data on the types and concentrations of chemicals in soil, dust, sediments, air, groundwater, surface water, and waste (tailings/slag) at the Anaconda Smelter NPL Site. Analyses have been performed using standard EPA Contract Laboratory Program (CLP) protocols as well as by X-ray fluorescence (XRF). Data were validated in accordance with procedures approved for the Clark Fork River Superfund Sites. Each data summary report prepared by ARCO was audited by EPA to determine the useability of each data point. EPA and ARCO have stipulated to the use of these data. As required for Clark Fork River Superfund Site investigations, data are classified into three data utilization categories: enforcement quality data, screening quality data, and unusable data. Enforcement quality data may be used for all Superfund program activities and purposes, screening quality data may be used for certain activities, and unusable (rejected) data are not usable for any Superfund purpose. Enforcement and screening data generated for Anaconda remedial investigations were used for the following purposes: site characterization, evaluation of alternatives, engineering design, risk assessment, determining presence or absence of contaminants, determining relative concentrations, and scoping and planning for future studies, investigations, or actions.

2.1.2 SELECTION OF DATA FOR USE IN THIS RISK ASSESSMENT

Prior risk assessments have been performed for the OW/EADA, Flue Dust, and Mill Creek OUs within the Anaconda Smelter NPL Site. This HHRA completes the risk assessment process by evaluating risks in areas of the Anaconda Smelter NPL Site that were not previously addressed. Data pertinent to these areas of the site are evaluated for useability in quantitative risk analysis. Data evaluation considers the following issues:

- Source and recentness of data
- Sampling locations
- Adequacy of documentation

- Data validation results
- Adequacy of analytical methods
- Detection limits
- Completeness
- Comparability

Reports containing data used for this HHRA include the Anaconda Soil Investigation (PTI 1992 and 1993), Anaconda Residential Urinary Arsenic Study (Bornschein 1992 and 1994), and CDM Federal (1994a). These studies are summarized in Table 2-1 and are evaluated in more detail below.

Data are available describing concentrations of arsenic, cadmium, copper, lead, and zinc in soil and groundwater. Table 2 - 2 provides a statistical summary of data for these chemicals in soil and compares concentrations to health-based screening criterion. As shown in Table 2 - 2, even maximum soil concentrations of cadmium, copper, and zinc are at or below health-based screening levels; therefore, these chemicals are not considered further in the risk assessment. The average concentration of lead is also less than the screening level; however, subareas within the town of Anaconda have soil lead concentrations higher than the screening level. Since subareas of the town have been identified as appropriate exposure units for this risk assessment (see Section 2.1.2.2), the higher average concentrations within these areas suggest a potential for unacceptable exposures for significant subpopulations within Anaconda. Based on mean lead concentrations within these areas, lead is retained as a COPC.

Table 2 - 3 provides summary statistics for groundwater data and compares concentrations to health-based screening criteria. Based on these comparisons, only arsenic is present in concentrations indicating a potential health hazard.

COPCs for the site are, therefore, arsenic and lead in soil and dust and arsenic in groundwater. Soil and groundwater data for these contaminants (Table 2 - 1) are evaluated below and used in Section 3.3.1 for estimating potential site-related exposures.

TABLE 2-1

Summary of Main Data Sources

Source	Description of Study
Anaconda Soil Investigation (PTI 1992a)	In order to characterize soil contamination in the Anaconda Smelter NPL Site, soil samples were collected from communities, including Anaconda, Opportunity, Warm Springs, Galen, and Fairmont. Areas of high use were targeted for additional sampling in Anaconda. Soil samples were also collected from areas near the communities, regional areas, and regional targeted areas such as streams, gulches, and the Yellow Ditch. Soil samples were analyzed for arsenic, cadmium, copper, lead, and zinc.
Anaconda Residential Urinary Arsenic Study (Bornschein 1992 and 1994)	To determine the extent of childhood arsenic exposure in residential environments in the Anaconda Smelter NPL Site, samples of soil, interior dust, exterior dust, and tapwater were collected from homes in Anaconda, Opportunity, Lost Creek, and Fairmont Ranches. Urine samples were collected from children living in these homes. Soil samples were analyzed for arsenic and lead; dust, water, and urine samples were analyzed for arsenic.
Domestic Water Sampling in and near Opportunity, Montana (CDM Federal 1994a)	A total of 20 groundwater samples were collected from 20 domestic wells in and near Opportunity. Samples were analyzed for metals and metalloids; lead data were not enforcement quality.

TABLE 2-2

Summary Statistical Data for Chemicals in Soil
Comparison to Residential Soil Screening Criterion[1]

Chemical	Mean (mg/kg) (Sample No.)	Range of Concentrations Detected (mg/kg)	Screening Criterion for Residential Soil (mg/kg)
Arsenic	172 (318)[a] *	38 - 409[a]	0.37[b]
Cadmium	5.01 (129)[c]	0.25 - 32.5[c]	39[b]
Copper	1337 (75)[c]	90 - 5070[c]	9,990[d]
Lead	384 (318)[a]	23 - 2153[a]	400[b]
Zinc	1662 (75)[c]	109 - 5210[c]	23,000[b]

[a]Source: Bornschein (1992 and 1994)
[b]Source: EPA 1994e
[c]Source: PTI (1991 and 1992)
[d]Calculated by CDM Federal

* Background (pg 2-20)
Arsenic 6-16 mg/kg

[1]Soil screening criteria are based on RME scenarios. Soil ingestions is the only pathway evaluated. Dust is equivalent to soil in these calculations.

TABLE 2-3

Summary Statistical Data for Chemicals in Groundwater
Comparison to Tapwater Screening Criterion[1]

Chemical	Range of Concentrations Detected (µg/L)	Screening Criterion for tapwater (µg/L)
Arsenic	1.0U - 13.8[a] ☆	0.038[b]
Cadmium	0.1 - 0.8[c]	18[b]
Copper	1.9U - 10.8[c]	1,400[b]
Lead	None Detected[c]	15[d]
Zinc	5.0U - 114.5[c]	11,000[b]

[a]Source: CDM 1994a and Bornschein (1992 and 1994)
[b]Source: EPA 1994e
[c]Source: CDM 1994a (Bornschein data contained only As concs.)
[d]Action Level
U = not detected

☆ Background (pg. 2-21)
1.6 – 12.6 ug/L

[1]Screening criterion based on RME scenario. No exposure pathways other than groundwater ingestion are included in the calculations.

2.1.2.1 PTI (1992 and 1993)

The soil investigation carried out by PTI characterized concentrations and spatial distribution of arsenic and metals in several areas near the former Anaconda Smelter. These areas include: (1) communities of Anaconda, Opportunity, Warm Springs, Galen, and Fairmont; (2) community target areas in Anaconda; (3) locations near the communities of Anaconda, Opportunity, Warm Springs, Galen, and Fairmont; (4) regional areas; and (5) regional target areas.

Community Soils

Soil samples totaling 97 were collected at 76 sampling stations within the communities of Anaconda, Opportunity, Warm Springs, Galen, and Fairmont. Of the 76 sampling stations, 30 were located in the town of Anaconda, 28 were located in Opportunity, 12 were located in the town of Warm Springs, and 3 each were located in the towns of Galen and Fairmont.

Seventy-nine of the 97 samples were collected from the 0 - 2 inch interval and are considered surface soil samples. The remaining samples were collected from the 2 - 10 inch interval to determine the extent of vertical migration of contaminants. These deeper samples are considered subsurface soil. Samples were collected from yards, and included composite soils from lawn areas. In addition, samples were collected from pasture and idle land located within town limits. Arsenic and lead samples were analyzed by XRF, and cadmium by CLP methods. CLP methods were also used to determine soil moisture, pH, and electrical conductivity.

Community Target Areas

A total of 51 samples were collected from 24 sampling locations in the community of Anaconda. Community target areas were defined as areas having the potential for extensive

public use. These areas included schools, residential yards, public parks, and playgrounds. No community soils target areas were identified in the towns of Opportunity, Warm Springs, Galen, and Fairmont. Thirty-two of the 51 samples were composites collected from the 0 - 2 inch interval, 16 were discrete opportunistic samples from the 0 - 2 inch interval, and 3 were composite opportunistic samples from the 0 - 2 inch interval. All samples are considered surface soil. Analyses were performed as described above.

Near Community Soils

Near community sampling areas are defined as 0.5-mile strips surrounding the five individual communities defined by the community soils sampling effort. A total of 117 soil samples were collected at 94 sampling stations. Of these, 40 samples were collected near Anaconda, 33 samples were collected near Opportunity, 16 samples were collected near Warm Springs, and 12 samples each were collected near Galen and Fairmont. These soil samples were analyzed for arsenic, cadmium, and lead as described above. Soil slurry pH and electrical conductivity were measured in a field laboratory. Of the 117 samples collected, 113 were composite samples, and 4 were grab opportunistic samples. Ninety-three of the 113 samples were collected from the 0 - 2 inch interval and are considered surface soil. Eighteen of the remaining samples were collected from the 2 - 10 inch interval to determine the extent of vertical migration of contaminants and are considered subsurface soil samples. Two samples were collected from the 0 - 10 inch interval. The remaining four soil samples were opportunistic surface samples collected at two near community sample stations.

Regional Soils

The regional area consists of nearly 77,000 acres and includes undisturbed lands, such as native rangeland and riparian zones, and disturbed lands characterized as agricultural or reclaimed land. Composite soil samples were collected from a total of 84 stations on a 1 square mile grid corresponding to section corners designated by the General Land Office grid

system (PTI 1992). Seventy-four of the 84 sample stations were defined as undisturbed (rangeland) and 10 stations were defined as regional disturbed sites (tilled/reclaimed). Of these 10 stations, 5 were reclaimed waste sites and 5 were tilled agricultural lands. Arsenic, copper, lead and zinc were analyzed using XRF methods, and cadmium by CLP methods. Soil slurry pH and electrical conductivity were determined in a field laboratory.

A total of 100 samples was collected; 90 were considered to represent regional undisturbed areas and 10 were considered to represent regional disturbed areas. Seventy-one of the 90 regional "undisturbed" samples were collected from the 0 - 2 inch interval and are considered surface soil. Nineteen of the remaining samples were collected from the 2 - 10 inch to determine extent of vertical migration of contaminants and are considered subsurface soil. Regional "disturbed" samples were all collected from the 0 - 10 inch depth interval. These samples are considered subsurface soil.

Regional Targeted Soils

Soil samples were collected at a total of 60 sample station transects designated as regional targeted sampling locations. Regional targeted sampling areas are defined as perennial streams, ephemeral drainages, and other areas within the regional boundaries (e.g., Yellow Ditch) possibly contaminated by arsenic and metals. Sampling locations consisted of a total of 60 station transects across five creeks, seven gulches, and the Yellow Ditch. The entire reach of each stream or gulch was characterized using sample stations located at evenly spaced distances across the area. Soil samples totaling 246 were collected. Arsenic, copper, lead and zinc were analyzed by XRF methods, and cadmium by CLP methods. Soil slurry pH and electrical conductivity were determined in a field laboratory.

Data Evaluation

Following an evaluation of the PTI (1992 and 1993) data, EPA determined that samples were collected and analyzed, and data were validated and properly qualified, according to the procedures set forth in planning documents and EPA guidance.

The majority of samples were collected from surface soil (0 - 2 inches). Receptors in Anaconda and the surrounding areas are much more likely to come into contact with this soil than with deeper soils. Thus, the majority of soil data collected by PTI is directly applicable to exposures at the site.

Sample locations and numbers of samples within the towns of Anaconda and Opportunity are sufficient for defining exposure. The samples are reasonably closely spaced and it is unlikely that significant "hot spots" for arsenic and metals exist in unsampled areas. This conclusion is supported by an examination of the data collected by Bornschein (1992, 1994, see Section 2.1.2.2). Sample locations within other areas may not be representative because of the small number of samples collected. The areas in question are large and samples are widely spaced. It is conceivable that hot spots of significant size could be present in some of these areas. However, the examination of data from the communities of Anaconda and Opportunity suggests a rather homogeneous distribution of contamination. If the same mechanisms of contaminant release are responsible for contamination outside these communities, it is reasonable to expect a relatively homogeneous contaminant distribution in these areas also. Thus, the uncertainties in data for areas outside Anaconda and Opportunity may not be as great as suggested by simple examination of sample numbers and locations. Nevertheless, no quantitative evaluation of exposures is presented for communities or areas other than Anaconda and Opportunity. Additional discussion of potential exposures and risks in outlying and surrounding areas is presented in Section 6.0.

FIGURE 2-1

Modified Bornschein Sub-Areas
Anaconda, Montana

Montana State Library
NRIS Natural Resource Information System

Map 95epa48j
October 16, 1995

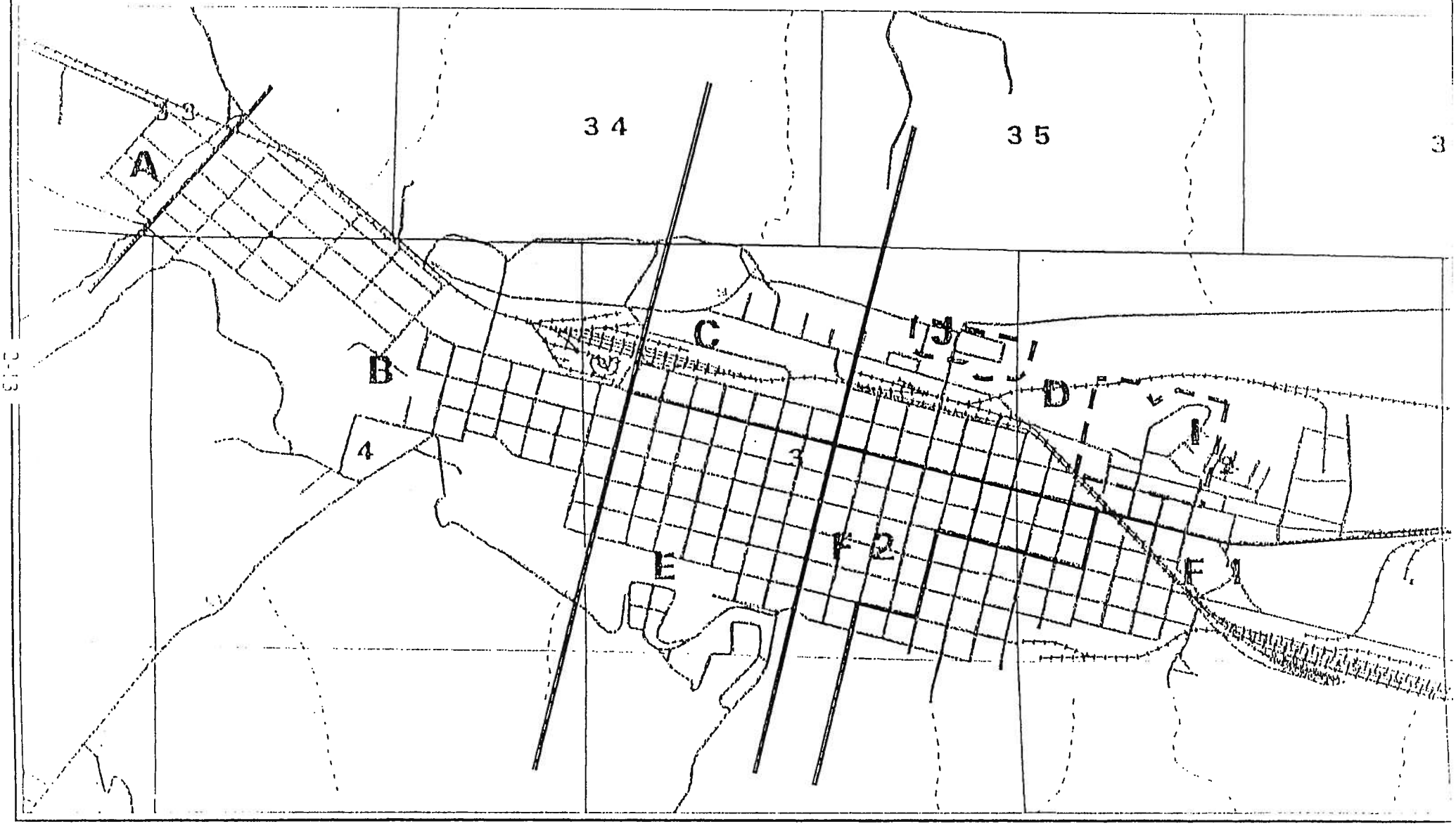


TABLE 2-4

Subarea Letter Descriptions Used in the Bornschein Study

Subarea	Description
A	This area is bounded by the west side of Evergreen Street through the West Valley, including North Cable Road, English Gulch, and American Gulch.
B	This area is bounded by the east side of Evergreen Street through the west side of Spruce Street, including the Sunnyside Addition.
C	This area is bounded by the east side of Spruce Street, north side of Park Street, and west side of Main Street, including Mount Haggin Homes.
D	This area is bounded by the east side of Main Street, north side of Park Street, and the edge of town. Excluded from this area are Area I (Teressa Ann Terrace) and Area J (Cedar Park Homes). Areas I and J are special abatement areas.
E	This area is bounded by the east side of Spruce Street, south side of Park Street, and west side of Main Street.
F	This is bounded by the east side of Main Street, south side of Park Street, and edge of town.
G	This area is the community of Opportunity, bounded by the north side of Highway 1, including all of Opportunity.
H	This area is Lost Creek, including all homes on Galen Road.
I	This area is Teressa Ann Terrace. Teressa Ann Terrace is on the east end of town and includes all homes on Elaine Drive, Heather Drive, Jefferson Way, and Pauline Drive.
J	This area is Cedar Park Homes which includes all Cedar Park Homes low-income housing, homes on North Cedar Street, north of the bridge and homes on North Cherry Street, and north of Warm Springs Creek.
K	This area is the Fairmont Ranches. It is bounded by the south side of Highway 1 and the Deer Lodge County/Silver Bow County line including Crackerville Road and Fairmont Road.

Source: Bornschein (1994)

characterized by generally lower soil contamination levels than is Anaconda. Thus, it may not be appropriate to extrapolate results of groundwater sampling directly from Opportunity to Anaconda. Lack of data for chemicals other than arsenic in Anaconda domestic groundwater is a potentially important data gap. Possible impacts of this data gap are discussed in Section 5.3.1.

Data Evaluation

Quality control results for the Bornschein data were presented in *Field and Laboratory Quality Control Results* (Roda 1995). A review of this report revealed that the lack of several key pieces of information prevented an assessment of the acceptability and useability of the data and an evaluation of bias and precision of the data. Much of the needed information was provided; however, data that would allow for the quantitative evaluation of data bias and precision were generally not available.

- For water samples, deficiencies included the lack of analysis of a continuing calibration blank and the lack of laboratory duplicates.
- In the interior dust data set, there were no analyses of preparation, method, or digestion blanks, nor was there an analysis of a continuing calibration blank. Laboratory duplicate analyses were conducted; however, it could not be determined whether duplicates were processed through the entire protocol, or if duplicate readings of the same sample were taken at the instrument.
- In the soil sampling investigation, no preparation blanks were prepared to assess whether cross-contamination occurred between samples. Independent reference material was not analyzed to check bias of the analytical system, nor were duplicate samples analyzed to assess precision.
- In the analysis of urine samples, key steps, including the digestion of organic arsenic and the use of an arsenic reducing agent, were not included in the written protocol. For the low standard (60 micrograms per liter [µg/L]), the mean reported value was 48 µg/L, with a range from 34 to 61 µg/L. On a percent recovery basis, the mean would be 80%, with a range from 56.7 to 101.7%. Urine values for arsenic near or below 60 µg/L are most likely biased low.

occupied room (usually living room or kitchen), and a floor area in the child's bedroom. Water samples were collected from the primary water faucet, normally the kitchen sink. Samples consisted of 100 milliliter (mL) taken immediately upon opening the tap. Water samples were collected in Anaconda only from a subset of 36 homes in subarea A that obtained drinking water from local groundwater.

In Anaconda, soil samples were collected from the yards of 280 homes, and indoor dust was sampled in 278 Anaconda homes. In Opportunity, soil and indoor dust were collected at 20 homes. Three homes in Lost Creek and 2 homes in Fairmont were sampled for soil and indoor dust. Tapwater samples were collected from a total of 61 homes: 36 in Anaconda, 20 in Opportunity, 3 in Lost Creek, and 2 in Fairmont. All of the tapwater samples were collected from homes using groundwater as the source of drinking water.

Soil samples were analyzed using atomic absorption (AA) for arsenic and lead; dust and water samples were only analyzed for arsenic. Method validation included cross checks with inductively coupled plasma-mass spectroscopy (ICP-MS). Analysis methods were consistent with EPA's Test Methods for Evaluating Solid Waste, Volume 1A: Laboratory Manual, Physical/Chemical Methods (EPA 1988a).

Indoor dust was not analyzed for lead. Since lead remains a COPC for soil in the communities, lead contamination of interior dust must be extrapolated from other data. This extrapolation is described in Section 3.3.1, and uncertainties associated with the extrapolation discussed in Section 5.3.3.

Tapwater was analyzed only for arsenic; therefore, it is possible that other contaminants could be present at significant concentrations. For Opportunity, this does not appear to be a significant data gap, since more complete metals analyses of drinking water in Opportunity (CDM Federal 1994a) did not detect any contaminants other than arsenic at significant concentrations. However, Opportunity is more distant from many waste sources and is

2.1.2.3 CDM Federal (1994a)

CDM Federal (1994a) collected a total of 20 groundwater samples from residential drinking water wells located in and near Opportunity. Sampled wells were chosen based on their location, depth, accessibility, tap location with respect to any storage tank, filtration device, or water softener, and owner permission. Because surface contamination is likely to affect the shallow portion of an aquifer first, samples were preferentially taken from wells completed less than 100 feet below grade. To the extent possible, samples were collected to provide the best representation of aquifer water quality (i.e., samples were collected before the water passed through any storage tank, filtration device, or water softener).

Samples were analyzed for metals and metalloids by ICP-MS according to EPA Method 200.8 with the exception of iron, which was analyzed according to EPA Method 6020 CLP-M. EPA Method 300.0 was used to analyze samples for sulfate.

Data Evaluation

Data were evaluated for precision, bias, and completeness. This evaluation concluded that all arsenic, copper, zinc, and sulfate data and 20% of the manganese data are enforcement quality. All cadmium, iron, and lead data and 80% of the manganese data were qualified because of elevated blanks and are considered screening quality. All data satisfied the Level B criteria.

Further, samples were collected from areas where exposure potential is high (i.e., where residents use local groundwater to supply drinking water), and sampling was focused on the shallowest wells, which are most likely to be impacted by surface contamination. A significant number of samples was collected from a variety of locations within the community. Given the number of wells sampled, and the relatively homogeneous distribution of surface contamination, it seems unlikely that there may be significant hot spots where

Evaluation of data quality is, therefore, based only on existing information. The results of this evaluation indicate that data from the environmental and biological samples can be assumed to be equivalent to screening quality data. This data evaluation is described in greater detail in a memorandum from D. Neuman, Reclamation Research Unit - Montana State University, to B. Alexander, CDM Federal, included as Appendix A.

Samples were collected from areas where exposure potential is considered high (i.e., yards and homes) and soil samples were collected from surface soil (0 to 2 cm). Further, a large number of samples is available for most subareas of the study. Thus, sampling protocols were sufficient to adequately characterize the distribution of surface contamination within reasonable exposure units for Opportunity and most of Anaconda. It is expected that data are representative of surface contamination in these communities, and groundwater contamination in subarea A of Anaconda and in Opportunity. Little or no data are available for Galen, Fairmont, and Warm Springs from this study, and no quantitative risk assessment would be appropriate for these areas based on the Bornschein data alone.

A more quantitative analysis of Bornschein data is consistent with the above conclusions. When these data are compared to data collected by PTI (1992 and 1993), there is little difference between the two data sets (Section 2.2). This increases the level of confidence in the soil data that were available.

Summary

The data are of sufficient quality and quantity to be used in a quantitative risk assessment of Anaconda and Opportunity. Data collected in Lost Creek and Fairmont are not of sufficient quantity to be used in a quantitative risk assessment. However, due to the proximity of Fairmont to Opportunity, these samples were combined into one area and referred to as Opportunity.

seems clear from examination of the analysis that similar results would be obtained regardless of which data set was used in the quantitative risk assessment. Thus, even if there are differences which are not readily detected statistically, they will have no substantive effect on the results of the risk assessment. The statistical analysis of these data sets is described in detail in Appendix B.

It is concluded that using either data set or a combination of the data will result in similar characterization of arsenic in surface soils for Anaconda and nearby communities. However, the Bornschein samples were collected from yards where actual exposure to children may occur. The PTI (1992 and 1993) soil samples were collected both from yards and pasture or idle land. Further, for arsenic, the Bornschein data contains paired soil and interior dust samples which provide a better characterization of the total exposure environment for children in Anaconda. Based on the above, it was concluded that the Bornschein data adequately characterizes concentrations of arsenic and lead in soil for the purposes of this assessment. Thus, the PTI data are not included in the quantitative risk assessment.

2.3 BACKGROUND SAMPLING

If site-specific background concentrations of COPCs are known, incremental risks (i.e., risks due to mine waste over and above any risks associated with exposure to background levels of chemicals) can be estimated. Site-specific background concentrations are defined in this HHRA as concentrations of chemicals present in soil or groundwater but unrelated to past smelting activities.

Background data compiled for the Mill Creek OU RI are suitable for use in this HHRA. For this investigation, background concentrations in soil and groundwater were established based upon available data for several regional Montana communities.

groundwater contamination is significantly higher than suggested in the data. The assumption that data can be used to represent potential groundwater quality in the community of Opportunity is reasonable.

Summary

The quality and quantity of the data collected by CDM Federal from residential wells in the community of Opportunity are sufficient for use in quantitative risk assessment.

2.2 COMPARABILITY OF AVAILABLE DATA

Soil investigations were conducted by PTI (1992 and 1993) and Bornschein (1992 and 1994), and there were initial concerns that soil arsenic concentrations from the two studies were not comparable. Therefore, data from both studies were evaluated statistically to determine:

(1) If significant differences exist between arsenic concentrations found in surface soil samples collected for these two studies in Anaconda and nearby communities on an area-by-area basis

(2) If significant differences do occur, whether these differences can be explained by differences in sampling methodology

If the differences between the two data sets were significant, a more extensive evaluation would have to be carried out to determine which data set best represents exposure conditions within the community.

Results of the statistical tests, however, indicate that PTI (1992 and 1993) data and Bornschein (1992 and 1994) data are not significantly different for eight of nine areas compared. Bornschein soil arsenic concentrations for subarea H were significantly greater (two-tailed p.= 0.05) than PTI soil arsenic concentrations. The statistical findings suggest that the two investigations sampled the same soil "population." Perhaps more importantly, it

2.3.2 BACKGROUND GROUNDWATER CONCENTRATIONS

The Mill Creek OU RI used background groundwater information gathered for the Anaconda Smelter RI/FS. For this study, a literature review and technical evaluation of background wells were conducted and nine background wells were sampled. Based on these data, ranges of background groundwater metals concentrations (µg/L) are:

Arsenic	1.6 - 12.6
Lead	0.9 - 5.0

Arsenic was detected infrequently in site samples collected from residential groundwater wells located in Anaconda, Opportunity, Lost Creek, and Fairmont. Concentrations of arsenic in these site groundwater samples, which ranged from non-detect to 13.8 µg/L, overlap with background concentrations of arsenic. Background arsenic may contribute significantly to total arsenic exposure via residential groundwater wells onsite.

Lead was not detected in site samples collected from residential groundwater wells in Opportunity.

2.4 SUMMARY OF DATA USED FOR QUANTITATIVE RISK ASSESSMENT

This section presents a brief description of the data used to calculated exposure point concentrations. Section 2.4.1 summarizes the overall data adequacy. Section 2.4.2 discusses the data for site soils, Section 2.4.3 discusses the data for site groundwater, and Section 2.4.4 discusses the data for interior dust.

Because of natural variations, background is considered as a distribution and not as a single value and is, therefore, reported as a range that represents the upper and lower 95% confidence interval of the mean.

2.3.1 BACKGROUND SOIL CONCENTRATIONS

Regional background soil samples were collected from non-impacted areas of Helena Valley and the Montana communities of Philipsburg, Townsend, and Livingston. Based on these regional data, ranges of background soil metals concentrations (mg/kg) are:

Arsenic	6 - 16
Lead	18 - 70

Soil concentrations of arsenic found at the site are significantly greater than background concentrations of arsenic in soil. It is unlikely that background concentrations of arsenic contribute significantly to total potential arsenic exposures. Background concentrations of lead in soil are generally less than reported for samples taken from the site. The mean concentration of lead in site soil is 384 mg/kg, compared to the maximum background value of 70 mg/kg. However, the lower end of the range of lead concentrations in site soil (23 - 2,153 mg/kg) overlaps background concentrations of lead in soil. These data suggest that background may not contribute greatly to potential lead exposures in areas where lead concentrations are high enough to present a significant risk. It is unknown whether background concentrations presented include potential contributions from lead-based paint. Background soil samples were collected from regional communities where lead-based paint could potentially be present. The latter is a potentially significant source of lead exposure in communities unrelated to past smelter operations.

2.4.3 GROUNDWATER

Anaconda

As described above, only the Bornschein study sampled water from the town of Anaconda. This study collected tapwater samples only from homes within subarea A, which use domestic groundwater as their drinking water source. Samples were analyzed only for arsenic. The public water supply of the town of Anaconda, used as the drinking water source for the other subareas, is from an area considered uncontaminated and is not contaminated by arsenic. Uncertainty regarding the presence of contaminants other than arsenic in domestic groundwater is discussed in Section 5.3.1.

Opportunity

Groundwater investigations in the town of Opportunity were conducted by Bornschein (1992 and 1994) and CDM Federal (1994a). Bornschein (1992 and 1994) collected tapwater samples from 20 homes in Opportunity that had private domestic wells. Samples were analyzed only for arsenic. CDM Federal (1994a) collected groundwater samples from 20 domestic wells in Opportunity and analyzed these samples for a suite of metals and metalloids. Only arsenic was detected in concentrations presenting a potential health hazard. Due to the relatively small number of samples available, groundwater data from both the CDM Federal (1994a) and Bornschein (1992 and 1994) studies are used to develop exposure point concentrations for arsenic in domestic groundwater in the town of Opportunity.

2.4.4 DUST

Residents may be exposed to contaminated interior dust in their home. As described above, Bornschein (1992 and 1994) collected a total of 479 interior dust samples from homes in Anaconda, Opportunity, Lost Creek, and Fairmont. These samples were analyzed only for

2.4.1 SUMMARY OF DATA ADEQUACY

The data evaluation identifies sufficient data to support quantitative risk assessment only for the communities of Anaconda and Opportunity. Sampling locations are too widely spread over the rest of the area addressed in this risk assessment to allow quantitative assessment. However, risk-based screening levels for arsenic are developed for receptors located in areas outside of Anaconda and Opportunity (Section 6.0). These screening levels can be used to help evaluate potential risks in these areas. For example, screening levels can be compared to isopleths for arsenic in surface soil to help identify geographic areas, if any, where current or future risks might be of concern. Likewise, screening levels can be compared with any additional data that may become available in the future, i.e., when land is developed, to identify geographic areas where potential risks may be unacceptable.

2.4.2 SOILS

As described above, surface soil samples used to calculate exposure point concentrations are selected from the Bornschein (1992 and 1994) study. In this study, soil and other media were sampled in the communities of Anaconda and Opportunity. Anaconda was separated into several subareas for this investigation to insure variation in potential risks within the town were adequately assessed. Numerous residential yards were sampled within each subarea, and several samples were collected from different locations within each yard, including the perimeter of the house, lawns, play areas, gardens and bare spots. All of these data are considered useful and are included in the exposure point concentrations calculations (Section 3.3.1).

arsenic. Anaconda was separated into several subareas for this investigation to insure a more representative assessment of potential risks. Data quality and quantity are considered sufficient for calculation of exposure point concentrations.

No data are available for lead in interior dust. Estimates of lead in dust are extrapolated from arsenic data (Bornschein 1992 and 1994) as described in Section 3.3.1.

3.0 EXPOSURE ASSESSMENT

The objectives of this exposure assessment are to identify potential human populations that may be exposed to site-related chemicals, determine the potential pathways through which exposure may occur, and estimate the magnitude, frequency, and duration of potential human exposures. Results of the exposure assessment for arsenic are presented as pathway-specific chronic daily intake (CDIs) for each receptor population. Lead exposures are estimated using the EPA IEUBK Lead Model, Version 0.99. The results of the exposure assessment for lead are presented as estimated blood-lead concentrations, integrated over possible exposure pathways, for each receptor population.

An exposure pathway generally consists of the following four elements:

- A chemical source and mechanism of release
- An environmental retention or transport mechanism for the released chemical
- A point of potential human contact with contaminated media
- A route of exposure (inhalation, ingestion, dermal absorption) at the point of contact

The absence of any one of the elements in an exposure pathway makes that pathway incomplete. No exposure is possible for incomplete pathways, and no CDIs can be calculated.

Section 3.1 describes the site setting, including the physical setting and potentially exposed populations. Section 3.2 identifies complete exposure pathways. Section 3.3 quantifies potential exposures. Section 3.4 compares predicted and measured exposures to arsenic. Section 3.5 discusses uncertainties associated with the exposure assessment.

3.1 CHARACTERIZATION OF SITE SETTING

The following sections characterize the physical setting and potentially exposed human populations within the Anaconda Smelter NPL Site. Discussion is focused on characteristics of the physical setting and of human populations that may influence potential exposures. This information supports the identification of complete exposure pathways in Section 3.2.

3.1.1 PHYSICAL SETTING

The Anaconda Smelter NPL Site is located in southwestern Montana, at the southern end of Deer Lodge Valley, approximately 25 miles northwest of the city of Butte (Figure 1-1). The site covers approximately 200 square miles, primarily in Deer Lodge County. The surface elevation in the study area ranges from 7,200 feet above mean sea level in the southwestern portion of the area to approximately 4,700 feet at its northeast corner.

3.1.1.1 Meteorology

The climate of Anaconda is classified as semi-arid with moderate wind conditions, long, cold winters, and cool summers (ARCO 1991). Climate in the higher mountain elevations is alpine to subalpine (MultiTech 1987). The average annual temperature measured in Anaconda is 43 degrees Fahrenheit (°F). The warmest month based on the 30-year average daily maximum temperature is July (79°F); the coldest month is January (14.5°F) based on the 30-year average daily minimum temperature.

Weather data collected for the period of 1951 to 1980 at the National Climatic Data Center (NCDC) site at East Anaconda (Montana No. 2604, elevation 5,511 feet) indicate the average annual precipitation is approximately 14 inches. The wettest months are May and June averaging 1.9 and 2.3 inches, respectively. The area receives at least 0.1 inch of precipitation

113 days/year. Mean annual snowfall in Anaconda is 63 inches, based on data for 1951 through 1974 (ARCO 1991).

Winds at the top of the smelter's smokestack generally blow at an average speed of about 11 miles per hour (mph), with gusts up to 80 mph (RCG 1995; Taskey 1972). Ground level winds range in speed from 3.6 to 4.1 meters per second (m/sec), or 7.9 to 9.1 mph (Life Systems 1993). Annual wind rose data indicate that prevailing winds are from the south to southeast, with lesser components from the north to northwest and southwest (CDM Inc. 1985).

3.1.1.2 Geology

The Anaconda Smelter NPL Site is located in and near the western margin of the southern Deer Lodge Valley in Deer Lodge County of southwestern Montana. This valley may be described as a north-south trending intermontaine valley bound at its margins by normal faults. The interior of the valley represents a structural downdropped block or graben. The foothills surrounding the valley are composed primarily of bedrock consisting of sedimentary, igneous, and metamorphic rocks of Tertiary to Pre-Cambrian geologic age.

The southern Deer Lodge Valley is predominantly filled with consolidated and semi-consolidated Tertiary sediments derived from weathering and erosion of the surrounding upland areas, and smaller amounts of Tertiary volcanics. Unconsolidated alluvium and glacial outwash deposits of Quarternary geologic age complete the stratigraphic section of valley fill material in the southern Deer Lodge Valley. As Quaternary valley fill deposits become saturated in the broad interior of the valley, they often represent the most prolific water-bearing material at the site.

3.1.1.3 Vegetation

Current vegetative cover is composed primarily of weedy grasses and shrubs, including Great Basin wildrye (*Elymus cinereus*), rabbit brush (*Chrysothamnus spp.*), and horsebrush (*Tetradymia canescens*) (Taskey 1972; ARCO 1991). Aspen (*Populus tremuloides*) are found on sheltered slopes and basins, and juniper (*Juniperus scopulorum* and *J. horizontalis*) are scattered on the hillsides (ARCO 1991; Taskey 1972). Willows (*Salix spp.*) occupy scattered portions of the drainages (ARCO 1991). Barren areas are found in the Anaconda area, including areas of Smelter Hill, Mount Haggin, the Old Works area, portions of Stucky Ridge, the Anaconda Ponds, the Opportunity Ponds, and the entire flatland between Willow Creek and Lost Creek east of Smelter Hill (RCG 1995). Generally, plant cover and diversity increase with distance from the smelter (Taskey 1972).

3.1.1.4 Hydrogeology

The principal aquifers at the site occur in the upper few hundred feet of alluvium, glacial outwash, and valley-fill located beneath the valley floor of the southern Deer Lodge Valley; alluvium and glacial outwash deposits in the Warm Springs Creek and Mill Creek tributary valleys; and in the lowland creek volcanics and Tertiary alluvial fan material underlying the surrounding foothills area. Typically, groundwater yields are highest from Quaternary alluvial and glacial outwash aquifers located beneath the valley floors of the southern Deer Lodge Valley and Warm Springs Creek and Mill Creek tributary valleys. These aquifers typically dominate groundwater use as a domestic and public water supply at the site.

The direction of groundwater flow is generally away from the upland areas of the site toward the central axis of the southern Deer Lodge Valley, then north following the direction of flow of the Clark Fork River. The alluvial aquifer at the site located beneath the southern Deer Lodge Valley is primarily recharged by valley through-flow from alluvial aquifers in the Warm Springs Creek, Mill Creek, and Silver Bow Creek, tributary valleys, in-flow of

groundwater from the surrounding bedrock aquifer through valley sidewalls, inflow from the underlying bedrock aquifer, infiltration of surface water along portions of perennial streams, infiltration of surface water from ponds and lakes, infiltration of surface water from irrigation, and direct infiltration of precipitation.

Depth to groundwater at the site is highly variable. The depth to groundwater below ground surface (bgs) in the alluvial aquifer in the vicinity of the southern Deer Lodge Valley ranges from less than 5 feet to approximately 50 feet. The depth to groundwater in the alluvial/glacial outwash aquifers in the Warm Springs Creek and Mill Creek tributary valleys ranges from approximately 10 feet to greater than 100 feet. Depth to groundwater bgs in the surrounding upland areas at the site range from approximately 25 feet to greater than 150 feet.

3.1.1.5 Hydrology

Five perennial streams, which are part of the Upper Clark Fork River system, are identified in the study area. These streams include Silver Bow Creek, Willow Creek, Mill Creek, Warm Springs Creek, and Lost Creek. The Mill-Willow Bypass, which is also located in the study area, redirects surface water flow from Willow Creek and Mill Creek around the Warm Springs Ponds. The confluence of Warm Springs Creek with discharge from the Warm Springs Ponds and the Mill-Willow Bypass forms the head waters of the Clark Fork River in the northeast portion of the study area.

Flow rates in perennial streams at the Anaconda Smelter NPL Site are typically high in the spring and early summer due to runoff of snowmelt and precipitation. Baseflow conditions typically prevail in late fall and winter.

Groundwater recharge of perennial streams at the site generally occurs along the lowermost reach of each stream, a short distance (1-3 miles) upstream of its confluence with the Clark

Fork River. Loss of surface water flow in perennial streams of the site to the alluvial aquifer typically occurs along their uppermost reach during periods of high flow.

3.1.2 POTENTIALLY EXPOSED POPULATIONS

A mixture of land uses in the study area suggest a variety of potential receptors. The focus of this assessment is on area residents, since data for non-residential areas outside of the communities of Anaconda and Opportunity are sparse and insufficient to support quantitative assessment. However, risk-based screening levels are developed for other receptors and land uses in Section 6.0. Thus, the following discussion includes characterization of current and likely future land uses throughout the study area.

3.1.2.1 Current Site Conditions

According to the *Anaconda-Deer Lodge County (ADLC) Comprehensive Master Plan* (Master Plan) (Peccia & Associates *et al.* 1990), 471,350 acres of the 472,320 total acres of county land area are identified as rural and the remaining 970 acres are urban. Much of the rural land is National Forest land used for conservation and recreational purposes. The majority of privately owned land is agricultural.

There are five communities located in the study area. These include Anaconda and Opportunity, for which risks will be quantitatively evaluated, and Fairmont, Warm Springs, and Galen. Anaconda is the largest community, with a population of approximately 10,000 persons (1990 census data). Anaconda has a public drinking water supply, which draws water from surface water and groundwater sources outside the area of potential impact of past smelter operations. Some homes in the Anaconda area, however, have private groundwater wells. Rural areas such as Opportunity, Warm Springs, Galen, and rural farm residences use groundwater wells to provide drinking water. Available information, however, suggests that contamination of currently used groundwater sources is minimal.

The portion of the Superfund Study Area in commercial and residential use is small, according to the Master Plan. Excluding the communities of Anaconda and Opportunity, the number of occupied housing units within the study area is 115, with the majority within Teressa Ann Terrace and Cedar Park Homes. Commercial uses cited by the Master Plan include the Town Pump store and gas station, a used car lot, and a racquetball club.

In the community of Anaconda, land is primarily residential, surrounding a commercial core area (Figure 3-1). The Opportunity area is a mixture of large- and small-lot residential with intermingled livestock grazing and mobile homes (Figure 3-2). The Master Plan also states that there are nine businesses located within Opportunity.

Residents of Anaconda and other communities participate in recreational activities such as dirt-bike riding, mountain biking, hiking, hunting, and swimming; these activities may result in exposure to arsenic and/or lead in soils within the study area.

Farms and residences are scattered throughout the site. Approximately 32% of Deer Lodge County is used for agricultural purposes, including crops like spring wheat, barley, oats, hay and potatoes; the average farm size in the county is 2,113 acres (personal communication, Montana Agriculture Line, 8/3/94). It is thought that local consumption of crops is minimal; crops are generally sold and dispersed to a wide range of areas. However, agricultural workers may be exposed directly to arsenic and lead in soils during agricultural activities, such as plowing, planting, field maintenance, and harvesting.

Residents may have private gardens in which fruits and vegetables are grown for personal consumption. Anaconda resident survey responses indicate consumption of locally grown fruits and vegetables is minimal (Bornschein 1993). Livestock production in Deer Lodge County is relatively low compared to other Montana counties; Deer Lodge County ranks as 53 out of 56 counties for beef production (personal communication, Montana Agriculture Line, 8/3/94). Farms may have cattle, sheep, and hogs; however, there are typically no more

FIGURE 3-1

Land Use in Anaconda

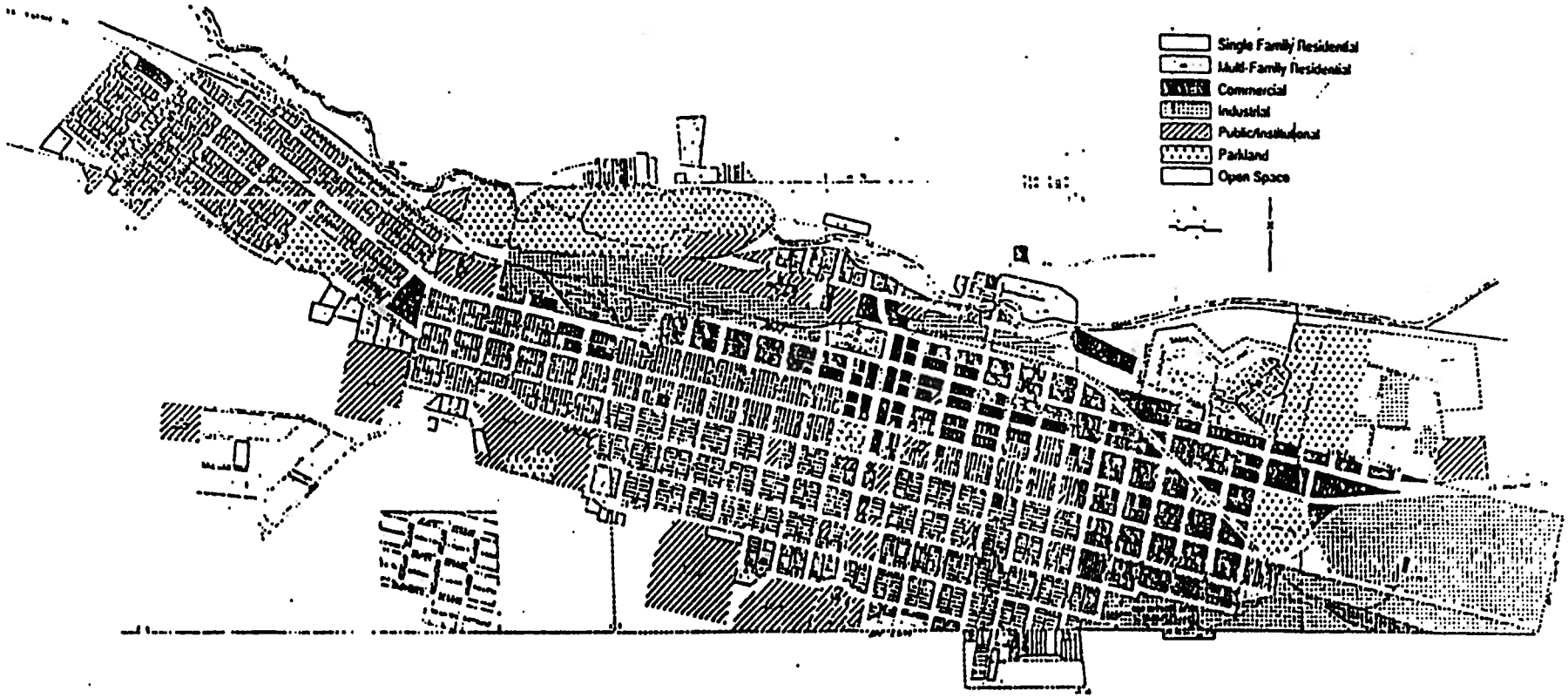
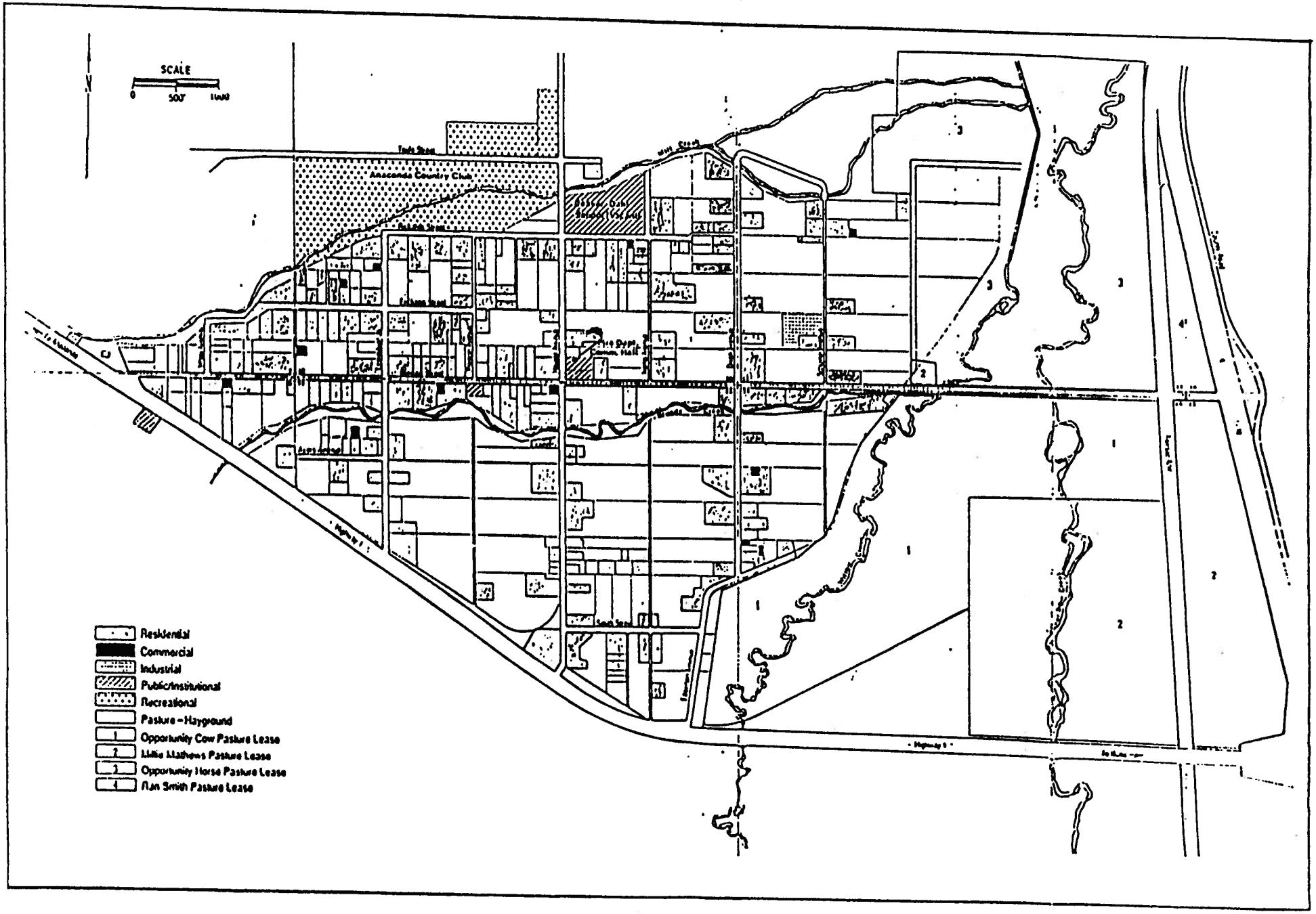


FIGURE 3-2

Land Use in Opportunity



than 2 animals per farm. Chickens are raised on most farms in the area. It is estimated that consumption of locally raised beef is low, as the majority of cattle raised are sold out of state (personal communication, Montana Agriculture Line, 8/3/94). Based on this information, it appears that exposure to arsenic and lead through the ingestion of local contaminated livestock is negligible. This assumption is supported by Anaconda resident survey responses (Bornschein 1993), which also indicated negligible consumption of locally grown livestock. Moreover, analyses in the Streamside Tailings (SST) OU HHRA (CDM Inc. 1994) indicates that, even if local livestock are consumed, exposure to arsenic and lead through this pathway is not expected to be significant due to the minimal concentrations sequestered in tissue.

3.1.2.2 Future Site Conditions

In the future, areas of the site that are currently undeveloped could be developed for a variety of purposes, including recreational, commercial, residential, or agricultural. Also, lands that are currently used for agricultural purposes could be developed for other uses, such as residential. Risk-based screening levels have been developed for such exposures.

In Anaconda, Opportunity, and the Superfund area, it is anticipated that county regulations and permit requirements described in the *ADLC Development Permit System* (ADLC DPS) (Peccia & Assoc. 1992) will facilitate the protection of Superfund remedies, and require future implementation of Superfund remedies when development occurs. The ADLC DPS was developed to carry out the policies of the Master Plan and is expected to be the primary public regulatory mechanism for controlling development in the Superfund and adjacent areas. It will set forth permissible arsenic levels for each land use (recreational, commercial, occupational, and residential) and a system for permitting based on these levels. Development would be prohibited unless a site has been, or as part of the development, will be remediated to protect human health. Also, the regulations adopted for the Superfund area are expected to protect sites with soil caps, barriers, or other structures from destruction through any proposed development. Limitations on development in sensitive areas, such as

wetlands, floodplains, in stream corridors, or in steep slopes, will also apply in the Superfund area.

Presently, permissible risk-based arsenic screening levels for recreational and commercial/occupational land uses have been established and incorporated into the ADLC DPS. These levels were derived in the *OW/EADA Baseline Risk Assessment* (Life Systems 1993). A permissible arsenic level for residential land use will be established as one outcome of this risk assessment.

3.1.2.3 Subpopulations of Concern

Subpopulations of concern are sensitive receptor populations who might be particularly susceptible to chemical exposure. They may include infants, the elderly, or individuals with respiratory problems depending on the COPCs and the nature of the exposures. Often exposure points for sensitive receptors include hospitals, nursing homes, schools, and day care centers. For this HHRA, sensitive receptors for exposures to lead have been identified as children ages 0 to 6 years. Children in this age range tend to have higher soil ingestion than older children and adults, and are more sensitive to adverse effects from exposure to lead.

3.1.2.4 Summary

Based on current and future land uses described above, the following populations are considered most likely to be exposed to arsenic and lead at the Anaconda Smelter NPL Site:

- Current and future residents
- Agricultural workers
- Recreational users
- Commercial workers

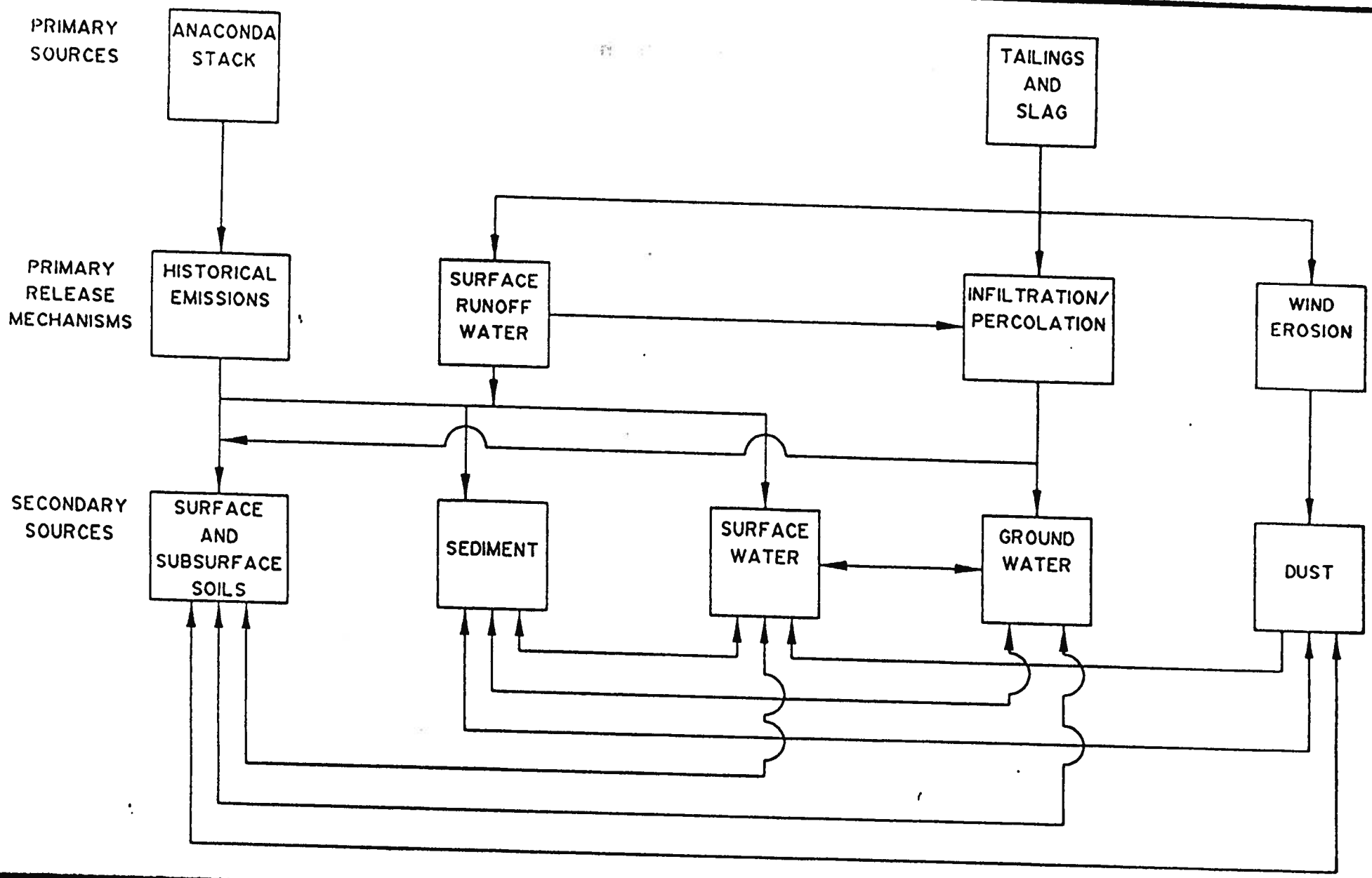
As described in Section 2, arsenic and lead concentrations in soil and groundwater outside of the towns of Anaconda and Opportunity are not adequately characterized due to the relatively small number of samples collected. Therefore, only risks to current residents of Anaconda and Opportunity are assessed quantitatively in this HHRA. Risk-based screening levels are, however, developed (Section 6.0) for other receptors.

3.2 IDENTIFICATION OF EXPOSURE PATHWAYS

The SCEM (Figure 3-3) for the Anaconda Smelter NPL Site presents primary sources of contamination, primary release mechanisms, secondary and tertiary sources of contamination, and potential human receptors. The SCEM presents reasonable pathways of exposure from primary sources of contamination to potential receptors. Each of these pathways is discussed below.

The two primary sources of contamination within the study area are historical air emissions from the Anaconda Smelter stack and from the tailings and slag remaining from the smelting process. Materials released from the stack were small particulates not captured by the emission controls in place at the plant. The primary release mechanism for tailings and slag is wind erosion, although some release via infiltration/percolation, and runoff has also occurred. Contamination in air emissions was/is transported via dry or wet deposition from the air into three secondary sources, soil, surface water, and sediment.

Contamination in the tailings and slag was also transported via infiltration/percolation into two secondary sources, soils and groundwater. In fact, some tailings are currently in contact with shallow groundwater. Finally, contamination in the tailings and slag is transported via runoff water into three secondary sources, soil, surface water, and sediment. The location of tailings and slag sources suggest that runoff would carry contaminants into sediments of nearby intermittent streams, and into permanent streams only indirectly.



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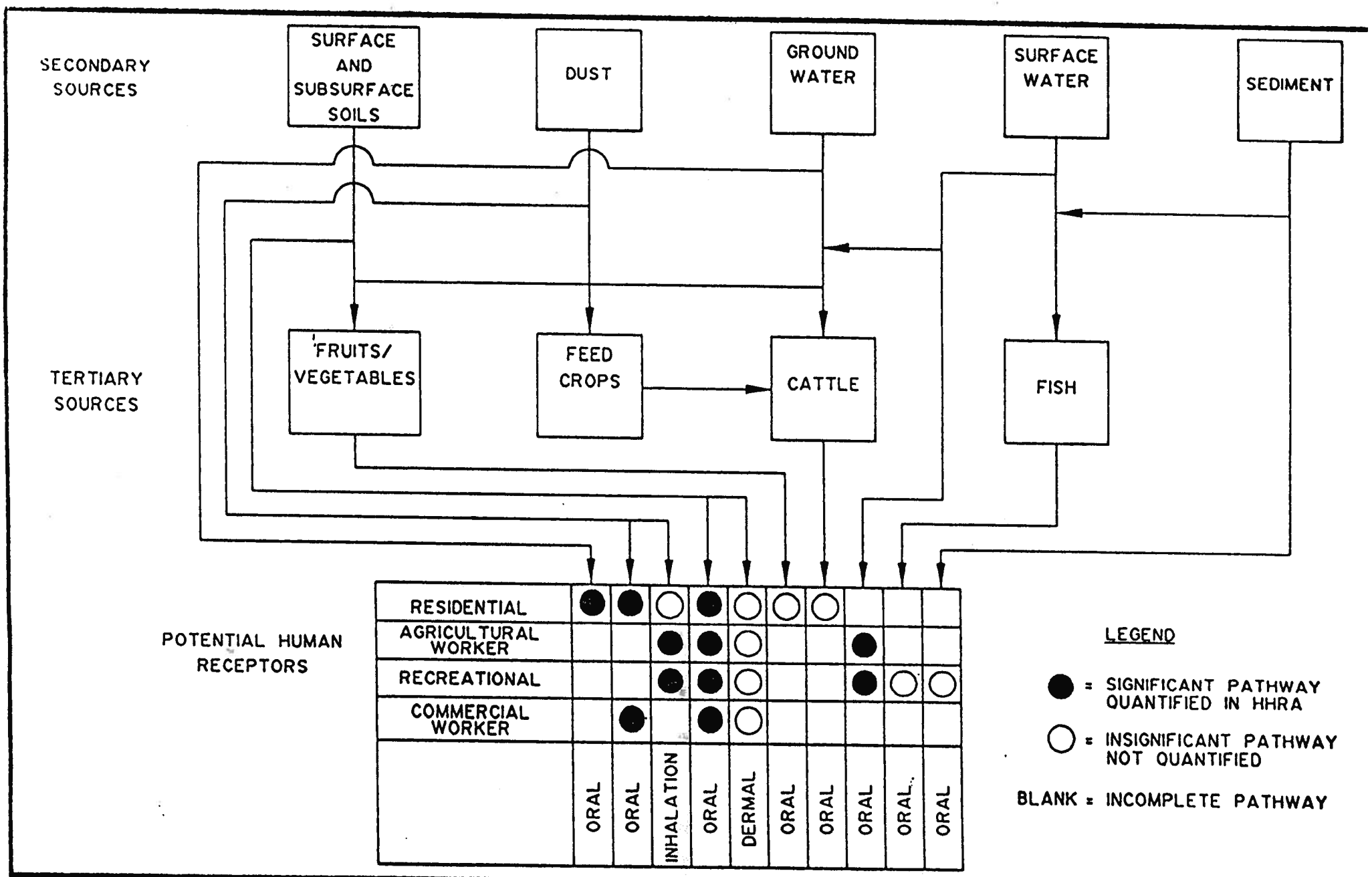
SITE CONCEPTUAL
EXPOSURE MODEL
ANACONDA

Figure 3-3



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SITE CONCEPTUAL EXPOSURE MODEL ANACONDA

Figure 3-3 cont.

