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This Public Health Statement summarizes the Division of Toxicology and Human Health Science's findings on hexachlorobenzene, tells you about it, the effects of exposure, and describes what you can do to limit that exposure.

The U.S. Environmental Protection Agency (EPA) identifies the most serious hazardous waste sites in the nation. These sites make up the National Priorities List (NPL) and are sites targeted for long-term federal clean-up activities. U.S. EPA has found hexachlorobenzene in at least 113 of the 1,699 current or former NPL sites. The total number of NPL sites evaluated for hexachlorobenzene is not known. But the possibility remains that as more sites are evaluated, the sites at which hexachlorobenzene is found may increase. This information is important because these future sites may be sources of exposure, and exposure to hexachlorobenzene may be harmful.

If you are exposed to hexachlorobenzene, many factors determine whether you'll be harmed. These include how much you are exposed to (dose), how long you are exposed (duration), and how you are exposed (route of exposure). You must also consider the other chemicals you are exposed to and your age, sex, diet, family traits, lifestyle, and state of health.

WHAT IS HEXACHLOROBENZENE?

Hexachlorobenzene is a white, crystalline solid at room temperature. Hexachlorobenzene is not currently manufactured as a commercial end product in the United States, and evidence indicates that it has not been commercially produced since the late 1970s. Hexachlorobenzene was used as a fungicide in the United States until 1984, when the last registered use of the compound as a pesticide was voluntarily cancelled. Small amounts of hexachlorobenzene can still be used in chemical laboratories for research purposes.

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WHERE IS HEXACHLOROBENZENE FOUND?

Hexachlorobenzene can mostly be found in treated and background soils, sediments, and oceans. It can also be found in air, surface water, and groundwater due to use and disposal of hexachlorobenzene products and as a byproduct of other processes. Hexachlorobenzene can accumulate up through the food chain and has been detected in breast milk.

Hexachlorobenzene is usually detected in air at low levels (typically in the picogram to nanogram per cubic meter [pg/m³ to ng/m³] range). Incineration of chlorinated materials is also a source of hexachlorobenzene. Hexachlorobenzene is very slow to break down in air and is subject to long-range transport in the atmosphere.

Hexachlorobenzene has been detected in groundwater, drinking water, and surface water. Levels are typically in the low parts per billion (ppb) to parts per trillion (ppt) range. Hexachlorobenzene is very slow to break down in water. It tends to adsorb to suspended particles and sediment in the water column and is highly bioaccumulated by aquatic organisms like fish.

Hexachlorobenzene has been detected in soil and sediment samples both in agricultural areas where it was formerly used and in urban soils near production and waste disposal sites. The levels of hexachlorobenzene can vary greatly in soil and sediment. Hexachlorobenzene levels as high as 53,000 ppb were observed in soil from a contaminated area. Hexachlorobenzene has low mobility in soil and may evaporate from soil surfaces. It is very persistent and takes many years to break down. It is slowly degraded by soil microorganisms.

Hexachlorobenzene has been detected in fish and food products. The Food and Drug Administration (FDA) Total Diet Study market basket surveys have found trace levels (<1 ppb) of hexachlorobenzene in many store-purchased food items. Fish from contaminated areas can contain levels of hexachlorobenzene greater than 100 ppb. The main exposure pathway for the general public to hexachlorobenzene is from the ingestion of food, typically only low-level exposure. Exposure to higher levels may occur through the

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contamination of food, such as consumption of fish caught in contaminated areas, and the ingestion of contaminated breast milk for infants.

Although hexachlorobenzene is not currently manufactured, it is formed as a waste product in the production of several chlorinated hydrocarbons, such as tetrachloroethylene and trichloroethylene, and is a contaminant in some pesticides, such as pentachloronitrobenzene and pentachlorophenol. Small amounts of hexachlorobenzene can also be produced during combustion processes, such as burning municipal waste. Hexachlorobenzene may also be produced as a byproduct in waste streams of chlor-alkali plants and wood preserving plants.

HOW MIGHT I BE EXPOSED TO HEXACHLOROBENZENE?

The primary route of exposure to hexachlorobenzene for the general population of the United States is from food. You may be exposed to very low levels of hexachlorobenzene through ingestion of contaminated foods, such as fatty fish. Young children may be exposed to hexachlorobenzene by playing in contaminated soil. Children who play in and on contaminated soil may have a higher potential for exposure through the skin and through inhalation of contaminated dust. Children who eat contaminated soil may ingest hexachlorobenzene. Hexachlorobenzene can also accumulate in breast milk. Breastfed babies may be exposed to hexachlorobenzene through their mother's breast milk. Other sources of exposure may include contact with water or air contaminated with hexachlorobenzene. Hexachlorobenzene has been found in ambient water samples at concentrations of less than 0.1 parts per trillion (ppt) and ambient air samples at concentration ranges of 0.1 pg/m³ to 1.5 ng/m³. Workers involved in the production of chlorinated hydrocarbons, which releases hexachlorobenzene as a byproduct, may also be exposed.

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HOW CAN HEXACHLOROBENZENE ENTER AND LEAVE MY BODY?

