ENVIRONMENTAL PROTECTION AGENCY
REGION III
1650 Arch Street
Philadelphia, Pennsylvania 19103
February 20, 2002

Dr. Bailus Walker
DC Mayor's Health Policy Council Office
441 4th Street, NW Suite 1150 South
Washington, DC 20001

RE: EPA's Response to the Spring Valley Mayor's Science Advisory Panel Recommendations

Dear Dr. Walker:

EPA appreciates the opportunity to respond to the recommendations made in the "Report of the District of Columbia Mayor's Spring Valley Scientific Advisory Panel Report". This report was issued following the second meeting of the Spring Valley Scientific Advisory Panel on December 7, 2001. EPA has no comments on the body of the report, but has responded in the attached document to the recommendations made in the panel's report.

EPA appreciates the Science Advisory Panel's interest and recommendations for EPA's documentation of the risk of arsenic in Spring Valley soils and the rationale supporting EPA's proposed cleanup levels. If you have any questions, please contact me at (215) 814-3221.

Sincerely,

Frank Vavra, Remedial Project Manager
Federal Facilities Section

Dawn Ioven, Senior Toxicologist
Technical Support Section

cc. Paul Leonard
Mark Stephens
Charles Howland
Hank Sokolowski
Abraham Ferdas
Thomas Voltaggio
Chris Ball
Richard Albright (DC Health Department)
Jim Sweeney (DC Health Department)
Lynette Stokes (DC Health Department)
Major Michael Peloquin (USACE Baltimore)
Sarah Shapley (RAB Co-Chair)

Attachments

EPA'S RESPONSE TO THE REPORT OF THE DISTRICT OF COLUMBIA MAYOR'S SPRING VALLEY SCIENTIFIC ADVISORY PANEL FEBRUARY 19, 2002

Introduction

The second meeting of the Spring Valley Scientific Advisory Panel (SVSAP) was held on December 7, 2001 in Washington DC. At that meeting, the Environmental Protection Agency (EPA) presented its rationale for its preferred cleanup level of 20 parts per million (ppm) arsenic in Spring Valley residential soils, with no limit on the depth of contamination. Subsequent to that meeting, the SVSAP issued a report which summarizes the meeting and makes several recommendations. EPA makes no comments on the body of the report, but will respond to the recommendations addressed to EPA.

Recommendation One

The panel recommends that the Environmental Protection Agency provide the scientific underpinning, or health-risk rationale, for the recommended remediation level of 20 ppm.

The basic toxicology of arsenic is complex and has been studied for a long time. The basic toxicological information serving as the foundation for EPA's assessment of arsenic risk can be found on the web at http://www.epa.gov/iris/subst/0278.htm. (attached). Additional information can be found in the 2001 update on Arsenic in Drinking Water, published by the National Academy Press, Washington D.C., and can be found at http://www.nap.edu. EPA's basic toxicological underpinning of arsenic risk has been fully debated and peer reviewed with industry and academia at the EPA Headquarters level during the recent reduction in the Maximum Contaminant Level (MCL) of arsenic allowed in drinking water. EPA Region 3 accepts the arsenic carcinogenic and systemic risks established by EPA Headquarters and refers the reader to the above information. Although EPA is setting soil cleanup levels, and the underlying science of arsenic toxicology is derived to a large extent from drinking water, the toxicology is essentially the same, with the exception of the bioavailability of arsenic in each media. Bioavailability is the percentage of a contaminant in drinking water or soil that will be absorbed into the body if the soil or water is ingested. In clear drinking water without suspended sediment, all of the arsenic is in solution and can therefore be absorbed by the body, while in soil, some arsenic is bound up in a mineralized insoluble compound and are not fully absorbed when ingested and passes through the digestive tract. However, in the absence of a reliable bioavailability study, EPA assumes that all of the arsenic is bioavailable. This is a conservative assumption and produces a very safe soil cleanup level.

The panel believes that risk assessment and risk management decisions should be conducted on a site-specific, not one size fits all, basis and should incorporate all available and relevant scientific information to achieve this objective.

EPA agrees that site specific information should be used when practical, especially if the situation is unique. However, when the situation is not unique, there is substantial merit to having standardized risk assessment methodologies and assumptions. For example, it would be expensive, redundant and unnecessary to do studies of childrens' soil ingestion rates at each site, since there is no reason to believe that they would vary substantially or on a consistent basis from national averages. EPA conservatively uses assumptions to afford protection under conditions of a reasonable maximum exposure, and uses a rate for ingestion that is sufficiently protective of even highly exposed children. The same approach is true regarding the 30 year duration of exposure. It could be argued that the typical duration of exposure in Spring Valley is much less, but again, someone *could* live in Spring Valley for 30 years and EPA chooses conservative exposure inputs to protect such individuals.

EPA also seeks a large degree of national consistency in its risk assessment methodology as a matter of fairness; to do otherwise would invite continual litigation and accusations of arbitrary or preferential decisions. The risk assessment procedures used to determine safe soil cleanup levels at Spring Valley were calculated by using the standard EPA approach employed at all the Superfund and Resource Conservation and Recovery Act (RCRA) hazardous waste sites across the United States. Most states have accepted in whole or have adopted and modified these risk assessment methodologies for application in their states. The procedures, assumptions of risk assessment and the toxicology of compounds have been peer reviewed by academia and industry. The detailed description of EPA's Risk Assessment Guidance Summary (RAGS) can be found on the web at http://www.epa.gov/superfund/programs/risk/ragsd/index.htm. For members of the public who may be interested in EPA's response to the SVSAP, EPA has attached a document titled "Superfund Risk Assessment Made Simple", which explains EPA's procedures and general assumptions.

Two parameters which can be important site specific factors in determining the appropriate cleanup level, are arsenic bioavailability and the species of arsenic present. Unfortunately, it is very difficult to determine the arsenic species present and only a handful of labs have demonstrated this capability. The U.S. Army Corps of Engineers (USACE) submitted a sample for analysis over one year ago, but the results were unusable. Additionally, because determining the species is so difficult, EPA has not developed separate toxicity factors for different arsenic species. Another problem is that unlike a copper foundry where arsenic may be present, there were numerous chemical warfare agents at Spring Valley the species may vary at different locations of the site.

Determining the bioavailability of arsenic requires properly conducted studies, but has been done successfully at other Superfund Sites. Modification of cleanup goals and toxicity based on bioavailability is scientifically sound and is fully acceptable to the EPA. However, EPA's toxicologists will only accept data from relatively long-term experimental studies conducted in

juvenile swine; these studies in young pigs mimic the human digestive system in terms of absorption. Several different chemical methods have been developed and then correlated with the results of animal studies. However, the correlation has not been strong enough for EPA's toxicologists to accept the results of such studies. EPA was not consulted in the development of the bioavailability study performed using Spring Valley soils, and when the report was circulated in the Fall of 2001, EPA was not supplied a copy on which to comment. The report was supplied to EPA just this month and was reviewed by our senior toxicologist. EPA concluded that the bioavailability study performed using Spring Valley soils did not rely on EPA-approved methods and had substantial data and quality assurance problems which rendered the results unusable. Also, as stated in the previous paragraph, an additional problem is that the bioavailability may vary dramatically from location-to-location at Spring Valley, because the arsenic may be due to different parent chemicals used in testing - unlike a copper foundry where the arsenic species will generally be the same across the site. To conduct a bioavailability study with enough samples from different site locations to bracket the possible bioavailabilities present at the site might not be cost effective. Additionally, to conduct such a study would require a substantial delay in the site cleanup while the tests were planned, completed and reviewed.

The paramount consideration for the remediation of the Spring Valley neighborhood should be the management of overall risk to human health, present and future.

EPA agrees, and would like to detail its rationale for the selection of 20 ppm as the appropriate soil cleanup level for the Spring Valley Site.

1) BACKGROUND - EPA is prohibited under the Superfund law from remediating a site to levels below background conditions. The average background level at the Spring Valley Site is about 5 ppm. The upper predicted limit for arsenic background at Spring Valley is about 13 ppm. These levels are based on studies performed by EPA using full QA/QC and were calculated by a statistician. The Corps of Engineers performed a simplistic standard deviation calculation using a different data base and came up with a very similar 95% confidence limit of 12.6 ppm and a 98% confidence limit of about 18 ppm. A more detailed discussion of background levels is contained in a memo to EPA's site file titled: "Determination of Arsenic Background Levels, Spring Valley - DC Munitions" (attached). The upper level of natural background sets a "floor", below which EPA cannot support remediation.

2) RISK - When EPA selects a remedy at a Superfund Site, EPA guidance urges Remedial Project Managers (RPMs) to consider remediation of contaminants to a 10-6 level, or one incremental cancer in a million people exposed. Based on site-specific factors, EPA may choose a contaminant level which is within the cancer risk range of 1x10-4 (43 ppm) to 1x10-6 (0.43 ppm). In other words, in terms risk considerations, EPA is instructed by law to try to select an arsenic cleanup level of 0.43 ppm if practical, but can allow a concentration as high as 43 ppm under some circumstances. This set of criteria is for carcinogenic risk only.

The second risk based consideration of risk is not related to cancer, but to the toxicity of arsenic to organ systems. The arsenic concentration in soil at which no harm (other than cancer) would

be expected is 23 ppm. This means that concentrations above 23 ppm could pose a non-cancer risk to some individuals.

Therefore, 13 ppm forms a floor for remediation based on background considerations at the site, while 23 ppm is a ceiling above which harm could occur. A level of 20 ppm is above EPA's calculation of the high end of background (13 ppm) and is even above the Corps' calculation of the 98% confidence level of 18 ppm. 18ppm was also the highest individual arsenic result in the background study. EPA is confident that at a cleanup level of 20 ppm, the USACE will not be remediating any areas below site background. Additionally, with 20 ppm as a cleanup goal, only safe arsenic levels for both carcinogenic risk and systemic risk will be left in site soils.

3) REGULATORY PRECEDENT - Several large states have set a soil cleanup level of 20 ppm, including New Jersey, Washington State, and Texas. These states have had to address widespread arsenic problems in their states and have experience addressing arsenic contamination. The only other large "arsenic" site in EPA - Region 3 is Whitmoyer Labs, which produced pesticides. The soil cleanup at Whitmoyer for residential use was 21 ppm. An internet survey of arsenic cleanup levels shows that 20 ppm is a common soil goal under conditions of residential exposure.

Dr. Lamm discussed arsenic cleanup levels in his presentation to the Spring Valley community. He cited the fact that at the ASARCO Site, a cleanup level of 230 ppm was selected for residential areas, with bioavailability playing an important role in the selection. This is accurate, but there are other factors that also influenced the selection of this cleanup level. Contamination was very widespread and ASARCO had other large environmental liabilities. Although 230 ppm was the level at which soil would be removed, institutional controls were employed at residences with arsenic levels above 20 ppm. Even at the ASARCO Site, 20 ppm was the cleanup level at which ***no additional controls were needed.***

Recommendation Two

The panel recommends that the agencies collect information on arsenic and related contaminants in household dust and debris in a selected number of Spring Valley homes.

Dust sampling in homes and interior sampling will be conducted by technical assistance to the DC Department of Health by the Agency for Toxic Substances and Disease Registry (ATSDR).

Recommendation Three

This recommendation is directed to the ATSDR and is in their area of expertise.

REPORT OF THE
DISTRICT OF COLUMBIA MAYOR'S
SPRING VALLEY SCIENTIFIC ADVISORY PANEL

INTRODUCTION

The second meeting of the Spring Valley Scientific Advisory Panel was held on December 7, 2001 in Washington, DC under the authority of the District of Columbia Mayor's Order 2001-32 (March 1, 2001).

The objective of the meeting was to review the progress of the District of Columbia Department of Health and the U.S. Army Corps of Engineers in characterizing and ameliorating the risk of potential adverse health effects resulting from human exposure to contaminants from World War I chemical weapons testing in the Spring Valley neighborhood located in the northwestern quadrant of the District of Columbia.

At it first meeting held in April 2001, the panel made several recommendations designed to expand the base of data/information on potential exposure to contaminants of interest, and evidence of health effects based on comparative epidemiological analysis (exposed versus unexposed population). The effect of concern was cancers for which there is evidence of arsenic as a risk factor. The panel also recommended that attention be given to risk communication including activities designed to enhance the Spring Valley residents' knowledge of process and procedures for assessing potential health impacts of exposure to chemicals released in the environment. The panel's recommendations provided the frame of reference for the presentations given at the December 7, 2001 meeting as listed in the agenda, which is attached. The detailed text of each presentation is on record, and available for public review in the Office of the Executive Director of the Mayor's Spring Valley Scientific Advisory Panel. In summary, the agencies have made substantial progress in "complying" with the panel's recommendation.

Potential Exposure Assessment

In determining the potential exposure, the U.S. Army Corps of Engineers has identified over 130 properties/lots for grid sampling and to date have sampled over 50 of these sites beginning in September of 2001. Given the trigger rate for additional sampling of 12%, the U.S. Army Corps of Engineers expects to have a grid-sample for nearly 200 properties.

Risk Management

Looking toward remediation of contaminated properties the U.S. Army Corps of Engineers discussed three different approaches to developing site wide remediation goals.

Option 1 – Hazard Based Remediation

0-2' feet of surface soil would be removed if:

(a) Exposure Point Concentration (EPC) $\geq$ 23.5ppm, the U.S. Army Corps of Engineers will clean the entire lot to background.

(b) Exposure Point Concentration (EPC) $\leq$ 23.5ppm, the U.S. Army Corps of Engineers will remove grid points $\geq$ 23.5.

Below 2' feet of subsurface soil would be removed if:

(a) Exposure Point Concentration (EPC) $\geq$ 41.4ppm, the U.S. Army Corps of Engineers will remove subsurface soil

Option 2 – Bioavailability-Based Remediation

0-2' feet of surface soil would be removed if:

(a) Exposure Point Concentration (EPC) $\geq$ 47ppm, the U.S. Army Corps of Engineers will clean the entire lot to background.

(b) Exposure Point Concentration (EPC) $\leq$ 47ppm, the U.S. Army Corps of Engineers will remove grid points $\geq$ 26.

Below 2' feet of subsurface soil would be removed if:

(a) Exposure Point Concentration (EPC) $\geq$ 56ppm (SPLP derived soil-to-groundwater protection level), the U.S. Army Corps of Engineers will remove subsurface soil

Option 3 -- Background-Based Remediation

0-2' feet of surface soil would be removed if:

(a) Exposure Point Concentration (EPC) $\geq$ 20ppm, the U.S. Army Corps of Engineers will remove all grid points

Below 2' feet of subsurface soil would be removed if:

(a) Exposure Point Concentration (EPC) $\geq$ 41.4ppm, the U.S. Army Corps of Engineers will remove subsurface soil

The Environmental Protection Agency's proposed arsenic cleanup level for soil is 20ppm, with no depth limitation. The cleanup level considers such factors as:

- 20ppm is slightly below the non-carcinogenic health effects level of 23.5ppm (HI = 1)
- It is within the EPA's cancer risk range (.43 to 43ppm)
- It is above background, so the U.S. Army Corps of Engineers wouldn't be cleaning up background arsenic
- 20ppm has been used as cleanup level in other states

Epidemiological Analysis

Responding to the panel's recommendation concerning epidemiological analysis of cancers for which exposure to arsenic is a risk factor, the District of Columbia Department of Health presented data that showed no excess cancer incidence and mortality in the Spring Valley neighborhood during 1987–1998 compared with U.S. populations in the Surveillance, Epidemiology and End Results (SEER) Program. SEER is an ongoing contract-supported program of the National Cancer Institute of the National Institutes of Health. It coordinates the collection of cancer data in population-based cancer registries located throughout the United States.

Comparing the Spring Valley ("exposed") neighborhood with Potomac, Maryland ("unexposed"), a community with a similar demographic profile, the analysis found no difference in cancer incidence and mortality rates. Limitations of the analysis – small number of cases – were reported.

Dr. Steven Lamm, an epidemiology and occupational health consultant for the U.S. Army Corps of Engineers, presented an epidemiological analysis of the health effects of arsenic. It included a basic overview of arsenic (chemistry and biology) and a recitation of known health effects. Dr. Lamm concluded that based on a hypothesized exposure levels to arsenic in the Spring Valley neighborhood the risk of adverse health effects is "low to zero". Dr. Lamm made a similar presentation to the members of the Spring Valley community, and his report was made available to the Spring Valley Scientific Advisory Panel for review.

Exposure Assessment

As indicated earlier, the U.S. Army Corps of Engineers' soil sampling and analysis program is underway. These measurements will define potential exposure. Actual exposure measurements, testing biological materials, specifically hair and urine, will be conducted by the Agency for Toxic Substance and Disease Registry (ATSDR). The draft protocol for this assessment was presented to the panel.