Transport of contaminants can occur among the secondary sources. Contaminants in surface soils can be transported to surface water (via runoff), groundwater (via infiltration/percolation), and fugitive dust (via wind). Contaminants in sediment can be transported to surface water (via desorption/dissolution), groundwater (via infiltration/percolation), and fugitive dust (from a intermittent stream bed via wind). Contaminants in groundwater can be transported to sediment (via groundwater flow), surface water (via groundwater flow), and soils (via groundwater flow or use of groundwater as irrigation water). Surface water can transport contaminants to groundwater (via infiltration/percolation), sediment (via sorption/precipitation), and surface soils (via runoff or use of surface water as irrigation water). Contaminants in fugitive dust can be transported to surface water (via dry or wet deposition) and surface soils (via dry or wet deposition).

Contaminants may also move from secondary sources to tertiary sources. Tertiary sources include vegetables/fruits or crops, cattle, and fish. Crops can uptake contaminants from soil, absorb contaminants from surface water or groundwater, or absorb contaminants (via leaf) in fugitive dust. Cattle can ingest contaminants from crops, soil, sediment, groundwater, or surface water, or inhale contaminants in fugitive dust. Fish can ingest contaminants in sediment or surface water, or absorb contaminants from surface water.

Ingestion of Arsenic and Lead in Contaminated Surface Soil

Soils may have been contaminated by airborne historic smelter emissions, re-entrainment of contaminated dust, and runoff and erosion from waste piles. Children and adults typically ingest small amounts of soil through hand-to-mouth contact. This pathway is considered complete for residents, agricultural workers, recreational users (dirt bikers), and commercial workers. Estimates of potential exposure via this pathway to residents of Anaconda and Opportunity are presented in this HHRA. All other receptors are evaluated using risk-based screening levels (Section 6.0).

Ingestion of Arsenic and Lead Contaminated Interior Dust

Contaminants in soil may be transported indoors in air, tracked in on shoes, carried in on clothes or pets fur, etc. Once indoors, soil particles become part of interior dust. Children and adults typically ingest small amounts of dust through hand-to-mouth contact. This pathway is considered complete for residents and commercial workers. Estimates of potential exposure to residents of Anaconda and Opportunity are presented in this HHRA. Commercial workers are evaluated using risk-based screening levels (Section 6.0).

Inhalation of Arsenic and Lead in Contaminated Soil and Waste Particles in Air

Arsenic and lead forms at this site are not volatile; however, they may be released to the air from contaminated soils, dust, and waste piles as respirable particulate matter by wind or mechanical disturbances. Monitoring data indicate that levels of arsenic and lead in air are below current regulatory limits (Life Systems 1993). Therefore, inhalation of particulate matter released by wind erosion is not assessed quantitatively for residents or commercial workers. However, persons engaged in activities that result in the short-term release of large quantities of dust (i.e., farming, dirt-bike riding) may be exposed to high concentrations of arsenic and/or lead via inhalation of dust. Data are insufficient to quantify such exposures, however, for most areas within the scope of this HHRA. Therefore, agricultural and recreational exposure scenarios are evaluated in Section 6.0 through the use of risk-based screening levels.

Indirect Exposure to Arsenic and Lead through Ingestion of Fruits/Vegetables Grown in Contaminated Soil

Current or future residents might grow fruits and vegetables in soil contaminated by surface runoff from waste piles and/or by deposition of contaminated dust. These fruits and vegetables may take up chemicals from the soil into the edible portion of the plant. However,

as described in the HHRA for the Mine Flooding OU, Silver Bow Creek/Butte NPL Site, exposure through this pathway is not expected to contribute significantly to site-related risks, and is, therefore, not further evaluated in this risk assessment.

Indirect Exposure to Arsenic and Lead through Ingestion of Contaminated Meats

Current or future residents might raise livestock, such as cattle. Livestock could, in theory, take up arsenic and/or lead from ingested soil and food and sequester these chemicals in their tissues. However, information presented in the SST OU HHRA indicates that this is unlikely to occur in significant amounts. Additionally, local residents consume little locally grown livestock. Exposure through this pathway is expected to be negligible for arsenic and lead even where local livestock is consumed based on information presented in Section 3.1.2.1. This pathway is not likely to significantly contribute to site-related risks and is, therefore, not further assessed in this HHRA.

Indirect Exposure to Arsenic and Lead through Ingestion of Contaminated Fish

Several creeks flow through the Anaconda Smelter NPL Site (Section 3.1.1.5). Fish in these creeks can ingest arsenic and lead in sediment or surface water, or absorb arsenic and lead from surface water. Current or future residents and recreational users could be exposed through ingestion of these fish. Although this is a plausible exposure pathway, screening level calculations presented in Life Systems (1993) indicate that risks resulting from fish ingestion would be very low. Therefore, exposure from ingestion of contaminated fish is not evaluated further in this HHRA.

Ingestion of Arsenic in Contaminated Groundwater

Current residents in Anaconda and Opportunity use surface water and groundwater as sources of drinking water. Residents could be exposed if these drinking water sources are

contaminated by arsenic. Exposure through this pathway is evaluated in the risk assessment for residents in Anaconda and Opportunity.

Ingestion of Arsenic and Lead in Contaminated Surface Water

Surface water runoff following rainstorms and snowmelt has led to contamination of surface water and sediment in site creeks. Area residents might visit affected creeks and be exposed to surface water through incidental ingestion during wading and other water play activities. Exposure to arsenic and lead might also occur through aquatic recreation in a small pool near Opportunity Ponds. It seems unlikely that such exposures would be associated with significant risks, based on the results of the risk assessment recently completed for the SST OU of the Silver Bow Creek NPL Site (CDM Inc. 1994). Surface water and sediment are heavily contaminated with arsenic and metals in this OU, yet even conservative estimates of potential exposures were not associated with significant risk. Risk-based screening concentrations are developed in Section 6.0 for this exposure pathway.

Dermal Exposure to Arsenic and Lead in Contaminated Surface Water

Only recreational users of surface water within the study area would be potentially exposed through this pathway. Lead is not expected to be significantly absorbed across the skin and several risk assessments performed for sites within the Clark Fork Basin have concluded that dermal exposure is insignificant for this metal. Dissolved arsenic in surface water may, however, be absorbed to some extent, although significant exposures are not expected based on results of the SST OU risk assessment (CDM Inc. 1994). This pathway is addressed using risk-based screening levels developed in Section 6.0.

Ingestion of Arsenic and Lead in Contaminated Sediment

Potential exposures for recreational visitors could occur during visits to surface water in the study area. Incidental ingestion of sediments might occur in much the same way as incidental ingestion of soils. However, recreational visitors are assumed to spend the majority of their time in the water, where sediments are not expected to adhere to skin. Additionally, visitors are assumed to bathe following swimming. Therefore, this HHRA assumes that contact with sediments would be minimal. This pathway is, therefore, considered insignificant and exposure to recreational users is not quantified in this HHRA.

Dermal Exposure to Arsenic and Lead in Contaminated Soil

It is expected that residents, recreational users, agricultural workers, and commercial workers might have dermal contact with contaminated soil. Only limited data are available on the rate at which metals cross the skin into the blood from soil or dust particles; therefore, dermal exposure to metals was not included in the quantitative assessment. It is not considered likely that omission of this pathway causes a significant underestimate of risk because uptake of metals across the skin, especially from soil, is generally believed to be minor.

Summary

From the information above, pathways of concern are:

Exposure Pathways for Residents (Adults and Children Ages 0 - 6):

- Ingestion of surface soils
- Ingestion of interior dust
- Ingestion of groundwater

Agricultural Workers (Adults):

- Ingestion of surface soils
- Inhalation of dust

Recreational Users (Dirt Bike Riders):

- Ingestion of surface soils
- Inhalation of dust

Recreational Visitors (Swimmers):

- Ingestion of surface water
- Dermal exposure to surface water

Commercial Workers (Adults):

- Ingestion of surface soils
- Ingestion of interior dust

3.3 QUANTIFICATION OF EXPOSURE

The amount of a chemical that receptor populations take into their bodies following exposure is referred to as chemical intake. The CDI is expressed in units of milligrams of chemical per kilogram of body weight per day (mg/kg-day) and is the standard expression of long-term daily exposure. Intake depends on the exposure point concentration of chemicals in a medium (e.g., groundwater), and exposure assumptions specific to the receptor population, including how often and how long the exposure occurs (exposure frequency and duration), body weight, and contact rate. Depending on the exposure route, contact rate is equivalent to the volume of food, water, or soil ingested, air inhaled, or surface water contacted dermally each day. The period of time over which exposure is averaged, or the averaging time, is used to convert total intake into daily intake.

Section 3.3.1 describes the estimation of exposure point concentrations. Pathway-specific and general exposure assumptions (e.g., frequency and duration of exposure) are provided in Section 3.3.2.

3.3.1 ESTIMATION OF EXPOSURE POINT CONCENTRATIONS

Exposure point concentrations are estimates of the level of a COPC in a medium at the exposure point. The approaches used in this HHRA to calculate exposure point concentrations for different media are as follows:

3.3.1.1 Soils

As described above, only Bornschein (1992 and 1994) soil sampling data are used to evaluate risks. In this study, Anaconda was separated into subareas (A, B, C, D, E, F, I, and J) to better characterize possible differences in exposure conditions within the community. For this assessment, subarea F, the subarea closest to Smelter Hill, was subdivided into areas F1 and F2 to ensure that potential exposures in this area were adequately addressed (Figure 2-1). Opportunity was retained as a separate study area (subarea G). Numerous yards within each subarea were sampled and soil was collected from several locations within each yard, including play, house perimeter, garden, hardpack, and bare areas. Soil concentrations for arsenic and lead from all of these samples were averaged for each yard[1]. An exposure point concentration for arsenic was derived for each area by calculating the 95% upper confidence limit (UCL) of the mean (EPA 1992b) of the arithmetic average soil concentrations for each residence assuming lognormal distribution. Use of the 95% UCL provides reasonable confidence that the average concentration will not be underestimated. Arsenic exposure point concentrations for soils of each subarea are shown in Table 3-1.

Lead intake is evaluated by the IEUBK Lead Model, Version 0.99. Average lead concentrations in soils of each subarea, rather than the 95% UCL of the mean, are used as lead exposure point concentrations (Table 3-2).

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[1] Averaging of all soil samples for each yard will tend to minimize any contribution of lead paint that is present.

TABLE 3-1

Anaconda Summary Statistics for Soil Data (Arsenic mg/Kg)

Sample Area	Sample Number	Geometric Mean	Arithmetic Mean	Ln_STD	Minimum Detection	Maximum Detection	95th UCL
Area A	44	82.27	86.92	0.34	38.40	171.20	95.76
Area B	60	130.84	138.97	0.35	59.33	229.80	150.52
Area C	17	183.46	191.43	0.30	107.50	306.33	221.65
Area D	11	214.86	225.26	0.34	136.00	340.00	282.23
Area E	47	190.57	195.31	0.22	92.00	292.50	206.31
Area F1	52	237.46	246.36	0.28	126.50	409.25	264.60
Area F2	36	190.57	204.30	0.39	82.50	373.50	231.64
Area I*	3	109.73	117.13	0.45	67.50	165.50	830.91
Area J	10	132.95	140.66	0.36	64.00	193.60	181.24
OPPORTUNITY	22	122.73	127.56	0.30	128.90	219.25	145.05

*Area I should use max detect because of limited sample number (3)

TABLE 3-2

Summary of Soil Lead Data

Exposure Area	Number of Residences	Minimum Concentration (mg/kg)	Maximum Concentration (mg/kg)	Average Concentration (mg/kg)	Standard Deviation
A	44	19.80	312.00	75.92	54.42
B	60	44.60	1183.00	256.65	215.04
C	17	57.20	851.00	476.49	245.23
D	11	110.20	812.50	419.37	230.53
E	47	110.00	1388.00	581.66	282.04
F1	52	111.00	2152.70	533.99	302.75
F2	36	60.00	1220.20	508.14	288.65
I	3	60.50	87.00	75.03	13.44
J	10	14.30	303.20	191.20	88.43
Opportunity	22	46.20	351.20	133.98	81.85
ALL AREAS	302	14.30	2152.70	364.03	297.24

3.3.1.2 Dust

The dust data for arsenic were provided in the Bornschein (1992 and 1994) study. Interior dust samples were collected from homes in Anaconda and Opportunity. Three interior dust samples were commonly taken for each residence. Data from a single residence were averaged prior to calculation of exposure point concentrations. Statistical tests of dust arsenic concentrations suggest a lognormal distribution. Therefore, data were logtransformed and arsenic exposure point concentrations derived for each subarea by calculating the 95% UCL of the arithmetic mean (EPA 1992b) for the lognormalized data (Table 3-3).

Dust samples were not analyzed for lead. However, analysis of paired soil and interior dust measurements for arsenic suggest a transfer coefficient of 0.43 for movement from soil to dust (Bornschein 1994). That is, concentrations of arsenic in indoor dust are about 43 percent of arsenic concentrations in outdoor soil. This value is derived from multiple regression analyses performed by Bornschein (1994) on data collected during the Anaconda arsenic exposure study, and represents information from paired soil and dust samples from over 300 locations. If arsenic and lead in smelter wastes are assumed to move in similar fashion from soil into dust, then the arsenic coefficient can be used to estimate transfer of lead.

In addition to a transfer coefficient, it is expected that there will be a "background" level of lead in homes unrelated to outdoor soil. This background may be represented by the y-intercept of the soil/dust regression line. Since no dust lead measurements have been made in Anaconda, the y-intercept must be obtained indirectly, again using the arsenic data. If arsenic is used as a surrogate for lead, a constant term for lead can be calculated assuming that the ratio of the constant term for average soil lead to indoor dust lead is the same as the parallel ratio for arsenic.

The approach used to estimate the above ratio for arsenic in this assessment follows that recommended by EPA (1995e). This guidance suggests that a "y-intercept", or constant term,

TABLE 3-3

Anaconda Summary Statistics for Dust Data (Arsenic mg/Kg)

Sample Area	Sample Number	Geometric Mean	Arithmetic Mean	Ln_STD	Minimum Detection	Maximum Detection	95th UCL
Area A	44	50.40	57.68	0.51	17.80	153.40	66.54
Area B	60	57.97	66.10	0.50	19.30	284.40	74.20
Area C	17	46.53	56.84	0.64	14.90	157.10	79.90
Area D	11	121.51	130.07	0.38	67.00	277.90	166.09
Area E	47	83.93	91.20	0.39	37.00	237.90	100.44
Area F1	51	116.75	130.74	0.49	29.00	393.60	149.90
Area F2	36	95.58	106.17	0.48	19.70	224.40	125.13
Area I*	3	44.26	54.30	0.77	23.10	103.40	16228.33 ?
Area J	9	52.98	57.79	0.47	20.65	95.87	86.72
OPPORTUNITY	22	75.19	83.07	0.45	33.30	205.40	100.76

*Area I should use max detect because of limited sample number (3)

can be estimated as the average of measured values that are less than some given percentage of the mean. It is found that only four measurements of arsenic in indoor dust contain arsenic at concentrations of 25 percent of the mean or less. These four measurements are thus taken to indicate "background" for indoor arsenic in dust. The average of these four measurements is about 18 mg/kg. Since the average arsenic concentration in outdoor soil for the same data set is 175 mg/kg, the constant term for arsenic is 10 percent of the site-wide average outdoor soil level.

Extrapolating measurements of arsenic in soil and dust to lead results in the following equation for estimating interior lead concentrations.

$$PB_{dust} = (0.43 \ x \ PB_{soil}) + (0.1 \ x \ mean \ PB_{soil})$$

Where:	PB_{dust}	=	the interior dust lead concentration (mg/kg)
	PB_{soil}	=	the average subarea soil lead concentration (mg/kg)
	mean PB_{soil}	=	the community-wide average lead concentration for Anaconda

Since the sitewide average lead concentration in outdoor soil is 364 mg/kg, the constant term for lead is estimated to be about 36 mg/kg. Interior dust lead concentrations for the different subareas are shown in Table 3-4. Use of the above equation assumes that transport of arsenic and lead from soil to dust is similar, and ignores any potential contribution from interior lead-based paint. This adds uncertainty to estimates of lead exposure within the study area.

3.3.1.3 Groundwater

Bornschein (1992 and 1994a) sampled tapwater in subarea A of Anaconda, from homes using groundwater as their source of drinking water, and in the town of Opportunity. CDM Federal (1994a) sampled domestic groundwater wells in Opportunity.

TABLE 3-4

Calculated Concentrations of Lead in Indoor Dust

Subarea	(mg/kg)
A	69.0
B	146.8
C	241.3
D	216.7
E	286.5
F1	266.1
F2	254.9
I	68.7
J	118.6
Opportunity	94.0
All Areas	192.9

Samples collected by Bornschein (1992 and 1994) were analyzed only for arsenic. Samples were not analyzed for lead. Lead was not detected in samples collected by CDM Federal (1994a). Therefore, default values for lead in drinking water were used in the IEUBK model.

Separate arsenic exposure point concentrations were developed for Anaconda and Opportunity drinking water (Table 3-5). The exposure point concentration for drinking water is the 95% UCL of the mean (EPA 1992b) for all of the arsenic concentrations measured in drinking water of subarea A and Opportunity. Although it is unlikely that individuals would be exposed to drinking water from multiple domestic wells, wells were combined to provide total population risk for the subareas. An arsenic concentration of nondetect was used for subareas in Anaconda which obtain drinking water from the public water supply. It should be noted that the large number of non-detects and low detections, especially in Opportunity, make it difficult to determine the appropriate data distribution. Thus, the default, using normal statistics, was used in accordance with EPA guidance (EPA 1992b).

3.3.1.4 Data Manipulation

When a chemical was detected in a medium (i.e., surface soils), samples having no detection for that chemical in the same medium were treated as if they contained the chemical at one-half the detection limit. Further, if the chemical is present in a sample below the sample quantitative limit (SQL), EPA recommends using one-half the SQL as a proxy concentration. This methodology follows recommendations in EPA's *Risk Assessment Guidance for Superfund, Part A* (1989a), which suggests that concentrations most representative of potential exposure at a site will consider both positively detected results and non-detected results within appropriate exposure units.

TABLE 3-5

Arsenic Exposure Point Concentrations
in Groundwater - Anaconda Smelter NPL Site

AREA	Sample Number	FOD	Min (ug/L)	MAX (ug/L)	Arithmetic Mean (ug/L)	95th[1] UCL (ug/L)
ANACONDA	36	92%(33/36)	1.1	9.9	2.46	2.91
OPPORTUNITY	42	21%(9/42)	1.1	13.8	1.73	2.45

[1]Because of the low frequency of detection (FOD) for the Opportunity data (21%), the data are neither normal or lognormally distributed. The distribution of the Anaconda data is rather flat. The 95th percent upper confidence limit of the arithmetic mean (UCL), used as the exposure point concentration, was calculated with the student-T normal distribution formula, shown below.

UCL= mean + t(standard deviation / square root of sample number).

3.3.2 EXPOSURE ASSUMPTIONS

Pathway-specific CDIs are estimated using exposure point concentrations and exposure assumptions specific to the receptor population. Generally, exposure assumptions are selected so that their combination results in an estimate of the reasonable maximum exposure (RME) for that pathway (EPA 1989a). RME is defined as an exposure well above the average but still within the range of those possible. Recent guidance (EPA 1992c) suggests that the RME should fall in the range of the 90th to the 99.9th percentile of possible exposures.

It is expected that different people will have different levels of contact with contaminated media, therefore, a range of exposures is also provided by estimating the central tendency exposure (CTE) for each exposure pathway. CTE uses exposure assumptions that predict an average or best estimate exposure to an individual. The presentation of risks for both RME and CTE scenarios provides the risk manager a range of risk for the site.

In keeping with EPA risk assessment guidelines (EPA 1989a), exposure assumptions derived from site-specific data are used when available, so that risks can be evaluated on a case-by-case basis. Where site-specific data are unavailable, standard EPA default assumptions for both RME and CTE exposures are used in accordance with EPA guidance (EPA 1989a, 1989b, 1991b, 1993a). The following is a discussion of exposure assumptions used to quantify intakes for the residential scenario.

Exposure assumptions are summarized in Tables 3-6 to 3-9.

3.3.2.1 Exposure Assumptions Common to All Pathways

The RME uses upper range estimates for some, but not all, exposure assumptions so that their combination results in a reasonable upper range estimate of exposure for that pathway. On the other hand, CTE uses best estimates for most exposure assumptions to estimate exposures

VARIABLES COMMON TO ALL EXPOSURE EQUATIONS
ANACONDA SMELTER SITE
CENTRAL TENDENCY EXPOSURE

Variable Symbol	Variable Definition	Variable Values That Could Be Selected	Variable Value Selected/Percentile	Reason for Variable Selection	Reference
BW	Body Weight	0 - 80 kg			
	Adult (residential)	67 - 72 kg	70 kg	Recommended by EPA	EPA 1993b
	Child (residential, age 0-6 years)	11 to 17 kg	15 kg	Recommended by EPA	EPA 1993b
AT	Averaging Time				
	Carcinogenic	365 days x 70 years	365 days x 70 years	Recommended by EPA	EPA 1989a
	Noncarcinogenic	Varies with ED	365 days x ED	Recommended by EPA	EPA 1989a
ED	Exposure Duration				
	Adult (residential)	0 - 70 years			
	Carcinogenic		7 years	Recommended by EPA	EPA 1993b
	Noncarcinogenic		7 years	Recommended by EPA	EPA 1993b
	Child (residential, age 0-6 years)	0 - 6 years			
	Carcinogenic		2 years	Recommended by EPA	EPA 1993b
	Noncarcinogenic		2 years	Recommended by EPA	EPA 1993b

VARIABLES COMMON TO ALL EXPOSURE EQUATIONS
ANACONDA SMELTER SITE
REASONABLE MAXIMUM EXPOSURE

Variable Symbol	Variable Definition	Variable Values That Could Be Selected	Variable Value Selected/Percentile	Reason for Variable Selection	Reference
BW	Body Weight	0 - 80 kg			
	Adult (residential)	67 - 72 kg	70 kg	Recommended by EPA	EPA 1993b
	Child (residential, age 0-6 years)	11 to 17 kg	15 kg	Recommended by EPA	EPA 1993b
AT	Averaging Time				
	Carcinogenic	365 days x 70 years	365 days x 70 years	Recommended by EPA	EPA 1989a
	Noncarcinogenic	Varies with ED	365 days x ED	Recommended by EPA	EPA 1989a
ED	Exposure Duration				
	Adult (residential)	0 - 70 years			
	Carcinogenic		24 years	Recommended by EPA	EPA 1993b
	Noncarcinogenic		24 years	Recommended by EPA	EPA 1993b
	Child (residential, age 0-6 years)	0 - 6 years			
	Carcinogenic		6 years	Recommended by EPA	EPA 1993b
	Noncarcinogenic		6 years	Recommended by EPA	EPA 1993b

VARIABLES ASSOCIATED WITH SPECIFIC PATHWAYS
ANACONDA SMELTER SITE
CENTRAL TENDENCY EXPOSURE

Variable Symbol	Variable Definition	Range of Variable Values	Variable Value Selected	Reason for Variable Selection	Reference
WATER					
IR - Used for Ingestion of Groundwater					
	Ingestion Rate	0 - 2.8 L/day			
	Adult (residential)	0.69-2.8L/day	1 L/day	Recommended by EPA	EPA 1993b
	Child (residential, age 0-6 years)	0.69 - 0.93 L/day	0.7 L/day	Consistent with CTE	
BAF - Bioavailability of Arsenic in Water					
	BAF of Arsenic in Water	0 - 100%	100% percent	Site-specific data	EPA 1995
EF - Used for Ingestion of Groundwater					
	Exposure Frequency	0 - 365 days/yr			
	Adult (residential)	0 -365 days/yr	234 days/yr	Recommended by EPA	EPA 1993b
	Child (residential, age 0-6 years)	0 -365 days/yr	234 days/yr	Recommended by EPA	EPA 1993b
SOIL AND DUST					
IR - Used for Ingestion of Surface Soil and Dust					
	Ingestion Rate	0 - 480 mg/day			
	Adult (residential)	0 - 480 mg/day	50 mg/day	Recommended by EPA	EPA 1993b
	Child (residential, age 0-6 years)	0 - 480 mg/day	100 mg/day	Recommended by EPA	EPA 1993b
FI - Used for Ingestion of Surface Soil					
	Fraction Ingested from Source	0 - 100%			
	Adult (residential)	0 - 100%	45%		
	Child (residential, age 0-6 years)	0 - 100%	45%		
BAF - Bioavailability of Arsenic in Soil					
	BAF of Arsenic in Soil	0 - 100%	18.30%	Site-specific data	EPA 1995
FI - Used for Ingestion of Interior Dust					
	Fraction Ingested from Source	0 - 100%			
	Adult (residential)	0 - 100%	55%		
	Child (residential, age 0-6 years)	0 - 100%	55%		
BAF - Bioavailability of Arsenic in Dust					
	BAF of Arsenic in Dust	0 - 100%	25.80%	Site-specific data	EPA 1995
EF - Used for Ingestion of Surface Soil and Interior Dust					
	Exposure Frequency	0 - 365 days/yr			
	Adult (residential)	0 -365 days/yr	350 days/yr	Recommended by EPA	EPA 1992a
	Child (residential, age 0-6 years)	0 -365 days/yr	350 days/yr	Recommended by EPA	EPA 1992a

VARIABLES ASSOCIATED WITH SPECIFIC PATHWAYS
ANACONDA SMELTER SITE
REASONABLE MAXIMUM EXPOSURE

Variable Symbol	Variable Definition	Range of Variable Values	Variable Value Selected	Reason for Variable Selection	Reference
WATER					
IR - Used for Ingestion of Groundwater					
	Ingestion Rate	0 - 2.8 L/day			
	Adult (residential)	0.69-2.8L/day	2 L/day	Recommended by EPA	EPA 1993b
	Child (residential, age 0-6 years)	0.69 - 0.93 L/day	1 L/day	Recommended by EPA	EPA 1993b
EF - Used for Ingestion of Groundwater					
	Exposure Frequency	0 - 365 days/yr			
	Adult (residential)	0 -365 days/yr	350 days/yr	Recommended by EPA	EPA 1993b
	Child (residential, age 0-6 years)	0 -365 days/yr	350 days/yr	Recommended by EPA	EPA 1993b
SOIL AND DUST					
IR - Used for Ingestion of Surface Soil and Dust					
	Ingestion Rate	0 - 480 mg/day			
	Adult (residential)	0 - 480 mg/day	100 mg/day	Recommended by EPA	EPA 1993b
	Child (residential, age 0-6 years)	0 - 480 mg/day	200 mg/day	Recommended by EPA	EPA 1993b
FI - Used for Ingestion of Surface Soil					
	Fraction Ingested from Source	0 - 100%			
	Adult (residential)	0 - 100%	45%		
	Child (residential, age 0-6 years)	0 - 100%	45%		
BAF - Bioavailability of Arsenic in Soil					
	BAF of Arsenic in Soil	0 - 100%	18.30%	Site-specific data	EPA 1995
FI - Used for Ingestion of Interior Dust					
	Fraction Ingested from Source	0 - 100%			
	Adult (residential)	0 - 100%	55%		
	Child (residential, age 0-6 years)	0 - 100%	55%		
BAF - Bioavailability of Arsenic in Dust					
	BAF of Arsenic in Dust	0 - 100%	25.80%	Site-specific data	EPA 1995
EF - Used for Ingestion of Surface Soil and Interior Dust					
	Exposure Frequency	0 - 365 days/yr			
	Adult (residential)	0 -365 days/yr	350 days/yr	Recommended by EPA	EPA 1992a
	Child (residential, age 0-6 years)	0 -365 days/yr	350 days/yr	Recommended by EPA	EPA 1992a

near the average of the possible range. Some assumptions are, however, common to both RME and CTE estimates. The following exposure assumptions are used for all CDI calculations. Table 3-6 presents the CTE assumptions common to all pathways, and RME assumptions are presented in Table 3-7.

Body Weights

For adult residents, the value selected for body weight (BW) is 70 kg. This is the representative mean BW for men and women between the ages of 18 and 75 (EPA 1993a). For child residents, a BW of 15 kg is used (EPA 1993a).

Averaging Time

Averaging time (AT) is the period in days over which chemical intakes are averaged. For noncarcinogenic chemicals, intakes are averaged over the exposure duration (ED) (ED X 365 days). For carcinogens, intake calculations average the total cumulative dose over a lifetime (assumed to be 25,550 days for a 70-year lifetime). Averaging times differ for carcinogens and noncarcinogens, because the effects of carcinogenic chemicals are assumed to have no threshold. Therefore, any exposure to a carcinogen carries a finite risk of causing cancer during the lifetime of the individual. Within reason, this means that a single large exposure to a carcinogen is expected to carry the same risk as the same total dose divided up into many small exposures. It is therefore most convenient to express intakes of carcinogens in terms of lifetime exposures, regardless of the actual exposure duration (EPA 1989a).

Exposure Frequency

For the soil and dust ingestion pathway, an exposure frequency (EF) of 350 days/year is used as the amount of time a person is at home for both the RME and CTE scenarios (EPA 1993a). This value assumes that a person spends part or all of each day of the year at home,

except for 15 vacation days and is considered appropriate for the soil ingestion pathway (EPA 1993a). For groundwater ingestion, an EF of 350 days/year is used for the RME scenario (EPA 1993a). For the CTE scenario, an EF of 234 days/year is used. This corresponds to the fraction of time estimated that is actually spent at home for both men and women (64%) (EPA 1993a).

Exposure Duration

EDs of 24 and 6 years are used for adult and child RME estimates, respectively (EPA 1993a). This results in ATs for adult and child noncarcinogenic exposures of 8,760 days and 2,190 days, respectively. For the CTE exposure duration, 7 and 2 years are used for adult and child residents, respectively, resulting in ATs for adult and child noncarcinogenic exposures of 2,555 and 730 days, respectively (EPA 1993a).

3.3.2.2 Site-Specific Exposure Assumptions

Pathway specific assumptions for CTE and RME exposures are described below, and presented in Tables 3-8 and 3-9, respectively.

Assumptions for Bioavailability of Arsenic from Soils and Dust

EPA has used the available data to derive site-specific arsenic bioavailability estimates for ingested soil and dust (EPA 1994a, 1995a). These data describe the arsenic concentrations in blood, urine, and feces collected from Cynomolgus monkeys exposed to arsenic by intravenous injection, gavage, and oral administration of capsules containing soil or dust collected in Community Soils OU (Battelle 1994). Arsenic bioavailability was measured as the ratio of the area under the curve (AUC) for arsenic in urine and blood following administration of soil or dust capsules, compared to that following intravenous administration adjusted for the difference in the size of the dose.

Mean absolute bioavailability estimates derived from urine arsenic concentrations were 91%, 18.3% and 25.8%, respectively, for gavage, soil, and dust. Absolute bioavailability estimates derived from blood arsenic concentrations were similar and ranged between 91% and 100% for gavage, 11% and 18% for soil ingestion and 8% and 11% for dust. The results of this study demonstrate that the absorption of arsenic from soils and dust is significantly less than absorption of soluble arsenic from water. Further, the results confirm the previous assumption of nearly complete absorption of ingested dissolved arsenic.

Results from the bioavailability study have been extensively reviewed and are thought to be reasonable site-specific estimates for human bioavailability. They are used directly in this assessment, as follows:

- 25.8% bioavailability for dust
- 18.3% bioavailability for soil
- 100% bioavailability for water

Further discussion of the derivation of these values can be found in an EPA (1995a) memorandum from C. Weis (EPA) to C. Coleman (EPA), describing the EPA review of the Battelle Columbus report: *Determination of the bioavailability of soluble Arsenic and Arsenic in soil and dust impacted by Smelter Activities following oral administration in Cyanomolgus monkeys. Amended Final Report.* This memorandum is included as Appendix C.

Selection of Soil and Dust Ingestion Rate for Children Living in Anaconda

A week-long measurement of soil and dust ingestion in 64 children living in Anaconda was performed by Dr. Edward Calabrese. Using a single "best tracer" methodology, the soil and dust ingestion rate median was 51 mg/day, the mean was 117 mg/day, and the 90th percentile was 277 mg/day. The "four best tracers" study resulted in an ingestion rate median of 39 mg/day, a mean of 83 mg/day and a 90th percentile of 273 mg/day. The findings in the Anaconda soil and dust ingestion study support the Superfund Program's usual approach of

assuming ingestion of 100 mg soil and dust per day as a CTE assumption and 200 mg soil and dust per day as a RME assumption for soil and dust ingestion rates (IRs) of children age 0 - 6 years. Though default assumptions are used for soil and dust IRs for children, these assumptions are clearly consistent with the available site-specific data.

3.3.2.3 Standard Default Exposure Assumptions

Site-specific data are unavailable for several exposure parameters. Default assumptions for these parameters are described below.

Ingestion of Surface Soils and Dust

Fraction Ingested

The IR values used for adults and children include both soil and interior dust. The fraction ingested (FI) values correct for the relative amount of soil or dust ingested. It was assumed for both adults and children that of the total soil and dust ingested, 55% derives from indoor dust and 45% from soil. An assumption for fractionating dose between soil and dust is necessary since (1) indoor dust and soil arsenic and lead concentrations are not the same at exposure points, (2) different bioavailability estimates are used for dust and soil for arsenic, and (3) many studies have found a significant contribution of indoor dust to exposure.

Adult Soil and Dust Ingestion Rate

The RME value selected for the IR for surface soils, soil-like material, and indoor dust for adult residents is 100 mg/day (EPA 1993a). The CTE value selected for IR for adult residents is 50 mg/day (EPA 1993a). This estimate is fractionated between soil and dust using the FI described above.

Ingestion of Water

Adult Water Ingestion Rate

The RME value selected for the IR for water for the adult resident is 2 L/day (EPA 1993b). This is close to the 90th percentile of values measured and/or estimated for the general population in the U.S., and is also the value currently used to establish drinking water standards by EPA's Office of Water (EPA 1993c). The CTE value selected for the IR of water for the adult resident is 1.4 L/day (EPA 1993b). This is based on the average intake observed from five studies in which the observed range was from 0.26 to 2.8 L/day (EPA 1993b).

Child Water Ingestion Rate

For child residents, the RME value selected for the IR of water is 1 L/day (EPA 1989b). The CTE value selected for the IR of water for child residents is 0.7 L/day. This estimate is in keeping with the definition of a CTE value, and is based on professional judgement

IEUBK Model Default Values

Default values provided in the IEUBK model are used for the following input parameters:

- Lead bioavailability
- Lead concentrations in groundwater
- Lead concentrations in air
- Lead dietary intake
- Maternal blood lead contribution

Model default values are shown in Table 3-10.

TABLE 3-10

Default Model Parameters

AIR CONCENTRATION: 0.100 µg Pb/m3

Indoor Air Pb Concentration: 30.0% of outdoor

Other Air Parameters:

Age (Years)	Time Outdoors (Hours)	Vent. Rate (m3/day)	Lung Abs. (%)
0-1	1.0	2.0	32.0
1-2	2.0	3.0	32.0
2-3	3.0	5.0	32.0
3-4	4.0	5.0	32.0
4-5	4.0	5.0	32.0
5-6	4.0	7.0	32.0
6-7	4.0	7.0	32.0

SOIL AND DUST

SOIL: Constant Concentration

DUST: Constant Concentration

Age (Years)	Soil (µg Pb/g)	House Dust (µg Pb/g)
0-1	Site Specific	Site Specific
1-2	Site Specific	Site Specific
2-3	Site Specific	Site Specific
3-4	Site Specific	Site Specific
4-5	Site Specific	Site Specific
5-6	Site Specific	Site Specific
6-7	Site Specific	Site Specific

DIET:

Age (Years)	0-1	1-2	2-3	3-4	4-5	5-6	6-7
(µg/day)	5.53	5.78	6.49	6.24	6.01	6.34	7.00

DRINKING WATER CONCENTRATION: 4.00 µg/L

WATER Consumption:

Age (Years)	0-1	1-2	2-3	3-4	4-5	5-6	6-7
(L/d)	0.20	0.5	0.52	0.53	0.55	0.58	0.59

ABSORPTION METHODOLOGY: Non-linear Active-Passive

PAINT INTAKE: 0.00 µg Pb/day

MATERNAL CONTRIBUTION: Infant Model

Maternal Blood Concentration: 2.50 µg Pb/dL

* Default values are shown, but site-specific values are used in the analysis.

A non-default value was used for the geometric standard deviation (GSD) in the IEUBK model. The GSD represents the variability of individual blood-lead levels with respect to the geometric mean blood level predicted by the IEUBK model. An inter-individual or individual GSD represents the variability remaining after environmental and age variability have been taken into account. The default GSD value of 1.6 is based on calculations of GSDs from specific sites ranging from 1.3 to 1.8 (Marcus 1992). A GSD of 1.4 was used in the model; this GSD was calculated from site-specific data on children at the Sandy City, Utah Smelter Site (EPA 1995a) and the Bingham Creek, Utah Site (EPA 1995b). The lead contamination originates from smelting activities at the Sandy City site and from historic mining operations at the Bingham Creek site. The lead concentrations in these soils, for the most part, appear to have a fairly homogenous and predictable distribution pattern. The Anaconda Smelter NPL Site is similar in that the lead in soil is distributed in a pattern which is consistent with the smelting activities and seems relatively homogenous within each of the gradients across the site. For this reason, it is reasonable to extrapolate the GSD from the site-specific data of the Sandy City Smelter Site and the Bingham Creek, Utah Site to the Anaconda Smelter NPL Site.

3.3.3 CALCULATION OF CHEMICAL INTAKES — RESIDENTIAL RECEPTOR

Chemical intakes by potentially exposed residential receptors are calculated using exposure point concentrations for each exposure area and the exposure assumptions described above. CDIs are estimated for each selected exposure pathway. In Section 5, CDIs are compared to toxicity values to quantify carcinogenic risks and noncarcinogenic hazards for each exposure pathway evaluated.

3.3.3.1 Ingestion of Chemicals in Surface Soil and Interior Dust

To determine CDIs associated with incidental ingestion of arsenic in surface soils and interior dust, the following equation is used (EPA 1989a).

$$CDI\ (mg/kg\text{-}day) = \frac{CS \times IR \times CF \times FI \times EF \times ED \times BAF}{BW \times AT}$$

Where:	CDI	=	Chronic Daily Intake ((mg/kg)/day)
	CS	=	Chemical Concentration in Soil or Dust (mg/kg)
	IR	=	Ingestion Rate (mg/day)
	CF	=	Conversion Factor (10^{-6} kg/mg)
	FI	=	Fraction Ingested from Contaminated Source (unitless)
	EF	=	Exposure Frequency (days/year)
	ED	=	Exposure Duration (years)
	BAF	=	Bioavailability Factor for COPC in Soil or Dust (unitless)
	BW	=	Body Weight (kg)
	AT	=	Averaging Time (days)

Example Calculations (Soil Ingestion, RME):

$$(NC):\ CDI\ ((mg/kg)/day) = \left[\frac{CS(mg/kg)*200(mg/d)*10^{-6}(kg/mg)*0.45*350(d/yr)*6(yr)*0.183}{15(kg)*(365(d/yr)*6(yr))}\right] + \left[\frac{CS(mg/kg)*100(mg/d)*10^{-6}(kg/mg)*0.45*350(d/yr)*24(yr)*0.183}{70(kg)*(365(d/yr)*24(yr))}\right]$$

$$(C):\ CDI\ ((mg/kg)/day) = \left[\frac{CS(mg/kg)*200(mg/d)*10^{-6}(kg/mg)*0.45*350(d/yr)*6(yr)*0.183}{15(kg)*(365(d/yr)*70(yr))}\right] + \left[\frac{CS(mg/kg)*100(mg/d)*10^{-6}(kg/mg)*0.45*350(d/yr)*24(yr)*0.183}{70(kg)*(365(d/yr)*70(yr))}\right]$$

Where:	NC	=	Noncarcinogenic
	C	=	Carcinogenic

Table 3-11 presents CDIs calculated for ingestion of arsenic in soil and interior dust. Both RME and CTE estimates are provided.

WATER

3.3.3.2 Ingestion of Water

To determine CDI for ingestion of arsenic in contaminated drinking water, the following equation is used (EPA 1989a).

$$CDI\ ((mg/kg)/day) = \frac{CW\ x\ IR\ x\ CF\ x\ EF\ x\ ED\ x\ BAF}{BW\ x\ AT}$$

Where:	CDI	=	Chronic Daily Intake ((mg/kg)/day)
	CW	=	Chemical Concentration in Water (micrograms/liter, or µg/L)
	IR	=	Ingestion Rate (liters/day)

TABLE 3-11
CHRONIC DAILY INTAKES
INGESTION OF ARSENIC IN GROUNDWATER, SOIL, AND DUST
RME AND CTE RESIDENTIAL SCENARIO
ANACONDA SMELTER SITE
(mg/kg-day)

SUBAREA	GROUNDWATER INGESTION				SOIL AND DUST INGESTION			
	Noncarcinogenic CDI (mg/kg-day)		Carcinogenic CDI (mg/kg-day)		Noncarcinogenic CDI (mg/kg-day)		Carcinogenic CDI (mg/kg-day)	
	RME	CTE	RME	CTE	RME	CTE	RME	CTE
Subarea A	1.01E-04	4.01E-05	2.51E-05	2.63E-06	6.33E-05	3.38E-05	1.03E-05	1.63E-06
Subarea B	0	0	0	0	8.37E-05	4.48E-05	1.36E-05	2.15E-06
Subarea C	0	0	0	0	1.08E-04	5.78E-05	1.76E-05	2.78E-06
Subarea D	0	0	0	0	1.71E-04	9.14E-05	2.78E-05	4.39E-06
Subarea E	0	0	0	0	1.14E-04	6.10E-05	1.86E-05	2.93E-06
Subarea F1	0	0	0	0	1.57E-04	8.41E-05	2.56E-05	4.04E-06
Subarea F2	0	0	0	0	1.35E-04	7.19E-05	2.19E-05	3.46E-06
Subarea I	0	0	0	0	1.03E-04	5.53E-05	1.68E-05	2.66E-06
Subarea J	0	0	0	0	9.95E-05	5.32E-05	1.62E-05	2.56E-06
Opportunity	8.50E-05	3.37E-05	2.11E-05	2.21E-06	9.59E-05	5.13E-05	1.56E-05	2.46E-06

CF	=	Conversion Factor (10^{-3} µg/mg)
EF	=	Exposure Frequency (days/year)
ED	=	Exposure Duration (years)
BAF	=	Bioavailability Factor for COPC in water (unitless)
BW	=	Body Weight (kg)
AT	=	Averaging Time (days)

Example Calculations (Ingestion of Water, RME):

$$NC\text{: } CDI\ ((mg/kg)/day) = \left[\frac{CW(ug/L)*1(L/d)*10^{-3}(ug/mg)*350(d/yr)*6(yr)*1}{15(kg)*(365(d/yr)*6(yr))}\right] + \left[\frac{CW(ug/L)*2(L/d)*10^{-3}(ug/mg)*350(d/yr)*24(yr)*1}{70(kg)*(365(d/yr)*24(yr))}\right]$$

$$C\text{: } CDI\ ((mg/kg)/day) = \left[\frac{CW(ug/L)*1(L/d)*10^{-3}(ug/mg)*350(d/yr)*6(yr)*1}{15(kg)*(365(d/yr)*70(yr))}\right] + \left[\frac{CW(ug/L)*2(L/d)*10^{-3}(ug/mg)*350(d/yr)*24(yr)*1}{70(kg)*(365(d/yr)*70(yr))}\right]$$

Table 3-11 presents CDIs for arsenic calculated for ingestion of arsenic in drinking water.

3.4 COMPARISON OF PREDICTED AND MEASURED EXPOSURES TO ARSENIC

When site-specific measurements of exposure are available, comparison of observed versus predicted exposures may be the best means to evaluate uncertainties in exposure calculations. Where exposure measurements have been carefully made, and can be assumed to be representative, observed and predicted exposures should be in reasonable agreement. Since careful and representative observations of arsenic exposure have been made for children in the communities of Anaconda and Opportunity (Bornschein 1994), a comparison of observed and

predicted exposures has been carried out for children living in these communities. Methodologies used to perform this comparison are presented in Appendix D, *Evaluation of the Data Collected in the Town of Anaconda Using EPA Risk Assessment Methodology* (CDM Federal 1995).

Exposure comparisons were based on observed and predicted urinary arsenic. To support this comparison, arsenic absorption and urinary excretion were assumed to be in equilibrium. This seems a reasonable assumption since children in the study had been living in the same exposure conditions (same residence) for several months to several years prior to the study. In addition, bioavailability estimates for arsenic in soil and dust were based on EPA (1994a, 1995a) analyses of data collected by Battelle (1994). The Battelle study measured arsenic in blood, urine and feces of monkeys following administration of soluble arsenic by injection and gavage, and soils and dust from Anaconda in capsules. These data form the basis for estimation of absolute bioavailability as described in Section 3.3.2.2.

add to uncertainty. Soluble As, which is a very available form, was used. Bio could be less.

Estimates for daily urine output were taken from measurements made by Bornschein (1994), and presented in Appendix D. For children less than 36 months of age, urine production was estimated to be 240 ml/day. Values for children 36 to 60 months and greater than 60 months were 355 and 432 ml/day, respectively.

Total daily absorption of arsenic was estimated as follows:

$$ABS = \frac{((C_s * 0.45 * BAF_s) + (C_d * 0.55 * BAF_d)) * IR_s * CF_s * EF)}{AT} + \frac{C_w * CF_w * IR_w * EF * BAF_w}{AT}$$

All variables are defined in Sections 3.3.3.1 and 3.3.3.2, Tables 3-6 to 3-9, and are also provided in Appendix D.

Urinary excretion was estimated from absorption estimates using:

$$EXC = \frac{ABS * CF_{abs}}{RATE * CF_{exe}}$$

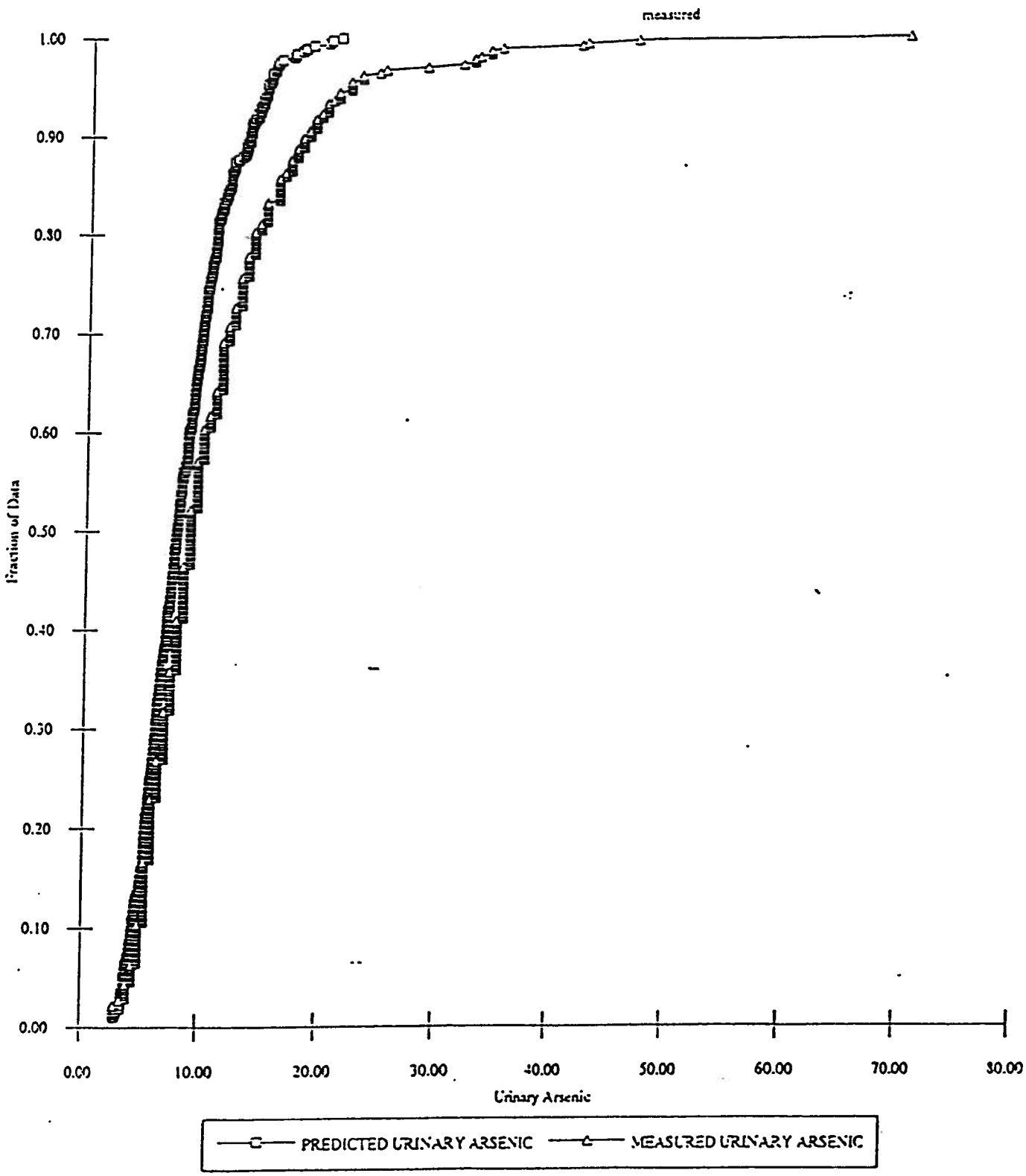
Where:

EXC	=	Urinary arsenic excretion (µg/L)
ABS	=	Estimated daily arsenic absorption (mg/d)
Cf_{abs}	=	Conversion factor (10^3 µg/mg)
RATE	=	Estimated urinary output (ml/d, varies with age)
Cf_{exe}	=	Conversion factor (10^{-3} L/ml)

Observed and predicted urinary arsenic, based on speciated arsenic measured by Bornschein, are presented in Figure 3-4. Kruskal-Wallis one-way analysis of variance does not eliminate the null hypothesis that populations of observed and predicted urinary arsenic levels have the same mean. However, it is apparent that calculated urinary arsenic underpredicts measured values when urinary arsenic concentrations exceed 10 µg/L.

Predicted urinary arsenic levels are based on exposure assumptions intended to represent central tendencies in exposures. Where observed exposures, as reflected in urinary arsenic values, are relatively low, these CTE estimates seem to reproduce measured exposures well. At higher observed exposures, CTE evaluation tends to underpredict exposures. Where arsenic in urine was measured at 20 µg/L, for example, the predicted value was 15.5, about 23 percent lower. Where arsenic was measured at 29 µg/L, the predicted value was about 45 percent lower (16 µg/L). The single child who had a measured arsenic level of 80 µg/L was predicted to excrete only about 20 µg/L. Thus, at the highest measured exposure, predicted values based on CTE could be low by a factor of four. This is currently the best estimate for uncertainty in calculations of arsenic exposure in the most exposed individuals.

FIGURE 3-4
MEASURED AND PREDICTED SPECIATED URINARY ARSENIC



SPUAGRPH.XLS Chart 2
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3.5 UNCERTAINTIES ASSOCIATED WITH EXPOSURE ASSESSMENT

The exposure assessment relies on assumptions for a variety of exposure parameters. Assumptions used are variously based on:

- Site-specific information
- EPA guidance
- Professional judgement

Exposure scenarios and assumptions used in this risk assessment are also based on discussions with EPA Region VIII personnel.

The combination of exposure assumptions used in the assessment is expected to provide realistic estimates for exposure of individuals living in Anaconda and Opportunity. As discussed in Section 3.4, urinary arsenic levels predicted from exposure assumptions used in this assessment, and those measured by Bornschein (1994), are in reasonable agreement for exposures based on central tendency. This increases confidence in exposure calculations for this assessment.

It should be noted, however, that the comparison of observed and predicted exposures can only be made for children. This risk assessment estimates exposure for longer durations including substantial periods of adulthood. Uncertainties in exposures for adults may therefore be important in defining the overall uncertainty in exposure estimates. For example, little information is available for evaluating soil/dust ingestion rates in adults. If default values for adults (50 and 100 mg/d for CTE and RME respectively), are substantially in error, total predicted exposures would be similarly under- or overestimated. Thus, it is not possible to evaluate some major sources of uncertainty using the comparison with Bornschein data.

Choices made for adult exposure parameters are within the ranges suggested by EPA and should be conservative for assessing adult exposure. For example, adults are likely to ingest

less soil than young children because of reduction in hand-to-mouth behavior with age. Adult ingestion rates in this assessment are half those suggested for young children. If this assumption underestimates exposures, it is likely to do so by a factor of less than two. It seems unlikely that soil/dust ingestion rate assumptions for adults result in significant underestimation of exposure.

Frequency and duration of exposure are also important determinants of exposure which may not be adequately addressed in the comparison of observed and predicted urinary arsenic levels in children. Much of the exposure for arsenic is anticipated to occur during adulthood. Adults, because of work and other out-of-home activities, may be exposed less frequently than young children. In addition, exposure duration is an important component of exposure evaluation, yet there is no site-specific information on residence times for Anaconda and Opportunity. If residence times in these communities are significantly different than national norms, exposures may be under- or overestimated.

Exposure frequency is estimated at the high end of those possible, allowing only for a two week per year vacation. Many individuals may spend more time than this away from home and/or may spend limited time at home on most weekdays because of work commitments. These individuals may receive less exposure than that estimated in this assessment. However, it is expected that significant numbers of individuals (for example non-working parents) will spend significant amounts of time each day at their homes. Moreover, many individuals will work close to their residences and thus be in a similar exposure environment both at home and at work. The high exposure frequency used in this assessment is not expected to be appropriate for all individuals in the potentially exposed population. However, it is assumed that a high exposure frequency is reasonable for a large fraction of the population and that this is not a major source of uncertainty in the risk estimates.

Exposure duration can have a significant impact on exposure estimates. National norms suggest that the 90th percentile for time at one residence is about 30 years, and that average

residence time is about 9 years. If the population in Anaconda and Opportunity is either more sedentary or more mobile than the nation as a whole, risks could be either under- or overestimated.

In many cases, small rural communities have many residents that stay in the community for long periods of time. It would not be surprising to see upper range estimates of a few decades for time at one residence. In addition, it is likely that people in the community may move within the community (e.g., from an apartment to a private residence). Anaconda has, however, seen a net loss in population since the closure of the smelter in 1980. This may suggest that residence times are dropping as children who grow up in the area, or adult residents, leave to find jobs, go to school, etc. It is, thus, difficult to determine how Anaconda and Opportunity may compare to national norms.

It seems unlikely, however, that uncertainties in exposure duration would be of great significance. For example, if an more reasonable upper range estimate for time at one residence was either 20 or 40 years, RME estimates would go down or up by only 33 percent. Anaconda and Opportunity would have to be very different from the national norms to greatly affect exposure calculations.

It should be noted that predicted blood lead levels based on lead exposure of children have not been confirmed through direct observations of blood lead levels. Default values were used in the IEUBK model for lead bioavailability, lead concentration in groundwater, air, and food, and maternal blood lead contribution. There is uncertainty associated with the default value for lead absorption from soil. The IEUBK model uses a default value of 30%, however, gastrointestinal absorption of lead has been reported to range from 5 to 72% depending upon soil geochemistry, species of lead, and age, nutritional status, and state of health of the exposed individual. In the absence of site-specific data regarding soil lead absorption, the IEUBK default value is considered the most acceptable for use.

A non-default value was used for the GSD in the IEUBK model; this value was calculated from site-specific data on children at the Sandy City, Utah Smelter site (EPA 1995a) and the Bingham Creek, Utah Site (EPA 1995b). The lead contamination orginates from smelting activities at the Sandy City site and from historic mining operations at the Bingham Creek site. The lead concentrations in these soils, for the most part, appear to have a fairly homogenous and predictable distribution pattern. The Anaconda Smelter NPL Site is similar in that the lead in soil is distributed in a pattern which is consistent with the smelting activities and seems relatively homogenous within each of the gradients across the site. For this reason, it is reasonable to extrapolate the GSD from the site-specific data of the Sandy City Smelter Site and the Bingham Creek, Utah Site to the Anaconda Smelter NPL Site.

Because of the uncertainties associated with these default values, the results of the IEUBK model (as with any risk assessment) should not be viewed as exact. Actual risks could vary by a factor of 2 or 3.

4.0 TOXICITY ASSESSMENT

The purpose of the toxicity assessment is to review and summarize the potential for each COPC to cause adverse effects in exposed individuals. Adverse effects of chemical agents are generally dependent on the route of exposure, the duration and frequency of exposure, the concentration of chemical at the exposure point, and the sensitivity of people exposed. Adverse health effects may follow acute (occurring soon after an exposure of a short duration), subchronic (occurring during or after an intermediate exposure period), or chronic (occurring during or after a long-term exposure) exposures to COPCs.

Of particular importance to many risk assessments is the potential for chemicals to cause cancer in exposed individuals. Cancer risks are assessed separately for chronic exposures to COPCs thought to have carcinogenic potential in humans.

For most adverse effects caused by chemicals, there is a positive relationship between dose and response. Generally, as dose increases, the type and severity of adverse responses also increases. For example, consumption of small amounts of alcohol, even on a daily basis, may have few effects other than slight euphoria. Consumption of larger amounts results in central nervous system depression (drunkenness) and even loss of consciousness. Consumed on a regular basis, larger amounts of alcohol can also cause severe disease such as liver cirrhosis. A key facet of any toxicity assessment is to use dose-response information to describe a quantitative relationship between human exposure and the potential for adverse health effects. For many chemicals, the assessment of dose-response has been completed (EPA 1995b). This report, therefore, includes only a summary of relevant dose-response information. References, which can provide detailed information, are cited at the end of this document.

Sources of toxicity information include, in order of priority, EPA's Integrated Risk Information System (IRIS) (EPA 1995b), Health Effects Assessment Summary Tables (HEAST) (EPA 1994d), EPA criteria documents, and Agency for Toxic Substances and

Disease Registry (ATSDR) Toxicological Profiles. This hierarchy of toxicological information sources is based on EPA guidance (EPA 1989a). However, only information from IRIS is used for toxicological evaluation of arsenic. Lead, which is the other COPC in the assessment, is unique in terms of risk assessment. Standard sources of toxicity information are not used for the evaluation of this metal. Lead risk assessment using the IEUBK Lead Model is discussed in more detail in Section 5.2.

Quantitative health risk assessment for most chemicals is based on the use of toxicological information to estimate toxicity criteria. These criteria are numerical expressions of the relationship between dose (exposure) and response (adverse health effects). As discussed below, separate criteria are developed for assessment of cancer and noncarcinogen health effects.

Toxicity criteria for carcinogens are provided as cancer slope factors (CSFs) in units of risk per milligram of chemical exposure per kilogram body weight per day. These factors are based on the assumption that no threshold for carcinogenic effects exists and any dose is associated with some finite cancer risk. Criteria for noncarcinogens, or for significant noncarcinogenic effects caused by carcinogens, are provided as reference doses (RfDs) in units of mg/kg-day. RfDs may be interpreted as thresholds below which adverse effects are not expected to occur even in the most sensitive populations.

Toxicity profiles are included for arsenic and lead, based in part on information in the documents cited above. These profiles outline major adverse effects, describe important toxicokinetic findings (absorption into, distribution in, metabolism by, and excretion from the body), discuss uncertainties and important data gaps, and summarize important studies used in the derivation of critical toxicity criteria.

Quantitative chemical dose-response information, in the form of critical toxicity criteria, is presented in Section 4.1. Uncertainties associated with toxicity criteria are discussed in

Section 4.2. Individual chemical profiles in support of toxicity criteria and a discussion of the uncertainty associated with the criteria are presented in Section 4.3.

4.1 TOXICITY CRITERIA

4.1.1 CARCINOGENS

Evidence of Carcinogenicity EPA has developed a system for stratifying evidence supporting classification of chemicals as carcinogens. This classification system characterizes the overall weight of evidence of carcinogenicity based on the availability of human, animal, and other supportive data (EPA 1989a). Three major factors are considered in characterizing weight of evidence of carcinogenicity: (1) the quality of evidence from human studies; (2) the quality of evidence from animal studies, and (3) other supportive data (e.g., studies of mutagenicity). The EPA classification system for the characterization of carcinogenicity has the following five categories:

- Group A – Human Carcinogen. This category indicates that there is sufficient evidence from human epidemiological studies to support a causal association between an agent and cancer.

- Group B – Probable Human Carcinogen. This category generally indicates that there is at least limited evidence from epidemiological studies of carcinogenicity to humans (Group B1) or that, in the absence of adequate data on humans, there is sufficient evidence of carcinogenicity in animals (Group B2).

- Group C – Possible Human Carcinogen. This category indicates that there is limited evidence of carcinogenicity in animals and no adequate data on humans.

- Group D – Not Classified. This category indicates that the evidence for carcinogenicity in both humans and animals is inadequate.

- Group E – Evidence of Noncarcinogenicity to Humans. This category indicates that there is evidence for noncarcinogenicity in at least two adequate animal tests in different species or in both epidemiological and animal studies.

