Appendices: A-G

Appendix A. Abstracts of ATSDR Documents for the American University/ Spring Valley Site, Washington, D.C.

The complete documents, abstracted in this section, can be found at the Palisades Library in Spring Valley or on ATSDR's Spring Valley Web site at www.atsdr.cdc.gov/sites/springvalley.

Health Consultation, Evaluation of Indoor Air Sampling, 4625 Rockwood Parkway, American University Experiment Station/Spring Valley, Washington, D.C.

December 2003

The U.S. Environmental Protection Agency (EPA) asked the Agency for Toxic Substances and Disease Registry (ATSDR) to review indoor air and soil gas sampling data to determine if exposure to chemical substances detected in indoor air posed an immediate or long-term health hazard to residents occupying a home at 4625 Rockwood Parkway, Spring Valley. EPA asked ATSDR to recommend actions necessary to protect the health of building occupants. The house was occupied at the time of sampling, but vacated at the time ATSDR received the data. The building occupants lived in the house for less than 1 year. They reportedly found laboratory glassware and other debris on the property and believed that it came from former AUES activities. The property is in an area adjacent to a debris field on American University Lot 18 and has the potential to be leased to another tenant. In June 2003, W. L. Gore and Associates, Inc. performed soil gas and indoor air sampling at the property. From a review and evaluation of the indoor air sampling data and available toxicological and medical information relevant to the substances of interest, ATSDR concludes that the presence of low levels of volatile and semivolatile substances in indoor air at 4625 Rockwood Parkway poses no apparent public health hazard to adult or child occupants. However, past detection of elevated carbon monoxide concentrations in the home indicate that carbon monoxide levels were elevated and may have contributed to reported health symptoms. ATSDR recommended that confirmatory sampling be conducted and that carbon monoxide levels be within a safe level prior to leasing.

Health Consultation, Exposure Investigation of Summer 2002 (Phase II), Arsenic Biomonitoring, Spring Valley Neighborhood

February 2003

Due to requests (from the Scientific Advisory Panel and others) to sample residents during summer months when the potential for exposure to soil arsenic should be higher, ATSDR and DC DOH conducted the Summer 2002 Exposure Investigation. Testing was offered to those individuals who participated in the March 2002 Exposure Investigation, individuals who were living on, or adjacent to, property which was being remediated, and individuals whose yards had the highest grid samples. Urine samples were collected from July to November 2002. Urine arsenic levels were tested in 40 individuals, 34 adults and 6 children. Three individuals had mild elevations (> 10 but <30 ug/L) of inorganic arsenic in their urine. Most participants (92%) had urine arsenic values less than 10 ug/L, indicating no significant exposures. Health effects are not expected in the adults with the mild elevations of urinary arsenic.

Health Consultation, Exposure Investigation of March 2002 (Phase I), Arsenic Biomonitoring, Spring Valley Neighborhood

June 28, 2002

In 2001, the DC DOH requested that additional biomonitoring be conducted in Spring Valley.

As a response to their request, ATSDR conducted an exposure investigation in March 2002 which included sampling hair, urine, and dust in homes. Participants were those individuals with yards having the highest composite soil samples of arsenic. A total of 32 individuals were tested; 23 adults and 9 children. Three individuals had levels of inorganic arsenic exceeding 10 ug/l.

Health Consultation, The Public Health Significance of Arsenic in Soil at the American University Child Development Center

March 14, 2001

The Army requested ATSDR to review new environmental sampling data from the American University Child Development Center (CDC) playground, to determine whether there is an increased risk of adverse health effects for the children and staff who worked and played at the CDC. The Army took 67 surface soil samples from the playground of the CDC, and analyzed them for arsenic. The average arsenic concentration in the samples was slightly less than 60 ppm, and the maximum was 498 ppm. ATSDR concluded that children and staff at the Child Development Center should not experience any adverse health effects from previous exposure to arsenic in soils at the playground. ATSDR concurred with the Army that the soil arsenic levels in the affected areas of the CDC playground be reduced to normal background levels.

Exposure Investigation, Spring Valley (a/k/a American University Child Development Center)

March 8, 2001

The Army reported that elevated concentrations of arsenic were detected in surface soil samples collected from some locations in the playground at the Child Development Center (CDC) at the American University in Washington, D.C. Parents of the children who attended the CDC expressed concern that their children may have been exposed to this contamination. In response to this concern, ATSDR collected hair samples from children who were attending the CDC and adult staff at the CDC and tested the samples for arsenic. Hair arsenic concentrations were not elevated in the 28 children and 4 adults who participated in this exposure investigation.

Health Consultation, Assessment of Soil Sampling Results at the American University Child Development Center

December 14, 2000

The Army Corps of Engineers requested that ATSDR review the environmental sampling data from the daycare playground, to determine whether there is an increased risk of adverse health effects to the children, their families, and the teachers. The Army sampled six areas within the playground, and mixed all six into a single soil sample. This sample was analyzed, and found to contain 31 ppm arsenic. We concluded that children attending the daycare, their families, and teachers, should not experience any adverse health effects from exposure to arsenic in soils at the level found by the Army. Nevertheless, should children eat large amounts of soils (a handful a day), they could experience gastrointestinal distress. Also, if this behavior continues over a period of a few weeks, children could begin developing pigmentation changes on their palms and the soles of their feet. ATSDR concurred with the Army's plan for additional sampling of the play area over 20 foot grids.

Health Consultation, Assessment of Arsenic in Creek Sediment at Four Residences in Spring Valley

March 2, 2000

EPA Region III requested that the Agency for Toxic Substances and Disease Registry (ATSDR) evaluate the public health significance of arsenic in creek sediments. Four sediment samples were taken from four residences on Glenbrook Road, near American University. The levels of arsenic in these samples were 4.0, 9.5, 9.6, and 9.7 ppm. We considered that children have ready access to the creek, and that a child might play in this creek every day. For this exposure scenario, ATSDR has derived a health protective comparison value for arsenic of 20 ppm. For arsenic, this level is based upon epidemiological studies of humans, including children, who were inadvertently exposed to arsenic. No adverse health effects were observed in these people

at a dose which is higher than would occur from the creek sediments at this site. For this reason, no adverse health effects are expected to result from this exposure.

Technical Assistance to the District of Columbia Department of Health, Potential Contaminants in Soils at American University

January 8, 1998

The Agency for Toxic Substances and Disease Registry (ATSDR) was requested to consider whether suspected chemical warfare agents, laboratory reagents, and associated degradation products in soils at the American University in Washington, DC, could pose a concern to public health. This question came about because many of these substances were not on the target compound list for the soil sampling analysis. After discussing the list of potential contaminants supplied by the DC government with the Army Corps of Engineer's contractor, Parsons Engineering, ATSDR was assured that the majority of substances in the list would have been tentatively identified during the sample analysis, since they were included in the reference library for the gas chromatograph/mass spectrograph during analysis. Contamination by other substances or their degradation products would have been observed as increased levels of inorganic substances, particularly arsenic. Remaining substances are chemical warfare agents, which are volatile and reactive in nature, making it unlikely that any of these substances would remain to contaminate soils in the area. ATSDR concluded that the potential for these substances to contaminate soils at the American University has been appropriately addressed during the analyses of soil samples.

Health Consultation, Assessment of Soil Sampling Results at the American University

August 26, 1997

The District of Columbia Public Health Commissioner requested ATSDR to review the EPA environmental data, to determine whether there is an increased risk of adverse health effects at the American University and vicinity. Several areas were sampled by the Army from December,

1993 through March, 1994. These areas are suspected to have been used as shell pits, storage areas, and testing fields and trenches. These samples were analyzed by the Army for chemical warfare agents and degradation products: mustard gas, oxathiane, dithiane, lewisite, and thiodiglycol. In addition, the samples were analyzed for explosives and metals. No chemical agents, degradation products, or explosives were detected. The same (split) samples were analyzed by the EPA for metals, volatile organic compounds (VOCs), semi-volatile organic compounds (SVOCs), pesticides, and metals. With the exception of one sample, the only substances which exceeded ATSDR comparison values are antimony, arsenic and manganese. This sampling information from the Army and the EPA do not indicate that adverse health effects might occur as a result of exposure to these soils. Still, arsenic was elevated above background in a few locations.

Chemical and conventional ordnance may remain buried at the American University or in the vicinity. In addition, laboratory or storage vessels may also be buried in these areas. These discarded weapons and glassware may hold explosives or noxious agents, and could pose serious health threats if they are unearthed.

Health Consultation, Spring Valley/ American University Experiment Station

June 3, 1997

This health consultation was sent to the D.C. Public Health Commissioner. It is a review of Remedial Investigations and other environmental reports for the American University Experiment Station (AUES) Formerly Used Defense Site. The purpose was to identify public health hazards resulting from chemical warfare research activities conducted at the site during World War I and recommend initial public health activities to mitigate or prevent human exposure to hazardous substances released into the environment from the site. Although previous remedial investigations have concluded that the AUES site poses no further public health hazards and that no additional actions are recommended, the subsequent unexpected encounter with hazardous substances by landscapers at the Presidents residence and evidence of open air

dispersion testing mentioned in the Operation Safe Removal RI indicate that the full range of potential hazards posed by releases of hazardous substances from the site may not yet have been identified and addressed. We recommended a focused health education program to inform residents, construction workers, emergency responders and health care providers about potential hazards related to the site, and to prepare them to respond to unexpected encounters with residual ordnance and contaminants. Other specific recommendations are also provided.

Appendix B. Environmental Fate of Chemicals Associated with the Spring Valley Formerly Utilized Defense Site

ATSDR also considered the fate and transport of potential contaminants in Spring Valley. Unless containerized or trapped, most chemicals used at American University Experiment Station (AUES), including warfare agents, are not persistent, especially after 80 years of being in the environment. However, breakdown products of organoarsenicals, such as lewisite and adamsite, can leave residual arsenic in soil. Some residual metals remain in soil as well. Additionally, explosives can be environmentally persistent but explosives have not been found in tested Spring Valley soils. The chemicals presented in this section have been selected based on detections in Spring Valley soils and an association with past AUES activities.

Generally, only chemicals with low vapor pressures (i.e., that tend not to volatilize), low water solubility (i.e., that tend not to dissolve well in water), and low rates of natural degradation are likely to persist in the environment. The main degradation processes include

- Photolysis—decomposition by the action of radiant energy,
- Hydrolysis—decomposition of a substance by reaction with the elements of water to form one or more new substances,
- Oxidation—oxygen combining with other elements, and
- Microbial degradation—the process of decomposition by microbes (tiny plants and animals).

Persistence in soils also depends on the form of the chemical (solids including crystalline forms, liquids, etc.), soil composition (organic matter content, cation exchange capacity, etc.), and environmental conditions (temperature, pH, etc.). These properties also influence the likelihood of chemicals moving from one environmental medium to another. Volatilization can be an important mechanism for the transfer of some chemical warfare agents from soil and water to air (Munro et al. 1999).

The specific properties of persistent chemicals or breakdown products of those chemicals associated with past AUES activities are described in the following sections. Toxicity of these chemicals and breakdown products is discussed in Appendix E.

Arsenic from Lewisite

Lewisite (Agent L), classified as an organic arsenical, is a complex mixture of several compounds, with dichloro(2-chlorovinyl)arsine predominating. Other compounds and impurities include bis(2-chlorovinyl)chloroarsine, tris(2-chlorovinyl)arsine, and arsenic trichloride. Lewisite (L) is considered nonvolatile, although with a vapor pressure of 0.58 mmHg at 25^{o}C, it is more volatile than sulfur mustard agent (Munro et al. 1999; ORNL 1997).

Lewisite is easily broken down in soil via hydrolysis. As such, its persistence is considered "intermediate" (i.e., it can persist for days, as opposed to hours or years) (USACHPPM 1999). Depending on the moisture content, it produces two hydrolysis products, 2-chlorovinyl arsonous acid or chlorovinylarsenious acid (CVAA) and lewisite oxide (chlorovinyl arsenous oxide or CVAO). Although lewisite is basically insoluble in water, its breakdown products, CVAA and CVAO, are soluble. Lewisite oxide can be converted (oxidized) to 2-chlorovinyl arsonic acid. The trivalent arsenic (As^{3+}) in lewisite oxide is generally oxidized to pentavalent arsenic (As^{5+}) (Munro et al. 1999). Generally, As^{5+} is more stable and more commonly found in the environment (Winski and Carter 1998).

Regardless of the degradation pathway, arsenical compounds will ultimately be formed. Depending on environmental conditions, various inorganic arsenic compounds can be formed in the course of complete lewisite mineralization as demonstrated by the presence of inorganic arsenic compounds in areas of past lewisite

Other Potential Sources of Arsenic

Other potential sources of arsenic include liquid arsine and arsenic-containing compounds such as: arsenic trifluoride; arsenic trichloride; arsenic trioxide; acetylene-arsenic trichloride; dimethylarsine, methyl dichlorarsine; ethyl dichloroarsine; diphenylcyanoarsine; phenyldichloroarsine; sodium arsenite; and aluminum, calcium, magnesium, and zinc arsenides (Parsons 1998; Smart 1993).

releases, such as Spring Valley. Some inorganic arsenic can be lost to the atmosphere via volatilization as a result of the production of methylarsines (ATSDR 2000; Kohler et al. 2001; Munro et al. 1999).

Arsenic from Adamsite

Adamsite (Agent DM) is the trade name for another organic arsenical, known as 10-chloro-9-10-dihydrophenarsazine, diphenylarsenious acid, or diphenylamine chloroarsine. It was first produced during World War I, but determined not to be toxic enough for the battlefield (USACHPPM 1998). Not being readily soluble or volatile, it is considered relatively persistent in the environment. Adamsite degradation products can leave residual arsenic in soil. Although it is basically insoluble in water, it can persist in water by forming an insoluble film.

Sulfur Mustard

Sulfur mustard[5] has been used in chemical warfare as early as World War I and as late as the Iran-Iraq War in 1980–1988. It has not been produced in the United States since 1968 (ATSDR 2001). The active ingredient in sulfur mustard is bis(2-chlorethyl)sulfide. Unlike other chemical warfare agents, sulfur mustard is considered to be somewhat persistent (can last for months under very cold conditions and can persist for years in bulk quantities or if trapped or containerized) (Munro et al. 1999). In military testing areas and land dumps, where large or bulk quantities of sulfur mustard had been deposited, persistence for weeks to decades has been reported (Munro et al. 1999).