PANEL COMMENTS AND RECOMMENDATIONS

The panel commends the efforts underway to address some of the scientific and health-related questions raised by the "discovery" of World War I chemical warfare agents in the Spring Valley neighborhood. The panel is also aware of the challenges in assessing the potential adverse effects of environmental chemicals and materials on human health.

A fundamental challenge in environmental health is relating the presence of a chemical or other contaminant with a valid prediction of ensuing hazards to potential biological (human) receptors. Adverse health effects in humans begin with exposure. No matter how hazardous an environmental toxicant is, without exposure there is no risk. Exposure can occur as a result of contact with a variety of elements (i.e., air, water, soil) that in turn influences the pathways of exposure (i.e., inhalation, ingestion, dermal) and may progress to damage of, or alteration in, the function of organs (i.e., lung, bladder, liver). Individuals' interactions with these elements are complex; and therefore it is not surprising that exposure assessment and dose estimation are formidable challenges to those investigating the health effects of environmental contaminants.

It bears repeating that individuals' exposure may be modified by factors such as activity patterns, which determine encounters with the sources of exposure; and the bioavailability of the agent in time and place (only a portion of the total quantity of a chemical or contaminant present in the environment is potentially available for uptake by individuals. This concept is referred to as biological availability or bioavailability.). The rate at which exposure occurs may also be a modifying factor. From a given exposure, a person's resultant dose – the amount of contaminant transferred to the exposed individual – will depend on host characteristics such as age, gender, occupation and proximity to source (time spent indoors versus out).

In summary, many types of variabilities enter into the risk assessment process: variability within individuals, among individuals, and among population groups. Types of variability include the nature and the intensity of exposure and susceptibility to toxic insults, related to age, gender and other factors. Infants and children are often considered more susceptible to the adverse effects of toxic contaminants. Referring to exposure to arsenic (a chemical of concern to the Spring Valley residents) in the drinking water, the Subcommittee on Arsenic in the Drinking Water for the National Research Council, National Academy of Sciences, concludes that it is unclear whether infants and young children might be more susceptible to arsenic-induced health effects, particularly those effects for non-cancer endpoints where less-than-lifetime exposures are important, and where children's greater water consumption per unit of body weight might put them at relatively greater risk. The Subcommittee states that more data are needed to better understand the susceptibility of children to arsenic-induced toxicity, particularly for non-cancer effects.

There are also issues of uncertainty – the lack of knowledge of the underlying science. There are numerous gaps in scientific knowledge regarding arsenic and other contaminants. Hence, there may be uncertainties in risk assessment. For instance, there

is little evidence of the level and species of arsenic consumed by different individuals and populations, and the role of arsenic in food remains somewhat uncertain.

In assessing the risk of arsenic and numerous other environmental contaminants, it is difficult, if not impossible, to entirely rule out the possibility that genetics, lifestyle differences such as smoking, food preference, cooking habits, and exposure to other environmental factors might play a role in explaining variability in the risks. In addition, human populations are exposed to multiple pollutants whose individual, let alone, joint effects are not known. To date, toxicology has remained primarily the science of individual toxicants, even though people are rarely, if ever, affected by a single agent in isolation from other agents that might influence risk. Understanding risks from simultaneous or sequential exposure to multiple agents, particularly at low levels of exposure, is a challenge to the health sciences (i.e., toxicology, epidemiology).

The sum vector of the challenges cited in the preceding paragraphs is a clear indication that risk characterization should present the state of knowledge, uncertainty and disagreements about the risk situation to reflect the range of relevant knowledge and perspectives. An accurate and balanced synthesis must treat the limits of scientific knowledge with an appropriate analytic process.

The Lamm Report

It is in this setting that the panel acknowledges and commends the progressive efforts of Dr. Lamm to enhance the awareness of the Spring Valley residents of the health effects of exposure to arsenic and related risk assessment parameters. Dr. Lamm's report attempts to address significant concerns of members of the community and to make the information understandable. However, the review inadequately describes the risks (and their accompanying uncertainties) that have been linked with exposure to inorganic arsenic in several populations. Findings of the report could well lead to the mistaken conclusion that some populations with demonstrated exposure may be at low or minimal risk.

The panel commends Dr. Lamm for the inclusion in his review of most of the important, well documented affects of arsenic. In addition, two important health effects of arsenic with highly suggestive, but preliminary information should also be included. These, specifically, are cardiovascular effects and diabetes. There is reference made to 'blackfoot disease', which results from effects of arsenic on the vascular system, but more information is available on other, related cardiovascular effects such as blood pressure (Rahman et al, 1999). Two suggestive studies of excess diabetes from southwest Taiwan are available and should be cited (Tsai et al, 1999; Tseng et al, 2000).

A general weakness of the report is the omission of data on dose-response relationships. In fact, it is this type of data that provides the basis for concluding that arsenic is a carcinogen of the skin, bladder, lung, and possibly other organs. The Lamm report indicated studies in the United States have not demonstrated a cancer risk

from exposure to drinking water. This is not accurate. Studies by Lewis (1999), Karagas (2001), and Bates (1995) have found elevated risk for one or another cancers either in the full study population or important subgroups. In addition, this statement must be carefully qualified. In fact, there have been no well conducted, large scale studies conducted in the US of populations exposed to arsenic in drinking water, and therefore it would not be surprising if none of the completed studies had observed elevated cancer risks. The studies cited above either were small or have other important methodological limitations. There are no data available from large, well-conducted studies in the United States that address the question of arsenic in drinking water and cancer risk. There is no reason to believe that the United States population differs in its susceptibility profile from populations in Chile, Argentina, or Taiwan where excess risk for several cancers has been observed after long-term exposure to waterborne arsenic at higher levels than are typical in the United States.

In addressing the risk of lung cancer from arsenic exposure, the Lamm review indicates, "There are some recent studies that relate lung cancer to arsenic absorbed from the ingestion of arsenic-containing water." In fact, several studies, from Taiwan, Chile, and Argentina have demonstrated a dose-response link between water-borne arsenic and lung cancer. The recent NAS Subcommittee to Update the 1999 Arsenic in Drinking Water Report (2001) concluded, "the database of epidemiological studies linking arsenic in drinking water with increased risk of skin, bladder, and lung cancer provides a sound and adequate basis for quantitative assessment of cancer risk."

The report is correct in stating, "... with bladder cancer, most of the associated arsenic exposure are with water containing one-half to one milligram of arsenic per liter and daily dosages measured in milligrams". The exposures in many high-arsenic/high risk areas of the world that have been studied average about ½ mg/L (500 micrograms/L). What isn't mentioned is that risk of bladder cancer has been observed in a dose-dependent fashion down to arsenic exposures much lower than ½ mg/L (eg. Chiou et al. 2001).

While arsenic below 150 micrograms/L may not cause skin cancer, there is but a thin data base currently available to demonstrate this. The report cites a study from Inner Mongolia in this regard. Dr Lamm's Inner Mongolia study involved a cross-sectional examination of 3,228 individuals, and observed 8 skin cancers, all among persons with "peak" arsenic exposures greater than 150 micrograms/liter. With only eight observed cases of skin cancer, the lack of statistical stability in this study severely limits the conclusions that can be based on its findings. In addition, the use of "peak" arsenic levels to define exposure can result in an underestimate of risk.

Other panel concerns about the report include the lack of an association in the U.S. observed "between bladder or lung cancer and drinking waters with arsenic levels between 3 and 60 ppb (ug/L)." This may be as much a consequence of inadequate study methods or study size as of a true lack of association. Again, it would be premature to draw the conclusion that there is no risk of arsenic exposure at these levels, given the limitations of studies that have been completed to date.

In summary, the Lamm review of the health effects of arsenic covers many important and relevant aspects of the chemical's toxicity, both with respect to inhalation and ingestion. But the review is incomplete and does not present a balanced picture of what is known and what is unknown about the effects of arsenic exposure. The report would be much stronger, useful and interpretable if it were fully referenced *(the references are cited at the end of this report)*.

RECOMMENDATIONS

Based on the presentations, the panel's discussion, its experience, and desire for a comprehensive database on which to base conclusions, the following recommendations are made:

Recommendation One

The panel recommends that the Environmental Protection Agency provide the scientific underpinning, or health-risk rationale, for the recommended remediation level of 20ppm. The panel believes that risk assessment and risk management decisions should be conducted on a site-specific, not-one-size-fits-all, basis and should incorporate all available and relevant scientific information to achieve this objective. The paramount consideration for the remediation of the Spring Valley neighborhood should be the management of overall risk to human health, present and future.

Recommendation Two

The panel recommends that the agencies collect information on arsenic and related contaminants in household dust/debris in a selected number of Spring Valley homes.

The objective is to determine the extent to which household dust/debris may contain arsenic or other contaminants of concern. In other words, is household dust/debris a potential pathway for chronic exposure to environmental toxicant of concern to Spring Valley residents.

There are a number of strategies that may be employed, including the collection of vacuum cleaner content, to get a "clue" as to the potential contribution of household dust to the overall exposure. The panel is aware of the potential for selection bias in this voluntary self-selection approach to exposure assessment.

The panel emphasizes that this recommendation should not be interpreted as suggesting a comprehensive home audit, the tools for which have been developed by environmental health specialists to assist in the assessment of exposure. Rather the focus here is on a simple "indicator" of potential exposures in well-selected samples of living quarters.

Recommendation Three

The panel recommends a revision in the Agency for Toxic Substance and Disease Registry (ATSDR) protocol for biomonitoring of the potentially exposed population. The panel's primary concern is that the monitoring be conducted when the "study cohort" is likely to have maximum exposure such as outdoor activities (i.e. children playing the yard), which is usually in the warmer months. Evidence abounds that a person's activity pattern is the single most important determinant of environmental exposure to most pollutants.

The panel also suggests that the selection of individuals for biological monitoring of exposure be accomplished according to the following scheme:

1. Top 10 homes with children and a high level of arsenic on the property as identified by the U.S. Army Corps of Engineers' soil sampling and testing programs.

2. Top 10 homes without children and a high level of arsenic as identified by the U.S. Army Corps of Engineers' soil sampling and testing programs.

3. A 5-10% random sample of individuals in the remaining homes.

The panel believes that this scheme will provide data/information on a range of exposure scenarios and may enhance efforts to address questions and issues of concern to interested and affected parties, or decision makers.

This scheme along with other data should facilitate analysis, for risk characterization, which includes various ways of reasoning and drawing conclusions by systematically applying theories and methods from the relevant sciences.

References:

Chiou H-Y, Wei M-L, Tseng C-H, et al. Arsenic and cancers: A follow-up study of 8102 residents in a northeastern arseniasis endemic area in Taiwan. Am J Epidemiol 2000; 108: 847-51.

Ferreccio C, Gonzalez C, Milosavjlevic V, et al. Lung cancer and arsenic concentrations in drinking water in Chile. Epidemiology 2000;11: 673-9.

Karagas MR, Stukel TA, Morris JS, et al. Skin cancer risk in relation to toenail arsenic concentrations in a US population-based case-control study. Am J Epidemiol 2001;153: 559-65.

Lewis DR, Southwick JW, Ouellet-Hellstrom R, et al. Drinking water arsenic in Utah: A cohort mortality study. Environ Health Perspect 1999;107: 359-65.

Lubin JH, Pottern LM, Stone BJ, et al. Respiratory cancer in a cohort of copper smelter workers: results from more than 50 years of follow-up. Am J Epidemiol 2000;151: 554-65.

National Research Council: Subcommittee to Update the 1999 Arsenic in Drinking Water Report. Arsenic in Drinking Water: 2001 Update. 2001. Washington, D.C., National Academy Press.

Rahman M, Tondel M, Ahmad SA, et al. Hypertension and arsenic exposure in Bangladesh. Hypertension 1999;33: 74-8.

Tsai SM, Wang TN, Ko YC. Mortality for certain diseases in areas with high levels of arsenic in drinking water. Arch Environ Health 1999;54: 186-93.

Tseng CH, Tai TY, Chong CK, et al. Long-term arsenic exposure and incidence of non-insulin-dependent diabetes mellitus: a cohort study in arseniasis-hyperendemic villages in Taiwan. Environ Health Perspect 2000;108: 847-51.

Wu M-M, Kuo T-L, Hwang Y-H, et al. Dose-response relation between arsenic concentration in well water and mortality from cancers and vascular diseases. Am J Epidemiol 1989;130: 1123-32.

Arsenic, inorganic (CASRN 7440-38-2)

MAIN CONTENTS

0278

Arsenic, inorganic; CASRN 7440-38-2 (04/10/1998)

Health assessment information on a chemical substance is included in IRIS only after a comprehensive review of chronic toxicity data by U.S. EPA health scientists from several Program Offices and the Office of Research and Development. The summaries presented in Sections I and II represent a consensus reached in the review process. Background information and explanations of the methods used to derive the values given in IRIS are provided in the Background Documents.

STATUS OF DATA FOR Arsenic, inorganic

File First On-Line 02/10/1988

Category (section)	Status	Last Revised
Oral RfD Assessment (I.A.)	on-line	02/01/1993
Inhalation RfC Assessment (I.B.)	no data	
Carcinogenicity Assessment (II.)	on-line	04/10/1988

_I. Chronic Health Hazard Assessments for Noncarcinogenic Effects

_I.A. Reference Dose for Chronic Oral Exposure (RfD)

Substance Name -- Arsenic, inorganic
CASRN -- 7440-38-2
Last Revised -- 02/01/1993

The oral Reference Dose (RfD) is based on the assumption that thresholds exist for certain toxic effects such as cellular necrosis. It is expressed in units of mg/kg-day. In general, the RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. Please refer to the Background Document for an elaboration of these concepts. RfDs can also be derived for the noncarcinogenic health effects of substances that are also carcinogens. Therefore, it is essential to refer to other sources of information concerning the carcinogenicity of this substance. If the U.S. EPA has evaluated this substance for potential human carcinogenicity, a summary of that evaluation will be contained in

Section II of this file.

NOTE: There was not a clear consensus among Agency scientists on the oral RfD. Applying the Agency's RfD methodology, strong scientific arguments can be made for various values within a factor of 2 or 3 of the currently recommended RfD value, i.e., 0.1 to 0.8 ug/kg/day. It should be noted, however, that the RfD methodology, by definition, yields a number with inherent uncertainty spanning perhaps an order of magnitude. New data that possibly impact on the recommended RfD for arsenic will be evaluated by the Work Group as it becomes available. Risk managers should recognize the considerable flexibility afforded them in formulating regulatory decisions when uncertainty and lack of clear consensus are taken into account.

__I.A.1. Oral RfD Summary

Critical Effect	Experimental Doses*	UF	MF	RfD
Hyperpigmentation, keratosis and possible vascular complications	NOAEL: 0.009 mg/L converted to 0.0008 mg/kg-day	3	1	3E-4 mg/kg-day
Human Chronic oral exposure	LOAEL: 0.17 mg/L converted to 0.014 mg/kg-day			
Tseng, 1977; Tseng et al., 1968				

*Conversion Factors -- NOAEL was based on an arithmetic mean of 0.009 mg/L in a range of arsenic concentration of 0.001 to 0.017 mg/L. This NOAEL also included estimation of arsenic from food. Since experimental data were missing, arsenic concentrations in sweet potatoes and rice were estimated as 0.002 mg/day. Other assumptions included consumption of 4.5 L water/day and 55 kg bw (Abernathy et al., 1989). NOAEL = [(0.009 mg/L x 4.5 L/day) + 0.002 mg/day] / 55 kg = 0.0008 mg/kg-day. The LOAEL dose was estimated using the same assumptions as the NOAEL starting with an arithmetic mean water concentration from Tseng (1977) of 0.17 mg/L. LOAEL = [(0.17 mg/L x 4.5 L/day) + 0.002 mg/day] / 55 kg = 0.014 mg/kg-day.

__I.A.2. Principal and Supporting Studies (Oral RfD)

Tseng, W.P. 1977. Effects and dose-response relationships of skin cancer and blackfoot disease with arsenic. Environ. Health Perspect. 19: 109-119.

Tseng, W.P., H.M. Chu, S.W. How, J.M. Fong, C.S. Lin and S. Yeh. 1968. Prevalence of skin cancer in an endemic area of chronic arsenicism in Taiwan. J. Natl. Cancer Inst. 40: 453-463.

