PLASTICS

THAT MAY BE HARMFUL TO CHILDREN AND REPRODUCTIVE HEALTH

ENVIRONMENT & HUMAN HEALTH, INC.

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Research and publication of this report was made possible by the Connecticut Health Foundation, the Forrest & Frances Lattner Foundation, the Patrick & Catherine Weldon Donaghue Medical Research Foundation, an anonymous donor, the Tortuga Foundation, and the Alida R. Messinger Charitable Lead Trust, No. 2.

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Printed on recycled paper with soy-based inks

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THE PLASTICS PROBLEM

Overview

Nearly 100 billion pounds of plastic are produced in the United States each year. Plastics are now heavily used in food and beverage packaging, building products, electrical wiring, vehicles, furniture, toys, and medical devices. Plastics now comprise nearly 70% of the synthetic chemical industry in the nation. Two plastic ingredients, *bisphenol A* (BPA) and *Di(2-ethylhexyl) phthalate* (DEHP), are the subject of this report because of increasing evidence that they disrupt normal growth and development in many different species of animals due to their hormonal activity.

The production of BPA has increased steadily since the 1990s, from about 16 million pounds per year in the early 1990s to nearly 2.3 billion pounds in 2007. It is used in the manufacture of clear, hard polycarbonate plastics and epoxy resins. More than 200 million pounds of DEHP are produced annually, most of which is added to polyvinyl chloride plastics (PVC). Both chemicals are used to package food and contain beverages, and they are found in surface and ground water, the oceans, fish, food, and many consumer products.

BPA and DEHP have been detected in the blood and urine of nearly everyone who has been tested. Each compound is commonly found in human breast milk, and both cross the placenta and the blood-brain barrier. The youngest children tested in the U.S. carry the highest concentrations of these molecules or their metabolites in their tissues.

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Both chemicals are hormonally active in test animals: BPA mimics estrogen, and DEHP blocks testosterone. Studies in humans are limited, but several have found effects also detected in animal experiments. The study of their environmental influence on human health is exceptionally difficult due to confounding exposures, the lag time between exposure and changes in health, and the need to reconstruct histories of exposure that occurred long ago. A growing number of government-sponsored scientists believe that effects found in animals may plausibly occur in humans, while manufacturers' scientists vigorously defend their claims of chemical safety. These government-sponsored studies have found that BPA is biologically active at exceptionally small doses in some animals, altering normal patterns of growth and development of a variety of organ systems and functions.

Although the U.S. government has authority under several federal statutes to regulate or prohibit the production, use, sale, and disposal of both chemicals, BPA remains virtually unregulated, while DEHP is ineffectively regulated. This is well demonstrated by the chemicals' presence in human tissues.

Prior to intense industrial production, use, and environmental release, neither chemical was tested to understand its behavior in the environment or its risk to human health. At present, no legal mechanism is in place at any level of government to assure warning or protection against exposure to these molecules. This report presents a summary of potential health risks associated with BPA and DEHP, patterns of exposure among women, children and others, and policy recommendations designed to reduce or prevent exposure among susceptible populations.

The DES history contains lessons and warnings about heightened human susceptibility to synthetic hormones during embryonic development, as well as the potential for multi-generational effects.[5]

Endocrine Disrupting Chemicals

During the last half of the twentieth century, scientists found that numerous synthetic chemicals can interfere with normal function of human hormones. Colborn and Colwell in 1992 termed these substances to be "*endocrine disrupting contaminants*" (EDCs) and in 1999 the U.S. National Academy of Science (NAS) called them "*hormonally active agents*" (HAAs).[1] The human endocrine system is composed of a complex network of glands that release hormones into the blood to signal and govern normal growth, development, metabolism and reproduction. Human hormones include estrogen, progesterone, testosterone, thyroid hormones, and melatonin, among others, and these can be biologically active at exceptionally small doses.

Evidence that synthetic estrogens could induce responses similar to human hormones developed early in the twentieth century. The drug diethyl-stilbestrol (DES)[2] was first marketed as a synthetic estrogen to prevent miscarriages, preterm birth, and other pregnancy problems. By 1953 published studies demonstrated that the drug neither prevented miscarriages nor preterm births; however, many physicians continued to prescribe it until 1971, when it was reported to cause clear cell adenocarcinoma, a rare form of vaginal cancer, among girls and young women who had been exposed to DES while in their mothers' wombs.[3] Daughters of women who took DES had other problems, including reduced fertility, premature births, miscarriages and an elevated risk of breast cancer. Sons of women who took the drug were more likely to experience undescended testicles and hypospadias (premature exit of the urethra before the end of the penis). Additional studies identified third-generation effects among DES exposed mice, suggesting possible risks to grandchildren of DES-exposed mothers that are not yet clear.[4] The DES history contains lessons and warnings about heightened human susceptibility to synthetic hormones during embryonic development, as well as the potential for multi-generational effects.[5]