Little information exists regarding the specific fate of sulfur mustard in soil, although it is considered relatively stable. Volatilization would be the main route of sulfur mustard loss expected in dry surface soil. Bulk quantities of sulfur mustard spilled or splashed on soils could persist for years depending on soil and weather conditions. Generally, sulfur mustard persists longer under cold wet conditions (Watson and Griffin 1992).

The primary fate of buried sulfur mustard is hydrolysis, leading to the production of thiodiglycol and hydrochloric acid. Thiodiglycol is the most persistent of the sulfur mustard degradation products. Thiodiglycol is not a unique degradation product of sulfur mustard degradation—it has been used as a solvent in antifreeze solutions, in dyestuffs for printing, and in the production of polyvinyl chloride (Munro et al. 1999). Other degradation products include 1,4-dithiane and 1,4-oxathiane; these are considered thermal degradation and dehydrohalogenation products, respectively. Sulfur mustard is not normally found in groundwater because of its low solubility and rapid hydrolysis when dissolved. However, its hydrolysis product, thiodiglycol, has been reported to leach into groundwater or surface water. In addition, 1,4-dithiane and 1,4-oxathiane have been reported in groundwater beneath other chemical warfare agent burial sites. Dithiane can be transported from surface soil and water to air, where it readily *photo*oxidizes to sulfoxides and sulfones (Munro et al. 1999).

In the presence of insufficient water to dissolve sulfur mustard (e.g., bulk mustard), sulfonium ion aggregates (mustard and hemimustard-thiodiglycol aggregates) can be formed. The H-thiodiglycol (undistilled mustard-thiodigylcol) aggregate has considerable toxicity when applied dermally (Munro et al. 1999). Theoretically, oxidation products can be formed, including mustard sulfoxide, mustard sulfone, and divinyl sulfone (ATSDR 2003, Munro et al. 1999; Watson and Griffin 1992). Again, hydrolysis is the primary degradation pathway for sulfur mustard, especially in the relatively moist soil in the Spring Valley area.

Sulfur mustard can also contain a variety of impurities or by-products formed during manufacturing as well as stabilizers and starters. Sulfur mustard can form metal complexes with the metal in the containers in which it is stored (e.g., with iron) or with metal sulfides present in the soil (Munro et al. 1999).

[5] Sulfur mustard is also referred to as “mustard gas,” but the term can be a little misleading because it is stored as a liquid and is not likely to change into a gas at ordinary temperatures.

Trinitrotoluene (TNT) and Dinitrotoluene (DNT)

DNT comes in several forms, including 2,4-dinitrotoluene and 2,6-dinitrotoluene.

2,4,6-Trinitrotoluene (TNT) and dinitrotoluene (DNT), which were detected at trace amounts (0.1 parts per million (ppm)) in only a few soil samples (less than 7%) are composed of a mixture of nitric and sulfuric acid. TNT and DNT are water soluble and do not tend to bind or sorb strongly with soil, increasing the likelihood that these substances would be carried from soil to groundwater. The estimated half-life of TNT in soil ranges from 1 to 6 months. But it could persist for decades in a crystalline form or in bulk quantities. DNT tends not to stay in the environment for a long time because it is broken down by sunlight and bacteria into substances such as carbon dioxide, water, and nitric acid. However, little information is available regarding the specific behavior of DNT in soil (ATSDR 1995, 1998).

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Appendix C. DC DOH Hotline Summary of Health Conditions

The District of Columbia Department of Health set up a Health Hotline in March 2001, for Spring Valley community members to report concerns and health problems. The following is a summary of health conditions that were reported to the Hotline:

Cancers

- Bone marrow
- Bone non-specific
- Brain
- Breast
- Fibro sarcoma
- Leukemia
- Lung √
- Skin √
- Prostate/Testicular
- Lymphoma
- Multiple myeloma
- Prostate
- Testicular

General

- Asthma
- Allergies
- Benign liver growth
- Bone condition **?**
- Chronic fatigue **?**
- Chronic infections
- Chronic auto-immune disease **?**
- Hair loss
- Lupus
- Neuropathy √
- Parkinson's disease
- Skin rashes **?**
- Thyroid growth
- Skin lesions √
- Stomach illness

Blood and Bone Marrow Disorders

- Aplastic anemia
- Blood disorder, non-specific √
- Lymphoma/Hodgkins lymphoma
- Multiple myeloma
- Myelofibrosis
- Pernicious anemia

Birth Defects

- Hydrocephalus
- Club feet

√ Disease known to be associated with arsenic exposures, but also associated with many other causes as well.

? Disease that could have a possible arsenic relation, but are associated with many other causes as well.

Appendix D. Descriptions of Reported Diseases and Health Conditions

This appendix describes the general characteristics of the *blood-related disorders* of reported concern in the Spring Valley neighborhood, as well as a general overview of *peripheral neuropathy* (final sections of Appendix D).

The primary purpose of this appendix is to help the reader understand the complexity of the systems in the body related to blood and the many factors that can lead to changes in and dysfunction of these systems. For example, many of the conditions reported by Spring Valley residents (e.g., anemia) come in many forms and may be non-specific in their etiology (i.e., they may be caused by multiple factors).

An overview of the general biology of the blood (hematological), blood-forming (hematopoietic), and lymphatic systems is presented first to provide some context for subsequent discussions. Next, a brief description of the specific blood-related disorders reported by Spring Valley residents is presented. Although not a blood-related disorder, peripheral neuropathy has been included in these discussions because of its association with arsenic ingestion. The known causes or risk factors, symptoms, incidence (i.e., the number of new cases diagnosed during a predetermined time period), prevalence (i.e., the total number of cases that are present in a given time period), and typical age of onset are detailed where possible. It is very important to understand the complexity of these disorders and the uncertainties regarding their cause(s) as one begins to evaluate the possible role of particular chemical substances in their development. Such data provide added perspective on the extent to which the described diseases or conditions might or might not be ordinarily expected to occur in a given population.

General Biology of the Blood and Lymphatic Systems

The human blood and lymphatic systems are complex systems responsible for specific and multiple functions that help maintain our bodies. Blood carries oxygen to our tissues from our lungs and carries carbon dioxide from our tissues to our lungs. Blood also carries nutrients from the food we eat to our tissues, transports waste products generated in our bodies, and helps fight disease. The lymphatic system is closely linked with the blood system. It is a drainage and

filtration system that helps remove excess fluids and filters out disease-causing agents from the body. Scientists continue to study how these systems work and factors that can disrupt the normal functioning of these systems.

Blood and Bone Marrow

Whole blood consists of three primary types of cells: red corpuscles (erythrocytes), white corpuscles (leukocytes), and platelets (thrombocytes). The main function of the red blood cells is to transport oxygen to all parts of the body. The primary function of white blood cells is to protect and help the body heal wounds and fight against infection and harmful agents. A deficiency in red blood cells, that carry oxygen from the lungs to all parts of the body, results in oxygen deficits and fatigue. A shortage of white blood cells challenges your ability to fight infections and a shortage of platelets makes clotting of the blood more difficult. Several types of white blood cells exist, including lymphocytes, monocytes, eosinophils, and basophils, each with a specific function in fighting infection. Platelets are needed for normal blood clotting. Increases and decreases in the number and quality of our blood cells can be a sign of disease; physicians therefore study the number and condition of our blood cells as a diagnostic tool.

Throughout life, blood cells are continuously being replaced. The average life span of a red cell, for example, is 120 days (Brobeck 1979). A healthy person produces about 1 million red blood cells and about 200,000 white blood cells every second of their life (Rich 2002). “Stem cells” or hemoatopoietic cells are the precursor cells that produce blood cells. This occurs in the bone marrow—the soft, spongy part of the bone. Inability of marrow to produce hematopoietic cells is a common feature of many hematologic diseases (Young 1994).

Bone marrow dysfunction can lead to various blood-related disorders (e.g., anemia, leukopenia [i.e., abnormally low number of white blood cells]). Factors that can injure bone marrow include:

- High-dose radiation and chemotherapy treatments
- Exposure to toxic chemicals such as hair dyes, benzene, herbicides, insecticides
- Use of certain drugs (e.g., those used to treat rheumatoid arthritis)
- Autoimmune disorders (e.g., lupus)
- Viral infection

- Pregnancy (on occasion)
- Bone marrow diseases (e.g., leukemia)

In general, however, it is important to remember that the extent to which chemical exposures could or could not result in illness is related to the amount and duration of exposure. This concept is addressed in Section IV of this report (Toxicological Assessment).

Lymphatic System

The lymphatic system is an extensive drainage system that returns water and proteins from various tissues back to the bloodstream. It consists of a network of ducts, called lymph vessels or lymphatics, and carries lymph, a clear, watery fluid that resembles the plasma of blood. If there were no way for excess fluid to return to the blood, our body tissues would become swollen. The lymph vessels collect that excess fluid and carry it to the veins through the lymphatic system.

The lymphatic system also acts as a filter and helps defend the body against invasion by disease-causing agents such as viruses or bacteria. Harmful foreign materials are filtered out by small masses of tissue called lymph nodes that lie along the network of lymphatic vessels. Because the lymphatic system extends throughout most of the body, disorders or diseases of the lymphatic system may affect multiple organ systems. The spleen, also considered part of the lymphatic system, filters the blood similar to the way lymph nodes serve as a major filter for the lymph (Amdur et al. 1991; Brobeck 1979).

Diseases of the Blood and Bone Marrow

Anemia

Anemia is the general name for the condition characterized by a decreased number of red blood cells and a decreased amount of hemoglobin (the substance in red blood cells which transports oxygen). Causes may include nutritional deficiencies, an underlying disease, or exposure to certain chemical agents (e.g, anti-cancer drugs, benzene, ionizing radiation) (A.D.A.M., Inc., 2001a; NCHS 2002).

A description of the specific types of anemia reported by Spring Valley residents follows:

Hemolytic Anemia

Hemolytic anemia occurs when red blood cells are being destroyed prematurely and the bone marrow simply cannot keep up with the demand for new cells. Hemolytic anemia can occur for many reasons, including heat stroke, parasites, viral infections, bacteriological and chemical toxins, and other non-specific conditions. Hemolytic anemia is typically classified by the location of the defect (i.e., intrinsic or extrinsic). Intrinsic hemolytic anemia involves the destruction of the red blood cells due to a defect within the red blood cells themselves. Intrinsic hemolytic anemias are often inherited, such as sickle cell anemia and thalassemia (thalassemia occurs as a result of a genetically determined defect in hemoglobin synthesis). These conditions produce abnormal red blood cells that do not live as long as normal red blood cells. Extrinsic hemolytic anemia (also referred to as autoimmune hemolytic anemia) occurs when healthy red blood cells are destroyed by becoming trapped in the spleen, destroyed by infection, or destroyed from drugs that can affect red blood cells (University of Maryland Medical System 2001a). The overall incidence of all types of hemolytic anemia in the United States is reported to be around 4 cases in 100,000 people.

How common is anemia?

The National Center for Health Statistics (NCHS) has collected national data on the prevalence of anemia in the United States. According to NCHS, approximately 3.4 million Americans have anemia. Over 2 million of these cases affect Americans under age 45. Anemia is far more prevalent among women than among men and more people in the southern portion of the United States have reported anemia than in any other region (based on 1996 statistics) (A.D.A.M., Inc., 2001a; NCHS 2002).

Aplastic Anemia

Aplastic anemia is a rare and serious bone marrow disorder. This form of anemia occurs when the bone marrow is unable to produce sufficient numbers of blood cells. The aplastic patient typically exhibits pancytopenia (a deficiency of all three major blood cells: red blood cells, white blood cells, and platelets) with bone marrow hypoplasia (or “empty” bone marrow) (NLM 2001; Foucar 1995; Young 1994, 1997).

Aplastic anemia can be inherited or acquired. Inherited or congenital aplastic anemia is a genetic disorder characterized by chronic bone marrow failure along with various congenital anomalies

(physical abnormalities present at birth) (Young 1994). Acquired (also referred to as secondary) aplastic anemia refers to bone marrow failure which appears to be triggered by certain environmental factors and physical conditions. The majority of cases of aplastic anemia, however, are of unknown cause.

Based on clinical reports and epidemiologic studies, drug or chemical exposures are the most frequently cited cause for aplastic anemia. An international study of aplastic anemia published in 1991, however, found that only about 25% of cases overall had a likely drug etiology (Kaufman et al. 1991 and 1997). The major drug associations were with gold salts and anti-thyroid drugs. Even in cases where the association is strong, the estimated risk of aplastic anemia remains extremely small relative to the use of the drug (Young 1994).

Several chemicals have been associated with aplastic anemia, with some more strongly linked than others. For example, a definitive association has been established between benzene and aplastic anemia, based on clinical and epidemiologic data, as well as animal and in vitro studies (Al Khouri and Ericson 1999). Researchers continue to examine benzene-exposed workers, however, to better understand the strength of the link between low-level benzene exposures and aplastic anemia (Hayes et al. 2000; Yin et al. 1996). Certain types of explosives, most notably trinitrotoluene (TNT), have also been linked to aplastic anemia. Numerous cases of aplastic anemia were observed in production workers during World War I as a result of inhalation and skin contact with TNT, but the levels and duration of exposure were not well documented for these workers (DOE 1998; ATSDR 1995). More recent occupational studies and animal studies suggest that blood effects, not necessarily aplastic anemia, represent a major sign of TNT toxicity (DOE 1998; ATSDR 1995). Documented effect levels, however, are more than 1 million times higher than estimated exposure doses at the Spring Valley site. As discussed in Appendix E, Toxicologic Assessment Methodology, TNT levels in Spring Valley soils would result in estimated exposure doses of approximately one million times lower than levels at which no effects were observed.

While research has shown that arsenic is associated with a variety of blood-related disorders (see Section V of the main text), no study data were identified that show a direct relationship between arsenic and aplastic anemia. Inorganic arsenic suppresses the hematopoietic system which may result in hypoplastic anemia (a low red blood cell count that results from the underproduction of red blood cells by the bone marrow). In severe cases of arsenic poisoning, agranulocytosis (characterized by a significant decrease in the number of a certain type of white blood cells referred to as neutrophils) may develop. However, most of the chemical agents that appear to contribute to the development of agranulocytosis are not linked to the development of aplastic anemia (Young 1994; WHO 2000).

Some infectious agents (especially those causing viral hepatitis, as well as Epstein-Barr virus and HIV, the virus which can cause AIDS) are also associated with aplastic anemia. The link between hepatitis and Epstein-Barr virus is relatively well established, however, associations with other viruses such as HIV are less clear (Young 1994, Al Khouri and Ericson 1999).