The data reported in Tseng (1977) show an increased incidence of blackfoot disease that increases with age and dose. Blackfoot disease is a significant adverse effect. The prevalences (males and females combined) at the low dose are 4.6 per 1000 for the 20-39 year group, 10.5 per 1000 for the 40-59 year group, and 20.3 per 1000 for the >60 year group. Moreover, the prevalence of blackfoot disease in each age group increases with increasing dose. However, a recent report indicates that it may not be strictly due to arsenic exposure (Lu, 1990). The data in Tseng et al. (1968) also show increased incidences of hyperpigmentation and keratosis with age. The overall prevalences of hyperpigmentation and keratosis in the exposed groups are 184 and 71 per 1000, respectively. The text states that the incidence increases with dose, but data for the individual doses are not shown. These data show that the skin lesions are the more sensitive endpoint. The low dose in the Tseng (1977) study is considered a LOAEL.

The control group described in Tseng et al. (1968; Table 3) shows no evidence of skin lesions and presumably blackfoot disease, although this latter point is not explicitly stated. This group is considered a NOAEL.

The arithmetic mean of the arsenic concentration in the wells used by the individuals in the NOAEL group is 9 ug/L (range: 1-17 ug/L) (Abernathy et al., 1989). The arithmetic mean of the arsenic concentration in the wells used by the individuals in the LOAEL group is 170 ug/L (Tseng, 1977; Figure 4). Using estimates provided by Abernathy et al. (1989), the NOAEL and LOAEL doses for both food and water are as follows: LOAEL- [170 ug/L x 4.5 L/day + 2 ug/day (contribution of food)] x (1/55 kg) = 14 ug/kg/day; NOAEL - [9 ug/L x 4.5 L/day + 2 ug/day (contribution of food)] x (1/55 kg) = 0.8 ug/kg/day.

Although the control group contained 2552 individuals, only 957 (approximately 38%) were older than 20, and only 431 (approximately 17%) were older than 40. The incidence of skin lesions increases sharply in individuals above 20; the incidence of blackfoot disease increases sharply in individuals above 40 (Tseng, 1968; Figures 5, 6 and 7). This study is less powerful than it appears at first glance. However, it is certainly the most powerful study available on arsenic exposure to people.

This study shows an increase in skin lesions, 22% (64/296) at the high dose vs. 2.2% (7/318) at the low dose. The average arsenic concentration in the wells at the high dose is 410 ug/L and at the low dose is 5 ug/L (Cebrian et al., 1983; Figure 2 and Table 1) or 7 ug/L (cited in the abstract). The average water consumption is 3.5 L/day for males and 2.5 L/day for females. There were about an equal number of males and females in the study. For the dose estimates given below we therefore assume an average of 3 L/day. No data are given on the arsenic exposure from food or the body weight of the participants (we therefore assume 55 kg). The paper states that exposure times are directly related to chronological age in 75% of the cases. Approximately 35% of the participants in the study are more than 20 years old (Figure 1).

Exposure estimates (water only) are: high dose - 410 ug/L x 3 L/day x (1/55 kg) = 22 ug/kg/day; low dose - 5-7 ug/L x 3 L/day x (1/55 kg) = 0.3-0.4 ug/kg/day.

The high-dose group shows a clear increase in skin lesions and is therefore designated a LOAEL. There is some question whether the low dose is a NOAEL or a LOAEL since there is no way of knowing what the incidence of skin lesions would be in a group where the exposure to arsenic is zero. The 2.2% incidence of skin lesions in the low-dose group is higher than that reported in the Tseng et al. (1968) control group, but the dose is lower (0.4 vs. 0.8 ug/kg/day).

The Southwick et al. (1983) study shows a marginally increased incidence of a variety of skin lesions (palmar and plantar keratosis, diffuse palmar or plantar hyperkeratosis, diffuse pigmentation, and arterial insufficiency) in the individuals exposed to arsenic. The incidences are 2.9% (3/105) in the control group and 6.3% (9/144) in the exposed group. There is a slight, but not statistically significant increase in the percent of exposed individuals that have abnormal nerve conduction (8/67 vs. 13/83, or 12% vs. 16% (Southwick et al., 1983; Table 8). The investigators excluded all individuals older than 47 from the nerve conduction portion of the study. These are the individuals most likely to have the longest exposure to arsenic.

Although neither the increased incidence of skin lesions nor the increase in abnormal nerve conduction is statistically significant, these effects may be biologically significant because the same abnormalities occur at higher doses in other studies. The number of subjects in this study was insufficient to establish statistical significance.

Table 3 (Southwick et al., 1983) shows the annual arsenic exposure from drinking water. No data are given on arsenic exposure from food or the body weight (assume 70 kg). Exposure times are not clearly defined, but are > 5 years, and dose groups are ranges of

exposure.

Exposure estimates (water only) are: dosed group - 152.4 mg/year x 1 year/365 days x (1/70) kg = 6 ug/kg/day; control group - 24.2 mg/year x year/365 days x (1/70) kg = 0.9 ug/kg/day.

Again because there are no data for a group not exposed to arsenic, there is some question if the control group is a NOAEL or a LOAEL. The incidence of skin lesions in this group is about the same as in the low-dose group from the Cebrian et al. (1983) study; the incidence of abnormal nerve conduction in the control group is higher than that from the low-dose group in the Hindmarsh et al. (1977) study described below. The control dose is comparable to the dose to the control group in the Tseng et al. (1968) and Hindmarsh et al. (1977) studies. The dosed group may or may not be a LOAEL, since it is does not report statisically significant effects when compared to the control.

This study shows an increased incidence of abnormal clinical findings and abnormal electromyographic findings with increasing dose of arsenic (Hindmarsh et al., 1977; Tables III and VI). However, the sample size is extremely small. Percentages of abnormal clinical signs possibly attributed to As were 10, 16, and 40% at the low, mid and high doses, respectively. Abnormal EMG were 0, 17 and 53% in the same three groups.

The exact doses are not given in the Hindmarsh et al. (1977) paper; however, some well data are reported in Table V. The arithmetic mean of the arsenic concentration in the high-dose and mid-dose wells is 680 and 70 ug/L, respectively. Figure 1 (Hindmarsh et al., 1977) shows that the average arsenic concentration of the low-dose wells is about 25 ug/L. No data are given on arsenic exposure from food. We assume daily water consumption of 2 liters and body weight of 70 kg. Exposure times are not clearly stated.

Exposure estimates (water only) are: low - 25 ug/L x 2 L/day x (1/70) kg = 0.7 ug/kg/day; mid - 70 ug/L x 2 L/day x (1/70) kg = 2 ug/kg/day; high -680 ug/L x 2 L/day x (1/70) kg = 19 ug/kg/day.

The low dose is a no-effect level for abnormal EMG findings. However, because there is no information on the background incidence of abnormal clinical findings in a population with zero exposure to arsenic, there is no way of knowing if the low dose is a no-effect level or another marginal effect level for abnormal clinical findings. The low dose is comparable to the dose received by the control group in the Tseng (1977) and Southwick et al. (1983) studies.

The responses at the mid dose do not show a statistically significant increase but are part of a statistically significant trend and are biologically significant. This dose is an equivocal NOAEL/LOAEL. The high dose is a clear LOAEL for both responses.

As discussed previously there is no way of knowing whether the low doses in the Cebrian et al. (1983), Southwick et al. (1983) and Hindmarsh et al. (1977) studies are NOAELs for skin lesions and/or abnormal nerve conduction. However, because the next higher dose in the Southwick and Hindmarsh studies only shows marginal effects at doses 3-7 times higher, the Agency feels comfortable in assigning the low doses in these studies as NOAELs.

The Tseng (1977) and Tseng et al. (1968) studies are therefore considered superior for the purposes of developing an RfD and show a NOAEL for a sensitive endpoint. Even discounting the people < 20 years of age, the control group consisted of 957 people that had a lengthy exposure to arsenic with no evidence of skin lesions.

The following is a summary of the defined doses in mg/kg-day from the principal and supporting studies:

1) Tseng (1977): NOAEL = 8E-4; LOAEL = 1.4E-2

2) Cebrian et al. (1983): NOAEL = 4E-4; LOAEL = 2.2E-2

3) Southwick et al. (1983): NOAEL = 9E-4; LOAEL = none (equivocal effects at 6E-3)

4) Hindmarsh et al., 1977: NOAEL = 7E-4; LOAEL = 1.9E-2 (equivocal effects at 2E-3)

__I.A.3. Uncertainty and Modifying Factors (Oral RfD)

UF -- The UF of 3 is to account for both the lack of data to preclude reproductive toxicity as a critical effect and to account for some uncertainty in whether the NOAEL of the critical study accounts for all sensitive individuals.

MF -- None

__I.A.4. Additional Studies/Comments (Oral RfD)

Ferm and Carpenter (1968) produced malformations in 15-day hamster fetuses via intravenous injections of sodium arsenate into pregnant dams on day 8 of gestation at dose levels of 15, 17.5, or 20 mg/kg bw. Exencephaly, encephaloceles, skeletal defects and genitourinary systems defects were produced. These and other terata were produced in mice and rats all at levels around 20 mg/kg bw. Minimal effects or no effects on fetal development have been observed in studies on chronic oral exposure of pregnant rats or mice to relatively low levels of arsenic via drinking water (Schroeder and Mitchner, 1971). Nadeenko et al. (1978) reported that intubation of rats with arsenic solution at a dose level of 25 ug/kg/day for a period of 7 months, including pregnancy, produced no significant embryotoxic effects and only infrequent slight expansion of ventricles of the cerebrum, renal pelves and urinary bladder. Hood et al. (1977) reported that very high single oral doses of arsenate solutions (120 mg/kg) to pregnant mice were necessary to cause prenatal fetal toxicity, while multiple doses of 60 mg/kg on 3 days had little effect.

Extensive human pharmacokinetic, metabolic, enzymic and long-term information is known about arsenic and its metabolism. Valentine et al. (1987) established that human blood arsenic levels did not increase until daily water ingestion of arsenic exceeded approximately 250 ug/day (approximately 120 ug of arsenic/L. Methylated species of arsenic are successively 1 order of magnitude less toxic and less teratogenic (Marcus and Rispin, 1988). Some evidence suggests that inorganic arsenic is an essential nutrient in goats, chicks, minipigs and rats (NRC, 1989). No comparable data are available for humans.

__I.A.5. Confidence in the Oral RfD

Study -- Medium
Database -- Medium
RfD -- Medium

Confidence in the chosen study is considered medium. An extremely large number of people were included in the assessment (> 40,000) but the doses were not well-characterized and other contaminants were present. The supporting human toxicity data base is extensive but somewhat flawed. Problems exist with all of the epidemiological studies. For example, the Tseng studies do not look at potential exposure from food or other source. A similar criticism can be made of the Cebrian et al. (1983) study. The U.S. studies are too small in number to resolve several issues. However, the data base does support the choice of NOAEL. It garners medium confidence. Medium confidence in the RfD follows.

__I.A.6. EPA Documentation and Review of the Oral RfD

Source Document -- This assessment is not presented in any existing U.S. EPA document.

This analysis has been reviewed by EPA's Risk Assessment Council on 11/15/1990. assessment was discussed by the Risk Assessment Council of EPA on 11/15/1990 and verified through a series of meetings during the 1st, 2nd and 3rd quarters of FY91.

Other EPA Documentation -- U.S. EPA, 1984, 1988

Agency Work Group Review -- 03/24/1988, 05/25/1988, 03/21/1989, 09/19/1989, 08/22/1990, 09/20/1990

Verification Date -- 11/15/1990

__I.A.7. EPA Contacts (Oral RfD)

Please contact the IRIS Hotline for all questions concerning this assessment or IRIS, in general, at (301)345-2870 (phone), (301)345-2876 (FAX) or Hotline.IRIS@epamail.epa.gov (internet address).

Back to top

_I.B. Reference Concentration for Chronic Inhalation Exposure (RfC)

Substance Name -- Arsenic, inorganic
CASRN -- 7440-38-2

Not available at this time.

Back to top

_II. Carcinogenicity Assessment for Lifetime Exposure

Substance Name -- Arsenic, inorganic
CASRN -- 7440-38-2
Last Revised -- 04/10/1998

Section II provides information on three aspects of the carcinogenic assessment for the substance in question; the weight-of-evidence judgment of the likelihood that the substance is a human carcinogen, and quantitative estimates of risk from oral exposure and from inhalation exposure. The quantitative risk estimates are presented in three ways. The slope factor is the result of application of a low-dose extrapolation procedure and is presented as the risk per (mg/kg)/day. The unit risk is the quantitative estimate in terms of either risk per ug/L drinking water or risk per ug/cu.m air breathed. The third form in which risk is presented is a drinking water or air concentration providing cancer risks of 1 in 10,000, 1 in 100,000 or 1 in 1,000,000. The rationale and methods used to develop the carcinogenicity information in IRIS are described in The Risk Assessment Guidelines of 1986 (EPA/600/8-87/045) and in the IRIS Background Document. IRIS summaries developed since the publication of EPA's more recent Proposed Guidelines for Carcinogen Risk Assessment also utilize those Guidelines where indicated (Federal Register 61(79):17960-18011, April 23, 1996). Users are referred to Section I of this IRIS file for information on long-term toxic effects other than carcinogenicity.

_II.A. Evidence for Human Carcinogenicity

II.A.1. Weight-of-Evidence Characterization

Classification -- A; human carcinogen

Basis -- based on sufficient evidence from human data. An increased lung cancer mortality was observed in multiple human populations exposed primarily through inhalation. Also, increased mortality from multiple internal organ cancers (liver, kidney, lung, and bladder) and an increased incidence of skin cancer were observed in populations consuming drinking water high in inorganic arsenic.

II.A.2. Human Carcinogenicity Data

Sufficient. Studies of smelter worker populations (Tacoma, WA; Magma, UT; Anaconda, MT; Ronnskar, Sweden; Saganoseki-Machii, Japan) have all found an association between occupational arsenic exposure and lung cancer mortality (Enterline and Marsh, 1982; Lee-Feldstein, 1983; Axelson et al., 1978; Tokudome and Kuratsune, 1976; Rencher et al., 1977). Both proportionate mortality and cohort studies of pesticide manufacturing workers have shown an excess of lung cancer deaths among exposed persons (Ott et al., 1974; Mabuchi et al., 1979). One study of a population residing near a pesticide manufacturing plant revealed that these residents were also at an excess risk of lung cancer (Matanoski et al., 1981). Case reports of arsenical pesticide applicators have also corroborated an association between arsenic exposure and lung cancer (Roth, 1958).

A cross-sectional study of 40,000 Taiwanese exposed to arsenic in drinking water found significant excess skin cancer prevalence by comparison to 7500 residents of Taiwan and Matsu who consumed relatively arsenic-free water (Tseng et al., 1968; Tseng, 1977). Although this study demonstrated an association between arsenic exposure and development of skin cancer, it has several weaknesses and uncertainties, including poor nutritional status of the exposed populations, their genetic susceptibility, and their exposure to inorganic arsenic from non-water sources, that limit the study's usefulness in risk estimation. Dietary inorganic arsenic was not considered nor was the potential confounding by contaminants other than arsenic in drinking water. There may have been bias of examiners in the original study since no skin cancer or preneoplastic lesions were seen in 7500 controls; prevalence rates rather than mortality rates are the endpoint; and furthermore there is concern of the applicability of extrapolating data from Taiwanese to the U.S. population because of different background rates of cancer, possibly genetically determined, and differences in diet other than arsenic (e.g., low protein and fat and high carbohydrate) (U.S. EPA, 1988).

A prevalence study of skin lesions was conducted in two towns in Mexico, one with 296 persons exposed to drinking water with 0.4 mg/L arsenic and a similar group with exposure at 0.005 mg/L. The more exposed group had an increased incidence of palmar keratosis, skin hyperpigmentation and hypopigmentation, and four skin cancers (histologically unconfirmed) (Cebrian et al. (1983). The association between skin cancer and arsenic is weak because of the small number of cases, small cohort size, and short duration follow-up; also there was no unexposed group in either town. No excess skin cancer incidence has been observed in U.S. residents consuming relatively high levels of arsenic in drinking water but the numbers of exposed persons were low (Morton et al., 1976; Southwick et al., 1981). Therapeutic use of Fowler's solution (potassium arsenite) has also been associated with development of skin cancer and hyperkeratosis (Sommers and McManus, 1953; Fierz, 1965); several case reports implicate exposure to Fowler's solution in skin cancer development (U.S. EPA, 1988).