The National Academy of Sciences considered the influence of hormonally active agents on wildlife and human health in 1999. They reported, *"Although it is clear that exposures to HAAs (hormonally active agents) at high concentrations can affect wildlife and human health, the extent of harm caused by exposure to these compounds in concentrations that are common in the environment is debated."* [6]

Manufacturers of commercially important HAAs vigorously support the safety of their chemicals, while government-sponsored scientists increasingly report effects in laboratory experiments at exceptionally low doses similar to those experienced by humans from environmental exposures.

Wildlife studies provided supporting evidence that some industrial chemicals and pollutants could also unintentionally behave like hormones.[7] The insecticide DDT, for example, was recognized to induce reproductive failure in many predatory birds, including eagles, ospreys, falcons and hawks, and some species of fish during the 1950s and 1960s. In later decades, other species yielded signs that they might be sentinels for human health. Fish swimming near paper mill sewage outfalls and exposed to dioxins in effluent exhibited estrogenic, androgenic, anti-androgenic and anti-thyroid effects. Alligators exposed to the insecticide dicofol developed reproductive abnormalities following a 1980 spill in Lake Apopka, Florida. Their egg survival rates declined and both males and females developed abnormal sexual organs. Alligators studied in nearby unpolluted lakes exhibited none of these conditions. Different species of birds suffered reproductive failures following exposures to DDT, PCBs and PAHs in the North American Great Lakes Region, as well as in the Puget Sound and the Baltic Sea in Northern Europe.[8]

Since 1971 scientists have reported that many other chemicals, including some pharmaceuticals, pesticides, plasticizers, solvents, metals, and flame retardants, have the potential to mimic or block endogenous human hormones. Some of these compounds mimic naturally occurring hormones like estrogens (the female sex hormones), androgens (the male sex hormones), and thyroid hormones. They can also bind to a receptor site within cells and thereby block endogenous hormones. Some of the best-known hormonally active contaminants other than synthetic hormones include dioxins, PCBs, organochlorine pesticides (including DDT), and BPA.[9]

Many scientists now believe that developing fetuses, infants, and children may be more vulnerable to harm than adults following exposures to hormonally active chemicals. This is because organ systems, hormone

Wildlife studies provided supporting evidence that some industrial chemicals and pollutants could also unintentionally behave like hormones.[7]

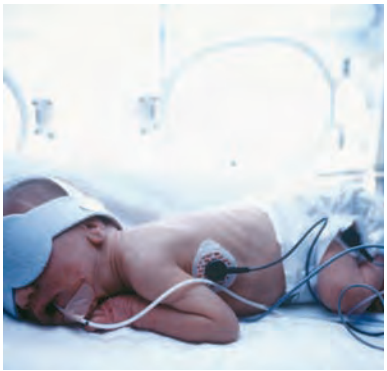
pathways, and metabolic systems are all still developing. In addition, young children breathe more air, consume more food and drink more water per pound of body weight than adults, and this increases their relative exposure to any chemicals present in their environment. The National Academy of Sciences in 1993 recognized the susceptibility of the very young to pesticides,[10] and in 1996 the *Food Quality Protection Act* was adopted by Congress and included the mandate that EPA develop an "*Endocrine Disruptor Screening Program*" to identify specific risks posed by hormonally active pesticides. A similar screening requirement was embedded into the Safe Drinking Water Act Amendments during the same year.[11] Both of these efforts have been under-funded and research has been stalled for more than a decade.

Support for policies that prevent childhood exposure to hazardous substances have deep roots in twentieth century environmental history. Many other substances once considered safe for everyone have been found to be harmful to fetuses, infants, and children during certain "critical windows" of development. Examples include lead, mercury, pesticides, tobacco, alcohol, pharmaceuticals, and vehicle emissions. Congress and EPA have responded to this more refined science by adopting laws and regulations that are more protective of the youngest in society. Importantly, the former absence of chemical testing had created the false impression of safety.

Many forms of human illness have increased in prevalence during the past several decades including infertility, miscarriage, breast cancer, prostate enlargement and cancer, obesity, and various neurological and neurobehavioral problems. Simultaneously, human reproductive and wildlife biologists have found an increase in developmental, reproductive and hormonal disorders in

wildlife associated with chemicals recognized to be hormonally active. More recently laboratory studies and *in vitro* experiments have noted health effects in laboratory animals similar to those found in wildlife studies.