Aplastic anemia affects approximately 2 to 6 in 1,000,000 people in the United States; approximately 500 to 1,000 new cases are reported each year. It affects males and females in equal numbers (Bakhshi et al. 2002). Incidence rates have been shown to vary depending on study location, gender, and age group. For example, the incidence of aplastic anemia in metropolitan Baltimore, Maryland, was reported to be as high as 7.1 per million among males and 5.4 per million among females between 1970 and 1978 (Szklo et al. 1985). A large difference in incidence rates has been observed among different age groups. Specifically, the incidence rate for individuals less than 60 years old has been observed to be approximately three cases per million compared with an incidence of 26 cases per million among those 60 years or greater (Bakhshi et al. 2002; Rawson et al. 1998). Acquired aplastic anemia affects children slightly less frequently than adults. However, children may also develop the disease from the less frequent inherited causes of bone marrow failure. In the United States and Europe, most cases occur in either the 15–24 year age group, or in the older than 60 age group (Bakhshi et al. 2002).

Pernicious Anemia (Commonly Referred to as Megaloblastic Anemia)

Pernicious anemia is a rare disorder in which the body does not absorb enough vitamin B12 from the digestive tract, resulting in an inadequate amount of red blood cells being produced (Conrad 2002; University of Maryland Medical System 2001b). Pernicious anemia may be associated with Type 1 diabetes, thyroid disease, and a family history of the disease. Other causes may include leukemia, myelofibrosis, multiple myeloma, certain hereditary disorders, chemotherapeutic agents, and excessive alcohol consumption. It is a disorder in which the incidence typically increases with age. Its frequency of occurrence has been estimated at about 0.1% of the population (Conrad 2002).

Pernicious anemia is more common in individuals of northern European descent and in the elderly. The adult form of pernicious anemia is most prevalent among individuals of either Celtic (i.e., English, Irish, Scottish) or Scandinavian origin. In these groups, 10 to 20 cases per 100,000 people occur per year (Conrad 2002). Pernicious anemia is reported less commonly in people of other racial backgrounds. Pernicious anemia from B12 deficiency tends to be an inherited tendency and is commonly seen in those over 60 years old. Researchers involved in a study done in California in 1996 used their results to estimate that as many as 800,000 elderly people in the United States have undiagnosed and untreated pernicious anemia (Carmel 1996).

Leukemia

Leukemia is a cancer that originates in the bone marrow. It is characterized by the uncontrolled growth of developing marrow cells. Leukemia actually consists of a group of different cancers of white blood cells. Leukemias are typically categorized based on their cellular origin, myeloid (i.e., myelogenous) or lymphoid (i.e., lymphocytic), and their stage of progression based on the course of the disease if left untreated (i.e., acute or chronic). Acute leukemias (e.g., acute lymphocytic leukemia [ALL] and acute myelogenous leukemia [AML]) often result in internal bleeding, anemia, or infection. Many patients with chronic leukemias (e.g., chronic lymphocytic leukemia [CLL] and chronic myelogenous leukemia [CML]) do not exhibit clinical symptoms (Landis et al. 1999; Wu and Martinez 2000).

The cause of the different forms of leukemia appears to be multi-factorial. Genetic, viral, environmental factors (e.g., ionizing radiation), drugs, and chemicals (e.g., benzene, trichloroethylene) all have been implicated in the development of leukemia. It is believed that the final common pathway is damage to the DNA in one way or another. Patients with an abnormal number of chromosomes (e.g., trisomy 21) and chromosomal translocations are at an increased risk of developing ALL. Of those patients diagnosed with CML, 90% have an acquired chromosomal abnormality (Wu and Martinez 2000). A review conducted by the Environment Committee of the Armed Forces Epidemiological Board suggested that *perhaps* an association exists between sulfur mustard and leukemia (Perrotta 1996), though no exposure data were available to support the existence or strength of the association. A more recent study of combatants in the Iran-Iraq war reports a possible link between exposures to mustard gas and CML, but authors acknowledge that previous studies have not shown such links and that further study is needed (Ghanei and Vosoghi 2002).

In 1999, 30,200 newly diagnosed cases of leukemia were reported in the United States. The incidence rates for each of the four primary types of leukemia ranges between 1 and 2.3 cases per 100,000 people per year. Of the leukemias diagnosed in the United States, approximately one-third were classified as AML (incidence = 2.3 cases per 100,000); About 26% were classified as CLL (Incidence rate = 2 cases per 100,000); about 15% were classified as CML (incidence rate = 1.3 cases per year); and about 10% were classified as ALL (incidence rate = 1 case per year). In general, males are diagnosed more often with each of the sub categories of leukemia (i.e., AML, CLL, CML, ALL) than females (Landis et al. 1999; Wu and Martinez 2000).

Multiple Myeloma

Multiple myeloma is a cancer of the plasma cells. Plasma cells are a type of white blood cell normally present in the bone marrow and responsible for producing antibodies to help fight infection. In multiple myeloma, uncontrolled growth of defective plasma cells (or myeloma cells) occurs. This disrupts the normal immune system as well as displacing normal bone marrow cells. Myeloma cells invade and damage bone and soft tissues such as nerves and muscles and

can travel through the blood stream to other bone marrow sites (Grethlein 2002; Sorenson et al. 2001; Medifocus.com 2002; NCI 2002a).

Multiple myeloma can lead to a wide variety of problems. The disease may interfere with the normal production of blood cells, resulting in leukopenia (decreased number of white blood cells), anemia (i.e., decreased number of red blood cells) and thrombocytopenia (i.e., decreased number of platelets). The defective cells may cause lesions in the skeleton or in soft tissue masses and result in a high incidence of infection in patients (Grethlein 2002).

In most cases, people who develop multiple myeloma have no clear risk factors. Multiple myeloma, like most diseases, may be the result of several factors (known and/or unknown) acting together. Some research suggests, however, that certain risk factors may increase a person's chance of getting multiple myeloma. For example, a person's family background appears to affect the risk of developing multiple myeloma; children and brothers and sisters of patients who have this disease have a slightly increased risk. Farmers and petroleum workers exposed to certain chemicals (e.g., some pesticides, benzene) also seem to have a higher-than-average chance of getting multiple myeloma. In addition, people exposed to large amounts of radiation (such as survivors of the atomic bomb explosions in Japan) have an increased risk for this disease. Scientists have some concern that smaller amounts of radiation (such as those radiologists and workers in nuclear plants are exposed to) also may increase the risk (Grethlein 2002; NCI 2002a; Eriksson and Karlsson 1992). One study was identified that investigated a possible link between arsenic and multiple myeloma; this study reported no statistically significant associations between arsenic and multiple myeloma (Eriksson and Karlsson 1992).

The overall incidence of multiple myeloma is approximately 3 to 4 cases per 100,000 persons (Grethlein 2002; Sorenson et al. 2001). In the United States, approximately 10,000 persons per year die from the disease. Without treatment, most patients die in less than 1 year; with treatment, life expectancy may be extended 2–3 years (Sorenson et al. 2001). Multiple myeloma is generally a disease of older people. Most patients who receive the diagnosis are aged 60–65 years. Only 3–5% of patients with multiple myeloma are younger than 45 years. The disease is

rare in children. Reported frequencies by age, sex, and race indicate that black males are at highest risk to develop multiple myeloma and the condition is very rare among Asian Americans. The age-adjusted annual incidence in the general U.S. population is 4.3 cases per 100,000 white men, 3 cases per 100,000 white women, 9.6 cases per 100,000 black men, and 6.7 cases per 100,000 black women (Grethlein 2002; Sorenson et al. 2001).

Myelofibrosis

Myelofibrosis, or fibrosis of the bone marrow, is another type of bone marrow disease in which fibrous scar tissue builds up inside the bone marrow cavity. The normal bone marrow has a very fine network of fibers supporting the blood-forming tissues. In myelofibrosis this network is coarsened and thickened so that normal blood cell production is blocked. It is generally triggered by a disturbance of the immune system. The disease results in the generation of poor quality blood made by the marrow. Although symptoms may not appear for a year or more, an enlarged spleen discovered at an annual medical examination may be the first clue. Eventually, symptoms become more prevalent (A.D.A.M., Inc., 2001b; The Thompson Corporation 2001).

The cause of myelofibrosis is unknown. Most cases arise secondarily to other diseases. The disorder is frequently associated, for example, with certain cancers of the hematologic system and may be seen prior to a clear diagnosis of acute leukemia, at the time of diagnosis with leukemia, or as a late event in patients previously treated for leukemia. Numerous nonmalignant diseases also have been reported in association with myelofibrosis (The Thompson Corporation 2001).

Myelofibrosis is an uncommon condition, and is especially rare in children. Most patients are over 50 years old, but it can occur at any age. Fewer than 100 cases in children have been described in the medical literature (The Thompson Corporation 2001; Johnston 2002).

Diseases of the Lymphatic System

Diseases may affect the lymph nodes, the spleen, or the collections of lymphoid tissue that occur in certain areas of the body. Lymphoma broadly describes cancers of the lymphatic system.

Lymphoma occurs when a lymphocyte (a type of white blood cell) undergoes malignant changes—multiplies, grows, and creates tumors. The two main types of lymphoma in people are Hodgkin's and non-Hodgkin's lymphomas. These two types of lymphomas are described in greater detail below (The Nemours Foundation 2001a, 2001b).

Hodgkin's Lymphoma

Hodgkin's lymphoma is a malignant disorder of the lymph node that is highly treatable. It is characterized by progressive enlargement of the lymph nodes, spleen, and liver and by progressive anemia. Since lymph tissues all over the body are connected, abnormal (cancerous) lymphocytes can circulate in the lymphatic vessels. As a result, Hodgkin's lymphoma often spreads from one lymph node to another throughout the body. Hodgkin's lymphoma can also spread to other areas and organs outside the lymph system (Lymphoma Research Foundation 2002).

The exact cause of Hodgkin's lymphoma is unknown. However, various triggers are suspected. For example, Epstein-Barr virus genes have been identified in tissue samples of approximately 20–50% of individuals with Hodgkin's lymphoma. The Epstein-Barr virus is a herpes virus that causes infectious mononucleosis. Workers who are exposed to benzene and other organic solvents may be at an increased risk of chromosome damage which may result in Hodgkin's lymphoma. However, strong evidence linking chemicals to Hodgkin's lymphoma is sparse. Hodgkin's lymphoma also is associated with a number of rare immune disorders. These include Wiskott-Aldrich syndrome (an immune deficiency disease), Klinefelter's syndrome (a chromosomal disorder) and ataxia telangiectasia (a progressive childhood disease that affects the nervous system and other body systems). Chronic inflammatory disorders such as rheumatoid arthritis and systemic lupus have also been associated with Hodgkin's lymphoma (Argiris and Kaklamani 2001; Hanson Centre for Cancer Research 1997). Recipients of heart, kidney, and other organ transplants have also been found to be at an increased risk of developing the illness. Also, Hodgkin's lymphoma is more common in western societies and in higher socio-economic groups. It is important to note, however, that most people with these possible risk factors never

develop the disease and many who are diagnosed have no identifiable risk factors (Lymphoma Research Foundation 2002).

The age-adjusted incidence rate for Hodgkin's lymphoma is 2.9 cases per 100,000 individuals. In the United States, 7,400 new cases were diagnosed during 2000 (Argiris and Kaklamani 2001). In the United States and northern Europe, Hodgkin's lymphoma is rare before the age of five, with a gradual rise in incidence until adolescence. After adolescence, there is a striking increase in incidence until age 30. Boys are more likely than girls to develop Hodgkin's lymphoma. Siblings of patients have a slightly increased risk of developing the disease (St. Jude Children's Research Hospital 2002; Argiris and Kaklamani 2001).

Non-Hodgkin's Lymphoma

Non-Hodgkin's lymphoma (NHL) is cancer that starts in lymphoid tissue (also called lymphatic tissue). NHL is a collection of more than a dozen different cancers of the lymphatic system. Cancers originating in other organs (e.g., the lung or colon) that then spread to lymphoid tissue are not considered lymphomas. Lymphomas starting in the lymphoid tissue can spread to other organs. Because NHL can develop in the body wherever lymphocytes are found, the cancer can develop nearly anywhere in the body. Symptoms can vary widely, depending on the cancer site. The most common symptom is a noticeable, usually painless swelling of a lymph node (NCI 2002b; Patlak 1996).

Little is known about exactly what causes NHL. Certain risk factors appear to exist. The likelihood of getting NHL increases with age and is more common in men than in women. NHL is more common among people with inherited immune deficiencies, autoimmune diseases, or HIV/AIDS, and among people taking immunosuppressant drugs following organ transplants. Human T-lymphotropic virus type I (HTLV-1) and Epstein-Barr virus are two infectious agents that may increase the chance of developing NHL. People who work extensively with or are otherwise exposed to certain chemicals, such as pesticides, solvents, or fertilizers, may have a greater chance of developing NHL (NCI 2002b; Patlak 1996). However, most people with these

risk factors do not get NHL, and many who do get this disease have none of the suspected risk factors (NCI 2002b).

The incidence of NHL has increased dramatically over the last couple of decades. This disease, which was historically relatively rare, is now the fifth most common cancer in the United States. According to the National Cancer Institute, NHL has increased by 75% over the last 20 years, making it the most rapidly rising cancer after lung cancer and melanoma. Nationwide, the incidence of NHL increased from 8.5 per 100,000 people in 1973 to 15.1 per 100,000 in 1991, and mortality from the disease increased from 4.8 per 100,000 people in 1973 to 6.5 per 100,000 in 1991 (Patlak 1996).The increase is a result of both better methods of detection and an actual increase in the number of new cases. Although some types of NHL are among the most common childhood cancers, more than 95% of NHL cases occur in adults. The average age at diagnosis is the early 40s. Whites are affected more often than African Americans or Asian Americans (Patlak 1996).

General Information About Peripheral Neuropathy

Peripheral neuropathy is a general term referring to disorders of peripheral nerves. The peripheral nervous system relays information back and forth from the central nervous system (brain and spinal cord) to muscles and other organs. Peripheral neuropathy is a clinical syndrome affecting a variety of peripheral nerve cells and fibers. The syndrome is characterized by pain, loss of sensation, muscle weakness and atrophy, decreased deep tendon reflexes, and vasomotor symptoms (singly or in combination). Effects may result from disease of a single nerve or many nerves simultaneously (Merck 1992; NIH/NLM 2002).