Several follow-up studies of the Taiwanese population exposed to inorganic arsenic in drinking water showed an increase in fatal internal organ cancers as well as an increase in skin cancer. Chen et al. (1985) found that the standard mortality ratios (SMR) and cumulative mortality rates for cancers of the bladder, kidney, skin, lung and liver were significantly greater in the Blackfoot disease endemic area of Taiwan when compared

with the age adjusted rates for the general population of Taiwan. Blackfoot disease (BFD, an endemic peripheral artery disease) and these cancers were all associated with high levels of arsenic in drinking water. In the endemic area, SMRs were greater in villages that used only artesian well water (high in arsenic) compared with villages that partially or completely used surface well water (low in arsenic). However, dose-response data were not developed (Chen et al. 1985).

A retrospective case-control study showed a significant association between duration of consuming high-arsenic well water and cancers of the liver, lung and bladder (Chen et al., 1986). In this study, cancer deaths in the Blackfoot disease endemic area between January 1980 and December 1982 were chosen for the case group. About 90% of the 86 lung cancers and 95 bladder cancers in the registry were histologically or cytologically confirmed and over 70% of the liver cancers were confirmed by biopsy orà-fetoprotein presence with a positive liver x-ray image. Only confirmed cancer cases were included in the study. A control group of 400 persons living in the same area was frequency-matched with cases by age and sex. Standardized questionnaires of the cases (by proxy) and controls determined the history of artesian well water use, socioeconomic variables, disease history, dietary habits, and lifestyle. For the cancer cases, the age-sex adjusted odds ratios were increased for bladder (3.90), lung (3.39), and liver (2.67) cancer for persons who had used artesian well water for 40 or more years when compared with controls who had never used artesian well water. Similarly, in a 15-year study of a cohort of 789 patients of Blackfoot disease, an increased mortality from cancers of the liver, lung, bladder and kidney was seen among BFD patients when compared with the general population in the endemic area or when compared with the general population of Taiwan. Multiple logistic regression analysis to adjust for other risk factors including cigarette smoking did not markedly affect the exposure-response relationships or odds ratios (Chen et al., 1988).

A significant dose-response relationship was found between arsenic levels in artesian well water in 42 villages in the southwestern Taiwan and age-adjusted mortality rates from cancers at all sites, cancers of the bladder, kidney, skin, lung, liver and prostate (Wu et al., 1989). An ecological study of cancer mortality rates and arsenic levels in drinking water in 314 townships in Taiwan also corroborated the association between arsenic levels and mortality from the internal cancers (Chen and Wang, 1990).

Chen et al.(1992) conducted a recent analysis of cancer mortality data from the arsenic-exposed population to compare risk of various internal cancers and compare risk between males and females. The study area and population have been described by Wu et al. (1989). It is limited to 42 southwestern coastal villages where residents have used water high in arsenic from deep artesian wells for more than 70 years. Arsenic levels in drinking water ranged from 0.010 to 1.752 ppm. The study population had 898,806 person-years of observation and 202 liver cancer, 304 lung cancer, 202 bladder cancer and 64 kidney cancer deaths. The study population was stratified into four groups according to median arsenic level in well water (< 0.10 ppm, 0.10- 0.29 ppm, 0.30-0.59 ppm and 60+ ppm), and also stratified into four age groups (< 30 years, 30-49 years, 50-69 years and 70+ years). Mortality rates were found to increase significantly with age for all cancers and significant dose- response relationships were observed between arsenic level and mortality from cancer of the liver, lung, bladder and kidney in most age groups of both males and females. The data generated by Chen et al. (1992) provide evidence for an association of the levels of arsenic in drinking water and duration of exposure with the rate of mortality from cancers of the liver, lung, bladder, and kidney. Dose-response relationships are clearly shown by the tabulated data (Tables II-V of Chen et al., 1992). Previous studies summarized in U.S. EPA (1988) showed a similar association in the same Taiwanese population with the prevalence of skin cancers (which are often non-fatal). Bates et al. (1992) and Smith et al. (1992) have recently reviewed and evaluated the evidence for arsenic ingestion and internal cancers.

__II.A.3. Animal Carcinogenicity Data

Inadequate. There has not been consistent demonstration of carcinogenicity in test

animals for various chemical forms of arsenic administered by different routes to several species (IARC, 1980). Furst (1983) has cited or reviewed animal carcinogenicity testing studies of nine inorganic arsenic compounds in over nine strains of mice, five strains of rats, in dogs, rabbits, swine and chickens. Testing was by the oral, dermal, inhalation, and parenteral routes. All oxidation states of arsenic were tested. No study demonstrated that inorganic arsenic was carcinogenic in animals. Dimethylarsonic acid (DMA), the end metabolite predominant in humans and animals, has been tested for carcinogenicity in two strains of mice and was not found positive (Innes et al., 1969); however, this was a screening study and no data were provided. The meaning of non-positive data for carcinogenicity of inorganic arsenic is uncertain, the mechanism of action in causing human cancer is not known, and rodents may not be a good model for arsenic carcinogenicity testing. There are some data to indicate that arsenic may produce animal lung tumors if retention time in the lung can be increased (Pershagen et al., 1982, 1984).

__II.A.4. Supporting Data for Carcinogenicity

A retrospective cohort mortality study was conducted on 478 British patients treated between 1945-1969 with Fowler's solution (potassium arsenite). The mean duration of treatment was 8.9 months and the average total oral consumption of arsenic was about 1890 mg (daily dose x duration). In 1980, 139 deaths had occurred. No excess deaths from internal cancers were seen after this 20-year follow-up. Three bladder cancer deaths were observed (1.19 expected, SMR 2.5) (Cuzick et al., 1982). A recent follow-up (Cuzick et al., 1992) indicated no increased mortality from all cancers but a significant excess from bladder cancer (5 cases observed/1.6 expected; SMR of 3.07). A subset of the original cohort (143 persons) had been examined by a dermatologist in 1970 for signs of arsenicism (palmar keratosis). In 1990, there were 80 deaths in the subcohort and 11 deaths from internal cancers. All 11 subjects had skin signs (keratosis-10, hyperpigmentation-5 and skin cancer-3). A case-control study of the prevalence of palmar keratoses in 69 bladder cancer patients, 66 lung cancer patients and 218 hospital controls (Cuzick et al., 1984), indicated an association between skin keratosis (as an indicator of arsenic exposure) and lung and bladder cancer. Above the age of 50, 87% of bladder cancer patients and 71% of lung cancer patients but only 36% of controls had one or more keratoses. Several case reports implicate internal cancers with arsenic ingestion or specifically with use of Fowler's solution but the associations are tentative (U.S. EPA, 1988).

Sodium arsenate has been shown to transform Syrian hamster embryo cells (Dipaolo and Casto, 1979) and to produce sister chromatid-exchange in DON cells, CHO cells, and human peripheral lymphocytes exposed in vitro (Wan et al., 1982; Ohno et al., 1982; Larramendy et al., 1981; Andersen, 1983; Crossen, 1983). Jacobson-Kram and Montalbano (1985) have reviewed the mutagenicity of inorganic arsenic and concluded that inorganic arsenic is inactive or very weak for induction of gene mutations in vitro but it is clastogenic with trivalent arsenic being an order of magnitude more potent than pentavalent arsenic.

Both the pentavalent and trivalent forms of inorganic arsenic are found in drinking water. In both animals and humans, arsenate (As+5) is reduced to arsenite (As+3) and the trivalent form is methylated to give the metabolites mononomethylarsinic acid (MMA) and dimethylarsonic acid (DMA) (Vahter and Marafante, 1988). The genotoxicity of arsenate (As+5) and arsenite (As+3) and the two methylated metabolites, MMA and DMA were compared in the thymidine kinase forward mutation assay in mouse lymphoma cells (Harrington-Brock et al. 1993; Moore et al., 1995, in press). Sodium arsenite (+3) and sodium arsenate (+5) were mutagenic at concentration of 1-2 ug/mL and 10-14 ug/mL, respectively, whereas MMA and DMA were significantly less potent, requiring 2.5-5 mg/mL and 10 mg/mL, respectively, to induce a genotoxic response. Based on small colony size the mutations induced were judged chromosomal rather than point mutations. The authors have previously shown that for chemicals having clastogenic activity (i.e., cause chromosomal mutations), the mutated cells grow more slowly than cells with single gene mutations and this results in small colony size. In the mouse lymphoma assay, chromosomal abberations were seen at approximately the

same arsenic levels as TK forward mutations. Arsenate, arsenite and MMA were considered clastogenic but the abberation response with DMA was insufficient to consider it a clastogen. Since arsenic exerts its genotoxicity by causing chromosomal mutations, it has been suggested by the above authors that it may act in a latter stage of carcinogenesis as a progressor, rather than as a classical initiator or promotor (Moore et al., 1994). A finding which supports this process is that arsenate (8-16 uM) and arsenite (3 uM) have been shown to induce 2-10 fold amplification of the dihydrofolate reductase gene in culture in methotrexate resistant 3T6 mouse cells (Lee et al., 1988). Although the mechanism of induction in rodent cells is not known, gene amplification of oncogenes is observed in many human tumors. Inorganic arsenic has not been shown to mutate bacterial strains, it produces preferential killing of repair deficient strains (Rossman, 1981). Sodium arsenite (As+3) induces DNA-strand breaks which are associated with DNA-protein crosslinks in cultured human fibroblasts at 3 mM but not 10 mM (Dong and Luo, 1993) and it appears that arsenite inhibits the DNA repair process by inhibiting both excision and ligation (Jha et al., 1992; Lee-Chen et al., 1993).

The inhibitory effect of arsenite on strand-break rejoining during DNA repair was found to be reduced by adding glutathione to cell cultures (Huang et al., 1993). The cytotoxic effects of sodium arsenite in Chinese hamster ovary cells also has also found to correlate with the intracellular glutathione levels (Lee et al., 1989).

In vivo studies in rodents have shown that oral exposure of rats to arsenate (As+5) for 2-3 weeks resulted in major chromosomal abnormalities in bone marrow (Datta et al., 1986) and exposure of mice to As (+3) in drinking water for 4 weeks (250 mg As/L as arsenic trioxide) caused chromosomal aberrations in bone marrow cells but not spermatogonia (Poma et al., 1987); micronuclei in bone marrow cells were also induced by intraperitoneal dosing of mice with arsenate (DeKnudt et al., 1986; Tinwell et al., 1991). Chromosomal aberrations and sister chromatid exchange have been seen in patients exposed to arsenic from treatment with Fowler's solution (Burgdorf et al., 1977) and subjects exposed occupationally (Beckman et al., 1977) but no increase in either endpoint was seen in lymphocytes of subjects exposed to arsenic in drinking water (Vig et al., 1984).

Back to top

_II.B. Quantitative Estimate of Carcinogenic Risk from Oral Exposure

__II.B.1. Summary of Risk Estimates

Oral Slope Factor -- 1.5E+0 per (mg/kg)/day

Drinking Water Unit Risk -- 5E-5 per (ug/L)

Extrapolation Method -- Time- and dose-related formulation of the multistage model (U.S. EPA, 1988)

Drinking Water Concentrations at Specified Risk Levels:

Risk Level	Concentration
E-4 (1 in 10,000)	2E+0 ug/L
E-5 (1 in 100,000)	2E-1 ug/L
E-6 (1 in 1,000,000)	2E-2 ug/L

__II.B.2. Dose-Response Data (Carcinogenicity, Oral Exposure)

The Risk Assessment Forum has completed a reassessment of the carcinogenicity risk associated with ingestion of inorganic arsenic (U.S. EPA, 1988). The data provided in Tseng et al., 1968 and Tseng, 1977 on about 40,000 persons exposed to arsenic in drinking water and 7500 relatively unexposed controls were used to develop dose-response data. The number of persons at risk over three dose intervals and four exposure durations, for males and females separately, were estimated from the reported prevalence rates as percentages. It was assumed that the Taiwanese persons had a constant exposure from birth, and that males consumed 3.5 L drinking water/day and females consumed 2.0 L/day. Doses were converted to equivalent doses for U.S. males and females based on differences in body weights and differences in water consumption and it was assumed that skin cancer risk in the U.S. population would be similar to the Taiwanese population. The multistage model with time was used to predict dose-specific and age-specific skin cancer prevalance rates associated with ingestion of inorganic arsenic; both linear and quadratic model fitting of the data were conducted. The maximum likelihood estimate (MLE) of skin cancer risk for a 70 kg person drinking 2 L of water per day ranged from 1E-3 to 2E-3 for an arsenic intake of 1 ug/kg/day. Expressed as a single value, the cancer unit risk for drinking water is 5E-5 per (ug/L). Details of the assessment are in U.S. EPA (1988).

Dose response data have not been developed for internal cancers for the Taiwanese population. The data of Chen et al. (1992) are considered inadequate at present.

__II.B.3. Additional Comments (Carcinogenicity, Oral Exposure)

Eastern Research Group, under contract to EPA, convened an Expert Panel on Arsenic Carcinogenicity on May 21 and 22, 1997 (Eastern Research Group, 1997). The Expert Panel believed that, "it is clear from epidemiological studies that arsenic is a human carcinogen via the oral and inhalation routes (p. 20)." They also concluded, "that one important mode of action is unlikely to be operative for arsenic". The panel agreed that arsenic and its metabolites do not appear to directly interact with DNA (pp. 30-31)." In addition, the panel agreed that, "for each of the modes of action regarded as plausible, the dose-response would either show a threshold or would be nonlinear (p. 31)". The panel agreed, however, "that the dose-response for arsenic at low doses would likely be truly nonlinear, i.e., with a decreasing slope as the dose decreased. However, at very low doses such a curve might be linear but with a very shallow slope, probably indistinguishable from a threshold (p. 31)."

__II.B.4. Discussion of Confidence (Carcinogenicity, Oral Exposure)

This assessment is based on prevalence of skin cancer rather than mortality because the types of skin cancer studied are not normally fatal. However, competing mortality from Blackfoot disease in the endemic area of Taiwan would cause the risk of skin cancer to be underestimated. Other sources of inorganic arsenic, in particular those in food sources have not been considered because of lack of reliable information. There is also uncertainty on the amount of water consumed/day by Taiwanese males (3.5 L or 4.5 L) and the temporal variability of arsenic concentrations in specific wells was not known. The concentrations of arsenic in the wells was measured in the early 1960s and varied between 0.01 and 1.82 ppm. For many villages 2 to 5 analyses were conducted on well water and for other villages only one analysis was performed; ranges of values were not provided. Since tap water was supplied to many areas after 1966, the arsenic-containing wells were only used in dry periods. Because of the study design, particular wells used by those developing skin cancer could not be identified and arsenic intake could not be assigned except by village. Several uncertainties in exposure measurement reliability existed and subsequent analysis of drinking water found fluorescent substances in water that are possible confounders or caused synergistic effects. Uncertainties have been discussed in detail in U.S. EPA (1988). Uncertainties in exposure measurement can affect the outcome of dose- response estimation.

Back to top

_II.C. Quantitative Estimate of Carcinogenic Risk from Inhalation Exposure

__II.C.1. Summary of Risk Estimates

Inhalation Unit Risk -- 4.3E-3 per (ug/cu.m)

Extrapolation Method -- absolute-risk linear model

Air Concentrations at Specified Risk Levels:

Risk Level	Concentration
E-4 (1 in 10,000)	2E-2 per (ug/cu.m)
E-5 (1 in 100,000)	2E-3 per (ug/cu.m)
E-6 (1 in 1,000,000)	2E-4 per (ug/cu.m)

__II.C.2. Dose-Response Data for Carcinogenicity, Inhalation Exposure

Tumor Type -- lung cancer
Test animals -- human, male
Route -- inhalation, occupational exposure
Reference -- Brown and Chu, 1983a,b,c; Lee-Feldstein, 1983; Higgins, 1982; Enterline and Marsh, 1982

Ambient Unit Risk Estimates (per µg/cu.m)				
Exposure Source	Study	Unit	Geometric Mean Unit Risk	Final Estimated Geometric Mean Unit Risk
Anaconda smelter	Brown and Chu Lee-Feldstein Higgins et al.	1.25E-3 2.80E-3 4.90E-3	2.56E-3	4.29E-3
ASARCO smelter	Enterline & Marsh	6.81E-3 7.60E-3	7.19E-3	4.29E-3

__II.C.3. Additional Comments (Carcinogenicity, Inhalation Exposure)

A geometric mean was obtained for data sets obtained with distinct exposed populations (U.S. EPA, 1984). The final estimate is the geometric mean of those two values. It was assumed that the increase in age-specific mortality rate of lung cancer was a function only of cumulative exposures.

The unit risk should not be used if the air concentration exceeds 2 ug/cu.m, since above this concentration the unit risk may not be appropriate.

__II.C.4. Discussion of Confidence (Carcinogenicity, Inhalation Exposure)

Overall a large study population was observed. Exposure assessments included air measurements for the Anaconda smelter and both air measurements and urinary arsenic for the ASARCO smelter. Observed lung cancer incidence was significantly increased over expected values. The range of the estimates derived from data from two different exposure areas was within a factor of 6.