Hexachlorobenzene can enter your body from the air, water, or contaminated food or soil. If you breathe air containing hexachlorobenzene, some of it will be absorbed through your lungs. Some of the hexachlorobenzene in contaminated drinking water, food, soil, or breast milk will be rapidly absorbed through the digestive tract. This is the most likely route of significant exposure to hexachlorobenzene.

Hexachlorobenzene rapidly spreads through your blood to many tissues, especially fat, where it can remain for years. Hexachlorobenzene easily moves from blood of pregnant mothers, across the placenta to the unborn child and into breast milk of a nursing mother, resulting in exposure to her baby. Because hexachlorobenzene accumulates in fat, levels in babies (particularly breast-fed babies) may be higher than those in the mothers.

Most hexachlorobenzene leaves your body as hexachlorobenzene in the feces. Some hexachlorobenzene is converted to other chemicals in your body and some of these chemicals leave your body in the urine.

HOW CAN HEXACHLOROBENZENE AFFECT MY HEALTH?

Exposure to very high levels of hexachlorobenzene for short periods caused effects on the nervous system such as weakness, tremors, and convulsions; skin sores; liver effects such as porphyria, which is a decrease in the production of the heme (iron-protein) portion of red blood cell hemoglobin that carries oxygen to cells; and thyroid effects such as decreased thyroid hormones. These types of effects were seen in some people in Turkey who were exposed to high levels of hexachlorobenzene in bread made from grain that had been treated with the chemical as a pesticide.

Long-term exposure to hexachlorobenzene can cause effects similar to those from short-term exposure. Because hexachlorobenzene accumulates in fat (including breast tissue) where it can remain for long periods, long-term exposure can result in a build-up of hexachlorobenzene in the body. Therefore, longterm exposure may be more serious than acute or short-term exposure.

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Studies in animals suggest that eating foods with hexachlorobenzene for months or years can cause cancer of the liver, kidney, and thyroid.

The U.S. Department of Health and Human Services (DHHS) considers hexachlorobenzene as reasonably anticipated to be a human carcinogen. The U.S. EPA says that hexachlorobenzene is a probable human carcinogen. The International Agency for Research on Cancer (IARC) says that hexachlorobenzene is possibly carcinogenic to humans.

HOW CAN HEXACHLOROBENZENE AFFECT CHILDREN?

This section discusses potential health effects of hexachlorobenzene exposure in humans from when they're first conceived to 18 years of age, and how you might protect against such effects.

Infants and young children appeared to be especially sensitive to the effects of hexachlorobenzene in the Turkish grain poisoning epidemic. Breastfed infants of mothers known to have eaten bread contaminated with high levels of hexachlorobenzene developed a skin disorder known as pembe yara or "pink sore". Other symptoms were weakness and convulsions. Many of the sickened infants died from this disease. Young children beyond 2 years of age did not get pink sore, but they did develop skin, nervous system, and bone abnormalities later in life.

Although hexachlorobenzene has been banned in the United States since 1966 and globally under the Stockholm Convention since 2004, it is ubiquitous in the environment. This environmental lingering exists because of its past production and use as an organic synthesis compound, and former applications as fungicides and pesticides. However, it is unlikely that hexachlorobenzene will be detected in soil samples in the United States at or near levels that caused the epidemic in Turkey during the 1950's when it was added as a fungicide to wheat seedlings. For more information on the releases, occurrences, and movements of this substance, see Chapters 5 and 6.

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One study found higher levels of hexachlorobenzene in the milk of breastfed babies who had ear infections than in milk of breastfed babies without ear infections. We do not know if hexachlorobenzene increased susceptibility to infection in these babies.

Young animals exposed to hexachlorobenzene before and soon after birth are especially sensitive to hexachlorobenzene. Liver lesions developed during adulthood in rats treated with combined pre- and postnatal exposure. Effects on the nervous system and immune function occurred at lower doses in the young developing animals than in adults. Animal studies also showed that hexachlorobenzene has effects on various endocrine organs, including the thyroid gland (hypothyroidism), parathyroid gland (hyperparathyroidism), adrenal gland, and ovaries. These tissues produce hormones that are important for normal growth and development of the organism.

Higher levels of hexachlorobenzene were found in the fat of boys with a specific type of birth defect, undescended testis, than in the fat of boys without this defect; however, we do not know if hexachlorobenzene caused the birth defect. Some studies evaluated possible associations between maternal serum hexachlorobenzene levels and developmental end points such as birth size (weight and/or length) or preterm birth, recurrent miscarriage, postnatal growth, postnatal neurodevelopment, sexual maturation, undescended testes, hypospadias (a congenital defect in which the urethra exits the penis on the underside rather than the tip), and indicators of postnatal thyroid function. Although most studies found no associations between maternal serum hexachlorobenzene levels and developmental effects, there were reports of associations between levels of hexachlorobenzene in maternal or umbilical cord blood and birth weight, postnatal growth, and hypospadias. There is some indication that hexachlorobenzene in the blood of young boys and girls may cause changes in blood sex hormone levels.