Cancer Slope Factors The EPA Cancer Review and Validation Effort (CRAVE) has used a variety of specialized models to estimate the upper-bound risk of carcinogenesis for over 50 compounds. Data from animal or epidemiological studies are used to determine CSFs. A CSF relates the increase in an individual's risk of developing cancer over a 70-year lifetime to a unit of exposure (mg/kg-day). Units for CSFs are, thus, $(mg/kg)/day)^{-1}$.

When a CSF is multiplied by the lifetime average dose of a potential carcinogen (CDI), the product is the upper-bound lifetime individual cancer risk associated with exposure at that dose. This calculated risk is an estimate of the increased likelihood of cancer resulting from exposure to a COPC. For example, if the product of the CSF and the lifetime average daily dose is $1x10^{-6}$, the predicted upper-bound excess cancer risk for the exposed population is one in one million (1:1,000,000). This risk would be in addition to any "background" risk of cancer not related to the chemical exposure. CSFs are provided in Table 4-1. Data used to develop these CSFs are found in the corresponding EPA health assessment and the open literature and are summarized in the toxicity profiles (Section 4.3).

The calculations of risk rely on the data derived from the results of human epidemiological studies or chronic animal bioassays. The likelihood that a chemical is a human carcinogen is a function of the weight of evidence of human and/or animal studies relating to:

- Increase in the number of tissues affected by the chemical
- Increase in the number of animal species, strains, sexes and number of experiments and doses showing a carcinogenic response
- Occurrence of clear dose-response relationships and a high level of statistical significance of the increased tumor incidence in treated compared to control groups

TABLE 4-1

TOXICITY VALUES: POTENTIAL CARCINOGENIC EFFECTS

ANACONDA SMELTER SITE

Chemical Oral Route	Oral Slope Factor (mg/kg-day)-1	Inhalation Slope Factor (mg/kg-day)-1	Weight of Evidence Classification	Type of Cancer	SF Basis/ SFSource	Date Online
Arsenic	1.50E+00	1.50E+01	A	lung/skin	water; inhalation/IRIS	10/95
Lead	not available	not available	B2	NA	food/IRIS	3/1/88

NA = not applicable for B2 carcinogens

- A dose-related shortening of time-to-tumor occurrence or time-to-death with tumor
- A dose-related increase in the proportions of tumors that are malignant

Animal studies are usually conducted using relatively high doses in order to observe possible adverse effects. Since human exposures are generally expected to occur at lower doses, animal data are adjusted using mathematical models to predict cancer risk at low doses. Human epidemiologic data must often also be extrapolated to low doses using mathematical models, since human exposures information generally comes from studies of workers who have received much higher exposures than those expected following many environmental releases. Models used assume a linear dose response at low doses, and are generally assumed to provide conservative estimates of carcinogenic potential. These models, thus, provide only rough, but plausible, estimates of the upper limits on lifetime risk. Actual risks calculated using EPA slope factors are unlikely to be higher than those estimated, but they could be considerably lower, and may even be zero.

4.1.2 NONCARCINOGENS

RfDs are toxicity values developed by EPA for chemicals exhibiting noncarcinogenic effects after oral exposure. RfDs are usually derived from no-observable-adverse-effect levels (NOAELs) or lowest-observable-adverse-effect levels (LOAELs) taken either from human studies (often involving workplace exposures) or from animal studies.

Derivation of RfDs usually involves the use of uncertainty and modifying factors to extrapolate animal data to humans and/or to ensure the protection of sensitive human subpopulations. Uncertainty factors are applied, for example, to address the possibility that humans are more sensitive than experimental animals. In addition, uncertainty factors may be applied to account for sensitive subpopulations of humans, such as children, pregnant women,

and individuals with hay fever or asthma. Depending on the information available, modifying factors may also be applied. Such factors are sometimes applied, for example, to address lack of information on reproductive toxicity.

The RfD is an estimate of the daily exposure to a chemical that would be without adverse effects even if the exposure occurred continuously over a lifetime. An RfD is probably associated with an uncertainty spanning an order of magnitude or more. RfDs are presented in units of mg/kg-day for comparison with intake into the body. Intakes that are less than the RfD are not likely to be of concern. CDIs that are greater than the RfD indicate a possibility for adverse effects, at least in sensitive populations. However, whether such exposures actually produce adverse effects will (depending on the chemical) be a function of a number of factors such as the accuracy of uncertainty factors applied to the NOAEL or LOAEL, the appropriateness of animal models used in studies extrapolated to humans, and the potential for the chemical to cause effects in organs or systems (e.g., reproductive and immune systems) that have not been adequately studied. However, it is generally accepted that the protective assumptions made by EPA in deriving RfDs will, in most cases, mean there may be small risk of noncarcinogenic health effects for exposures slightly in excess of RfDs, with the probability of adverse effects increasing with increasing exposure. RfDs for noncarcinogenic effects are presented in Table 4-2.

4.2 UNCERTAINTIES ASSOCIATED WITH TOXICITY ASSESSMENT

There are many uncertainties associated with the use of toxicological information in health risk assessments that are related to uncertainties intrinsic to toxicology. Important among these are:

- The use of dose-response information from high-dose studies to predict adverse health effects at low doses

TABLE 4-2

TOXICITY VALUES: POTENTIAL NONCARCINOGENIC EFFECTS

ANACONDA SMELTER SITE

Chemical Oral Route	Chronic RfD (mg/kg-day)	Confidence Level	Critical Effects	RfD Source/ RfD Basis	Uncertainty/ Modifying Factors	Date Online
Arsenic	3.00E-04	medium	hyperpigmentation, etc.	epidemiology/IRIS	3	10/1/91
Lead	use IEUBK lead model		neurobehavioral development, etc			3/1/88

- The applicability of experimental animal studies to predict accurate health effects in humans
- The use of dose-response information from short-term exposure studies to predict adverse health effects of long-term exposures
- The use of toxicity values derived from homogenous animal populations or healthy human populations to predict adverse health effects in the general population, which is likely to contain sensitive individuals
- Quality of the study (i.e., design and conduct of the study)
- The selection criteria for the appropriate study used in the development of toxicity values

These and other uncertainties are limitations to the risk assessment process, which cannot be resolved quantitatively given the current understanding of toxicology and human health and using current risk assessment methodology. These uncertainties are addressed in part by consistent application of conservative assumptions regarding the toxic effects of chemicals, such as uncertainty factors for RfDs and upper bound estimates for CSFs. Such procedures are intended to protect public health in the absence of data and may, in many cases, overstate potential impacts on human health.

4.3 TOXICITY PROFILES

4.3.1 ARSENIC

Arsenic (As) is a naturally occurring element found in a variety of complex sulfidic ores. Arsenic trioxide, produced primarily from flue dust that is generated at copper and lead smelters, is the most important commercial arsenic compound. Production of arsenic trioxide in the United States ceased in 1985. Since then, importation of elemental arsenic and arsenic trioxide has increased dramatically. Arsenic is used in wood preservatives and in agricultural insecticides and herbicides.

Toxicokinetics

Absorption of arsenic from the gastrointestinal tract is dependent on the solubility of the arsenic compound. Soluble forms of both As(III) and As(V) are almost completely absorbed in laboratory animals (Vahter 1983, Battelle 1994) and humans (EPA 1984a, b). Bettley and O'Shea (1975, in ATSDR 1991a) reported that 5% of arsenite was recovered in the feces of humans orally exposed to arsenite. Insoluble forms may not be available for absorption in humans as indicated by the lack of increase in urinary excretion of arsenic in human volunteers administered arsenic selenide orally (Mappes 1977).

Site-specific estimates of arsenic absorption from ingested soil were developed by EPA for this HHRA (EPA 1994a, 1995a). Data used to develop site-specific arsenic absorption estimates describe the arsenic concentrations in blood, urine, and feces collected from Cynomologus monkeys exposed to arsenic by intravenous injection, gavage, and oral administration of capsules containing soil or dust collected in Community soils OU (Battelle 1994). Mean absolute absorption estimates derived from urine arsenic estimates were 91%, 18.3%, and 25.8% for gavage, soil, and dust, respectively. Absolute absorption estimates derived from blood arsenic concentrations were similar and ranged between 91% and 100% for gavage, 11% and 18% for soil ingestion, and 8% and 11% for dust ingestion. Discussion of the derivation of these values is provided in Appendix C.

Following inhalation, absorption of arsenic is dependent on particle size, with larger particles being quickly cleared from the lungs with little absorption. In one study, Holland *et al.* (1959, in ATSDR 1991a) examined the absorption and deposition of arsenic in lung cancer patients exposed to arsenic in arsenite-containing cigarette smoke and arsenic-containing aerosols. In the patients, approximately 40% of arsenic particulates were deposited in the lungs and approximately 75-85% of the deposited arsenic was absorbed by the lungs. Smaller particles penetrate into alveolar spaces and may remain there for extended periods, increasing the chances for inhaled arsenic to be absorbed (EPA 1984a, b). Absorption from the lung

may be rapid for soluble arsenic forms, but is much slower for more insoluble forms (ATSDR 1991a).

No studies are available regarding the absorption of arsenic in humans following dermal exposure. Animal studies indicate that arsenic may bind to the skin following dermal exposure, and be slowly absorbed even after exposure ends (ATSDR, 1991a). In one study in which the tails of rats were immersed in sodium arsenate for 1 hour, arsenic uptake was not detected for up to 24 hours after exposure; however, over the next five days arsenic concentrations rose in the blood, liver and spleen. The rate of uptake was estimated to be 1 to 33 micrograms per squared centimeter per hour ($\mu g/cm^2/hr$) (ATSDR 1991a).

Following absorption, arsenic is distributed throughout the body. Analysis of autopsy tissues collected from humans exposed to background levels of arsenic in food show that arsenic was present in all tissues of the body (ATSDR 1991a). Similarly, elevated levels of arsenic were noted in all tissues of mice and hamsters given oral doses of arsenate or arsenite (ATSDR 1991a). Rhoads and Sanders (1985, in ATSDR 1991a) reported that distribution of arsenic trioxide after intratracheal administration to rats was to the liver, kidneys, skeleton, gastrointestinal tract, and other tissues. No organ appears to preferentially accumulate arsenic.

Metabolism of inorganic arsenic takes place via two major processes: (1) oxidation/reduction reactions that interconvert arsenate and arsenite, and (2) methylation reactions which convert arsenite to monomethyl arsenic acid (MMA) and dimethyl arsenic acid (DMA). These processes appear to be used for metabolism regardless of the route of exposure.

Arsenic is efficiently metabolized to methylated forms in the liver in both animals (ATSDR 1991a) and humans (Buchet, *et al.* 1981). Because acute toxicity of these methylated forms is much less than for inorganic arsenic, methylation is considered detoxification. At high arsenic doses, methylation pathways may become saturated (Buchet, *et al.* 1981). This may

result in a "threshold" determined by the ability to metabolize arsenic, where low doses are relatively nontoxic due to conversion to methylated forms, and higher doses are more toxic since greater amounts of inorganic arsenic will be available for distribution to target tissues. This is especially important for carcinogenesis following oral exposure, where small daily intakes could be much less effective in inducing cancer than higher doses that saturate metabolism. Unfortunately, available information is insufficient to determine the saturation point in humans (EPA 1988b) and it is not possible at this time to make adjustments to the oral CSF for low CDIs.

Most arsenic is promptly excreted in the urine in the form of metabolic products, including As(+3), As(+5), DMA, and MMA (ATSDR 1991a). Vahter *et al.* (1986, in ATSDR 1991a) reported that urinary arsenic levels in smelter workers rose within hours of starting work on a Monday and then fell over the weekend. This indicates that excretion is rapid, an observation supported by experimental studies in animals (Rhoads and Sanders 1985, Marafante and Vahter 1987, both in ATSDR 1991a). Human oral exposure to known amounts of arsenite or arsenate indicate that very little is excreted in the feces (Bettley and O'Shea 1975, in ATSDR 1991a), while 45-85% is excreted in the urine between 1-3 days (Buchet *et al.* 1981, Crecelius 1977, Mappes 1977, Tam *et al.* 1979, all in ATSDR 1991a). Small amounts of arsenic may remain bound to tissues, depending inversely on the rate and extent of methylation (ATSDR 1991a).

Qualitative Description of Health Effects

Acute exposure to ingested arsenic may result in death (ATSDR 1991a). Although the information on lethal doses to humans is sparse, Armstrong *et al.* (1984, in ATSDR 1991a) reported that two people in a family of eight died after ingesting 110 ppm of arsenic in water. A number of serious cardiovascular effects may result after acute and chronic ingestion. These effects include myocardial depolarization, cardiac arrhythmias, and damage to the vascular system (Glazener *et al.* 1968, Goldsmith and From 1986, Heyman *et al.* 1956, Little

et al. 1990, Mizuta *et al.* 1956, Tseng 1977, all in ATSDR 1991a). An example of vascular damage is "blackfoot disease," a disease characterized by loss of circulation in hands and feet which leads to necrosis and gangrene (Chen *et al.* 1988, Chi and Blackwill 1968, Tseng 1977 1989, Tseng *et al.* 1968, all in ATSDR 1991a). The disease was endemic in an area of Taiwan where the population was exposed to arsenic ranging from 0.17 to 0.8 ppm in well water. Oral ingestion of arsenic can affect the skin. Hyperkeratosis, hyperpigmentation, and hypopigmentation have been observed on the faces, necks, and backs of workers following chronic oral exposure (ATSDR 1991a). Studies indicate that arsenic may be fetotoxic, teratogenic, and embryotoxic in animal tests (ATSDR 1991a).

There is convincing evidence from a large number of studies that ingestion of arsenic increases the risk of skin cancer. EPA (1995b) has classified arsenic via oral exposure in Group A – Human Carcinogen. Squamous cell carcinomas are the most common types of skin cancer and appear to develop from hyperkeratinized corns. Basal cell carcinomas also occur. In a key study by Tseng *et al.* (1968, in ATSDR 1991a), ingestion of contaminated drinking water from wells in Taiwan was correlated with an increased skin cancer rate. Based on an examination of over 40,000 people in Taiwan, the skin cancer rate was 10.6/1,000. There is also mounting evidence that ingestion of arsenic may increase the risks of internal cancers. These include tumors of the bladder, kidney, liver, and lung (ATSDR 1991a, EPA 1995b).

After acute exposure to arsenic compounds via inhalation, humans may experience irritation of the mucous membranes in the nose and throat, which may lead to laryngitis, bronchitis, rhinitis, and in very high doses, perforation of the nasal septum (Dunlap 1921, Morton and Caron 1989, Pinto and McGill 1953, all in ATSDR 1991a). Chronic inhalation of arsenic compounds may lead to an increased risk of mortality from cardiovascular disease (Axelson *et al.* 1978, Lee-Feldstein 1983, Wall 1980, all in ATSDR 1991a), but this effect has not been observed in all studies. An increased incidence of Raynaud's disease (cyanosis of the digits due to arterial and arteriolar contraction) and increased constriction of blood vessels in

response to cold, suggests that long-term inhalation exposure to arsenic compounds (0.05-0.5 mg As/m^3) may injure blood vessels and/or the heart (Lagerkvist *et al.* 1986, Lagerkvist *et al.* 1988, both in ATSDR 1991a).

There is convincing evidence that chronic arsenic inhalation exposure increases the risk of lung cancer. EPA (1995b) has classified arsenic according to its weight of evidence criteria in Group A – Human Carcinogen (via inhalation). Most studies involved workers in copper smelters exposed to arsenic trioxide in the air, but an increased risk of lung cancer has also been observed at chemical plants where workers were exposed to arsenate. Several studies also suggest that residents living near smelters or arsenic chemical plants may also have an increased risk of lung cancer, although an increased cancer risk was not observed in all cases (ATSDR 1991a, EPA 1995b).

Quantitative Description of Health Effects

EPA derived an oral RfD based on a study by Tseng *et al.* (1968, in ATSDR 1991a) and Tseng (1977, in ATSDR 1991a). Tseng *et al.* (1968, in ATSDR 1991a) and a follow-up study by Tseng (1977, in ATSDR 1991a) observed a population in Taiwan where well water was contaminated with arsenic. The Tseng (1977, in ATSDR 1991a) study reported an increased incidence of blackfoot disease that was both age- and dose-specific. For the low-dose group (170 µg/L), blackfoot disease was observed in 4.6 per 1,000 for the 20–39-years-of-exposure group, 10.5 per 1,000 for the 40–59-years-of-exposure group, and 20.3 for the "greater-than-60-years-of-exposure" group. In addition, an increased incidence of hyperpigmentation and keratosis occurred with increasing age (Tseng *et al.* 1968, in ATSDR 1991a). Based on effects of hyperpigmentation, keratosis, and blackfoot disease, the LOAEL was 0.014 (mg/kg)/day = ((170 µg/L x 4.5 L/day) + 2 µg/day [contribution of food]). The NOAEL was 0.0008 (mg/kg)/day = ((9 µg/L x 4.5 L/day) + 2 µg/day). This estimate is based on the arithmetic mean concentration of arsenic in the well used by the individuals in the control group (9 µg/L, range 1-17 µg/L) (Abernathy *et al.* 1989, in EPA 1995b). To

derive an oral RfD, an uncertainty factor of 3 was applied to the NOAEL to account for the lack of reproductive toxicity data and to account for sensitive individuals. Thus, the oral RfD is 3E-4 mg/kg-day (EPA 1995b).

The studies on which the RfD are based have been given a medium level of confidence, based on the presence of other contaminants and poor characterization of the exposure doses. The supporting human toxicity database is extensive but lacking in some important areas. However, it does support the choice of NOAEL and is given a medium degree of confidence. Therefore, medium confidence is placed in the oral RfD (EPA 1995b).

Tseng (1977, in ATSDR 1991a) observed a population in Taiwan where well water contaminated with arsenic was used for 60 years. The study found significantly elevated standard mortality ratios for cancer of the bladder, lung, liver, kidney, skin, and colon. The study was extensive, but did not define a control population. Concentrations of arsenic in the water ranged from 0.01 to 1.82 mg/L. The overall prevalence rate for skin cancer was 10.6 per 1,000 and for peripheral vascular disorder of the extremities was 8.9 per 1,000. Three dose groups were designated as "low" (below 0.3 mg/L), "mid" (0.3-0.6 mg/L), and "high" (above 0.6 mg/L). Tseng (1977, in ATSDR 1991a) reported a dose-response relationship between concentrations of arsenic in the water and skin cancer. Based on this study, the oral CSF is 1.50 $((mg/kg)/day)^{-1}$ (EPA 1995b).

EPA has derived an inhalation CSF of 15 $(mg/kg\text{-}day)^{-1}$ based on six occupational exposure studies of two different exposed populations (Brown and Chu 1983a, Brown and Chu 1983b, Brown and Chu 1983c, Lee-Feldstein 1983, Higgins *et al.* 1982, Enterline and Marsh 1982, all in ATSDR 1991a). These studies have reported an association between occupational exposure to arsenic and lung cancer mortality. To derive the inhalation CSF, the geometric mean was taken within each of the exposed populations and the final inhalation CSF was the geometric mean of the two exposed populations. Supporting evidence of the carcinogenicity

of arsenic has also been found in residents drinking arsenic-containing water and residents living near a pesticide manufacturing plant (EPA 1995b).

The described CSFs are based on the absorbed dose in contrast to those for most other chemicals which are based on administered doses. EPA assumed 100% absorption of arsenic following oral exposure from water and 30% absorption following inhalation exposure (EPA 1988b; EPA 1995b).

The maximum contaminant level goal (MCLG) of 0.05 mg/L has been proposed, based on the current maximum contaminant level (MCL) of 0.05 mg/L. Although arsenic is potentially carcinogenic, its potential essential nutrient value was considered in determining the MCLG (EPA 1995b).

SUMMARY OF ARSENIC CRITERIA		SOURCE
EPA Carcinogenic Classification	Group A	EPA 1995b
Maximum Contaminant Level (MCL)	0.05 mg/L	EPA 1993b
Chronic Oral RfD	3.0E-04 (mg/kg)/day	EPA 1995b
Oral SF	1.5E+007 $((mg/kg)/day)^{-1}$	EPA 1995b
Inhalation SF	1.5E+01 $((mg/kg)/day)^{-1}$	EPA 1995b
EPA Drinking Water Health Advisory (HA)	Not Available	EPA 1993b
Ambient Water Quality Criteria (AWQC)		
Human – Water and Fish Consumption	2.2E-03 µg/L	EPA 1995b
Aquatic Organisms		
Freshwater		
Acute	3.6E+02 µg/L	EPA 1995b
Chronic	1.9E+02µg/L	EPA 1995b
Marine		
Acute	6.9E+01 µg/L	EPA 1995b
Chronic	3.6E+01 µg/L	EPA 1995b

4.3.2 LEAD (INORGANIC)

Lead (Pb) is a naturally occurring, ubiquitous metal. Concentrations in rocks and soils in the western United States range from 10 to 700 mg/kg (Shacklette and Boerngen 1984). Lead is often found in association with cadmium, zinc, and silver ores. Lead is obtained through

underground mining, as a by-product from open pit copper mines, and from secondary sources including scrap, product wastes, refinery drosses, and residues. During 1989, United States mine production of recoverable lead was 905 million pounds and production of refined lead from primary sources was 874 million pounds. Lead production by recovery from secondary sources was 1.783 billion pounds. Lead imports have been decreasing: in 1977, 719 million pounds were imported, while in 1989, 281 million pounds of lead were imported into the United States. Lead is commercially important because it is very soft, highly malleable, ductile, and a poor conductor. In addition, it is resistant to corrosion, is an effective sound absorber, and makes an excellent radiation shield. Historically, major uses of lead included battery casings, pigments in paint, solders, and as gasoline additives. Because of its extensive use and its ubiquitous distribution, exposure to lead is common.

Toxicokinetics

Oral absorption of inorganic lead in humans ranges from as low as 3% to as high as 80% (ATSDR 1991b). The percentage of absorbed lead appears to be dependent on the solubility of the lead salt ingested as well as age, nutritional status, and fasting time. Dietary absorption of lead has been reported as 50% and 15% for children and adults, respectively (Chamberlain *et al.* 1978; in ATSDR 1991b). Animal studies indicate that particle size also influences lead absorption from the gastrointestinal tract (EPA 1986a in ATSDR 1991). For example, in rats an inverse relationship was shown between lead absorption for metallic lead. Tissue concentrations of lead increased by 2.3-fold when particle size of small lead particles less than (<) 38 micrometers (μm) were administered as compared to lead particles measuring 150 to 250 μm (ATSDR 1991b). As described in Section 3.3.2.3, this HHRA uses a default value of 30% for lead absorption from soil and dust ingestion (EPA 1991e).

Absorption of inhaled lead is thought to reach 100%; however, not all inhaled particles are deposited in the respiratory tract. The deposition rate of lead-containing particles is

influenced by factors such as particle size and ventilation rate, and is estimated to be between 30% and 50% of the inhaled particles.

Dermal absorption of lead is not considered a significant pathway. Route of absorption does not effect distribution of lead. After absorption, lead is distributed among several physiologically distinct compartments, including blood, soft tissue, particularly brain, kidney and liver, and bone (ATSDR 1991b). In adults, approximately 94% of the total body burden is in bone (ATSDR 1991b). Estimates of elimination half-times for lead from blood range from 15 to 35 days and elimination half times from other soft tissues are probably similar (Harley and Kneip 1985; in ATSDR 1991b). Elimination half-times for lead from mineralized bone are expressed in years. Because metabolic stress such as pregnancy may result in increased bone turnover or demineralization, there is potential for a portion of the parental bone lead-burden to be transferred to the fetus.

Inorganic lead is not metabolized or biotransformed in the body (ATSDR 1991b). All absorbed lead that is not retained is excreted by the kidney or through biliary clearance into the gastrointestinal tract. Infants (0 to 2 years of age) retain approximately 32% of the lead absorbed (Ziegler *et al.* 1978; in ATSDR 1991b) whereas adults retain only about 1% of absorbed lead (Rabinowitz *et al.* 1977; in ATSDR 1991b). Most toxicity endpoints associated with exposure to lead can be correlated with blood-lead levels. Blood-lead levels are, therefore, a useful index of toxicity.

Qualitative Description of Health Effects

Cases of severe lead encephalopathy have resulted in death in both adults and children. Blood-lead levels associated with death in children have ranged from approximately 125 micrograms of lead per deciliter blood (µg Pb/dL) to 750 µg Pb/dL. Lead encephalopathy (non-fatal) has been seen at blood-lead levels of 60-300 µg/dL. At lower blood-lead levels, systemic effects associated with lead intoxication include increased systolic and diastolic

blood pressure (Harlan 1988; Pocock *et al.* 1984, 1985; in ATSDR 1991b). Harlan's analysis, which is based on National Health and Nutrition Examination Survey (NHANES II) data, estimated an increase in blood pressure of 7 mm Hg at blood-lead levels between 14 and 30 µg Pb/dL. Pirkle *et al.* (1985; in ATSDR 1991b) evaluated the same data set for 40–59-year-old white males and found no threshold for increased blood pressure associated with increased blood-lead levels across the range of 7-34 µg Pb/dL. Gastrointestinal symptoms such as colic, abdominal pain, constipation and anorexia are typically seen at blood-lead levels of 100-200 µg Pb/dL but have been reported at blood-lead levels as low as 40 µg Pb/dL.

Lead is known to depress heme synthesis and this effect appears to have no threshold in the range of available blood-lead concentration data. Cytochrome P450 formation is also inhibited in the presence of lead. Kidney damage occurs with both acute and chronic exposures to lead. Acute renal toxicity has been reported in lead-intoxicated children and is considered reversible, whereas chronic renal toxicity has been observed in lead-exposed workers and is considered irreversible. Lead interferes with vitamin D metabolism and may have some effect on the cellular component of the immune system.

The lowest-observed-effect-level (LOEL) for overt neurotoxic toxicity in adults is estimated to be 40 µg Pb/dL (ATSDR 1991b). Early symptoms include irritability, poor attention span, headache, muscular tremor, loss of memory and hallucinations. As the condition worsens, symptoms include delirium, convulsions, paralysis and coma and may lead to death. Decreased peripheral nerve conduction velocities (NCVs) have been seen in workers at blood-lead levels ranging from 30-48µg Pb/dL; these effects are probably reversible.

Neurotoxicity in children is seen at very low blood-lead levels. Low-level prenatal exposure to lead has been shown to result in reduced birth weight and gestation age, as well as neurobehavioral deficits or delays (ATSDR 1991b). Prenatal exposure was generally estimated through maternal or cord blood-lead concentrations. Postnatal lead exposures may

result in fine motor dysfunction, hyperactivity, and altered behavioral patterns (ATSDR 1991b). Several studies have demonstrated a statistically significant decrement in children's intelligence quotients (IQs) when correlated with blood-lead levels. Subtle signs of lead-induced effects begin to be apparent at blood-lead levels of 10 µg/dL or even lower, with effects becoming clearer by 30 to 40 µg/dL. Some researchers claim that some of the effects of lead, including neurobehavioral effects, heme synthesis depression, and fetal developmental problems, do not have a threshold value (EPA 1994c).

Studies on association of occupational exposure to lead with increased cancer risks are insufficient to determine the carcinogenicity of lead in humans. Ingestion of lead acetate and lead phosphate produced renal tumors in laboratory rats and mice.

The literature on lead is difficult to summarize briefly. The Toxicological Profile for Lead (ATSDR 1991b) contains over 1,000 references, and much of the brief synopsis above is taken from the profile.

Quantitative Description of Health Effects

EPA has not published a RfD or acceptable intakes for chronic or subchronic periods of human exposure in IRIS (EPA 1995b) or HEAST (EPA 1994d) because available data suggest no threshold for adverse effects even at exposure levels that might be considered background. Any significant increase above such exposures could represent a cause for concern. In lieu of acceptable intake for chronic exposure (AIC) or RfDs, EPA has developed a biokinetic computer model for prediction of blood-lead levels in children exposed to lead from a variety of sources, including soil, dust, air, diet, lead-based paint, and maternal blood. Estimated blood-lead levels are compared to target blood-lead concentrations to assess possible risks.

The model can be used to assess risks to individual children or a population of children. For a single child, risk is calculated as the probability that the child's blood-lead level will exceed

the level of concern (10 μg/dL) (EPA 1991c). The single-child assessment is generally used to evaluate remedial options on a house-by-house or yard-by-yard basis (EPA 1991e). For a population of children, risk is expressed as the percentage of children that are likely to have a blood lead level greater than 10 μg/dL. This HHRA evaluates lead risks to populations of children. Protection of young children is considered achieved when model results indicate that less than 5% of the population of children will have blood-lead levels greater than 10 μg/dL (EPA 1994c). Because children between the ages of 0-6 are thought to be most susceptible to the adverse effects of lead, protection for this age group (0-6 years old) is assumed to also protect older individuals.

No inhalation reference concentration (RfC) is available for lead, and, as discussed above, it is not clear that there is a practical threshold below which there are no risks from exposure to lead. Since RfCs are based on the assumption that such a threshold exists, the estimation of an RfC for lead is not appropriate.

Oral ingestion of certain lead salts (lead acetate, lead phosphate, lead subacetate) have been associated with increased renal tumor frequency in rats (Azar *et al.* 1973; Koller *et al.* 1985; both in ATSDR 1991b), but no quantitative estimate of excess cancer risk has been developed by CRAVE. EPA (1987, in EPA 1995b) has noted that the available data provide an insufficient basis on which to regulate lead acetate, lead phosphate, and lead subacetate as human carcinogens. However, applying the criteria described in EPA's Guidelines for Carcinogenic Risk Assessment (EPA 1986a), these lead salts have been classified by EPA (1987; in EPA 1995b) in Group B2 – probable human carcinogen.

At present, standards for lead in soil have not been established in the United States. The United Kingdom Directorate of the Environment has developed a tentative guideline of 550 ppm for lead in soil in residential areas (Smith *et al.* 1981, in ATSDR 1991b). Vernon Houk of the Centers for Disease Control has been quoted as indicating that levels of lead in soil of 300-400 ppm are acceptable based on studies of childhood lead poisoning (Mielke *et al.* 1984,

in ATSDR 1991b). Recently, EPA has proposed a screening level of 400 ppm for lead in residential soils (EPA 1994c).

The current MCL for lead (at source) is 0.05 mg/L, as stated in the Code of Federal Regulations at 40 CFR 141.11. The Treatment Technique Action Level of 0.015 mg/L has been finalized (EPA 1991d, in ATSDR 1991b) by the Office of Drinking Water. The MCLG for lead at the source and at the tap is zero.

The EPA Office of Drinking Water issued a draft health advisory of 20 µg/day for all extended periods of exposure (EPA 1985, in ATSDR 1991b). Blood-lead levels above 10 µg/dL are identified as of concern, and children under six years of age are assumed to be the most sensitive subpopulation (CDC 1991).

The National Primary and Secondary Ambient Air Quality Standard for lead is 1.5 µg/m^3. This standard is currently being re-evaluated (40 CFR 50.12).

SUMMARY OF LEAD CRITERIA		SOURCE
EPA Carcinogenic Classification	**Group B2**	**EPA 1995b**
Maximum Contaminant Level (MCL)	**0.05 mg/L**	**40 CFR 141.11**
Maximum Contaminant Level Goal (MCLG)	**0 mg/L**	**40 CFR 141.11**
Treatment Technique Action Level	**0.015 mg/L**	**EPA 1995b**
EPA Drinking Water Health Advisory (HA)	**NA**	
Ambient Water Quality Criteria (AWQC)		
Human Water and Fish Consumption	**0.05 mg/L**	**EPA 1992c**
Aquatic Organisms		
Freshwater		
Acute	**8.2E+1 µg/L**	**EPA 1992c**
Chronic	**3.2E+0 µg/L**	**EPA 1992c**
Marine		
Acute	**2.2E+2 µg/L**	**EPA 1992c**
Chronic	**8.5E+0 µg/L**	**EPA 1992c**

5.0 RISK CHARACTERIZATION

In this section, potential site-related risks are characterized for exposure to arsenic and lead for exposure pathways selected in Section 3.2. In Section 5.1, toxicity values for arsenic (Section 4.0) are combined with estimates of CDI (Section 3.3.3) to calculate cancer and noncarcinogenic health risks for each exposure pathway. Total risks, assuming exposure from each pathway, are also discussed. Risks associated with exposure to lead are assessed in Section 5.2 using the IEUBK Lead Model, Version 0.99. Children (aged 0-6) are considered the sensitive subpopulation at risk for adverse effects due to exposure to lead in environmental media. Risks to adults from lead exposure are not evaluated. Uncertainties in the risk assessment are presented in Section 5.3. A summary of risk estimates and associated uncertainties is provided in Section 5.4.

5.1 ARSENIC HEALTH RISKS

Arsenic is known to cause both systemic toxicity and cancer following prolonged exposure. Therefore, both cancer and noncancer health risks are assessed.

5.1.1 CANCER HEALTH RISKS FROM ARSENIC EXPOSURE

To evaluate cancer risks due to exposure to arsenic, pathway-specific CDI estimated previously are multiplied by the arsenic-specific oral CSF. Since inhalation exposures are not considered significant, the inhalation slope factor is not used in the assessment.

Table 5-1 presents pathway-specific and total cancer risks for RME and CTE scenarios. Potential risks based on RME estimates associated with ingestion of soil/interior dust are in the range of 2×10^{-5} to 4×10^{-5} for all subareas, reflecting the relatively homogeneous distribution of arsenic in the study area. The highest risks are estimated for subareas D and F1, perhaps reflecting the proximity of these areas to Smelter Hill. However, differences in

TABLE 5-1
CANCER RISKS
INGESTION OF ARSENIC IN GROUNDWATER, SOIL, AND DUST
RME AND CTE RESIDENTIAL SCENARIO
ANACONDA SMELTER SITE
(mg/kg-day)

SUBAREA	RME SCENARIO			CTE SCENARIO		
	Groundwater Ingestion Cancer Risk	Soil and Dust Ingestion Cancer Risk	Total Arsenic Cancer Risk	Groundwater Ingestion Cancer Risk	Soil and Dust Ingestion Cancer Risk	Total Arsenic Cancer Risk
Subarea A	3.76E-05	1.55E-05	5.30E-05	3.94E-06	2.44E-06	6.38E-06
Subarea B	0	2.05E-05	2.05E-05	0	3.23E-06	3.23E-06
Subarea C	0	2.64E-05	2.64E-05	0	4.17E-06	4.17E-06
Subarea D	0	4.18E-05	4.18E-05	0	6.59E-06	6.59E-06
Subarea E	0	2.79E-05	2.79E-05	0	4.40E-06	4.40E-06
Subarea F1	0	3.84E-05	3.84E-05	0	6.06E-06	6.06E-06
Subarea F2	0	3.29E-05	3.29E-05	0	5.19E-06	5.19E-06
Subarea I	0	2.53E-05	2.53E-05	0	3.98E-06	3.98E-06
Subarea J	0	2.43E-05	2.43E-05	0	3.83E-06	3.83E-06
Opportunity	3.16E-05	2.34E-05	5.51E-05	3.32E-06	3.69E-06	7.01E-06

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risk estimates among subareas are small and may not be significant. Risks based on CTE estimates are about 16% of those based on RME.

Potential risks from ingestion of arsenic in groundwater are somewhat higher than those for soil/dust ingestion in subarea A and in Opportunity, although they still fall within the EPA risk range. Groundwater risks are not evaluated for other subareas since data from these areas are lacking. All estimated risks fall within the risk range of 1×10^{-4} and 1×10^{-6}, which are generally considered acceptable by EPA (1991b).

5.1.2 NONCARCINOGENIC HEALTH RISKS FROM ARSENIC EXPOSURE

To evaluate noncarcinogenic health risks, CDI (Section 3.3.3) are compared to toxicity criteria to determine if exposure might exceed the nominal threshold established by the RfD. The ratio of exposure estimate to toxicity criteria for a single chemical is called a hazard quotient (HQ) and provides a measure of risk for systemic health effects. The ratio is calculated as:

$$\text{Hazard quotient} = \frac{CDI}{RfD}$$

Where: CDI = Chronic Daily Intake ((mg/kg)/day)
RfD = Reference Dose ((mg/kg)/day)

The HQ assumes that there is a level of exposure (the RfD) below which it is unlikely for even a sensitive population to experience adverse health effects. If the CDI exceeds the RfD, a potential for non-cancer adverse health effects may exist. Although a quantitative estimate of risk cannot be established for noncancer effects, it is assumed that a small exceedance of the RfD might be associated with a small risk and that risks would increase with larger CDIs.

At most Superfund Sites, one must assess potential health effects of more than one chemical. The Hazard Index (HI) is used to assess the overall potential for systemic effects posed by exposure to multiple chemicals, and is equal to the sum of HQs for all of the COPCs for a

group of receptors. When the HI exceeds one, there may be a potential for adverse health effects from exposure to all of the chemicals at the site, and further evaluation of mechanisms of toxic action is required. For this HHRA, however, HQs are calculated only for arsenic. As described in Section 4.0, lead risks are evaluated through the use of the EPA IEUBK Lead Model, Version 0.99. This model evaluates health risks based on blood-lead levels. It would be inappropriate to attempt to combine arsenic and lead toxicity values because of the different evaluation methodologies. Additionally, lead and arsenic do not induce similar toxic effects, nor does their toxicity occur through the same mechanism of action. Therefore, the HI approach is not applicable to this HHRA.

Table 5-2 presents noncarcinogenic HQs for arsenic for each subarea. Based on RME estimates, HQs for ingestion of soil and dust range from about 0.1 to 0.3 for all subareas. As with cancer risk estimates, the highest HQs are found in subareas D and F1, though differences among subareas are small. HQs based on CTE estimates are about 53% of those based on RME.

Potential risks due to ingestion of groundwater are similar to those for ingestion of soil/dust in subarea A and in Opportunity, and overall these risks fall in the lower half of the range of HQs for soil/dust ingestion. The highest HQ (0.34 for subarea A) is less than one suggesting that exposures to arsenic in groundwater will not exceed the target HQ of 1.

All HQs estimated are less than unity, suggesting little potential for impacts to human health. Thus, neither cancer risks nor hazard quotients exceed common criteria used to establish acceptable risk levels. Considering these criteria alone, potential arsenic exposure in the communities of Anaconda and Opportunity does not appear to be associated with unacceptable health risks.

TABLE 5-2
NONCANCER RISKS
INGESTION OF ARSENIC IN GROUNDWATER, SOIL, AND DUST
RME AND CTE RESIDENTIAL SCENARIO
ANACONDA SMELTER SITE
(mg/kg-day)

SUBAREA	RME SCENARIO			CTE SCENARIO		
	Groundwater Ingestion HQ	Soil and Dust Ingestion HQ	Total Arsenic Risk	Groundwater Ingestion HQ	Soil and Dust Ingestion HQ	Total Arsenic Risk
Subarea A	3.37E-01	2.11E-01	5.48E-01	1.34E-01	1.13E-01	2.46E-01
Subarea B	0	2.79E-01	2.79E-01	0	1.49E-01	1.49E-01
Subarea C	0	3.60E-01	3.60E-01	0	1.93E-01	1.93E-01
Subarea D	0	5.70E-01	5.70E-01	0	3.05E-01	3.05E-01
Subarea E	0	3.80E-01	3.80E-01	0	2.03E-01	2.03E-01
Subarea F1	0	5.24E-01	5.24E-01	0	2.80E-01	2.80E-01
Subarea F2	0	4.48E-01	4.48E-01	0	2.40E-01	2.40E-01
Subarea I	0	3.45E-01	3.45E-01	0	1.84E-01	1.84E-01
Subarea J	0	3.32E-01	3.32E-01	0	1.77E-01	1.77E-01
Opportunity	2.83E-01	3.20E-01	6.03E-01	1.12E-01	1.71E-01	2.83E-01

5.1.3 COMBINED RISKS

Residents of Anaconda and Opportunity might be exposed to both contaminated soil/dust and to contaminated groundwater. Thus, total risks for receptor populations may be higher than risks estimated for individual pathways. It may be appropriate to combine risks based on RME estimates if it is likely that the same individual might experience RME exposures in more than one pathway. For Anaconda and Opportunity, it is conceivable that the same individuals could be exposed at high levels to both soil/dust and groundwater. In fact, within a single subarea, soil concentrations are relatively consistent, suggesting that the occurrence of high soil/dust levels and high local groundwater contamination in the same location is likely. Though this alone does not indicate that people at such location will be maximally exposed to both soil/dust and groundwater, it does increase the likelihood for co-occurrence of such exposures. Thus, it seems reasonable to combine risks based on RME for subarea A and Opportunity.

Combined RME cancer risks for subarea A (5.3×10^{-5}) and Opportunity (5.5×10^{-5}) are still within the EPA acceptable risk range (Table 5-1). Likewise, combined HQs (0.55 and 0.6 for subarea A and Opportunity respectively) are still below the target HQ of one (Table 5-2). Thus, combining risks from soil/dust ingestion and groundwater ingestion pathways does not result in risk estimates that exceed common criteria for acceptable risk.

5.2 POTENTIAL HEALTH RISKS ASSOCIATED WITH EXPOSURE TO LEAD

Risks from exposure to lead cannot be assessed using standard methods, because toxicological criteria for lead are not available. The EPA's position is that current data are insufficient to determine an RfD or RfC for lead. Further, EPA feels that the primary threat to human health from exposure to lead is subtle neurological effects in young children. For this reason, the EPA has not derived a CSF for lead, despite the chemical's Group B2 status as a probable human carcinogen.

The best available quantitative tool for evaluating health effects from exposure to lead is the IEUBK model (EPA 1994b). This model uses current information on the uptake of lead following exposure from different routes, its distribution among various internal body compartments, and its excretion, to predict impacts of lead exposure on blood-lead concentrations in young children. Predicted blood-lead concentration can then be compared with target blood-lead concentrations associated with subtle neurological effects in children. Because children are thought to be most susceptible to the adverse effects of lead, protection for this age group is assumed to also protect older individuals. Protection of young children is considered achieved when the model predicts that less than 5% of children will have blood-lead levels greater than 10 µg/dL (EPA 1994c).

The IEUBK Lead Model, Version 0.99, is used to evaluate potential risks from exposure to lead associated with the Anaconda Smelter NPL Site. Young children (0 to 6 years old) who live near the Anaconda Smelter NPL Site are evaluated for potential exposure to lead in soil and dust.

IEUBK Modeling Results

Results from IEUBK modeling runs are presented in Appendix E to this document. The probability plots for blood-lead concentrations for exposure subareas in Anaconda and Opportunity are presented on Figures 5-1 to 5-11. Table 5-3 summarizes the modeling results. Modeling predicted that 5% of children in exposure subarea E may have blood-lead levels in excess of 10 µg/dL. The estimated percentage of individuals in exposure subarea E having blood-lead levels above 10 µg/dL is 5.4. Based on the combined data for all subareas, only 0.68% of children are predicted to have blood-lead levels above 10 µg/dL (Figure 5-11).