Back to top

_II.D. EPA Documentation, Review, and Contacts (Carcinogenicity Assessment)

__II.D.1. EPA Documentation

U.S. EPA. 1984, 1988, 1993

A draft of the 1984 Health Assessment Document for Inorganic Arsenic was independently reviewed in public session by the Environmental Health Committee of the U.S. EPA Science Advisory Board on September 22-23, 1983. A draft of the 1988 Special Report on Ingested Inorganic Arsenic; Skin Cancer; Nutritional Essentiality was externally peer reviewed at a two-day workshop of scientific experts on December 2-3, 1986. A draft of the Drinking Water Criteria Document for Arsenic was reviewed by the Drinking Water Committee of the U.S. EPA Science Advisory Board on March 10, 1993. The comments from these reviews were evaluated and considered in the revision and finalization of these reports.

__II.D.2. EPA Review (Carcinogenicity Assessment)

Agency Work Group Review -- 01/13/1988, 12/07/1989, 02/03/1994

Verification Date -- 02/03/1994

__II.D.3. EPA Contacts (Carcinogenicity Assessment)

Please contact the IRIS Hotline for all questions concerning this assessment or IRIS, in general, at (301)345-2870 (phone), (301)345-2876 (FAX) or Hotline.IRIS@epamail.epa.gov (internet address).

Back to top

_III. [reserved]
_IV. [reserved]
_V. [reserved]

_VI. Bibliography

Substance Name -- Arsenic, inorganic
CASRN -- 7440-38-2
Last Revised -- 04/10/1998

_VI.A. Oral RfD References

Abernathy, C.O., W. Marcus, C. Chen, H. Gibb and P. White. 1989. Office of Drinking Water, Office of Research and Development, U.S. EPA. Memorandum to P. Cook, Office of Drinking Water, U.S. EPA and P. Preuss, Office of Regulatory Support and Scientific Management, U.S. EPA. Report on Arsenic (As) Work Group Meetings. February 23.

Cebrian, M.E., A. Albores, M. Aguilar and E. Blakely. 1983. Chronic arsenic poisoning in the north of Mexico. Human Toxicol. 2: 121-133.

Ferm, V.H. and S.J. Carpenter. 1968. Malformations induced by sodium arsenate. J. Reprod. Fert. 17: 199-201.

Hindmarsh, J.T., O.R. McLetchie, L.P.M. Heffernan et al. 1977. Electromyographic abnormalities in chronic environmental arsenicalism. J. Analyt. Toxicol. 1: 270-276.

Hood, R.D., G.T. Thacker and B.L. Patterson. 1977. Effects in the mouse and rat of prenatal exposure to arsenic. Environ. Health Perspect. 19: 219-222.

Lu, F.J. 1990. Blackfoot disease: Arsenic or humic acid? The Lancet. 336: 115-116.

Marcus, W.L. and A.S. Rispin. 1988. Threshold carcinogenicity using arsenic as an example. In: Advances in Modern Environmental Toxicology, Vol. XV. Risk Assessment and Risk Management of Industrial and Evironmental Chemicals, C.R. Cothern, M.A. Mehlman and W.L. Marcus, Ed. Princeton Scientific Publishing Company, Princeton, NJ. p. 133-158.

Nadeenko, V.G., V. Lenchenko, S.B. Genkina and T.A. Arkhipenko. 1978. The influence of tungsten, molibdenum, copper and arsenic on the intrauterine development of the fetus. TR-79-0353. Farmakologiya i Toksikologiya. 41: 620-623.

NRC (National Research Council). 1989. Recommended Dietary Allowances, 10th ed. Report of the Food and Nutrition Board, National Academy of Sciences, Washington, National Academy Press, Washington, DC. 285 p.

Schroeder, H.A. and M. Mitchner. 1971. Toxic effects of trace elements on the reproduction of mice and rats. Arch. Environ. Health. 23(2): 102-106.

Southwick, J.W., A.E. Western, M.M. Beck, et al. 1983. An epidemiological study of arsenic in drinking water in Millard County, Utah. In: Arsenic: Industrial, Biomedical, Environmental Perspectives, W.H. Lederer and R.J. Fensterheim, Ed. Van Nostrand Reinhold Co., New York. p. 210-225.

Tseng, W.P. 1977. Effects and dose-response relationships of skin cancer and blackfoot disease with arsenic. Environ. Health Perspect. 19: 109-119.

Tseng, W.P., H.M. Chu, S.W. How, J.M. Fong, C.S. Lin and S. Yeh. 1968. Prevalence of skin cancer in an endemic area of chronic arsenicism in Taiwan. J. Natl. Cancer. Inst. 40(3): 453-463.

Valentine, J.L., L.S. Reisbord, H.K. Kang and M.D Schluchter. 1987. Arsenic effects on population health histories. In: Trace Elements in Man and Animals- TEMA 5, C.F. Mills, I. Bremner and J.K. Chesters, eds. Commonwealth Agricultural Bureaux, Aberdeen, Scotland.

U.S. EPA. 1984. Health Assessment Document for Inorganic Arsenic. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Research Triangle Park, NC. EPA 600/8-83-021F.

U.S. EPA. 1988. Quantitative Toxicological Evaluation of Ingested Arsenic. Office of Drinking Water, Washington, DC. (Draft)

Back to top

_VI.B. Inhalation RfD References

None

Back to top

_VI.C. Carcinogenicity Assessment References

Axelson, O., E. Dahlgren, C.D. Jansson and S.O. Rehnlund. 1978. Arsenic exposure and mortality: A case referent study from a Swedish copper smelter. Br. J. Ind. Med. 35: 8-15.

Andersen, O. 1983. Effects of coal combustion products and metal compounds on sister chromatid exchange (SCE) in a macrophage like cell line. Environ. Health Perspect. 47: 239-253.

Bates, M.N., A.H. Smith and C. Hopenhayn-Rich. 1992. Arsenic ingestion and internal cancers: A review. Am. J. Epidemiol. 135(5): 462-476.

Beckman, G., L. Beckman and I. Nordenson. 1977. Chromosome aberrations in workers exposed to arsenic. Environ. Health Perspect. 19: 145-146.

Brown, C.C. and K.C. Chu. 1983a. Approaches to epidemiologic analysis of prospective and retrospective studies: Example of lung cancer and exposure to arsenic. In: Risk Assessment Proc. SIMS Conf. on Environ. Epidemiol. June 28-July 2, 1982, Alta, VT. SIAM Publications.

Brown, C.C. and K.C. Chu. 1983b. Implications of the multistage theory of carcinogenesis applied to occupational arsenic exposure. J. Natl. Cancer Inst. 70(3): 455-463.

Brown, C.C. and K.C. Chu. 1983c. A new method for the analysis of cohort studies: Implications of the multistage theory of carcinogenesis appled to occupational arsenic exposure. Environ. Health Perspect. 50: 293-308.

Burgdorf, W., K. Kurvink and J. Cervenka. 1977. Elevated sister chromatid exchange rate in lymphocytes of subjects treated with arsenic. Hum. Genet. 36(1): 69-72.

Cebrian, M.E., A. Albores, M. Aquilar and E. Blakely. 1983. Chronic arsenic poisoning in the north of Mexico. Human Toxicol. 2: 121-133.

Chen, C-J. and C-J. Wang. 1990. Ecological correlation between arsenic level in well water and age-adjusted mortality from malignant neoplasms. Cancer Res. 50(17): 5470-5474.

Chen, C-J., Y-C. Chuang, T-M. Lin and H-Y. Wu. 1985. Malignant neoplasms among residents of a Blackfoot disease-endemic area in Taiwan: High-arsenic artesian well water and cancers. Cancer Res. 45: 5895-5899.

Chen, C-J., Y-C. Chuang, S-L. You, T-M. Lin and H-Y. Wu. 1986. A retrospective study on malignant neoplasms of bladder, lung, and liver in blackfoot disease endemic area in Taiwan. Br. J. Cancer. 53: 399-405.

Chen, C-J., M-M. Wu, S-S. Lee, J-D. Wang, S-H. Cheng and H-Y. Wu. 1988. Atherogenicity and carcinogenicity of high-arsenic artesian well water. Multiple risk

factors and related malignant neoplasms of Blackfoot disease. Arteriosclerosis. 8(5): 452-460.

Chen, C-J., CW. Chen, M-M. Wu and T-L. Kuo. 1992. Cancer potential in liver, lung bladder and kidney due to ingested inorganic arsenic in drinking water. Br. J. Cancer. 66 (5): 888-892.

Crossen, P.E. 1983. Arsenic and SCE in human lymphocytes. Mutat. Res. 119: 415-419.

Cuzick, J., S. Evans, M. Gillman and D.A. Price Evans. 1982. Medicinal arsenic and internal malignancies. Br. J. Cancer. 45(6): 904-911.

Cuzick, J., R. Harris, P.S. Mortimer. 1984. Palmar keratoses and cancers of the bladder and lung. March 10. The Lancet. 1(8376): 530-533.

Cuzick, J., P. Sasieni and S. Evans. 1992. Ingested arsenic, keratoses, and bladder cancer. Am. J. Epidemiol. 136(4): 417-421.

Datta, S., G. Talukder and A. Sharma. 1986. Cytotoxic effects of arsenic in dietary oil primed rats. Sci. Culture. 52: 196-198.

DeKnudt, G., A. Leonard, A. Arany, G.D. Buisson and E. Delavignette. 1986. In vivo studies in male mice on the mutagenic effects of inorganic arsenic. Mutagenesis. 1(1): 33-34.

DiPaolo, J.A. and B.C. Casto. 1979. Qantitative studies of in vitro morphological transformation of Syrian hamster cells by inorganic metal salts. Cancer Res. 39: 1008-1013.

Dong, J-T., X-M. Luo. 1993. Arsenic-induced DNA-strand breaks associated with DNA-protein crosslinks in human fetal lung fibroblasts. Mutat. Res. 302(2): 97-102.

Eastern Research Group. 1997. Report on the expert panel on arsenic carcinogenicity: review and workshop. Prepared by Eastern Research Group, Lexington, MA, for the National Center for Environmental Assessment, Washington, DC, under EPA contract no. 68-C6-0041.

Enterline, P.E. and G.M. Marsh. 1982. Cancer among workers exposed to arsenic and other substances in a copper smelter. Am. J. Epidemiol. 116(6): 895-911.

Fierz, U. 1965. Catamnestic investigations of the side effects of therapy of skin diseases with inorganic arsenic. Dermatologica. 131: 41-58.

Furst, A. 1983. A new look at arsenic carcinogenesis. In: Arsenic: Industrial, Biomedical, and Environmental Perspectives, W. Lederer and R. Fensterheim, Ed. Van Nostrand Reinhold, New York. p. 151-163.

Harrington-Brock, K., T.W. Smith, C.L. Doerr, and M.M. Moore. 1993. Mutagenicity of the human carcinogen arsenic and its methylated metabolites monomethylarsonic and dimethylarsenic acids in L5178Y TK+/- mouse lymphoma cells (abstract). Environ. Mol. Mutagen. 21(Supplement 22): 27.

Higgins, I. 1982. Arsenic and respiratory cancer among a sample of Anaconda smelter workers. Report submitted to the Occupatinal Safety and Health Administration in the comments of the Kennecott Minerals Company on the inorganic arsenic rulemaking. (Exhibit 203-5)

Higgins, I., K. Welch and C. Burchfield. 1982. Mortality of Anaconda smelter workers in relation to arsenic and other exposures. University of Michigan, Dept. Epidemiology, Ann Arbor, MI.

Huang, H., C.F. Huang, D.R. Wu, C.M. Jinn and K.Y. Jan. 1993. Glutathione as a cellular defence against arsenite toxicity in cultured Chinese hamster ovary cells. Toxicology. 79(3): 195-204.

IARC (International Agency for Research on Cancer). 1980. IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Man, Vol. 23. Some metals and metallic compounds. World Health Organization, Lyon, France.

Innes, J.R.M., B.M. Ulland, M.G. Valerio, et al. 1969. Bioassay of pesticides and industrial chemicals for tumorigenicity in mice: A preliminary note. JNCI. 42: 1101-1114.

Jacobson-Kram, D. and D. Montalbano. 1985. The reproductive effects assessment group's report on the mutagenicity of inorganic arsenic. Environ. Mutagen. 7(5): 787-804.

Jha, A.N., M. Noditi, R. Nilsson and A.T. Natarajan. 1992. Genotoxic effects of sodium arsenite on human cells. Mutat. Res. 284(2): 215-221.

Larramendy, M.L., N.C. Popescu and J.A. DiPaolo. 1981. Induction by inorganic metal salts of sister chromatid exchanges and chromosome aberrations in human and Syrian hamster strains. Environ. Mutagen. 3: 597-606.

Lee, Te-Chang, J. Ko and K.Y. Jan. 1989. Differential cytotoxocity of sodium arsenite in human fibroblasts and chinese hamster ovary cells. Toxicology. 56(3): 289-300.

Lee, Te-Chang, N. Tanaka, P.W. Lamb, T.M. Gilmer and J.C. Barrett. 1988. Induction of gene amplification by arsenic. Science. 241(4861): 79-81.

Lee-Chen, S.F., J.R. Gurr, I.B. Lin and K.Y. Jan. 1993. Arsenite enhances DNA double-strand breaks and cell killing of methyl methanesulfonate-treated cells by inhibiting the excision of alkali-labile sites. Mutat. Res. 294(1): 21-28.

Lee-Feldstein, A. 1983. Arsenic and respiratory cancer in man: Follow-up of an occupational study. In: Arsenic: Industrial, Biomedical, and Environmental Perspectives, W. Lederer and R. Fensterheim, Ed. Van Nostrand Reinhold, New York.

Mabuchi, K., A. Lilienfeld and L. Snell. 1979. Lung cancer among pesticide workers expsoed to inorganic arsenicals. Arch. Environ. Health. 34: 312-319.

Matanoski, G., E. Landau, J. Tonascia, et al. 1981. Cancer mortality in an industrial area of Baltimore. Environ. Res. 25: 8-28.

Moore, M.M., K. Harrington-Brock and C.L. Doerr. 1995. Genotoxicity of arsenic and its methylated metabolites. Mutagenesis and Cellular Toxicology Brance, Genetic Toxicology Dividion, Health Effects Research Laboratory, U.S. Environmental Protection Agency, Research Triangle Park, NC. (In press).

Morton, W., G. Starr, D. Pohl, J. Stoner, S. Wagner, and P. Weswig. 1976. Skin cancer and water arsenic in Lane County, Oregon. Cancer. 37: 2523-2532.

Ohno, H., F. Hanaoka and M. Yamada. 1982. Inductibility of sister chromatid exchanges by heavy-metal ions. Mutat. Res. 104(1-3): 141-146.

Ott, M.G., B.B. Holder and H.L. Gordon. 1974. Respiratory cancer and occupational exposure to arsenicals. Arch. Environ. Health. 29: 250-255.

Pershagen, G., B. Lind and N.E. Bjorklund. 1982. Lung retention and toxicity of some inorganic arsenic compounds. Environ. Res. 29: 425-434.

Pershagen, G., G. Norberg and N.E. Bjorklund. 1984. Carcinomas of the respiratory tract in hamsters given arsenic trioxide and/or benxo(a)pyrene by the pulmonary route. Environ. Res. 34: 227-241.

Poma, K., N. Degraeve and C. Susanne. 1987. Cytogenic effects in mice after chronic exposure to arsenic followed by a single dose of ethyl methanesulfonate. Cytologia. 52 (3): 445-450.

Rencher, A.C., M.W. Carter and D.W. McKee. 1977. A retrospective epidemiological study of mortality at a large western copper smelter. J. Occup. Med. 19(11): 754-758.

Rossman, T.G. 1981. Enhancement of UV-mutagenesis by low concentrations of arsenite in Escherichia coli. Mutat. Res. 91: 207-211.

Roth, F. 1958. Uber den Bronchialkrebs Arsengeschadigter Winzer. Virchows Arch. 331: 119-137.

Smith, A.H., C. Hopenhayn-Rich, M.N. Bates, et al. 1992. Cancer risks from arsenic in drinking water. Environ. Health Perspect. 97: 259-267.

Sommers, S.C. and R.G. McManus. 1953. Multible arsenical cancers of the skin and internal organs. Cancer. 6: 347-359.

Southwick, J., A. Western, M. Beck, et al. 1981. Community health associated with arsenic in drinking water in Millard County, Utah. Health Effects Research Laboratory, Cincinnati, OH. EPA-600/1-81-064.