Peripheral neuropathy is a very common disorder. However, incidence rates are difficult to determine and vary depending on geographic region and other factors such as the specific type of neuropathy and the precise case definition. The population prevalence of non-specific peripheral neuropathy reported by one investigator has been estimated to be 2,400 per 100,000 people (2.4%), with prevalence increasing with age to 8,000 per 100,000 people (8.0%) (Hughes 2002).

One Web site reports that peripheral neuropathy affects at least 20 million people in the United States (Neurologychannel 2004).

Common Causes of Peripheral Neuropathy

Many diseases and conditions can cause or increase the risk of peripheral neuropathy. In some cases, the cause is unknown. The most common risk factors are summarized below (Merck 1992; Hughes 2002; NIH/NLM 2002):

- Systemic or metabolic disorders (e.g., diabetes). [Diabetes is considered the most common cause of neuropathy.]
- Heavy alcohol use.
- Infectious or inflammatory conditions (e.g., AIDS, HIV infection, rheumatoid arthritis).
- Nutritional deficiencies and metabolic disorders.
- Trauma or localized injury.
- Certain medicines or toxic substances (e.g., chemotherapeutic agents, lead, mercury, organic solvents, carbon monoxide, and arsenic).
- Hereditary disorders/predisposition.

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Appendix E. Estimates of Human Exposure Doses and Determination of Health Effects

ATSDR focused its health effects evaluation on exposures to *arsenic* levels detected in surface soil in the Spring Valley neighborhood because it was a completed exposure pathway (elevated arsenic levels were present in surface soil of some residential yards). This appendix presents the methods and findings of ATSDR's health effects assessment. It describes how ATSDR estimated exposure doses for Spring Valley residents contacting soils with detected levels of arsenic and then discusses what estimated doses mean—that is, how do the doses compare to those shown in the scientific literature to result in adverse health effects? *As is detailed below, doses associated with exposure to the detected levels of arsenic in Spring Valley soils are lower than those expected to result in illness, including the symptoms and diseases of concern reported by some area residents.*

This appendix also presents a brief overview of the toxicity data related to chemical warfare agents, lewisite and sulfur mustard, found in containers of surface disposal areas or burial pits. The potential for exposure in this scenario is extremely limited because people would need to be in a disposal area disturbing the soil and glassware containing the agent. There are four former burial pits with completion of remediation pending at one Glenbrook Road pit and one surface disposal area that contained or contain chemical warfare agents. Detected levels in soil are well below those associated with health-based comparison values and harmful effects. Soil gas migration from disposal areas into homes has not been thoroughly investigated and would be another limited but not impossible exposure scenario.

Lastly, we evaluate TNT because of its strong association with toxic effects on the blood. ATSDR looked closely at TNT toxicity in the context of site-related exposures. We also looked at phosphorus due to its concentration in residential surface soils.

Methodology

Deriving Exposure Doses

ATSDR estimated exposure doses, which are estimates of how much contaminant a person may be exposed to on a daily basis. Variables considered when estimating exposure doses include the contaminant concentration in the environmental media, the exposure amount (how much of the substance the person was actually exposed to), the exposure frequency (how often), and the exposure duration (how long). Together, these factors influence an individual's physiological response to chemical contaminant exposure and potential outcomes. Where possible, ATSDR used site-specific information about the frequency and duration of exposures. In cases where site-specific information was not available, ATSDR applied several conservative exposure assumptions to estimate exposures for Spring Valley residents. ATSDR also considered the extent to which arsenic is actually absorbed into the human body.

The following equation was used to estimate exposure doses for contaminants detected in Spring Valley soils, for both children and adults:

$$\textit{Estimated exposure dose} = \frac{C \times IR \times EF \times ED \times AF}{BW \times AT}$$

where:

- C: Contaminant concentration in soil (mg/kg or ppm)
- IR: Ingestion rate (EPA 1997):
  - IRa: 100 mg/day for an adult (0.0001 kg/day)
  - IRc: 200 mg/day for a child (0.0002 kg/day)
  - 5,000 mg/day for a pica child (0.005 kg/day)
- EF: Exposure frequency (exposure events per year of exposure): 365 days/year
- ED: Exposure duration (the duration over which exposure occurs):
  - Adult = 30 years (high end duration at one residence)
  - Child = 6 years
- AF: Absorption factor: 0.5 (ATSDR 2000a and b; Parsons 2002a)[6]
- BW: Body weight (EPA 1997):
  - BWa: Adult = 70 kg (154 pounds)
  - BWc: Child = 16 kg (35 pounds; average weight of child 1–6 years)

[6] See main text discussion regarding selection of the most appropriate absorption factor.

AT: Averaging time or the period over which cumulative exposures are averaged (ED x 365 days/year)

ATSDR also estimates "age-adjusted" doses, which take into account an integrated exposure dose over time. The approach considers changes in daily soil ingestion rates, body weight, and exposure duration for children from 1 to 6 years (EDc = 6 years) and for individuals aged 7–30 years (EDa = 24 years). The age-adjusted dose may be considered a more realistic estimate of a chronic dose a person living at a single residence for 30 years might get. Integrating in the higher intake rate of soil by children typically leads to a more conservative estimate of dose compared to an adult-only exposure scenario.

The following equation was used to estimate the age-adjusted dose:

$$\textit{Age-adjusted exposure dose} = \left(\frac{C \times EF \times AF}{AT}\right)\left(\frac{EDc \times IRc}{BWc} + \frac{EDa \times IRa}{BWa}\right)$$

Using Exposure Doses to Evaluate Potential Health Hazards

ATSDR performs an in-depth evaluation to determine whether exposures might be associated with adverse health effects (non-cancer and cancer). As part of this process, ATSDR examines relevant toxicologic, medical, and epidemiologic data to determine whether estimated doses are likely to result in adverse health effects. As a first step in evaluating non-cancer effects, ATSDR compares estimated exposure doses to standard health guideline values, including ATSDR's minimal risk levels (MRLs) and the U.S. Environmental Protection Agency's (EPA's) reference doses (RfDs). The MRLs and RfDs are estimates of daily human exposure to substances that are unlikely to result in non-cancer effects over a specified duration. Estimated exposure doses that are less than these values are not considered to be of health concern. To be very protective of human health, MRLs and RfDs have built in "uncertainty" or "safety" factors that make them much lower than levels at which health effects have been observed. Therefore, if an exposure dose is much higher than the MRL or RfD, it does not necessarily follow that adverse health effects will occur.

To evaluate carcinogens, ATSDR compares the exposure levels to cancer effect levels that have been shown to cause cancer in animals or humans. In addition, ATSDR may calculate quantitative estimates of risk using EPA's cancer slope factors. These cancer estimates are based on conservative models and assumptions, so the actual risk may be substantially less than the calculated value.

If health guideline values are exceeded, ATSDR examines the effect levels seen in the literature and more fully reviews exposure potential to help predict the likelihood of adverse health outcomes. Specifically, ATSDR examines "no-observed-adverse-effect levels" (NOAELs) or the "lowest-observed-adverse-effect levels" (LOAELs) for the most sensitive outcome for a given route of exposure (e.g., ingestion or skin contact). ATSDR looks at human studies, when available, as well as experimental animal studies. In the case of arsenic, a great deal of human data is available, though most is related to water and air exposures versus soil exposures. This information is used to describe the disease-causing potential of a particular contaminant and compare site-specific dose estimates with doses shown to result in illness in applicable studies (known as the margin of exposure). For cancer effects, ATSDR also reviews genotoxicity studies to further understand the extent to which a contaminant might be associated with cancer outcomes. This process enables ATSDR to weigh the available evidence, in light of uncertainties, and offer perspective on the plausibility of adverse health outcomes under site-specific conditions. Reviewing the scientific literature in this way enabled ATSDR to evaluate the range of dose levels that may be associated with the substance being evaluated and the characteristics of that substance that may make adverse health effects less or more likely.

Health Effects Evaluation Findings

Arsenic

How estimated arsenic doses compare to MRLs and observed effect levels

Based on ATSDR's analysis, arsenic doses associated with possible Spring Valley soil exposures are below doses shown in the scientific literature to cause harmful health effects.

Using the dose equation presented above, ATSDR estimated doses for chronic (long-term) and acute (short-term) exposures. ATSDR considered the highest composite arsenic concentration (202 ppm) detected in the most contaminated residential yard and assumed that children and adults could have had regular contact with these soils over a long period of time. For acute exposures, ATSDR assumed exposure to the highest detected concentration (529 ppm) in a single spot (discrete sample) in that same yard. Both standard child soil intakes and those associated with possible pica behavior were evaluated.[7] ATSDR also estimated exposure doses associated with exposure to the highest arsenic level detected in yards of people reporting health concerns (85 ppm). As shown in Table E-1, the estimated chronic doses are more than 14 times lower than the most sensitive endpoint related to chronic arsenic exposure (skin lesions and skin cancer). In fact, for adults, chronic dose estimates are lower than the chronic MRL and doses at which no adverse effects have been reported. Acute doses generally fall below the acute MRL, clearly indicating that no observable adverse effects are expected (e.g., gastrointestinal disturbance). For the hypothetical pica child, however, estimated doses associated with exposures to the highest arsenic levels detected at the site would be in the range at which symptoms characteristic of acute arsenic "poisoning" (e.g., facial swelling, nausea, vomiting, and diarrhea) have been reported. This would only happen if relatively *large* amounts of the *most* contaminated soil were ingested in a short amount of time. The highest levels of soil arsenic in yards were removed during the time critical removal actions; remaining concentrations are not expected to result in harmful doses, even to a pica child.

[7] Some children have a much higher tendency to ingest soil and other non-food items. This is known as pica behavior. Pica children could conceivably consume a teaspoon or more of contaminated soil each day. No documentation of this type of exposure has been identified at Spring Valley, so its consideration is purely hypothetical.

Table E-1. Estimated Arsenic Exposure Doses Compared to Screening Values and Observed Effect Levels

Exposure Situation	Exposure Concentration	Estimated Exposure Dose (mg/kg/day)			MRL (mg/kg/day)	NOAEL** (mg/kg/day)	LOAEL** (mg/kg/day)
		Adult	Child	Age-Adjusted			
Acute	529 ppm	0.0004	0.003 0.08*	--	0.005	--	0.05
Chronic	202 ppm	0.0001	0.001	0.0004	0.0003	0.0008	0.014
Chronic	85 ppm	0.00006	0.0005	0.0002	0.0003	0.0008	0.014

* Represents the dose for a hypothetical pica child.

** Screening levels and observed effect levels are based on the following principle studies: Mizuta et al. 1956 and Tseng et al. 1968.

The discussion below provides additional perspective, including discussion of some of the uncertainties associated with the data used in our evaluation.

Arsenic-related health effects

As already discussed, whether harmful effects will occur depends—as with all toxins—on both the intensity (how much) and duration (how long) of the exposure. Much of what is known about arsenic toxicity relates to high or "poisonous" levels of exposure (e.g., occupational exposures following an accidental release). Health effects associated with arsenic have been relatively well studied. But much uncertainty still exists regarding the effects caused by arsenic at relatively low environmental exposures, such as those associated with the Spring Valley site.

While researchers have studied situations in which people have been exposed to arsenic in drinking water, little data exist specifically describing the effects resulting from exposure to arsenic in soils. Further, deficiencies in the drinking water studies make interpretation difficult. Examples of such deficiencies include:

- exposure levels are not well documented,
- the study fails to account for a number of complicating factors, including exposure to other non-water sources of arsenic or genetic susceptibility to arsenic, and
- nutritional status of the exposed populations is missing.

Exposure situations described in the literature might not be fully analogous and exposure data might be sparse. Still, the available health effects data provide a relative sense of the magnitude of arsenic exposures shown to result in harmful effects.

Further, study data suggest that our bodies have the capacity to safely handle arsenic doses such as those estimated for the Spring Valley site. Various studies indicate that at low-level exposures, arsenic compounds are detoxified (or metabolized)—that is, changed into less harmful forms—and then excreted in the urine. When the body's capacity to detoxify is exceeded, blood levels of arsenic increase and adverse health effects can occur. Limited data suggest that the dose at which this happens is somewhere between 0.003–0.015 mg/kg/day (ATSDR 2000a). All of the estimated site-specific exposure doses fall below this range, indicating that the effective breakdown and excretion of arsenic could very well be expected at the exposure levels documented in Spring Valley.

The text below reviews what is known—and what is not known—about the toxicity of arsenic in general. We studied information on the toxicity of inorganic arsenic (arsenite and arsenate), and, where possible, examined the toxicity of its metabolites.

What bodily systems does arsenic affect?

Inorganic arsenic has been shown to affect multiple systems in the human body, including the gastrointestinal (stomach and intestines), hepatic (liver), renal (kidney), cardiovascular (heart and circulatory), blood and bone marrow, central nervous, skin, respiratory, and reproductive systems.

Does arsenic cause cancer?

EPA, IARC, and NTP have classified arsenic as a known human carcinogen. Chronic ingestion of soluble forms of inorganic arsenic is strongly associated with an increased risk of skin cancer. Arsenic is possibly associated with cancers of the lung, liver, bladder, kidney, and colon, but less is known about the association between inorganic arsenic and these internal organ cancers.

ATSDR estimated the theoretical cancer risk from chronic (lifetime) exposure to the highest detected concentration of arsenic in a composite soil sample (202 ppm). Using this soil arsenic concentration and conservative assumptions for soil ingestion, the estimated cancer risk was 6 x 10^{-4}. However, soil with the highest levels of arsenic contamination has been removed, so exposures at this risk level are no longer occurring. Furthermore, the estimated exposure dose of arsenic (0.0004 mg/kg/day) is 35-times less than the lowest dose of arsenic (0.014 mg/kg/day) that has been shown to cause cancer in humans (Tseng et al. 1968).

What characteristic health conditions are related to arsenic exposure?

The hallmarks of chronic (long-term) inorganic soluble arsenic ingestion include skin changes, peripheral neuropathy (a condition characterized by weakness in the extremities caused by damage to the nerves leading to these areas), and anemia (ATSDR 2000b). Hyperpigmentation (darkening of the skin in small blotches) and hyperkeratosis (the formation of excess keratin, in the form of warts or corns) are the most common or characteristic effects of arsenic ingestion. Spring Valley residents reported neither of these skin conditions[8], though some residents did report rashes. The lowest dose at which hyperpigmentation and hyperkeratosis has been reported in the literature is 0.014 mg/kg/day. This value is based on observations in a Taiwanese population exposed to arsenic in drinking water for about 45 years (Tseng et al. 1968). Estimated site doses are at least 14 times lower than the effect level reported in this particular study. Note also that exposure has to occur for 10 to 40 years before damage to the skin occurs.