FIGURE 5-1

IEUBK Modeling Blood Lead Results - Subarea A

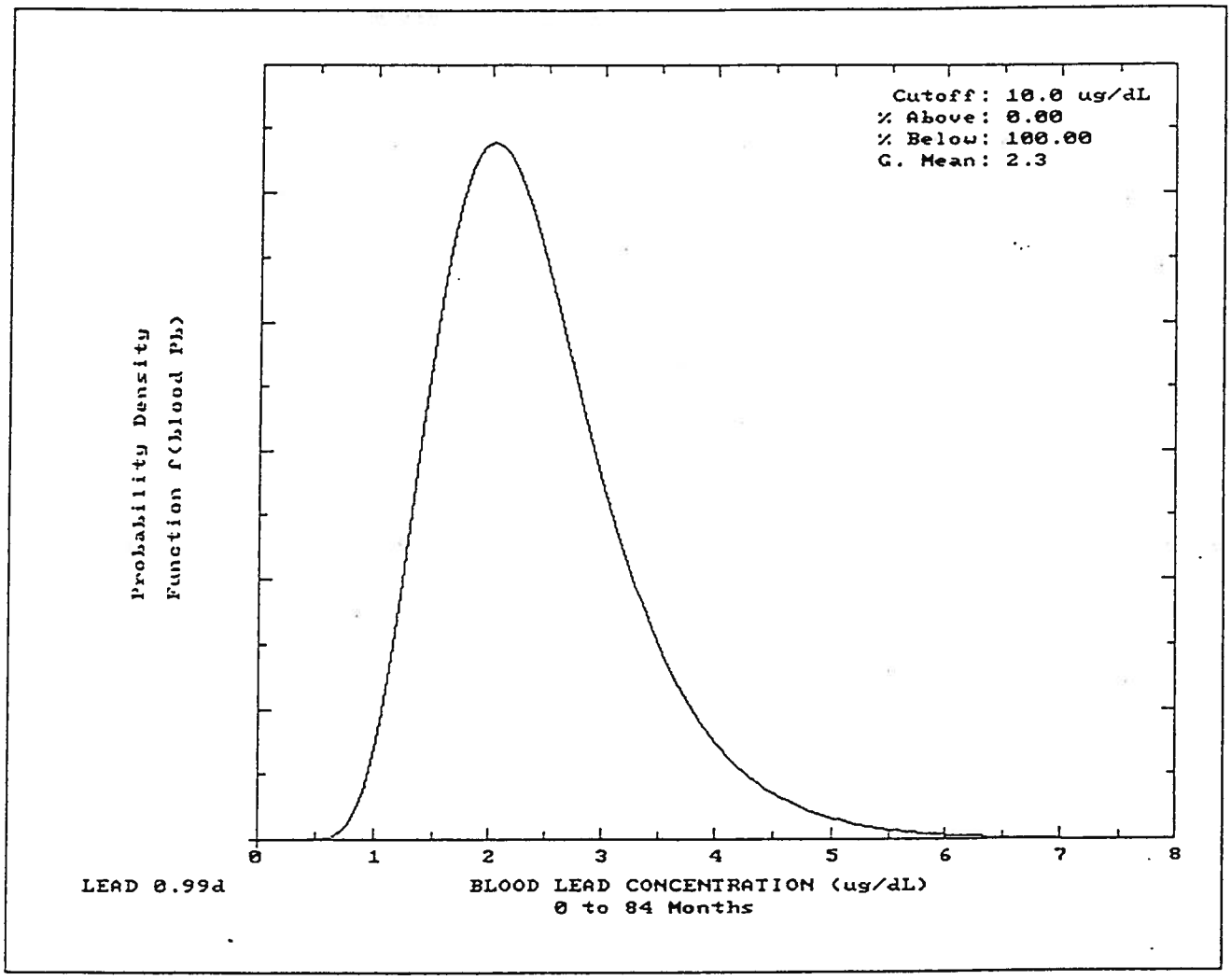

FIGURE 5-2

IEUBK Modeling Blood Lead Results - Subarea B

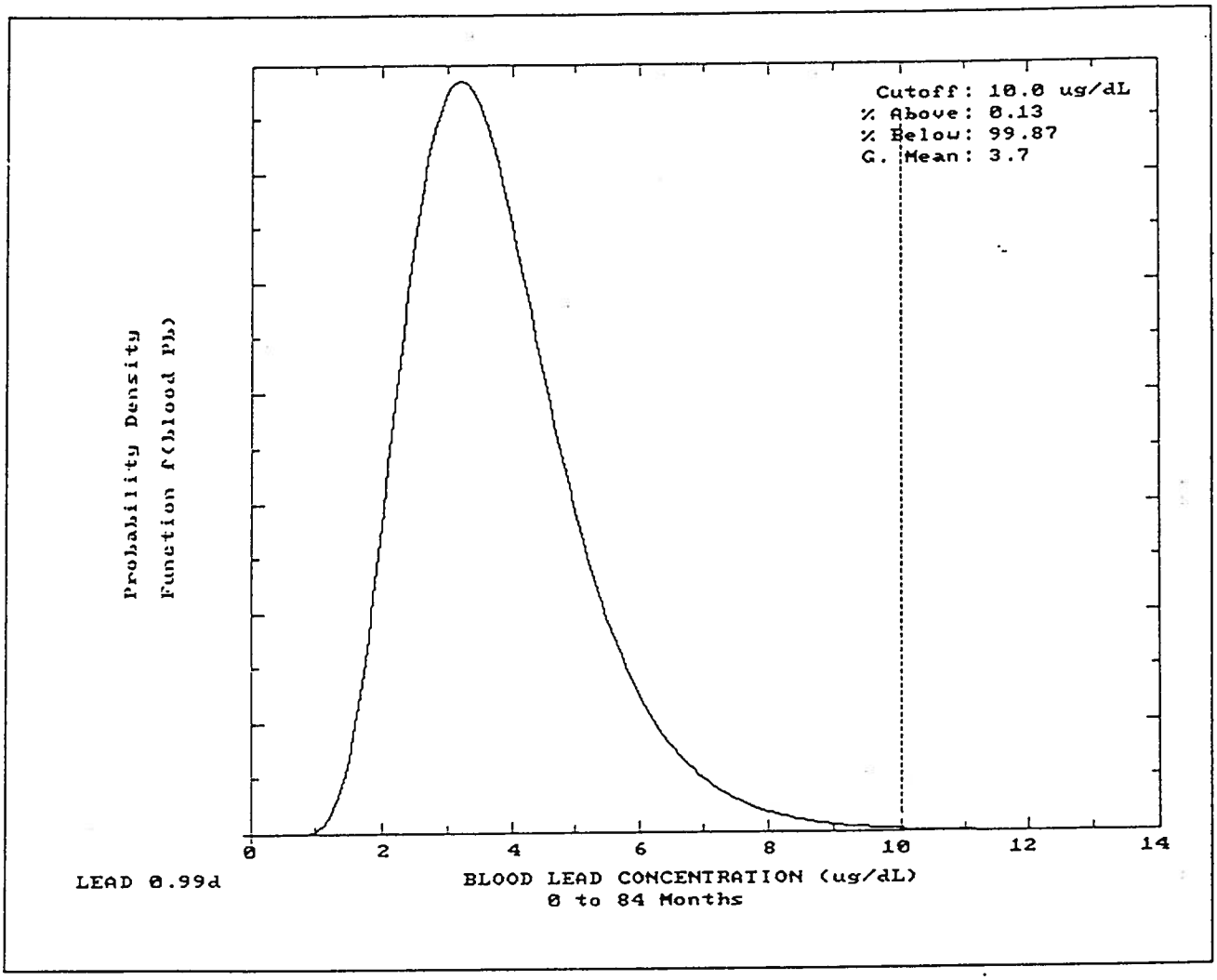

FIGURE 5-3

IEUBK Modeling Blood Lead Results - Subarea C

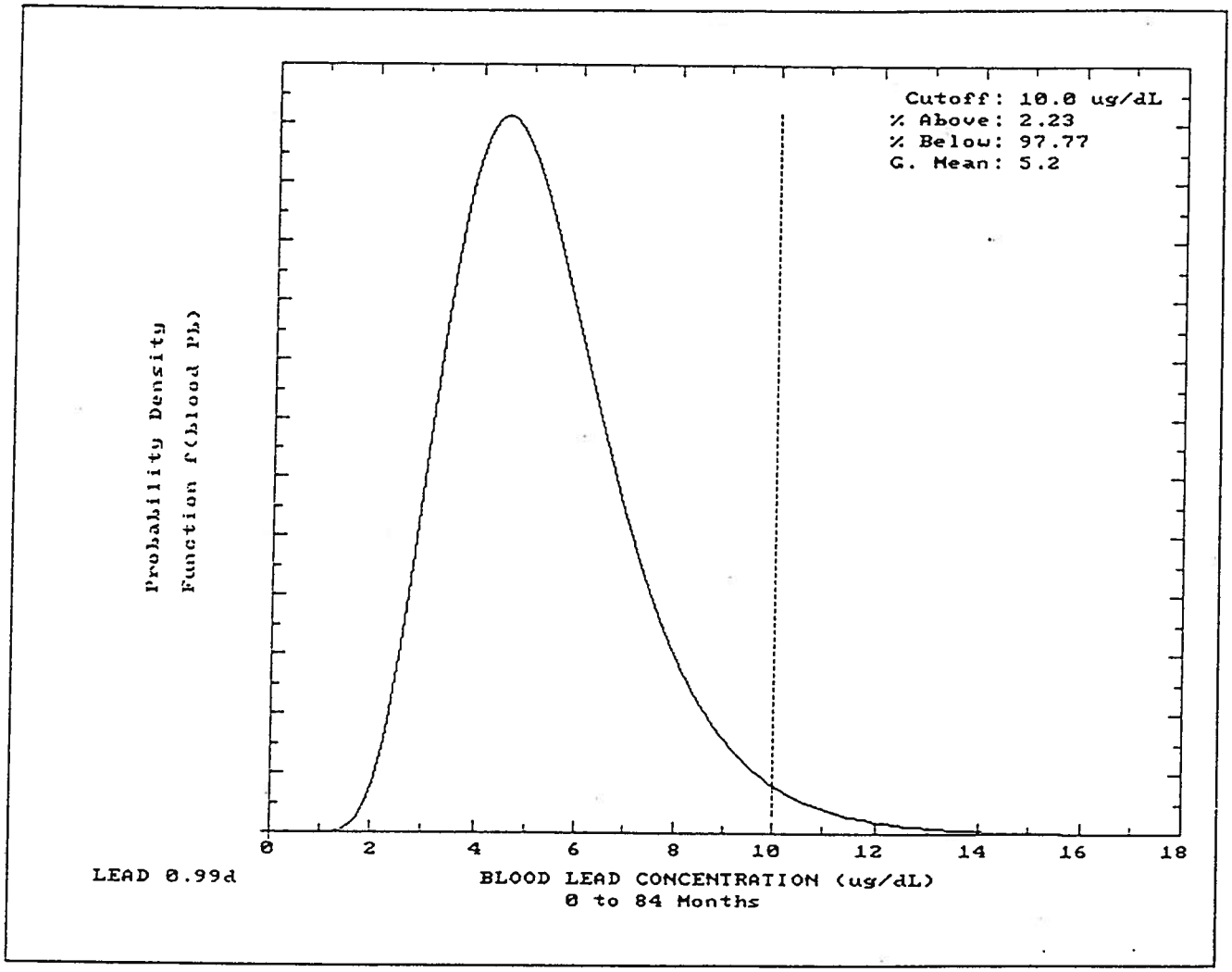

FIGURE 5-4

IEUBK Modeling Blood Lead Results - Subarea D

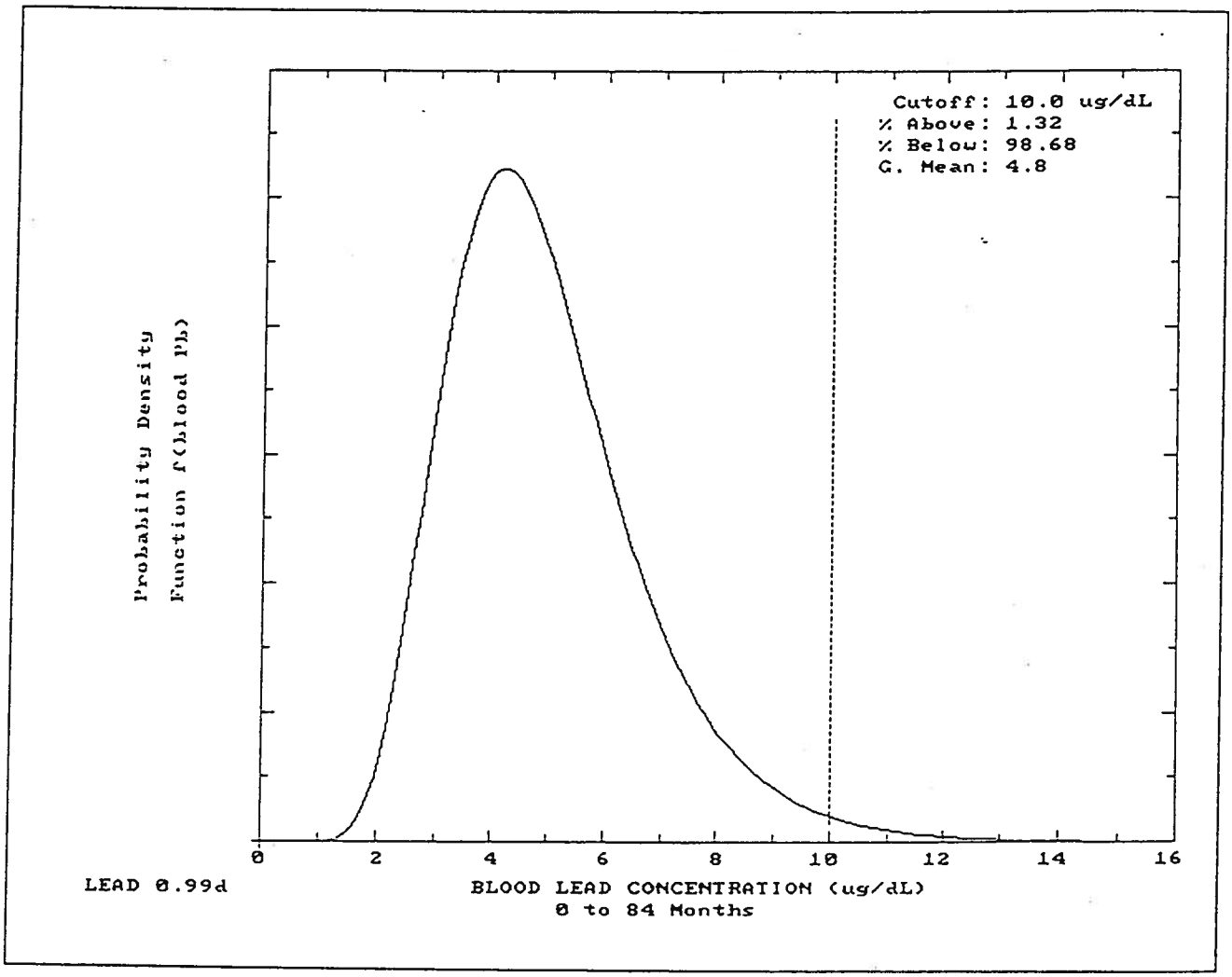

FIGURE 5-5

IEUBK Modeling Blood Lead Results - Subarea E

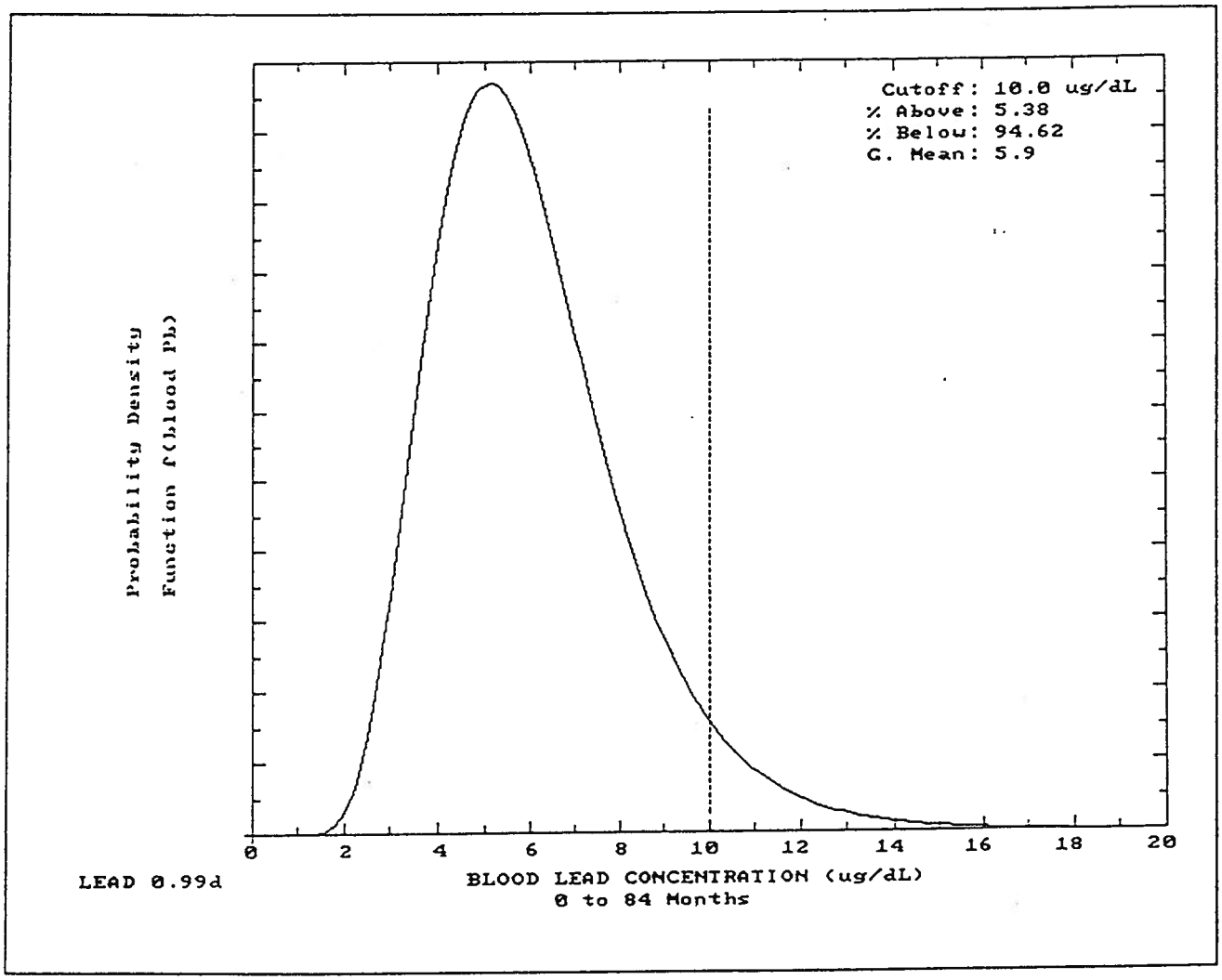

FIGURE 5-6

IEUBK Modeling Blood Lead Results - Subarea F_1

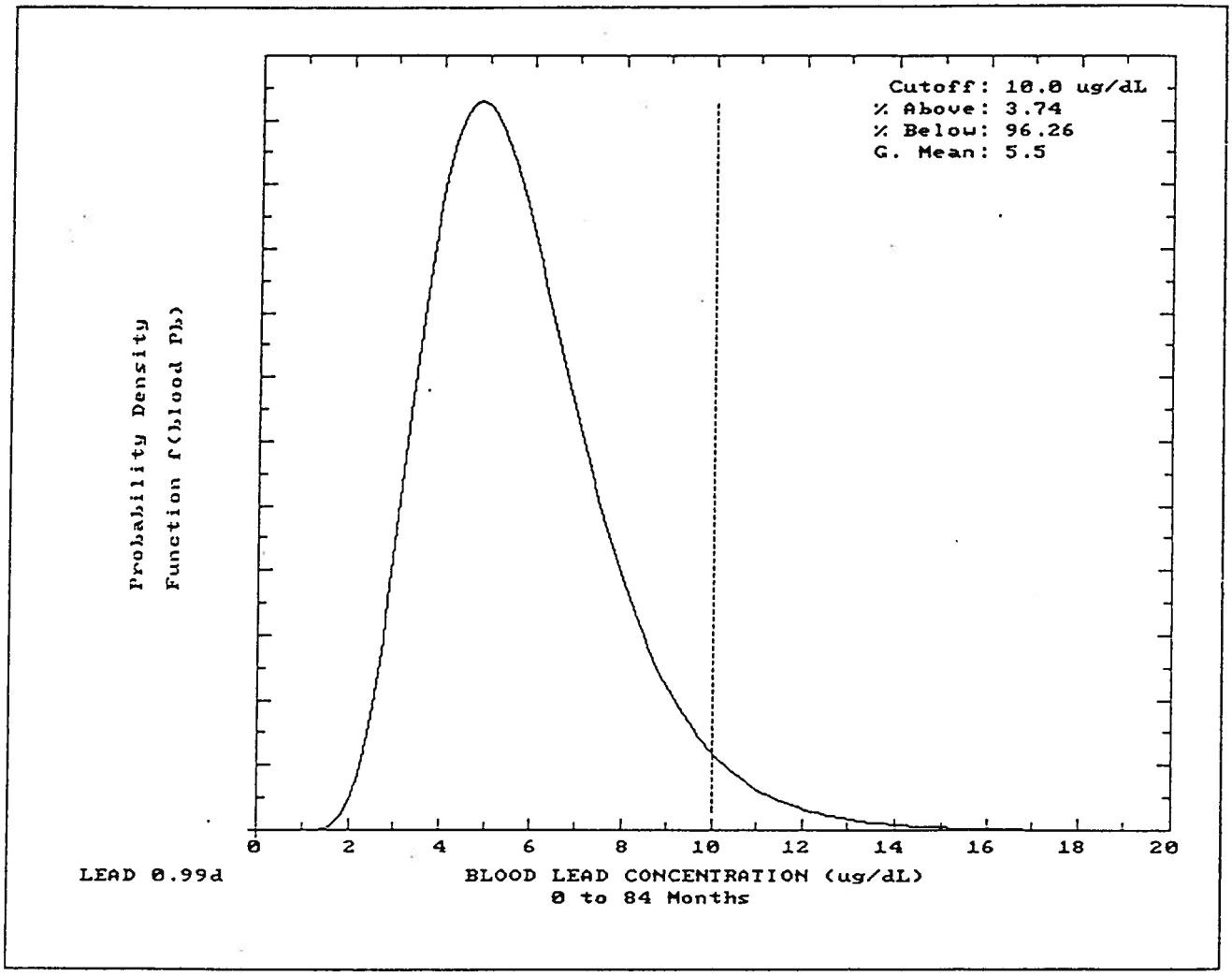

FIGURE 5-7

IEUBK Modeling Blood Lead Results - Subarea F_2

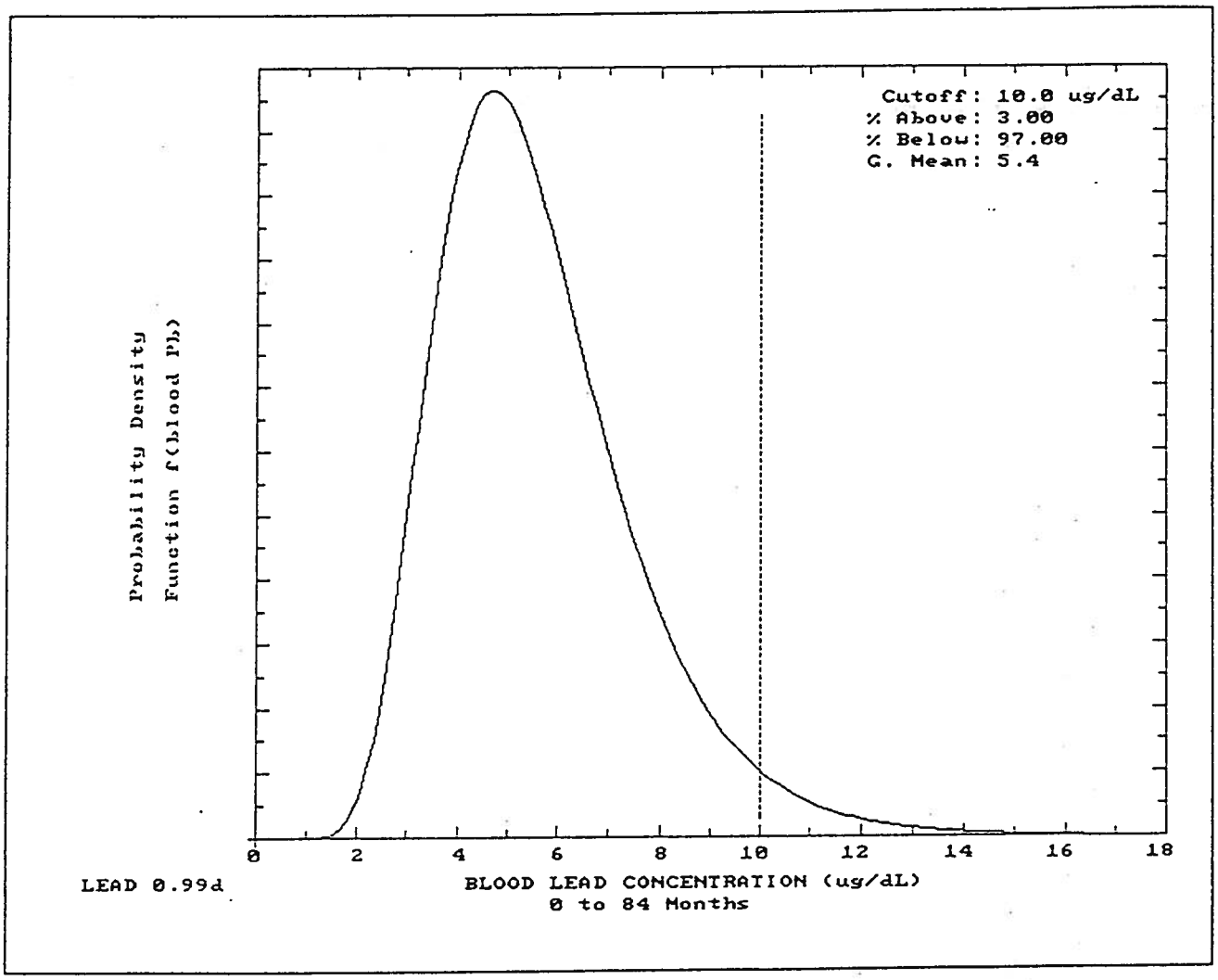

FIGURE 5-8

IEUBK Modeling Blood Lead Results - Subarea I

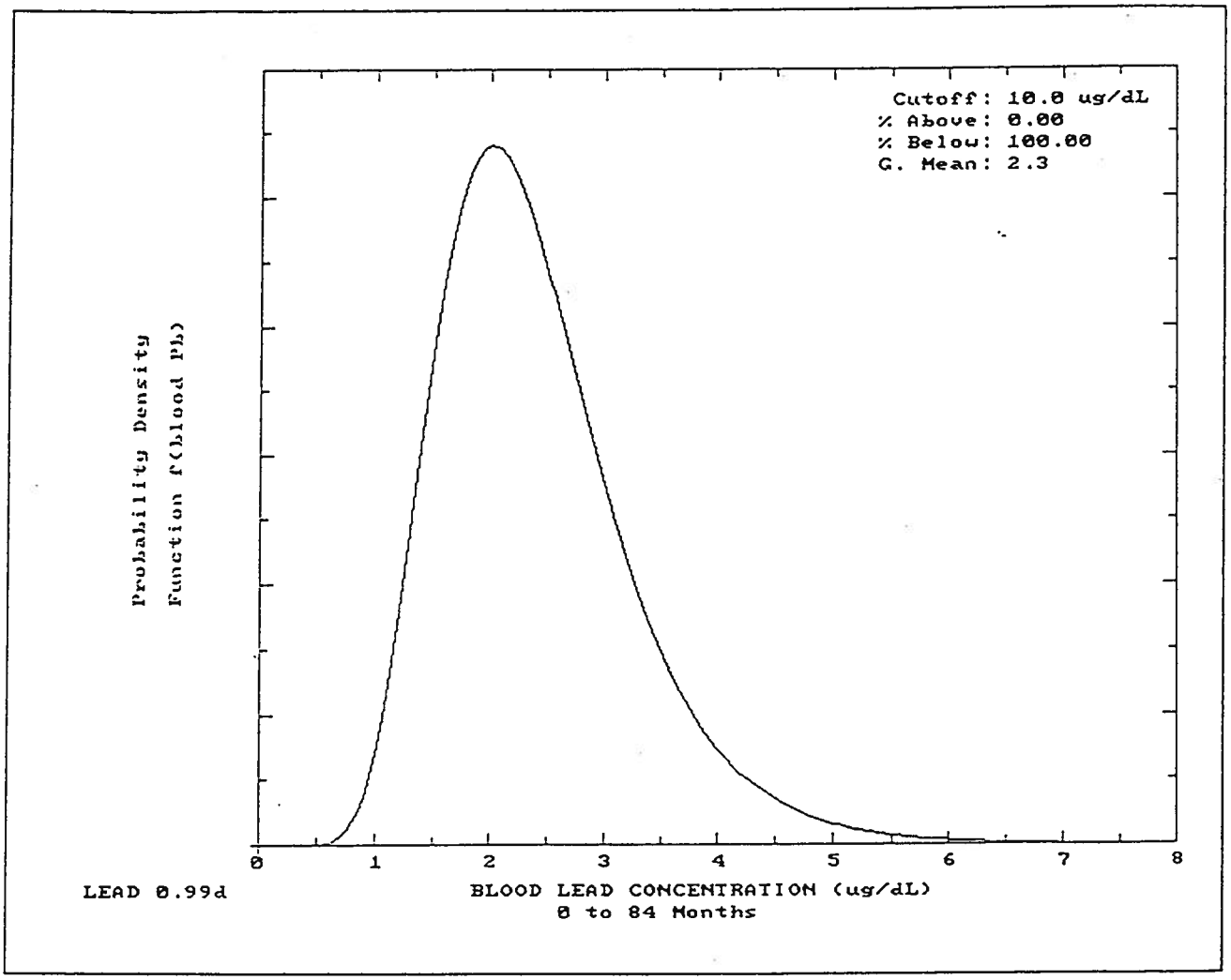

FIGURE 5-9

IEUBK Modeling Blood Lead Results - Subarea J

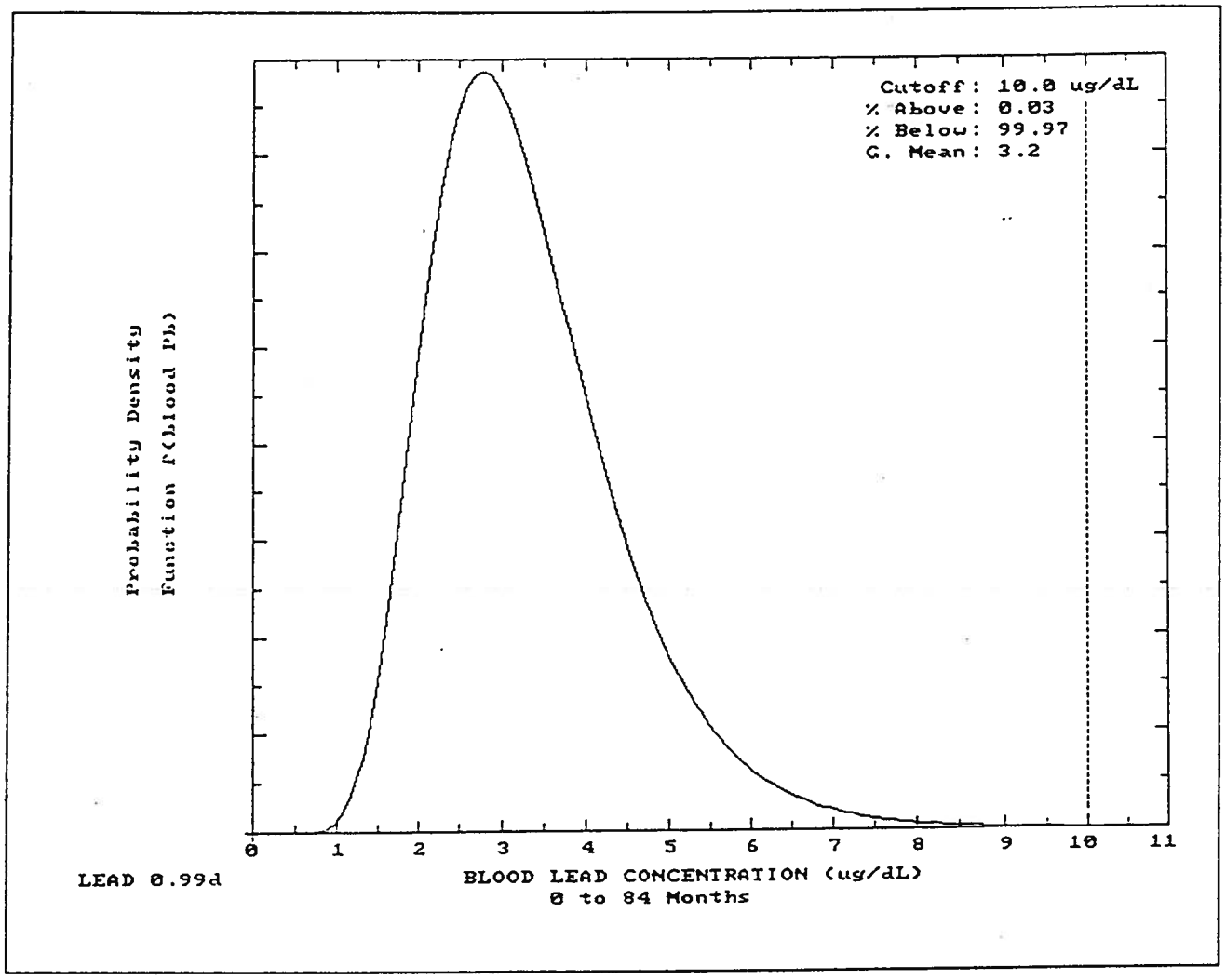

FIGURE 5-10

IEUBK Modeling Blood Lead Results - Subarea G (Opportunity)

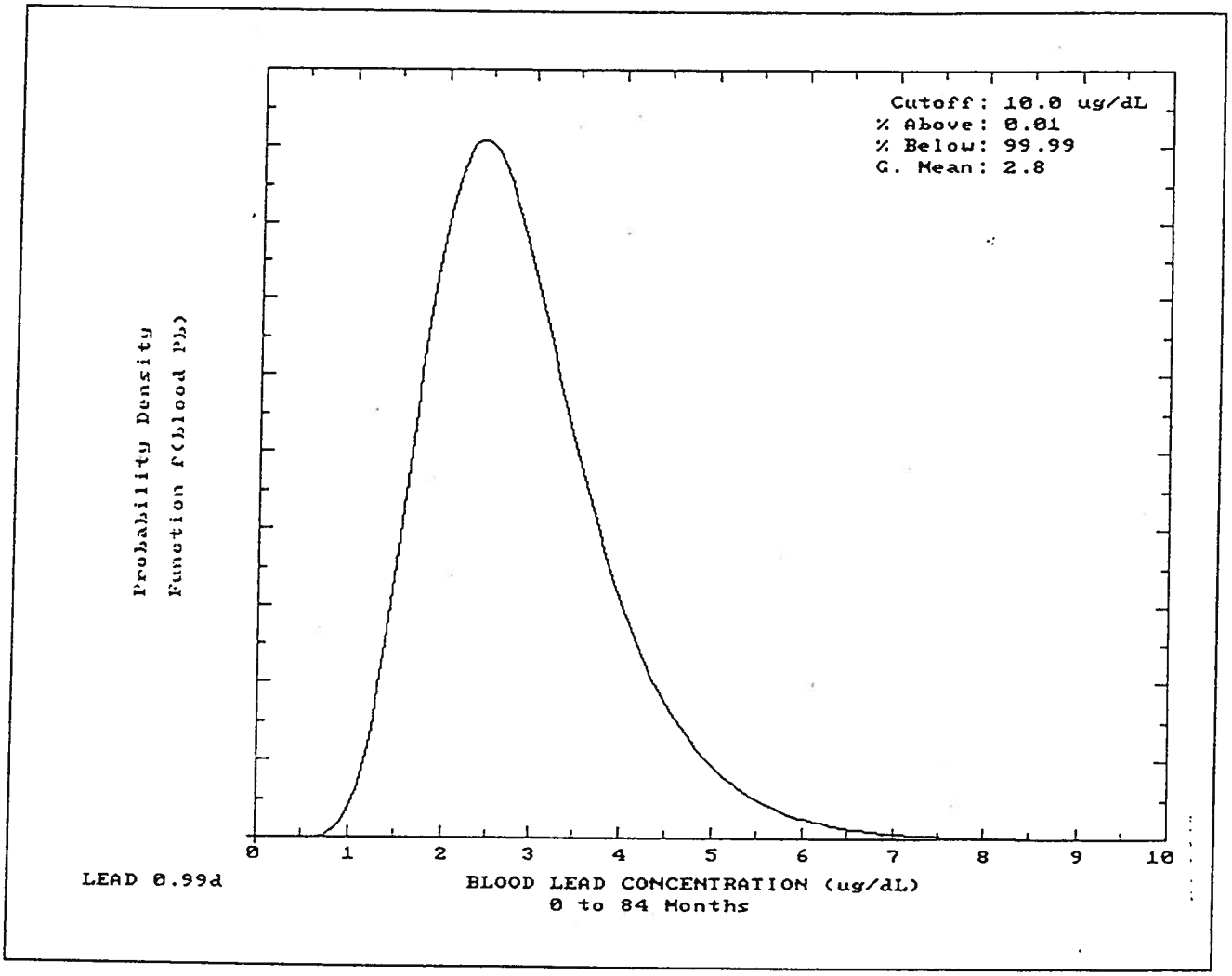

FIGURE 5-11

IEUBK Modeling Blood Lead Results - All Subareas Combined

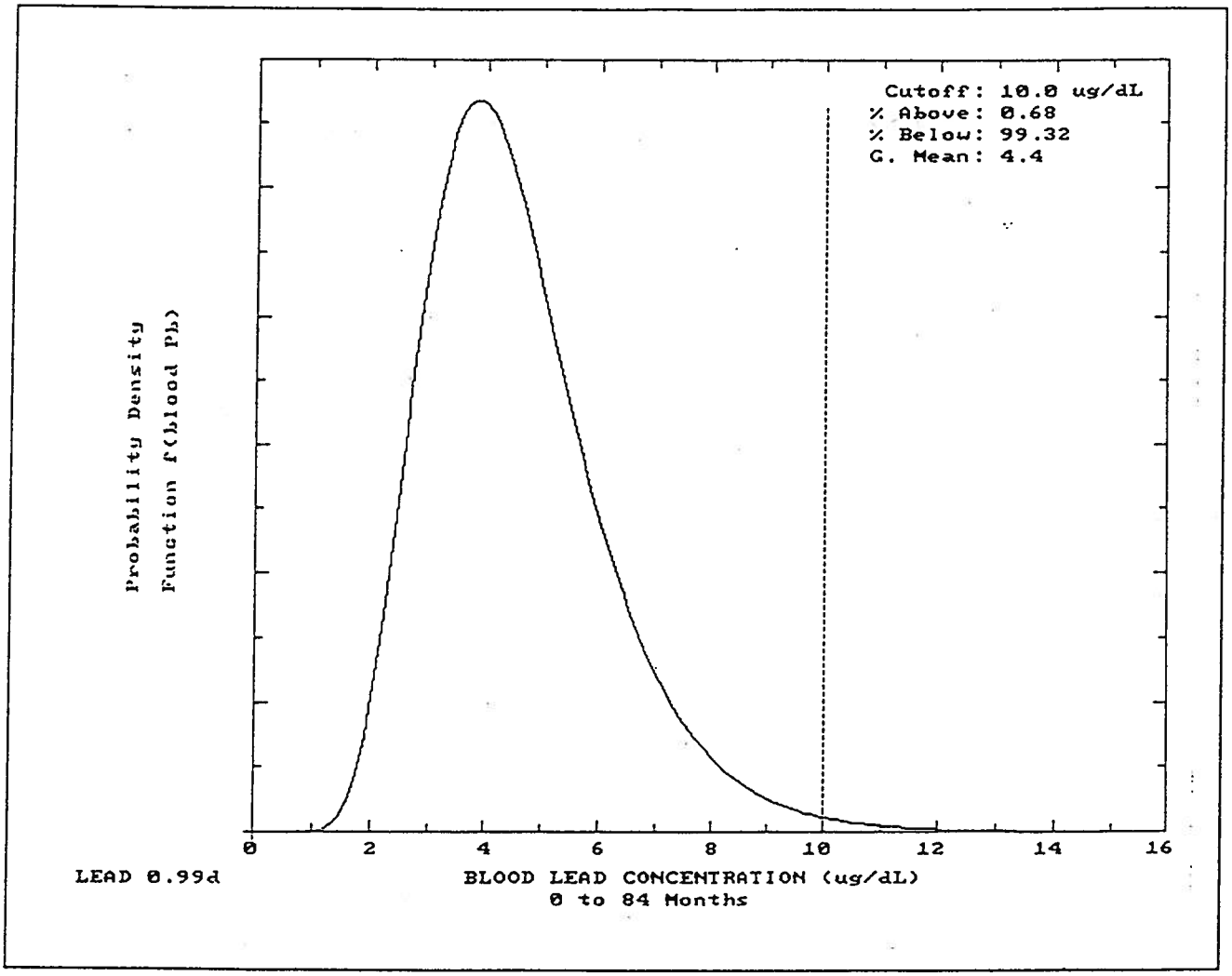

TABLE 5-3

IEUBK Modeling Results Summary

Subarea	Predicted Percentage of Individuals with Blood Lead Levels Above 10 µg/dL	Predicted Geometric Mean Blood Lead Level (µg/dL)
A	0.00	2.3
B	0.13	3.7
C	2.23	5.2
D	1.32	4.8
E	5.38	5.9
F1	3.74	5.5
F2	3.00	5.4
I	0.00	2.3
J	0.03	3.2
Opportunity	0.01	2.8
All Areas	0.68	4.4

Generally, EPA (1994c) considers risks from exposure to lead unacceptable if more than 5% of children have blood-lead levels in excess of 10 μg/dL. Thus, risk from lead exposure would be considered unacceptable for exposure subarea E.

5.3 ANALYSIS OF UNCERTAINTIES

Quantitative risk estimates are based on site-specific information, national default assumptions, toxicology literature and professional judgement. There are uncertainties associated with all of these sources, and, hence, there is uncertainty in all quantitative estimates of risk. In order to appropriately interpret and use quantitative risk estimates, uncertainties must be recognized and understood. Several sources of uncertainty have been identified in previous sections, including:

- Lack of groundwater data for most of Anaconda
- Limited environmental data for areas outside Anaconda and Opportunity
- Lack of data for lead in interior dust
- Toxicity criteria for arsenic
- Lack of bioavailability data for lead in soils and dust from the study area
- Lack of suitable methodology for evaluating dermal exposure to contaminated soils
- Use of default exposure assumptions and professional judgement in estimating CDI for arsenic and blood-lead levels for lead

In the following discussions, these uncertainties are further evaluated relative to their potential influence on the use of quantitative risk estimates in risk management decisions for the site.

5.3.1 LACK OF DATA FOR CHEMICALS OTHER THAN ARSENIC IN ANACONDA GROUNDWATER

Domestic drinking water samples collected from subarea A in Anaconda were analyzed only for arsenic; therefore, it is possible that other contaminants could be present at significant concentrations. This is not a data gap for Opportunity, since analyses of domestic groundwater in Opportunity did not detect any contaminants other than arsenic at significant concentrations. However, Opportunity is more distant from many waste sources and is characterized by generally lower soil contamination levels than is Anaconda. It may be inappropriate to extrapolate results of groundwater sampling directly from Opportunity to Anaconda.

There are three reasons that suggest that actual effects on the risk assessment are not substantial. First, concentrations of arsenic in subarea A domestic groundwater overlap significantly with background concentrations of arsenic in regional groundwater (Section 2.3.2), indicating that groundwater in this subarea is relatively unimpacted by site contamination.

Second, groundwater downgradient of contamination is not currently used as a source of drinking water within most of the community of Anaconda since municipal water is readily available. Municipal water is supplied by groundwater upgradient of contamination and is unimpacted. Thus, the exposure pathway is incomplete throughout most of the community.

Third, soil levels of cadmium, copper, and zinc were below health-based screening levels, indicating that concentrations in groundwater may be insignificant.

5.3.2 LIMITED ENVIRONMENTAL DATA FOR AREAS OUTSIDE ANACONDA AND OPPORTUNITY

The study area is large, and few data are available for undeveloped or agricultural lands. It is difficult statistically to justify these data as representative, and no quantitative risk estimates are provided outside of Anaconda and Opportunity. Because of the relative sparsity of sampling locations, it is possible that areas with significantly elevated levels of arsenic and lead exist, but have not been recognized. In these areas, risks could be greater than those estimated for Anaconda and Opportunity.

"Hot spot" areas with substantially higher concentrations of contamination are not expected given the primary transport mechanism, air, for contaminants from the smelter and associated wastes. Where data have been collected from more closely spaced locations, results are consistent with a relatively homogeneous distribution of contamination. However, there may be secondary transport mechanisms, such as runoff, which could concentrate contaminants in areas where pooling occurs. Thus, it is theoretically possible that some areas with higher than expected arsenic and/or lead concentrations might exist within the study area. It is not possible to determine the extent of any potential risks that might be associated with such areas. Therefore, screening levels are provided in Section 6.0 for application to areas outside Anaconda and Opportunity. When additional data become available for such areas, screening levels can be used to help assess potential human health risks for current or projected land uses.

5.3.3 LACK OF DATA FOR LEAD IN INTERIOR DUST

No measurements have been made for lead in interior dust for any of the communities within the Anaconda Smelter NPL Site. However, exposures to contaminated dust have been shown to be significant for arsenic in Anaconda and Opportunity, and, in fact, 55% of incidental ingestion of soil-derived contamination is assumed to come via interior dust. In order to

estimate lead concentrations in indoor dust, it was necessary to extrapolate from the available data on arsenic (Bornschein 1992, 1994). This extrapolation required the assumption that arsenic and lead would move in similar fashion from soil to dust, and that there are no significant indoor sources of lead or arsenic that would alter the baseline or "background" concentrations in homes.

The former assumption seems reasonable since one expects that transport from soil to dust will depend mainly on the physical characteristics of soil particles rather than their chemical composition. However, wastes from different sources may have both different particle size distributions and different arsenic and lead concentrations. If such sources contributed differentially to total arsenic and total lead concentrations in the community, there could be differences in transport of arsenic and lead into homes.

The maximum influence different sources might have on dust concentrations would be about a factor of 2 either higher or lower, since concentrations of arsenic in dust are about 43% of those indoors. If lead was transported very efficiently into homes, soil and dust lead concentration might in the worst theoretical case be equal (in several studies there has been no suggestion that soil contaminants might be concentrated in dust). If transport was very inefficient, little or no lead in soil would be transported into homes. Studies at several sites across the country suggest that neither of the above extreme alternatives is likely, implying that any uncertainty in estimates for lead concentrations in dust would be less than a factor of two. This is a relatively small uncertainty and, therefore, lack of interior dust data for lead is not expected to have significant impact on site-related lead exposures[2].

The baseline or "background" level of lead in indoor dust might be greatly influenced by lead-based paint; a source which would not contribute significantly to interior arsenic contamination. Therefore, the assumption that non-soil sources of arsenic and lead are similar

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[2] This analysis does not consider input from interior lead paint, which can cause indoor dust levels to greatly exceed those in outdoor soils.

is probably incorrect. This assumption, in fact, eliminates consideration of indoor lead-based paint in estimating lead exposures. This may significantly underestimate the potential for exposure in areas where homes have been painted in the past with lead-based paints. Estimates for lead exposure presented in this assessment should not be used to predict potential total lead exposures unless it is known that lead-based paint is not present, or, preferably, measurements for lead in indoor dust have been made.

5.3.4 UNCERTAINTY IN TOXICITY CRITERIA FOR ARSENIC

There continues to be discussion of the oral CSF for arsenic. Recent reviews and letters (Carlson-Lynch, et al. 1994; Beck et al. 1995) present one view of evidence that the oral CSF for arsenic is too high. Several lines of evidence are advanced to support this conclusion, and all are based on criticisms of the studies of the Taiwanese population from which toxicity criteria for ingested arsenic are derived.

First, a recent study (Yost et al. 1994) suggests that estimates of inorganic arsenic in the diet of the Taiwanese population may have been underestimated in the past, resulting in an exaggerated estimate of cancer potency. The study measured inorganic arsenic in rice and sweet potatoes, two staples in the Taiwanese diet, and results were interpreted to indicate that inorganic arsenic in these food stuffs was much greater than previously assumed.

Second, several studies in both humans and laboratory animals were interpreted to indicate that arsenic metabolism is saturable, and that saturation occurs at exposures less than those received by the Taiwanese population. This, in turn, would suggest that the apparent potency of inorganic arsenic as a carcinogen is exaggerated at high doses by reduction in detoxification. At lower doses, efficient metabolism to organic forms would reduce the effectiveness of a given exposure to inorganic arsenic in producing cancer.

Third, inadequate dietary methionine, an essential amino acid, may be present in the Taiwanese diet to support both basic metabolic needs and the metabolic demands caused by the ingestion of large amounts of inorganic arsenic. Methionine is likely to be a methyl donor in the conversion of inorganic arsenic to methylated forms, and lack of sufficient methionine in the diet could limit the capacity for arsenic metabolism in the body. This would result in a higher apparent potency of arsenic, since less metabolic detoxification could take place.

Finally, the presence of humic acids in the water supply for the Taiwanese population is suggested as causative or interactive in the production of human cancer. If humic acids do play such a role, exposure to arsenic in the absence of humic acids may not have the same high potential to cause cancer as that seen in the study population.

Though the above studies seem, on the surface, to make a reasonable case for lowering the arsenic oral CSF, objective examination of all the evidence demonstrates significant flaws in all of the above arguments. An appropriate CSF can only be developed if the limitations of all information is understood and factored into the analysis. On more thorough examination, it does not appear that sufficient information is currently available on which to base a reevaluation of the arsenic CSF.

Data presented by Yost et al. (1994) are dramatically counter to other measurements of inorganic arsenic in rice and potatoes grown in soils treated with inorganic arsenic. This discrepancy is unexplained, but could be due to strong acid treatment used to extract arsenic in the Yost study. This could have resulted in the artifactual production of inorganic arsenic (Mushak and Crocetti 1995). The forms of organic arsenic in plants are poorly known, and it is not clear how easily inorganic arsenic can be produced from these forms, nor how this may vary among different plant species. Until such problems are resolved, it will not be possible to revise the cancer slope factor based on the single least conservative study.

Information available on biotransformation in humans is generally weak and difficult to interpret. Moreover, there are conflicting reports which variously suggest that the saturation point for human methylation of inorganic arsenic falls above or below the exposures received by the Taiwanese population (Mushak and Crocetti 1995). That some reports suggest the former is an important observation. For example, similar percentages for inorganic arsenic, monomethyl arsenic, and dimethyl arsenic were found in urine of subjects in Nevada, exposed on average to levels of arsenic similar to those for the "high dose" group in Taiwan, and in subjects in a control group. The results did not support saturation of metabolism and, in fact, indicated that organic arsenic made up 78 percent of total arsenic in exposed subjects and 86 percent in controls (Warner et al. 1994). Such a small difference is probably not statistically or biologically significant and is not consistent with a low threshold for saturation of arsenic metabolism.

Similarly, in the study by Buchet et al. (1981), which is often cited in support of a relatively low metabolic threshold, data seem to indicate significant metabolic capability at all doses. Individuals receiving 1,000 µg of inorganic arsenic per day, for example, formed nearly the same proportion of total methyl metabolites as did individuals receiving only 125 µg (74 versus 84 percent), respectively. Such differences are small enough to be due to sampling errors and individual variation. On the basis of metabolite formation, it is difficult to conclude that metabolism has reached saturation.

The key to resolving the issue of metabolism in arsenic would seem to be characteristic of mechanisms of methylation and the study of these biochemical pathways in human systems. In addition, empirical studies should focus on the kinetics of the inorganic arsenic rather than on metabolite formation and metabolite ratios. The latter are indirect measures of the amount of the ultimate carcinogen (assumed to be inorganic arsenic) which reaches target tissues. Moreover, metabolite ratios especially are difficult to interpret and have no demonstrated connection with the amounts of inorganic arsenic which reach target tissues.

The nutritional status of the Taiwanese appears to be sufficient for normal metabolic processes (Engel and Receveur 1993). In addition, a simple calculation (Mushak and Crocetti 1995) suggests that the amount of methionine which might be necessary to support metabolism of ingested arsenic is at best a small fraction of total daily intake, on the average of less than 1 percent. It seems likely that the "problem" related to nutritional status is really a "red herring." Until such time as new data become available which challenge the above conclusions, it seems safe to dismiss the argument for nutritional deficits as a factor influencing cancer potency in the Taiwanese populations.

Finally, the presence of humic acids in water consumed by the Taiwanese seems unlikely to be a causative factor in cancer. It appears that arsenic, not humic acids, are the constant in the various stages of both Blackfoot disease and precancerous skin lesions (Mushak and Crocetti 1995). Moreover, both skin cancer and internal cancers are found in patients treated with Fowler's solution where humic acids were not a factor (EPA 1986). Thus, it has been reasonably concluded that humic acids are not necessary for the carcinogenic activity of arsenic. It is possible that humic acids could alter the carcinogenic response in humans through some as yet unknown mechanism. Available data are, however, apparently not sufficient to establish this as a possibility, much less quantify such an effect. Until substantial additional data are available, it will not be possible to assess the contribution, if any, of humic acids to carcinogenesis in the Taiwanese population.

Currently, regional guidance recommends recognizing uncertainties in the arsenic oral CSF, but making no changes in the CSF for the purposes of quantitative risk assessment, and this approach is taken in this assessment. It is, thus, assumed that uncertainties in the arsenic oral CSF are best taken into account in the risk management process.

5.3.5 LACK OF DATA ON BIOAVAILABILITY OF LEAD IN SOILS AND INTERIOR DUST

Bioavailability of lead in wastes from mining and smelting activities is recognized as an important factor in human exposure. In some cases, such as Butte, Montana, bioavailability of lead has been shown to be much reduced from the default value of 30 percent in the IEUBK model. These findings in animal studies are consistent with a large exposure study of young children living in Butte (Bornschein 1991).

Some wastes in Anaconda, such as the mill tailings in the Opportunity Ponds, may be similar to wastes found in Butte. These wastes were both derived from the same area and from similar processes. However, other wastes in Butte (e.g., waste rock) are not found in Anaconda. Further, large quantities of lead may have been released from the smelter in Anaconda, whereas only limited smelting occurred in Butte. Due to these differences, it is not possible to extrapolate bioavailability estimates from Butte to Anaconda.

Correlations with other studies can often be drawn based on geochemistry in soil. However, no speciation data are available to determine the dominant forms of lead in soils at the Anaconda site. Without such data, one must consider measurements of high bioavailability of lead in wastes at the Smuggler Mine NPL site in Colorado, and the Jasper County, Missouri NPL site (Griffin 1995) where considerable lead smelting occurred, and the blood lead studies in East Helena, Montana (EPA 1986). Such studies support bioavailability estimates at or above the model default of 30 percent (unpublished results from swine bioavailability studies show absolute bioavailabilities in excess of 40% for the Smuggler Mine and Jasper County sites).

It is conceivable that bioavailability of lead in soils at Anaconda is less than the IEUBK model default. However, site-specific data on which to base a quantitative estimate of bioavailability are lacking. Thus, it is reasonable to assume that the default assumption in the

IEUBK model is protective. It is not possible to determine at this time, however, if the default is overly conservative.

5.3.6 LACK OF METHODOLOGY FOR EVALUATING DERMAL EXPOSURE TO METALS IN SOIL

Little information is available on which to base estimates of dermal absorption of arsenic or metals in soil. However, a few reports suggest that absorption will be very inefficient, even for soluble arsenic or metal forms (ATSDR 1991a). This information is difficult to extrapolate directly to human exposure, but it does suggest that dermal exposure should be a minor pathway. It is not likely that dermal absorption of arsenic or metals from soil contributes significantly to overall exposures within the study area.

5.3.7 USE OF DEFAULT EXPOSURE ASSUMPTION AND PROFESSIONAL JUDGEMENT

Default exposure assumptions and professional judgement are used throughout the exposure assessment to estimate potential chronic daily intakes. Data are not available to determine quantitatively how each of these assumptions and judgements might influence CDI calculations. However, as discussed in Section 3.4, urinary arsenic concentrations predicted using the basic assumptions also used in the exposure assessment are in good agreement with those actually measured in the community of Anaconda. This suggests that assumptions and judgements made are reasonable and uncertainty in the results of the exposure assessment is relatively small, at least for young children.

It should be also be noted that uncertainties in exposure assumptions not directly assessed by the comparison of observed and predicted urinary arsenic in children are not expected to greatly influence exposure estimates. As discussed in section 3.5, factors such as soil/dust ingestion rates for adults, and exposure frequency and duration, are at least conservative (i.e.,

are unlikely to underestimate possible exposures) and probably do not result in substantial overestimation.

It is reasonable to conclude that exposures calculated in this assessment are acceptable for both CTE and RME estimates.

5.4 SUMMARY

Section 5.1 presents cancer and noncancer risks associated with exposure to arsenic in groundwater, soil, and dust. Cancer risks based on RME for soil/dust for all subareas of the site evaluated fall into a narrow range of about 1×10^{-5} to 3×10^{-5}. This narrow range reflects the relatively even distribution of arsenic within Anaconda and Opportunity. A similar narrow range of hazard quotients (0.1 to 0.3) is estimated for the same exposures. Cancer risk estimates all fall within the EPA risk range, and all hazard quotients fall below the target level of one.

In subarea A and in Opportunity, cancer risks based on RME for groundwater are in the same range as those for exposure to soil/dust; this is also true for hazard quotients. Again, all estimates are within acceptable ranges, or below risk targets.

Combined risks and hazard quotients from RME to both groundwater and soil/dust (subarea A and Opportunity only) remain within the ranges of risks and HQs established for RME for soil/dust ingestion. This suggests that even where near maximum exposures to both groundwater and soil/dust occur simultaneously, exposures will remain within acceptable levels.

EPA (1994c) generally considers risks from lead exposure unacceptable if more than 5% of children have blood-lead levels exceeding 10 µg/dL. Five percent of the children in subarea E are estimated to have blood-lead levels exceeding 10 µg/dL.

Analysis of uncertainties in the above risk estimates suggests that it is unlikely that risks have been significantly underestimated, especially for the well characterized communities of Anaconda and Opportunity. The sparsity of data in other areas, however, leaves open the question of whether significant "hot spots" might exist within the study area. In the absence of data, screening levels are provided in Section 6.0 to assist in assessing specific locations when additional data become available.

6.0 RISK-BASED SCREENING LEVELS

This section of the HHRA develops risk-based screening levels for the Anaconda Smelter NPL Site. Screening levels are developed for arsenic in soil and surface water, and are based on exposure assumptions for residential, agricultural, occupational, and recreational exposure scenarios. Exposure assumptions for agricultural, occupational, and recreational scenarios are taken from other risk assessments prepared for the Anaconda Smelter NPL Site or adjacent areas. Screening levels are intended to be used together with site maps that illustrate chemical concentration boundaries (generated using the kriging technique) to identify potential areas of risk. Also, screening levels can be used to evaluate any additional data collected from specific locations. Finally, comparison of screening levels for scenarios not evaluated quantitatively in this HHRA provides further evidence regarding the potential significance of exposures associated with non-residential land use. Such comparisons may provide useful information pertinent to evaluation of remedial options for different areas of the site.

Screening levels are developed for the following scenarios:

- Resident
- Agricultural worker (exposure during plowing/tilling)
- Commercial worker
- Recreational visitor (dirt-bike rider)
- Recreational visitor (adolescent playing in pooled water)

Screening levels for soil are developed based on the following exposure pathways:

Residents (Adults and Children Ages 0 - 6):

- Ingestion of surface soils
- Ingestion of interior dust

Agricultural Workers (Adults):

- Ingestion of surface soils
- Inhalation of dust

Recreational Users (Dirt Bike Riders):

- Ingestion of surface soils
- Inhalation of dust

Recreational Visitors (Swimmers/Waders):

- Ingestion of surface water
- Dermal exposure to surface water

Commercial Workers (Adults):

- Ingestion of surface soils
- Ingestion of interior dust

Screening levels are developed based on the carcinogenic and noncarcinogenic effects of arsenic. Screening levels are developed for a carcinogenic risk range of 10^{-3} to 10^{-7}, and a noncarcinogenic HI of 1. Screening levels are developed for both RME and CTE exposure scenarios.

6.1 EXPOSURE ASSUMPTIONS

6.1.1 RESIDENTIAL EXPOSURE SCENARIO

Screening levels for the residential exposure scenario are calculated using the exposure assumptions used in this HHRA to evaluate residential exposures at the Anaconda Smelter NPL Site. Screening levels for this exposure scenario are based on ingestion of surface soil/interior dust. Exposure assumptions for the residential scenario are presented in Table 6-1 and are discussed below. Screening levels for residential exposures are calculated according to the following formulas:

TABLE 6-1

Exposure Parameters for the Residential Scenario

Symbol	Units	Definition	Value	Source
SL	(mg arsenic/kg soil)	risk-based screening level	Section 6-2	-
TR	(unitless)	target risk	Section 6-2	-
AT	(days)	averaging time	Carcinogens = 25,550 Noncarcinogens RME = 10,950 CTE = 3,285	EPA 1989a
CF	(kg/mg)	conversion factor	.000001	EPA 1989a
EF	(days/year)	exposure frequency	350	EPA 1989a
SF_o	$(mg/kg\text{-}day)^{-1}$	oral slope factor for arsenic	1.5	EPA 1995b
IR_{child}	(mg/day)	soil ingestion rate for children	RME=200 CTE=100	EPA 1993a EPA 1993a
ED_{child}	(years)	exposure duration for children	RME=6 CTE=2	EPA 1993a EPA 1993a
BW_{child}	(kg)	average body weight for children	15	EPA 1989a
IR_{adult}	(mg/day)	soil ingestion rate for adults	RME=100 CTE=50	EPA 1993a EPA 1993a
ED_{adult}	(years)	exposure duration for adults	RME=24 CTE=7	EPA 1993a EPA 1993a
BW_{adult}	(kg)	average body weight for adults	70	EPA 1989a
FS	(unitless)	fraction of soil ingested	0.45	Professional Judgement
BAF_S	(unitless)	bioavailability of soil	0.183	EPA 1995a
C	(unitless)	Contribution of soil arsenic to arsenic in dust	0.43	Calculated, see text.
FD	(unitless)	fraction of dust ingested	0.55	Professional Judgement
BAF_D	(unitless)	bioavailability of interior dust	0.258	EPA 1995a

posures:

$$\frac{(TR \times AT)}{SF_O \left(\frac{IR_{child} \times ED_{child}}{BW_{child}} + \frac{IR_{adult} \times ED_{adult}}{BW_{adult}}\right) \times [(FS \times BAF_S) + (C \times FD \times BAF_D)]}$$

exposures:

$$\frac{(TR \times AT \times RfD)}{) \times \left(\frac{IR_{child} \times ED_{child}}{BW_{child}} + \frac{IR_{adult} \times ED_{adult}}{BW_{adult}}\right) \times [(FS \times BAF_S) + (C \times FD \times BAF_D)]}$$

= Screening Level for Soil (mg/kg)
= Target Risk (unitless)
= Averaging Time (days)
= Reference Dose for Arsenic (mg/kg-day)
= Conversion Factor for Soil (kg/mg)
= Exposure Frequency (days/year)
= Oral Slope Factor for Arsenic (mg/kg-day^{-1})
= Soil Ingestion Rate (mg/kg)
= Exposure Duration (years)
= Body Weight (kg)
= Fraction of Soil Ingested (unitless)
= Bioavailability Factor for Soil (unitless)
= Contribution of Soil Arsenic to Arsenic in Dust (unitless)
= Fraction of Dust Ingested (unitless)
= Bioavailability Factor for Dust (unitless)

es are averaged over 70 years or 25,550 days (EPA 1989a). AT for
sures is equal to ED x 365 days/year. AT for RME noncarcinogens is,
s and AT for CTE is 3,285 days.

ssumed to be 350 days/year (EPA 1989a). This value assumes that
single two-week vacation per year. An EF of 350 days/year is used to
ingestion by residents. This value is conservative, since soil in

Montana is likely to be frozen for several months out of the year, and ingestion of soil during this time is unlikely.

Ingestion Rate

Soil/dust IRs for young children (0 to 6 years old) and adult residents are 200 and 100 mg/day for RME, and 100 and 50 mg/day for CTE (EPA 1993a). Time-weighted CTE and RME soil/dust IR are calculated assuming 6 years of exposure for children and 24 years for adults.

Exposure Duration

The EPA (1993a) recommended ED for RME is 30 years for residents, spanning a time period from birth into adulthood. Exposures are time-averaged over 30 years, assuming 6 years of exposures for children and 24 years for adults. For evaluation of CTE, EPA (1993a) recommends using EDs of two years for children and 7 years for adults for a total ED of nine years.

Body Weight

The default BW parameters for young children and adults are 15 and 70 kg, respectively (EPA 1989a). These values are used to calculate screening levels based on residential exposures.

Fraction of Soil and Dust Ingested

Of the total amount of soil/dust ingested (see Ingestion Rate above), 45% is assumed to come from soil and 55% from interior dust.

Bioavailability of Soil and Dust

The values selected for soil and dust bioavailability (BAF_S and BAF_D) were derived by EPA (1994a, 1995a) from data presented in "Determination of Bioavailability of Soluble Arsenic and Arsenic in Soil and Dust Impacted by Smelter Activities Following Oral Administration

in Cynomolgus Monkeys" (Battelle 1994). The selected values (18.3% for soil and 25.8% for dust) are the mean absolute bioavailabilities identified in this study.

Contribution of Soil Arsenic to Arsenic in Dust

The contribution of soil arsenic to arsenic in dust was derived from multiple regression analyses performed by Bornschein (1994) on data collected during the Anaconda arsenic exposure study. This is described in detail in Section 3.3.1.2.

6.1.2 AGRICULTURAL WORKER SCENARIO

Screening levels for soil are developed for the agricultural worker scenario for the exposure pathways of soil ingestion and inhalation of windblown dust. Agricultural workers at the site could come into contact with contaminants in soils during plowing, planting, field maintenance, and harvesting, and incidental ingestion of soil and inhalation of dust may result in significant exposure. Incidental ingestion of soil may occur when contaminated soil adheres to hands and is subsequently ingested via hand-to-mouth behavior (e.g., when eating lunch), and dust may be inhaled when it is resuspended during field work.

Exposure assumptions used for the agricultural worker scenario are derived from the Draft Baseline Risk Assessment for the SST OU, Silver Bow Creek NPL Site (CDM Inc. 1994) and from relevant EPA guidance documents. Exposure assumptions are summarized in Table 6-2 and are discussed below. Screening levels for soil based on the agricultural worker scenario are calculated using the following formula based on carcinogenic exposures:

$$SL = (TR \times AT \times BW)/((EF \times IRs \times ED \times CFs \times SF_O \times BAF_S) + (EF \times ED \times IR \times SFi \times DL \times ET))$$

Where:	SFi	=	Inhalation Slope Factor for Arsenic (mg/kg-day)
	DL	=	Dust Loading Factor (kg/m^3)
	ET	=	Exposure Time (hours/day)

All other parameters are previously defined.

Screening levels based on noncarcinogenic exposure cannot be calculated for the agricultural worker scenario. The exposure pathways evaluated for this scenario are ingestion of soil and inhalation of dust. However, a reference concentration that can be used to evaluate noncarcinogenic inhalation exposure is not available for arsenic. Screening levels based on noncarcinogenic exposure are, therefore, not calculated for this scenario.

Averaging Time

Carcinogenic exposures are averaged over 70 years or 25,550 days (EPA 1989a). This value is used to calculate screening levels based on exposure by agricultural workers.

Body Weight

The default BW parameters for adults is 70 kg, respectively (EPA 1989a). This value is used to calculate screening levels based on the agricultural worker scenario.

Exposure Frequency

To calculate screening levels for the agricultural worker scenario, CTE and RME EFs of three and five days per week, respectively are assumed. It is also assumed that ingestion of soil is not possible at times when the soil is frozen (approximately five months each year). Exposures are therefore only evaluated for seven months out of the year, and EFs of 140 and 84 days per year are assumed to calculate screening levels based on RME and CTE exposure, respectively. These EFs may be high, as agricultural workers may not be engaged in activities during which they could contact soil each working day.

Exposure Duration

EPA (1991c) recommends using an ED of 25 years to evaluate worker exposures. However, most agricultural workers near the Anaconda Smelter are expected to also be residents of the area. Residential EDs are, therefore, considered more appropriate for evaluation of these workers. For development of screening levels based on RME, an ED of 30 years is used, which is an upper range (90th percentile) estimate for residency at one address (EPA 1989a).

Screening levels for CTE are based on an ED of nine years, the average estimate for residency at one address (EPA 1989a).

Soil Ingestion Rate

EPA (1993a) recommends a soil IR of 480 mg/day to evaluate RME from soil ingestion for professions during which intensive contact with soil may occur. For agricultural worker exposures at the Anaconda Smelter NPL Site, intensive contact with soil is only expected during plowing. Based on the types of crops grown at the site, plowing is assumed to be limited to a maximum of 14 days per year. During non-contact intensive activities (e.g., watering, planting, and harvesting), lower soil IR are considered more appropriate. For such activities the EPA (1993a) default soil IR of 100 mg/day for workers is used for the RME. The EF for RME for agricultural workers is 140 days/year. To calculate screening levels based on RME, it is assumed that farmers ingest 480 mg of soil for 14 days per year and 100 mg/day for 126 days per year.

Current data are insufficient to estimate a CTE soil ingestion rate for workers who may have intensive contact with soil (i.e., during plowing) (EPA 1993a). Based on professional judgement, an average soil IR of 100 mg/kg is considered reasonable for such exposures. This value is used for CTE soil ingestion during plowing. The default soil IR for activities associated with non-intensive contact with soil (50 mg/day) (EPA 1991c) is used for CTE during agricultural activities other than plowing. The EF for CTE worker exposures is 84 days/year. Screening levels based on CTE are calculated assuming a soil IR of 100 mg/day for 14 days per year and 50 mg/day for 70 days per year.

Bioavailability of Soil

The BAF_S of 18.3% was derived by EPA (1994a, 1995a) from data presented in "Determination of Bioavailability of Soluble Arsenic and Arsenic in Soil and Dust Impacted by Smelter Activities Following Oral Administration in Cynomolgus Monkeys" (Battelle 1994), and presents the mean absolute bioavailability identified in this study.

Inhalation Rate

Agricultural workers are assumed to be moderately active when working in the fields. EPA (1989b) presents an inhalation rate of 2.5 m^3/hour for adults at moderate activity levels. This inhalation rate is used here.

Dust Loading Factor

As for soil ingestion (see above), quantities of dust inhaled are assumed to be highest during plowing and relatively lower during other activities generally not associated with intensive contact with soil. Two dust leading factors are, therefore, estimated, one for plowing and one for other agricultural activities. A particulate emission factor that estimates the concentration of respirable particles that may be present in the air, due to wind erosion, was derived by Cowherd, et al. (1985) and is presented by EPA (1991a). The estimated value is based on the assumptions that the surface material has unlimited erosion potential, and would erode at low wind speed. These assumptions result in a conservative estimate for particulate intake. Cowherd, et al. (1985) used the following formula to derive the particulate emission factor:

$$PEF\ (m^3/kg) = \frac{LS\ x\ V\ x\ DH\ x\ 3600\ s/hr}{A}\ x\ \frac{1000\ g/kg}{0.036\ x\ (1-G)\ x\ (U_m/U_t)^3\ x\ F(x)}$$

Where:	PEF	=	Particulate emission factor (m^3/kg) (default = 4.63 x 10^9 m^3/kg)
	LS	=	Width of contaminated area (m) (default = 45 m)
	V	=	Wind speed in mixing zone (m/s) (default = 2.25 m/s)
	DH	=	Diffusion height (m) (default = 2 m)
	A	=	Area of contamination (m^2) (default = 2025 m^2)
	0.036	=	Respirable fraction (g/m^2-hr) (default 0.36 g/m^2-hr)
	G	=	Fraction of vegetative cover (unitless) (default = 0)
	U_m	=	Mean annual wind speed (m/s) (default = 4.5 m/s)
	U_t	=	Equivalent threshold value of wind speed at 10 m (m/s) (default = 12.8 m/s)
	F(x)	=	Function dependent on U_m/U_t (unitless) (default = 0.0497 [determined by Cowherd, et al. 1985])

The resulting value, 4.63×10^9 m^3/kg or 2.2×10^{-10} kg/m^3 is the dust loading factor that is used to evaluate exposure associated with agricultural activities such as watering and planting. This value is used to evaluate exposure for 126 days and 70 days for RME and CTE exposure, respectively.

Dust loading while plowing has not been measured in the Anaconda area, and little information could be found to support a choice for the dust-loading term. The value for the dust loading parameter during plowing, 0.15 mg/m^3, was selected primarily on the basis of professional judgement. However, the following analysis was carried out to determine if this choice was in a plausible range for actual dust loading during plowing.

Dust emissions from agricultural plowing, discing, harrowing, etc. may be estimated by:

$$E = k(5.38)s^{0.6}$$ (Cowherd, et al. 1985)

Where:	E	=	Emissions in kilograms per hectare (kg/ha)
	k	=	Particle size multiplier (unitless)
	s	=	Silt content (percent)

The equation is derived from field testing information and is, therefore, empirical.

An appropriate value for k, 0.21, is provided for particulate size. Silt content may vary considerably; a range of 1.7 to 88% is reported in the literature. A default value of 18% is provided in this reference, without documentation. Without data on silt content of arable soils near Anaconda, this value is used in the analysis.

Assuming that working a hectare would take about 1 hour and that dust emissions would be constant during this time, an emission rate of 69,390 µg/sec is estimated (equivalent to about 0.16 kg/ha). A mixing volume in air for these emissions can be estimated by using a windfield approach. A windfield is calculated by multiplying estimates for wind speed,

horizontal length of emitting surface perpendicular to wind direction, and vertical mixing height. A windfield can be presented in units of m^3/sec, and represents an estimate of the volume of air into which the emitted dust is mixed.

An annual average wind speed of about 9 mph has been estimated for the Anaconda area. Agricultural workers are expected to be in the field frequently during the growing season, and a long term average is appropriate for assessing exposures spanning many days per year for several years.

Emissions during tilling are expected to be caused by mechanical disturbance rather than creation of loose soil which can then be suspended by wind. Thus, the length of the emitting surface is expected to be the length of tractor and plow (or other implement) when the tractor is traveling at right angles to the wind. This length is assumed to be 12 meters (about 40 feet). It is assumed that plowing at different angles to the wind would approximately average out over the course of many days and years and that the above length is plausible.

Assuming a dust load of 150 $\mu g/m^3$, a vertical mixing height necessary for an emission rate of 69,390 μg/sec is estimated to be about 8.7 meters (approximately 28 feet). This appears to be a reasonable mixing height, suggesting that the assumed dust load of 150 $\mu g/m^3$ is at least in the plausible range. Therefore, this value is used in calculation of screening levels for the agricultural scenario. The value is used to evaluate exposure during plowing (i.e., 14 days per year).

Uncertainties in the above approach should be noted. The equation provided is sensitive to the silt content of soil. Keeping the windfield constant, dust loading predicted from a silt content of 36% is more than 220 $\mu g/m^3$, while that for a silt content of 9% is less than 100 $\mu g/m^3$. Differences in silt content within a factor of 2 from the default value of 18% would, thus, have a significant affect on screening level calculations.

Screening level estimates are also sensitive to windfield assumptions. For example, if the length of the emitting area perpendicular to wind direction is doubled or halved, the resulting dust-loading estimates (18% silt, all other assumptions held constant) are 198 and 49 $\mu g/m^3$, respectively.

Screening levels calculated using a dust loading factor of 150 $\mu g/m^3$ are expected to be conservative even in light of the above uncertainties. Exposure time, frequency and duration used for screening level calculations can be considered maximum for agricultural workers in the Anaconda region, and most workers would not be exposed as intensely as assumed. Even if average long term dust loading were underestimated by the above analyses, it seems unlikely that actual exposures and risks implied by the screening level estimate will be underestimated.

Exposure Time

Agricultural workers are assumed to work outside for eight hours per day. This value is used to calculate screening levels based on RME and CTE.

6.1.3 COMMERCIAL WORKER SCENARIO

Commercial workers who may become exposed to site contaminants include shopkeepers, office workers, sales people and others that may work at the site. Screening levels for this scenario are based on ingestion of soil and interior dust. Exposure assumptions for the commercial worker scenario are taken from relevant EPA guidance documents and from the Baseline Risk Assessment for the OW/EADA OU (Life Systems 1993). However, different bioavailability factors than were used in Life Systems (1993) are used to calculate screening levels for this HHRA. As discussed above, the BAF_s and BAF_d were derived by EPA (1994a, 1995a) from a recent laboratory study (Battelle 1994).

Exposure assumptions for the commercial worker scenario are shown in Table 6-3 and are discussed below. Screening levels for soil based on this scenario are calculated using the following formulas:

For carcinogens:

$$SL = (TR \times AT \times BW)/(EF \times ED \times IRs \times CFs \times SF_O \times ((FS \times BAF_S) + (C \times FD \times BAF_D))$$

For noncarcinogens:

$$SL = (TR \times AT \times BW \times RfD)/(EF \times ED \times IRs \times CFs) \times ((FS \times BAF_S) + (C \times FD \times BAF_D))$$

All parameters are described in previous sections.

Averaging Time

Carcinogenic exposures are averaged over 70 years or 25,550 days (EPA 1989a). This value is used to calculate screening levels based on carcinogenic exposure by commercial workers. ATs for noncarcinogenic exposure are 9,125 days for RME and 2,555 days for CTE.

Body Weight

The default BW parameters for adults is 70 kg, respectively (EPA 1989a). This value is used here.

Exposure Frequency

EPA (1993a) presents EFs for evaluation of RME and CTE for commercial workers. These values, 250 and 234 days/year, respectively, are used to calculate screening levels based on the commercial worker scenario.

TABLE 6-3

Exposure Assumptions for the Commercial Worker Scenario

Symbol	Units	Definition	Value	Source
SL	(mg arsenic/kg soil)	risk-based screening level	Section 6-2	-
TR	(unitless)	target risk	Section 6-2	-
AT	(days)	averaging time	Carcinogens = 25,550 Noncarcinogens RME = 9,125 CTE = 2,555	EPA 1989a
BW	(kg)	body weight	70	EPA 1989a
EF	(days/year)	exposure frequency	RME = 250 CTE = 234	EPA 1993a EPA 1993a
ED	(years)	exposure duration	RME = 25 CTE = 7	EPA 1989a Professional Judgement
IRs	(mg/day)	soil ingestion rate	RME = 100 CTE = 50	EPA 1993a EPA 1993a
CFs	(kg/mg)	conversion factor for soil	0.000001	EPA 1989a
SF_O	(mg/kg-day)-1	oral slope factor for arsenic	1.5	EPA 1995b
BAF_S	(unitless)	bioavailability factor for soil	0.183	EPA 1995a
FS	(unitless)	fraction of soil ingested	0.45	Professional Judgement
C	(unitless)	contribution of soil arsenic to arsenic in dust	0.43	Calculated see text
FD	(unitless)	fraction of dust ingested	0.55	Professional Judgement
BAF_D	(unitless)	bioavailability of interior dust	0.258	EPA 1995a

Exposure Duration

EPA (1989a) recommends using an ED of 25 years to evaluate worker exposures. This value is used to calculate screening levels based on RME to evaluate commercial workers. An ED of seven years is used to calculate screening levels based on CTE. This value is based on professional judgment.

Soil and Dust Ingestion Rate

EPA (1993a) recommends soil and dust IR of 100 mg/day and 50 mg/day for evaluation of RME and CTE, respectively, for workers who may have limited contact with soil. These values are used here.

Fraction of Soil and Dust Ingested

Of the total amount of soil/dust ingested (see Ingestion Rate above), 45% is assumed to be soil and 55% for interior dust.