Tinwell, H., S.C. Stephens, J. Ashby. 1991. Arsenite as the probable active species in the human carcinogenicity of arsenic: Mouse micronucleus assays on Na and K arsenite, orpiment, and Fowler's solution. Environ. Health Perspec. 95: 205-210.

Tokudome, S. and M. Kuratsune. 1976. A cohort study on mortality from cancer and other causes among workers at a metal refinery. Int. J. Cancer. 17: 310-317.

Tseng W.P., H.M. Chu, S.W. How, J.M. Fong, C.S. Lin, and S. Yen. 1968. Prevalence of skin cancer in an endemic area of chronic arsenicism in Taiwan. J. Natl. Cancer Inst. 40(3): 453-463.

Tseng W.P. 1977. Effects and dose-response relationships of skin cancer and Blackfoot disease with arsenic. Environ. Health Perspect. 19: 109-119.

U.S. EPA. 1984. Health Assessment Document for Inorganic Arsenic. Prepared by the Office of Research and Development, Environmental Criteria and Assessment Office, Reasearch Triangle Park, NC.

U.S. EPA. 1988. Special Report on Ingested Inorganic Arsenic; Skin Cancer; Nutritional Essentiality Risk Assessment Forum. July 1988. EPA/625/3-87/013.

U.S. EPA. 1993. Drinking Water Criteria Document for Arsenic. Office of Water, Washington, DC. Draft.

Vahter, M. and E. Marafante. 1988. In vivo methylation and detoxification of arsenic. Royal Soc. Chem. 66: 105-119.

Vig, B.K., M.L. Figueroa, M.N. Cornforth, S.H. Jenkins. 1984. Chromosome studies in human subjects chronically exposed to arsenic in drinking water. Am. J. Ind. Med. 6(5): 325-338.

Wan, B., R.T. Christian and S.W. Soukup. 1982. Studies of cytogenetic effects of sodium arsenicals on mammalian cells in vitro. Environ. Mutag. 4: 493-498.

Welch, K., I. Higgins, M. Oh and C. Burchfield. 1982. Arsenic exposure, smoking, and respiratory cancer in copper smelter workers. Arch. Environ. Health. 37(6): 325-335.

Wu, M-M., T-L. Kuo, Y-H Hwang and C-J. Chen. 1989. Dose-response relation between arsenic concentration in well water and mortality from cancers and vascular diseases. Am. J. Epidemiol. 130(6): 1123-1132.

Back to top

_VII. Revision History

Substance Name -- Arsenic, inorganic
CASRN -- 7440-38-2

Date	Section	Description
06/30/1988	II.B.	Revised last paragraph
06/30/1988	II.C.1.	Inhalation slope factor changed
06/30/1988	II.C.3.	Paragraph 2 added
09/07/1988	II.B.	Major text changes
12/01/1988	II.A.2.	Mabuchi et al. citation year corrected
12/01/1988	II.A.3.	Pershagen et al. citation year corrected
09/01/1989	II.C.2.	Citations added to anacondor smelter
09/01/1989	VI.	Bibliography on-line
06/01/1990	II.A.2.	2nd and 3rd paragraph - Text revised
06/01/1990	II.A.4.	Text corrected
06/01/1990	II.C.1.	Inhalation slope factor removed (format change)
06/01/1990	IV.F.1.	EPA contact changed
06/01/1990	VI.C.	References added
12/01/1990	II.B.	Changed slope factor to "unit risk", 2nd para, 1st sen
02/01/1991	II.C.3.	Text edited
09/01/1991	I.A.	Oral RfD summary now on-line
09/01/1991	I.A.	Oral RfD bibliography added
10/01/1991	I.A.1.	Conversion factor text clarified
10/01/1991	IV.B.1.	MCLG noted as pending change
01/01/1992	IV.	Regulatory actions updated
08/01/1992	II.	Note added to indicate text in oral quant. estimate
10/01/1992	VI.C.	Missing reference added to bibliography
02/01/1993	I.A.4.	Citations added to second paragraph
02/01/1993	VI.A.	References added to bibliography

03/01/1993	VI.A.	Corrections to references
03/01/1994	II.D.2.	Work group review date added
06/01/1994	II.	Carcinogen assessment noted as pending change
01/01/1995	II.	Pending change note revised
01/01/1995	II.B.	Dates and document no. added to oral quant. estimate
06/01/1995	II.	Carcinogenicity assessment replaced
06/01/1995	VI.C.	Carcinogenicity references replaced
07/01/1995	II.D.1.	Documentation year corrected; review statement revised
07/01/1995	VI.C.	U.S. EPA, 1994 corrected to 1993
08/01/1995	II.D.2.	EPA's RfD/RfC and CRAVE workgroups were discontinued in May, 1995. Chemical substance reviews that were not completed by September 1995 were taken out of IRIS review. The IRIS Pilot Program replaced the workgroup functions beginning in September, 1995.
04/01/1997	III., IV., V.	Drinking Water Health Advisories, EPA Regulatory Actions, and Supplementary Data were removed from IRIS on or before April 1997. IRIS users were directed to the appropriate EPA Program Offices for this information.
04/10/1998	II.B.3	Added discussion on expert panel workshop
02/11/2000	II.C.2	Corrected alignment of unit risks in table with corresponding studies

Back to top

_VIII. Synonyms

Substance Name -- Arsenic, inorganic
CASRN -- 7440-38-2
Last Revised -- 02/10/1988

7440-38-2
Arsenic
Arsenic, inorganic
gray-arsenic

Back to top

List of IRIS Substances

[Send Comments | What's New| Search IRIS]
[IRIS Home | NCEA Home | ORD Home | EPA Home]
URL: http://www.epa.gov/iris/subst/0278.htm
This page last updated: August 13, 2001

10-6-93

SUPERFUND RISK ASSESSMENT MADE SIMPLE

WHAT IS SUPERFUND? AN OVERVIEW

Superfund is EPA's program to clean up hazardous waste sites. Most of the sites in this program are abandoned or no longer active.

For each site, EPA tries to figure out the best solution. Some sites may look bad to begin with, but investigation reveals that there really is no danger to anyone. For example, people may have thought certain chemicals were dumped there, but this turns out not to be the case. Or the chemicals may have broken down into a harmless form. At some sites, EPA takes immediate action for urgent or emergency situations, and that immediate action may turn out to solve the problems of the site for good. At sites like these, EPA may decide that no action, or no further action, is appropriate.

At many other sites, EPA decides that an action is necessary. Sometimes the waste is burned in an incinerator to destroy the dangerous chemicals. Sometimes special bacteria are used to break down the waste into harmless products. Sometimes well water is filtered to remove the chemicals. EPA has many choices. To select the best one, EPA has to know:

Is the site polluted, or contaminated?

If so, what chemicals are at the site, where are they, and at what amounts?

What levels of these chemicals would be safe?

Risk assessment helps to answer some of these questions.

WHAT IS RISK ASSESSMENT?

Suppose we go to a site and take samples. We find that in every kilogram of soil (about 2.2 pounds), there are about 5000 milligrams (about 0.01 pounds) of lead. Since lead occurs in nature, and a certain amount of lead is usually found in most soils, how do we know whether this amount of lead is bad?

Risk assessment tries to answer questions like this by comparing the levels of chemicals found at the site to safe levels. The safe levels of chemicals are based on earlier scientific studies. Most of these studies use animals. However, some of the studies involve people (who may have been exposed to the chemical because it occurs naturally, or as the result of a chemical accident).

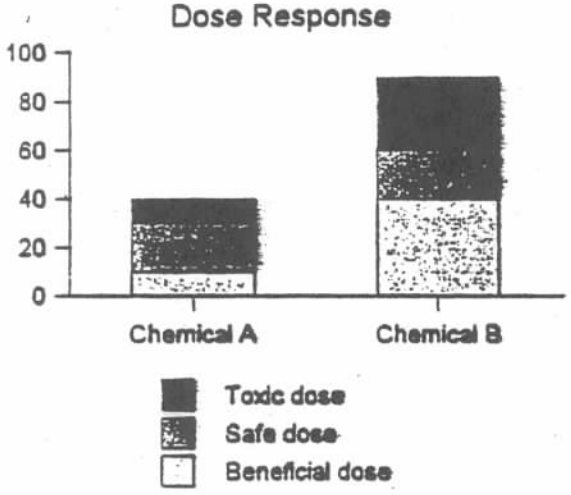
EPA is concerned about two types of dangers from chemicals: cancer and toxic effects other than cancer (such as liver disease or rashes).

Non-Cancer

For non-cancer effects, the level of chemical from the site is simply compared to the safe level. If the amount at the site is lower than the safe level, then EPA considers the risk to be acceptable.

If the amount at the site is higher than the safe level, there may be a cause for concern. However, this does not mean that people near the site would definitely be harmed. Above the safe level, there will

ultimately be a harmful level, but scientists can not usually pinpoint exactly where the harmful levels begin. Also, not every person reacts the same way to chemicals: the same level of chemical in two different people may cause symptoms in one person but not the other. (EPA's safe levels are designed to be safe even for sensitive people.) Because of these unknown factors, EPA's goal is to make sure that exposures stay at, or below, the safe level.



This graph shows the safe and toxic doses of two chemicals. Chemical A is actually helpful, or beneficial, up to a dose of about 10. Chemical B is beneficial up to a dose of about 40. The chemical dose is no longer helpful, but is not yet harmful, up to about 30 for Chemical A and 60 for chemical B. Above the safe dose, the toxic or dangerous dose starts.

Not every chemical has all three levels like this, however. Many chemicals do not have a beneficial dose. Some chemicals are not toxic until such high levels that it would be hard to actually take in a toxic amount; in a practical sense, they are non-toxic.

However, the graph does illustrate the basic ideas that are important to risk assessment. In reality, the line between the safe and toxic dose is not as sharp and clear as on the graph. EPA therefore tries to keep the dose of an environmental chemical somewhere within the middle gray zone, or the safe-dose range.

Advanced Concepts

HOW TO CALCULATE NON-CANCER RISK

The non-cancer evaluation can be expressed mathematically. If a person might receive a dose of 5 from a site, and the safe dose is 10, then the site dose divided by the safe dose is 0.5. EPA calls the safe dose a "Reference Dose," abbreviated RfD. The resulting answer, in this case 0.5, is called a "Hazard Quotient." (A quotient is the answer one gets after dividing numbers; the term "Hazard" is used to describe what we are measuring.) As an equation, this concept is written:

Dose from Site / Reference Dose = Hazard Quotient

Example:

5 / 10 = 0.5

In this example, we can see that the dose one would get from the site is not expected to be dangerous, since people would receive half of the safe dose. When the Hazard Quotient is less than 1, the safe dose has not yet been exceeded, and harm is not expected.

However, what if the site had more than one chemical? This is usually the case

at Superfund sites. The risk assessor would then evaluate a Hazard Quotient for each chemical, and would add them together to get a total "Hazard Index:"

Hazard Quotient #1 + Hazard Quotient #2 + Hazard Quotient #3 . . . + Hazard Quotient #n = Hazard Index

For example, if EPA found three chemicals at a site, each with a Hazard Quotient of 0.8, the Hazard Index would be 0.8 + 0.8 + 0.8 = 2.4. This is higher than the expected safe level of 1, so at first glance it appears that this site is potentially dangerous, and needs to be cleaned up. Indeed, this may be the case if all three chemicals harm the same part of the body.

If all three could injure the kidney, then it is right to add them, and the Hazard Index of 2.4 means that there is 2.4 times the safe dose to the kidney. However, if the first chemical causes a skin rash, the second chemical causes an upset stomach, and the third can injure the heart, it is not right to add the Hazard Quotients. There is not enough of chemical #1 to cause a skin rash, because only 80% of the safe dose is present. Chemicals 2 and 3 do not affect the skin at these levels, and therefore do not increase the overall risk of skin rash. Therefore, the Hazard Indexes for such a case might be expressed as follows:

Hazard Quotient for skin = 0.8
Hazard Quotient for stomach = 0.8
Hazard Quotient for heart = 0.8

Lead

Lead is an unusual chemical because scientists have not been able to identify the safe level with confidence. Very subtle changes in blood enzymes seem to be possible at low levels. For this reason, EPA's goal is to keep lead exposure to a level that does not cause noticeable harm for most people. That level is 10 micrograms of lead per deciliter of blood.

Risk assessors use a computer model to predict how much lead people might get in their bloodstreams from a Superfund site. EPA's goal is for at least 95% to have less than 10 micrograms per deciliter of lead in the blood.

Cancer

A person's risk of getting cancer is evaluated differently from the way of estimating non-cancer risks. Cancer is a type of uncontrolled cell growth. One current theory is that, when a chemical injures a cell in a way that can cause cancer, just one instance of this damage can be enough to trigger the chain of events that leads to the full development of cancer. Because the body can often repair itself, cancer does not always result from such exposure, but it may result. The higher the amount of chemical and the more times that a person comes in contact with it, the greater the chances of developing cancer.

EPA therefore uses the results of scientific studies to figure out how likely it is that a chemical causes cancer, and how much of the chemical is associated with what chance of getting cancer. Therefore, cancer risk is described as a probability, or the odds of getting cancer.

The background risk in the general population for getting cancer is believed to be anywhere from 1 in 2 to 1 in 5. Most of this cancer risk is believed to come from family history, diet, smoking, exposure to sun, etc. Risks from environmental sources,

such as hazardous waste sites, are believed to play only a small part in a person's total cancer risk. EPA believes that the risks from waste sites should stay small, that waste sites should not become a disproportionate source of cancer risk. In general, EPA requires that Superfund site risks should not be higher than 1 in 10,000. Ideally, EPA recommends that waste-site cancer risks should be as low as 1 in 1,000,000 if possible.

Cancer risks are often written in special formats. For example, the risk of "1 in 1,000,000" can also be expressed as the number 0.000001. Because it can be awkward to write numbers with so many zeroes (and increase the chance of accidentally adding or dropping a zero), EPA usually uses scientific notation. In scientific notation, the number 0.000001 is written as 1×10^{-6}, meaning that the number 1 is 6 places to the right of the decimal point. Another way to write this is 1E-6.

EPA also describes the likelihood that a chemical can cause cancer in people. For some chemicals, scientists have found a strong link between chemical exposure and cancer in people. These are called "Group A" chemicals, or human carcinogens. For other chemicals, scientists have strong evidence of cancer in animals, but little or no evidence of cancer in people. These are "Group B," or probable human carcinogens. If only some animal data exist, the chemical may be a "Group C," or possible human carcinogen. "Group D" chemicals can not be classified as to cancer causation. "Group E" chemicals have evidence of not causing cancer in people. EPA is considering changing these descriptions: for example, the categories might become "known/likely," "cannot be determined," and "not likely" to cause cancer. Currently, the A/B/C/D/E system is still in use. These descriptions are called "weight of evidence," because they summarize the weight of scientific evidence that a chemical causes cancer.

Note that the weight of evidence and the potency of a chemical are not the same thing. For example, a chemical can seem to cause cancer at a very high rate (which would be a strong potency), but this may be based on very limited evidence (a weak weight of evidence).

Advanced Concepts

HOW TO CALCULATE CANCER RISK

As described above, the higher the dose of a cancer-causing chemical, the higher the chances of getting cancer. The rate at which the chances increase is different for every chemical. For some chemicals, the chances go up sharply and steeply. For other chemicals, the chances go up more slowly.

This relationship can be expressed as a number, called the Cancer Slope Factor (CSF). The higher the CSF, the more potent the chemical is believed to be at causing cancer.

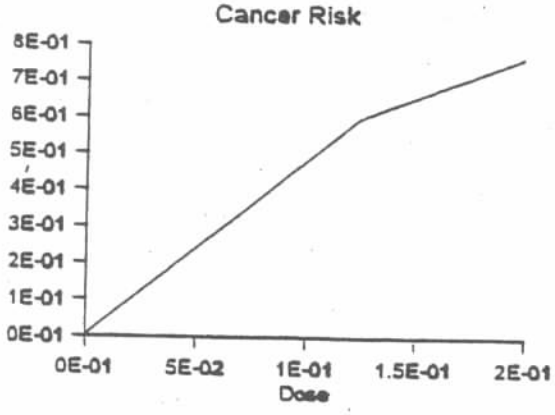
When the cancer risk is less than 1 in 100, the cancer risk is estimated by this simple equation:

Risk = CSF x Dose

where "Dose" is the amount of the chemical that a person would receive from the site. For example, if a person could receive 0.0005 milligrams of material per kilogram of body weight each day, and the CSF were 7.3 per milligram per kilogram per day, the cancer risk would be:

0.0005 mg/kg/day x 7.3/mg/kg/day = 0.00365, or about 3.65 per thousand

Of course, risk cannot keep increasing indefinitely, because a risk of 1 in 1, or 100%, is not possible. At very high doses, the cancer risk curve levels off and approaches, but does not attain, 1 in 1.