Government-sponsored scientists now express concern that hormonally active chemicals may be a possible cause for the rising human incidence of adverse developmental and reproductive system effects such as breast, testicular, and prostate cancer.[12, 13, 14, 15] Other scientists report the importance of a human's age at time of exposure. Fetal and neonatal exposures shortly after birth may result in health effects that are difficult to detect until later in life.[16] Yet industry-sponsored scientists maintain that animal studies do not necessarily imply a similar level of hazard to humans, and that risks will vary with differences in species, age, gender, genetic traits, exposure and other factors. A prominent committee convened by the U.S. National Academy of Sciences to consider the nature of risk posed by hormonally active chemicals has agreed that the health effects seen in animals are important signals of human health risks, especially when well correlated with increasing trends in human illness.[17] Indeed, pesticide regulation and pesticide bans have relied almost exclusively on animal evidence as a surrogate for human data to estimate health risks since 1970, the year EPA was created.



Fetal and neonatal exposures shortly after birth may result in health effects that are difficult to detect until later in life.[16]

Growth of the Plastics Industry

The importance of the BPA and DEHP problem is tied closely to the enormity of their markets. A few statistics clarify the scale:[18]

- The U.S. plastics industry now accounts for $379 billion in sales, and employs nearly 850,000 people.[19]
- Plastics comprise nearly 70% of the synthetic chemical industry and include nearly 500 different chemical resins.[20]
- Plastic product manufacturing is the fourth largest manufacturing segment in the U.S. with over 21,000 companies manufacturing plastic products or plastics raw materials.[21]

Given the scale of this industry, it should not be a surprise that plastics in children's environments have steadily increased in recent years.

- Nearly 113 billion pounds of resins were produced in 2006, including more than 2.3 billion pounds of BPA, and nearly 240 million pounds of DEHP (2002) used to create 14.5 billion pounds of polyvinyl chloride (PVC).[22]

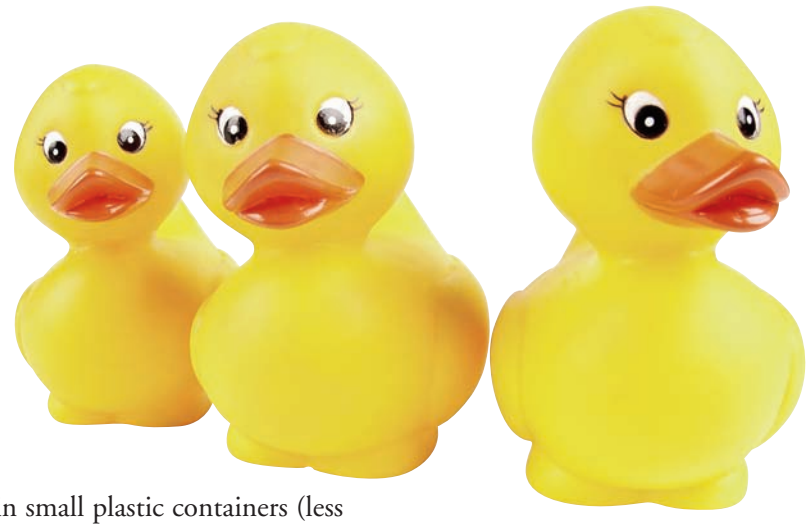
- By the late 1990s, packaging materials were the largest and fastest growing market for plastics, including bags, bottles, and food containers (consuming 26 percent of all plastics).[23] These often include DEHP and BPA.

- BASF estimated consumption of plastic in the U.S. at 223 pounds/person/year. It also estimated that consumption would increase to 300 pounds per year by 2010.[24]

Given the scale of this industry, it should not be a surprise that plastics in children's environments have steadily increased in recent years. Most homes built since 1985 are wrapped in plastic such as Tyvek™, first made by DuPont in 1959. Many homes are enclosed by PVC siding, serviced by PVC water lines, and wired with PVC-coated electrical lines. Walls are coated with plastic/epoxy paints, countertops are commonly plastic, wood floors are often coated with polyurethane finishes or covered with polypropylene rugs or vinyl tiles, and some homes have plastic insulation. Many infants, children, and adults sleep on PVC covered mattresses.