Peripheral neuropathy has been associated with arsenic doses ranging from 0.03–0.1 mg/kg/day. Researchers generally have not found neurological effects of any kind in populations chronically exposed to arsenic doses of 0.006 mg/kg/day or less. Some fatigue, headache, and numbness of the extremities were reported in a single study looking at inhabitants of Chinese villages exposed to arsenic via drinking water at 0.005 mg/kg/day. However, in another study no such symptoms were reported at slightly lower doses of 0.004 mg/kg/day (ATSDR 2000a). Spring Valley chronic dose estimates are generally lower than these reported effect levels. Although two

reports of "neuropathy" were recorded on the DC DOH hotline, the maximum arsenic concentration detected in surface soils from these two residences was 4 ppm, which would result in doses of 0.000006 mg/kg/day (adult) and 0.00005 mg/kg/day (child). These estimated doses are more than 100 times lower than the lowest dose found to result in neurological effects.

Case reports have shown decreased white blood cell counts, fatigue, malaise, and gastrointestinal symptoms associated with arsenic exposures. However, these conditions are experienced by many people and from multiple causes. These non-specific conditions are generally not considered arsenic-induced until more obvious findings of pigmentation, keratosis, and peripheral neuropathy occur (Kyle and Pease 1965).

How estimated arsenic doses compare to observed effect levels associated with blood-related disorders reported by community members

Based on the findings of our research, no blood-related disorders were shown to occur in the range of arsenic doses estimated for Spring Valley. In fact, arsenic-related blood conditions have generally not been reported in the absence of skin lesions, the most sensitive arsenic-related endpoint. For several of the reported conditions (e.g., leukemia and lymphoma), no documentation was found linking them to arsenic exposures.

The findings of the health effects assessment described in Section V reveal that exposures to the levels of arsenic detected in the Spring Valley neighborhood soils are not expected to result in adverse health effects. This conclusion was based on comparison of site-specific doses to the arsenic doses associated with the most sensitive effects or endpoints in the human body. Nonetheless, to thoroughly address community concerns, ATSDR further reviewed the scientific literature to document if and how site exposure doses relate to doses associated with the documented illness reported by some Spring Valley residents (see Appendix C). In the process, we attempted to identify information that could confirm or dispel possible links between arsenic and those health conditions reported by Spring Valley residents. The research was conducted in

[8] One child at the American University Child Development Center was reported as having a "rash" and "warts."

two phases: (1) literature search and (2) evaluation and comparison of available dose-response data to site-specific doses. We focused on blood, blood-forming, and lymphatic system disorders. Our research strategy and findings are detailed below.

Literature search methodology

An extensive search of the current scientific literature was conducted to identify information pertaining to: (1) the characteristics, known/suspected causes, and prevalence of the reported diseases (see Appendices C and D); (2) the behavior of arsenic and other site-related contaminants in the environment and within the human body; and (3) possible relationships between detected levels of contaminants in soil and dust/air and the diseases of concern.

The literature search was conducted in a step-wise manner. We first reviewed the secondary literature to identify pertinent studies already assembled and peer-reviewed, including ATSDR's Toxicological Profile for Arsenic (ATSDR 2000a), EPA's Integrated Risk Information System (IRIS), and the World Health Organization (WHO) Environmental Health Criteria (WHO 2001). Water quality criteria documentation was also reviewed (NAS 1999, 2001). Original references cited in these documents were obtained and reviewed, as appropriate. A literature search was then conducted to identify additional toxicity data published that might not have been captured in the secondary sources, including study data published since the release of the secondary sources. Search dates generally covered the years 1990–2002. The primary on-line libraries searched include PubMed and TOXLINE. Primary terms searched included: inorganic arsenic (CAS# 7440-38-2), inorganic arsenic compounds, arsine, and specific organoarsenical chemical warfare agents (e.g., adamsite and lewisite).[9] A secondary search was conducted to identify studies specific to arsenic associated with chemical warfare weapons and arsenic in soils. A search was also performed for dimethylarsinate (DMA)/cacodylic acid, a primary metabolite of arsenic.

[9] For example: arsenic trioxide, *arsenite, and *arsenate.

Key words used in the search included[10]: anemia* (e.g., anemia, aplastic anemia, megaloblastic anemia, and pernicious anemia), autoimmun*, blood disorders, bone marrow, eosinophilia, erythro* (e.g., erythropoiesis), granulocytopenia, hemato*, immunotox*, leuk* (e.g., leukemia and leukopenia), lymph* (e.g., lymphatic and lymphoma), multiple myeloma, myelofibrosis, and plasma* (e.g., plasmacytoma).

More than 400 abstracts were considered relevant to this effort. A subset of articles was retrieved and critically reviewed.

Findings

Table E-2 summarizes how Spring Valley exposure doses compare with doses observed to result in anemia and other blood-related disorders (referred to as the "margin of exposure"). As can be seen, site doses are 20 to thousands of times lower than these documented adverse effect levels. The table presents the type of exposures (e.g., acute, intermediate and chronic) and the medium by which the dose was received (e.g., water or food). None of the exposure situations are directly analogous to the Spring Valley soil exposures under study. They do, however, provide some basis for comparison. Note also that dose-response data available for hematological effects are drawn primarily from case reports. As such, dose-response data come from a relatively small data pool. Many of the larger-scale epidemiologic studies that have studied environmental exposures to arsenic (e.g., drinking water studies) either lack the exposure data necessary to define dose-response relationships or do not specifically evaluate blood-related conditions. Nonetheless, these comparisons offer a fair amount of perspective, as does the narrative that follows.

[10] * Indicates that any word that includes that fragment was captured.

Table E-2. In the Scientific Literature, How Do Site-Specific Estimated Exposure Doses Compare to Levels Associated with Blood-related Effects?

Observed Effect*	Observed Effect Level (mg/kg/day)	Matrix	Form	Reference	Margin of Exposure†
Pancytopenia, leukopenia	0.2 (A)	water	NS	Armstrong et al. 1984‡	67
Hemolysis	8 (A)	NS	As^{3+}	Fincher and Koerker 1987‡	2,667
Increase in blood enzyme levels	13 (A)	acute poisoning	As^{3+}	Kamijo et al. 1998‡	4,333
Increase in blood enzyme levels	22 (A)	acute poisoning	As^{3+}	Levin-Scherz et al. 1987‡	7,333
High leukocyte count, low hematocrit	6 (A)	acute poisoning	As^{3+}	Lugo et al. 1969‡	2,000
Mild anemia, leukopenia	0.05 (A)	dietary	As^{5+}	Mizuta et al. 1956‡	17
Decrease polychromatic erythrocytes in bone marrow (mouse)	6 (A)	gavage in water	As^{3+}	Tice et al. 1997‡	2,000
Anemia, leukopenia	0.1 (I)	water	As^{3+} As^{5+}	Franzblau and Lilis 1989‡	100
Anemia, leukopenia, erythroid hyperplasia of bone marrow	0.06 (I)	water	NS	Wagner et al. 1979‡	60
Anemia	0.06 (C)	water	NS	Guha Mazumder et al. 1988‡	60
Anemia	0.05 (C)	water	NS	Zaldivar and Guillier 1977‡	50
Slight transient decrease in hemoglobin values (rat)	20 (C)	dietary	As^{3+}	Byron et al. 1967‡	20,000
Slight to moderate anemia (dog)	2.4 (C)	dietary	As^{5+}	Byron et al. 1967‡	2,400

Key:
A = acute exposures
I = intermediate exposures
C = chronic exposures
mg/kg/day = milligram per kilogram per day
NS = not specified

* The observed effects are reported from human studies, unless otherwise noted.

† The margin of exposure (MOE) represents the ratio between estimated doses at Spring Valley and the observed effect level reported in the table. For intermediate and chronic effects, we compared the most conservative chronic dose estimate of 0.001 mg/kg/day (child dose) to the observed effect levels reported in the table. Similarly for acute effects, we compared the estimated acute dose estimate of 0.003 mg/kg/day (child dose). For example, for the first entry in the table, the MOE = 0.2 mg/kg/day (observed effect level) ÷ 0.003 mg/kg/day (estimated acute dose at Spring Valley) = 67.

‡ Cited in ATSDR 2000a.

Anemia often accompanies the skin lesions and neuropathy seen in patients chronically poisoned by arsenic. But these conditions tend to be associated with high or intense exposures. Exposures of several milligrams of arsenic a day, for example, can result in anemia within a few weeks to months (ATSDR 2000b). Estimated Spring Valley exposures, however, are believed to be in the range of 0.02–0.04 milligrams per day, assuming ingestion of the highest detected concentration of arsenic in soil (202 ppm).

Anemia is a common feature of arsenic poisoning following oral (ingestion) exposures. Anemia and leukopenia (a reduced number of white blood cells) have been observed in humans following acute, intermediate, and chronic oral exposures at doses of 0.05 mg/kg/day or more. Still, anemia has not been observed in all cases of arsenic exposure or poisonings. Observed effects could be due to direct action on the blood cells or suppression of the formation of blood cells in the bone marrow (ATSDR 2000a; Chang et al. 1996).

Arsenic has not been directly linked to aplastic anemia. While some references list arsenic among substances possibly associated with aplastic anemia, no data were identified that showed any specific dose-response relationships between arsenic exposures and aplastic anemia (Young 1994).

No identified studies found statistically significant associations between arsenic and cancers of the blood, bone marrow, or lymphatic systems (e.g., leukemia, multiple myeloma, and lymphoma). As mentioned above, arsenic is strongly associated with skin cancer; some studies suggest that associations could also exist for tumors of the bladder, kidney, liver, lung, and prostate (ATSDR 2000a; EPA 2002).

Chemical Warfare Agents Found in Containers of Disposal Areas

Some chemical warfare agents and associated breakdown products were detected at trace levels (below health-based comparison values) in only a few soil samples. Based on soil concentrations, exposure to these substances via the soil pathway has no adverse health consequences. Information regarding the toxicity of the chemical warfare agents found in

disposal areas is presented below to give readers an overview of the toxicity of these agents. Containerized chemical warfare agents, if contacted, are clearly toxic and at high enough doses can have some debilitating effects. *However, as previously stated, direct exposure to these agents at such levels in Spring Valley is only a remote possibility.*

Organoarsenicals: Lewisite and Adamsite

During World War I, chemical warfare agents, lewisite and adamsite, were reportedly handled at the American University Experiment Station (AUES). Although the U.S. Army Corps of Engineers (USACE) identified lewisite and its breakdown products in some of the buried bottles removed from the Spring Valley site, these agents were not prevalent in area soils. Therefore, while no question remains regarding whether these agents are highly toxic, in all likelihood most area residents would not come in contact with them at all, let alone at harmful levels. Workers involved in soil excavations might have had some short-term exposures to higher levels, consistent with some reports of burning eyes and respiratory system reaction.

Exposure potential

The extent to which people might have been directly exposed to lewisite and adamsite chemical warfare agents (e.g., during past excavations or contact with containers) and some of the breakdown products is not fully known. Nevertheless, as discussed in Section IV and Appendix B, these chemical warfare agents are broken down (degrade) fairly rapidly in soil. Samples of materials from buried bottles removed from the Glenbrook Road area in the summer of 2001 were analyzed for lewisite derivatives.[11] Nine of 33 samples detected concentrations up to 148,220 ppm (U.S. Army Soldier Biological Chemical Command 2001). This maximum concentration was identified as L3 [tris-(2-chlorovinyl)arsine]. A small amount of lewisite was also detected in a bottle from a surface disposal area on American University Lot 18. One

[11] The results of bottle contents were reported as L1+CVAA [2-chlorovinyl arsine dichloride +2-chlorovinyl arsonous acid], L2+L2-acid [bis-(2-chlorovinyl)chloroarsine +bis-(2-chlorovinyl) arsinous acid], and L3 [tris-(2-chlorovinyl)arsine]. The sums were used because gas chromatograph methods could not distinguish between the compounds.

surface soil sample for which lewisite was tested did not contain detectable concentrations (Parsons 2002b). No lewisite breakdown products (CVAA/CVAO [2-chlorovinyl arsonous acid/chlorovinyl arsenous oxide]) were detected in sampled soils.

These data show that human contact with organoarsenicals from surface disposal areas and burial pits is feasible, but not likely, especially at harmful levels. Because detectable levels were found in excavated containers, some future potential remains for digging up the soil in yet undiscovered surface disposal areas/burial pits to depths of several feet and becoming exposed to agents in broken or degraded containers. However, as discussed in Appendix B, lewisite and its breakdown products are not likely to persist in the environment.

Physiologic effects

Both blister agent, lewisite, and vomiting agent, adamsite, are harmful upon direct contact. More lewisite than adamsite toxicity information was identified in the literature.

Lewisite can cause painful blistering on contact with the skin or mucous membranes. It can be absorbed by the skin and act as a "systemic" poison, producing effects such as pulmonary edema, diarrhea, restlessness, and low blood pressure (NRC 1995). Tissues and organs that could be affected by lewisite include the liver, gall bladder, bladder, lungs, and kidneys. Regarding the specific doses of lewisite required to produce toxic effects, however, a large knowledge gap remains (ORNL 1997). Still, some acute toxicity studies in rats and rabbits are available. The Army developed an interim RfD for lewisite of 0.0001 mg/kg/day (ORNL 1997).[12] But in an independent assessment of the RfD, the National Research Council (NRC) reported that because of the poor data, the strength of evidence for deriving the RfD for lewisite is weak. To account for the uncertainty, the National Research Council recommended using a rabbit study and

[12] An RfD represents a dose at or below which no harmful health effects would be expected. It is calculated by critically reviewing studies to identify the highest dose at which a critical or sensitive effect is not observed and applying a series of "safety" factors to account for uncertainties. For lewisite, the RfD is based on a NOAEL of 0.44 mg/kg/day, reported in a reproductive study in rats. An uncertainty factor of 3,000 was applied to account for differences between humans and animals and variability among individuals. (The same RfD has been recommended for lewisite oxide [USACHPPM 1999]).

applying more uncertainty factors. The resulting RfD is 0.00001 mg/day/day—10 times lower than the Army value (NRC 1999). No mammalian toxicity data are available for the CVAA or CVAO, but are presumed to have comparable toxicity to lewisite (Munro et al. 1999).