The full equation of this line is

$Risk = 1 - e^{(-Dose \times CSF)}$

where e is the base of natural logarithms (approximately 2.71).

Estimating Dose

To get non-cancer or cancer risk, scientists must use dose, or the amount of chemical that a person receives from a site. How do risk assessors figure this out? If we know how much of a chemical is in the water, we still do not know how much of that chemical will end up inside a person, until we know how much water he or she drinks. Body weight is also important, because a high dose of a chemical will usually affect a lighter person more than a heavier person.

Scientists have collected information about how much water people drink, how much they weigh, how much soil they accidentally swallow, how much skin they have, and many similar things. These pieces of information are called "exposure factors." Risk assessors use these exposure factors to estimate people's doses of chemicals from soil, water, air, plants, fish, and so forth.

CLEANUP LEVELS: ASSESSMENT VS. MANAGEMENT

Risk assessors estimate the risks for cancer and for effects other than cancer. Managers then use this information to figure out whether the site needs cleanup and, if so, what type of cleanup and how much. The decision they reach is called the "remedy" for the site. Managers must balance many factors, such as the state laws, the future uses of the site, the cost of various cleanup options, the likely success of each option, the availability of the technology, and so on. At a minimum, every Superfund remedy must protect human health and the environment.

Therefore, while the risk assessment alone does not determine the remedy, it is an important piece of the puzzle.

CONFIDENCE AND UNCERTAINTY

Risk assessment is not an exact science. Some information is unknown, or is only known within certain limits. For example, the safe dose of a chemical is often estimated from animal studies. Because we do not know exactly how to relate animal doses to human doses, we do this in a conservative way by applying safety factors.

Other information varies from person to person, so that any single risk estimate will apply more closely to some people than others. For example, body weight is not the

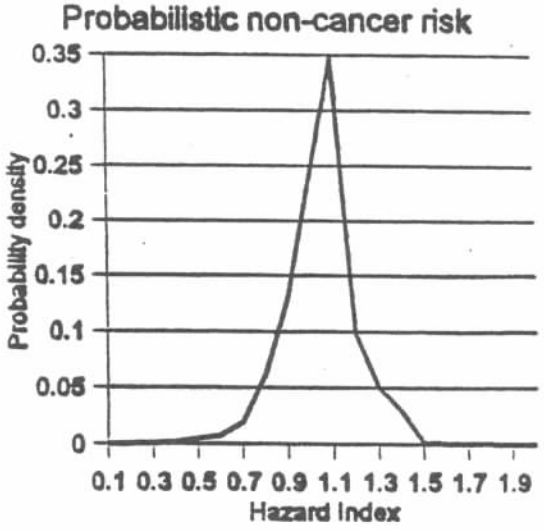
same for every person, and people do not all drink the same amount of water.

To take these unknown and varying factors into account, EPA tries to make its risk estimates protective of most people, yet still realistic. This type of estimate is called "Reasonable Maximum Exposure" (abbreviated RME), which is the highest exposure that most people would reasonably be expected to encounter. It is not, however, a worst-case scenario; the worst case would be the highest possible exposure.

When EPA estimates the more typical, or middle-of-the-road exposure, this is called a "Central Tendency" estimate. Because the Central Tendency estimate is protective of fewer people, Superfund decisions are based on the Reasonable Maximum Exposure, although the Central Tendency numbers can be used to refine or influence the decision.

Sometimes, instead of showing a single risk for a single set of circumstances, EPA will consider all of the possibilities at once. (For example, instead of a single typical body weight, the whole range of possible body weights can be considered.) This type of risk assessment is called a "probabilistic" risk assessment. Because many scenarios are considered at once, the result is not a single risk number, but a whole range of risk numbers. Along with the range, we can also see the most and least likely risks.

In the example on the right, the probability of non-cancer risks is shown. The most likely Hazard Index is about 1.1. A Hazard Index above 1.5 or below 0.4 is not expected.



ATTACHMENT: SAMPLE RISK ASSESSMENT

Use the principles you have just learned to interpret this sample risk assessment summary:

At Site X, two substances called benzene and hexavalent chromium were found in drinking water at 13 micrograms per liter and 18 micrograms per liter, respectively. Cancer and non-cancer risks were evaluated using the exposure factors described below.

Exposure Factors: Adults are assumed to drink 2 liters of water per day, to weigh 70 kilograms (about 150 pounds) on average, to drink the water 350 days/year (assuming some days are spent away from the home), and to live at the same residence for 30 years. Non-cancer risks are averaged over 365 days/year for the 30 years; cancer risks are averaged over 365 days/year for 70 years (a lifetime). Therefore, the benzene dose from this water is 0.00015 mg/kg/day; the chromium dose is 0.00049 mg/kg/day.

Toxicity Factors: The Reference Dose for chromium is 0.003 mg/kg/day. The Cancer Slope Factor is 2.9E-2 per mg/kg/day for benzene. Benzene is a Group A, or human carcinogen, while chromium is Group D (not classifiable) for oral exposure.

For adults drinking this water, the Hazard Index (HI) for chromium is estimated at 0.16. The HI is below EPA's level of concern of an HI of 1.

For adults drinking this water, the cancer risk from benzene is estimated at 4E-6, or 4 in a million. The cancer risk is below EPA's upper level of concern for cancer risk (1E-4 or 1 in 10,000), but is above the ideal target risk of (1E-6 or 1 in 1,000,000).

BIBLIOGRAPHY

This paper was based on the following sources, which may be consulted for more information:

Clay, Don R., USEPA Assistant Administrator. "Role of the Baseline Risk Assessment in Superfund Remedy Selection Decisions." Memorandum to USEPA Division Directors. OSWER Directive 9355.0-30. 22 April 1991.

Fields, Timothy Jr., Acting Director of USEPA Office of Emergency and Remedial Response, and Bruce Diamond, Director of USEPA Office of Waste Programs Enforcement. "Human Health Evaluation Manual, Supplemental Guidance: 'Standard Default Exposure Factors.'" Memorandum to USEPA Division Directors. OSWER Directive 9285.6-03. 25 March 1991.

Laws, Elliott P., USEPA Assistant Administrator. "Revised Interim Soil Lead Guidance for CERCLA Sites and RCRA Corrective Action Facilities." Memorandum to USEPA Regional Administrators. OSWER Directive 9355.4-12. 14 July 1994.

United States Environmental Protection Agency (USEPA). Risk Assessment Guidance for Superfund, Volume I. Human Health Evaluation Manual (Part A). Interim Final. EPA/540/1-89/002. Washington, DC: Office of Emergency and Remedial Response, 1989.

USEPA. Integrated Exposure Uptake Biokinetic Model for Lead in Children (IEUBK). Version 0.99d. PB93-963511. Diskette.

USEPA. National Oil and Hazardous Substances Pollution Contingency Plan. Title 40, Code of Federal Regulations, Part 300. July 1, 1996.

USEPA. "Benzene." Integrated Risk Information System (IRIS). Online. Internet. 9 September 1999.

USEPA. "Chromium." Integrated Risk Information System (IRIS). Online. Internet. 9 September 1999.

ENVIRONMENTAL PROTECTION AGENCY
REGION III
1650 Arch Street
Philadelphia, Pennsylvania 19103
November 28, 2001

SUBJECT: Determination of Arsenic Background Levels
Spring Valley - DC Munitions

FROM: Frank Vavra, RPM
Federal Facilities Section

TO: Site File

Several efforts have been made to define background levels of arsenic at the Spring Valley Site, potentially causing confusion. The purpose of the memo to the file is to document the past efforts and avoid any confusion regarding use of the data.

The first effort by EPA to quantify background levels is contained in a report titled: "Review of Statistical Tests and Approaches for Assessing Site Data, Spring Valley Washington DC Munitions Site, A.Singh and R.W. Gerlach, March 24, 1998. This report is attached to EPA's October 1999 Draft Risk Assessment for Spring Valley. Twelve background samples were collected by EPA from 12 locations and these locations were within four different soil types. Compounds of concern in this Risk Assessment were compared to their background levels. The mean arsenic level was 3.3 ppm and the soil results ranged from 1 ppm to 17 ppm.

The second effort to define background levels was more extensive. There had been some concern that some of the soil samples in the first effort might have been within the influence of arsenic contamination and that the mean might be consequently biased high. The purpose of the investigation was to obtain defensible background soil concentrations in the vicinity of Spring Valley. Gannet Fleming performed the study for EPA and subcontracted Mr. Terry W. Schulz, a statistician to analyze the data. The data was derived from four soil types. Twenty five samples were derived from Piedmont rock derived soils. The remaining five samples were derived from Coastal Plain Sediments. This complicated the statistical analysis of the data and the methodology is described in detail in the report titled: " Spring Valley Munitions Facility, Background Investigation, prepared by Gannet Fleming, Inc. and Terry W. Schulz, April 2000." The summary table and the description of the statistical method is attached. All of the data used was taken by EPA and subjected to full QA/QC and data validation. This report is attached to EPA Region 3's Human Health Risk Assessment Report for OU3, dated August 2000. For arsenic, 25 of the 30 samples taken were used in the background calculations. The reasons that five of the samples were not used is detailed in the report. The Upper Prediction Limit (UPL)and the Upper Tolerance Level (UTL) were calculated. The UTL is intended to limit the likelihood of a false positive (leading to erroneously cleaning an area that is already clean) to 5%. The UPL is considered the more conservative value for risk assessment purposes. The UPL is intended to limit the likelihood of a false negative (leading to erroneously no cleaning up and area that is contaminated) to 5%. The calculated UTL was 15.6 ppm and the calculated UPL was

TABLE I

SUMMARY TABLE

RESULTS OF BACKGROUND SOIL STATISTICAL ANALYSIS

	Al	As	Cr	Fe	Pb
Distribution Type	lognormal	lognormal	lognormal	normal	lognormal
Data Set Used to Develop Background for Use in Risk Assessment	Piedmont	Combined	Combined	Combined	Piedmont
Number of Samples in Data Set Used to Develop Background Value for Use in Risk Assessment	25	25	30	30	25
Recommended UPL (mg/Kg)	22654	12.5	42.5	30679	99
Recommended UTL (mg/Kg)	26879	15.6	49.8	33159	119

1.0 INTRODUCTION

The purpose of this investigation is to obtain defensible background concentrations in the vicinity of the Spring Valley Army (SPVA) Munitions Facility. The elements of interest are: aluminum (Al), arsenic (As), chromium (Cr), iron (Fe) and lead (Pb). The analytical data source is a report prepared by Roy F. Weston, Inc. for USEPA Region III (Weston 2000). Two cases are presented here. The first case assumes all the background data derive from one parent geologic population, while the second case considers background data grouped by actual known geologic parent populations.

The 95% upper prediction limit (UPL) of the mean element background concentration will constitute an upper limit of assumed naturally occurring concentration (Singh and Brown 1999). The 95% UPL is calculated using the same formula as the 95% upper tolerance limit with 95% average coverage. The UPL for a specific element, such as arsenic, can be used to calculate background human health risks that can be compared to contaminant-specific human health risks calculated for each site.

A statistically more conservative estimate than the UPL is the UTL with at least 95% coverage (UTL). This UTL supposedly guarantees limiting the likelihood of a false positive (leading to erroneously cleaning an area that is already clean) to 5%. The average coverage of this UTL averages 98% or more (USEPA 1992). Concentrations in excess of this upper limit at any site location can be considered elevated and most likely attributable to the activities of man.

The UPL is considered the more conservative value for risk assessment purposes. The UPL supposedly guarantees limiting the likelihood of a false negative (leading to erroneously not cleaning up an area that is contaminated) to 5%.

All of the statistical results provided in this report were performed in Office 97 Excel spreadsheets (Microsoft Corp.), SYSTAT v. 9 (SPSS, Inc.), IMSL FORTRAN subroutines in

FORTRAN Powerstation v. 4.0 (Microsoft Corp.) or in customized software using algorithms referenced in Law and Kelton (1991).

2.0 METHODOLOGY

2.1 Case I - Consider All Background Data to derive from One Geologic Parent Population

Distribution Fitting

It is first necessary to determine whether the data of interest follow a normal or lognormal distribution in order to determine whether to calculate the UPL and UTL using the raw data or the natural logs of the data. If the natural logs of the data are used to calculate the UPL and UTL, the result is raised to the power of e. If the data do not follow a normal or lognormal distribution, a non-parametric UTL method is used.

Data and natural logs of data of the elements of interest were fit to normal and lognormal distributions, respectively, and the resulting goodness-of-fit was assessed using the Shapiro-Wilk (USEPA 1992), one-sample Kolmogorov-Smirnov (Law and Kelton 1991) and Anderson-Darling (Law and Kelton 1991 and Sinclair and Spurr 1988) tests. Probabilities for all three tests vary between 0 and 1. The results for the elements of interest are shown in Table 1. Any probability > 0.05 indicates acceptance of that particular distribution fit. In general, it is seen that the Shapiro-Wilk test is the most stringent test of normality as indicated by the lower probabilities of fit for a given element and distribution type.

The Shapiro-Wilk test probability of normality for aluminum is 0.19 and that of lognormality is 0.39. Both test results indicate an acceptable fit to the respective distribution ($p > 0.05$), however, the data are twice as better fit to a lognormal distribution than to a normal distribution. Acceptable fits to a normal or lognormal distribution occur for all elements except lead.

Probability plots are also provided (immediately following the tables) for normal and natural log transformed data for each element of interest to provide visual support of the probability test results. The closer the data points are to the line the better the fit. Note the strong deviation from normality and lognormality for lead.

Outliers

Outliers are data with extremely high or low values with respect to the rest of the values of a data set. Outliers have strong leverage on averages and standard deviations and consequently on UPL and UTL results (see equations for UPL and UTL below).

The test on page 8-11 of the RCRA Groundwater Monitoring Guidance (USEPA 1989) is used to check for outliers. This test calculates:

$$T_n = (X_n - \bar{X}) / S$$

where X_n is the largest observation, $\bar{x}$ is the sample mean and S is the sample standard deviation. The value for T_n is compared to the critical value given for the sample size, n, in Table 8 of Appendix B of USEPA (1989). If T_n exceeds the critical value in the table, there is statistical evidence that the suspect observation is an outlier. Results for all data combined are shown in Table 1 for the best fitting distribution or for both distributions when neither fits the data. This test indicates the only element containing possible outliers is lead.

Visual corroboration is supplied by boxplots that follow the P-P plots. The box in a boxplot contains the middle 50% of the values of a data set. The line inside the box indicates the median. The whiskers show the range of values that fall within the inner fences. Outside values are plotted with an asterisk. Far outside values are plotted with an open circle. Outside and far outside values are outliers. Only the boxplots for lead indicate the presence of outliers.

95% Upper Prediction Limit

The 95% Upper Prediction Limit hereinafter referred to as the UPL is calculated according to Singh and Brown (1999). The equation is given by:

$$UPL = \bar{X} + t_{(n-1),\alpha}\, S\sqrt{1/n + 1}$$

where $\bar{x}$ and S are the arithmetic mean and standard deviation obtained using the background data, t (n-1),α is Student's t critical value with n-1 degrees of freedom and α, the error level is 0.05 for a one-sided 95% UPL. A UPL was calculated for each element of interest if the data were normally or lognormally distributed as determined by distribution fitting. The results are shown in Table 1.

95% Upper Tolerance Limit

The 95% Upper Tolerance Limit with guaranteed 95% coverage hereinafter referred to as the UTL is calculated according to USEPA (1989). The equation is given by:

$$UTL = \bar{x} + KS$$

where $\bar{x}$ and S are the arithmetic mean and standard deviation of the background data and K is obtained from Table 5 page B-8 of USEPA (1989). Results are shown in Table 1.

Non-Parametric UTL

If the background data are not normal or lognormal, a non-parametric UTL can be approximated by the largest value of the data set (USEPA 1992). This method requires at least 19 values to

obtain 95% coverage. Coverage percentage is calculated as [n / (n + 1)] * 100. A value of 1660 mg/kg lead is obtained with 96.8% coverage for n = 30. However, this value should not be used because the samples are derived from two parent geologic parent populations. As will be shown in the section on hypothesis testing, the background samples from the two types of parent material have significantly different means at the 95% level of confidence for lead. In addition, the Coastal Plain sediment samples appear to have elevated lead concentrations making their use as background samples suspect.

