1. PUBLIC HEALTH STATEMENT

This public health statement tells you about phosphate ester flame retardants and the effects of exposure to them.

This profile discusses the following phosphate ester flame retardants: tris(2-chloroethyl) phosphate (TCEP), tributyl phosphate (TnBP), tris(2-butoxyethyl) phosphate (TBEP), tris(1,3-dichloro-2-propyl) phosphate (TDCP), triphenyl phosphate (TPP), tris(2-chloroisopropyl) phosphate (TCPP), triisobutyl phosphate (TiBP), and tricresyl phosphate (TCP).

The Environmental Protection Agency (EPA) identifies the most serious hazardous waste sites in the nation. These sites are then placed on the National Priorities List (NPL) and are targeted for long-term federal clean-up activities. Phosphate ester flame retardants have been found in at least 8 of the 1,699 current or former NPL sites. Although the total number of NPL sites evaluated for these substances is not known, the possibility exists that the number of sites at which phosphate ester flame retardants are found may increase in the future as more sites are evaluated. This information is important because these sites may be sources of exposure and exposure to these substances may be harmful.

When a substance is released either from a large area, such as an industrial plant, or from a container, such as a drum or bottle, it enters the environment. Such a release does not always lead to exposure. You can be exposed to a substance only when you come in contact with it. You may be exposed by breathing, eating, or drinking the substance, or by skin contact.

If you are exposed to phosphate ester flame retardants, many factors will determine whether you will be harmed. These factors include the dose (how much), the duration (how long), and how you come in contact with them. You must also consider any other chemicals you are exposed to and your age, sex, diet, family traits, lifestyle, and state of health.

1.1 WHAT ARE PHOSPHATE ESTER FLAME RETARDANTS?

Description	Phosphate ester flame retardants are human-made chemicals added to consumer and industrial products for the purpose of reducing flammability. Phosphate ester flame retardants are composed of a group of chemicals with similar properties but slightly different structures. Phosphate esters are typically liquids at room temperature; however, some are solids.
Uses	Phosphate esters are flame retardants, plasticizers, hydraulic fluids, solvents, extraction agents, antifoam agents, and coatings for electronic devices.

For more information on the physical and chemical properties of phosphate esters and their production, disposal and use, see Chapters 4 and 5.

1.2 WHAT HAPPENS TO PHOSPHATE ESTER FLAME RETARDANTS WHEN THEY ENTER THE ENVIRONMENT?

Sources	Phosphate ester flame retardants are released to the environment from industrial sources and disposal of consumer products containing flame retardants.
Breakdown	Phosphate ester flame retardants can change chemical composition in the environment.
• **Air**	There is no specific information available for the eight phosphate ester flame retardants discussed in this document; however, in general, these compounds are degraded by chemical reactions in the air. If they attach themselves to particles, they can settle out onto the ground. .
• **Water and soil**	Generally, most phosphate esters are poorly soluble in water and adsorb strongly to soils. These compounds are commonly detected in water due to their widespread use in commercial products. Phosphate esters are subject to biodegradation in aquatic and terrestrial environments.

1.3 HOW MIGHT I BE EXPOSED TO PHOSPHATE ESTER FLAME RETARDANTS?

Routes of exposure	Humans can be exposed by a combination of oral, inhalation, and dermal routes.
Food—primary source of exposure	Ingesting contaminated food: Most foods have been found to contain trace amounts of phosphate ester flame retardants due to their wide use in plastics and presence in the environment.
Air	Breathing contaminated outdoor air: Hydraulic fluid is the primary source of phosphate esters in outdoor air. Breathing contaminated indoor air: Indoor air can contain phosphate ester flame retardants from certain plastics, adhesives, foams, or electronics.
Water and soil	Drinking water contaminated with phosphate esters due to leaching from plastics or industrial waste water discharge. By skin contact with contaminated soil: Hydraulic fluid spills or industrial waste water used for agriculture can result in the presence of phosphate esters in soil.
Children	Young children may be at a higher risk of exposure since they are more likely to put phosphate ester flame retardant treated materials in their mouths.