The cancer-causing potential of lewisite is uncertain. No studies were identified in which the carcinogenicity of lewisite was specifically evaluated or quantified. Genotoxicity studies (e.g., mutation assays), which can provide some supporting evidence for a chemical's carcinogenic potential, have been conducted for lewisite. Most test results were negative, but the overall data set is considered inconclusive (NRC 1995; ORNL 1997). We do know, however, that lewisite breakdown products are carcinogenic (e.g., the arsenicals).

Adamsite is a nose and throat irritant. The Army described it as a vomiting agent. First produced during World War I, it was not considered "toxic enough" for battlefield use (USACHPPM 1998). Comparative *in vitro* studies looking at the inhibition of cell proliferation reveals adamsite to be less toxic than lewisite (Henriksson et al. 1996). The human body "will detoxify" the effects of mild exposures within 30 minutes of evacuation (USACHPPM 1998). Little other toxicity data for adamsite were identified.

Sulfur Mustard

Available sampling data indicate that neither sulfur mustard (also referred to as "HD" or "mustard HD") nor its breakdown products are present in Spring Valley soils at harmful levels. The Army has established an RfD of 0.000007 mg/kg/day for sulfur mustard (USACHHPM 1999). Detected levels of the mustard breakdown product thiodiglycol in Spring Valley soils are lower than the RfD established for the more toxic parent compound.

Exposure potential

Sulfur mustard was detected in some of the materials sampled from buried bottles. Its primary breakdown product (thiodiglycol) was detected in a few soil samples, but at very low levels. Resulting exposures to these levels are well below health-based screening values. Assuming some individuals could be exposed to even the maximum detected concentration of thiodiglycol

(2.1 ppm) on a regular basis, estimated doses would only be 0.000003 mg/kg/day. As described below, no known evidence suggests that dose levels this low could result in harmful effects.

Biological fate

Sulfur mustard is fat-soluble and therefore, readily absorbed through exposed tissues. It can affect multiple tissues, depending on the route, extent, and duration of exposure. Sulfur mustard is considered an "alkylating" agent and can harm cells through chemical reactions with proteins, enzymes, and nucleic acids in the cells (Reutter 1999; Watson and Griffin 1992).

Physiological effects

Like lewisite, sulfur mustard is a blister agent. It can produce direct or delayed toxicity. Sulfur mustard is directly toxic to the various components of human cells (e.g., DNA, RNA, and proteins) and produces cellular damage in a manner similar to radiation. For example, mustard can be directly toxic to hematopoietic tissues, leading to decreased white blood cell counts (ATSDR 2003; USACHPPM 1998; Watson and Griffin 1992). The effects of battlefield exposure have been well described, but the doses that produced them are not specifically known. Upon acute exposure, sulfur mustard has been shown to produce chemical burns on tissues that come in contact with the vapors or with the aerosols containing the agent. Affected tissues include the eyes, nose, throat, skin, bronchial, and upper gastrointestinal tract (Reutter 1999; Watson and Griffin 1992). Wartime exposures include eye and skin lesions, with respiratory and gastrointestinal problems observed in more severe cases. Soldiers exposed to sulfur mustard in World War I also seemed to have a higher rate of respiratory cancers (Reutter 1999). Exposures to mustard high enough to cause acute symptoms (such as might occur on the battlefield or in test chambers) are associated with an increased risk of respiratory and skin cancers, and perhaps leukemia (Perrotta 1996). Nothing in the published literature, however, points to associations between sulfur mustard or its breakdown products with aplastic anemia, or any cancers of the blood or hematopoietic systems.

Unlike the parent sulfur mustard, the mustard degradation products—including thiodiglycol—appear to have relatively low toxicity. The acute toxicity of sulfur mustard degradation products has been fairly well studied in animals, but no dose-response data were identified for humans. Only mild effects (decreased body weights and mild kidney effects) were observed in rats exposed to doses of thiodiglycol as high as 5,000 mg/kg/day; no effects at all were reported at 500 mg/kg/day (Munro et al. 1999). While no human studies were identified and uncertainty remains regarding the effects that could be seen at lower doses, what is known is that the estimated exposure thiodiglycol doses (0.000003 mg/kg/day) are more than a million times lower than doses shown to cause no effects at all.

Both 1,4-dithiane and 1,4-oxathiane are of low acute toxicity to mammalian species (Munro et al. 1999), and although few longer-term (chronic) studies were identified in a recent review, available data suggest only very high doses triggered adverse health effects. Similarly, only mild effects were observed in a study of mustard breakdown product 1,4-dithiane at doses ranging from 105 mg/kg/day (nasal lesions) to 420 mg/kg/day (liver and kidney effects) (Munro et al. 1999; EPA 2002). Neither of these chemicals were detected in tested soil samples.

The Army has compiled some data on the toxic properties of mustard-lewisite mixture. The mixture, like its single components, is considered a blister and alkylating agent that can affect multiple tissues (USACHPPM 1998). The mixture degrades into hydrochloric acid, thiodiglycol, and nonvesicant arsenic compounds.

Explosives

2,4,6-Trinitrotoluene (TNT)

Soils samples showed that TNT is not present at harmful levels. As noted earlier, TNT was not detected in burial areas (reported less than 0.1 ppm). The reported detection limit of 0.1 ppm is 200 times lower than ATSDR's health-based comparison value, which represents a level of TNT considered to be safe. Because of TNT's strong association with toxic effects on the blood,

ATSDR looked a little more closely at TNT toxicity in the context of what is known about site-related exposures.

Exposure potential

Based on available sampling data, exposure to harmful levels of TNT is not occurring. General information on TNT toxicity is presented below for some general perspective.

Physiological effects

At levels associated with its use as an explosive, TNT can be a potent toxicant. At high doses, the blood, lymphatic, and immune systems have all become severely impaired. Anemia is one of the signs of TNT toxicity. During World War I numerous reports of anemia and some cases of aplastic anemia were reported among munition workers exposed to airborne TNT. In animal studies moderate anemia was seen at doses ranging from 8–200 mg/kg/day. In these same studies no anemia was reported at doses below approximately 1–5 mg/kg/day (ATSDR 1995).

Although available cancer data for TNT are sparse, both human and animal studies report possible links between TNT and leukemias and lymphomas. EPA has therefore classified TNT as a possible human carcinogen. This is based largely on a preliminary study of a German population living near World War II munitions plants. The study supposedly established an association between humans living near wastes from the plants and some types of leukemia. While a causal relationship is suggested, further investigation is needed to identify possible confounding factors (e.g., other exposures), environmental conditions (no environmental data are available), and overall living conditions (Kolb 1993). In addition, leukemias and lymphoma of the spleen have been reported in mice exposed to 1.5 mg/kg/day TNT in their food (Army 1984). The data from the mice study at least suggest that cancer effects, like the anemias described above, have been linked with TNT. But those links appear at doses far greater than those known to be present in Spring Valley.

Phosphorus

Phosphorus was reported at concentrations up to 1,530 parts per million (ppm) in residential soil. Estimated exposure doses associated with this concentration of phosphorus are 0.019 mg/kg/day for a child and 0.002 mg/kg/day for an adult. These estimated doses are close to or below the dose (0.015 mg/kg/day) at which *no* effects were reported in animal studies following exposure to white (or elemental) phosphorus, the most toxic form of phosphorus. However, they are above ATSDR's child and adult EMEG (10 and 100 ppm, respectively) for white phosphorus and are within an order of magnitude of LOAELs for adverse health effects that have been observed in animals and humans. White phosphorus is used mainly for producing phosphoric acid and other chemicals used to make fertilizers, food additives, cleaning compounds, etc. In the military, it has been used in ammunitions (ATSDR 1997). The form of phosphorus detected at the site is not specified; different chemical forms of phosphorus differ greatly in their toxicity. Assuming that all of the phosphorus is white phosphorus overestimates toxicity; total phosphorus actually includes other less toxic forms such as phosphates. It is unlikely that phosphorus in surface soil remains predominantly elemental in the form of white phosphorus.

Note that phosphorus also can occur naturally (less toxic forms from phosphate-bearing minerals and rocks) and is part of the normal diet. Reported background levels range up to 6,800 ppm in eastern U.S. soils (Boerngen and Shacklette 1984). Tolerable upper intake levels of phosphorus have been developed: 4 grams per day (g/day) for adolescents and adults (ages 9–70 years), 3 g/day for toddlers and children (1–8 years) and older adults (>70 years), and 3.5 g/day for pregnant women (Institute of Medicine 1999). For perspective, estimated phosphorus intakes associated with the incidental ingestion of 1,530 ppm phosphorus in soil would be much lower—approximately 0.0003 g/day for a child (assuming an intake of 200 milligrams of soil per day) and 0.00015 g/day for an adult (assuming an intake of 100 milligrams of soil per day).

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Appendix F. Brochure: Safe Gardening, Safe Play, and a Safe Home

Safe Gardening, Safe Play, and a Safe Home

An interim guide to reducing arsenic exposure in Spring Valley

This pamphlet was designed for residents of Spring Valley. The purpose is to provide residents with good health practice tips for the home, lawn and garden work, and play. By following the tips in this pamphlet, residents can greatly reduce their exposure to arsenic as well as to other potentially harmful materials such as pesticides and germs that might be in the soil.

Introduction

Approximately 146 properties in the Spring Valley area have some soil arsenic levels greater than 20 parts per million (ppm), a level designated by local and federal officials as a clean-up level for this community. Although the levels of arsenic detected in this community are in some cases elevated in soil, limited exposure studies to date suggest that the arsenic is not getting into residents' bodies in any greater amounts than what you would find in the general public. Although this is reassuring, it is recognized that some residents may still be concerned until the cleanup of their yards has occurred. For those and other concerned residents, the good practice tips in this pamphlet will be effective in reducing exposures to arsenic, pesticides, and germs that might be present in the soil.

Enjoying Your Lawn and Garden

Eating fruits and vegetables and getting plenty of exercise are essential parts of a healthy lifestyle. People enjoy many activities on their lawn and in their garden, which provide places both for exercise and for growing fresh fruits and vegetables. The levels of arsenic found in the soil of most properties in Spring Valley are at or below background (natural) levels and present no health hazard for people doing lawn or garden activities. Still, some families have arsenic in their soil at levels higher than the clean-up level and wish to reduce their exposure to the lowest possible level. Activities such as playing, gardening, and working on your lawn can increase your opportunity for exposure even though they are healthful. The information in this pamphlet will help you understand how to reduce your chances of exposure so you do not feel you have to give up the outdoor activities that you and your family enjoy. Understand that each property is different. Some of the tips outlined may apply to your situation and some may not.

Arsenic

A major source of elevated arsenic in Spring Valley surface soils is from degradation of chemical warfare agents tested there during World War I (WWI).

The U.S. Environmental Protection Agency (EPA), Army Corps of Engineers (ACOE), and the D.C. Department of Health set an arsenic cleanup level of 20 ppm for yards in Spring Valley. ACOE has removed soil from some contaminated properties and is planning to continue soil removals over the next several years. Until the contaminated soil is replaced, residents may

reduce their chances of exposure by following the guidelines in this pamphlet. Additional information about arsenic can be found at the ATSDR Spring Valley Information Repository at Palisades Library (4901 V Street N.W. at 49th Street N.W.) or through the ATSDR Spring Valley Web site at www.atsdr.cdc.gov/sites/springvalley.

Arsenic and Gardening

Arsenic is a naturally occurring element. Two types of arsenic are found in the environment. The first is **inorganic arsenic**, which is usually found in the environment combined with other elements such as oxygen, iron, and sulfur. The second type of arsenic is **organic arsenic**. Organic arsenic is formed by arsenic combined with carbon and hydrogen. It is found in plants, fish, and shellfish and is considered less harmful than inorganic arsenic.

For most properties in Spring Valley the soil arsenic levels are not high enough to cause any health problems associated with eating homegrown vegetables. Indeed, even for those areas showing elevated levels of arsenic, the uptake into home grown vegetables or fruits, is not likely to be sufficient to cause any health effects to persons gardening in the soil or eating vegetables grown in the garden. This will be explained below.

Gardening in soil with elevated levels of arsenic has two main issues: cleaning soil from the edible portion of the plant and absorption of arsenic by the plant. It is always a good health practice to wash all fruits and vegetables thoroughly whether they are bought or homegrown. Washing the soil from your homegrown fruits and vegetables is one of the most effective ways of reducing your exposure to not only arsenic but to pesticides and germs as well.

Most edible plants absorb some small amounts of arsenic, but usually do not contain enough arsenic to be of health concern. The amount of arsenic absorbed by plants can depend on many factors. Some of the most important factors are soil acidity, nutrient content, iron, organic matter, and plant type. Plants can absorb more arsenic if you have acidic soil. Keeping your soil at a near-neutral range (pH 6–7) can help reduce the amount of arsenic absorbed in plants. Maintaining adequate levels of plant nutrients in your soil can help reduce arsenic absorption. Adding a balanced commercial fertilizer to soil can help maintain correct levels of key plant nutrients. Iron can prevent arsenic from being absorbed. The iron combines with arsenic to form iron arsenate, a form of arsenic that is not well absorbed by plants. Increased amounts of organic matter are also helpful; the organic matter binds to arsenic and reduces how much plants take up. Some lawn and garden products contain arsenic, so it is a good idea to check with your lawn and garden store for products that do not contain arsenic.

Another important thing to keep in mind is that arsenic deposited by the chemical weapons tests in Spring Valley has been in the soil for 80 years. The longer the arsenic stays in the soil, the more it becomes bound to the soil, making it less available to plants and humans.

Arsenic levels in garden areas tend to be lower than in other areas of the property because most gardeners add soil conditioners such as compost and topsoil. By adding these conditioners, the concentration of arsenic in the soil is diluted. Some gardeners might want to add additional compost or topsoil from an area of their yard that does not have elevated levels of arsenic. In some cases it may be best to remove the soil from the place you want to garden and replace it with topsoil from a commercial garden center.