Bioavailability of Soil and Dust

The BAF_s and BAF_d (18.3% and 25.8%, respectively) were derived by EPA (1994a, 1995a) from data presented in "Determination of Bioavailability of Soluble Arsenic and Arsenic in Soil and Dust Impacted by Smelter Activities Following Oral Administration in Cynomolgus Monkeys" (Battelle 1994).

Contribution of Soil Arsenic to Arsenic in Dust

The contribution of soil arsenic to arsenic in dust was derived from multiple regression analyses performed by Bornschein (1994) on data collected during the Anaconda arsenic exposure study. This is described in detail in Section 3.3.1.2.

6.1.4 RECREATIONAL VISITOR SCENARIO (ADOLESCENT PLAYING IN POOLED WATER)

Adolescents may potentially be exposed to contaminants in surface water, particularly in the surface water adjacent to the Opportunity Ponds. Screening levels for surface water are, therefore, developed for this exposure scenario. Screening levels are based on ingestion of surface water and dermal contact with arsenic in surface water by 4- to 12-year-old children. Exposure assumptions used to calculate screening levels for this exposure scenario are presented in CDM Inc. (1994). Exposure assumptions are summarized in Table 6-4 and are discussed below. Screening levels for this exposure scenario are calculated using the following equations:

For carcinogens:

$$SL = (TR \times AT \times BW)/((EF \times ED \times SF_O) \times ((IR_{sw} \times CF_{sw} \times ET) + (SA \times PC \times ET \times CF)))$$

For noncarcinogens:

$$SL = (TR \times AT \times BW \times RfD)/((EF \times ED) \times ((IR_{sw} \times CF_{sw} \times ET) + (SA \times PC \times ET \times EF)))$$

Where:

	SL	=	Screening Level for Surface Water (µg/L)
	IR_{SW}	=	Surface Water Ingestion Rate (ml/hr)
	CF_{SW}	=	Conversion Factor for Surface Water (L/ml)
	SA	=	Skin Surface Area Available for Contact (cm^2)
	PC	=	Dermal Permeability Constant (cm/hr)
	CF	=	Volumetric Conversion Factor (L/cm^3)

All other parameters are defined in previous sections.

Averaging Time

Carcinogenic exposures are averaged over 70 years or 25,550 days (EPA 1989a). This value is used to calculate screening levels based on carcinogenic exposure for the recreational

TABLE 6-4

Exposure Parameters for the Recreational Visitor Scenario

Symbol	Units	Definition	Value	Source
SL	(mg arsenic/L surface water)	risk-based screening level	Section 6-2	-
TR	(unitless)	target risk	Section 6-2	-
AT	(days)	averaging time	Carcinogens = 25,550 Noncarcinogens = 2,920	EPA 1989a
BW	(kg)	body weight	27	EPA 1989b
EF	(days/year)	exposure frequency	RME = 40 CTE = 10	Site-specific Site-specific
ED	(years)	exposure duration	8	Site-specific
IRsw	(ml/hour)	surface water ingestion rate	25	Site-specific
CFsw	(L/ml)	conversion factor	0.001	EPA 1989a
SFo	(mg/kg-day)-1	oral slope factor for arsenic	1.5	EPA 1995b
SA	(cm^2)	skin surface area available for contact	10,500	EPA 1989b
PC	(cm/hr)	dermal permeability constant	0.001	EPA 1992a
ET	(hours/day)	exposure time	2	Site-specific
CF	(L/cm^3)	volumetric conversion factor	0.001	EPA 1989a

visitor scenario. AT for noncarcinogens is 2,920 days.

Body Weight

EPA (1989b) presents BW for different age groups of children. These data are used to calculate a representative BW for 4- to 12-year-old children. This value (27 kg) is used here.

Exposure Frequency

Based on the climate in southwestern Montana, exposure to surface water is assumed likely for only five months out of the year. During this time children are assumed to swim or play in the water two times per month and two times per week for evaluation of CTE and RME, respectively. CTE and RME EFs are, therefore, 10 and 40 days per year, respectively.

Exposure Duration

Children from 4-12 years old are evaluated for potential exposure to surface water. The ED for this scenario is therefore eight years.

Surface Water Ingestion Rate

EPA (1989a) suggests that swimmers may ingest 50 mL of surface water per hour. For the exposure scenario evaluated in this HHRA, continuous swimming for 2 hours per day is considered unrealistic. Children are assumed to be playing in the water rather than swimming for most of the 2 hours that they are assumed to be in the water. While some ingestion of water may occur during play, surface water IRs are likely lower during playing activities than during swimming. An IR of 25 mL per hour is therefore considered conservative for this exposure scenario and is used here.

Skin Surface Area Available for Contact

Dermal contact with surface water is expected to occur over the entire body surface. The total body skin surface area for 4- to 12-year-old children is 10,500 cm^2, respectively. This surface area has been calculated from data for different age groups presented in EPA (1989b).

Life Systems (1993) reported that adults represent the majority of people that bike in the Anaconda Smelter Area. The default BW parameters for adults is 70 kg (EPA 1989a). This value is used to calculate screening levels based on the recreational dirt biker scenario.

Exposure Frequency

Life Systems (1993) interviewed trail users at the Anaconda Smelter NPL Site and identified representative EF from these data. Based on this analysis, CTE and RME exposure frequencies of 13 and 26 days per year, respectively, were identified (Life Systems 1993). These values are used to calculate screening levels for the dirt biker scenario.

Exposure Duration

Recreational trail users are assumed to be nearby residents. Residential ED are therefore used for development of screening levels. The RME ED is 30 years, and the CTE ED is nine years. These values represent a 90th percentile and an average estimate for residency at one address (EPA 1989a).

Soil Ingestion Rate

For evaluation of RME and CTE scenarios, dirt bikers are assumed to ingest 100 and 50 mg of soil per day, respectively. These values are based on professional judgement and are selected because a relatively large amount of soil is assumed to be resuspended by trail-bike riding.

Bioavailability of Soil and Dust

The BAF_s of 18.3% was derived by EPA (1994a, 1995a) from data presented in "Determination of Bioavailability of Soluble Arsenic and Arsenic in Soil and Dust Impacted by Smelter Activities Following Oral Administration in Cynomolgus Monkeys" (Battelle 1994).

Inhalation Rate

TABLE 6-5

Exposure Assumptions for the Dirt Biker Scenario

Symbol	Units	Definition	Value	Source
SL	(mg arsenic/kg soil)	risk-based screening level	Section 6-2	-
TR	(unitless)	target risk	Section 6-2	-
AT	(days)	averaging time	25550	EPA 1989a
BW	(kg)	body weight	70	EPA 1989a
EF	(days/year)	exposure frequency	RME = 26 CTE = 13	Life Systems 1993 Life Systems 1993
ED	(year)	exposure duration	RME = 30 CTE = 9	EPA 1989a EPA 1989a
IRs	(mg/day)	soil ingestion rate	RME = 100 CTE = 50	Professional Judgement
CFs	(kg/mg)	conversion factor for soil	0.000001	EPA 1989a
SFo	(mg/kg-day)-1	oral slope factor for arsenic	1.5	EPA 1995b
BAF_s	(unitless)	bioavailability of soil	0.183	EPA 1995a
IR	(m3/hour)	inhalation rate	RME = 2.5 CTE = 1.3	EPA 1989b EPA 1989b
SFi	(mg/kg-day)-1	slope factor for inhalation	15	EPA 1995b
DL	(kg/m3)	dust loading factor	3.8×10^{-7}	Professional Judgement
ET	(hours/day)	exposure time	RME = 5 CTE = 2	Lifesystems 1993 Lifesystems 1993

T The number of tires (wheels) per dirt-bike is two.

Based on these parameters, a value of 0.16 kg/VKT/hr was calculated for E. Multiplying by VKT and dividing by area yields the emission rate in units of kg/hr/m^2. The value of VKT is given by the number of bikes (assumed to be three) times the speed of each (30 km/hr). Dividing by 3,600 sec/hr results in an estimate of E of 2.0×10^{-8} kg/sec/m^2.

The concentration of particulate matter in air resulting from dirt-bike riding at each area were calculated using the estimated soil emission rate and a box model. The following formula was used (Hanna et al. 1982).

$$C = E \times X/(H/2 \times u)$$

Where:	C	=	Concentration of particulate matter in air (kg/m^3)
	E	=	Particulate matter emission rate (kg/sec/m^2)
	X	=	Distance from upwind to downwind edge of the box (m)
	H	=	Mixing height of the box (m)
	u	=	Windspeed (m/sec) across the box

Values of these parameters were derived as follows:

E The emission rate was calculated as described above.

X The "box" in which riding occurs was assumed to be square. Based on the assumed area of 2E+05 m^2, this corresponds to a side of about 450 m.

H The mixing height of the box is a function of distance from the source and turbulence of the air which, in turn, is a function of the roughness of the terrain. The value of H at the upwind edge of the site is assumed to be zero. At the downwind edge, the value of H was calculated from the following equation:

$$X = 6.25Z_0 \, [(H/Z_0) - 1.58(H/Z_0) + 1.58]$$

The BAF_s of 18.3% was derived by EPA (1994a, 1995a) from data presented in "Determination of Bioavailability of Soluble Arsenic and Arsenic in Soil and Dust Impacted by Smelter Activities Following Oral Administration in Cynomolgus Monkeys" (Battelle 1994).

Inhalation Rate

EPA (1989b) presents inhalation rates for adults at moderate and light activity levels. Moderate activity is assumed to evaluate RME and light activity is assumed to evaluate CTE. Inhalation rates for moderate and light activity are 2.5 and 0.8 m^3/hour. These rates are used to calculate screening levels for the dirt biker recreational scenario.

Dust Loading Factor

Dust loading during dirt bike riding was estimated using the following approach adopted from Life Systems (1993). A soil emission rate from dirt bike riding is calculated using the following equation based on Cowherd, et al. (1985):

$$E = 0.85 \times (S/10) \times (V/24)^{0.8} \times (W/7)^{0.3} \times (T/6)^{1.2}$$

Where:	E	=	Particulate emission rate (kg/vehicle kilometer traveled (VKT)/hr)
	S	=	Silt content of the soil (%)
	V	=	Vehicle speed (km/hr)
	W	=	Vehicle weight (Mg, where 1 Mg = 1,000 kg)
	T	=	Number of tires (wheels) per vehicle

No adjustment was used to account for days with rain or snow, since this form of the equation calculates emission rates during the dirt-bike riding event (rather than an annual average), and dirt-bike riding is assumed to occur only on dry days. The values of the parameters above were derived as follows:

TABLE 6-6

Risk-Based Screening Levels for Arsenic for the Anaconda Smelter Site

Medium	Soil								Surface Water	
Screening Level Based on Carcinogenic Risk	Residential Scenario (mg/kg)		Agricultural Scenario (mg/kg)		Commercial Worker Scenario (mg/kg)		Recreational Dirt Biker Scenario (mg/kg)		Recreational Youth/ Swimmer Scenario (mg/L)	
Carcinogenic Risk	RME	CTE	RME	CTE	RME	CTE	RME	CTE	RME	CTE
1×10^{-7}	0.30	1.85	1.00	10.04	1.33	10.15	2.32	53.55	0.002	0.008
1×10^{-6}	2.97	18.5	10.03	100.4	13.3	101.5	23.2	535.5	0.020	0.081
1×10^{-5}	29.7	185.2	100.3	1,003	133	1,015	232.3	5,355	0.20	0.81
1×10^{-4}	297	1,852	1,003	10,038	1331	10,155	2,323	53,551	2.0	8.1
1×10^{-3}	2,970	18,516	10,033	100,385	13,307	101,546	23,231	535,517	20.2	81.0
Screening Level Based on Noncarcinogenic Effects (HI = 1)	573	1,071	NC	NC	2,139	4,570	NC	NC	1.04	4.16

NC = Not calculated. Risk-based screening levels for these exposure scenarios are based on inhalation and ingestion exposures. A RfC for inhalation is not available; screening levels based on noncarcinogenic effects can, therefore, not be calculated for these exposure scenarios.

Where: X = Upwind to downwind distance (m)
Z_o = Roughness height (m)

As noted above, X is assumed to be about 450 m. The roughness height is a function of the height of natural and man-made objects (trees, buildings, etc.) in the vicinity of the source. Areas on the Anaconda Site, where dirt-bike riding is assumed to take place, are devoid of buildings and have very few trees. The value of Z_o was, therefore, estimated to be 4 cm (0.04 m), based on the graph presented in Figure 3-6 of Cowherd, et al. (1985).

u The average wind speed was taken to be 3.6 m/sec, based on annual average values measured at Hiway Junction (MDHES 1988).

Using these input parameters, Life Systems (1993) calculated a dust loading factor of 3.8 x 10^{-7} kg/m^3.

Exposure Time

Based on interviews with recreational trail users at the Anaconda Smelter NPL Site, RME and CTE exposure times of 5 and 2 hours per day, respectively, have been selected as representative. These values are used to calculate screening levels for the dirt biker recreational scenario.

6.2 SCREENING LEVELS FOR THE ANACONDA SMELTER NPL SITE

This section of the HHRA presents screening levels for arsenic based on residential, agricultural and commercial worker and recreational swimmer and dirt biker exposure scenarios. Screening levels for the different exposure scenarios are based on exposure assumptions presented in Section 6.1, and have been developed for a carcinogenic risk range of 10^{-7} to 10^{-3} and a noncarcinogenic HI of 1. Screening levels for the Anaconda Smelter NPL Site are presented in Table 6-6.

- Inhalation of dust

Recreational Users (Dirt Bike Riders):

- Ingestion of surface soils
- Inhalation of dust

Recreational Visitors (Swimmers):

- Ingestion of surface water
- Dermal exposure to surface water

Commercial Workers (Adults):

- Ingestion of surface soils
- Ingestion of interior dust

Data quantity is sufficient to perform a quantitative risk assessment only in the towns of Anaconda and Opportunity. Data quantity is inadequate to quantitatively evaluate risks to receptors throughout the rest of the site. Risk-based screening levels of arsenic in media will be developed for receptors located in areas outside of Anaconda and Opportunity (Section 6.0). These screening levels will be used in conjunction with maps of kriged data to evaluate risks in other areas of the site.

Statistical comparisons of soil data indicate that arsenic concentrations in PTI (1992 and 1993) and Bornschein (1992 and 1994) data are comparable; however, Bornschein (1992 and 1994) data were collected from areas where receptors might have actual exposure. Therefore, only Bornschein (1992 and 1994) soil sampling data are used to evaluate risks. In this study, Anaconda was separated into subareas (A, B, C, D, E, F1, F2, I, and J) to better characterize possible differences in exposure conditions within the community. Opportunity was retained as a separate study (area G). Numerous yards within each subarea were sampled. Soil samples were collected from several locations within each yard, including play, house perimeter, garden, hardpack, and bare areas. Soil concentrations were averaged for each yard.

7.0 SUMMARY AND CONCLUSIONS

A baseline HHRA was conducted to evaluate the potential human health risks associated with the Anaconda Smelter NPL Site in the absence of remedial (corrective) action. The no action alternative was evaluated in accordance with Sect. 300.430(d) of the NCP. This HHRA focuses on the risks associated with chemicals present in surface soils and groundwater.

7.1 IDENTIFICATION OF CHEMICALS OF POTENTIAL CONCERN

The selection of COPCs for this HHRA is abbreviated due to prior identification of COPCs for OUs of the Anaconda Smelter NPL Site, and for other sites in the upper Clark Fork Basin. COPCs for the remaining areas of the Anaconda Smelter NPL Site are expected to be similar to those for OUs within the site and for sites in the region. Selection of COPCs is limited, therefore, to determination of whether arsenic, cadmium, copper, lead, and zinc should be included in the quantitative assessment. Following a review of the available data, COPCs for the site were determined to be arsenic and lead in soil and arsenic in groundwater.

7.2 EXPOSURE ASSESSMENT

Potential pathways by which humans could be exposed to COPCs at the Anaconda Smelter NPL Site were identified and selected for evaluation. The potential receptors and pathways of exposure selected for evaluation in this HHRA were as follows:

Exposure Pathways for Residents (Adults and Children Ages 0 - 6):

- Ingestion of surface soils
- Ingestion of interior dust
- Ingestion of groundwater

Agricultural Workers (Adults):

- Ingestion of surface soils

Findings in the Anaconda soil ingestion study support the Superfund Program's usual approach of assuming ingestion of 100 mg soil and dust per day as a CTE assumption and 200 mg soil and dust per day as a RME assumption for IRs of children age 0 - 6 years. Though default assumptions are used for soil IR for children, these assumptions are clearly consistent with available site-specific data.

Predictions of exposure obtained from calculations of CDIs were compared to measured exposures of urine arsenic concentrations for children living in Anaconda. The arithmetic and geometric means of predicted and measured urinary arsenic concentrations for these children were compared to evaluate the appropriateness of the exposure assumptions used. Kruskal-Wallis one-way analysis of variance demonstrated that measured and predicted urinary arsenic are not statistically different. However, EPA exposure calculations underpredict urinary arsenic concentrations where measured levels are greater than 10 μg/L. Overall, the results of the comparison support the use of the described exposure calculations in risk assessment for the Anaconda Smelter NPL Site.

7.3 HUMAN RISK CHARACTERIZATION

This section presents the risk characterization based on exposure to arsenic and lead through the pathways selected in Section 3.2. Toxicity values for arsenic (Section 4.1) are combined with CDI to estimate quantitative health risk estimates for exposure to arsenic. Lead toxicity was assessed using the IEUBK Lead Model, Version 0.99. Children (aged 0-6) are considered the sensitive subpopulation at risk for adverse effects due to exposure to lead in environmental media. Risks to adults from lead exposure were not evaluated. A summary of toxicity estimates is presented in Section 5.3.

An exposure point concentration was derived for each area by calculating the 95% UCL of the mean (EPA 1992b) of the arithmetic average soil concentrations for each residence.

Dust data was provided in the Bornschein (1992 and 1994) study. Interior dust samples were collected from homes in Anaconda and Opportunity. Samples were collected from several locations inside each home, and an average concentration for each home was developed. Statistical tests of dust COPC concentrations demonstrated a lognormal distribution. Therefore, the data were logtransformed. The exposure point concentration was derived for each area by calculating the upper 95% confidence limit of the arithmetic mean (EPA 1992b) for the lognormalized average interior dust concentrations for each residence.

For Opportunity, both Bornschein (1992 and 1994) and CDM Federal (1994a) groundwater data were used to evaluate risks. Only Bornschein (1992 and 1994) presented groundwater data for the town of Anaconda. Groundwater data were available only for subarea A; all other subareas used public water supply. The exposure point concentration for groundwater is the upper 95% confidence limit of the mean (EPA 1992b) for the groundwater concentrations measured in each subarea.

Arsenic CDI was estimated for each residential exposure pathway based on estimates regarding the extent, frequency, and duration of exposures and the exposure point concentrations. Site-specific exposure assumptions were used when available; these include estimates of arsenic bioavailability in dust, soil, and water. EPA has used available data to derive site-specific arsenic bioavailability estimates for ingested soil and dust (EPA 1994a, 1995a). The following are the bioavailability values used in the HHRA:

- 25.8% bioavailability for dust
- 18.3% bioavailability for soil
- 100% bioavailability for water

- Use of default exposure assumptions and professional judgement in estimating CDI for arsenic and blood-lead levels for lead

7.3.1 SUMMARY OF CANCER RISKS

Carcinogenic risks were calculated by multiplying estimates of arsenic CDI by the arsenic-specific oral CSF. The total cancer risks for all pathways for each subarea range from 2.0E-05 to 5.5E-05 for the RME scenario, and from 3.2E-06 to 7.0E-06 for the CTE scenario.

7.3.2 SUMMARY OF NONCARCINOGENIC RISKS

Noncarcinogenic risks were calculated by dividing CDI of arsenic for each pathway by the arsenic-specific oral RfD. The total noncancer risks for all pathways for each subarea range from 0.28 to 0.60 for the RME scenario, and from 0.15 to 0.31 for the CTE scenario. These risks are less than unity, indicating there is little potential for adverse noncarcinogenic effects.

7.3.3 LEAD TOXICITY

EPA generally considers risks from exposure to lead unacceptable if more than 5% of the children have blood-lead levels in excess of 10 µg/dL. Results of the IEUBK modeling indicate that 5% of children in subarea E may have blood-lead levels in excess of 10 µg/dL.

7.4 UNCERTAINTIES

Uncertainties associated with this risk assessment include the following:

- Limited environmental data for areas outside of Anaconda and Opportunity
- Lack of data for lead in interior dust
- Toxicity criteria for arsenic
- Lack of bioavailability data for lead in soils and dust from the study area
- Lack of suitable methodology for evaluating dermal exposure to contaminated soils

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APPENDIX A

DATA EVALUATION

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MEMORANDUM

TO: Bob Alexander, CDM/FPC, Helena
FROM: Dennis Neuman
DATE: 14 June 1995
SUBJECT: Data Quality

Introduction

The purpose of this Memorandum is to review and comment on the quality of environmental (waters, soils and dusts) and human (urine) data generated by the Kettering Laboratory, Department of Environmental Health, University of Cincinnati Medical Center. This analytical work and subsequent data were in support of the Arsenic Residential Exposure Study conducted in Anaconda, Montana by the Kettering Laboratory. Preliminary review of a document, *Field and Laboratory Quality Control Results* (Roda, S.M., Univ. Of Cincinnati, January 23, 1995), revealed that there were several key pieces of information missing that would prevent such an evaluation. A memorandum (Neuman/MSU to Alexander/CDM-FPC of 24 March 1995) identified information that would allow assessment of the acceptability and useability of the data, and permit calculation of the bias and precision of these data. Ms. Sandy Roda provided (in a Memorandum of 10 May 1995) much of the identified information, and the following text describes the quality of the data to terms of its equivalence to Clark Fork River environmental data produced under CERCLA activities. It was hoped that data would be received that wold allow for the quantitative evaluation of data bias and precision. These data are generally not available.

Results of Data Assessment

* The arsenic water data were judged to be equivalent to Screening Quality Data.

* The arsenic interior dust/dustfall data were judged to be equivalent to Screening Quality Data.

* The arsenic soil and exterior dustfall data were judged to be equivalent to Screening Quality Data.

* The arsenic handwipe data were judged to be equivalent to Screening Quality Data.

* The arsenic urine data were judged to be equivalent to Screening Quality Data, and concentrations near or below 60 ug/l are most likely biased low.

Detailed Assessments by Matrix

Water

1. Evaluation of written analytical protocols.

Written protocols include the following: For the Perkin Elmer Z-3030 atomic absorption instrument.

* Analytical standard preparation (10, 25, 50 and 75 ug/l As).
* Matrix modifier was nickel nitrate.
* QC samples were made from different source than the calibration standards. Concentration levels were 5 and 10 ug/l.
* QC sample NIST # 1643C at 82.1 ± 1.2 ug/l was used and diluted to be within the calibration of the instrument.
* Analytical blank was identified.
* In every set of 25 samples, there were three QC samples: 5 ug/l, 10 ug/l, and the NIST Standard.
* Duplicate injections into the ZGFAA were required.
* Every sample was spiked with 200 ul of 100 ug/l As solution.
* No separate laboratory duplicate was analyzed.

The protocols for a second instrument, A PE 5100 ZL, was essentially the same, except analytical standards were lower at 5, 10, 20, and 30 ug/l. QC samples were 10 ug/l (from a different source than the calibration standards), and two NIST SRMs. QC samples were run at a frequency of 10%, with the following control limits:

* QC limits of 17.5 to 21.7 ug/l for 20.5 ug/l standard.
* QC limits of 27.7 to 33.1 ug/l for 30.0 ug/l standard.
* QC limits of 10.5 to 14.9 ug/l for 12.5 ug/l continuing calibration standard.
* Every sample was spiked with As.

2. Evaluation of raw analytical data.

The data set received from Roda was labeled as "dated 1.4.93 (am). As in water." Standards were at 0, 5, 10, 20, 50, 75, and 100 ug/l. The standard curve was acceptable. Sample were analyzed with duplicate injections; coefficients of variation (CV) were acceptable, but somewhat high due to the low absorbance values. QC samples included 5 ug/l SPEX (reported value was 5.2 ug/l), 10 ug/l SPEX (reported value was 10.2 ug/l), and 82.1 ug/l NIST Standard (reported value was 95.2 ug/l). Spike recoveries for the 25 samples in this batch ranged from 93 to 111.3 %. The only analytical deficiency was the lack of analysis of a continuing calibration blank.

3. Evaluation of QC data.

There were approximately 143 water samples analyzed for their As concentration. Each was spiked with As solution. The average recovery ± std. deviation was 103 ± 6 %, with a range from 88 to 113 %. Results of QC samples were 4.7 ± 0.5 ug/l for the SPEX 5 ug/l standard, 10.0 ± 0.8 for the SPEX 10 ug/l standard, and 81.9 ± 1.8 ug/l for the NIST standard. No laboratory duplicates were analyzed.

4. Evaluation of detection limit information.

The reported detection limit value of 1 ug/l was verified.

5. Summary for As water data.

Based on the analytical protocol, the raw data for the analysis of the first 25 samples, the QC summary, and the recovery of added As, as well as the results for the NIST standard, these water As data are considered to be of acceptable quality. Based on my knowledge of the *Level A/B Criteria*, and the validation protocols established for environmental data at the Clark Fork River NPL Sites, I rate these water As data to be equivalent to *Screening Quality Data.*

Interior Dust and Dustfall Samples

1. Evaluation of written analytical protocols.

The written protocol for the preparation and analysis of interior dust and dustfall samples was very detailed, and included the use of QC samples - reagent blank, method blank, and NIST standards. The digestion technique with 1M and 7M nitric acid should provide complete digestion and recovery of added As. The analytical protocol for As determinations using graphite furnace atomic absorption included the following:

* Acceptable glassware cleaning method.
* Analytical standards were 0, 20,40,60, 75, and 90 ug/l made from Fisher stock solution.
* Matrix modifier was nickel nitrate.
* General protocol was to run set of samples which were diluted 1:10. Samples which required further dilution or concentration were run in a second set.

2. Evaluation of raw analytical data.

The data set received from Rhoda was labeled "Interior dust for As, 10-14-93". Standards were 0, 10,25,75, and 90 ug/l, and the standard curve was acceptable. Samples were run with duplicate injections, and the CV values were acceptable. Results for the SPEX 10 and 70 ug/l standards were 9 and 72 ug/l. In the data set provided there were no analysis of preparation, method, or digestion blanks. There was also no analysis of a continuing calibration blank.

3. Evaluation of QC results.

In Roda's memorandum of 10 May 1995, acceptable QC limits were given for blank types including reagent blank, method blank, and the digestion blank. Only one method blank exceeded the QC limit. Acceptable QC limits were also provided for the NIST standards.

Recovery of As added to interior dust samples averaged 101.2 $\pm$ 6.6% (N =58), with a range from 86 to 114 %. Recovery of As added to dustfall samples averaged 105.1 $\pm$ 4.1 % (N = 7), with a range from 100 - 110 %.

3. Evaluation of QC results

Table 4 of Roda's Memorandum shows recovery of As added to the control wipes. The average recovery varied from 85% for the 4 ug spike to 98.7% for wipes spiked with 100 ug. The range of individual recoveries was very broad - from 52.5 to 142%. Results of duplicate analysis were very good, generally less than 10 % RPD. The precision did not vary with concentration.

4. Evaluation of detection limit.

The reported detection limit of 0.1 ug was verified.

5. Summary for handwipe samples.

These As data for handwipes are judged acceptable and to be equivalent to *Screening Quality Data.*

Urine Samples

1. Evaluation of written analytical protocols.

The method presented was based on a literature procedure published in 1981. A mixed standard containing As(III), As(V), methylarsonic acid, and dimethlyarsinic acid was prepared and dilutions made to produce working standards. When these standards and/or acidified urine samples were mixed (in a controlled reaction flask) with a solution of $NaBH_4$, arsine gas (AsH_3) is formed. This gas is then swept into an absorption tube of an atomic absorption instrument. Only inorganic As is the 3+ valence state will form arsine. Organic forms of As require digestion and As in the 5+ valence state must be reduced to As (III) using a strong reducing reagent, typically potassium iodide, KI. Neither the digestion step or the use of a reducing agent were part of the written protocol.

2. Evaluation of raw analytical data.

The instrument was calibrated with mixed standards ranging from 0 to 75 ug/l. A blank, followed by a spiked urine sample, additional calibration standards, and the NIST standards, were then analyzed. The analytical sequence was then 10 urine samples, calibration standard and blank, etc. A duplicate was analyzed every 20 samples.

3. Evaluation of QC data.

In the data set provided, four NIST standards and three spiked controls were analyzed. Results were 42 and 45 ug/l for the 60 ug/l NIST standard, 460 and 436 ug/l for the 480 ug/l NIST standard, 26 ug/l for the 20 ug/l urine control, and 50 ug/l for the 69 ug/l urine control. In Table 5 of Roda's Memorandum results of the determination of As in the NIST standards is given. For the low standard (60 ug/l As) the mean reported value was 48 ug/l (N=86), with a

range of 34 to 61 ug/l. On a percent recovery basis the mean would be 80%, with a range from 56.7 to 101.7%. The high As NIST standard (480 ± 100 ug/l) was analyzed 61 times with an average reported value of 492 ug/l. Reported values ranged from 388 ug/l (80.8% recovery) to 598 ug/l (121.5%). Urine values for As near the 60 ug/l may be biased low. No information on the results of the reference urine samples was provided.

4. Evaluation of the detection limit.

The reported detection limit of 1 ug/l was verified.

5. Summary for urine samples.

Based on the written analytical methods, the raw laboratory data and the results of the analysis of NIST standards, these data are judged as acceptable, with a notation that low level As values (less than 60 ug/l) are mostly likely biased low. These data are equivalent to *Screening Quality Data.*

APPENDIX B

STATISTICAL COMPARISON OF PTI AND BORNSCHEIN SOIL DATA

STATISTICAL COMPARISON OF BORNSCHEIN ANACONDA SURFACE SOIL ARSENIC DATA WITH ANACONDA SOILS INVESTIGATION SURFACE SOIL ARSENIC DATA

This analysis has been performed to resolve two disparate observations made for the Anaconda Superfund Site. First, soil arsenic concentrations for the Anaconda Residential Urinary Arsenic Study (Bornschein, 1992 and 1994) appeared to be less than soil arsenic concentrations found by the Draft Anaconda Soil Investigation Preliminary Site Characterization Report (PSCR) (PTI 1992) for community soils. Second, an ARCO Anaconda representative expressed concern that the Bornschein soil arsenic data would overestimate soil arsenic concentrations in Anaconda because the soil analyzed was a sieved fraction.

This analysis examines the data from both studies to determine (1) if significant differences do exist between arsenic concentrations found in surface soil samples collected for these two studies in Anaconda and nearby communities on an area-by-area basis. And (2) if significant differences do occur, could these differences be explained by differences in sampling methodology. A finding of widespread significant differences would raise the issue of what data set(s) are to be used in the Anaconda Human Health Risk Assessment.

SOILS DATA SOURCES

Arsenic concentrations from results of "Community Soils" were presented in the PSCI Report prepared by PTI Environmental Services for ARCO Anaconda (PTI 1992). Analytical results of the ASI are maintained in the Clark Fork Data Management System by the Clark Fork Data System Manager (CFDSM) for the Department of Health and Environmental Sciences Superfund Section of the State of Montana. Two dBASE files (CDMRISK.DBF and CDMQDV.DBF) containing community, near community, and regional soils analytical data were obtained from the CFDSM. CDM Federal Programs Corporation added additional

information to these files and retained the original file names.

Results of the Anaconda Childhood Arsenic Exposure Study prepared under the direction of Dr. Robert Bornschein of the University of Cincinnati for Anaconda - Deer Lodge County and sponsored by ARCO have not been finalized. However, raw dBASE files containing soils data analytical results (ANAC_S.DBF) and form files necessary to link samples with descriptive data including area location (FM2108.DBF and FM2308.DBF) have been provided and were used for this analysis.

SAMPLING AND ANALYTICAL METHODS

The Community Soils surface soil sampling procedure was described in PTI (1991). On page seven of responses to comments, the following addition was to be made to SOP-39 discussing procedures for surface soil sampling:

> The following procedures are designed to be used to collect a surface soil sample (0-2 inches). The procedures listed below may be modified in the field based on field and site conditions after appropriate annotations have been made in the appropriate field log book.
>
> 1) Locate the site as directed in the appropriate sampling and analysis plan.
>
> 2) Dig a 12-inch square pit to a depth of approximately 8 inches. If an organic layer is present, this layer will be peeled back.
>
> 3) A stainless steel bowl will be placed in the pit and a sample collected by scraping the face of the pit from the mineral soil (0-2 inch interval) steel spoon.
>
> 4) All coarse fragments greater than 0.5 inches will be removed from the bowl. The remaining sample will be disaggregated and homogenized in the collection bowl with a stainless steel spoon.
>
> 5) In the field laboratory, a sufficient quantity of sample will be saved for measurement of soil slurry pH and conductivity.

6) The sample will be sent to a laboratory for analysis per the Anaconda Smelter remedial investigation and feasibility study analytical laboratory protocol (i.e., air dried and sieved to 2mm prior to subsampling for metals.

Surface soil sampling methods for the Bornschein data were described in the first draft of a protocol to study arsenic exposure in children living in or near Anaconda (Bornschein 1992). The following quotes were excerpted from this document. "Soil cores, of 2 cm depth, will be taken in grassy areas and gardens." "A composite sample of soil cores will be taken from grassy yards adjacent to a residence i.e. from the front, back and sides, with 8 to 12 samples per composite. Cores will be taken at approximately equal spacings along the sides of the building, at a distance of one meter (3 feet) from the building wall. Small lot sizes and fences preclude taking building perimeter samples at a distance of one meter on some properties. For large multi-family buildings, proportionately more composite samples will be taken. A composite of soil cores will also be collected from cultivated areas (vegetable and flower gardens) accessible to children, bare areas in yards, obvious play areas and sand boxes. Field duplicates will be collected at 10% of the sample sites." "Soil and dust samples will be air dried overnight. They will then be sieved into two fractions: a 'Large Soil Fraction' which passed a 2mm sieve but not a 250um sieve and a 'Fine Fraction' which passed a 250 um sieve." The Fine Fractions were analyzed by a laboratory based X-ray fluorescence (XRF) unit. Lead (Pb) and arsenic were analyzed in these samples so that spectral Pb interference on arsenic could be corrected (Bornschein, 1994). Samples less than two grams were insufficient for XRF and were consequently analyzed by a Zeiss Graphite Furnace Atomic Absorption Spectrophotometer (ZGFAAS).

DATA SELECTION AND FILE PREPARATION

ASI arsenic data used in this analysis came from data records with the following location acronyms (dBASE field STATION in file CDMRISK.DBF):

CMA = Anaconda residences

CTA1 through CTA6, CTA15, CTA21 = Anaconda targeted residences

CMO = Opportunity residences

CMG = Lost Creek residences, homes on Galen Road

CMF = Fairmont Ranches

Only the composited subsample data results were selected for use in this analysis (designated by a "1" in field SS and no "L" in SAMNO). Replicate data (designated by "A" and "B" in field FREP) were averaged so that no one location could bias the results. Non-detects were used at full value. These data have been validated. Therefore, reported arsenic concentrations were used as presented under the assumption that any modification in the concentration caused by blank contamination (designated by "B" in field ASQUAL) was made by the data validator.

A new field (AREA) was added to the database to incorporate the Bornschein Anaconda Geographic Letter Description according to page seven of Bornschein (1994). The descriptions of area boundaries were plotted on a copy of Figure 6, Community and Community Targeted Sampling Station Locations - Anaconda, from the PSCI report (PTI 1992). Areas A through F were assigned to CMA and CTA samples, accordingly. Area G was assigned to Opportunity Samples. Area H was assigned to Lost Creek Samples. Areas I (Teresa Ann Terrace) and J (Cedar Park Homes) are not considered in this analysis, because no community soils data were collected for these areas. Area K was assigned to Fairmont Ranches data.

The Bornschein soils data were drawn from the dBASE file ANAC_S.DBF and linked to areas A through K via form files FM2108.DBF and FM2308.DBF. Data for perimeter, bare ground, hardpack, garden, and play soil types were available. A new field (SOILAVG) was added that contains the calculated arithmetic average across soil types for each yard. It has already been demonstrated (unpublished descriptive statistical analysis of Bornschein

Anaconda media and urinary arsenic data by CDM Federal Corp 1994) that arsenic concentrations from different soil types may come from different populations, thus bringing into question averaging across soil types within yards. The rationale of averaging across a yard is supported by the assumption, in the absence of behavioral data, that the child spends an equal amount of time in each soil type and receives an equal amount of exposure from each soil type. The quality of the Bornschein data is unknown at this time, because insufficient Quality Assurance/Quality Control information has been provided to date to make such a determination.

STATISTICAL TREATMENT

The ASI data are compared with the Bornschein calculated yard soil averages using multiple box plots and the Mann-Whitney U test. All statistics were performed using STATGRAPHICS PLUS version 6.1 (Manguistics, Inc. 1991).

Multiple box plots are a useful exploratory data analysis technique that summarizes data and makes no distributional assumptions about the data. The scales on all three accompanying figures are the same to make direct comparisons more convenient. Each "box" represents the middle 50 percent of the data concentration values. The lower end of the box is essentially at the 25th percentile or lower quartile and the upper end of the box is at the 75th percentile or upper quartile. The difference between the upper quartile and lower quartile is called the interquartile range. The horizontal line drawn inside the box is the median value (close to the geometric mean for a large number of samples). Vertical lines, called whiskers, extend from each end of the box. The lower whisker is drawn from the first quartile to the smallest data point within 1.5 interquartile ranges from the first quartile. The other whisker is drawn from the third quartile to the largest data point within 1.5 interquartile ranges from the third quartile. Data points beyond the whiskers are outliers and are indicated by "+" on the figures.

The Mann-Whitney U test is analogous to the unpaired t-test. The unpaired t-test compares

two samples to support or refute the hypothesis that the two samples are drawn from the same population. The t-test would be appropriate if the data were normally distributed. Previous statistical analysis of the Bornschein soils data indicated the data are not normally distributed, so using the t-test would be inappropriate. The Mann Whitney U test performs an unpaired t-test on the ranks of the data and makes no distributional assumption. The error level was set at 0.05. If the two-tailed probability of equalling or exceeding the test statistic (Z) is less than 0.05, the hypothesis that both samples come from the same population is rejected. If this probability equals or exceeds 0.05, the hypothesis that both samples come from the same population is accepted. Results for each area comparison follow the boxplot figures. Sample 1 is always the Bornschein data and Sample 2 is always the ASI data.

RESULTS

Boxplots were sandwiched and placed on a light table for a quick area comparison. If the boxes for a given area have much overlap, the samples will likely be from the same population. If the boxes do not overlap the samples will likely be from different populations. The light table comparison was made for the ASI data and the Bornschein calculated soil average data. It appeared that data for Areas A, C, and H could be from different populations.

Average Bornschein soil arsenic concentrations across soil types by yard were greater in seven (A-D, F, H-K) of nine areas compared. ASI soil arsenic averages were greater in areas E and G. Mann-Whitney U tests for all areas only confirmed data for Area H probably came from different populations.

CONCLUSIONS

Results of statistical tests indicate that ASI arsenic data and Bornschein arsenic data are not significantly different for eight of nine areas compared. Bornschein soil arsenic

concentrations for Area H were significantly greater (two-tailed $p = 0.05$) than ASI soil arsenic concentrations. These results refute both observations made at the beginning of this analysis, because the two data sets appear to come from one population.

It is suggested that using either data set will result in similar characterization of arsenic in surface soils for Anaconda and nearby communities. Combining the two data sets to maximize sample size appears attractive. If kriging is to be performed, the ASI data have the advantage that sample locations are already known. However, the Bornschein data are about eight times more numerous in Anaconda for Areas A - F than ASI data and more closely approximate the soil fraction to which children are exposed.

REFERENCES

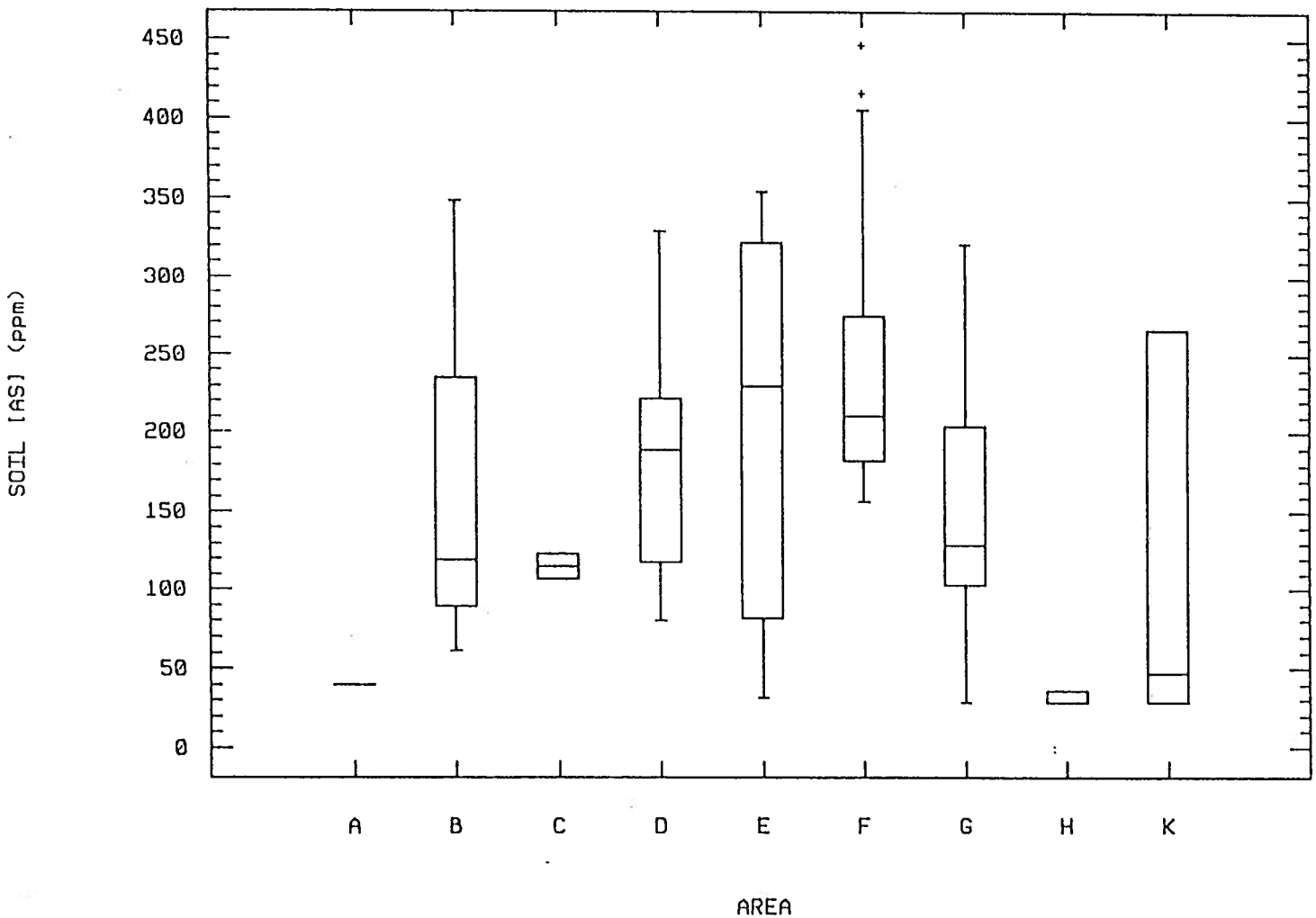
Bornschein, R. 1992. Anaconda Childhood Arsenic Exposure Study Department of Environmental Health. Draft. January 1992. Prepared for Deer Lodge County. Prepared by University of Cincinnati. Sponsored by Atlantic Richfield Co.

Bornschein, R. 1994. The Anaconda Study: An Assessment of Residential Arsenic Exposures Among Children Living in the Vicinity of a Former Copper Smelter. UPDATE September 6, 1994. University of Cincinnati.

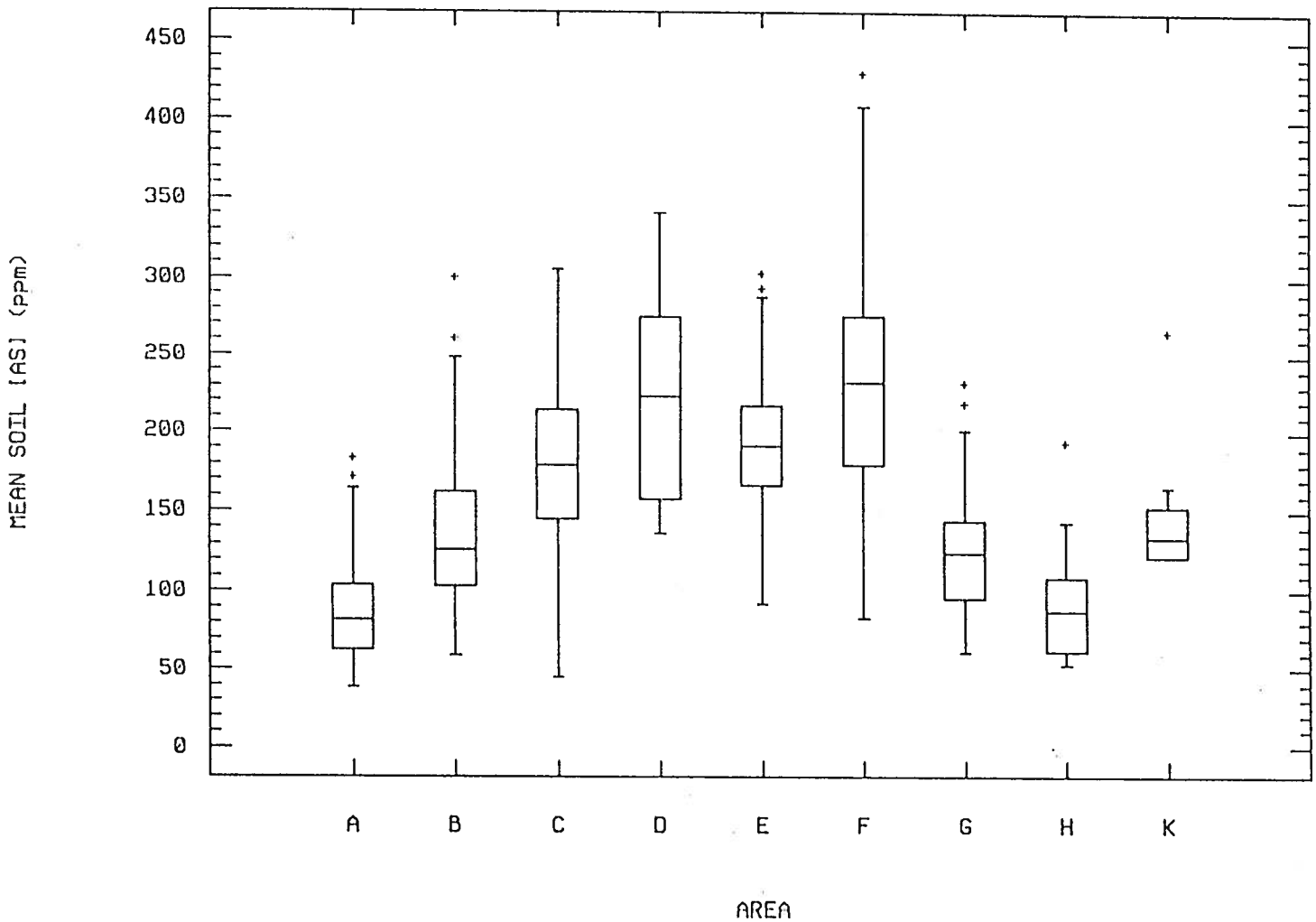
PTI. 1991. Draft Sampling and Analysis Plan Anaconda Regional and Community Soil Investigation. Draft. Prepared by PTI Environmental Services. July 1991. Prepared for ARCO Anaconda, Montana

PTI. 1992. Anaconda Soil Investigation Preliminary Site Characterization Information Report. Draft. Prepared by PTI Environmental Services. March 1992. Prepared for ARCO Anaconda, Montana. Attached Responses to Comments.

ANACONDA SOILS INVESTIGATION
ARSENIC DATA



BORNSCHEIN COMMUNITY SOILS
ARSENIC DATA



Comparison of Two Samples

Sample 1: BORN1.SOILAVG SELECT AREA_ID='A'

Sample 2: BORNCOMM.AVGAS SELECT AREA='A'

Test: Unpaired

Average rank of first group = 30.9661 based on 59 values.
Average rank of second group = 3 based on 1 values.
Large sample test statistic Z = -1.55958
Two-tailed probability of equaling or exceeding Z = 0.118858

NOTE: 60 total observations.

Comparison of Two Samples

Sample 1: BORN1.SOILAVG SELECT AREA_ID='B'

Sample 2: BORNCOMM.AVGAS SELECT AREA='B'

Test: Unpaired

Average rank of first group = 37.65 based on 70 values.
Average rank of second group = 34.875 based on 4 values.
Large sample test statistic Z = -0.239067
Two-tailed probability of equaling or exceeding Z = 0.811049

NOTE: 74 total observations.

Comparison of Two Samples

Sample 1: BORN1.SOILAVG SELECT AREA_ID='C'

Sample 2: BORNCOMM.AVGAS SELECT AREA='C'

Test: Unpaired

Average rank of first group = 20.8243 based on 37 values.
Average rank of second group = 4.75 based on 2 values.
Large sample test statistic Z = -1.91053
Two-tailed probability of equaling or exceeding Z = 0.0560646

NOTE: 39 total observations.

Comparison of Two Samples

Sample 1: BORN1.SOILAVG SELECT AREA_ID='D'

Sample 2: BORNCOMM.AVGAS SELECT AREA='D'

Test: Unpaired

Average rank of first group = 20.3261 based on 23 values.
Average rank of second group = 15.2692 based on 13 values.
Large sample test statistic Z = -1.36688
Two-tailed probability of equaling or exceeding Z = 0.171663

NOTE: 36 total observations.

Comparison of Two Samples

Sample 1: BORN1.SOILAVG SELECT AREA_ID='E'

Sample 2: BORNCOMM.AVGAS SELECT AREA='E'

Test: Unpaired

Average rank of first group = 37.2721 based on 68 values.
Average rank of second group = 40.0833 based on 6 values.
Large sample test statistic Z = 0.297086
Two-tailed probability of equaling or exceeding Z = 0.766397

NOTE: 74 total observations.

Comparison of Two Samples

Sample 1: BORN1.SOILAVG SELECT AREA_ID='F'

Sample 2: BORNCOMM.AVGAS SELECT AREA='F'

Test: Unpaired

Average rank of first group = 83.0037 based on 136 values.
Average rank of second group = 82.9828 based on 29 values.
Large sample test statistic Z = 0
Two-tailed probability of equaling or exceeding Z = 1

NOTE: 165 total observations.

Comparison of Two Samples

Sample 1: BORN1.SOILAVG SELECT AREA_ID='G'

Sample 2: BORNCOMM.AVGAS SELECT AREA='G'

Test: Unpaired

Average rank of first group = 24.4821 based on 28 values.
Average rank of second group = 28.8542 based on 24 values.
Large sample test statistic Z = 1.02809
Two-tailed probability of equaling or exceeding Z = 0.303907

NOTE: 52 total observations.

Comparison of Two Samples

Sample 1: BORN1.SOILAVG SELECT AREA_ID='H'

Sample 2: BORNCOMM.AVGAS SELECT AREA='H'

Test: Unpaired

Average rank of first group = 12 based on 17 values.
Average rank of second group = 2 based on 3 values.
Large sample test statistic Z = -2.64827
Two-tailed probability of equaling or exceeding Z = 0.00809049

NOTE: 20 total observations.

Comparison of Two Samples

Sample 1: BORN1.SOILAVG SELECT AREA_ID='K'

Sample 2: BORNCOMM.AVGAS SELECT AREA='K'

Test: Unpaired

Average rank of first group = 6.5 based on 8 values.
Average rank of second group = 4.66667 based on 3 values.
Large sample test statistic Z = -0.721019
Two-tailed probability of equaling or exceeding Z = 0.470895

NOTE: 11 total observations.

APPENDIX C

DEVELOPMENT OF ARSENIC BIOAVAILABILITY FACTORS

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
REGION VIII
999 18th STREET - SUITE 500
DENVER, COLORADO 80202-2466

NOV 10 1994

MEMORANDUM

SUBJECT: Review of the Battelle Columbus report: ***Determination of the Bioavailability of Soluble Arsenic and Arsenic in Soil and Dust Impacted by Smelter Activities Following Oral Administration in Cynomolgus Monkeys*** (August, 1994) Laboratory Project ID# SC930261.

TO: Charlie Coleman, RPM
Montana Operations Branch

Susan Griffin, Ph.D., D.A.B.T., Toxicologist
Superfund Management Branch

FROM: Christopher Weis, Ph.D., D.A.B.T., Toxicologist
Superfund Management Branch

I have completed a review of the subject report prepared by Battelle for the Atlantic Richfield Company (ARCO) under the direction of Dr. Gary B. Freeman. The work was initiated on November 15, 1993 and completed on August 5, 1994. The purpose of the work was to "***determine and compare the extent of absorption of arsenic in soil and dust impacted from smelter activities near Anaconda, Montana***". The objectives of the work were to: "***determine the extent of absorption and to characterize the rates and routes of excretion of arsenic in Cynomolgus monkeys following a single oral administration of a soluble arsenic solution (sodium arsenate) or a single oral administration (via capsules) of a test soil or dust containing arsenic.***" The authors administered a single dose of arsenic (As) as either intravenous, gavage (soluble arsenic) or capsules (soil or dust) to cynomolgus monkeys weighing between 2.42 and 2.88 kg and monitored urinary and fecal excretion of As over a 72 hour period. Absolute percent estimates of arsenic bioavailability were determined by comparing urinary and fecal excretion of arsenic in the IV dose group with urinary and fecal excretion in the oral dose groups.

This work augments earlier work by Battelle aimed at determining the extent of arsenic absorption in lagomorphs. As such, this work adds to the growing database of studies aimed at determining the role of physico-chemical characteristics (concentration, matrix, chemical species, and particle size) in the bioavailability of arsenic. This investigation, if completed and interpreted in juxtaposition with other work in the area of soil/dust exposure characterization for arsenic, might add significantly to the Agency's growing understanding of human exposure to environmental arsenic. The subject work is particularly important as a component of a comprehensive set of data (including an epidemiological investigation conducted by the University of Cincinnati, and a study of childhood soil and dust ingestion conducted by investigators at the University of Massachusetts) collected in the area of Anaconda, Montana during the summer of 1993.

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However, the investigation reviewed herein contains considerable evidence of technical aberration and interpretational inconsistency which may limit its direct application to the stated purpose. Alternative interpretations of the results of the study along with a technical review of the work and suggestions for study completion are presented below.

Comments:

Study Design:

The study was conducted under the general guidelines of Good laboratory Practice (CFR part 792). the work appears to have been generally well planned and carried out with a reasonable amount of care. The introduction to the study presents considerable discussion of a "pilot study" from which the authors draw several conclusions relevant the comparative absorption of arsenic from rabbits and Cynomolgus monkeys; however, no data is presented from the pilot work. Unfortunately, the study design used a limited number of animals and rotated those animals through dose groups as indicated in Table 1. The study design employed animals which had been purchased by Battelle for purposes other than the subject study. The animals employed in the work were received by Battelle on 9/7/90 whereas the study start date was 12/9/93. Therefore the animals had been under observation for considerable time prior to the start of the work. The study design employed three female animals in each of five treatment cycles. The treatment cycles were staggered such that each animal participated in more than one treatment group and such that there were three animals per treatment group at the termination of the study. While certainly an efficient use of resources, several difficulties with the study may have been averted had the investigators employed a full compliment of individual animals to fill the dose groups. The general study design along with treatment groups and animal identifiers is reproduced below:

TABLE 1: Study Design

Treatment Cycle	Date	Animal Number		
		30-537	20-784	30-544
1	12-15-93	Gavage sodium arsenate	Oral Soil (capsules)	IV Sodium Arsenate
2	1-12-94	Oral Soil (capsules)	IV Sodium Arsenate	Oral Dust (capsules)
3	2-2-94	IV Sodium Arsenate	Oral Dust (capsules)	Gavage Sodium Arsenate
4	2-17-94	Oral Dust (capsules)	Gavage Sodium Arsenate	Oral Soil (capsules)
5	3-16-94	—	—	Oral Dust (capsules)

Test Substance Characterization:

Characterization of the **soils** test substance used in the study was completed by PTI of Boulder, Colorado. The test substance was a composite of six play area or bare area soils collected from the 0-2" soil horizon. The samples were dried at 80C then sieved to a particle size of <250 µm. The samples were analyzed for arsenic concentration using XRF then blended to yield a final concentration of 410 ppm. This test substance was analyzed by electron microprobe for mineralogical determination.

House dusts used for dosing were composited samples collected by Hoover Brush vacuum (Model S1137). Samples were collected from carpets in living areas and childrens bedrooms. A decontamination procedure was used between sample collections. Dust samples were then dried at 80C and sieved to < 250 µm.

Frequency of arsenic-bearing particles and mass distributions were calculated. The authors indicate that the averaged results of three "representative" splits of the composite soil sample indicate that the arsenic mineral mass was present primarily as metal-arsenic oxide and iron-arsenic oxide, with lesser contributions from metal-arsenic silicate, enargite, slag, arsenic phosphate and iron-arsenic sulfate. The authors indicate that "*the arsenic mineralogy of the housedust was nearly identical to that of the soil sample*"

Arsenic particle size was <50 µm in diameter with a large number of particles occurring in the < 10 µm fraction. the authors indicate that the house dust particles size was "*slightly larger*" than the soil sample.

The phase association is characterized by the authors as liberated, cemented, and rimmed association, with a high percentage of iron-arsenic oxide phases occurring as liberated particles. The authors state that "*the more frequent occurrence of liberated arsenic particles in the house-dust sample than in the soil could explain the higher observed bioavailability in the house dust*". This statement, made in the test substance characterization report, indicates that the substance characterization was completed **after** the in life phase of the dosing. According to GLP protocol, test substance characterization should have been completed prior to dosing. ***This is an important and potentially serious broach of GLP protocol.***

Dosing Regimen:

The animals were delivered a single dose of arsenic as indicated in the table below following an overnight fast. Feed was made available to the animals at four hours post dosing and water was made available *ad libitum*. Target doses are as indicated below:

In order to deliver the target dose of arsenic indicated in table 2, and assuming the animal body weights were 2.5 kg, the authors administered approximately 3 grams of soil and approximately 3.8 grams of dust to each animal. The amount of material given to the test system is approximately 20 fold greater than the amount material EPA typically assumes a child might be exposed to and approximately 190 fold greater than the assumed adult dose. It is plausible that such high doses may have a negative influence on the estimates of arsenic absorption made by the authors. However, further work is

necessary to determine the relationship between arsenic dose and percent absorption.

TABLE 2: Dosing Regimen

Treatment	Dose Group (mg As/kg BW)	Number of animals
IV sodium arsenate	0.62*	3
Gavage sodium arsenate	0.62	3
Oral test soil	0.62†	3
Oral test dust	0.26‡	3

* The animal weights were approximately 2.5 kg. Therefore the single dose delivered was approximately 1,240 ug of As.

† arsenic concentration in soil was 410 ppm.

‡ arsenic concentration in dust was 170 ppm.

Data collection:

Urine, fecal and cage rinse samples were collected prior to dosing and every 24 hour period for 168 hours (7 days). Assuming that the animals were not chronically dehydrated and that glomerular filtration rate remained stable, such collection protocol should negate the need to normalize urinary arsenic concentrations to creatinine excretion. **Recovery of urinary and fecal arsenic from the IV dose groups was consistently lower than for the other groups (Figure 1).** A one way analysis of variance (ANOVA) of the means shows that there is a significant difference (P=0.019) between the IV group and the oral groups. The authors have normalized the results of urinary recovery from other dose groups to compensate for the poor recovery from the IV group. This correction for poor recovery significantly effects downward the estimates of absorption made by the authors. The observation that recovery of arsenic in the IV group was below that of the oral dose groups does not, by itself, justify the adjustment in absorption calculations which have been made by the authors. No attempt has been made to provide a physiological explanation for the poor recovery observed in the IV group. Nor have the authors taken steps to conduct blood arsenic analysis which may shed light on the observed phenomenon even though significant effort was invested to obtain blood samples. Assuming, as the authors clearly indicate, that delivery of the IV doses was successful and considering the accurate dose verification obtained by the authors, it is likely that arsenic was indeed absorbed by the test system. It is likely that the IV dose remained bound to tissue components, cellular blood components or plasma proteins making it more inaccessible to glomerular filtration or biliary excretion than the oral doses.