1.4 HOW CAN PHOSPHATE ESTER FLAME RETARDANTS ENTER AND LEAVE MY BODY?

Enter the body	
• **Humans**	There is virtually no information about the entrance of these substances into the body. However, TDCP had been found in human tissues and body fluids, so we know that this substance can enter the body possibly by inhaling aerosols or dusts or ingesting contaminated food or water. Adverse health effects seen in humans after exposure to TCP indicate that this substance can enter the body and pass into the bloodstream.
• **Animals**	Oral – Studies found that TDCP, TCEP, TCP, and TnBP can easily pass from the stomach and intestines into the blood stream. Dermal – Less amounts entered the body through the skin of rats and only very small amounts through the skin of pigs.

Leave the body	
• **Humans**	There is no information on how these chemicals leave your body, but based on studies in animals, phosphate ester flame retardants may be broken down in the body and the breakdown product may be eliminated in the urine. However, there are no studies in humans to prove that this actually happens.
• **Animals**	Neither phosphate ester flame retardants nor their breakdown products seemed to accumulate in the body. Most breakdown products were eliminated in the urine in 2–3 days.

1.5 HOW CAN PHOSPHATE ESTER FLAME RETARDANTS AFFECT MY HEALTH?

This section looks at animal and human studies concerning potential health effects.

Workers	Long-term exposure of workers to TDCP, TCP, or TPP was not associated with adverse health effects. No information was available regarding exposure to other phosphate ester flame retardants.
General population	Almost no information is available regarding health effects in members of the general population exposed to the phosphate ester flame retardants discussed in this profile. However, accidental ingestion of a component of TCP, tri-*o*-cresyl phosphate, has caused adverse effects on the nervous system. There have been a few cases of allergic reactions to consumer products that contain TPP, but a study that examined several hundred people exposed to plastics and glues that contained TPP or TCP did not find any allergic reactions.

Laboratory animals	One way to learn about the effects of phosphate ester flame retardants is to see how they affect test animals. Almost all studies in animals have administered these substances orally and generally at levels much higher than what can be expected from environmental exposures. TCEP given to rats for 16 weeks or longer caused brain lesions. When given for 2 years, it also caused lesions in the kidneys. TCEP also decreased the fertility of mice that were exposed for 18 weeks before mating. TnBP induced lesions in the urinary bladder of rats when given for 10 weeks or longer. TBEP caused liver lesions in rats after the rats ate food that contained TBEP for 18 weeks. A study showed that rats that ate food containing TCP for 2 years developed lesions in the ovary and adrenal gland and male mice developed liver lesions. TCP also decreased fertility in rats and mice. Rats that ate food containing TDCP for 2 years developed lesions in the kidneys and liver. The few studies that examined the effects of TPP, TiBP, and TCPP in animals did not report significant adverse health effects.
Cancer	There is not enough information available to determine with certainty whether or not phosphate ester flame retardants produce cancer in humans. Studies of workers employed in the manufacture of TDCP and TCP did not find significant associations between exposure and cancer. No information was available regarding the carcinogenic potential of the other phosphate esters to humans. Rats that received oral doses of TCEP for 2 years developed kidney tumors. Feeding mice a diet that contained TCEP for 18 months induced tumors in the kidney, liver, and stomach, and also induced leukemia. Long-term administration of TnBP to rats and mice induced tumors in the urinary bladder and the liver, respectively. Feeding rats with a diet that contained TDCP for 2 years produced tumors in the liver, kidneys, testes, and adrenal gland. Neither the EPA nor the Department of Health and Human Services (DHHS) has classified the carcinogenic potential of the phosphate esters discussed in this profile. The International Agency for Research on Cancer (IARC) determined that TCEP is not classifiable as to its carcinogenicity to humans.

1.6 HOW CAN PHOSPHATE ESTER FLAME RETARDANTS AFFECT CHILDREN?

This section discusses potential health effects in humans from exposures during the period from conception to maturity at 18 years of age.