Plants vary in the amount of arsenic they absorb from the soil and where they store arsenic. Some plants move arsenic from the roots to the leaves, while others absorb and store it in the roots only. Fruit-type vegetables such as tomatoes concentrate arsenic in the roots and very little arsenic is taken up in the edible portion of the plant. Leafy vegetables also store arsenic in their roots, but some is also stored in the stems and leaves. Lettuce and some members of the Brassica plant family such as collards, kale, mustard, and turnip greens store more arsenic in the leaves than do other crops, but not at concentrations high enough to cause concern. Root crops such as beets, turnips, carrots, and potatoes absorb most of the arsenic in the surface skin of the vegetable. By peeling the skins of root crops, you can eliminate the portion of the plant that contains arsenic. Again, garden vegetables grown in Spring Valley should not contain enough arsenic to be of health concern. Recommendations for conditioning your soil, washing vegetables, and peeling root crops are intended to provide you the property owner with additional options for reducing exposure to arsenic.

For some properties with limited space for gardens, a raised garden bed might be an option. Instructions for building a raised garden bed can be found in most gardening books. The raised beds can be filled with soil from commercial gardening centers or from an area of your yard that does not contain elevated levels of arsenic. Your local agricultural extension office is an excellent source of for all types of gardening information.

Can I Eat Fruits and Vegetables Grown in My Garden?

Yes. Homegrown fruits and vegetables are highly unlikely to contain arsenic levels that would affect your health. Vegetables grown in soils with arsenic will take up some small amounts of arsenic. However, we believe the benefits from the eating your homegrown fruits and vegetables outweigh the risk presented by their arsenic content. By following the recommendations in the Tips for Safe Gardening, Safe Play, and a Safe Home section, you can greatly reduce your exposure to arsenic from the soil.

Unknown Buried Material

As the result of activities performed at the American University Experimental Station during WWI, dangerous materials used in the war effort were often buried as a means of disposal. ACOE, using historical records, has identified several areas of concern and continues to investigate. Buried items already discovered include buried munitions (both conventional and those containing chemical warfare agents), chemical weapon agents in ceramic jugs, laboratory waste, and other related items. These items have been buried since WWI and many have rusted and deteriorated to a point that they pose little health risk but it is possible for some to contain chemical agents. There have been very few reports of these items being uncovered through normal yard work, but the possibility does exist. Existing gardens and flowerbeds that have already been tilled or dug in are considered very low risk, but you should follow precautions. If you dig up any suspicious glass or metal object, do not attempt to remove the item yourself. Call ACOE at 1-800-434-0988, 410-962-7522, or 202-686-3359 for assistance.

Tips for Safe Gardening, Safe Play, and a Safe Home

Preparing Your Garden Soil

We are all exposed to a little arsenic every day. The recommendations below are for people who want to keep their exposure to the minimum possible. These recommendations are intended to be on the safe side. Under normal circumstances, a lapse in following these recommendations will not, by itself, lead to health problems.

- Increase the organic matter in your soil by adding compost or manure from outside sources such as commercial garden centers.
- Keep soil pH in the near-neutral range (pH 6–7). For a soils test, check with your local agricultural extension office or purchase a soils test kits at a garden center.
- Maintain adequate levels of plant nutrients by using a balanced commercial fertilizer.
- Maintain adequate levels of iron in your soil.
- Consider building a raised-bed garden. Fill it with topsoil and compost from outside sources or areas of your yard that do not have elevated levels of arsenic.

Note: Do not use chromated copper arsenate (CCA)-treated wood to build your raised garden beds. CCA contains arsenic that can leach into your soil. Use a safer nonarsenic pressure-treated wood such as ammoniacal copper quaternary (ACQ). Bricks, stone, or other wood products such as cedar or redwood can be used to build a raised garden bed.

Working in the Garden and Yard

- Avoid eating or drinking while working in the yard or garden because contaminated soil and dust might get on your food and you could accidentally swallow it.
- Dampen soils with water before you garden to limit the amount of dust you inhale.

- Avoid working in the yard on windy days, when dust can be stirred up and possibly increase your exposure.
- Consider wearing a mask if you spend time in dusty areas.
- Wash your hands after gardening.
- Wash work clothes to remove dust and dirt.
- Take your shoes off at the door to avoid tracking soil into your home.

Preparing Fruits and Vegetables

- Clean your hands, cutting boards, and kitchen tools with hot, soapy water and rinse well before and after handling your fruits and vegetables.
- Soak garden produce in cool water and rinse thoroughly until the water runs clear. Commercial vegetable-cleaning products are available in supermarkets to help free soil residues from your produce. These products work well with leafy vegetables. Vinegar can also be used for cleaning produce.
- Scrub firm fruits and root crops with a vegetable-cleaning brush to remove dust and dirt before peeling or eating.
- Peel root crops like carrots, rutabagas, radishes, and turnips.
- Wash berry fruits like strawberries and blackberries, and remove the "caps" (the tops of the berries where the stem and leaves attach).

Buy Some, Grow Some

- Eat some fruits and vegetables from your garden and some from the farmer's market or grocery store. Eating a mix of homegrown and commercial products can help reduce your potential exposure.

Creating Play Areas for Children

- Fill sandboxes with sand or soil from an outside source such as a commercial gardening center.
- Cover bare soil with grass or other material such as mulch.
- Keep children from playing in contaminated soil. The most likely way for children to become exposed to arsenic is from ingesting (eating) dirt.
- Have children wash hands and faces after they play in the yard.

Cleaning Your Home

- Remove work and play shoes before entering your house.
- Damp-mop floors and wipe down counters, tables, and window ledges regularly.
- To reduce dust levels in the home, consider upgrading your vacuum cleaner bags to those that filter better or simply change your bags more often. Some persons may want to buy a vacuum cleaner with a HEPA (high-efficiency particulate air) filter to better reduce dust levels.
- Wash the soil from homegrown fruits and vegetables before bringing them into your home.
- Keep pets out of areas of contaminated soil. Dogs and cats carry contaminated soil on their feet and fur into the home. Bathe your pets frequently.

For more information about ATSDR's work at Spring Valley, visit our web site at www.atsdr.cdc.gov/sites/springvalley or contact any of ATSDR's Spring Valley Team members:

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Note: (Personal communication from Dr. David Stilwell, Department of Analytical Chemistry, The Connecticut Agricultural Experiment Station, New Haven, CT).

Appendix G. ATSDR Glossary of Terms

ATSDR Glossary of Terms

The Agency for Toxic Substances and Disease Registry (ATSDR) is a federal public health agency with headquarters in Atlanta, Georgia, and 10 regional offices in the United States. ATSDR's mission is to serve the public by using the best science, taking responsive public health actions, and providing trusted health information to prevent harmful exposures and diseases related to toxic substances. ATSDR is not a regulatory agency, unlike the U.S. Environmental Protection Agency (EPA), which is the federal agency that develops and enforces environmental laws to protect the environment and human health. This glossary defines words used by ATSDR in communications with the public. It is not a complete dictionary of environmental health terms. If you have questions or comments, call ATSDR's toll-free telephone number, 1-888-42-ATSDR (1-888-422-8737).

Absorption
The process of taking in. For a person or an animal, absorption is the process of a substance getting into the body through the eyes, skin, stomach, intestines, or lungs.

Acute
Occurring over a short time [compare with chronic].

Acute exposure
Contact with a substance that occurs once or for only a short time (up to 14 days) [compare with intermediate duration exposure and chronic exposure].

Additive effect
A biologic response to exposure to multiple substances that equals the sum of responses of all the individual substances added together [compare with antagonistic effect and synergistic effect].

Adverse health effect
A change in body function or cell structure that might lead to disease or health problems

Aerobic
Requiring oxygen [compare with anaerobic].

Ambient
Surrounding (for example, ambient air).

Anaerobic
Requiring the absence of oxygen [compare with aerobic].

Analyte
A substance measured in the laboratory. A chemical for which a sample (such as water, air, or blood) is tested in a laboratory. For example, if the analyte is mercury, the laboratory test will determine the amount of mercury in the sample.

Analytic epidemiologic study
A study that evaluates the association between exposure to hazardous substances and disease by testing scientific hypotheses.

Antagonistic effect
A biologic response to exposure to multiple substances that is less than would be expected if the known effects of the individual substances were added together [compare with additive effect and synergistic effect].

Background level
An average or expected amount of a substance or radioactive material in a specific environment, or typical amounts of substances that occur naturally in an environment.

Biodegradation
Decomposition or breakdown of a substance through the action of microorganisms (such as bacteria or fungi) or other natural physical processes (such as sunlight).

Biologic indicators of exposure study
A study that uses (a) biomedical testing or (b) the measurement of a substance [an analyte], its metabolite, or another marker of exposure in human body fluids or tissues to confirm human exposure to a hazardous substance [also see exposure investigation].

Biologic monitoring
Measuring hazardous substances in biologic materials (such as blood, hair, urine, or breath) to determine whether exposure has occurred. A blood test for lead is an example of biologic monitoring.

Biologic uptake
The transfer of substances from the environment to plants, animals, and humans.

Biomedical testing
Testing of persons to find out whether a change in a body function might have occurred because of exposure to a hazardous substance.

Biota
Plants and animals in an environment. Some of these plants and animals might be sources of food, clothing, or medicines for people.

Body burden
The total amount of a substance in the body. Some substances build up in the body because they are stored in fat or bone or because they leave the body very slowly.

CAP [see Community Assistance Panel.]

Cancer
Any one of a group of diseases that occur when cells in the body become abnormal and grow or multiply out of control.

Cancer risk
A theoretical risk for getting cancer if exposed to a substance every day for 70 years (a lifetime exposure). The true risk might be lower.

Carcinogen
A substance that causes cancer.

Case study
A medical or epidemiologic evaluation of one person or a small group of people to gather information about specific health conditions and past exposures.

Case-control study
A study that compares exposures of people who have a disease or condition (cases) with people who do not have the disease or condition (controls). Exposures that are more common among the cases may be considered as possible risk factors for the disease.

CAS registry number
A unique number assigned to a substance or mixture by the American Chemical Society Abstracts Service.

Central nervous system
The part of the nervous system that consists of the brain and the spinal cord.

CERCLA [see Comprehensive Environmental Response, Compensation, and Liability Act of 1980]

Chronic
Occurring over a long time [compare with acute].

Chronic exposure
Contact with a substance that occurs over a long time (more than 1 year) [compare with acute exposure and intermediate duration exposure]

Cluster investigation
A review of an unusual number, real or perceived, of health events (for example, reports of cancer) grouped together in time and location. Cluster investigations are designed to confirm case reports; determine whether they represent an unusual disease occurrence; and, if possible, explore possible causes and contributing environmental factors.

Community Assistance Panel (CAP)
A group of people from a community and from health and environmental agencies who work with ATSDR to resolve issues and problems related to hazardous substances in the community. CAP members work with ATSDR to gather and review community health concerns, provide information on how people might have been or might now be exposed to hazardous substances, and inform ATSDR on ways to involve the community in its activities.

Comparison value (CV)
Calculated concentration of a substance in air, water, food, or soil that is unlikely to cause harmful (adverse) health effects in exposed people. The CV is used as a screening level during the public health assessment process. Substances found in amounts greater than their CVs might be selected for further evaluation in the public health assessment process.

Completed exposure pathway [see exposure pathway].

Comprehensive Environmental Response, Compensation, and Liability Act of 1980 (CERCLA)
CERCLA, also known as Superfund, is the federal law that concerns the removal or cleanup of

hazardous substances in the environment and at hazardous waste sites. ATSDR, which was created by CERCLA, is responsible for assessing health issues and supporting public health activities related to hazardous waste sites or other environmental releases of hazardous substances. This law was later amended by the Superfund Amendments and Reauthorization Act (SARA).

Concentration
The amount of a substance present in a certain amount of soil, water, air, food, blood, hair, urine, breath, or any other media.

Contaminant
A substance that is either present in an environment where it does not belong or is present at levels that might cause harmful (adverse) health effects.

Delayed health effect
A disease or an injury that happens as a result of exposures that might have occurred in the past.

Dermal
Referring to the skin. For example, dermal absorption means passing through the skin.

Dermal contact
Contact with (touching) the skin [see route of exposure].

Descriptive epidemiology
The study of the amount and distribution of a disease in a specified population by person, place, and time.

Detection limit
The lowest concentration of a chemical that can reliably be distinguished from a zero concentration.

Disease prevention
Measures used to prevent a disease or reduce its severity.

Disease registry
A system of ongoing registration of all cases of a particular disease or health condition in a defined population.

DOD
United States Department of Defense.

DOE
United States Department of Energy.

Dose (for chemicals that are not radioactive)
The amount of a substance to which a person is exposed over some time period. Dose is a measurement of exposure. Dose is often expressed as milligram (amount) per kilogram (a measure of body weight) per day (a measure of time) when people eat or drink contaminated water, food, or soil. In general, the greater the dose, the greater the likelihood of an effect. An "exposure dose" is how much of a substance is encountered in the environment. An "absorbed dose" is the amount of a substance that actually got into the body through the eyes, skin, stomach, intestines, or lungs.

Dose (for radioactive chemicals)
The radiation dose is the amount of energy from radiation that is actually absorbed by the body. This is not the same as measurements of the amount of radiation in the environment.

Dose-response relationship
The relationship between the amount of exposure [dose] to a substance and the resulting changes in body function or health (response).

Environmental media
Soil, water, air, biota (plants and animals), or any other parts of the environment that can contain contaminants.

Environmental media and transport mechanism
Environmental media include water, air, soil, and biota (plants and animals). Transport mechanisms move contaminants from the source to points where human exposure can occur. The environmental media and transport mechanism is the second part of an exposure pathway.

EPA
United States Environmental Protection Agency.

Epidemiologic surveillance [see Public health surveillance].

Epidemiology
The study of the distribution and determinants of disease or health status in a population; the study of the occurrence and causes of health effects in humans.

Exposure
Contact with a substance by swallowing, breathing, or touching the skin or eyes. Exposure may be short-term [acute exposure], of intermediate duration, or long-term [chronic exposure].

Exposure assessment
The process of finding out how people come into contact with a hazardous substance, how often and for how long they are in contact with the substance, and how much of the substance they are in contact with.

Exposure-dose reconstruction
A method of estimating the amount of people's past exposure to hazardous substances. Computer and approximation methods are used when past information is limited, not available, or missing.

Exposure investigation
The collection and analysis of site-specific information and biologic tests (when appropriate) to determine whether people have been exposed to hazardous substances.

Exposure pathway
The route a substance takes from its source (where it began) to its end point (where it ends), and how people can come into contact with (or get exposed to) it. An exposure pathway has five parts: a source of contamination (such as an abandoned business); an environmental media and transport mechanism (such as movement through groundwater); a point of exposure (such as a private well); a route of exposure (eating, drinking, breathing, or touching), and a receptor population (people potentially or actually exposed). When all five parts are present, the exposure pathway is termed a completed exposure pathway.