HOW CAN FAMILIES REDUCE THE RISK OF EXPOSURE TO HEXACHLOROBENZENE?

If your doctor finds that you have been exposed to significant amounts of hexachlorobenzene, ask whether your children might also be exposed. Your doctor might need to ask your state health department to investigate.

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The primary way that most people are exposed to hexachlorobenzene is through food. Fatty food may be higher in hexachlorobenzene than less fatty food. Additionally, when hexachlorobenzene is present in food, more may be absorbed when the food is fatty than when the food is less fatty. Therefore, eating less fatty food may reduce the risk of exposure to hexachlorobenzene.

Exposure to contaminated drinking water should be limited. Hexachlorobenzene has been detected in some drinking water supplies. For bottled water, consumers should contact the bottler with specific questions on potential contaminants.

If you live near an industrial site where hexachlorobenzene was produced or is produced as an unintentional byproduct, or if you live near a hazardous waste site where it has been discarded, there may be high levels of hexachlorobenzene in the water and soil. Substituting cleaner sources of water and limiting contact with soil (for example, through use of a dense ground cover or thick lawn) would reduce family exposure to hexachlorobenzene. Produce grown in hexachlorobenzene-contaminated soil should not be eaten. By paying careful attention to dust and dirt control in the home (air filters, frequent cleaning), you can reduce family exposure to hexachlorobenzene-contaminated dirt. Some children eat a lot of dirt. You should prevent your children from eating dirt. You should discourage your children from putting objects in their mouths. Make sure that they wash their hands frequently and before eating. Discourage your children from putting their hands in their mouths or from other hand-to-mouth activity.

Check labels for hexachlorobenzene. In the past, some technical-grade pesticides or solvents when produced were found to contain trace amounts of hexachlorobenzene as an impurity. However, levels of hexachlorobenzene would be expected to be much lower than those causing health problems.

ARE THERE MEDICAL TESTS TO DETERMINE WHETHER I HAVE BEEN EXPOSED TO HEXACHLOROBENZENE?

Blood, breast milk, urine, and feces may be tested to determine if you have ever been exposed to hexachlorobenzene. These tests are not usually available at a doctor's office because they require special

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equipment found at county, state, university, and independent analytical laboratories. Because hexachlorobenzene can deposit and remain in human fat for several years, tests for hexachlorobenzene and its breakdown products (metabolites) can tell you only that you have been exposed to hexachlorobenzene, but not when or to how much. Furthermore, the detection of hexachlorobenzene or its metabolites cannot predict the kind of health effects that might develop from that exposure. Blood, urine, and feces can also be monitored for porphyrins. High porphyrin levels indicate slowed formation of heme, which is a major effect of hexachlorobenzene in the body. The production of persistent purple urine is diagnostic. The usefulness of this test as a sign of hexachlorobenzene exposure is limited, because there are many other potential causes of high porphyrin levels.

WHAT RECOMMENDATIONS HAS THE FEDERAL GOVERNMENT MADE TO PROTECT HUMAN HEALTH?

The federal government develops regulations and recommendations to protect public health. Regulations can be enforced by law. Federal agencies that develop regulations for toxic substances include the Environmental Protection Agency (EPA), the Occupational Safety and Health Administration (OSHA), and the Food and Drug Administration (FDA). Recommendations provide valuable guidelines to protect public health but cannot be enforced by law. Federal organizations that develop recommendations for toxic substances include the Agency for Toxic Substances and Disease Registry (ATSDR) and the National Institute for Occupational Safety and Health (NIOSH).

Regulations and recommendations can be expressed as "not-to-exceed" levels; that is, levels of a toxic substance in air, water, soil, or food that do not exceed a critical value usually based on levels that affect animals; levels are then adjusted to help protect humans. Sometimes these not-to-exceed levels differ among federal organizations. Different organizations use different exposure times (an 8-hour workday or a 24-hour day), different animal studies, or emphasize some factors over others, depending on their mission.

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Recommendations and regulations are also updated periodically as more information becomes available. For the most current information, check with the federal agency or organization that issued the regulation or recommendation.

The U.S. EPA has determined that exposures to hexachlorobenzene in drinking water of adults or children (10 years old or younger) at concentrations less than or equal to 0.05 milligrams per liter (mg/L) for up to 10 days or adults at less than or equal to 0.03 mg/L for a lifetime (assuming 100% of hexachlorobenzene exposure is from drinking water) are not expected to cause any adverse noncancer effects.

WHERE CAN I GET MORE INFORMATION?

If you have any questions or concerns, please contact your community or state health or environmental quality department, or contact ATSDR at the address and phone number below. ATSDR can also provide publically available information regarding medical specialists with expertise and experience recognizing, evaluating, treating, and managing patients exposed to hazardous substances.

- Call the toll-free information and technical assistance number at 1-800-CDCINFO (1-800-232-4636) or
- Write to:

Agency for Toxic Substances and Disease Registry Division of Toxicology and Human Health Sciences 1600 Clifton Road NE Mailstop F-57 Atlanta, GA 30329-4027

Toxicological profiles and other information are available on ATSDR's web site: http://www.atsdr.cdc.gov.

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