Effects in humans	There are no studies that examined the health effects of the phosphate ester flame retardants discussed in this profile on pregnant women or on their embryo or fetus. There are no studies that examined the health effects in children of the phosphate ester flame retardants discussed in this document.
Laboratory animals	In general, exposure of rodents during gestation to TCEP, TnBP, TBEP, TDCP, TPP, or TCPP did not result in adverse effects to the fetuses or newborn animals. However, continuous exposure of two generations of mice to TCEP reduced the number of male pups born alive in the third generation. A similar study with TnBP in rats found that pups born to exposed rats had lower body weight during the first weeks of life than pups born to untreated rats. Studies in rats and mice also found that exposure to TCP before and during pregnancy can increase the number of pups born dead.
Exposure of the fetus	There is no information regarding transfer of phosphate ester flame retardants to the fetus across the placenta in pregnant women.
Human breast milk	No studies have been conducted to determine whether phosphate ester flame retardants can be detected in human breast milk from women exposed at work or from the general population.

1.7 HOW CAN FAMILIES REDUCE THE RISK OF EXPOSURE TO PHOSPHATE ESTER FLAME RETARDANTS?

Food	Avoid food that is generally high in phosphate ester content as indicated by the current market basket for the U.S. Total Diet study.
Air	Avoid installation or use of materials that are known to contain phosphate ester-based flame retardants in indoor environments to minimize exposure to them via air and particulate matter.

1.8 IS THERE A MEDICAL TEST TO DETERMINE WHETHER I HAVE BEEN EXPOSED TO PHOSPHATE ESTER FLAME RETARDANTS?

Detecting exposure	Phosphate ester flame retardants can be measured in blood and urine, but this is not a routine test that can be performed in a doctor's office. You should, however, see a physician if you believe that you have been exposed to high levels of these substances. No studies have been conducted to measure these chemicals in blood samples from groups of people representative of the U.S. general population.
Measuring exposure	The presence of phosphate ester flame retardants in your blood may indicate that you have been exposed to these substances and some amount entered your bloodstream. The presence of phosphate ester flame retardants in your blood does not necessarily indicate that adverse health effects will occur. Additional studies are needed to help to determine the health effects associated with exposure to these substances.

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

Regulations and recommendations can be expressed as "not-to-exceed" levels. These are levels of a toxic substance in air, water, soil, or food that do not exceed a critical value. This critical value is usually based on levels that affect animals; they are then adjusted to levels that will help protect humans. Sometimes these not-to-exceed levels differ among federal organizations because they used different exposure times (an 8-hour workday or a 24-hour day), different animal studies, or other factors.

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 provides it.

Some regulations and recommendations for phosphate ester flame retardants include the following:

Levels in workplace air set by OSHA	OSHA set a legal limit of 3 and 5 mg/m^3 for TPP and TnBP, respectively, in air averaged over an 8-hour work day.
Food	The EPA has permitted TnBP, TBEP, and TPP for use in nonfood pesticide products.

1.10 WHERE CAN I GET MORE INFORMATION?

If you have any more 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 tell you the location of occupational and environmental health clinics. These clinics specialize in recognizing, evaluating, and treating illnesses that result from exposure to hazardous substances.

Toxicological profiles are also available on-line at www.atsdr.cdc.gov and on CD-ROM. You may request a copy of the ATSDR ToxProfiles™ CD-ROM by calling the toll-free information and technical assistance number at 1-800-CDCINFO (1-800-232-4636), by e-mail at cdcinfo@cdc.gov, or by writing to:

Agency for Toxic Substances and Disease Registry
Division of Toxicology and Human Health Sciences (proposed)
1600 Clifton Road NE
Mailstop F-62
Atlanta, GA 30333
Fax: 1-770-488-4178

Organizations for-profit may request copies of final Toxicological Profiles from the following:

National Technical Information Service (NTIS)
5285 Port Royal Road
Springfield, VA 22161
Phone: 1-800-553-6847 or 1-703-605-6000
Web site: http://www.ntis.gov/