2.2 Case II - Consider All Data to Derive from More than One Geologic Parent Population

The Soil Survey of the District of Columbia (SCS 1976) was consulted to determine parent geologic populations for the SPVA background data. Two distinct parent populations encompass all the background samples. The Manor Glenelg (10 samples), Urban Land Manor Glenelg (10 samples) and Urban Land Brandywine (5 samples) Soil Associations all derive from the weathering of Piedmont Rocks. The Urban Land Sassafras Chillum (5 samples) Soil Association derive from deposition of Coastal Plain Sediment.

PIEDMONT ROCKS & COASTAL PLAIN SEDIMENT

Distribution Fitting

Distribution Fitting was performed for the grouped data deriving from Piedmont Rock weathering and Coastal Plain Sediment deposition as described above. The results are shown in Tables 2 and 3, respectively. Note that when the lead data are assumed to derive from more than one geologic parent material, good lognormal fits are observed for both Piedmont Rock (25 samples) (Shapiro-Wilk p = 0.60) and Coastal Plain Sediment (5 samples) (Shapiro-Wilk p = 0.95) parent material background samples. Again, visual corroboration of distribution fitting via P-P plots can be found following the tables.

Outliers

A check for outliers was performed for the data deriving from Piedmont Rock and Coastal Plain Sediment as described above. Note that no statistical outliers occur when the geologic parent material is used to group soils background data (Tables 2 and 3). Boxplots provide visual corroboration of all outlier results except iron deriving from Coastal Plain Sediment deposition. This boxplot shows one outside value at each end of the plot. No action was taken with respect to these possible outliers for reasons explained in the discussion section below.

UPL & UTL

Ninety-five percent UPLs and UTLs were calculated as described above. Results for background samples derived from Piedmont Rocks and Coastal Plain Sediment are shown in Tables 2 and 3, respectively.

Non-Parametric UTL

A non-parametric UTL was calculated as described above for arsenic derived from Piedmont Rocks, since the Shapiro-Wilk test probability is only marginally significant ($p = 0.06$). The resulting value compares favorably with the UPL and UTL values. Note that non-parametric UTLs could not be calculated for Coastal Plain Sediment, even if needed, because at least 19 samples are required for 95% coverage and only 5 samples were available.

Hypothesis Testing

It is desirable to use the largest appropriate sample size in the UPL and UTL calculations. Hypothesis testing can suggest when it is appropriate to combine Piedmont Rock and Coastal Plain Sediment samples to obtain larger sample sizes. Since only two parent materials and

non-paired data are involved the tests of choice would be the parametric Student t-test of the means or the comparable non-parametric Mann-Whitney U test. The Mann-Whitney U test was preferred to the Student t-test, because the data were better approximated by lognormal distributions (except for Fe from Piedmont Rock), and application of the t-test to log transformed data has been questioned by some statisticians.

The results of Mann-Whitney U hypothesis tests of data derived from Piedmont Rock weathering and Coastal Plain Sediment deposition follows:

Element	prob.
Al	0.02
As	0.09
Cr	0.33
Fe	0.85
Pb	<0.001

It is seen that at the 95% level of confidence (ie, probability ≥ 0.05), the mean concentrations for chromium and iron samples are not significantly affected by parent material origin. The arsenic mean is marginally affected. The aluminum and lead means are significantly affected by parent material origin. Therefore, it is appropriate to combine data from the two parent material sample sets for arsenic, chromium and iron. It is not appropriate to combine data for aluminum and lead.

3.0 REFERENCES

Law, Averill M. and Kelton, W. David. 1991. Simulation Modeling & Analysis. Second Edition. McGraw-Hill, Inc. New York.

Sinclair, C. D. and Spurr, B. D. 1988. Approximation to the Distribution Function of the Anderson-Darling Test Statistic. Journal of the American Statistical Association 83:

Upper ... used by USACE to get mean of 5.05 and 95% Conf Level of 12.6

Sample	Detection Limit	Concentration		LN Background
BS-ULMG-01		4.5	Background	1.504077397
BS-ULMG-02		3.4	Background	1.223775432
BS-ULMG-03		4.2	Background	1.435084525
BS-ULMG-04		4.4	Background	1.481604541
BS-ULMG-05		3.7	Background	1.30833282
BS-ULMG-06		5	Background	1.609437912
BS-ULMG-07		3.5	Background	1.252762968
BS-ULMG-08		3.3	Background	1.193922468
BS-ULMG-09		3.7	Background	1.30833282
BS-ULMG-10		5	Background	1.609437912
BS-MG-11		5.9	Background	1.774952351
BS-MG-12		5.5	Background	1.704748092
BS-MG-13		4	Background	1.386294361
BS-MG-14		5.2	Background	1.648658626
BS-MG-15		4.2	Background	1.435084525
BS-ULSC-16		13.2	Background	2.58021683
BS-ULSC-17		5.7	Background	1.740466175
BS-ULSC-18		6.9	Background	1.931521412
BS-ULSC-19		4.4	Background	1.481604541
BS-ULSC-20		18	Background	2.890371758
BS-ULB-21		6.6	Background	1.887069649
BS-ULB-22		9	Background	2.197224577
BS-ULB-23		8.3	Background	2.116255515
BS-ULB-24		9.7	Background	2.272125886
BS-ULB-25		11.1	Background	2.406945108
BS-MG-26		4.6	Background	1.526056303
BS-MG-27		5.4	Background	1.686398954
BS-MG-28		8.4	Background	2.128231706
BS-MG-29		11.1	Background	2.406945108
BS-MG-30		7.5	Background	2.014903021
Back-01		2.8	Background	1.029619417
Back-02		4.1	Background	1.410986974
Back-03		0.97	Background	-0.030459207
Back-04		2.3	Background	0.832909123
Back-05		3.7	Background	1.30833282
Back-06		2.9	Background	1.064710737
Back-07		3	Background	1.098612289
Back-08		16.7	Background	2.815408719
Back-09		3.5	Background	1.252762968
Back-10		4.3	Background	1.458615023
Back-11		2.7	Background	0.993251773
Back-12		5.4	Background	1.686398954
	mean	5.055977765		1.620571259

SHAPIRO-WILK GOODNESS OF FIT TEST

95th Percentile	x(0.95) = exp(mean + (Z(0.95)*SD)	Using equation for esti
mean	1.620571259	
Standard Deviation	0.555776468	
Z(0.95)	1.645	
95th Percentile	12.61420480	
2*95th Percentile	25.22840972	

Mean	1.620571259
Standard Error	0.085758171
Median	1.51506685
Mode	1.30833282
Standard Deviation	0.555776468
Sample Variance	0.308887482
Kurtosis	1.236610812
Skewness	0.046714403
Range	2.920830965
Minimum	-0.030459207
Maximum	2.890371758
Sum	68.06399288
Count	42
Confidence Level(95.0%)	0.173192235

TABLE 1. CONCENTRATION OF INORGANICS IN SURFACE SOILS OF THE U.S. [IN PPM-DRY WEIGHT, DW), EQUIVALENT TO mg/kg-dw] (SOURCE: KABATA-PENDIAS AND PENDIAS 1984).

Arsenic, ppm

Soil	Elements											
	As		Ba		Co		Cr		Cu		Hg	
	Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean
Sandy soils and loamsoils on sandstones	<0.1-30.0	5.1	20-1500	400	0.4-20	3.5	3-200	40	1-70	14	<0.01-0.54	0.08
Light loamy soils	0.4-31.0	7.3	70-1000	555	3-30	7.5	10-100	55	3-70	25	0.01-0.60	0.07
Loess and soils on silt deposits	1.9-16.0	6.6	200-1500	675	3-30	11.0	10-100	55	7-100	25	0.01-0.38	0.08
Clay and clay loamy soils	1.2-27.0	7.7	150-1500	535	3-30	8.0	20-100	55	7-70	29	0.01-0.90	0.13
Alluvial soils	2.1-22.0	8.2	200-1500	660	3-20	9.0	15-100	55	5-50	27	0.02-0.15	0.05
Soils over granites and gneisses	0.7-15.0	3.6	300-1500	785	3-15	6.0	10-100	45	7-70	24	0.01-0.14	0.06
Soils over volcanic rocks	2.1-11.0	5.9	500-1500	770	5-50	17.0	20-700	85	10-150	41	0.01-0.18	0.05
Soils over limestones and calcareous rocks	1.5-21.0	7.8	150-1500	520	3-20	9.5	5-150	50	7-70	21	0.01-0.50	0.08
Soils on glacial till and drift	2.1-12.0	6.7	300-1500	765	5-15	7.5	30-150	80	15-50	21(a)	0.02-0.36	0.07
Light desert soils	1.2-18.0	6.4	300-2000	835	3-20	10.0	10-200	60	5-100	24	0.02-0.32	0.06(a)
Salty prairie soils	2.0-12.0	5.6	200-1500	765	3-15	7.5	20-100	50	10-50	20(a)	0.02-0.06	0.04(a)
Chernozems and dark prairie soils	1.9-23.0	8.8	100-1000	595	3-15	7.5	15-150	55	10-70	27	0.02-0.53	0.10
Organic light soils	<0.1-48.0	5.0	10-700	265	3-10	6.0	1-100	20	1-100	15	0.01-4.60	0.28
Forest soils	1.5-16.0	6.5	150-2000	505	5-20	10.0	15-150	55	7-150	17(a)	0.02-0.14	0.06(a)
Various soils	<1.0-93.2	7.0	70-3000	560	3-50	10.5	7-1500	50	3-300	26	0.02-1.50	0.17

Naturally Occurring Background Levels of Arsenic – By State

Table 2

State	Range 2a.	Established 2b.	Use 2c.
AK	17.3 mg/kg	Geochemical Atlas of Alaska	Compare the statistical mean conc for each Hazd substance/compare the max hazd substance conc detected.
AL	1 - 10	US Geological Survey 1984	RCRA clean closure: to indicate disposal activities
AZ	1.4 - 97 mg/kg	USGS sampling of surficial soils in Boerngen & Shacklette, 1981, USGS Open-file Report 81-197.	Naturally occuring contaminate levels can be used as cleanup levels.
AR	1.1 - 16.7 ppm	Regional numbers	Considered on site specific basis after screening process.
CA	5-40(SF Bay Area) 5-20(southern cal.) thousands(gold country)	Background levels of trace elements in Southern California soils. Contract #89-T0081. Cal. EPA/Protocol for determining background conc of metals in soils at Lawrence Berkeley National Laboratory, 1995.	Realistic standard in setting cleanup levels.
CO	4 - 40 ppm	Site-specific data collection	If risk-based clean-up levels fall below background, the background values are used as the clean-up standards
CT	Up to 10 ppm	DEP paper covering New England w/CT data	Criterion for soil cleanup
DE	0.4 mg/kg	From historical site investigations	Risk assessments, remediation standard requirements
FL	0 - 3 mg/kg	Empirically	To modify the SCTL (Soil Concentration Target Limit)
HI	0.93 to 5 mg/kg	The background samples are collected from noncontaminated areas or from subsurface of the study areas. Statistical analyses were applied. Further studies are needed to confirm naturally occurring background concentrations.	To establish action levels
IL	0.35 - 24.0 ppm	Survey of data reported to agency during site investigation.	Chemicals may be excluded as chemical of concern for a site by comparison to background and background conc. may be used as remediation objectives.
IA	5 - 10 mg/kg	Approximation based on experience	Informally, no action required when near background levels.
KS	Non detect - <100 mg/kg	Review of data selected from various sites across the state.	As a Tier 1 approach, use background if exceeds 10^{-6} cancer or H.I. = 1.0
KY	0.1 - 10 mg/kg	Based on analyzing samples from across the state which were labeled as "background"	To determine presence or absence of contamination.
ME	1 - 28 mg/kg	Based on data available from 5 sites in Maine	Inorganic contaminants present at concentrations greater than soil criteria; background is considered the critical benchmark
MD	No background est.	Not available	No state soil criteria
MI	0.1 - 11.0 mg/kg	Background as conc established through a MI background soil survey conducted by Waste Management Division.	A background concentration is used as a default cleanup criterion when it is higher than the calculated criteria.
MS	0 - 26 ppm (4 - 10 Avg.)	USGS paper 1270- Elemental Concentration in Soils & Other Surficial Materials...	Background concentration can be considered as an alternative cleanup standard.
MO	Not available	Chemical analysis of many soil samples taken during an agriculture soil survey which included soil chemical characteristic information.	Don't usually set cleanup goals lower than proven background concentrations.
MT	Non detect – 100's ppm in geothermic areas.	Via soil testing (mostly XRF).	Take them into account, but use risk based human health numbers as action levels.
NH	0 - 12 mg/kg	From a database of soil samples from playgrounds and background levels at sites that are then used for biosolid applications. The 95th percentile value of the data is used.	Background is used as a cleanup standard when risk based numbers are lower.
NM	.015 - 17.00 mg/kg	Testing done by Sandia Labs	To establish cleanup of contaminated sites.
NJ	0.02 – 350 ppm	DEP background testing and review of sites under DEP oversight	Legislation states that remediation is not to be required below regional natural background levels.
NY	3 - 12 ppm	Site specific data is preferred but literature data is used	For inorganic materials, background is used as the starting point in determining the soil cleanup level.
ND	<0.1 - 34 mg/kg	Use of documented studies by USGS in Region	Comparative background to established contamination
OH	Non detect - 30 ppm	Using site data from several RCRA facilities that established background conc. for their sites	Setting up cleanup standards for metals only.
OK	0 - 32 mg/kg	USGS Soil survey and site specific background determinations for a variety of sites.	Sometimes criteria for no further action – sometimes for screening.
OR	1 - 10 ppm	Limited survey of cleanup sites	Natural background is considered to be protective of human health & the environment. Cleanup to background concentration, if higher than risk-based concentration.

Source: "Study of State Soil Arsenic Regulations Association for the Environmental Health of Soils"

Table 2 (continued)

State	Range 2a.	Established 2b.	Use 2c.
SC	2 - 11 mg/kg	Average of sites sampled statewide	To determine clean-up levels in most cases.
TN	0.1 - 120 ppm	TN Division of Superfund - from EPA or state site inspections.	Used to evaluate whether concentrations at a site are within natural background. Not all Divs. use background
TX	1 - 18 ppm	US Geological Survey	It can be used to screen contaminants from a risk assessment; it can be used as a cleanup level.
VA	Varies from site to site	By sampling	Not available
WA	0.5 - 28.6 mg/kg	Background soil survey	Background concentration of 20 mg/kg is used as the cleanup standard if the human health value is below background. 1.67 mg/kg for human health
WY	Not available	Not available	Site specific only - won't allow use of regional background

TABLE 4. AGRICULTURAL SOURCES OF INORGANIC CONTAMINATION IN SOILS (PPM DW)[a] (KABATA-PENDIAS AND PENDIAS 1984).

Element	Sewage sludges	Phosphate fertilizers	Limestones	Nitrogen fertilizers	Manure	Pesticides (%)
As Arsenic	2–26	2–1,200	0.1–24.0	2.2–120	3–25	22–60
B	15–1,000	5–115	10	–	0.3–0.6	–
Ba	150–4,000	200	120–250	–	270	–
Be	4–13	–	1	–	–	–
Br	20–165	3–5	–	185–716	16–41	20–85
Cd	2–1,500	0.1–170	0.04–0.1	0.05–8.5	0.3–0.8	F
Ce	20	20	12	–	–	–
Co	2–260	1–12	0.4–3.0	5.4–12	0.3–24	–
Cr	20–40,600	66–245	10–15	3.2–19	5.2–55	–
Cu	50–3,300	1–300	2–125	<1–15	2–60	12–50
F	2–740	8,500–38,000	300	–	7	18–45
Ge	1–10	–	0.2	–	19	–
Hg	0.1–55	0.01–1.2	0.05	0.3–2.9	0.09–0.2	0.8–42
In	–	–	–	–	1.4	–
Mn	60–3,900	40–2,000	40–1,200	–	30–550	–
Mo	1–40	0.1–60	0.1–15	1–7	0.05–3	–
Ni	16–5,300	7–38	10–20	7–34	7.8–30	–
Pb	50–3,000	7–225	20–1,250	2–27	6.6–15	60
Rb	4–95	5	3	–	0.06	–
Sc	0.5–7	7–36	1	–	5	–
Se	2–9	0.5–25	0.08–0.1	–	2.4	–
Sn	40–700	3–19	0.5–4.0	1.4–16.0	3.8	–
Sr	40–360	25–500	610	–	80	–
Tc	–	20–23	–	–	0.2	–
U	–	30–300	–	–	–	–
V	20–400	2–1,600	20	–	–	45
Zn	700–49,000	50–1,450	10–450	1–42	15–250	1.3–25
Zr	5–90	50	20	–	5 5	–

a. Equivalent to mg/kg-DW.