Percent Recovery of Dose (F+U)

FIGURE 1

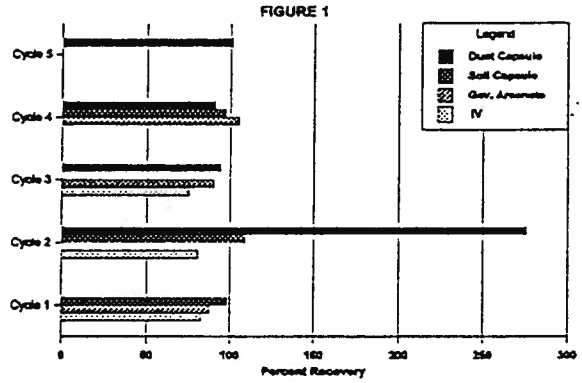
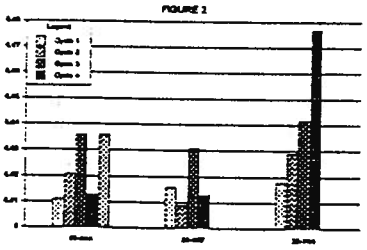


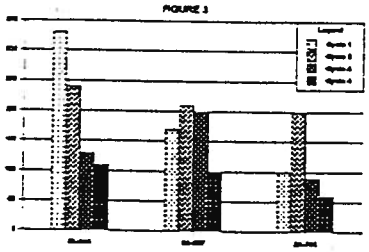
TABLE 3: Percent recovery of Urinary and Fecal Arsenic

	Percent Recovery of Urinary and Fecal Arsenic			
	IV Sodium Arsenate	Sodium Arsenate via Gavage	Soil Capsule	Dust Capsule
	82.9	88	98.1	94.4
	81	90.3	109	90.8
	75.3	105	97.2	101
Mean	79.7	94.4	101.4	95.4
Std. Dev.	3.96	9.22	6.57	5.17
SEM	2.28	5.32	3.79	2.99

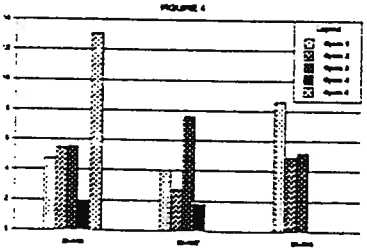
Predose Urinary As Concentration (ug



Predose Urinary Volume (mL)



Total Predose Urinary As (ug)



The authors also collected blood samples at 2,3,4,8,24,48,72,96,120, and 144 hours following oral dose and 2,5,10,15,30,60 minutes and 2,4,8,24,48,72,96, and 120 hours post IV dose (page 21). The blood samples have not been analyzed. **This information is critical to the interpretation and assessment of internal consistency of the Battelle report and the analysis of blood arsenic levels should be completed immediately.** The text of the report (page 23) indicates that the IV doses were delivered slowly over a period of 2-3 minutes which means that the investigators were both delivering the IV dose and collecting the first blood sample at the same time. Unfortunately, this practice is likely to have rendered the first 2 time points unusable for quantitative pharmacokinetics.

The authors indicate that predose urinary arsenic **concentrations** rose throughout the course of the study (Figure 2). They attribute this rise in predose urinary arsenic concentration to an endogenous arsenic source and "correct" for each animal's background arsenic level which had been determined prior to the treatment cycle in question (page 33). However, this interpretation and subsequent data correction appears to be incorrect. Urinary arsenic concentration is increasing due to a concurrent decrease in urinary volume for the predose collection periods and not due to any endogenous arsenic source (Figure 3). Acquisition of concurrent measurements of urinary creatinine may have resolved this question more clearly. In fact, total urinary excretion of arsenic is unchanged during the predose collection and even appears to decrease somewhat over the course of the dosing cycles (Figure 4). Total urinary arsenic measured at predose is not statistically

different as measured by one way ANOVA. Since the estimate of arsenic bioavailability presented in the report is based upon **total arsenic** excreted ([As] in urine x urine volume), it follows that predose correction for background arsenic should be based upon total arsenic rather than **arsenic concentration**. Table 4 (below) presents summary data on total predose arsenic.

TABLE 4 **Summary Statistics for Total Predose Arsenic (µg)**

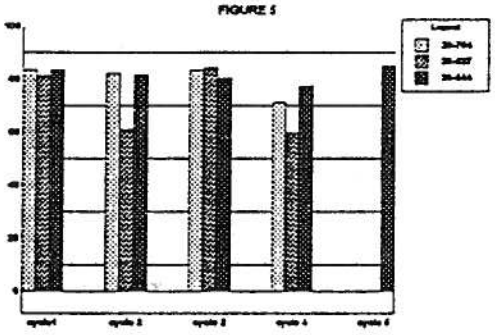
	Animal Number			
	30-544	30-537	20-784	All
Mean	6.18	4.06	6.25	5.49
Std. Dev	4.13	2.56	2.04	3.14
SEM	1.85	1.28	1.18	0.91
Max	13.1	7.64	8.60	13.1
Min	2	1.18	4.49	1.81
Med	5.49	3.39	5.22	5.08

Correction of predose arsenic using total arsenic excreted in urine averaged across animals and cycles would provide a more defensible approach to background correction. As indicated in table 4, the mean arsenic background across the study is 5.49 µg total urinary arsenic.

Food Consumption:

Food consumption for animal number 30-537 was irregular as evidenced in the figure 5. Following each gavage dosing, animal number 30-537's food intake decreased dramatically. The authors indicate that no clinical signs of toxicity were evident and that, perhaps the animal experienced some nausea as a result of the dosing procedure or as a result of the soil or dust dose. The animal's weight remained stable throughout the washout period.

Average Food Consumption (grms)



Clinical Observations:

The authors state that "*clinical observations were made frequently immediately following dosing, the afternoon of the day of dosing, and each day prior to study termination*". However, **no data is presented to substantiate the finding** that "*[t]here were no abnormal behavioral or clinical signs of toxicity observed in any of the animals during the in-life period of [the] study*". Given the substantial investment of effort in the study, I would have expected the authors to regularly assess the clinical health of the

animals through; 1) analysis of complete blood counts (CBCs), 2) standard measurements of serum chemistry; 3) assessment of possible disturbance of creatinine metabolism, 4) regular monitoring of body temperature of the animals, and 5) specific observations related to digestive disorders associated with Keflin administration. Perhaps more importantly to the interpretation of study results is the likelihood of systemic staphylococcus or streptococcus infection as a result of surgical implantation of the indwelling catheters used for vascular access. The catheters were implanted on November 19, 1993 whereas the study did not begin until December 9, 1993. The animals were treated with Keflin (a broad-spectrum cephalosporin antibiotic) twice daily indicating that the investigators recognized the possibility of bacteriological infection associated with catheter implantation. One animal (20-784) received treatments of urokinase to re-establish patency of the catheter indicating the possibility of hematoma associated with the access port.

The absence of adequate clinical data and veterinary observations of the animals within the study report is a serious oversight which limits the interpretation of the results. This data may, however, be available within the laboratory notebooks associated with the study and should be requested from the authors.

Study Interpretation:

The authors present graphical results of their estimates of arsenic bioavailability in terms of total excretory arsenic in figures 1 and 2 of the report. Evidence is presented which supports the hypothesis that arsenic in soils is less bioavailable to the test system than soluble IV or soluble oral arsenic. Estimates of absorption of soluble arsenic delivered orally are more or less consistent with literature values available for these forms of arsenic. Due to aberrations in study implementation, two correction methods were used by the authors to estimate bioavailability which were, in my opinion, inappropriate. First, the authors argue that, since the recovery of the IV dose was significantly less than the oral doses, a correction should be made to account for the discrepancy. Second, the authors argue that the predose urinary arsenic concentrations increase throughout the study and consequently should be corrected for endogenous arsenic. Neither adjustment is justifiable based upon the data presented in the Battelle report.

Recommendations:

This investigation could plausibly provide important insight into the physiology and pharmacokinetics of arsenic absorption. With some exceptions, the study is well designed and appears to have been carefully conducted. Additionally, if completed, the investigation may provide a basis for site specific adjustments in arsenic bioavailability for the Anaconda NPL site. However, in its present state, I recommend that the study be rejected as a tool for site specific decision-making. Steps to be taken which might improve the usefulness of the study include: (1) complete analysis of all archived blood samples and thorough comparison of these analysis with data on urinary and fecal excretion in an attempt to resolve the enigma of poor IV dose recovery; (2) provision of adequate information on the clinical chemistry and health of the animals beyond an assessment of arsenic toxicity to include CBCs if available, and clinical observations of the attending veterinarian; (3) reassessment of arsenic absorption without the assumption of an increasing predose endogenous arsenic source. The background arsenic should be

treated as stable and bioavailability estimates presented as corrected for study mean arsenic background; and (4) estimates of arsenic bioavailability should be made assuming that the intravenous dose was delivered as was clearly indicated by the investigators and that it was fully absorbed and physiologically unrecoverable. This approach would be generally more supportable than assuming, as the authors have, that some portion of the IV arsenic was lost in the analysis.

Thank you for the opportunity to review this important and interesting study. I look forward to reviewing it again upon its completion. If you have any questions, please call me at (303) 294-7566.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
REGION VIII
999 18th STREET - SUITE 500
DENVER, COLORADO 80202-2466

JUL 3 1995

MEMORANDUM

SUBJECT: Addendum to the Review of the Battelle Columbus report: ***Determination of the Bioavailability of Soluble Arsenic and Arsenic in Soil and Dust Impacted By Smelter Activities Following Oral Administration in Cynomolgus Monkeys. Amended Final Report*** (March 1995)

TO: Charlie Coleman, RPM
Montana Operations Branch

Susan Griffin, Ph.D., D.A.B.T., Toxicologist
Superfund Management Branch

FROM: Christopher Weis, Ph.D., D.A.B.T., Toxicologist
Superfund Management Branch

After review of the initial report (December 1994) EPA requested that the archived blood samples be analyzed and compared to the urinary and fecal excretion data. This memorandum, prepared with technical assistance from Dr. Susan Walker of CDM Federal Programs, Inc.,presents the review of the amended subject report prepared by Battelle for the Atlantic Richfield Company (ARCO) under the direction of Dr. Gary B. Freeman.

Study design, test substance characterization, dosing regimen, data collection, food consumption and clinical observations were discussed in the review of the initial report and will not be repeated here.

Analysis of Blood Arsenic Data:

The percent recovery from both matrix spiked samples and the solvent samples was within a technically acceptable range of recovery. Percent recovery in samples of blood spiked with arsenic ranged from 133 percent in the blood samples spiked with 0.02 µg arsenic/sample to 83 percent in the blood samples spiked with 5.00 µg arsenic/sample. The resulting percent residual errors were 20.5 to -3.0 (Figure 1, blood). Percent recovery in samples of solvent spiked with arsenic ranged from 85 percent in the solvent samples spiked with 0.02 µg arsenic/sample to 103 percent in the solvent samples spiked with 5.00 µg arsenic/sample. The resulting percent residual errors were -14.2 to 3.4 (Figure 2). Accuracy of the blood samples was within the technically acceptable range at 0.05 µg/sample. Precision of the study, as measured by the reproducibility of analytical results for the same sample, was not reported.

Absolute bioavailability, measured by evaluating area under the curve (AUC) was

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estimated using the trapezoidal method and using AutoCAD. The formula used for the trapezoidal method was as follows:

$$\int_{t_0}^{t_n} \phi(t)\ dt = \int_{t_0}^{t_1} \phi(t)\ dt + \ldots \int_{t_{n-1}}^{t_n} \phi(t)\ dt$$

Where:
$\phi(t)$ is linear between two consecutive blood level-time points, and
n is the number of trapezoids into which the curve is divided. Both sets of results were compared to the results reported by Battelle using Sigma Plot to develop estimates (Table 1).

Absolute bioavailability, as estimated using AUC for gavaged dosing with sodium arsenate ranged from 0.67 to 1.07 using Sigma Plot, 0.73 to 1.32 using AutoCAD and 0.9 to 1.22 using the trapezoidal method. These data suggest that the mean absolute bioavailability for gavaged arsenic approaches 100 percent. High absorption efficiencies for gavaged arsenic may be expected and are generally supported in the available literature. The equation used to determine absolute bioavailability was:

$$\frac{\textit{AUC for gavage treatment}}{\textit{AUC for intravenous treatment}} \times \frac{\textit{Total administered dose for intravenous treatment (mg/kg)}}{\textit{Total administered dose for gavage treatment (mg/kg)}} \times 100$$

Soil and dust absorption demonstrated a higher variability between monkeys. The range of absolute bioavailability for arsenic in ingested soils among individual animals was from 0.05 to 0.42 resulting in absolute mean bioavailabilities of from 11 to 18 percent. The range of absolute bioavailability for arsenic in ingested dusts were from 0.04 to 0.18 resulting in absolute mean bioavailabilities from 8 to 11 percent.

Monkey 30-537 demonstrated higher absorption of arsenic from ingested soil than did either other monkey when using blood AUC to determine absorption. The 72 hour blood sample from this monkey was extremely high and resulted in an aberrant arsenic absolute bioavailability for ingested soil. According to Dr. Freeman, the sample was re-analyzed with the same analytical results, indicating that the result was not likely to be due to an analytical error. Curve averaging or smoothing were used to limit the impact of the aberrant arsenic value. A second method attempted was to truncate all AUCs at 72 hours. While this had no effect on the intravenous AUC, all other AUCs decreased dramatically. Mean absolute bioavailability estimates decreased from 99 percent to 22 percent for arsenic absorbed from gavage; 22 percent to 4 percent for arsenic absorbed from soil, and 11 percent to 1 percent for arsenic absorbed from dust when curves were truncated, suggesting that bioavailabilities were grossly underestimated using this method (Table 2).

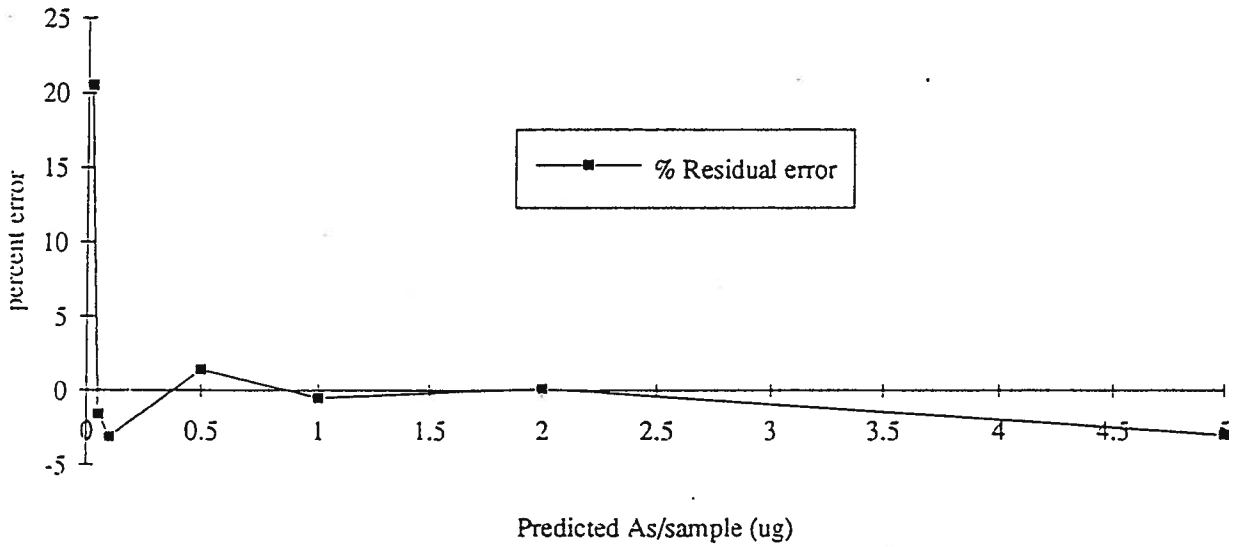
Comparison of mean bioavailability estimates:

As was discussed in the first review, the authors normalized the results of urinary arsenic recovery from other dose groups to compensate for the poor recovery from the IV group. This correction for poor urinary arsenic recovery significantly reduced the estimates of arsenic absorption. Table 3 presents a comparison of the mean aboslute bioavailability estimated for urinary arsenic recoveries with and without normalizing the data for poor urinary arsenic recovery. Comparison of the bioavailabilities for gavage, soil ingestion, and dust ingestion developed from the blood arsenic data and the urinary arsenic data demonstrate that the mean absolute bioavailabilities are more comparable (particularly for gavage) when the urinary arsenic bioavailabilities are not normalized for poor arsenic recovery for the IV group (Table 4).

Summary:

The mean absolute bioavailability estimated from urine arsenic concentrations were 91 percent, 18.3 percent and 25.8 percent respectively for gavage, soil and dust (Table 3). The mean absolute bioavailability estimated from blood arsenic concentrations were between 91 and 100 percent for gavage, 11 and 18 percent for soil ingestion and 8 and 11percent for dust. This study demonstrates that the absorption of arsenic from soils and dust is significantly less than absorption of soluble arsenic from water, and should be used to provide site-specific adjustments in arsenic bioavailability for the Anaconda NPL site.

Figure 1
Percent Residual Error for Spiked Blood



RESERROR.XLS Chart 1
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Figure 2
Percent Residual Error for Solvent

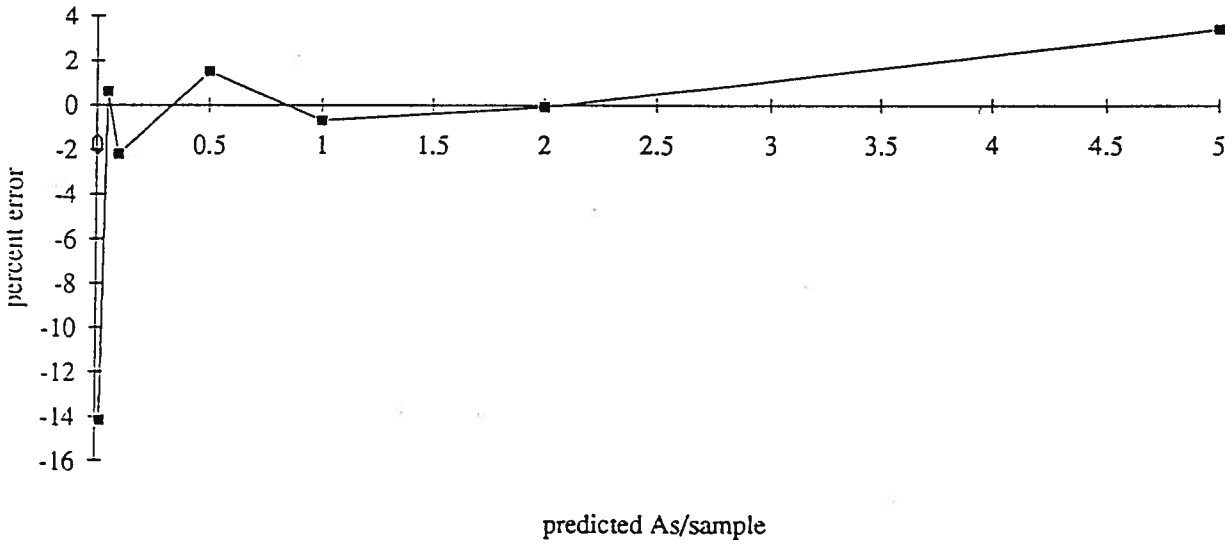

TABLE I
BIOAVAILABILITY ESTIMATED BY AUC MEASUREMENT
BLOOD ARSENIC MEASUREMENTS

Treatment	Monkey	Dose	AREA UNDER THE CURVE					ABSOLUTE BIOAVAILABILITY					MEAN ABSOLUTE BIOAVAILABILITY		
			Uncorrected		corrected			uncorrected		corrected					
			AutoCAD	Trapezoidal	AutoCAD	Trapezoidal	Batelle	AutoCAD	Trapezoidal	AutoCAD	Trapezoidal	Batelle	AutoCAD	Trapezoidal	Batelle
iv	30-544	0.63	4.00	3.80	3.16	3.06	3.18								
iv	20-784	0.60	4.50	3.30	3.90	3.00	4.24								
iv	30-537	0.64	5.20	4.80	3.80	3.75	4.72								
gavage	30-544	0.61	3.69	3.30	3.10	3.10	3.10	0.95	0.90	1.01	1.05	1.01			
gavage	20-784	0.60	3.34	3.00	2.83	2.70	2.83	0.74	0.91	0.73	0.90	0.67	102%	106%	91%
gavage	30-537	0.63	5.31	4.70	4.95	4.50	4.95	1.04	0.99	1.32	1.22	1.07			
soil	30-544	0.58	1.00	0.10	0.20	0.19	0.20	0.27	0.03	0.07	0.07	0.07			
soil	20-784	0.62	0.94	0.42	0.20	0.18	0.20	0.20	0.12	0.05	0.06	0.05	15%	18%	11%
soil*	30-537	0.62	3.46	3.40	1.25	1.54	0.97	0.69	0.73	0.34	0.42	0.21			
dust	30-544	0.26	1.02	0.82	0.24	0.18	0.24	0.62	0.53	0.18	0.14	0.18			
dust	20-784	0.26	0.87	0.41	0.08	0.06	0.08	0.45	0.28	0.05	0.05	0.04	11%	8%	10%
dust	30-537	0.26	0.92	0.51	0.13	0.10	0.13	0.43	0.26	0.09	0.07	0.07			

* = Batelle believed the value for 72 hr blood arsenic in 30-537 to be discrepant. Batelle omitted the value when calculating AUC
AutoCAD used Batelle's corrected numbers to measure area under the curve. Trappezoidal included the 72 hr blood arsenic number

TABLE 2
BIOAVAILABILITY ESTIMATED BY AUC METHOD
TRUNCATED AT 72 HOURS

Treatment	Monkey	Dose	AREA UNDER THE CURVE		ABSOLUTE BIOAVAILABILITY		MEAN ABSOLUTE BIOAVAILABILITY	
			FULL	TRUNCATED	FULL	TRUNCATED	FULL	TRUNCATED
iv	30-544	0.63	183.20	183.20				
iv	20-784	0.60	171.00	171.00				
iv	30-537	0.64	229.12	229.12				
gavage	30-544	0.61	176.16	38.58	0.99	0.22		
gavage	20-784	0.60	152.69	30.32	0.89	0.18	98.8%	19.6%
gavage	30-537	0.63	243.00	43.46	1.08	0.19		
soil	30-544	0.58	3.79	3.79	0.02	0.02		
soil	20-784	0.62	7.28	7.28	0.04	0.04	22.4%	3.8%
soil*	30-537	0.62	135.18	11.34	0.61	0.05		
dust	30-544	0.26	13.83	1.05	0.18	0.01		
dust	20-784	0.26	4.60	0.38	0.06	0.01	10.9%	0.8%
dust	30-537	0.26	7.54	0.46	0.08	0.00		

* = Batelle believed the value for 72 hr blood arsenic in 30-537 to be discrepant. Batelle omitted the value when calculating A
AutoCAD used Batelle's corrected numbers to measure area under the curve. Trappezoidal included the 72 hr bloo

TABLE 3
BIOAVAILABILITY ESTIMATED BY AUC MEASUREMENT
URINARY ARSENIC MEASUREMENTS

Treatment	Monkey	ABSOLUTE BIOAVAILABILITY		MEAN ABSOLUTE BIOAVAILABILITY	
		abs	normal	abs	normalized
iv	30-544				
iv	20-784				
iv	30-537				
gavage	30-544	94%	73%		
gavage	20-784	86%	64%	90.9%	67.6%
gavage	30-537	93%	66%		
soil	30-544	26%	20%		
soil	20-784	16%	12%	18.3%	13.8%
soil*	30-537	13%	9%		
dust	30-544	28%	22%		
dust	20-784	22%	16%	25.8%	19.2%
dust	30-537	28%	20%		

TABLE 4
COMPARISON OF MEAN ABSOLUTE BIOAVAILABILITIES

Treatment	Blood	Urine	Normalized Urine
Gavage	99%	91%	68%
Soil	22%	18%	14%
Dust	11%	26%	19%

APPENDIX D

COMPARISON OF PREDICTED AND MEASURED URINARY ARSENIC

EVALUATION OF THE DATA COLLECTED IN THE TOWN OF ANACONDA USING EPA RISK ASSESSMENT METHODOLOGY

In keeping with EPA risk assessment guidelines, the Exposure Assessment for the Anaconda Smelter NPL site uses factors derived from site-specific data so that risks can be evaluated on a case-by-case basis. Where site-specific data are unavailable, standard EPA default assumptions are used. The following is a discussion of the site-specific data and the EPA default assumptions that will be used to quantify intakes and risks for the residential scenario at the Anaconda Smelter site.

ASSUMPTIONS FOR COMPARISON OF MEASURED TO PREDICTED URINARY ARSENIC LEVELS

Assumptions for Bioavailability of Arsenic from Soils and Dust

Determination of the Bioavailability of Soluble Arsenic and Arsenic in Soil and Dust Impacted By Smelter Activities Following Oral Administration in Cynomolgus Monkeys. Final Report (Battelle December 1994) and Amended Final Report (Battelle March 1995) presented blood arsenic, urine arsenic and feces arsenic data collected from Cynomolgus monkeys exposed to arsenic by intravenous injection, gavage, and capsules containing soil and dust collected at the Anaconda Smelter site. EPA has used these data to derive a site-specific arsenic bioavailability estimates for ingested soil and dust (EPA 1994, 1995)

Bioavailability is defined as the fraction of the amount of arsenic in the system after oral dosing compared to the amount of arsenic in the system after intravenous administration adjusted for the difference in the size of the dose. The mean absolute bioavailability estimated from urine arsenic concentrations were 91 percent, 18.3 percent and 25.8 percent respectively for gavage, soil and dust. The absolute bioavailability estimated from blood arsenic concentrations ranged between 91 and 100 percent for gavage, 11 and 18 percent for soil ingestion and 8 and 11 percent for dust. This study demonstrates that the absorption of arsenic from soils and dust is significantly less than absorption of soluble arsenic from water, and should be used to provide site-specific adjustments in arsenic bioavailability for the Anaconda NPL site. The mean absolute availability estimated from urine arsenic concentrations were used to compare measured and predicted urinary levels in children.

Selection of Exposure Assumptions

This evaluation of the media data (water, soil, dust) collected in Anaconda by Dr. Robert Bornschein using EPA risk assessment methodology serves several purposes. First, the large number of soil and dust samples collected, the data should allow a more accurate analysis of the community than other media data sets. Second, by having measured urinary arsenic, we are able to compare predicted urinary arsenic levels to the measured spot urinary arsenic levels.

The assumptions presented in Table 1 were used to predict excretion of speciated arsenic in ug/L for those children where ages were available (n = 373). The estimates were then graphed

against speciated arsenic for those children where it was measured (n = 366). Total arsenic excretion was also predicted, however, the uncertainty associated with the predicted total arsenic excretion is greater than the uncertainty associated with the predicted speciated arsenic excretion.

It was assumed that all children were in a steady state condition, i.e., the amount of arsenic absorbed (from soil, dust, water, and in the case of total arsenic, food) equals the amount of arsenic excreted in urine.

$$ABSORBED\ ARSENIC = EXCRETED\ ARSENIC$$

The formula used to estimate daily absorption was as follows: No dermal!

$$ABS = \frac{C_s \ X \ IR_s \ X \ CF_s \ X \ EF \ X \ BAF_s}{AT} + \frac{C_w \ X \ CF_w \ X \ IR_w \ X \ EF \ X \ BAF_w}{AT}$$

The resulting value (ABS) in mg/day is the estimated absorbed arsenic per day for each individual child. (Refer to the Table below for an explanation of the other terms.)

The following formula was used to estimate the amount of speciated arsenic excreted in the urine:

$$EXC = \frac{ABS \ X \ CF_{abs}}{RATE \ X \ CF_{exc}}$$

Where:
EXC (µg/L) = amount of arsenic excreted in the urine
ABS (mg/day) = The result from the equation above.
CF_{abs} (µg/mg) = Conversion factor for µg/mg = 10^3 µg/mg
RATE (ml/day) = The estimated urinary output per day for a given age in months
CF_{exc} (L/ml) = Conversion factor for milliliters to liters = 10^{-3} L/ml

During the Anaconda study, Dr. Bornschein measured the 24-hour urine output of a subset of 25 children. The mean urine volume measured by Dr. Robert Bornschein for each age group is used as the estimated urinary output per day (RATE).

Selection of Ingestion Rate for Children in Living in Anaconda

Dr. Edward Calabrese conducted a soil ingestion study in Anaconda. The study was a week-long measurement of soil ingestion in 64 children. Using a single "best tracer" methodology, the ingestion rate median was 51 mg/day, the mean was 117 mg/day, the 90th percentile was 277 mg/day. The "four best tracers" study resulted in an ingestion rate median of 39 mg/day, a mean of 83 mg/day and a 90th percentile of 273 mg/day. The findings in the Anaconda

soil ingestion study support the Superfund Program's usual approach of 100 mg/day as a central tendency exposure assumption and 200 mg/day as a reasonable maximum exposure assumption for ingestion rates.

Predicting Total Urinary Arsenic Excretion

As a substudy in the soil ingestion study by Edward Calabrese, daily food samples of a subset of 30 children were collected. The mean mg arsenic in food per day was 0.00705 with a standard deviation of 0.0065. To predict total urinary arsenic excretion, it was assumed that children over the age of 18 months ate "solid food". It was also assumed that 100 percent of the arsenic in food was bioavailable and therefore was excreted in the urine. Because of the large standard deviation in the arsenic concentration in food and because of the lack of information on the bioavailability of arsenic in food, there is a large degree of uncertainty associated with predicted total urinary arsenic excretion.

RESULTS OF THE COMPARISON OF PREDICTED SPECIATED URINARY ARSENIC TO MEASURED URINARY ARSENIC IN CHILDREN

Using the assumptions described above, predicted urinary arsenic concentrations were developed for each child. Table 2 presents the measured and predicted speciated and total urinary arsenic levels for each child. The arithmetic and geometric means and standard deviations for measured and predicted urinary arsenic are presented in Table 3.

Kruskal-Wallis one-way analysis of variance demonstrated that the populations from which the measured and predicted data sets were drawn have the same mean. Figure 1 is a comparison of the measured and predicted speciated urinary arsenic and demonstrates that predicted urinary arsenic excretion is similar to the measured urinary arsenic levels. However, the EPA model underpredicts urinary arsenic at measured levels greater than 10 ug/L. Figure 2 compares the measured and predicted total urinary arsenic.

USE OF EPA DEFAULT EQUATION TO PREDICT POTENTIAL CARCINOGENIC RISK

To determine the overall risk for the Anaconda Community Soils data, the soil and dust data from Dr Robert Bornschein's Anaconda Study were evaluated using the following formula:

$$RISK = \frac{C_s \text{ X } EF \text{ X } ED \text{ X } IR \text{ X } CF \text{ X } BAF \text{ X } SF_o}{BW \text{ X } AT}$$

C_s (mg/kg) = the concentration of the contaminant in soils and dust.
EF (days/year) = exposure frequency.
ED (years) = exposure duration.

IR (mg/day) = ingestion rate.
CF (kg/mg) = conversion factor of 10^{-6}.
BAF = bioavailability factor
SF_o $(mg/kg/day)^{-1}$= the oral slope factor.
BW (kg) = body weight in kg.
AT (days) = Averaging time.

- The dust mean and soil mean were calculated for each area sampled by Dr. Bornschein as well as the entire population.
- The soil concentration was estimated for each yard by calculating the average of all yard soil samples collected.
- The 95% upper confidence limit of the arithmetic mean (ucl of the mean) was calculated for each area as well as the entire population.
- The exposure point concentration (C_s) for each area, and for the entire population assumed 55% dust and 45% soil was ingested. [For the relative bioavailability analysis, the actual ucl of the mean for dust and soil was used.]
- The reasonable maximum exposure ingestion rate for children (0 to 6) (RME) was assumed to be 200 mg/day.
- The central tendency exposure ingestion rate for children (0 to 6) (CTE) was assumed to be 100 mg/day.
- The RME ingestion rate for all others was assumed to be 100 mg/day.
- The CTE ingestion rate for all others was assumed to be 50 mg/day.
- Body weight for children was assumed to be 15 kg.
- Body weight for all others was assumed to be 70 kg.
- Exposure frequency was assumed to be 350 days/year.
- The RME exposure duration was assumed to be 30 years
- The CTE exposure duration was assumed to be 9 years (2 years as a child 0 to 6 and 7 years as an adult
- Averaging time was assumed to be 365 days/year times 70 years or 25550 days.
- Bioavailability factors were selected from the Cynomolgus monkey study by Battelle for ARCO. The absolute bioavailability selected for dust absorption was 25.8 percent and for soil absorption was 18.3 percent.
- The oral slope factor was 1.75 $(mg/kg/day)^{-1}$.

Table 4 presents the residential risks for Anaconda using the media data collected by Dr. Bornschein and the reasonable maximum exposure assumptions. The range of risks when assuming 25.8 percent bioavailibility for arsenic in dust and 18.3 percent bioavailability for arsenic in soils is from 4.9×10^{-5} to 1.2×10^{-4}. The overall community risk would be 7.9×10^{-5}. Area D has the highest overall concentration of arsenic in soil and dust with Area A having the lowest concentration.

Table 5 presents the residential risks for Anaconda using the media data collected by Dr. Bornschein and the central tendency exposure assumptions. The range of risks when assuming 25.8 percent and 18.3 percent bioavailability for soils is from 7.9×10^{-6} to 1.9×10^{-5}. The overall community risk would be 1.3×10^{-5}.

FIGURE 1
MEASURED AND PREDICTED SPECIATED URINARY ARSENIC

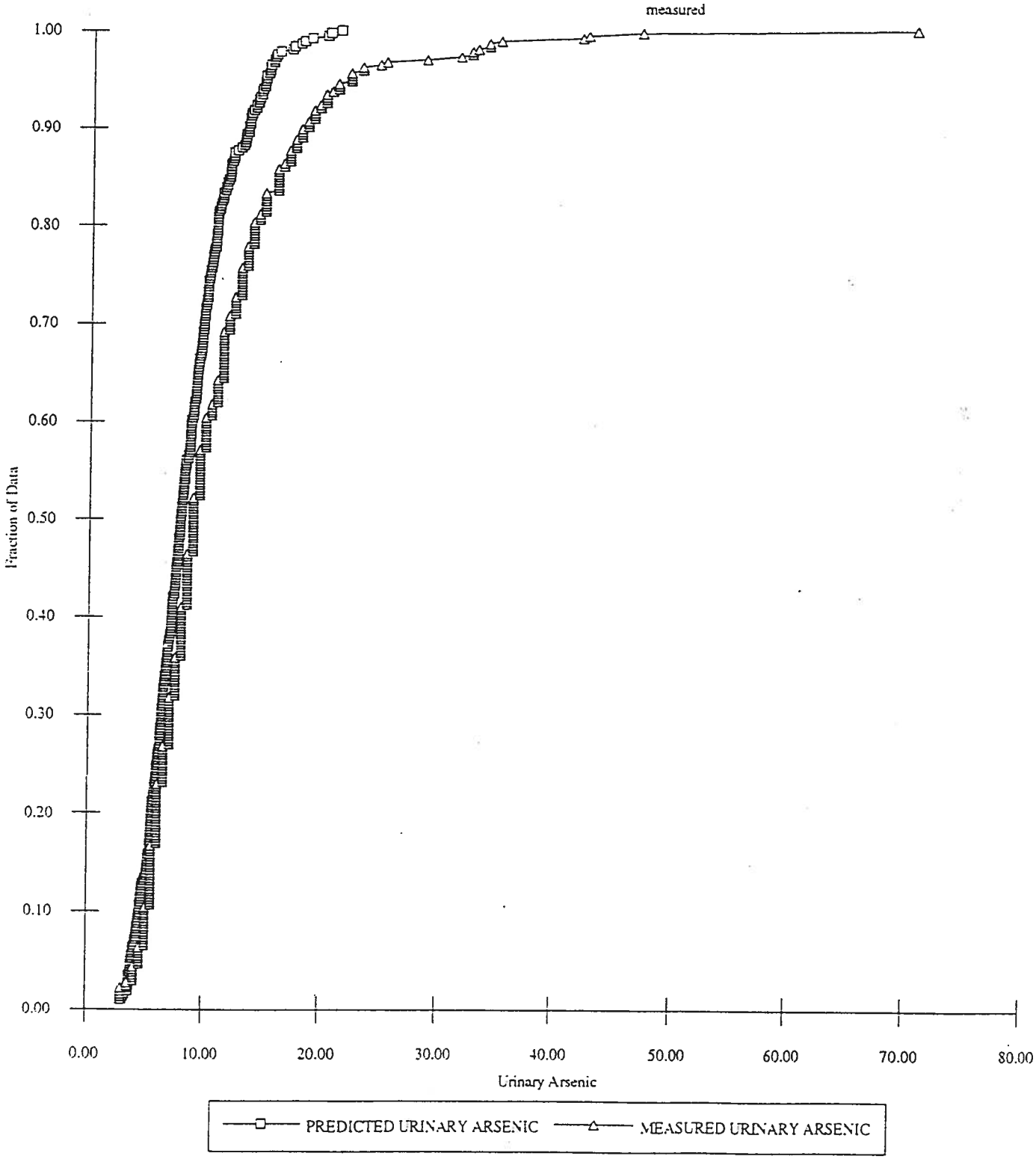

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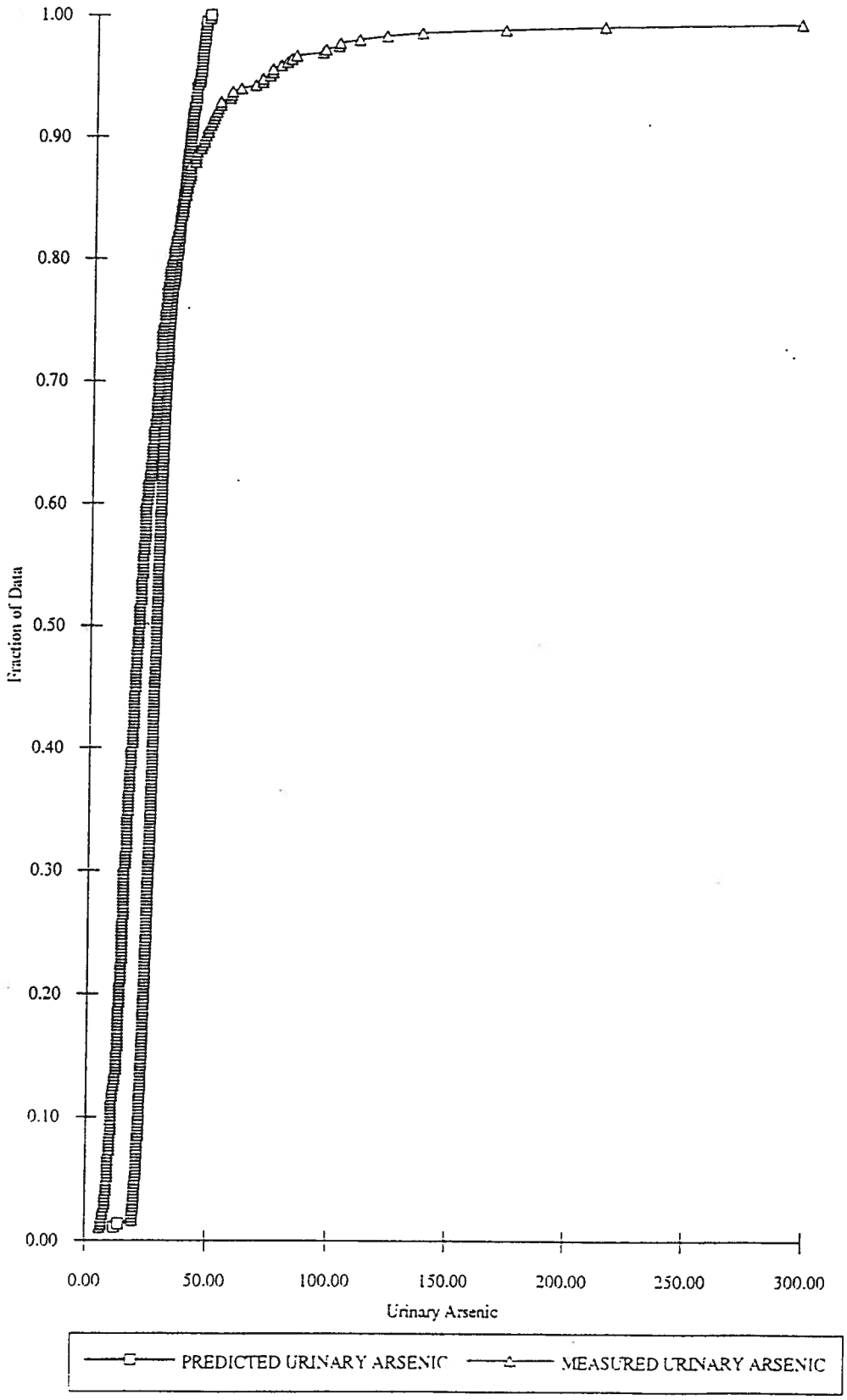
FIGURE 2
COMPARISON OF MEASURED AND PREDICTED TOTAL URINARY ARSENIC



TOTASGRH.XLS Chart 2
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TABLE 1

Symbol	Definition	Value Used
C_s	Arsenic concentration of ingested soil and dust (mg/kg)	55% sampled interior dust As 45% sampled average yard As
IR_s	Ingestion rate of combined soil and dust (mg/day)	100 mg/day
CF_s	Conversion Factor (kg/mg)	10^{-6} kg/mg
EF	Exposure Frequency (days)	350 days
AT	Averaging Time (days)	365 days
C_w	Arsenic concentration of ingested water (µg/L)	Measured water arsenic concentration (or 1/2 detection limit - 0.5 µg/L)
CF_w	Conversion Factor (mg/µg)	10^{-3} mg/µg
IR_w	Ingestion Rate (L/day)	0.7 L/day
BAF_s	Bioavailability for soil and dust	25.8 % for dust 18.3 % for soil
BAF_w	Bioavailability for water	100 %
ABS	Estimated absorbed arsenic per day for each individual child (mg/day)	Calculated for each individual child
CF_{abs}	Conversion factor for µg/mg	10^3 µg/mg
RATE	The estimated urinary output per day for a given age in months (ml/day)	Children less than 36 months of age excrete 240 ml urine/day Children between 36 and 60 months of age excrete 355 ml urine/day Children greater than 60 months of age excrete 432 ml urine/day
CF_{exc}	Conversion factor for milliliters to liters	10^{-3} L/ml

TABLE 2

ACTUAL AND PREDICTED URINARY ARSENIC LEVELS

AGE IN MONTHS	ESTIMATED URINE PRODUCTION	ARSENIC IN WATER (ug/L)	ARSENIC IN DUST (ug/g)	ARSENIC IN SOIL (ug/g)	55% DUST 45% SOIL (ug/g) ABSORBED	MEAN SPEC URINARY AS NORMALIZED (ug/L)	NATURAL LOG MEAN SPEC URINARY AS NORMALIZED	MEAN TOTAL URINARY AS NORMALIZED (ug/L)	NATURAL LOG MEAN TOTAL URINARY AS NORMALIZED	EPA PREDICTED SPECIATED AS CTB (ug/L)	NATURAL LOG EPA PREDICTED SPECIATED AS CTB (ug/L)	DIFFERENCE BETWEEN SPECIATED MEASURED AND PREDICTED	EPA PREDICTED TOTAL AS CTB (ug/L)	NATURAL LOG EPA PREDICTED TOTAL AS CTB (ug/L)	DIFFERENCE BETWEEN TOTAL MEASURED AND PREDICTED
8	240	0.5	22.3	154	16	16.00	2.77	35.50	3.57	7.72	2.04	8	7.72	2.04	27.78
14	240	0.5	62.2	266	31	5.00				13.68		(9)	13.68		
15	240	0.5	67.4	206	27	11.50	2.44	23.50	3.16	12.00	2.48	0	12.00	2.48	11.50
20	240	0.5	23.4	181	18					8.69			38.07		
21	240	0.5	23.1	166	17	32.50	3.48	44.50	3.80	8.15	2.10	24	37.53	3.63	6.97
21	240	0.5	72.1	191	26	17.00	2.83	36.00	3.58	11.83	2.47	5	41.20	3.72	(5.20)
23	240	0.5	65.3	246	30	10.00	2.30	10.00	2.30	13.19	2.58	(3)	42.56	3.75	(12.56)
23	240	0.5	40.7	110	17	35.00	3.56	65.50	4.18	7.99	2.08	27	37.37	3.62	28.13
23	240	0.5	110.2	288	39	9.50	2.25	15.00	2.71	17.12	2.84	(8)	46.50	3.84	(31.50)
23	240	0.5	59.9	100	17	19.00	2.94	120.00	4.79	8.08	2.09	11	37.46	3.62	82.54
25	240	3.2	153.4	82	28	19.50	2.97	30.00	3.40	20.33	3.01	(1)	49.70	3.91	(19.70)
25	240	0.5	112.8	136	27	42.00	3.74	76.00	4.33	12.27	2.51	30	41.64	3.73	34.36
25	240	0.5	84.2	140	23	17.00	2.83	27.50	3.31	10.79	2.38	6	40.16	3.69	(12.66)
25	240	0.5	36.4	68	11	16.00	2.77	48.00	3.87	5.68	1.74	10	35.06	3.56	12.94
25	240	0.5	133.2	151	31	12.50	2.53	39.00	3.66	13.91	2.63	(1)	43.29	3.77	(4.29)
26	240	0.5	61.2	306	34	14.00	2.64	38.50	3.65	14.95	2.70	(1)	44.32	3.79	(5.82)
26	240	0.5	124.5	198	34	12.50	2.53	30.00	3.40	14.96	2.71	(2)	44.34	3.79	(14.34)
26	240	0.5	62.2	163	22	17.50	2.86	27.00	3.30	10.29	2.33	7	39.66	3.68	(12.66)
27	240	0.5	71.4	248	31	5.50	1.70	26.50	3.28	13.60	2.61	(8)	42.97	3.76	(16.47)
27	240	0.5	109.2	220	34	13.00	2.56	22.50	3.11	14.82	2.70	(2)	44.20	3.79	(21.70)
27	240	0.5	103.4	178	29	12.50	2.53	26.50	3.28	13.11	2.57	(1)	42.48	3.75	(15.98)
27	240	0.5	34.9	108	14	11.50	2.44	19.50	2.97	6.91	1.93	5	36.29	3.59	(16.79)
28	240	0.5	60.4	154	21	6.00	1.79	9.00	2.20	9.90	2.29	(4)	39.27	3.67	(30.27)
28	240	0.5	77.5	254	32	14.00	2.64	23.00	3.14	14.14	2.65	0	43.51	3.77	(20.51)
28	240	0.5	199.1	258	50	10.00	2.30	37.50	3.62	21.19	3.05	(11)	50.56	3.92	(13.06)
29	240	0.5	224.4	374	63	21.00	3.04	30.00	3.40	26.41	3.27	(5)	55.78	4.02	(25.78)
29	240	0.5	41.8	50	10	18.50	2.92	24.00	3.18	5.41	1.69	13	34.78	3.55	(10.78)
29	240	0.5	75.2	122	21	20.00	3.00	29.00	3.37	9.67	2.27	10	39.04	3.66	(10.04)
29	240	0.5	31.3	82	11	17.50	2.86	33.00	3.50	5.87	1.77	12	35.25	3.56	(2.25)
30	240	0.5	51.4	112	17	15.00	2.71	18.50	2.92	8.00	2.08	7	37.37	3.62	(18.87)
31	240	0.5	83.0	93	19	6.00	1.79	45.00	3.81	9.15	2.21	(3)	38.53	3.65	6.47
31	240	0.5	99.1	253	35	7.00	1.95	20.50	3.02	15.33	2.73	(8)	44.71	3.80	(24.21)
31	240	0.5	83.7	242	32	14.00	2.64	28.00	3.33	14.12	2.65	0	43.49	3.77	(15.49)
31	240	0.5	91.7		13	9.00	2.20	14.50	2.67	6.60	1.89	2	35.97	3.58	(21.47)
31	240	0.5	37.0	160	18	11.00	2.40	25.50	3.24	8.74	2.17	2	38.12	3.64	(12.62)
31	240	0.5	81.9	134	23	31.50				10.44		21	39.82		
32	240	0.5	52.0	186	23	9.50	2.25	19.00	2.94	10.48	2.35	(1)	39.85	3.69	(20.85)
32	240	0.5	63.1	145	21	15.00	2.71	25.50	3.24	9.75	2.28	5	39.12	3.67	(13.62)
32	240	8.9	74.7	166	24	12.00	2.48	19.00	2.94	34.59	3.54	(23)	63.96	4.16	(44.96)
32	240	0.5	73.0	83	17	18.00	2.89	21.00	3.04	8.25	2.11	10	37.63	3.63	(16.63)
32	240	0.5	224.4	374	63	10.00	2.30	18.00	2.89	26.41	3.27	(16)	55.78	4.02	(37.78)
33	240	0.5	65.8	190	25	16.00	2.77	21.00	3.04	11.38	2.43	5	40.76	3.71	(19.76)
33	240	0.5	49.9	97	15	13.50	2.60	23.50	3.16	7.41	2.00	6	36.79	3.61	(13.29)
33	240	0.5	16.1	159	15	11.50	2.44	22.00	3.09	7.53	2.02	4	36.91	3.61	(14.91)
33	240	0.5	56.3	224	26	8.50	2.14	16.00	2.77	11.97	2.48	(3)	41.35	3.72	(25.35)
33	240	0.5	48.0	92	14	10.50	2.35	15.50	2.74	7.15	1.97	3	36.52	3.60	(21.02)
33	240	0.5	93.2	243	33	9.50	2.25	20.50	3.02	14.66	2.69	(5)	44.04	3.79	(23.54)
33	240	0.5	49.8	217	25	7.50	2.01	30.00	3.40	11.35	2.43	(4)	40.72	3.71	(10.72)
33	240	2.9	121.8	194	33	14.00	2.64	35.00	3.56	21.41	3.06	(7)	50.78	3.93	(15.78)
33	240	0.5	45.0	84	13	7.50	2.01	21.00	3.04	6.71	1.90	1	36.08	3.59	(15.08)
34	240	0.5	277.9	275	62	28.50	3.35	47.50	3.86	26.22	3.27	2	55.59	4.02	(8.09)
34	240	0.5	42.7	165	20	6.00	1.79	12.00	2.48	9.24	2.22	(3)	38.62	3.65	(26.62)
34	240	1.4	125.6	82	25	10.50	2.35	27.00	3.30	13.74	2.62	(3)	43.12	3.76	(16.12)
34	240	0.5	50.4	171	21	6.00	1.79	12.00	2.48	9.89	2.29	(4)	39.26	3.67	(27.26)
34	240	0.5	151.0	303	47	42.50	3.75	68.50	4.23	20.11	3.00	22	49.48	3.90	19.02
34	240	0.5	246.1	289	59	18.00	2.89	29.00	3.37	24.87	3.21	(7)	51.24	3.99	(25.24)
34	240	0.5	58.5	260	30	5.50	1.70	12.00	2.48	13.26	2.58	(8)	42.63	3.75	(30.63)
35	240	0.5	0.0	321	26	13.00	2.56	22.00	3.09	11.95	2.48	1	41.32	3.72	(19.32)
35	240	0.5	144.3	189	36	13.00	2.56	25.00	3.22	15.80	2.76	(3)	45.17	3.81	(20.17)
35	240	0.5	52.9	174	22	5.50	1.70	17.00	2.83	10.12	2.31	(5)	39.50	3.68	(22.50)
35	240	0.5	91.7	228	32	9.00	2.20	18.00	2.89	14.27	2.66	(5)	43.64	3.78	(25.64)
35	240	2.0	30.5	69	10	5.50	1.70	32.50	3.48	9.60	2.26	(4)	38.97	3.66	(6.47)
35	240	1.4	42.8	43	10	8.50	2.14	19.50	2.97	7.77	2.05	1	37.14	3.61	(17.64)

TABLE 2

ACTUAL AND PREDICTED URINARY ARSENIC LEVELS

AGE IN MONTHS	ESTIMATED URINE PRODUCTION	ARSENIC IN WATER (ug/L)	ARSENIC IN DUST (ug/kg)	ARSENIC IN SOIL (ug/kg)	55%DUST 45%SOIL (ug/kg) ABSORBED	MEAN SPEC URINARY AS NORMALIZED (ug/L)	NATURAL LOG MEAN SPEC URINARY AS NORMALIZED	MEAN TOTAL URINARY AS NORMALIZED (ug/L)	NATURAL LOG MEAN TOTAL URINARY AS NORMALIZED	EPA PREDICTED SPECIATED AS CTE (ug/L)	NATURAL LOG EPA PREDICTED SPECIATED AS CTE (ug/L)	DIFFERENCE BETWEEN SPECIATED MEASURED AND PREDICTED	EPA PREDICTED TOTAL AS... CTE (ug/L)	NATURAL LOG EPA PREDICTED TOTAL AS CTE (ug/L)	DIFFERENCE BETWEEN TOTAL MEASURED AND PREDICTED
35	240	0.5	105.3	106	24	20.00	3.00	39.00	3.66	10.86	2.39	9	40.24	3.69	(1.24)
35	240	0.5	49.3	138	18	22.00	3.09	29.50	3.38	8.73	2.17	13	38.10	3.64	(8.60)
35	240	0.5	102.1	259	36	12.50	2.53	25.50	3.24	15.69	2.75	(3)	45.07	3.81	(19.57)
35	240	0.5	113	163	20	23.00	3.14	25.00	3.22	9.24	2.22	14	38.61	3.65	(13.61)
36	240	0.5	125.1	268	40	5.50	1.70	13.50	2.60	17.30	2.85	(12)	46.68	3.84	(33.18)
36	240	0.5	125.5	179	33	10.00	2.30	16.00	2.77	14.40	2.67	(4)	43.78	3.78	(27.78)
36	240	0.5	135.6	187	35	8.00	2.08	14.50	2.67	15.23	2.72	(7)	44.60	3.80	(30.10)
36	355	0.5	14.9	128	13	9.00	2.20	20.00	3.00	4.36	1.47	5	24.22	3.19	(4.22)
36	355	0.5	40.7	123	16	13.50	2.60	20.00	3.00	5.24	1.66	8	25.10	3.22	(5.10)
37	355	0.5	69.9	162	23	9.00	2.20	27.50	3.31	7.23	1.98	2	27.09	3.30	0.41
37	355	0.5	36.4	68	11	8.00	2.08	43.00	3.76	3.84	1.35	4	23.70	3.17	19.30
37	355	0.5	104.7	228	34	16.00	2.77	33.50	3.51	10.03	2.31	6	29.89	3.40	3.61
37	355	0.5	54.3	258	29	11.50	2.44	18.00	2.89	8.76	2.17	3	28.62	3.35	(10.62)
37	355	0.5	81.4	149	24	9.00	2.20	10.00	2.30	7.49	2.01	2	27.35	3.31	(17.35)
37	355	0.5	101.8	265	36	6.00	1.79	28.00	3.33	10.73	2.37	(5)	30.59	3.42	(2.59)
37	355	0.5	119.7	193	33	14.00	2.64	37.00	3.61	9.83	2.29	4	29.69	3.39	7.31
38	355	1.6	149.8	96	29	18.00	2.89	43.50	3.77	10.89	2.39	7	30.75	3.43	12.75
38	355	4.7	43.3	62	11	20.00	3.00	36.50	3.60	11.93	2.48	8	31.78	3.46	4.72
38	355	2.9	49.2	72	13	25.00	3.22	39.00	3.66	8.97	2.19	16	28.83	3.36	10.17
38	355	0.5	103.4	118	24	15.00	2.71	21.00	3.04	7.54	2.02	7	27.40	3.31	(6.40)
38	355	0.5	49.4	73	13	8.50	2.14	135.00	4.91	4.45	1.49	4	24.31	3.19	110.69
38	355	0.5	53.6	151	20	11.00	2.40	20.50	3.02	6.36	1.85	5	26.22	3.27	(5.72)
38	355	0.5	190.2	239	47	24.50	3.20	51.00	3.93	13.55	2.61	11	33.41	3.51	17.59
38	355	0.5	237.9	248	54	11.50	2.44	20.00	3.00	15.57	2.75	(4)	35.43	3.57	(15.43)
38	355	0.5	39.7	81	12	21.00	3.04	31.00	3.43	4.26	1.45	17	24.12	3.18	6.88
39	355	0.5	85.3	313	38	11.00	2.40	22.50	3.11	11.17	2.41	0	31.03	3.43	(8.53)
39	355	0.5	70.5	161	23	11.50	2.44	25.00	3.22	7.23	1.98	4	27.09	3.30	(2.09)
39	355	0.5	69.8	205	27					8.18			28.03		
40	355	0.5	150.9	263	43	9.00	2.20	15.50	2.74	12.58	2.53	(4)	32.44	3.48	(16.94)
40	355	0.5	85.7	148	24	16.50	2.80	38.00	3.64	7.51	2.02	9	27.37	3.31	10.63
40	355	0.5	65.8	194	25	17.50	2.86	17.50	2.86	7.77	2.05	10	27.63	3.32	(10.13)
40	355	0.5	47.6	69	12	5.50	1.70	14.50	2.67	4.31	1.46	1	24.17	3.19	(9.67)
40	355	0.5	67.3	203	26	7.00	1.95	15.50	2.74	8.03	2.08	(1)	27.89	3.33	(12.39)
40	355	0.5	89.4	126	23	11.50	2.44	21.50	3.07	7.18	1.97	4	27.04	3.30	(5.54)
40	355	0.5	63.6	134	20	19.50	2.97	28.00	3.33	6.36	1.85	13	26.22	3.27	1.78
40	355	0.5	70.6	223	28	17.00	2.83	19.50	2.97	8.62	2.15	8	28.48	3.35	(8.98)
41	355	0.5	115.5	214	34	8.00	2.08	17.50	2.86	10.13	2.32	(2)	29.99	3.40	(12.49)
41	355	0.5	38.2	229	24	17.00	2.83	41.00	3.71	7.51	2.02	9	27.37	3.31	13.63
41	355	0.5	31.0	142	16	9.50	2.25	9.00	2.20	5.30	1.67	4	25.16	3.23	(16.16)
41	355	0.5	168.3	349	53	14.50	2.67	46.00	3.83	15.15	2.72	(1)	35.01	3.56	10.99
41	355	0.5	124.5	198	34	3.00	1.10	18.00	2.89	10.12	2.31	(7)	29.98	3.40	(11.98)
41	355	2.6	47.8	62	12	15.00	2.71	27.50	3.31	8.13	2.10	7	27.99	3.33	(0.49)
41	355	0.5	64.2	129	20	34.00	3.53	51.00	3.93	6.28	1.84	28	26.14	3.26	24.86
41	355	0.5	175.8	310	50	13.50	2.60	26.00	3.26	14.57	2.68	(1)	34.43	3.54	(8.43)
41	355	0.5	25.1	162	17					5.51			25.36		
41	355	0.5	151.6	341	50	11.50	2.44	34.00	3.53	14.33	2.66	(3)	34.19	3.53	(0.19)
41	355	0.5	98.5	158	27	6.00	1.79	18.50	2.92	8.24	2.11	(2)	28.09	3.34	(9.59)
41	355	0.5	129.8	240	38	18.50	2.92	29.50	3.38	11.25	2.42	7	31.11	3.44	(1.61)
42	355	0.5	110.8	187	31	9.00	2.20	31.50	3.45	9.36	2.24	0	29.22	3.37	2.28
42	355	3.9	17.8	80	9	8.00	2.08	17.00	2.83	9.84	2.29	(2)	29.70	3.39	(12.70)
42	355	0.5	81.0	151	24					7.42			27.28		
42	355	0.5	160.0	174	37	14.00	2.64	34.50	3.54	10.95	2.39	3	30.81	3.43	3.69
42	355	0.5	81.2	232	31	19.00	2.94	212.50	5.36	9.21	2.22	10	29.07	3.37	183.43
42	355	3.3	83.4	86	19	11.00	2.40	20.50	3.02	11.35	2.43	0	31.21	3.44	(10.71)
43	355	0.5	81.4	293	36	13.00	2.56	23.00	3.14	10.57	2.36	2	30.43	3.42	(7.43)
43	355	1.6	85.2	94	20	21.00	3.04	28.00	3.33	8.38	2.13	13	28.24	3.34	(0.24)
43	355	0.5	91.9	204	30	5.50	1.70	12.00	2.48	9.01	2.20	(4)	28.87	3.36	(16.87)
43	355	0.5	260.1	232	56	19.00	2.94	47.00	3.85	16.08	2.78	3	35.94	3.58	11.06
43	355	0.5	119.8	278	40	8.50	2.14	10.00	2.30	11.72	2.46	(3)	31.57	3.45	(21.57)
43	355	0.5	63.2	192	25	47.00	3.85	100.00	4.61	7.65	2.03	39	27.51	3.31	72.49
43	355	0.5	178.5	256	46	9.50	2.25	18.50	2.92	13.47	2.60	(4)	33.33	3.51	(14.83)
43	355	2.7	38.7	79	12	7.00	1.95	34.00	3.53	8.35	2.12	(1)	28.21	3.34	5.79
43	355	0.5	37.3	78	12	11.00	2.40	21.00	3.04	4.11	1.41	7	23.97	3.18	(2.97)