Exposure registry
A system of ongoing followup of people who have had documented environmental exposures.

Feasibility study
A study by EPA to determine the best way to clean up environmental contamination. A number of factors are considered, including health risk, costs, and what methods will work well.

Geographic information system (GIS)
A mapping system that uses computers to collect, store, manipulate, analyze, and display data. For example, GIS can show the concentration of a contaminant within a community in relation to points of reference such as streets and homes.

Grand rounds
Training sessions for physicians and other health care providers about health topics.

Groundwater
Water beneath the earth's surface in the spaces between soil particles and between rock surfaces [compare with surface water].

Half-life (t½)
The time it takes for half the original amount of a substance to disappear. In the environment, the half-life is the time it takes for half the original amount of a substance to disappear when it is changed to another chemical by bacteria, fungi, sunlight, or other chemical processes. In the human body, the half-life is the time it takes for half the original amount of the substance to disappear, either by being changed to another substance or by leaving the body. In the case of radioactive material, the half life is the amount of time necessary for one half the initial number of radioactive atoms to change or transform into another atom (that is normally not radioactive). After two half lives, 25% of the original number of radioactive atoms remain.

Hazard
A source of potential harm from past, current, or future exposures.

Hazardous Substance Release and Health Effects Database (HazDat)
The scientific and administrative database system developed by ATSDR to manage data collection, retrieval, and analysis of site-specific information on hazardous substances, community health concerns, and public health activities.

Hazardous waste
Potentially harmful substances that have been released or discarded into the environment.

Health consultation
A review of available information or collection of new data to respond to a specific health question or request for information about a potential environmental hazard. Health consultations are focused on a specific exposure issue. Health consultations are therefore more limited than a

public health assessment, which reviews the exposure potential of each pathway and chemical [compare with public health assessment].

Health education
Programs designed with a community to help it know about health risks and how to reduce these risks.

Health investigation
The collection and evaluation of information about the health of community residents. This information is used to describe or count the occurrence of a disease, symptom, or clinical measure and to evaluate the possible association between the occurrence and exposure to hazardous substances.

Health promotion
The process of enabling people to increase control over, and to improve, their health.

Health statistics review
The analysis of existing health information (i.e., from death certificates, birth defects registries, and cancer registries) to determine if there is excess disease in a specific population, geographic area, and time period. A health statistics review is a descriptive epidemiologic study.

Indeterminate public health hazard
The category used in ATSDR's public health assessment documents when a professional judgment about the level of health hazard cannot be made because information critical to such a decision is lacking.

Incidence
The number of new cases of disease in a defined population over a specific time period [contrast with prevalence].

Ingestion
The act of swallowing something through eating, drinking, or mouthing objects. A hazardous substance can enter the body this way [see route of exposure].

Inhalation
The act of breathing. A hazardous substance can enter the body this way [see route of exposure].

Intermediate duration exposure
Contact with a substance that occurs for more than 14 days and less than a year [compare with acute exposure and chronic exposure].

In vitro
In an artificial environment outside a living organism or body. For example, some toxicity testing is done on cell cultures or slices of tissue grown in the laboratory, rather than on a living animal [compare with in vivo].

In vivo
Within a living organism or body. For example, some toxicity testing is done on whole animals, such as rats or mice [compare with in vitro].

Lowest-observed-adverse-effect level (LOAEL)
The lowest tested dose of a substance that has been reported to cause harmful (adverse) health effects in people or animals.

Medical monitoring
A set of medical tests and physical exams specifically designed to evaluate whether an individual's exposure could negatively affect that person's health.

Metabolism
The conversion or breakdown of a substance from one form to another by a living organism.

Metabolite
Any product of metabolism.

mg/kg
Milligram per kilogram.

mg/cm^2
Milligram per square centimeter (of a surface).

mg/m^3
Milligram per cubic meter; a measure of the concentration of a chemical in a known volume (a cubic meter) of air, soil, or water.

Migration
Moving from one location to another.

Minimal risk level (MRL)
An ATSDR estimate of daily human exposure to a hazardous substance at or below which that substance is unlikely to pose a measurable risk of harmful (adverse), noncancerous effects. MRLs are calculated for a route of exposure (inhalation or oral) over a specified time period (acute, intermediate, or chronic). MRLs should not be used as predictors of harmful (adverse) health effects [see reference dose].

Morbidity
State of being ill or diseased. Morbidity is the occurrence of a disease or condition that alters health and quality of life.

Mortality
Death. Usually the cause (a specific disease, a condition, or an injury) is stated.

Mutagen
A substance that causes mutations (genetic damage).

Mutation
A change (damage) to the DNA, genes, or chromosomes of living organisms.

National Priorities List for Uncontrolled Hazardous Waste Sites (National Priorities List or NPL)
EPA's list of the most serious uncontrolled or abandoned hazardous waste sites in the United States. The NPL is updated on a regular basis.

National Toxicology Program (NTP)
Part of the Department of Health and Human Services. NTP develops and carries out tests to predict whether a chemical will cause harm to humans.

No apparent public health hazard
A category used in ATSDR's public health assessments for sites where human exposure to contaminated media might be occurring, might have occurred in the past, or might occur in the future, but where the exposure is not expected to cause any harmful health effects.

No-observed-adverse-effect level (NOAEL)
The highest tested dose of a substance that has been reported to have no harmful (adverse) health effects on people or animals.

No public health hazard
A category used in ATSDR's public health assessment documents for sites where people have never and will never come into contact with harmful amounts of site-related substances.

NPL [see National Priorities List for Uncontrolled Hazardous Waste Sites]

Physiologically based pharmacokinetic model (PBPK model)
A computer model that describes what happens to a chemical in the body. This model describes how the chemical gets into the body, where it goes in the body, how it is changed by the body, and how it leaves the body.

Pica
A craving to eat nonfood items, such as dirt, paint chips, and clay. Some children exhibit pica-related behavior.

Plume
A volume of a substance that moves from its source to places farther away from the source. Plumes can be described by the volume of air or water they occupy and the direction they move. For example, a plume can be a column of smoke from a chimney or a substance moving with groundwater.

Point of exposure
The place where someone can come into contact with a substance present in the environment [see exposure pathway].

Population
A group or number of people living within a specified area or sharing similar characteristics (such as occupation or age).

Potentially responsible party (PRP)
A company, government, or person legally responsible for cleaning up the pollution at a hazardous waste site under Superfund. There may be more than one PRP for a particular site.

ppb
Parts per billion.

ppm
Parts per million.

Prevalence
The number of existing disease cases in a defined population during a specific time period [contrast with incidence].

Prevalence survey
The measure of the current level of disease(s) or symptoms and exposures through a questionnaire that collects self-reported information from a defined population.

Prevention
Actions that reduce exposure or other risks, keep people from getting sick, or keep disease from getting worse.

Public availability session
An informal, drop-by meeting at which community members can meet one-on-one with ATSDR staff members to discuss health and site-related concerns.

Public comment period
An opportunity for the public to comment on agency findings or proposed activities contained in draft reports or documents. The public comment period is a limited time period during which comments will be accepted.

Public health action
A list of steps to protect public health.

Public health advisory
A statement made by ATSDR to EPA or a state regulatory agency that a release of hazardous substances poses an immediate threat to human health. The advisory includes recommended measures to reduce exposure and reduce the threat to human health.

Public health assessment (PHA)
An ATSDR document that examines hazardous substances, health outcomes, and community

concerns at a hazardous waste site to determine whether people could be harmed from coming into contact with those substances. The PHA also lists actions that need to be taken to protect public health [compare with health consultation].

Public health hazard
A category used in ATSDR's public health assessments for sites that pose a public health hazard because of long-term exposures (greater than 1 year) to sufficiently high levels of hazardous substances or radionuclides that could result in harmful health effects.

Public health hazard categories
Public health hazard categories are statements about whether people could be harmed by conditions present at the site in the past, present, or future. One or more hazard categories might be appropriate for each site. The five public health hazard categories are no public health hazard, no apparent public health hazard, indeterminate public health hazard, public health hazard, and urgent public health hazard.

Public health statement
The first chapter of an ATSDR toxicological profile. The public health statement is a summary written in words that are easy to understand. The public health statement explains how people might be exposed to a specific substance and describes the known health effects of that substance.

Public health surveillance
The ongoing, systematic collection, analysis, and interpretation of health data. This activity also involves timely dissemination of the data and use for public health programs.

Public meeting
A public forum with community members for communication about a site.

Radioisotope
An unstable or radioactive isotope (form) of an element that can change into another element by giving off radiation.

Radionuclide
Any radioactive isotope (form) of any element.

RCRA [see Resource Conservation and Recovery Act (1976, 1984)]

Receptor population
People who could come into contact with hazardous substances [see exposure pathway].

Reference dose (RfD)
An EPA estimate, with uncertainty or safety factors built in, of the daily lifetime dose of a substance that is unlikely to cause harm in humans.

Registry
A systematic collection of information on persons exposed to a specific substance or having specific diseases [see exposure registry and disease registry].

Remedial investigation
The CERCLA process of determining the type and extent of hazardous material contamination at a site.

Resource Conservation and Recovery Act (1976, 1984) (RCRA)
This Act regulates management and disposal of hazardous wastes currently generated, treated, stored, disposed of, or distributed.

RFA
RCRA Facility Assessment. An assessment required by RCRA to identify potential and actual releases of hazardous chemicals.

RfD [see reference dose]

Risk
The probability that something will cause injury or harm.

Risk reduction
Actions that can decrease the likelihood that individuals, groups, or communities will experience disease or other health conditions.

Risk communication
The exchange of information to increase understanding of health risks.

Route of exposure
The way people come into contact with a hazardous substance. Three routes of exposure are breathing [inhalation], eating or drinking [ingestion], or contact with the skin [dermal contact].

Safety factor [see uncertainty factor]

SARA [see Superfund Amendments and Reauthorization Act]

Sample
A portion or piece of a whole. A selected subset of a population or subset of whatever is being studied. For example, in a study of people the sample is a number of people chosen from a larger population [see population]. An environmental sample (for example, a small amount of soil or water) might be collected to measure contamination in the environment at a specific location.

Sample size
The number of units chosen from a population or an environment.

Solvent
A liquid capable of dissolving or dispersing another substance (for example, acetone or mineral spirits).

Source of contamination
The place where a hazardous substance comes from, such as a landfill, waste pond, incinerator, storage tank, or drum. A source of contamination is the first part of an exposure pathway.

Special populations
People who might be more sensitive or susceptible to exposure to hazardous substances because of factors such as age, occupation, sex, or behaviors (for example, cigarette smoking). Children, pregnant women, and older people are often considered special populations.

Stakeholder
A person, group, or community who has an interest in activities at a hazardous waste site.

Statistics
A branch of mathematics that deals with collecting, reviewing, summarizing, and interpreting data or information. Statistics are used to determine whether differences between study groups are meaningful.

Substance
A chemical.

Substance-specific applied research
A program of research designed to fill important data needs for specific hazardous substances identified in ATSDR's toxicological profiles. Filling these data needs would allow more accurate assessment of human risks from specific substances contaminating the environment. This research might include human studies or laboratory experiments to determine health effects resulting from exposure to a given hazardous substance.

Superfund [see Comprehensive Environmental Response, Compensation, and Liability Act of 1980 (CERCLA) and Superfund Amendments and Reauthorization Act (SARA)

Superfund Amendments and Reauthorization Act (SARA)
In 1986, SARA amended the Comprehensive Environmental Response, Compensation, and Liability Act of 1980 (CERCLA) and expanded the health-related responsibilities of ATSDR. CERCLA and SARA direct ATSDR to look into the health effects from substance exposures at hazardous waste sites and to perform activities including health education, health studies, surveillance, health consultations, and toxicological profiles.

Surface water
Water on the surface of the earth, such as in lakes, rivers, streams, ponds, and springs [compare with groundwater].

Surveillance [see public health surveillance]

Survey
A systematic collection of information or data. A survey can be conducted to collect information from a group of people or from the environment. Surveys of a group of people can be conducted by telephone, by mail, or in person. Some surveys are done by interviewing a group of people [see prevalence survey].

Synergistic effect
A biologic response to multiple substances where one substance worsens the effect of another substance. The combined effect of the substances acting together is greater than the sum of the effects of the substances acting by themselves [see additive effect and antagonistic effect].

Teratogen
A substance that causes defects in development between conception and birth. A teratogen is a substance that causes a structural or functional birth defect.

Toxic agent
Chemical or physical (for example, radiation, heat, cold, microwaves) agents that, under certain circumstances of exposure, can cause harmful effects to living organisms.

Toxicological profile
An ATSDR document that examines, summarizes, and interprets information about a hazardous substance to determine harmful levels of exposure and associated health effects. A toxicological profile also identifies significant gaps in knowledge on the substance and describes areas where further research is needed.

Toxicology
The study of the harmful effects of substances on humans or animals.

Tumor
An abnormal mass of tissue that results from excessive cell division that is uncontrolled and progressive. Tumors perform no useful body function. Tumors can be either benign (not cancer) or malignant (cancer).

Uncertainty factor
Mathematical adjustments for reasons of safety when knowledge is incomplete. For example, factors used in the calculation of doses that are not harmful (adverse) to people. These factors are applied to the lowest-observed-adverse-effect-level (LOAEL) or the no-observed-adverse-effect-level (NOAEL) to derive a minimal risk level (MRL). Uncertainty factors are used to account for variations in people's sensitivity, for differences between animals and humans, and for differences between a LOAEL and a NOAEL. Scientists use uncertainty factors when they have some, but not all, the information from animal or human studies to decide whether an exposure will cause harm to people [also sometimes called a safety factor].

Urgent public health hazard
A category used in ATSDR's public health assessments for sites where short-term exposures (less than 1 year) to hazardous substances or conditions could result in harmful health effects that require rapid intervention.

Volatile organic compounds (VOCs)
Organic compounds that evaporate readily into the air. VOCs include substances such as benzene, toluene, methylene chloride, and methyl chloroform.

Other glossaries and dictionaries:
Environmental Protection Agency (http://www.epa.gov/OCEPAterms/)
National Center for Environmental Health (CDC)
(http://www.cdc.gov/nceh/dls/report/glossary.htm)
National Library of Medicine (NIH)
(http://www.nlm.nih.gov/medlineplus/mplusdictionary.html)

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