TABLE 2

ACTUAL AND PREDICTED URINARY ARSENIC LEVELS

AGE IN MONTHS	ESTIMATED URINE PRODUCTION	ARSENIC IN WATER (ug/L)	ARSENIC IN DUST (ug/kg)	ARSENIC IN SOIL (ug/kg)	55%DUST 45%SOIL (ug/kg) ABSORBED	MEAN SPEC URINARY AS NORMALIZED (ug/L)	NATURAL LOG MEAN SPEC URINARY AS NORMALIZED	MEAN TOTAL URINARY AS NORMALIZED (ug/L)	NATURAL LOG MEAN TOTAL URINARY AS NORMALIZED	EPA PREDICTED SPECIATED AS CTE (ug/L)	NATURAL LOG EPA PREDICTED SPECIATED AS CTE (ug/L)	DIFFERENCE BETWEEN SPECIATED MEASURED AND PREDICTED	EPA PREDICTED TOTAL AS CTE (ug/L)	NATURAL LOG EPA PREDICTED TOTAL AS CTE (ug/L)	DIFFERENCE BETWEEN TOTAL MEASURED AND PREDICTED
11	355	0.5	112.8	136	27	20.50	3.02	55.00	4.01	8.29	2.12	12	28.15	3.34	26.85
11	355	0.5	190.3	229	46	16.00	2.77	295.00	5.69	13.32	2.59	3	33.18	3.50	261.82
11	355	0.5	68.8	105	18	5.50	1.70	10.00	2.30	5.92	1.78	0	25.78	3.25	(15.78)
11	355	0.5	102.7	137	26	11.50	2.44	24.50	3.20	7.93	2.07	4	27.79	3.32	(3.29)
11	355	0.5	91.8	233	32	16.50	2.80	32.50	3.48	9.61	2.27	7	29.49	3.38	3.01
11	355	0.5	114.1	252	37	15.00	2.71	20.00	3.00	10.92	2.39	4	30.78	3.43	(10.78)
11	355	1.5	40.9	87	13	7.00	1.95	14.00	2.64	6.34	1.85	1	26.20	3.27	(12.20)
11	355	9.9	29.5	71	10	3.00	1.10	8.00	2.08	21.43	3.06	(18)	41.29	3.72	(33.29)
11	355	8.9	74.7	166	24	15.00	2.71	82.50	4.41	23.38	3.15	(8)	43.24	3.77	39.26
15	355	0.5	35.1	156	18	8.00	2.08	12.50	2.53	5.77	1.75	2	25.63	3.24	(13.13)
15	355	2.9	45.4	129	17	9.00	2.20	18.00	2.89	10.09	2.31	(1)	29.95	3.40	(11.95)
15	355	0.5	71.8	187	26	6.00	1.79	17.00	2.83	7.86	2.06	(2)	27.72	3.32	(10.72)
15	355	0.5	154.0	303	47	22.00	3.09	41.50	3.73	13.59	2.61	8	33.45	3.51	8.05
15	355	0.5	77.4	190	27	9.00	2.20	13.50	2.60	8.15	2.10	1	28.00	3.33	(14.50)
15	355	0.5	41.8	50	10	32.50	3.48	41.00	3.71	3.66	1.30	29	23.51	3.16	17.49
15	355	0.5	80.5	164	25	14.00	2.64	31.00	3.43	7.67	2.04	6	27.53	3.32	3.47
15	355	0.5	117.9	159	30	12.50	2.53	56.00	4.03	8.99	2.20	4	28.85	3.36	27.15
15	355	0.5	35.6	64	10	13.00	2.56	22.00	3.09	3.73	1.32	9	23.59	3.16	(1.59)
15	355	0.5	69.8	183	25	7.00	1.95	18.00	2.89	7.68	2.04	(1)	27.54	3.32	(9.54)
15	355	0.5	142.3	202	37	6.50	1.87	13.00	2.56	10.90	2.39	(4)	30.76	3.43	(17.76)
15	355	0.5	126.5	238	38	12.00	2.48	28.00	3.33	11.08	2.41	1	30.94	3.43	(2.94)
15	355	0.5	60.5	156	21	20.00	3.00	37.00	3.61	6.73	1.91	13	26.59	3.28	10.41
15	355	0.5	133.5	145	31	23.00	3.14	59.50	4.09	9.28	2.23	14	29.14	3.37	30.36
16	355	0.5	76.1	127	21	5.50	1.70	14.00	2.64	6.69	1.90	(1)	26.55	3.28	(12.55)
16	355	0.5	164.5	268	45	16.00	2.77	26.00	3.26	13.21	2.58	3	33.07	3.50	(7.07)
16	355	0.5	61.2	306	34	9.50	2.25	27.50	3.31	10.11	2.31	(1)	29.96	3.40	(2.46)
16	355	0.5	58.8	131	19	5.50	1.70	20.50	3.02	6.10	1.81	(1)	25.96	3.26	(5.46)
16	355	0.5	72.3	323	37	10.50	2.35	17.50	2.86	10.91	2.39	0	30.77	3.43	(13.27)
16	355	0.5	45.3	128	17	6.00	1.79	12.50	2.53	5.52	1.71	0	25.38	3.23	(12.88)
16	355	0.5	25.6	203	20	16.00	2.77	41.00	3.71	6.44	1.86	10	26.30	3.27	14.70
16	355	0.5	175.8	510	50	11.00	2.40	17.00	2.83	14.57	2.68	(4)	34.43	3.54	(17.43)
16	355	0.5	71.7	92	18	8.00	2.08	21.50	3.07	5.86	1.77	2	25.72	3.25	(4.22)
17	355	0.5	86.3	164	26	5.00	1.61	9.50	2.25	7.90	2.07	(3)	27.75	3.32	(18.25)
17	355	0.5	40.7	130	17	34.00	3.53	44.50	3.80	5.40	1.69	29	25.26	3.23	19.24
17	355	0.5	73.0	138	22	13.00	2.56	24.50	3.20	6.82	1.92	6	26.68	3.28	(2.18)
17	355	0.5	32.6	197	21	9.50	2.25	18.50	2.92	6.57	1.88	3	26.43	3.27	(7.93)
17	355	0.5	133.2	151	31	11.50	2.44	27.00	3.30	9.41	2.24	2	29.26	3.38	(2.26)
17	355	0.5	76.9	208	28	5.00	1.61	6.50	1.87	8.52	2.14	(4)	28.38	3.35	(21.88)
17	355	0.5	19.3	104	11	19.00	2.94	19.00	2.94	3.99	1.38	15	23.85	3.17	(4.85)
17	355	0.5	72.5	174	25	6.00	1.79	11.00	2.40	7.59	2.03	(2)	27.45	3.31	(16.45)
18	355	0.5	59.6	125	19	13.50	2.60	49.50	3.90	6.02	1.79	7	25.88	3.25	23.62
18	355	0.5	23.9	107	12	8.50	2.14	10.00	2.30	4.25	1.45	4	24.11	3.18	(14.11)
18	355	0.5	145.4	140	32	9.00	2.20	19.50	2.97	9.64	2.27	(1)	29.50	3.38	(10.00)
18	355	0.5	64.7	119	19	8.50	2.14	20.50	3.02	6.07	1.80	2	25.93	3.26	(5.43)
18	355	0.5	135.6	187	35	7.50	2.01	22.00	3.09	10.29	2.33	(3)	30.15	3.41	(8.15)
18	355	0.5	25.2	159	17	14.00	2.64	31.00	3.43	5.44	1.69	9	25.30	3.23	5.70
18	355	0.5	146.4	311	46	14.00	2.64	28.00	3.33	13.46	2.60	1	33.32	3.51	(5.32)
18	355	0.5	49.2	140	18	11.00	2.40	26.50	3.28	5.93	1.78	5	25.79	3.25	0.71
19	355	0.5	82.2	209	29	18.00	2.89	16.50	2.80	8.74	2.17	9	28.60	3.35	(12.10)
19	355	2.2	48.3	63	12	5.50	1.70	12.50	2.53	7.41	2.00	(2)	27.27	3.31	(14.77)
19	355	0.5	83.3	360	41	5.00	1.61	13.00	2.56	12.14	2.50	(7)	32.00	3.47	(19.00)
19	355	0.5	73.0	202	27	6.00	1.79	55.50	4.02	8.24	2.11	(2)	28.10	3.34	27.40
19	355	0.5	157.1	266	44	9.50	2.25	13.00	2.56	12.89	2.56	(3)	32.75	3.49	(19.75)
19	355	3.3	25.2	66	9	5.50	1.70	26.00	3.26	8.67	2.16	(3)	28.53	3.35	(2.53)
50	355	0.5	122.2	142	29	8.00	2.08	23.00	3.14	8.80	2.17	(1)	28.65	3.36	(5.65)
50	355	0.5	39.9	103	14	6.00	1.79	27.50	3.31	4.77	1.56	1	24.63	3.20	2.87
50	355	0.5	42.4	138	17	7.50	2.01	6.00	1.79	5.63	1.73	2	25.49	3.24	(19.49)
50	355	0.5	191.3	294	51	9.50	2.25	14.50	2.67	14.81	2.70	(5)	34.67	3.55	(20.17)
50	355	0.5	63.7	106	18	8.00	2.08	17.00	2.83	5.75	1.75	2	25.61	3.24	(8.61)
50	355	2.2	95.7	84	20	13.00	2.56	25.00	3.22	9.69	2.27	3	29.54	3.39	(4.54)
51	355	0.5	11.9	215	19	13.50	2.60	26.50	3.28	6.18	1.82	7	26.04	3.26	0.46
51	355	0.5	202.5	276	51	11.50	2.44	17.50	2.86	14.86	2.70	(3)	34.71	3.55	(17.21)
51	355	0.5	91.5	226	32	7.50	2.01	22.00	3.09	9.48	2.25	(2)	29.34	3.38	(7.34)

TABLE 2

ACTUAL AND PREDICTED URINARY ARSENIC LEVELS

AGE IN MONTHS	ESTIMATED URINE PRODUCTION	ARSENIC IN WATER (ug/L)	ARSENIC IN DUST (ug/kg)	ARSENIC IN SOIL (ug/kg)	55% DUST 45% SOIL (ug/kg) ABSORBED	MEAN SPEC URINARY AS NORMALIZED (ug/L)	NATURAL LOG MEAN SPEC URINARY AS NORMALIZED	MEAN TOTAL URINARY AS NORMALIZED (ug/L)	NATURAL LOG MEAN TOTAL URINARY AS NORMALIZED	EPA PREDICTED SPECIATED AS CTE (ug/L)	NATURAL LOG EPA PREDICTED SPECIATED AS CTE (ug/L)	DIFFERENCE BETWEEN SPECIATED MEASURED AND PREDICTED	EPA PREDICTED TOTAL AS CTE (ug/L)	NATURAL LOG EPA PREDICTED TOTAL AS CTE (ug/L)	DIFFERENCE BETWEEN TOTAL MEASURED AND PREDICTED
51	355	0.5	82.5	214	29	13.50	2.60	37.50	3.62	8.86	2.18	5	28.72	3.36	8.78
52	355	1.2	127.8	101	26	9.50	2.25	17.50	2.86	9.42	2.24	0	29.28	3.38	(11.78)
52	355	0.5	75.5	314	37	8.00	2.08	26.00	3.26	10.82	2.38	(3)	30.68	3.42	(4.68)
52	355	0.5	73.5	138	22	6.50	1.87	23.00	3.14	6.84	1.92	0	26.70	3.28	(3.70)
52	355	0.5	109.2	220	34	12.00	2.48	15.00	2.71	10.02	2.30	2	29.88	3.40	(14.88)
52	355	0.5	67.8	119	19	8.50	2.14	94.50	4.55	6.19	1.82	2	26.04	3.26	68.46
52	355	1.1	26.1	87	11	15.00	2.71	30.50	3.42	5.01	1.61	10	24.87	3.21	5.63
52	355	1.5	51.5	62	12	6.50	1.87	20.00	3.00	6.19	1.82	0	26.05	3.26	(6.05)
53	355	0.5	33.6	81	11	10.00	2.30	20.00	3.00	4.02	1.39	6	23.88	3.17	(3.88)
53	355	0.5	33.1	257	26	6.50	1.87	10.50	2.35	7.94	2.07	(1)	27.80	3.32	(17.30)
53	355	0.5	136.6	153	32	17.00	2.83	32.00	3.47	9.59	2.26	7	29.45	3.38	2.55
53	355	0.5	29.7	208	21	8.50	2.14	18.00	2.89	6.72	1.90	2	26.58	3.28	(8.58)
54	355	0.5	147.0	254	42	5.00	1.61	12.50	2.53	12.23	2.50	(7)	32.09	3.47	(19.59)
54	355	0.5	22.6	128	14	9.00	2.20	6.50	1.87	4.67	1.54	4	24.53	3.20	(18.03)
54	355	0.5	237.9	248	54	11.50	2.44	18.00	2.89	15.57	2.75	(4)	35.43	3.57	(17.43)
54	355	0.5	23.6	127	14	9.00	2.20	22.00	3.09	4.67	1.54	4	24.53	3.20	(2.53)
54	355	0.5	74.0	269	33	9.50	2.25	16.50	2.80	9.76	2.28	0	29.62	3.39	(13.12)
54	355	0.5	62.3	218	27	6.00	1.79	16.50	2.80	8.17	2.10	(2)	28.03	3.33	(11.53)
54	355	2.3	84.1	88	19	4.00	1.39	7.00	1.95	9.52	2.25	(6)	29.38	3.38	(22.38)
55	355	0.5	70.9	184	25	13.00	2.56	12.50	2.53	7.76	2.05	5	27.61	3.32	(15.11)
55	355	0.5	53.6	151	20	8.50	2.14	28.50	3.35	6.36	1.85	2	26.22	3.27	2.28
55	355	0.5	59.9	100	17	9.00	2.20	80.50	4.39	5.47	1.70	4	25.32	3.23	55.18
55	355	3.5	56.1	127	18	7.00	1.95	16.00	2.77	11.58	2.45	(5)	31.44	3.45	(15.44)
55	355	4.0	23.7	79	10	8.00	2.08	16.00	2.77	10.22	2.32	(2)	30.08	3.40	(14.08)
55	355	0.5	124.5	198	31	3.00	1.10	26.00	3.26	10.12	2.31	(7)	29.98	3.40	(3.98)
56	355	0.5	38.2	57	10	5.00	1.61	18.50	2.92	3.68	1.30	1	23.54	3.16	(5.04)
56	355	0.5	174.1	197	41	9.00	2.20	15.50	2.74	12.00	2.48	(3)	31.86	3.46	(16.36)
56	355	0.5	79.6	212	29	7.50	2.01	19.00	2.94	8.71	2.16	(1)	28.57	3.35	(9.57)
56	355	0.5	50.0	59	12	5.50	1.70	14.50	2.67	4.18	1.43	1	24.04	3.18	(9.54)
56	355	0.5	101.3	272	37	70.50	4.26	78.50	4.36	10.87	2.39	60	30.73	3.43	47.77
56	355	0.5	45.5	202	23	10.00	2.30	18.00	2.89	7.19	1.97	3	27.05	3.30	(9.05)
56	355	0.5	32.9	106	13	4.50	1.50	20.00	3.00	4.56	1.52	0	24.42	3.20	(4.42)
56	355	0.5	101.0	179	29	10.50	2.35	17.00	2.83	8.80	2.17	2	28.66	3.36	(11.66)
56	355	0.5	73.5	61	16	7.00	1.95	14.50	2.67	5.19	1.65	2	25.05	3.22	(10.55)
56	355	0.5	99.1	253	35	6.00	1.79	16.50	2.80	10.37	2.34	(4)	30.23	3.41	(13.73)
57	355	0.5	62.7	102	17	7.50	2.01	15.00	2.71	5.61	1.73	2	25.47	3.24	(10.47)
57	355	0.5	178.5	256	46	7.50	2.01	24.00	3.18	13.47	2.60	(6)	33.33	3.51	(9.33)
57	355	0.5	19.7	110	12	10.00	2.30	72.50	4.28	4.14	1.42	6	24.00	3.18	48.50
57	355	0.5	68.8	174	24	13.00	2.56	15.50	2.74	7.45	2.01	6	27.31	3.31	(11.81)
57	355	0.5	124.8	261	39	11.50	2.44	18.00	2.89	11.53	2.44	0	31.39	3.45	(13.39)
57	355	0.5	0.0	120	10	7.00	1.95	10.50	2.35	3.62	1.29	3	23.48	3.16	(12.98)
57	355	0.5	49.8	217	25	7.00	1.95	21.50	3.07	7.67	2.04	(1)	27.53	3.32	(6.03)
57	355	0.5	70.7	121	20	8.00	2.08	34.50	3.54	6.34	1.85	2	26.20	3.27	8.30
58	355	0.5	119.3	136	28	8.50	2.14	46.00	3.83	8.55	2.15	0	28.41	3.35	17.59
58	355	0.5	156.3	215	40	12.00	2.48	18.50	2.92	11.71	2.46	0	31.57	3.45	(13.07)
58	355	0.5	70.5	161	23	8.50	2.14	21.50	3.07	7.23	1.98	1	27.09	3.30	(5.59)
58	355	0.5	45.9	143	18	10.50	2.35	8.00	2.08	5.89	1.77	5	25.75	3.25	(17.75)
58	355	1.5	38.4	56	10	8.00	2.08	22.00	3.09	5.56	1.72	2	25.42	3.24	(3.42)
58	355	0.5	107.4	162	29	10.00	2.30	24.50	3.20	8.67	2.16	1	28.53	3.35	(4.03)
58	355	0.5	224.4	374	63	9.00	2.20	14.00	2.64	17.85	2.88	(9)	37.71	3.63	(23.71)
58	355	0.5	59.6	125	19	12.00	2.48	31.00	3.43	6.02	1.79	6	25.88	3.25	5.12
58	355	0.5	103.4	118	24	13.50	2.60	12.50	2.53	7.54	2.02	6	27.40	3.31	(14.90)
58	355	0.5	110.1	180	30	9.50	2.25	24.50	3.20	9.18	2.22	0	29.04	3.37	(4.54)
58	355	0.5	42.2	117	16	8.50	2.14	71.50	4.27	5.17	1.64	3	25.03	3.22	46.47
58	355	0.5	36.4	68	11	18.50	2.92	22.00	3.09	3.84	1.35	15	23.70	3.17	(1.70)
59	355	2.9	49.2	72	13	33.00	3.50	48.50	3.88	8.97	2.19	24	28.83	3.36	19.67
59	355	0.5	118.6	305	42	7.50	2.01	19.00	2.94	12.26	2.51	(5)	32.12	3.47	(13.12)
59	355	0.5	31.8	118	15	9.00	2.20	8.50	2.14	4.91	1.59	4	24.77	3.21	(16.27)
59	355	0.5	55.5	186	23					7.21			27.07		
59	355	0.5	85.6	83	19	5.00	1.61	11.00	2.40	6.07	1.80	(1)	25.92	3.26	(14.92)
59	355	0.5	90.3	221	31	4.50	1.50	13.50	2.60	9.32	2.23	(5)	29.18	3.37	(15.68)
59	355	0.5	91.5	212	31	10.00	2.30	68.50	4.23	9.27	2.23	1	29.13	3.37	39.37
59	355	0.5	62.2	163	22	5.50	1.70	8.50	2.14	6.96	1.94	(1)	26.81	3.29	(18.31)

TABLE 2

ACTUAL AND PREDICTED URINARY ARSENIC LEVELS

AGE IN MONTHS	ESTIMATED URINE PRODUCTION	ARSENIC IN WATER (ug/L)	ARSENIC IN DUST (mg/kg)	ARSENIC IN SOIL (mg/kg)	55% DUST 45% SOIL (mg/kg) ABSORBED	MEAN SPEC URINARY AS NORMALIZED (ug/L)	NATURAL LOG MEAN SPEC URINARY AS NORMALIZED	MEAN TOTAL URINARY AS NORMALIZED (ug/L)	NATURAL LOG MEAN TOTAL URINARY AS NORMALIZED	EPA PREDICTED SPECIATED AS CTE (ug/L)	NATURAL LOG EPA PREDICTED SPECIATED AS CTE (ug/L)	DIFFERENCE BETWEEN SPECIATED MEASURED AND PREDICTED	EPA PREDICTED TOTAL AS CTE (ug/L)	NATURAL LOG EPA PREDICTED TOTAL AS CTE (ug/L)	DIFFERENCE BETWEEN TOTAL MEASURED AND PREDICTED
60	355	0.5	104.6	249	35	9.00	2.20	14.00	2.64	10.50	2.35	(2)	30.36	3.41	(16.36)
60	355	0.5	52.0	186	23	8.00	2.08	16.00	2.77	7.08	1.96	1	26.94	3.29	(10.94)
60	355	2.0	30.5	69	10	5.00	1.61	12.50	3.48	6.49	1.87	(1)	26.35	3.27	6.15
60	355	0.5	81.2	232	31	16.00	2.77	100.50	4.61	9.21	2.22	7	29.07	3.37	71.43
60	432	0.5	60.1	151	21	7.50	2.01	21.50	3.16	5.50	1.70	2	21.82	3.08	1.68
60	432	0.5	34.0	69	10	3.50	1.25	108.50	4.69	3.11	1.13	0	19.42	2.97	89.08
61	432	0.5	97.6	112	23	6.50	1.87	5.50	1.70	5.89	1.77	1	22.21	3.10	(16.71)
61	432	0.5	97.6	112	23	8.50	2.14	6.00	1.79	5.89	1.77	3	22.21	3.10	(16.21)
61	432	2.3	60.8	72	15	8.50	2.14	9.00	2.20	6.80	1.92	2	23.12	3.14	(14.12)
61	432	0.5	56.4	250	29	9.50	2.25	19.50	2.97	7.12	1.96	2	23.44	3.15	(3.94)
61	432	0.5	105.6	162	28	10.00	2.30	14.00	2.64	7.06	1.95	3	23.37	3.15	(9.37)
61	432	0.5	70.1	122	20	8.50	2.14	93.50	4.54	5.21	1.65	3	21.53	3.07	71.97
61	432	0.5	43.5	163	20	11.50	2.44	14.00	2.64	5.13	1.64	6	21.45	3.07	(7.45)
61	432	0.5	210.7	171	44	6.50	1.87	20.50	3.02	10.54	2.36	(4)	26.86	3.29	(6.36)
62	432	0.5	393.6	272	78	15.00	2.71	36.50	3.60	18.15	2.90	(3)	31.47	3.54	2.03
62	432	0.5	81.9	134	23	5.50	1.70	14.50	2.67	5.80	1.76	0	22.12	3.10	(7.62)
62	432	0.5	73.0	138	22	11.50	2.44	20.50	3.02	5.60	1.72	6	21.92	3.09	(1.42)
62	432	0.5	170.3	321	51	10.00	2.30	21.00	3.04	12.01	2.49	(2)	28.33	3.34	(7.33)
62	432	0.5	67.0	341	38	13.00	2.56	24.50	3.20	9.11	2.21	4	25.43	3.24	(0.93)
62	432	0.5	50.9	176	22	12.50	2.53	31.50	3.45	5.59	1.72	7	21.91	3.09	9.59
62	432	0.5	59.9	141	20	5.00	1.61	9.00	2.20	5.25	1.66	0	21.56	3.07	(12.56)
62	432	0.5	38.2	229	24	8.50	2.14	26.00	3.26	6.17	1.82	2	22.49	3.11	3.51
62	432	0.5	60.0	98	17	7.50	2.01	15.50	2.74	4.47	1.50	3	20.78	3.03	(5.28)
62	432	0.5	92.2	237	33	9.50	2.25	19.50	2.97	8.01	2.08	1	24.33	3.19	(4.83)
62	432	0.5	49.5	187	22	9.00	2.20	9.00	2.20	5.75	1.75	3	22.07	3.09	(13.07)
63	432	0.5	190.2	239	47	7.00	1.95	13.50	2.60	11.13	2.41	(4)	27.45	3.31	(13.95)
63	432	0.5	63.7	199	25	6.00	1.79	14.50	2.67	6.43	1.86	0	22.74	3.12	(8.24)
63	432	0.5	33.6	81	11	5.50	1.70	15.50	2.74	3.31	1.20	2	19.63	2.98	(4.13)
63	432	0.5	132.0	305	44	14.50	2.67	33.50	3.51	10.52	2.35	4	26.84	3.29	6.66
64	432	0.5	42.7	165	20	9.00	2.20	14.00	2.64	5.13	1.64	4	21.45	3.07	(7.45)
64	432	0.5	25.1	162	17	16.00	2.77	14.50	2.67	4.52	1.51	11	20.84	3.04	(6.34)
64	432	3.3	83.4	86	19	7.00	1.95	26.50	3.28	9.33	2.23	(2)	25.65	3.24	0.85
64	432	0.5	64.4	100	17	5.00	1.61	14.50	2.67	4.63	1.53	0	20.95	3.04	(6.45)
64	432	0.5	100.6	226	33	5.00	1.61	16.50	2.80	8.08	2.09	(3)	24.40	3.19	(7.90)
64	432	0.5	114.5	131	27	6.00	1.79	12.50	2.53	6.84	1.92	(1)	23.16	3.14	(10.66)
64	432	0.5	114.5	131	27	7.00	1.95	14.00	2.64	6.84	1.92	0	23.16	3.14	(9.16)
65	432	0.5	95.6	189	29	8.50	2.14	11.50	2.44	7.25	1.98	1	23.57	3.16	(12.07)
65	432	0.5	48.0	124	17	6.00	1.79	16.00	2.77	4.55	1.52	1	20.87	3.04	(4.87)
65	432	0.5	62.7	203	26	12.00	2.48	29.00	3.37	6.46	1.87	6	22.78	3.13	6.22
65	432	0.5	62.7	203	26	11.50	2.44	30.00	3.40	6.46	1.87	5	22.78	3.13	7.22
65	432	0.5	41.1	96	14	8.50	2.14	15.50	2.74	3.82	1.34	5	20.14	3.00	(4.64)
65	432	0.5	136.6	153	32	14.50	2.67	25.00	3.22	7.88	2.06	7	24.20	3.19	0.80
65	432	0.5	73.7	191	26	6.00	1.79	72.50	4.28	6.59	1.89	(1)	22.91	3.13	49.59
65	432	0.5	25.2	91	11	2.50	0.92	9.50	2.25	3.23	1.17	(1)	19.55	2.97	(10.05)
65	432	0.5	49.4	73	13	8.00	2.08	170.50	5.14	3.66	1.30	4	19.98	2.99	150.52
65	432	0.5	103.6	147	27	7.00	1.95	18.00	2.89	6.73	1.91	0	23.05	3.14	(5.05)
65	432	0.5	63.2	146	21	6.00	1.79	14.50	2.67	5.44	1.69	1	21.76	3.08	(7.26)
66	432	0.5	67.3	203	26	10.00	2.30	13.00	2.56	6.60	1.89	3	22.92	3.13	(9.92)
66	432	0.5	72.5	174	25	5.00	1.61	10.00	2.30	6.24	1.83	(1)	22.56	3.12	(12.56)
66	432	0.5	114.4	149	28	8.00	2.08	10.00	2.30	7.10	1.96	1	23.42	3.15	(13.42)
66	432	0.5	164.5	268	45	13.50	2.60	16.50	2.80	10.86	2.38	3	27.18	3.30	(10.68)
66	432	0.5	69.8	183	25	5.00	1.61	13.00	2.56	6.31	1.84	(1)	22.63	3.12	(9.63)
66	432	2.7	74.4	164	24	6.00	1.79	9.00	2.20	9.54	2.26	(4)	25.86	3.25	(16.86)
66	432	0.5	102.1	259	36	9.50	2.25	30.50	3.42	8.72	2.17	1	25.04	3.22	5.46
66	432	0.5	52.2	109	16	7.50	2.01	12.00	2.48	4.41	1.48	3	20.73	3.03	(8.73)
67	432	0.5	59.0	214	26	9.50	2.25	14.00	2.64	6.54	1.88	3	22.86	3.13	(8.86)
67	432	0.5	51.6	169	21	7.00	1.95	13.00	2.56	5.49	1.70	2	21.80	3.08	(8.80)
67	432	1.6	106.0	132	26	6.50	1.87	22.00	3.09	8.24	2.11	(2)	24.56	3.20	(2.56)
67	432	0.5	124.5	198	34	3.00	1.10	15.00	2.71	8.31	2.12	(5)	24.63	3.20	(9.63)
67	432	0.5	129.0	163	32	8.50	2.14	14.50	2.67	7.82	2.06	1	24.14	3.18	(9.64)
67	432	9.9	29.5	71	10	4.00	1.39	8.50	2.14	37.40	3.62	(33)	33.93	3.52	(25.43)
67	432	0.5	119.7	193	33	22.00	3.09	26.50	3.28	8.08	2.09	14	24.40	3.19	2.10
67	432	0.5	56.9	77	14	6.50	1.87	9.50	2.25	3.97	1.38	3	20.29	3.01	(10.79)

TABLE 2

ACTUAL AND PREDICTED URINARY ARSENIC LEVELS

AGE IN MONTHS	ESTIMATED URINE PRODUCTION	ARSENIC IN WATER (ug/L)	ARSENIC IN DUST (ug/kg)	ARSENIC IN SOIL (ug/kg)	55% DUST 45% SOIL (ug/kg) ABSORBED	MEAN SPEC URINARY AS NORMALIZED (ug/L)	NATURAL LOG MEAN SPEC URINARY AS NORMALIZED	MEAN TOTAL URINARY AS NORMALIZED (ug/L)	NATURAL LOG MEAN TOTAL URINARY AS NORMALIZED	EPA PREDICTED SPECIATED AS CIE (ug/L)	NATURAL LOG EPA PREDICTED SPECIATED AS CIE (ug/L)	DIFFERENCE BETWEEN SPECIATED MEASURED AND PREDICTED	EPA PREDICTED TOTAL AS CIE (ug/L)	NATURAL LOG EPA PREDICTED TOTAL AS CIE (ug/L)	DIFFERENCE BETWEEN TOTAL MEASURED AND PREDICTED
67	432	0.5	18.1	122	17	5.00	1.61	13.50	2.60	4.53	1.51	0	20.85	3.04	(7.35)
68	432	0.5	62.7	192	37	7.50	2.01	15.50	2.74	4.61	1.53	3	20.93	3.04	(5.43)
68	432	0.5	29.0	212	22	9.00	2.20	19.00	2.94	5.56	1.72	3	21.88	3.09	(2.88)
68	432	1.1	85.5	150	24					7.13			23.45		
68	432	0.5	159.6	213	40	6.50	1.87	14.50	2.67	9.69	2.27	(3)	26.01	3.26	(11.51)
68	432	0.5	126.2	137	29	3.50	1.25	9.50	2.25	7.25	1.98	(4)	23.57	3.16	(14.07)
68	432	0.5	86.3	161	26	4.50	1.50	10.50	2.35	6.49	1.87	(2)	22.81	3.13	(12.31)
68	432	0.5	150.7	240	41	17.50	2.86	36.00	3.58	9.90	2.29	8	26.22	3.27	9.78
68	432	0.5	99.3	166	28	6.50	1.87	14.00	2.64	6.95	1.94	0	23.27	3.15	(9.27)
69	432	0.5	142.3	202	37	4.00	1.39	8.50	2.14	8.95	2.19	(5)	25.27	3.23	(16.77)
69	432	1.4	23.4	38	6	4.00	1.39	17.50	2.86	3.61	1.28	0	19.93	2.99	(2.43)
69	432	0.5	47.4	87	14	6.50	1.87	6.00	1.79	3.85	1.35	3	20.17	3.00	(14.17)
69	432	0.5	46.1	94	14	6.00	1.79	21.00	3.04	3.95	1.37	2	20.27	3.01	0.73
69	432	2.9	47.6	108	16	7.50	2.01	14.00	2.64	7.97	2.08	0	24.29	3.19	(10.29)
70	432	1.1	101.7	70	21	8.00	2.08	13.00	2.56	6.29	1.84	2	22.61	3.12	(9.61)
70	432	0.5	48.7	115	16	4.50	1.50	14.50	2.67	4.42	1.49	0	20.74	3.03	(6.24)
70	432	0.5	206.3	140	41	6.00	1.79	9.50	2.25	9.83	2.29	(4)	26.15	3.26	(16.65)
70	432	0.5	39.1	152	18	9.50	2.25	9.00	2.20	4.79	1.57	5	21.11	3.05	(12.11)
70	432	0.5	77.3	127	21	7.00	1.95	11.50	2.44	5.54	1.71	1	21.86	3.08	(10.36)
70	432	0.5	180.5	227	44	12.50	2.53	23.00	3.14	10.61	2.36	2	26.93	3.29	(3.93)
70	432	0.5	63.6	131	20	11.50	2.44	18.50	2.92	5.23	1.65	6	21.55	3.07	(3.05)
70	432	0.5	60.5	156	21	9.50	2.25	22.00	3.09	5.53	1.71	-1	21.85	3.08	0.15
71	432	0.5	85.3	360	41	6.50	1.87	15.50	2.74	9.98	2.30	(3)	26.30	3.27	(10.80)
71	432	1.8	58.0	87	15	2.50	0.92	6.50	1.87	6.21	1.83	(4)	22.53	3.11	(16.03)
71	432	0.5	108.7	202	32	8.00	2.08	24.00	3.18	7.89	2.07	0	24.21	3.19	(0.21)
71	432	0.5	76.1	127	21	5.50	1.70	15.00	2.71	5.50	1.70	0	21.82	3.08	(6.82)
71	432	0.5	95.6	217	31	7.50	2.01	12.50	2.53	7.75	2.05	0	24.07	3.18	(11.57)
71	432	2.6	140.1	90	27	5.50	1.70	10.00	2.30	10.10	2.31	(5)	26.42	3.27	(16.42)
71	432	0.5	97.1	290	38	7.00	1.95	12.00	2.48	9.13	2.21	(2)	25.45	3.24	(13.45)
71	432	0.5	98.7	213	32	4.50	1.50	12.50	2.53	7.78	2.05	(3)	24.09	3.18	(11.59)
71	432	0.5	65.8	161	23					5.78			22.10		
71	432	0.5	95.2	270	36	7.00	1.95	16.00	2.77	8.70	2.16	(2)	25.02	3.22	(9.02)
72	432	0.5	83.7	242	32	8.50	2.14	11.50	2.44	7.84	2.06	1	24.16	3.18	(12.66)
72	432	0.5	101.3	272	37	22.00	3.09	39.00	3.66	8.93	2.19	13	25.25	3.23	13.75
72	432	0.5	132.5	128	29	5.50	1.70	8.00	2.08	7.28	1.99	(2)	23.60	3.16	(15.60)
72	432	0.5	110.1	180	30	5.50	1.70	12.00	2.48	7.54	2.02	(2)	23.86	3.17	(11.86)
72	432	2.6	42.0	60	11	4.00	1.39	9.00	2.20	6.46	1.87	(2)	22.78	3.13	(13.78)
72	432	0.5	126.5	301	43	13.00	2.56	29.00	3.37	10.26	2.33	3	26.58	3.28	2.42
72	432	0.5	182.3	238	45	9.00	2.20	12.50	2.53	10.87	2.39	(2)	27.19	3.30	(14.69)
73	432	0.5	284.4	300	65	7.00	1.95	7.50	2.01	15.21	2.72	(8)	31.53	3.45	(24.03)
73	432	0.5	107.6	120	25	4.00	1.39	10.00	2.30	6.37	1.85	(2)	22.69	3.12	(12.69)
73	432	0.5	60.6	89	16	5.50	1.70	12.50	2.53	4.31	1.46	1	20.63	3.03	(8.13)
73	432	1.4	71.7	134	21	4.50	1.50	8.00	2.08	6.87	1.93	(2)	23.19	3.14	(15.19)
73	432	0.5	46.2	88	14	4.50	1.50	9.50	2.25	3.84	1.34	1	20.16	3.00	(10.66)
73	432	0.5	129.8	240	38	11.50	2.44	36.00	3.58	9.25	2.22	2	25.57	3.24	10.43
74	432	0.5	38.2	57	10	6.00	1.79	22.00	3.09	3.03	1.11	3	19.35	2.96	2.65
74	432	0.5	35.5	213	23	6.50	1.87	12.50	2.53	5.79	1.76	1	22.11	3.10	(9.61)
74	432	0.5	55.2	120	18	11.00	2.40	16.50	2.80	4.71	1.55	6	21.03	3.05	(4.53)
74	432	0.5	138.7	309	45	5.00	1.61	14.00	2.64	10.80	2.38	(6)	27.12	3.30	(13.12)
74	432	0.5	205.4	139	41	8.00	2.08	28.50	3.35	9.79	2.28	(2)	26.11	3.26	2.39
74	432	0.5	153.8	280	45	5.50	1.70	10.00	2.30	10.74	2.37	(5)	27.06	3.30	(17.06)
75	432	0.5	43.2	84	13	11.00	2.40	15.50	2.74	3.68	1.30	7	20.00	3.00	(4.50)
75	432	0.5	333.4	409	81	8.00	2.08	13.50	2.60	18.76	2.93	(11)	35.08	3.56	(21.58)
75	432	0.5	32.6	197	21	5.50	1.70	14.50	2.67	5.40	1.69	0	21.72	3.08	(7.22)
76	432	0.5	122.1	131	28	6.00	1.79	50.00	3.91	7.01	1.95	(1)	23.33	3.15	26.67
76	432	0.5	75.1	157	24	6.50	1.87	12.50	2.53	6.01	1.79	0	22.33	3.11	(9.83)
76	432	0.5	74.2	44	14	2.50	0.92	14.00	2.64	3.92	1.37	(1)	20.24	3.01	(6.24)
76	432	0.5	51.6	127	18	3.00	1.10	7.00	1.95	4.72	1.55	(2)	21.04	3.05	(14.04)

TABLE 3

Urinary Arsenic Levels	Arithmetic Mean and Standard Deviation	Geometric Mean and Standard Deviation
Measured Speciated Urinary Arsenic	10.9 ± 7.1	9.4 ± 1.7
Predicted Speciated Urinary Arsenic	9.0 ± 4.4	8.1 ± 1.5
Measured Total Urinary Arsenic	26.1 ± 25.9	20.8 ± 1.8
Predicted Total Urinary Arsenic	29.2 ± 7.6	28.4 ± 1.3

TABLE 4

REASONABLE MAXIMUM EXPOSURE CALCULATIONS FOR RISKS IN COMMUNITY SOILS OU

		Dust Mean	Soil Mean	Risk	Bioavailability assumption
Area A	count	59	59		
	mean	56.11	99.91		
	standard deviation	30.95	41.10		
	95% u c l of mean	62.85	108.86	4.89E-05	assumes 25.8% bioavailability for dust; 18.3% bioavailability for soil
Area B	count	70	70		
	mean	65.97	145.79		
	standard deviation	40.82	53.81		
	95% u c l of mean	74.12	156.53	6.40E-05	assumes 25.8% bioavailability for dust; 18.3% bioavailability for soil
Area C	count	36	37		
	mean	59.56	194.03		
	standard deviation	66.47	51.31		
	95% u c l of mean	78.29	208.28	7.72E-05	assumes 25.8% bioavailability for dust; 18.3% bioavailability for soil
Area D	count	23	23		
	mean	114.20	256.34		
	standard deviation	43.79	84.04		
	95% u c l of mean	129.88	286.43	1.15E-04	assumes 25.8% bioavailability for dust; 18.3% bioavailability for soil
Area E	count	68	68		
	mean	87.55	219.80		
	standard deviation	37.69	51.97		
	95% u c l of mean	95.18	230.32	8.87E-05	assumes 25.8% bioavailability for dust; 18.3% bioavailability for soil
Area F	count	135	135		
	mean	118.99	255.75		
	standard deviation	63.15	76.97		
	95% u c l of mean	127.93	266.64	1.10E-04	assumes 25.8% bioavailability for dust; 18.3% bioavailability for soil
Area G	count	28	28		
	mean	79.44	150.32		
	standard deviation	40.41	61.62		
	95% u c l of mean	92.44	170.16	7.41E-05	assumes 25.8% bioavailability for dust; 18.3% bioavailability for soil
Area H	count	17	17		
	mean	70.19	103.46		
	standard deviation	33.41	47.94		
	95% u c l of mean	84.33	123.77	6.06E-05	assumes 25.8% bioavailability for dust; 18.3% bioavailability for soil
Area I	count	12	12		
	mean	79.90	162.85		
	standard deviation	34.54	50.38		
	95% u c l of mean	97.81	188.97	8.05E-05	assumes 25.8% bioavailability for dust; 18.3% bioavailability for soil
Area J	count	21	21		
	mean	54.95	155.30		
	standard deviation	27.52	38.31		
	95% u c l of mean	65.31	169.72	6.35E-05	assumes 25.8% bioavailability for dust; 18.3% bioavailability for soil
Area K	count	10	8		
	mean	99.46	196.96		
	standard deviation	40.72	85.66		
	95% u c l of mean	123.06	254.36	1.05E-04	assumes 25.8% bioavailability for dust; 18.3% bioavailability for soil
Total Pop	count	479	478		
	mean	86.10	191.23		
	standard deviation	54.14	83.64		
	95% u c l of mean	90.17	197.52	7.94E-05	assumes 25.8% bioavailability for dust; 18.3% bioavailability for soil

TABLE 5
CENTRAL TENDENCY EXPOSURE CALCULATIONS FOR RISKS IN COMMUNITY SOILS OU

		Dust Mean	Soil Mean	Risk	Bioavailability assumption
Area A	count	59	59		
	mean	56.11	99.91		
	standard deviation	30.95	41.10		
	95% u c l of mean	62.85	108.86	7.86E-06	assumes 25.8% bioavailable arsenic in dust; 18.3% bioavailable arsenic in soil
Area B	count	70	70		
	mean	65.97	145.79		
	standard deviation	40.82	53.81		
	95% u c l of mean	74.12	156.53	1.03E-05	assumes 25.8% bioavailable arsenic in dust; 18.3% bioavailable arsenic in soil
Area C	count	36	37		
	mean	59.56	194.03		
	standard deviation	66.47	51.31		
	95% u c l of mean	78.29	208.28	1.24E-05	assumes 25.8% bioavailable arsenic in dust; 18.3% bioavailable arsenic in soil
Area D	count	23	23		
	mean	114.20	256.34		
	standard deviation	43.79	84.04		
	95% u c l of mean	129.88	286.43	1.85E-05	assumes 25.8% bioavailable arsenic in dust; 18.3% bioavailable arsenic in soil
Area E	count	68	68		
	mean	87.55	219.80		
	standard deviation	37.69	51.97		
	95% u c l of mean	95.18	230.32	1.43E-05	assumes 25.8% bioavailable arsenic in dust; 18.3% bioavailable arsenic in soil
Area F	count	135	135		
	mean	118.99	255.75		
	standard deviation	63.15	76.97		
	95% u c l of mean	127.93	266.64	1.76E-05	assumes 25.8% bioavailable arsenic in dust; 18.3% bioavailable arsenic in soil
Area G	count	28	28		
	mean	79.44	150.32		
	standard deviation	40.41	61.62		
	95% u c l of mean	92.44	170.16	1.19E-05	assumes 25.8% bioavailable arsenic in dust; 18.3% bioavailable arsenic in soil
Area H	count	17	17		
	mean	70.19	103.46		
	standard deviation	33.41	47.94		
	95% u c l of mean	84.33	123.77	9.74E-06	assumes 25.8% bioavailable arsenic in dust; 18.3% bioavailable arsenic in soil
Area I	count	12	12		
	mean	79.90	162.85		
	standard deviation	34.54	50.38		
	95% u c l of mean	97.81	188.97	1.29E-05	assumes 25.8% bioavailable arsenic in dust; 18.3% bioavailable arsenic in soil
Area J	count	21	21		
	mean	54.95	155.30		
	standard deviation	27.52	38.31		
	95% u c l of mean	65.31	169.72	1.02E-05	assumes 25.8% bioavailable arsenic in dust; 18.3% bioavailable arsenic in soil
Area K	count	10	8		
	mean	99.46	196.96		
	standard deviation	40.72	85.66		
	95% u c l of mean	123.06	254.36	1.69E-05	assumes 25.8% bioavailable arsenic in dust; 18.3% bioavailable arsenic in soil
Total Pop	count	479	478		
	mean	86.10	191.23		
	standard deviation	54.14	83.64		
	95% u c l of mean	90.17	197.52	1.28E-05	assumes 25.8% bioavailable arsenic in dust; 18.3% bioavailable arsenic in soil

APPENDIX E

LEAD MODELING RUN

SUBAREA A

LEAD MODEL Version 0.99d

AIR CONCENTRATION: 0.100 ug Pb/m3 DEFAULT
Indoor AIR Pb Conc: 30.0 percent of outdoor.
Other AIR Parameters:

Age	Time Outdoors (hr)	Vent. Rate (m3/day)	Lung Abs. (%)
0-1	1.0	2.0	32.0
1-2	2.0	3.0	32.0
2-3	3.0	5.0	32.0
3-4	4.0	5.0	32.0
4-5	4.0	5.0	32.0
5-6	4.0	7.0	32.0
6-7	4.0	7.0	32.0

DIET: DEFAULT

DRINKING WATER Conc: 4.00 ug Pb/L DEFAULT
WATER Consumption: DEFAULT

SOIL & DUST:
Soil: constant conc.
Dust: constant conc.

Age	Soil (ug Pb/g)	House Dust (ug Pb/g)
0-1	75.9	69.0
1-2	75.9	69.0
2-3	75.9	69.0
3-4	75.9	69.0
4-5	75.9	69.0
5-6	75.9	69.0
6-7	75.9	69.0

Additional Dust Sources: None DEFAULT

PAINT Intake: 0.00 ug Pb/day DEFAULT

MATERNAL CONTRIBUTION: Infant Model
Maternal Blood Conc: 2.50 ug Pb/dL

CALCULATED BLOOD Pb and Pb UPTAKES:

YEAR	Blood Level (ug/dL)	Total Uptake (ug/day)	Soil+Dust Uptake (ug/day)
0.5-1:	2.6	4.76	1.74
1-2:	2.7	6.47	2.76
2-3:	2.6	6.91	2.78
3-4:	2.4	6.87	2.80
4-5:	2.1	6.13	2.09
5-6:	1.9	6.19	1.89
6-7:	1.8	6.43	1.79

YEAR	Diet Uptake (ug/day)	Water Uptake (ug/day)	Paint Uptake (ug/day)	Air Uptake (ug/day)
0.5-1:	2.62	0.33	0.00	0.02
1-2:	2.73	0.95	0.00	0.03
2-3:	3.03	0.99	0.00	0.06

SUBAREA A

3-4:	2.99	1.02	0.00	0.07
4-5:	2.91	1.06	0.00	0.07
5-6:	3.08	1.13	0.00	0.09
6-7:	3.40	1.15	0.00	0.09

SUBAREA B

LEAD MODEL Version 0.99d

AIR CONCENTRATION: 0.100 ug Pb/m3 DEFAULT
Indoor AIR Pb Conc: 30.0 percent of outdoor.
Other AIR Parameters:

Age	Time Outdoors (hr)	Vent. Rate (m3/day)	Lung Abs. (%)
0-1	1.0	2.0	32.0
1-2	2.0	3.0	32.0
2-3	3.0	5.0	32.0
3-4	4.0	5.0	32.0
4-5	4.0	5.0	32.0
5-6	4.0	7.0	32.0
6-7	4.0	7.0	32.0

DIET: DEFAULT

DRINKING WATER Conc: 4.00 ug Pb/L DEFAULT
WATER Consumption: DEFAULT

SOIL & DUST:
Soil: constant conc.
Dust: constant conc.

Age	Soil (ug Pb/g)	House Dust (ug Pb/g)
0-1	256.6	146.8
1-2	256.6	146.8
2-3	256.6	146.8
3-4	256.6	146.8
4-5	256.6	146.8
5-6	256.6	146.8
6-7	256.6	146.8

Additional Dust Sources: None DEFAULT

PAINT Intake: 0.00 ug Pb/day DEFAULT

MATERNAL CONTRIBUTION: Infant Model
Maternal Blood Conc: 2.50 ug Pb/dL

CALCULATED BLOOD Pb and Pb UPTAKES:

YEAR	Blood Level (ug/dL)	Total Uptake (ug/day)	Soil+Dust Uptake (ug/day)
0.5-1:	4.1	7.52	4.59
1-2:	4.5	10.80	7.23
2-3:	4.2	11.31	7.31
3-4:	4.0	11.35	7.40
4-5:	3.4	9.55	5.59
5-6:	2.9	9.30	5.07
6-7:	2.7	9.38	4.80

YEAR	Diet Uptake (ug/day)	Water Uptake (ug/day)	Paint Uptake (ug/day)	Air Uptake (ug/day)
0.5-1:	2.54	0.37	0.00	0.02
1-2:	2.63	0.91	0.00	0.03
2-3:	2.98	0.96	0.00	0.06

SUBAREA B

3-4:	2.90	0.99	0.00	0.07
4-5:	2.85	1.04	0.00	0.07
5-6:	3.03	1.11	0.00	0.09
6-7:	3.36	1.13	0.00	0.09

SUBAREA C

LEAD MODEL Version 0.99d

AIR CONCENTRATION: 0.100 ug Pb/m3 DEFAULT
Indoor AIR Pb Conc: 30.0 percent of outdoor.
Other AIR Parameters:

Age	Time Outdoors (hr)	Vent. Rate (m3/day)	Lung Abs. (%)
0-1	1.0	2.0	32.0
1-2	2.0	3.0	32.0
2-3	3.0	5.0	32.0
3-4	4.0	5.0	32.0
4-5	4.0	5.0	32.0
5-6	4.0	7.0	32.0
6-7	4.0	7.0	32.0

DIET: DEFAULT

DRINKING WATER Conc: 4.00 ug Pb/L DEFAULT
WATER Consumption: DEFAULT

SOIL & DUST:
Soil: constant conc.
Dust: constant conc.

Age	Soil (ug Pb/g)	House Dust (ug Pb/g)
0-1	476.5	241.3
1-2	476.5	241.3
2-3	476.5	241.3
3-4	476.5	241.3
4-5	476.5	241.3
5-6	476.5	241.3
6-7	476.5	241.3

Additional Dust Sources: None DEFAULT

PAINT Intake: 0.00 ug Pb/day DEFAULT

MATERNAL CONTRIBUTION: Infant Model
Maternal Blood Conc: 2.50 ug Pb/dL

CALCULATED BLOOD Pb and Pb UPTAKES:

YEAR	Blood Level (ug/dL)	Total Uptake (ug/day)	Soil+Dust Uptake (ug/day)
.5-1:	5.7	10.65	7.83
1-2:	6.4	15.65	12.23
2-3:	6.0	16.29	12.44
3-4:	5.7	16.48	12.65
4-5:	4.8	13.55	9.67
5-6:	4.1	12.96	8.80
6-7:	3.7	12.87	8.36

YEAR	Diet Uptake (ug/day)	Water Uptake (ug/day)	Paint Uptake (ug/day)	Air Uptake (ug/day)
.5-1:	2.45	0.35	0.00	0.02
1-2:	2.51	0.37	0.00	0.03
2-3:	2.37	0.32	0.00	0.06

3-4:	2.81	0.95	0.00	0.07
4-5:	2.79	1.02	0.00	0.07
5-6:	2.98	1.09	0.00	0.09
6-7:	3.31	1.11	0.00	0.09

SUBAREA D

LEAD MODEL Version 0.99d

AIR CONCENTRATION: 0.100 ug Pb/m3 DEFAULT
Indoor AIR Pb Conc: 30.0 percent of outdoor.
Other AIR Parameters:

Age	Time Outdoors (hr)	Vent. Rate (m3/day)	Lung Abs. (%)
0-1	1.0	2.0	32.0
1-2	2.0	3.0	32.0
2-3	3.0	5.0	32.0
3-4	4.0	5.0	32.0
4-5	4.0	5.0	32.0
5-6	4.0	7.0	32.0
6-7	4.0	7.0	32.0

DIET: DEFAULT

DRINKING WATER Conc: 4.00 ug Pb/L DEFAULT
WATER Consumption: DEFAULT

SOIL & DUST:
Soil: constant conc.
Dust: constant conc.

Age	Soil (ug Pb/g)	House Dust (ug Pb/g)
0-1	419.4	216.7
1-2	419.4	216.7
2-3	419.4	216.7
3-4	419.4	216.7
4-5	419.4	216.7
5-6	419.4	216.7
6-7	419.4	216.7

Additional Dust Sources: None DEFAULT

PAINT Intake: 0.00 ug Pb/day DEFAULT

MATERNAL CONTRIBUTION: Infant Model
Maternal Blood Conc: 2.50 ug Pb/dL

CALCULATED BLOOD Pb and Pb UPTAKES:

YEAR	Blood Level (ug/dL)	Total Uptake (ug/day)	Soil+Dust Uptake (ug/day)
0.5-1:	5.3	9.86	7.01
1-2:	6.0	14.43	10.97
2-3:	5.6	15.03	11.14
3-4:	5.3	15.18	11.32
4-5:	4.4	12.52	8.62
5-6:	3.8	12.02	7.84
6-7:	3.4	11.98	7.45

YEAR	Diet Uptake (ug/day)	Water Uptake (ug/day)	Paint Uptake (ug/day)	Air Uptake (ug/day)
.5-1:	2.47	0.36	0.00	0.02
1-2:	2.54	0.38	0.00	0.03
2-3:	2.90	0.93	0.00	0.06

SUBAREA D

3-4:	2.83	0.96	0.00	0.07
4-5:	2.81	1.03	0.00	0.07
5-6:	2.99	1.09	0.00	0.09
6-7:	3.32	1.12	0.00	0.09

SUBAREA E

LEAD MODEL Version 0.99d

AIR CONCENTRATION: 0.100 ug Pb/m3 DEFAULT
Indoor AIR Pb Conc: 30.0 percent of outdoor.
Other AIR Parameters:

Age	Time Outdoors (hr)	Vent. Rate (m3/day)	Lung Abs. (%)
0-1	1.0	2.0	32.0
1-2	2.0	3.0	32.0
2-3	3.0	5.0	32.0
3-4	4.0	5.0	32.0
4-5	4.0	5.0	32.0
5-6	4.0	7.0	32.0
6-7	4.0	7.0	32.0

DIET: DEFAULT

DRINKING WATER Conc: 4.00 ug Pb/L DEFAULT
WATER Consumption: DEFAULT

SOIL & DUST:
Soil: constant conc.
Dust: constant conc.

Age	Soil (ug Pb/g)	House Dust (ug Pb/g)
0-1	581.7	286.5
1-2	581.7	286.5
2-3	581.7	286.5
3-4	581.7	286.5
4-5	581.7	286.5
5-6	581.7	286.5
6-7	581.7	286.5

Additional Dust Sources: None DEFAULT

PAINT Intake: 0.00 ug Pb/day DEFAULT

MATERNAL CONTRIBUTION: Infant Model
Maternal Blood Conc: 2.50 ug Pb/dL

CALCULATED BLOOD Pb and Pb UPTAKES:

YEAR	Blood Level (ug/dL)	Total Uptake (ug/day)	Soil+Dust Uptake (ug/day)
0.5-1:	6.5	12.08	9.30
1-2:	7.3	17.84	14.49
2-3:	6.9	18.55	14.76
3-4:	6.5	18.82	15.05
4-5:	5.5	15.40	11.56
5-6:	4.6	14.67	10.54
6-7:	4.2	14.50	10.02

YEAR	Diet Uptake (ug/day)	Water Uptake (ug/day)	Paint Uptake (ug/day)	Air Uptake (ug/day)
0.5-1:	2.41	0.35	0.00	0.02
1-2:	2.47	0.35	0.00	0.03
2-3:	2.82	0.90	0.00	0.06

SUBAREA E

3-4:	2.76	0.94	0.00	0.07
4-5:	2.76	1.01	0.00	0.07
5-6:	2.95	1.08	0.00	0.09
6-7:	3.28	1.11	0.00	0.09

SUBAREA F1

3-4:	2.78	0.95	0.00	0.07
4-5:	2.77	1.02	0.00	0.07
5-6:	2.96	1.08	0.00	0.09
6-7:	3.29	1.11	0.00	0.09

SUBAREA F1

LEAD MODEL Version 0.99d

AIR CONCENTRATION: 0.100 ug Pb/m3 DEFAULT
Indoor AIR Pb Conc: 30.0 percent of outdoor.
Other AIR Parameters:

Age	Time Outdoors (hr)	Vent. Rate (m3/day)	Lung Abs. (%)
0-1	1.0	2.0	32.0
1-2	2.0	3.0	32.0
2-3	3.0	5.0	32.0
3-4	4.0	5.0	32.0
4-5	4.0	5.0	32.0
5-6	4.0	7.0	32.0
6-7	4.0	7.0	32.0

DIET: DEFAULT

DRINKING WATER Conc: 4.00 ug Pb/L DEFAULT
WATER Consumption: DEFAULT

SOIL & DUST:
Soil: constant conc.
Dust: constant conc.

Age	Soil (ug Pb/g)	House Dust (ug Pb/g)
0-1	534.0	266.1
1-2	534.0	266.1
2-3	534.0	266.1
3-4	534.0	266.1
4-5	534.0	266.1
5-6	534.0	266.1
6-7	534.0	266.1

Additional Dust Sources: None DEFAULT

PAINT Intake: 0.00 ug Pb/day DEFAULT

MATERNAL CONTRIBUTION: Infant Model
Maternal Blood Conc: 2.50 ug Pb/dL

CALCULATED BLOOD Pb and Pb UPTAKES:

YEAR	Blood Level (ug/dL)	Total Uptake (ug/day)	Soil+Dust Uptake (ug/day)
0.5-1:	6.1	11.44	8.64
1-2:	6.9	16.86	13.48
2-3:	6.5	17.54	13.72
3-4:	6.2	17.77	13.97
4-5:	5.2	14.56	10.71
5-6:	4.4	13.90	9.76
6-7:	3.9	13.77	9.27

YEAR	Diet Uptake (ug/day)	Water Uptake (ug/day)	Paint Uptake (ug/day)	Air Uptake (ug/day)
0.5-1:	2.42	0.35	0.00	0.02
1-2:	2.49	0.36	0.00	0.03
2-3:	2.34	0.31	0.00	0.06

SUBAREA F2

3-4:	2.79	0.95	0.00	0.07
4-5:	2.78	1.02	0.00	0.07
5-6:	2.97	1.09	0.00	0.09
6-7:	3.30	1.11	0.00	0.09

SUBAREA F2

LEAD MODEL Version 0.99d

AIR CONCENTRATION: 0.100 ug Pb/m3 DEFAULT
Indoor AIR Pb Conc: 30.0 percent of outdoor.
Other AIR Parameters:

Age	Time Outdoors (hr)	Vent. Rate (m3/day)	Lung Abs. (%)
0-1	1.0	2.0	32.0
1-2	2.0	3.0	32.0
2-3	3.0	5.0	32.0
3-4	4.0	5.0	32.0
4-5	4.0	5.0	32.0
5-6	4.0	7.0	32.0
6-7	4.0	7.0	32.0

DIET: DEFAULT

DRINKING WATER Conc: 4.00 ug Pb/L DEFAULT
WATER Consumption: DEFAULT

SOIL & DUST:
Soil: constant conc.
Dust: constant conc.

Age	Soil (ug Pb/g)	House Dust (ug Pb/g)
0-1	508.1	254.9
1-2	508.1	254.9
2-3	508.1	254.9
3-4	508.1	254.9
4-5	508.1	254.9
5-6	508.1	254.9
6-7	508.1	254.9

Additional Dust Sources: None DEFAULT

PAINT Intake: 0.00 ug Pb/day DEFAULT

MATERNAL CONTRIBUTION: Infant Model
Maternal Blood Conc: 2.50 ug Pb/dL

CALCULATED BLOOD Pb and Pb UPTAKES:

YEAR	Blood Level (ug/dL)	Total Uptake (ug/day)	Soil+Dust Uptake (ug/day)
0.5-1:	5.9	11.09	8.28
1-2:	6.7	16.32	12.92
2-3:	6.3	16.98	13.15
3-4:	6.0	17.19	13.38
4-5:	5.0	14.11	10.24
5-6:	4.3	13.48	9.33
6-7:	3.8	13.37	8.86

YEAR	Diet Uptake (ug/day)	Water Uptake (ug/day)	Paint Uptake (ug/day)	Air Uptake (ug/day)
0.5-1:	2.43	0.35	0.00	0.02
1-2:	2.50	0.86	0.00	0.03
2-3:	2.86	0.92	0.00	0.06

SUBAREA I

LEAD MODEL Version 0.99d

AIR CONCENTRATION: 0.100 ug Pb/m3 DEFAULT
Indoor AIR Pb Conc: 30.0 percent of outdoor.
Other AIR Parameters:

Age	Time Outdoors (hr)	Vent. Rate (m3/day)	Lung Abs. (%)
0-1	1.0	2.0	32.0
1-2	2.0	3.0	32.0
2-3	3.0	5.0	32.0
3-4	4.0	5.0	32.0
4-5	4.0	5.0	32.0
5-6	4.0	7.0	32.0
6-7	4.0	7.0	32.0

DIET: DEFAULT

DRINKING WATER Conc: 4.00 ug Pb/L DEFAULT
WATER Consumption: DEFAULT

SOIL & DUST:
Soil: constant conc.
Dust: constant conc.

Age	Soil (ug Pb/g)	House Dust (ug Pb/g)
0-1	75.0	68.7
1-2	75.0	68.7
2-3	75.0	68.7
3-4	75.0	68.7
4-5	75.0	68.7
5-6	75.0	68.7
6-7	75.0	68.7

Additional Dust Sources: None DEFAULT

PAINT Intake: 0.00 ug Pb/day DEFAULT

MATERNAL CONTRIBUTION: Infant Model
Maternal Blood Conc: 2.50 ug Pb/dL

CALCULATED BLOOD Pb and Pb UPTAKES:

YEAR	Blood Level (ug/dL)	Total Uptake (ug/day)	Soil+Dust Uptake (ug/day)
0.5-1:	2.6	4.75	1.73
1-2:	2.7	6.45	2.74
2-3:	2.6	6.89	2.75
3-4:	2.4	6.85	2.78
4-5:	2.1	6.12	2.08
5-6:	1.9	6.17	1.88
6-7:	1.8	6.42	1.77

YEAR	Diet Uptake (ug/day)	Water Uptake (ug/day)	Paint Uptake (ug/day)	Air Uptake (ug/day)
0.5-1:	2.62	0.38	0.00	0.02
1-2:	2.73	0.95	0.00	0.03
2-3:	3.08	0.99	0.00	0.06

SUBAREA 1

3-4:	2.99	1.02	0.00	0.07
4-5:	2.91	1.06	0.00	0.07
5-6:	3.08	1.13	0.00	0.09
6-7:	3.40	1.15	0.00	0.09

SUBAREA J

LEAD MODEL Version 0.99d

AIR CONCENTRATION: 0.100 ug Pb/m3 DEFAULT
Indoor AIR Pb Conc: 30.0 percent of outdoor.
Other AIR Parameters:

Age	Time Outdoors (hr)	Vent. Rate (m3/day)	Lung Abs. (%)
0-1	1.0	2.0	32.0
1-2	2.0	3.0	32.0
2-3	3.0	5.0	32.0
3-4	4.0	5.0	32.0
4-5	4.0	5.0	32.0
5-6	4.0	7.0	32.0
6-7	4.0	7.0	32.0

DIET: DEFAULT

DRINKING WATER Conc: 4.00 ug Pb/L DEFAULT
WATER Consumption: DEFAULT

SOIL & DUST:
Soil: constant conc.
Dust: constant conc.

Age	Soil (ug Pb/g)	House Dust (ug Pb/g)
0-1	191.2	118.6
1-2	191.2	118.6
2-3	191.2	118.6
3-4	191.2	118.6
4-5	191.2	118.6
5-6	191.2	118.6
6-7	191.2	118.6

Additional Dust Sources: None DEFAULT

PAINT Intake: 0.00 ug Pb/day DEFAULT

MATERNAL CONTRIBUTION: Infant Model
Maternal Blood Conc: 2.50 ug Pb/dL

CALCULATED BLOOD Pb and Pb UPTAKES:

YEAR	Blood Level (ug/dL)	Total Uptake (ug/day)	Soil+Dust Uptake (ug/day)
0.5-1:	3.6	6.54	3.58
1-2:	3.9	9.27	5.65
2-3:	3.6	9.75	5.70
3-4:	3.4	9.76	5.76
4-5:	2.9	8.33	4.34
5-6:	2.6	8.18	3.93
6-7:	2.4	8.32	3.72

YEAR	Diet Uptake (ug/day)	Water Uptake (ug/day)	Paint Uptake (ug/day)	Air Uptake (ug/day)
0.5-1:	2.57	0.37	0.00	0.02
1-2:	2.66	0.92	0.00	0.03
2-3:	3.02	0.97	0.00	0.06

SUBAREA J

3-4:	2.93	1.00	0.00	0.07
4-5:	2.87	1.05	0.00	0.07
5-6:	3.05	1.12	0.00	0.09
6-7:	3.37	1.14	0.00	0.09

OPPORTUNITY

LEAD MODEL Version 0.99d

AIR CONCENTRATION: 0.100 ug Pb/m3 DEFAULT
Indoor AIR Pb Conc: 30.0 percent of outdoor.
Other AIR Parameters:

Age	Time Outdoors (hr)	Vent. Rate (m3/day)	Lung Abs. (%)
0-1	1.0	2.0	32.0
1-2	2.0	3.0	32.0
2-3	3.0	5.0	32.0
3-4	4.0	5.0	32.0
4-5	4.0	5.0	32.0
5-6	4.0	7.0	32.0
6-7	4.0	7.0	32.0

DIET: DEFAULT

DRINKING WATER Conc: 4.00 ug Pb/L DEFAULT
WATER Consumption: DEFAULT

SOIL & DUST:
Soil: constant conc.
Dust: constant conc.

Age	Soil (ug Pb/g)	House Dust (ug Pb/g)
0-1	134.0	94.0
1-2	134.0	94.0
2-3	134.0	94.0
3-4	134.0	94.0
4-5	134.0	94.0
5-6	134.0	94.0
6-7	134.0	94.0

Additional Dust Sources: None DEFAULT

PAINT Intake: 0.00 ug Pb/day DEFAULT

MATERNAL CONTRIBUTION: Infant Model
Maternal Blood Conc: 2.50 ug Pb/dL

CALCULATED BLOOD Pb and Pb UPTAKES:

YEAR	Blood Level (ug/dL)	Total Uptake (ug/day)	Soil+Dust Uptake (ug/day)
0.5-1:	3.1	5.67	2.68
1-2:	3.3	7.90	4.23
2-3:	3.1	8.35	4.26
3-4:	2.9	8.34	4.30
4-5:	2.5	7.24	3.23
5-6:	2.3	7.20	2.92
6-7:	2.1	7.39	2.76

YEAR	Diet Uptake (ug/day)	Water Uptake (ug/day)	Paint Uptake (ug/day)	Air Uptake (ug/day)
0.5-1:	2.59	0.38	0.00	0.02
1-2:	2.70	0.93	0.00	0.03
2-3:	3.05	0.98	0.00	0.06

OPPORTUNITY

3-4:	2.96	1.01	0.00	0.07
4-5:	2.89	1.06	0.00	0.07
5-6:	3.06	1.12	0.00	0.09
6-7:	3.39	1.14	0.00	0.09

ALL AREAS

LEAD MODEL Version 0.99d

AIR CONCENTRATION: 0.100 ug Pb/m3 DEFAULT
Indoor AIR Pb Conc: 30.0 percent of outdoor.
Other AIR Parameters:

Age	Time Outdoors (hr)	Vent. Rate (m3/day)	Lung Abs. (%)
0-1	1.0	2.0	32.0
1-2	2.0	3.0	32.0
2-3	3.0	5.0	32.0
3-4	4.0	5.0	32.0
4-5	4.0	5.0	32.0
5-6	4.0	7.0	32.0
6-7	4.0	7.0	32.0

DIET: DEFAULT

DRINKING WATER Conc: 4.00 ug Pb/L DEFAULT
WATER Consumption: DEFAULT

SOIL & DUST:
Soil: constant conc.
Dust: constant conc.

Age	Soil (ug Pb/g)	House Dust (ug Pb/g)
0-1	364.0	192.9
1-2	364.0	192.9
2-3	364.0	192.9
3-4	364.0	192.9
4-5	364.0	192.9
5-6	364.0	192.9
6-7	364.0	192.9

Additional Dust Sources: None DEFAULT

PAINT Intake: 0.00 ug Pb/day DEFAULT

MATERNAL CONTRIBUTION: Infant Model
Maternal Blood Conc: 2.50 ug Pb/dL

CALCULATED BLOOD Pb and Pb UPTAKES:

YEAR	Blood Level (ug/dL)	Total Uptake (ug/day)	Soil+Dust Uptake (ug/day)
0.5-1:	4.9	9.08	6.20
1-2:	5.5	13.22	9.73
2-3:	5.1	13.79	9.86
3-4:	4.9	13.90	10.00
4-5:	4.1	11.52	7.60
5-6:	3.5	11.10	6.91
6-7:	3.2	11.10	6.55

YEAR	Diet Uptake (ug/day)	Water Uptake (ug/day)	Paint Uptake (ug/day)	Air Uptake (ug/day)
0.5-1:	2.49	0.36	0.00	0.02
1-2:	2.57	0.89	0.00	0.03
2-3:	2.93	0.94	0.00	0.06

ALL AREAS

3-4:	2.86	0.97	0.00	0.07
4-5:	2.82	1.03	0.00	0.07
5-6:	3.00	1.10	0.00	0.09
6-7:	3.33	1.12	0.00	0.09

Journal of Toxicology and Environmental Health, Part A, 76:449–457, 2013
Copyright © Taylor & Francis Group, LLC
ISSN: 1528-7394 print / 1087-2620 online
DOI: 10.1080/15287394.2013.771562

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MEASUREMENT OF ARSENIC RELATIVE BIOAVAILABILITY IN SWINE

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This study describes a method for measuring the relative oral bioavailability (RBA) of arsenic (As) in soil and other soil-like media using young swine as the animal model. Groups of animals are exposed to site soil or sodium arsenate orally for 12 d. Forty-eight-hour urine samples were collected from each animal on d 6–7, 8–9, and 10–11 and were analyzed for total As. The urinary excretion fraction (UEF) for each group was estimated by plotting the mass of As excreted in urine by each animal as a function of the dose administered, and then fitting a linear model to the data using simultaneous weighted linear regression. The RBA of a test material is calculated as the ratio of the UEF value for the test material divided by the UEF of the reference material. Uncertainty around the RBA estimate is calculated using Fieller's theorem. Application of this method to a series of test soils indicates that RBA values for As can range from 18 to 52%. This wide variability supports the conclusion that there may be important differences in RBA between sites, and that use of a site-specific RBA value is likely to increase the accuracy of risk estimates for exposure to As in soil.

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Accurate assessment of the human health risks resulting from oral exposure to As requires knowledge of the amount of As absorbed from the gastrointestinal (GI) tract into the body (Orloff et al., 2009). This information on GI absorption may be described either in absolute or relative terms:

Absolute bioavailability (ABA) is the ratio of the amount of As absorbed to the amount ingested:

$$\text{ABA} = (\text{Absorbed dose}) / (\text{Ingested dose})$$

Relative bioavailability (RBA) is the ratio of the absolute bioavailability of As present in some test material to the absolute bioavailability of As in some appropriate reference material:

$$\text{RBA} = \text{ABA (test)} / \text{ABA (reference)}$$

When measuring RBA, the form of As used as the reference material is usually an As compound dissolved in water or a readily soluble form (e.g., sodium arsenate) that is expected to completely dissolve when ingested.

Received 16 October 2012; accepted 9 January 2013.

This work was supported by the U.S. Environmental Protection Agency (contract number GS-00F-0019L, order number, 0818 and order number EP-S8-11-030). The work described in this report is the product of a team effort involving a large number of people. Most of the studies described in this report were planned and sponsored by the United States Environmental Protection Agency, Region 8. The technical and managerial direction for the project was provided mainly by Christopher P. Weis, PhD, DABT, and Gerry M. Henningsen, DVM, PhD, DABT/DABVT. Dr. Casteel was supported in his work by Genny Fent, DVM, Larry D. Brown, DVM, MPH, Ross P. Cowart, DVM, MS, DACVIM, James R. Turk, DVM, PhD, DACVP, John T. Payne, DVM, MS, DACVS, Steven L. Stockham, DVM, MS, DACVP, Margaret E. Dunsmore, BS, and Roberto E. Guzman, DVM, MS. Dr. Brattin was supported in his efforts by Angela Wahlquist and Penny Hunter. Analysis of urine and other biological samples was performed by Dr. Edward Hindenberger, of L.E.T., Inc., Columbia, MO. Dr. Timothy Barry, U.S. Environmental Protection Agency, National Center for Environmental Economics, provided ongoing support in the development, testing, and evaluation of the statistical methods used in dose-response curve fitting and data reduction.

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When a reliable RBA value is available for a particular site medium (e.g., soil), the RBA can be used to adjust the default reference dose (RfD) and cancer slope factor (CSF) for As to account for differences in absorption between As ingested in water and As ingested in the site medium, as follows:

$$RfD_{adj} = \frac{RfD_{default}}{RBA}$$

$$CSF_{adj} = CSF_{default} \cdot RBA$$

Alternatively, it is also acceptable to adjust the dose (rather than the toxicity factors) as follows:

$$Dose_{adj} = Dose_{default} \cdot RBA$$

This dose adjustment is mathematically equivalent to adjusting the toxicity factors as described above.

Scientists from the U.S. Environmental Protection Agency (EPA) Region 8 have been engaged in a multiyear investigation of As absorption from a variety of different environmental media, especially soils and solid wastes associated with mining, milling, and smelting sites. The protocol described here is the end product of these many years of research, and represents the current approach used by the U.S. EPA for measuring As RBA in vivo. This investigation, along with other related studies, has been described in a report prepared by the U.S. EPA (2010).

MATERIALS AND METHODS

Experimental Animals

Juvenile swine are used in these studies because their GI physiology is more similar to humans than most other animal models (Weis and LaVelle, 1991). For the studies reported here, all animals were young males of the Pig Improvement Corporation (PIC) genetically defined Line 26, and were purchased from Chinn Farms, Clarence, MO. The number of animals purchased for each study was typically six to eight more than required by the protocol. These animals were usually purchased at age 4–5 wk (weaning occurs at age 3 wk), and were held in individual stainless-steel cages. Any animals that appeared to be in poor health were excluded. To minimize weight variations between animals and groups, extra animals most different in body weight (either heavier or lighter) 4 d prior to exposure (d −4) were also excluded from the study. The remaining animals were assigned to dose groups at random. When exposure began (d 0), the animals were about 5–6 wk old and weighed approximately 7–12 kg.

Diet

Animals provided by the supplier were weaned onto standard pig chow purchased from MFA, Inc., Columbia, MO. In order to minimize As exposure from the diet, the animals were gradually transitioned from the MFA feed to a special feed (Zeigler Brothers, Inc., Gardners, PA) over a time interval from d −7 to d −3; this feed was then maintained for the duration of the study. The feed was nutritionally complete and met all requirements of the National Institutes of Health–National Research Council. Each day every animal was given an amount of feed equal to 5% of the mean body weight of all animals on study. Feed amounts were adjusted every 3 d, when pigs were weighed. Feed was administered in 2 equal portions of 2.5% of the mean body weight at 11:00 a.m. and 5:00 p.m. daily. Periodic analysis of feed samples indicated that the As level was generally below the detection limit (0.1 ppm), which corresponds to a dose contribution from food of less than 5 μg/kg-d. Drinking water was provided ad libitum via self-activated watering nozzles within each cage. Periodic analysis of samples from randomly selected drinking water nozzles indicated the As concentration was less than the detection limit (about 1 μg/L). Assuming water intake of about 0.1 L/kg-d, this corresponds to a dose contribution from water of less than 0.1 μg/kg-d.

Test Materials

Test materials were obtained from a number of sites being investigated by the U.S. EPA

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TABLE 1. Test Materials

Site	Sample designation	Sample description	Arsenic concentration (ppm)	Target doses (μg/d)
Vasquez Boulevard and I-70 NPL Site, Denver, CO	VBI70 TM1	Soil composite from impacted residential property (Eastern Swansea/Elyria neighborhood)	312	500, 1250
	VBI70 TM2	Soil composite from impacted residential property (Western Swansea/Elyria neighborhood)	983	500, 1250
	VBI70 TM3	Soil composite from impacted residential property (Eastern Cole neighborhood)	390	500, 1250
	VBI70 TM4	Soil composite from impacted residential property (Western Cole neighborhood)	813	300, 600
	VBI70 TM5	Soil composite from impacted residential property (Clayton neighborhood)	368	300, 600
	VBI70 TM6	Clean site soil (from the Swansea/Elyria neighborhood) plus added PAX pesticide	516	300, 600
Silver Bow Creek/Butte Area NPL Site, Butte, MT	Butte TM1	Soil composite collected from waste rock dumps in Butte Priority Soils Operable Unit (BPSOU)	234	300, 600, 900
	Butte TM2	Soil composite collected from a residential property located adjacent to a railroad grade in Butte, MT	367	300, 600, 900
Wells G & H Superfund Site, Woburn, MA	Aberjona River TM1	Composite of sediment samples containing arsenic concentrations greater than 500 ppm, collected along the Aberjona River, Massachusetts	676	300, 600, 900
	Aberjona River TM2	Composite of sediment samples containing arsenic concentrations from 180 to 460 ppm, collected along the Aberjona River, Massachusetts	313	300, 600, 900
El Paso/Dona Ana County Metals Survey site, El Paso County, Texas, and Dona Ana County, NM	El Paso TM1	Soil sample collected approximately 1.5 miles east of the American Canal in El Paso County, Texas	74	400, 800, 1600
	El Paso TM2	Soil sample collected approximately 1.5 miles east of the American Canal in El Paso County, Texas	73	400, 800, 1600
Confidential (Study sponsored by American Chemistry Council)	ACC utility pole soil	Soil affected by chromated copper arsenate (CCA)-treated wood utility poles (poles were in place for more than 10 yr)	320	600, 1200
	ACC dislodgeable arsenic	Dislodgeable material obtained from the surface of chromated copper arsenate (CCA)-treated wood (boards from in-service residential decks, aged outdoors for 1 to 3 yr)	3,500	300, 600, 1200

where As was present at elevated levels in soil or sediment (Table 1). In general, the test materials were prepared for study by drying and sieving to <250 μm grain size. This was done because it is generally assumed that fine-grained soil particles are more likely to adhere to hands and be ingested than coarse-grained soil particles.

Dosing

Each experiment included two or three dose groups for sodium arsenate and each test soil (either two or three test soils per study). Animals (typically 5 per dose group) were exposed to sodium arsenate or test material for 12 d, with the dose for each day being administered in 2 equal portions given at 9:00 a.m. and

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3:00 p.m. (2 h before feeding). This schedule was used to minimize any potential effects of GI contents on As absorption rates. Dose levels of As ranged from 300 to 1600 μg/d (Table 1). In most studies, these dose levels were held constant over the course of the experiment, even though the animals gained weight during the study. Control animals (typically 3 per study) were not exposed to As.

Dose material was placed in the center of a small portion (approximately 5 g) of moistened feed (referred to as a "doughball"). Sodium arsenate was dispensed into the doughballs from a stock solution using a micropipette, while test material was weighed and placed into the doughballs as a solid. In cases where the mass of soil was too large to fit into one doughball, the test material was distributed among two or more doughballs. Doughballs were administered to the animals by hand. Occasionally, some animals did not consume some or all of the dose (usually because the dose dropped from their mouth while chewing). All missed doses were recorded and the time-weighted average dose calculation for each animal was adjusted downward accordingly.

Collection and Preservation of Urine

Samples of urine were collected from each animal on d 6–7, 8–9, and 10–11 during the study. Collection began at about 8:00 a.m. and ended 48 h later. The urine was collected in a stainless-steel pan placed beneath each cage, and the pan drained into a plastic storage bottle. Each collection pan was fitted with a nylon screen to minimize contamination with feces, spilled food, or other debris. At the end of each collection period, the urine was well mixed, the volume was measured, and two 60-ml portions were removed for analysis. Each 60-ml sample was preserved by addition of 0.6 ml concentrated nitric acid. These samples were refrigerated until sample analysis.

Sample Digestion

As concentrations in urine were measured using a hydride generation approach. This method requires that all As exist in the form of inorganic As before hydride generation. Because some As in urine may exist in organic forms such as monomethylarsonic acid and dimethylarsinic acid (Buchet et al., 1981a, 1981b; Orloff et al., 2009), vigorous digestion of the urine prior to analysis is required. This was performed as follows. A 25-ml aliquot of acidified urine was removed and placed in a clean 100-ml beaker. To this were added 3 ml methanol, 5 drops antifoam agent, 10 ml 40% (w/v) magnesium nitrate hexahydrate, and 10 ml concentrated trace metal grade nitric acid. The beaker was covered with a watch glass and placed on a hot plate to reflux for 8–12 h at 70–80°C. After this, the temperature was increased to 200°C, and the watch glass was moved back to allow faster evaporation. The sample was then heated to complete dryness (8–12 h), covered with a watch glass, and allowed to cool. Dried samples were transferred to a cool muffle furnace that was heated at a rate of 1°C/min to a temperature of 500°C, and then held at 500°C for 3 h before cooling. Ashed samples were dissolved by adding 5 ml distilled water and 5 ml concentrated trace metal grade hydrochloric acid (HCl), and boiling gently until the white residue was completely dissolved. After cooling, the dissolved sample was diluted with distilled water to 50 ml and held until analysis.

Arsenic Analysis by Hydride Generation

Samples were prepared for hydride generation by dilution with a solution of 10% HCl, 10% potassium iodide, and 5% ascorbic acid. The samples were diluted 1/10 or 1/5 (v/v), depending on the detection limit desired. Samples were held in the diluting fluid for at least 30 min before analysis, but overnight was preferred. Analysis was performed using a Perkin-Elmer 3100 atomic absorption spectrometer (AAS) equipped with an FIAS 200 flow injection system. Calibration standards were prepared in dilution fluid (10% HCl, 10% KI, 5% ascorbic acid) at concentrations of 0, 0.2, 1, 5, 10, and 15 μg/L.

The detection limit of the method was evaluated by performing 10 replicate analyses of

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a low standard (about 1 μg/L). The detection limit was defined as 3 times the standard deviation of these 10 analyses. A 1/10 dilution typically gave a detection limit of about 2 μg/L, while a dilution of 1/5 typically yielded a detection limit of about 1 μg/L. All responses below the detection limit were evaluated at one-half the detection limit.

Estimation of Urinary Excretion Fraction

Data from each study were analyzed by plotting the amount of As excreted in urine (μg/48 h) against the amount of As administered (μg/48 h) for each animal and finding the slope of the best fit straight line for each dose material:

$$\text{Mass excreted } (\mu g) = a + b \times \text{dose administered } (\mu g)$$

The slope of the line for each dose material is the urinary excretion fraction (UEF) (μg excreted/μg administered) for that dose material. Fitting was performed in Microsoft Excel using matrix functions. All of the data were evaluated simultaneously to ensure that the intercept term (a) is the same for all dose materials, as described by Finney (1978). Weighted regression was used because the between-sample variability tended to increase as a function of the mass of As excreted (heteroscedasticity). In this approach (Draper and Smith, 1998), the squared error for each observation is assigned a weight that is inversely proportional to the variance of the response in that group:

$$\textit{Weighted square error}_{i,j,m} = \frac{1}{\sigma_j^2}\left(x_{i,j,m} - a - b_m \cdot dose_{j,m}\right)^2$$

where:

σ^2_j = variance of responses in animals in dose group j
$x_{i,j,m}$ = mass of As excreted by animal i in dose group j of test material m
a = mass of As excreted by control animals
b_m = urinary excretion fraction for dose material m
$dose_{j,m}$ = dose of As administered to animals in dose group j of test material m

One approach for estimating the weight is to assume that σ^2_j is identical to the observed value of the sample variance (s^2_j) for each dose group. This approach was not employed because observed sample variance is a relatively unstable statistic, especially when the number of animals is only 5. That is, due to random variation, the observed sample variance may be substantially smaller or larger than the true variance, and this might result is assignment of inappropriately high or low weights to the data during the fitting process. In order to minimize this problem, σ^2_j was estimated using an "external" variance model developed from observation of the relationship between variance and mean response across many studies. Based on the combined data from multiple experiments, the variance was modeled as:

$$ln\left(\sigma_j^2\right) = k1 + k2 \cdot ln(\bar{y}_j)$$

where:

σ^2_j = expected between-animal variance in As excretion for exposure group j
$\bar{y}_j$ = average As excretion by exposure group j

Based on this analysis, the intercept and slope terms for the variance model are as follows:

$$k1\ (\text{intercept}) = -1.10$$
$$k2\ (\text{slope}) = 1.64$$

Overall goodness of fit was evaluated using analysis of variance (Draper and Smith, 1998).

Calculation of RBA

Given the UEF for each dose material, the best estimate of the RBA for each test material is calculated as:

$$RBA_m = UEF_m/UEF_{ref}$$

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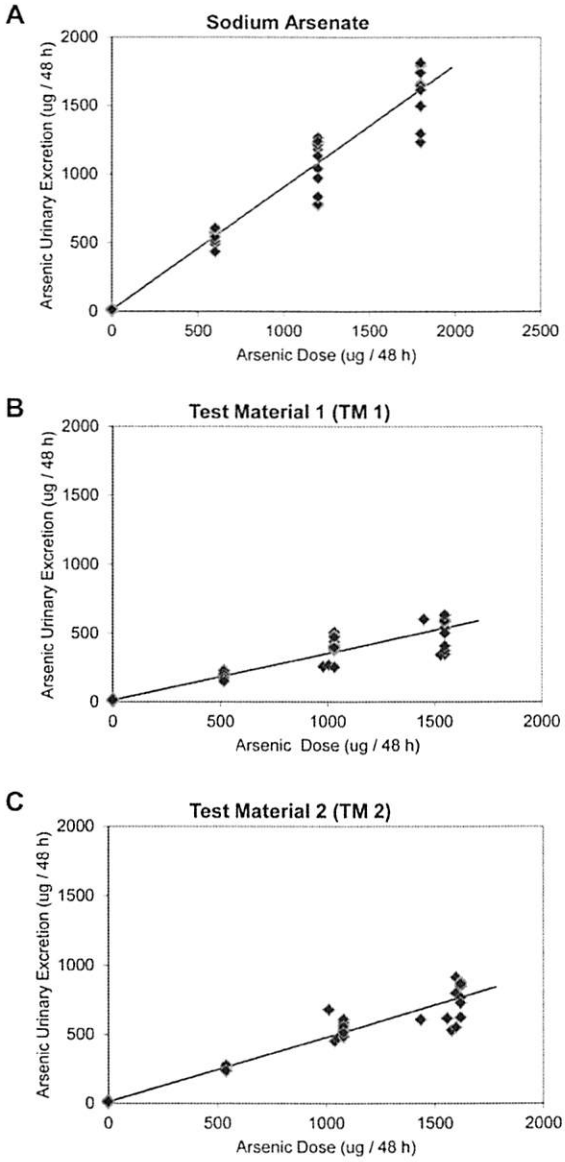

FIGURE 1. Example results for a study with two test materials. The three graphs show the raw data (solid diamonds) for (A) sodium arsenate (reference material), (B) test material 1, and (C) test material 2, along with the simultaneous best-fit variance-weighted linear regression models (color figure available online).

where RBA_m is the best estimate of the RBA for test material m, UEF_m the urinary excretion fraction for test material m, and UEF_{ref} the urinary excretion fraction for the reference material (sodium arsenate).

As described by Finney (1978), the uncertainty around this point estimate may be estimated using Fieller's theorem:

$$LB, UB = \frac{RBA - g\frac{covar_{r,t}}{var_r} \pm \frac{t}{b_r}\sqrt{W}}{1-g}$$

where LB is the lower bound of the fiduciary range on RBA, UB the upper bound of the fiduciary range on RBA, var_r the variance in the slope coefficient for the reference material, $covar_{r,t}$ the covariance in the slope coefficients for the reference and test materials, b_r the slope coefficient for the reference material, and t the t statistic for alpha (0.05) and $(n - p)$ degrees of freedom, where n is the total number of data points and p the total number of fitting parameters in the combined model,

$$g = \frac{t^2}{b_r^2} var_r$$

$$W = var_t - 2 \cdot R \cdot covar_{t,r} + R^2 \cdot var_r - g\left(var_r - \frac{covar_{r,t}^2}{var_r}\right)$$

The interval between the LB and the UB is the 95% confidence interval for the RBA.

RESULTS

Figure 1 presents the results of an example study in which two test soils were evaluated (Aberjona River sediments TM1 and TM2). As seen, the exposure-response data (mass of As excreted *vs.* mass of As administered) are well characterized by linear models. Table 2 provides the fitting statistics and calculated RBA values for this study. The slope of the line (the UEF) for sodium arsenate (0.89) is steeper than the slopes (UEF) for the two test materials (0.34 and 0.47), indicating lower excretion (and hence lower absorption) of As from the test materials than the reference material. Based on these values, the RBA values for test material 1 and 2 are 38 ± 2% and 52 ± 2%. Overall goodness of fit of the model to the data was assessed by analysis of variance (ANOVA). As indicated, the fit in this example is quite good ($R^2 = .969$, $p < .001$). Close inspection of Figure 1 reveals a tendency for increased

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TABLE 2. Example Fitting Statistics

Summary of fitting	Estimate	SE	
a	12.0	1.4	
b1	0.89	0.02	
b2	0.34	0.01	
b3	0.47	0.01	
Covariance (*b1*, *b2*)	0.0082	—	
Covariance (*b1*, *b3*)	0.0063	—	
Degrees of freedom	113	—	
RBA and uncertainty	TM 1	TM 2	
RBA	38%	52%	
Lower bound	36%	49%	
Upper bound	41%	56%	
Standard error	1.6%	2.0%	
ANOVA	SSE	DF	MSE
Fit	2963.80	3	987.93
Error	92.38	112	0.82
Total	3056.18	115	26.58
Goodness-of-fit statistic	Estimate		
F	1197.7		
p	<.001		
Adjusted R^2	.969		

variance in As excretion as the average mass of As excreted rises. This is why weighted regression is judged to be appropriate. Other studies display similar attributes (data not shown).

Table 3 summarizes the RBA results for all test material analyzed using this protocol. As seen, using sodium arsenate as a relative frame of reference the estimated RBA values for these test materials range from 18 to 52%. This wide variability supports the conclusion that there may be important differences in RBA between different types of samples and that use of a site-specific RBA value is likely to increase the accuracy of risk estimates for As.

DISCUSSION

The results of this investigation indicate that juvenile swine are a useful model for quantifying GI absorption of As from different test materials, using urinary As excretion as the measurement endpoint. The approach is applicable to almost any type of As-contaminated medium that may be ingested including a wide variety of soils, sediments, and solid waste streams.

TABLE 3. Relative Bioavailability Estimates

Sample	RBA ± SE
VBI70 TM1	40 ± 4%
VBI70 TM2	42 ± 4%
VBI70 TM3	37 ± 3%
VBI70 TM4	24 ± 2%
VBI70 TM5	21 ± 2%
VBI70 TM6	24 ± 3%
Butte TM1	18 ± 3%
Butte TM2	24 ± 2%
Aberjona River TM1	38 ± 2%
Aberjona River TM2	52 ± 2%
El Paso TM1	44 ± 3%
El Paso TM2	37 ± 3%
ACC utility pole soil	47 ± 3%
ACC dislodgeable arsenic	26 ± 1%

Comparison to Other Models

Several other animal models were developed for assessing the RBA of As, including cynomolgus monkeys (Roberts et al., 2002, 2007) and mice (Bradham et al., 2011). In terms of experimental design, the swine model has several potential advantages compared to the other models. First, because of the size of juvenile swine (approximately 10 kg at the beginning of the study), it is usually possible to administer doses of test soils that are relatively close to the range thought to be of concern to humans. For example, for a soil with an As concentration of 500 ppm (500 μg/g), the amount of soil administered in the low dose group (25 μg As/d) is 500 mg/d, which corresponds to an intake of about 50 mg soil/kg body weight/d (mg/kg/d). This value is relatively close to the reasonable maximum exposure (RME) value of 13 mg/kg/d generally assumed for human children. In contrast, the monkey and mouse bioassay systems usually use soil doses that approach 1000 mg/kg/d. Thus, in the swine assay, most measurements are obtained in a portion of the dose-response curve that is more relevant to humans than is achieved in most other animal models. In addition, the swine model employed a repeated dosing protocol, with sampling not beginning until 5 d of exposure have elapsed. This allows the exposed animal to approach a quasi-steady state with regard to As intake and excretion.

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An advantage of this protocol is that it reflects a more realistic human exposure scenario (continuous exposure for many months or years) than does a single dose protocol such as Roberts et al. (2002, 2007) used in the monkey model. Further, multiple measurements can be made from the same animal on different days to ensure that a steady state has been reached and to increase the number of observations upon which the fitting is performed.

Recently, the U.S. EPA (2012) compiled and compared RBA measurements from swine, monkey, and mouse studies to investigate whether the animal models yield the same or different outcomes. For swine compared to monkey, only four soil samples (all from the same site) have been analyzed in both systems. The results are too limited to draw a firm conclusion, and uncertainty bounds between paired RBA values often overlap. Nevertheless, there is a suggestion that RBA values measured in swine tend to be somewhat higher than for monkeys. For swine compared to mice, there are 11 paired samples available, and the results are qualitatively similar to monkeys. There is a tendency for swine RBA values to be somewhat higher than for mice, although the differences are not always statistically significant. At present, there is no firm basis for determining if the observed tendencies reflect authentic and significant differences between the animal models, and if so, which animal model is the most appropriate for estimating RBA in humans.

Potential Utility of RBA Data

The RBA results for different test materials investigated in the swine model support the view that absorption of As from soils and mine wastes may vary substantially, both within and between sites. The detailed chemical mechanism accounting for this variable and reduced bioavailability of As in soil-like media is not known, but almost certainly is related to variations in the chemical and physical form(s) of As in the sample.

Because As in most test materials is absorbed less extensively than soluble forms of As, and because soluble forms of As are the basis of the oral RfD and oral CSF for As, the use of the unadjusted toxicity factors for assessing human health risk (i.e., assuming an RBA value of 100%) will usually lead to an overestimate of hazard. Consequently, measurement and application of site-specific RBA values to adjust the toxicity factors to account for the lower level of absorption are expected to increase the accuracy and decrease the uncertainty in human health risk assessments for As. At sites where As is the principal source of risk from soil, this adjustment may allow for reduced remedial costs due to decreases in the estimated level of risk and hence the extent or magnitude of soil cleanup needed to protect public health.

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APPENDIX E

Crystal Ball Modeling Output – Arsenic Cancer Risk

Crystal Ball Report - Custom

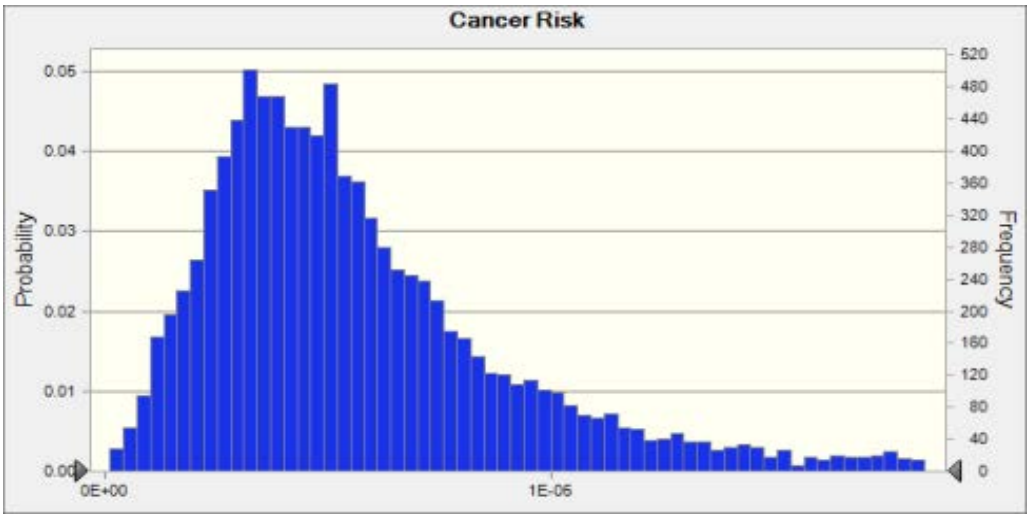
Simulation started on 4/16/2014 at 4:59 PM
Simulation stopped on 4/16/2014 at 4:59 PM

Run preferences:	
Number of trials run	10,000
Monte Carlo	
Random seed	
Precision control on	
Confidence level	95.00%
Run statistics:	
Total running time (sec)	2.86
Trials/second (average)	3,493
Random numbers per sec	52,400
Crystal Ball data:	
Assumptions	15
Correlations	0
Correlation matrices	0
Decision variables	0
Forecasts	1

Forecasts

Forecast: Cancer Risk

Summary:
Entire range is from 1E-07 to 5E-05
Base case is 6E-06
After 10,000 trials, the std. error of the mean is 4E-08



Statistics:	Forecast values
Trials	10,000
Base Case	6.E-06
Mean	6.E-06
Median	5.E-06
Mode	---
Standard Deviation	4.E-06
Variance	2.E-11
Skewness	2.49
Kurtosis	12.81
Coeff. of Variation	0.7312
Minimum	1.E-07
Maximum	5.E-05
Range Width	5.E-05
Mean Std. Error	4.E-08

Forecast: Cancer Risk (cont'd)

Percentiles:	Forecast values
0%	1.E-07
5%	2.E-06
10%	2.E-06
15%	3.E-06
20%	3.E-06
25%	3.E-06
30%	4.E-06
35%	4.E-06
40%	4.E-06
45%	5.E-06
50%	5.E-06
55%	5.E-06
60%	6.E-06
65%	6.E-06
70%	7.E-06
75%	7.E-06
80%	8.E-06
85%	9.E-06
90%	1.E-05
95%	1.E-05
100%	5.E-05

End of Forecasts

Assumptions

Assumption: Adult Body Weight (kg)

Custom distribution with parameters:

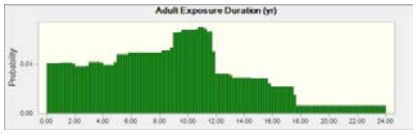
Minimum	Maximum	Probability
44.0	52.3	5.00
---	57.6	10.00
---	68.7	35.00
---	84.4	35.00
---	97.0	10.00
---	107.0	5.00

Assumption: Adult Exposure Duration (yr)

Custom distribution with parameters:

Minimum	Maximum	Probability
0.01	0.98	5.00
---	1.94	5.00
---	2.97	5.00
---	3.91	5.00
---	4.91	5.00
---	5.73	5.00
---	6.53	5.00
---	7.33	5.00
---	8.13	5.00
---	8.90	5.00
---	9.50	5.00
---	10.08	5.00
---	10.66	5.00
---	11.22	5.00
---	11.81	5.00
---	13.03	5.00
---	14.38	5.00
---	15.75	5.00
---	17.57	5.00
---	24.00	5.00

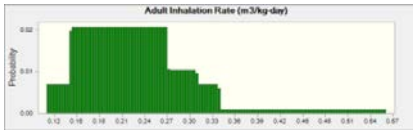
Assumption: Adult Exposure Duration (yr) (cont'd)



Assumption: Adult Inhalation Rate (m3/kg-day)

Custom distribution with parameters:

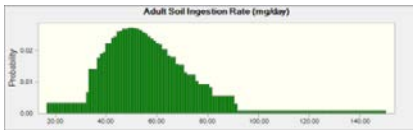
Minimum	Maximum	Probability
0.11	0.14	5.00
---	0.15	5.00
---	0.16	5.00
---	0.17	5.00
---	0.18	5.00
---	0.19	5.00
---	0.20	5.00
---	0.21	5.00
---	0.22	5.00
---	0.23	5.00
---	0.24	5.00
---	0.25	5.00
---	0.26	5.00
---	0.27	5.00
---	0.29	5.00
---	0.31	5.00
---	0.34	5.00
---	0.56	5.00



Assumption: Adult Soil Ingestion Rate (mg/day)

Custom distribution with parameters:

Minimum	Maximum	Probability
16.57	32.78	5.00
---	36.70	5.00
---	39.60	5.00
---	42.07	5.00
---	44.33	5.00
---	46.43	5.00
---	48.48	5.00
---	50.50	5.00
---	52.53	5.00
---	54.61	5.00
---	56.79	5.00
---	59.12	5.00
---	61.59	5.00
---	64.29	5.00
---	67.37	5.00
---	70.92	5.00
---	75.43	5.00
---	81.33	5.00
---	91.03	5.00
---	150.07	5.00

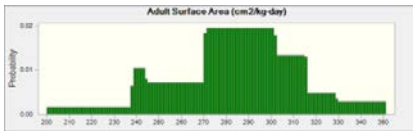


Assumption: Adult Surface Area (cm2/kg-day)

Custom distribution with parameters:

Minimum	Maximum	Probability
200	238	5.00
---	244	5.00
---	270	15.00
---	286	25.00
---	302	25.00
---	316	15.00
---	329	5.00
---	351	5.00

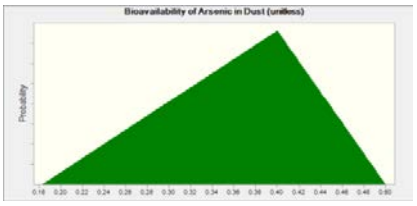
Assumption: Adult Surface Area (cm2/kg-day) (cont'd)



Assumption: Bioavailability of Arsenic in Dust (unitless)

Triangular distribution with parameters:

Minimum	0.18
Likeliest	0.40
Maximum	0.50



Assumption: Bioavailability of Arsenic in Soil (unitless)

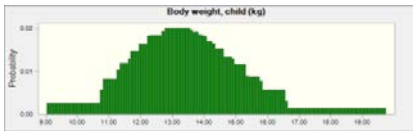
Triangular distribution with parameters:

Minimum	0.18
Likeliest	0.40
Maximum	0.50

Assumption: Child Body Weight (kg)

Custom distribution with parameters:

Minimum	Maximum	Probability
9.03	10.75	5.00
---	11.28	5.00
---	11.65	5.00
---	11.95	5.00
---	12.22	5.00
---	12.46	5.00
---	12.70	5.00
---	12.92	5.00
---	13.14	5.00
---	13.36	5.00
---	13.58	5.00
---	13.81	5.00
---	14.05	5.00
---	14.31	5.00
---	14.60	5.00
---	14.93	5.00
---	15.31	5.00
---	15.81	5.00
---	16.58	5.00
---	19.73	5.00



Assumption: Child Exposure Duration (yr)

Custom distribution with parameters:

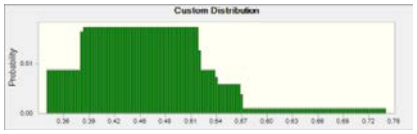
Minimum	Maximum	Probability
0.01	0.59	5.00
---	1.18	5.00
---	1.77	5.00
---	2.36	5.00
---	2.96	5.00
---	3.37	5.00
---	3.76	5.00
---	4.16	5.00
---	4.56	5.00
---	4.95	5.00
---	5.37	5.00
---	5.78	5.00
---	6.00	40.00

Assumption: Child Exposure Duration (yr) (cont'd)

Assumption: Child Inhalation Rate (m3/kg-day)

Custom distribution with parameters:

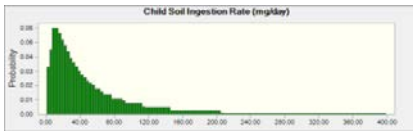
Minimum	Maximum	Probability
0.34	0.36	5.00
---	0.38	5.00
---	0.39	5.00
---	0.40	5.00
---	0.41	5.00
---	0.42	5.00
---	0.43	5.00
---	0.44	5.00
---	0.45	5.00
---	0.46	5.00
---	0.47	5.00
---	0.48	5.00
---	0.49	5.00
---	0.50	5.00
---	0.51	5.00
---	0.52	5.00
---	0.54	5.00
---	0.57	5.00
---	0.74	5.00



Assumption: Child Soil Ingestion Rate (mg/day)

Custom distribution with parameters:

Minimum	Maximum	Probability
0.52	5.52	5.00
---	8.34	5.00
---	11.04	5.00
---	13.78	5.00
---	16.67	5.00
---	19.81	5.00
---	23.21	5.00
---	26.95	5.00
---	31.17	5.00
---	35.94	5.00
---	41.39	5.00
---	47.83	5.00
---	55.44	5.00
---	64.66	5.00
---	76.34	5.00
---	91.54	5.00
---	112.85	5.00
---	145.10	5.00
---	205.24	5.00
---	398.75	5.00

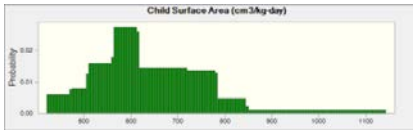


Assumption: Child Surface Area (cm3/kg-day)

Custom distribution with parameters:

Minimum	Maximum	Probability
421	470	5.00
---	507	5.00
---	563	15.00
---	617	25.00
---	719	25.00
---	784	15.00
---	846	5.00
---	1142	5.00

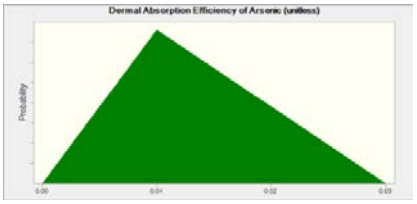
Assumption: Child Surface Area (cm3/kg-day) (cont'd)



Assumption: Dermal Absorption Efficiency of Arsenic (unitless)

Triangular distribution with parameters:

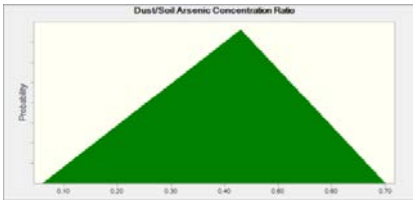
Minimum	0.00
Likeliest	0.01
Maximum	0.03



Assumption: Dust/Soil Arsenic Concentration Ratio

Triangular distribution with parameters:

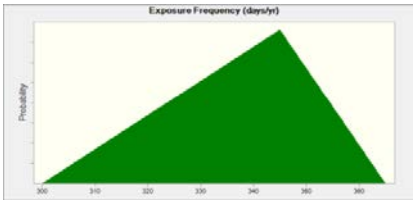
Minimum	0.06
Likeliest	0.43
Maximum	0.70



Assumption: Exposure Frequency (days/yr)

Triangular distribution with parameters:

Minimum	300
Likeliest	345
Maximum	365



End of Assumptions

APPENDIX F

Crystal Ball Modeling Output – Arsenic Hazard Quotient

Crystal Ball Report - Custom

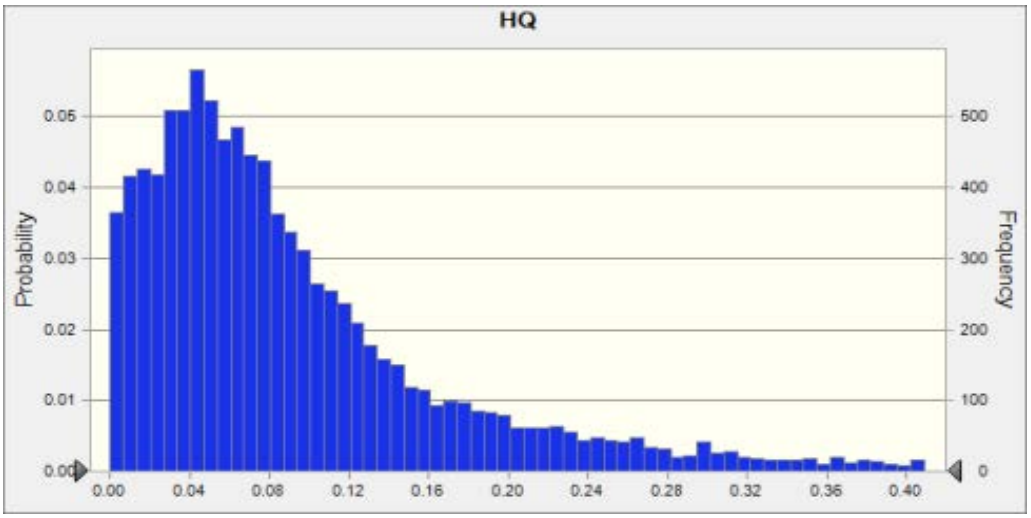
Simulation started on 4/16/2014 at 5:11 PM
Simulation stopped on 4/16/2014 at 5:11 PM

Run preferences:	
Number of trials run	10,000
Monte Carlo	
Random seed	
Precision control on	
Confidence level	95.00%
Run statistics:	
Total running time (sec)	2.74
Trials/second (average)	3,654
Random numbers per sec	36,543
Crystal Ball data:	
Assumptions	10
Correlations	0
Correlation matrices	0
Decision variables	0
Forecasts	1

Forecasts

Forecast: HQ

Summary:
Entire range is from 0.00 to 1.05
Base case is 0.10
After 10,000 trials, the std. error of the mean is 0.00



Statistics:	Forecast values
Trials	10,000
Base Case	0.10
Mean	0.10
Median	0.07
Mode	---
Standard Deviation	0.11
Variance	0.01
Skewness	2.75
Kurtosis	13.42
Coeff. of Variation	1.05
Minimum	0.00
Maximum	1.05
Range Width	1.05
Mean Std. Error	0.00

Forecast: HQ (cont'd)

Percentiles:	Forecast values
0%	0.00
5%	0.01
10%	0.02
15%	0.02
20%	0.03
25%	0.04
30%	0.04
35%	0.05
40%	0.06
45%	0.06
50%	0.07
55%	0.08
60%	0.09
65%	0.10
70%	0.11
75%	0.13
80%	0.15
85%	0.18
90%	0.22
95%	0.31
100%	1.05

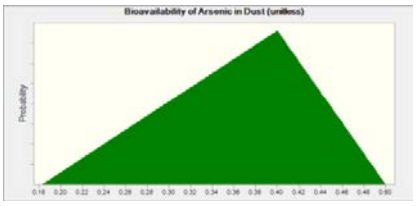
End of Forecasts

Assumptions

Assumption: Bioavailability of Arsenic in Dust (unitless)

Triangular distribution with parameters:

Minimum	0.18
Likeliest	0.40
Maximum	0.50



Assumption: Bioavailability of Arsenic in Soil (unitless)

Triangular distribution with parameters:

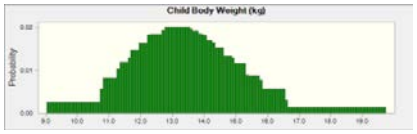
Minimum	0.18
Likeliest	0.40
Maximum	0.50

Assumption: Child Body Weight (kg)

Custom distribution with parameters:

Minimum	Maximum	Probability
9.0	10.8	5.00
---	11.3	5.00
---	11.7	5.00
---	12.0	5.00
---	12.2	5.00
---	12.5	5.00
---	12.7	5.00
---	12.9	5.00
---	13.1	5.00
---	13.4	5.00
---	13.6	5.00
---	13.8	5.00
---	14.1	5.00
---	14.3	5.00
---	14.6	5.00
---	14.9	5.00
---	15.3	5.00
---	15.8	5.00
---	16.6	5.00
---	19.7	5.00

Assumption: Child Body Weight (kg) (cont'd)



Assumption: Child Exposure Duration (yr)

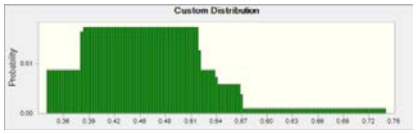
Custom distribution with parameters:

Minimum	Maximum	Probability
0.01	0.59	5.00
---	1.18	5.00
---	1.77	5.00
---	2.36	5.00
---	2.96	5.00
---	3.37	5.00
---	3.76	5.00
---	4.16	5.00
---	4.56	5.00
---	4.95	5.00
---	5.37	5.00
---	5.78	5.00
---	6.00	40.00

Assumption: Child Inhalation Rate (m3/kg-day)

Custom distribution with parameters:

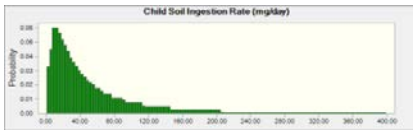
Minimum	Maximum	Probability
0.34	0.36	5.00
---	0.38	5.00
---	0.39	5.00
---	0.40	5.00
---	0.41	5.00
---	0.42	5.00
---	0.43	5.00
---	0.44	5.00
---	0.45	5.00
---	0.46	5.00
---	0.47	5.00
---	0.48	5.00
---	0.49	5.00
---	0.50	5.00
---	0.51	5.00
---	0.52	5.00
---	0.54	5.00
---	0.57	5.00
---	0.74	5.00



Assumption: Child Soil Ingestion Rate (mg/day)

Custom distribution with parameters:

Minimum	Maximum	Probability
0.52	5.52	5.00
---	8.34	5.00
---	11.04	5.00
---	13.78	5.00
---	16.67	5.00
---	19.81	5.00
---	23.21	5.00
---	26.95	5.00
---	31.17	5.00
---	35.94	5.00
---	41.39	5.00
---	47.83	5.00
---	55.44	5.00
---	64.66	5.00
---	76.34	5.00
---	91.54	5.00
---	112.85	5.00
---	145.10	5.00
---	205.24	5.00
---	398.75	5.00

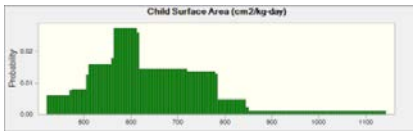


Assumption: Child Surface Area (cm2/kg-day)

Custom distribution with parameters:

Minimum	Maximum	Probability
421	470	5.00
---	507	5.00
---	563	15.00
---	617	25.00
---	719	25.00
---	784	15.00
---	846	5.00
---	1142	5.00

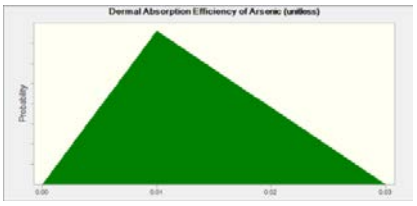
Assumption: Child Surface Area (cm2/kg-day) (cont'd)



Assumption: Dermal Absorption Efficiency of Arsenic (unitless)

Triangular distribution with parameters:

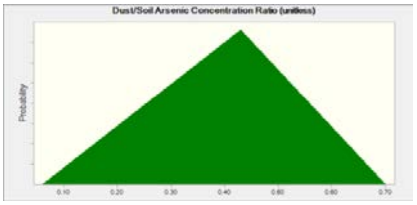
Minimum	0.00
Likeliest	0.01
Maximum	0.03



Assumption: Dust/Soil Arsenic Concentration Ratio (unitless)

Triangular distribution with parameters:

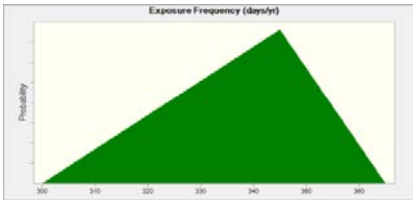
Minimum	0.06
Likeliest	0.43
Maximum	0.70



Assumption: Exposure Frequency (days/yr)

Triangular distribution with parameters:

Minimum	300
Likeliest	345
Maximum	365



End of Assumptions

APPENDIX G

Crystal Ball Modeling Output – Copper Hazard Quotient

Crystal Ball Report - Custom

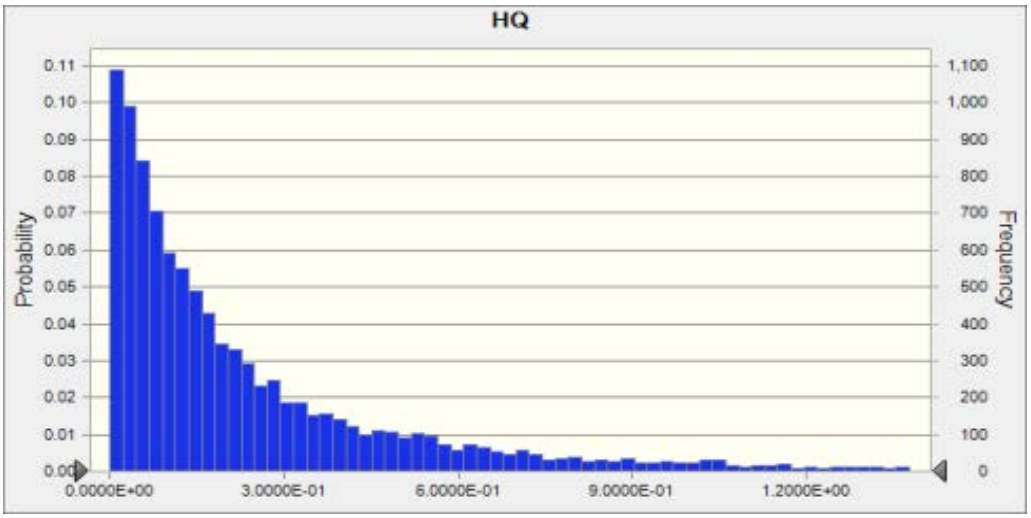
Simulation started on 4/11/2014 at 2:14 PM
Simulation stopped on 4/11/2014 at 2:14 PM

Run preferences:	
Number of trials run	10,000
Monte Carlo	
Random seed	
Precision control on	
Confidence level	95.00%
Run statistics:	
Total running time (sec)	2.61
Trials/second (average)	3,828
Random numbers per sec	26,799
Crystal Ball data:	
Assumptions	7
Correlations	0
Correlation matrices	0
Decision variables	0
Forecasts	1

Forecasts

Forecast: HQ

Summary:
Entire range is from 1.8783E-05 to 3.3666E+00
Base case is 2.8433E-01
After 10,000 trials, the std. error of the mean is 3.9113E-03



Statistics:	Forecast values
Trials	10,000
Base Case	2.8433E-01
Mean	2.8222E-01
Median	1.4620E-01
Mode	---
Standard Deviation	3.9113E-01
Variance	1.5298E-01
Skewness	3.10
Kurtosis	15.37
Coeff. of Variation	1.39
Minimum	1.8783E-05
Maximum	3.3666E+00
Range Width	3.3666E+00
Mean Std. Error	3.9113E-03

Forecast: HQ (cont'd)

Percentiles:	Forecast values
0%	0.00
5%	0.01
10%	0.02
15%	0.03
20%	0.04
25%	0.06
30%	0.07
35%	0.09
40%	0.10
45%	0.12
50%	0.15
55%	0.17
60%	0.20
65%	0.24
70%	0.28
75%	0.34
80%	0.42
85%	0.53
90%	0.69
95%	1.03
100%	3.37

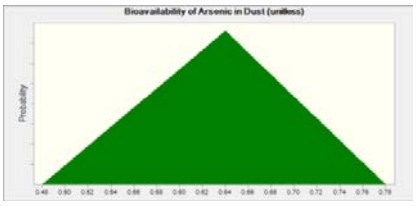
End of Forecasts

Assumptions

Assumption: Bioavailability of Arsenic in Dust (unitless)

Triangular distribution with parameters:

Minimum	0.48
Likeliest	0.64
Maximum	0.78



Assumption: Bioavailability of Arsenic in Soil (unitless)

Triangular distribution with parameters:

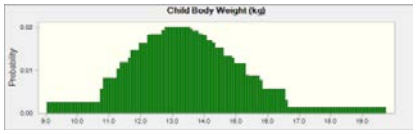
Minimum	0.48
Likeliest	0.64
Maximum	0.78

Assumption: Child Body Weight (kg)

Custom distribution with parameters:

Minimum	Maximum	Probability
9.0	10.8	5.00
---	11.3	5.00
---	11.7	5.00
---	12.0	5.00
---	12.2	5.00
---	12.5	5.00
---	12.7	5.00
---	12.9	5.00
---	13.1	5.00
---	13.4	5.00
---	13.6	5.00
---	13.8	5.00
---	14.1	5.00
---	14.3	5.00
---	14.6	5.00
---	14.9	5.00
---	15.3	5.00
---	15.8	5.00
---	16.6	5.00
---	19.7	5.00

Assumption: Child Body Weight (kg) (cont'd)



Assumption: Child Exposure Duration (yr)

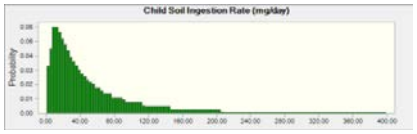
Custom distribution with parameters:

Minimum	Maximum	Probability
0.01	0.59	5.00
---	1.18	5.00
---	1.77	5.00
---	2.36	5.00
---	2.96	5.00
---	3.37	5.00
---	3.76	5.00
---	4.16	5.00
---	4.56	5.00
---	4.95	5.00
---	5.37	5.00
---	5.78	5.00
---	6.00	40.00

Assumption: Child Soil Ingestion Rate (mg/day)

Custom distribution with parameters:

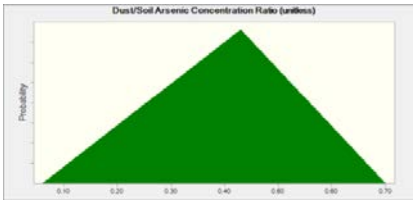
Minimum	Maximum	Probability
0.52	5.52	5.00
---	8.34	5.00
---	11.04	5.00
---	13.78	5.00
---	16.67	5.00
---	19.81	5.00
---	23.21	5.00
---	26.95	5.00
---	31.17	5.00
---	35.94	5.00
---	41.39	5.00
---	47.83	5.00
---	55.44	5.00
---	64.66	5.00
---	76.34	5.00
---	91.54	5.00
---	112.85	5.00
---	145.10	5.00
---	205.24	5.00
---	398.75	5.00



Assumption: Dust/Soil Arsenic Concentration Ratio (unitless)

Triangular distribution with parameters:

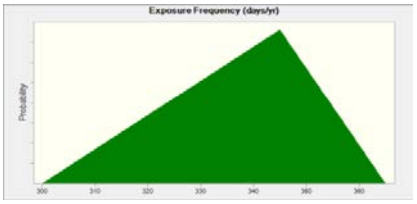
Minimum	0.06
Likeliest	0.43
Maximum	0.70



Assumption: Exposure Frequency (days/yr)

Triangular distribution with parameters:

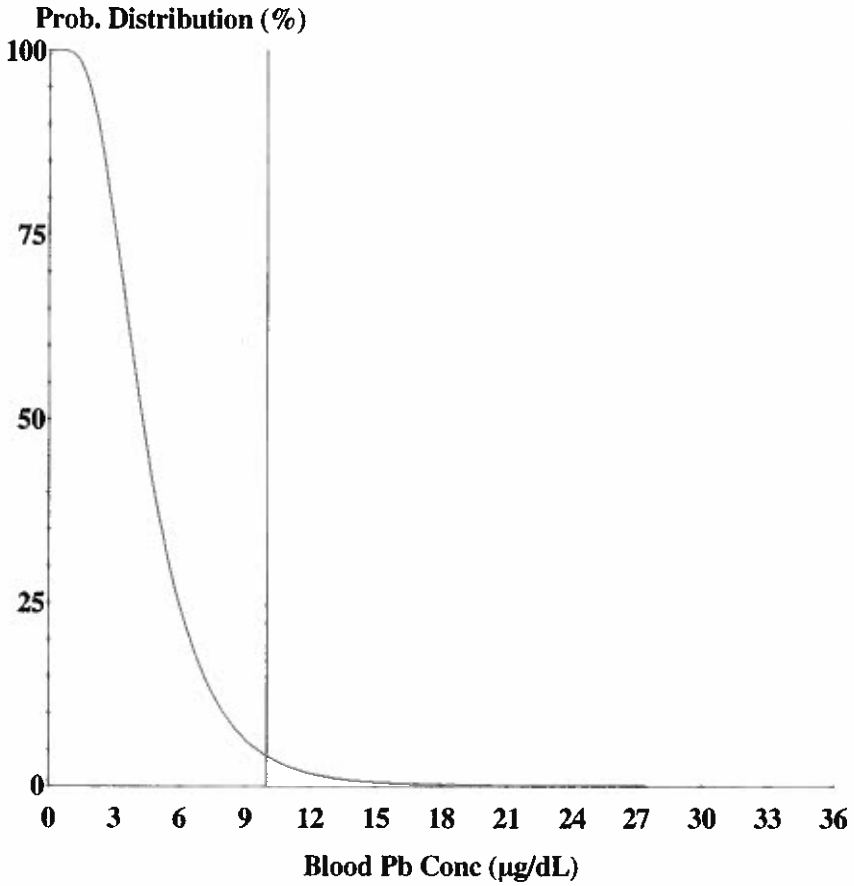
Minimum	300
Likeliest	345
Maximum	365



End of Assumptions

APPENDIX H

IEUBK Model Output



Cutoff = 10.000 µg/dl
Geo Mean = 4.485
GSD = 1.600
% Above = 4.398

Age Range = 0 to 84 months

Run Mode = Research