Most foods and beverages consumed by children are packaged in plastic, including soda and soups (can linings sometimes made with BPA epoxy) juice boxes (made of polyethylene),[25] frozen juice concentrates,[26] and single-serve plastic milk bottles (expected to replace the half-pint milk carton in school lunch programs).[27] Snack-sized food and beverage packages made of plastic are on the rise due to their convenience. As package size diminishes, use of plastic increases.[28]

The growth in bottled water consumption is an example of the dramatic increase in the use of plastic for food packaging that has occurred in the last decade. A decade ago, most children did not drink from plastic containers but today many arrive at school with plastic juice boxes, or purchase beverages in similar containers. Milk once sold only in glass is now sold almost exclusively in plastic containers or cardboard cartons



lined with plastic. Sales of bottled water in small plastic containers (less than one liter in size) increased more than seven-fold in the U.S. between 1997 and 2005, rising from four billion to nearly 30 billion bottles sold.[29]

Children's toys increasingly are made from plastic, and nearly 80% of the world's toys are made in China.[30] The European Council of Vinyl Manufacturers stated that almost all soft plastic toys are made with PVC, including dolls, bath ducks, inflatable toys, balls, and baby care items.[31] Children's video games, computers, MP3 players, cameras and cell phones collectively exceed billions in individual sales each year in the U.S. alone. Most of the components are plastic, and the devices' life-spans are rarely more than three years. Planned obsolescence guarantees extraordinary waste.

Children ride to and from school in cars, buses, and other vehicles that are increasingly made from plastic. New cars contain nearly 332 pounds of many different types of plastic. Some of these give off gases inside the passenger compartments, contributing to the "new car smell." Nearly 7.5 million new vehicles are sold in the U.S. each year, meaning that 2.5 billion pounds of plastic in vehicles has little hope of being recycled.

The European Council of Vinyl Manufacturers stated that almost all soft plastic toys are made with PVC, including dolls, bath ducks, inflatable toys, balls, and baby care items.[31]

Consumer Confusion

What chemicals are in the plastics just described? It's virtually impossible to know for all but the simplest products, such as polyethylene (PETE) beverage bottles. Why? Ingredients used to make plastics are not required to be labeled, and many manufacturers are unwilling to disclose the plastic ingredients or sources. Given the complexity of international plastics markets, it is not surprising that many manufacturers or distributors cannot identify ingredients or sources of plastics in their products.

Some plastics are labeled to facilitate recycling, not to identify chemicals used in their manufacture. The only clue a consumer has when identifying chemical ingredients in plastic products is the resin identification code on the plastic product, intended to facilitate recycling. The code was designed to indicate the type of resin used in the manufacturing process and to identify which products should or should not be recycled.[32] There is no federal law requiring this code, although many states have legislation mandating the use of the codes on some types of bottles.[33] There are no federal methods to ensure the proper use of the codes. Currently, the Federal Trade Commission only offers guidelines for environmental marketing claims designed to have an effect on labeling, but not requiring or enforcing it.[34]

Table 1. Recycling Symbols for Plastic Resins

Symbol	Type of Plastic	Products Packaged (Examples)
1 PETE	PET Polyethylene Terephthalate	Most convenience-size beverage bottles, mouthwash bottles, boil-in-bag pouches
2 HDPE	HDPE High Density Polyethylene	Milk jugs, trash bags, ice cube trays, storage containers
3 PVC	PVC Polyvinyl Chloride (DEHP)	Cooking oil bottles, packaging around meat, some baby bottle nipples, beverage pitchers
4 LDPE	LDPE Low Density Polyethylene	Produce bags, food wrap, bread bags, zip-lock bags, baby bottle liners
5 PP	PP Polypropylene	Yogurt containers, straws, margarine tubs, spice containers
6 PS	PS Polystyrene	Styrofoam cups and containers, take-home boxes, egg cartons, meat trays
7 OTHER	**Other (Bisphenol A)**	**Polycarbonate baby bottles, 5-gallon water cooler bottles, meat trays, toddler fruit cups**

The American Plastics Council estimates that only about 5% of all plastics manufactured are recycled, and this is optimistic compared with other approximations.

The code identifies the six resins that account for most of the plastics used in packaging (Table 1). Polyvinyl chloride (#3) contains DEHP and polycarbonate (#7) contains BPA. The code for BPA provides an excellent example of confusion, given its title: "Other."

Recycling Failure

The American Plastics Council estimates that only about 5% of all plastics manufactured are recycled, and this is optimistic compared with other approximations. Some types of plastic are recycled more often, including PET soft drink bottles (34% recycled) and HDPE milk and water bottles (29%).[35] Others, including DEHP-containing PVC plastics, BPA-containing polycarbonate plastics, and polystyrene (its production involves the use of known and suspected human carcinogens), are rarely recycled.

Recycling failure occurs for many reasons, including inconvenience and low redemption fees. It is also clear that the true costs of plastics including energy, environmental contamination, health loss, regulation, environmental restoration and waste management are not reflected in product prices. Collection, recycling, and redistribution costs are so high that the price of virgin resin has recently been 40% lower than that of recycled resin.[36]

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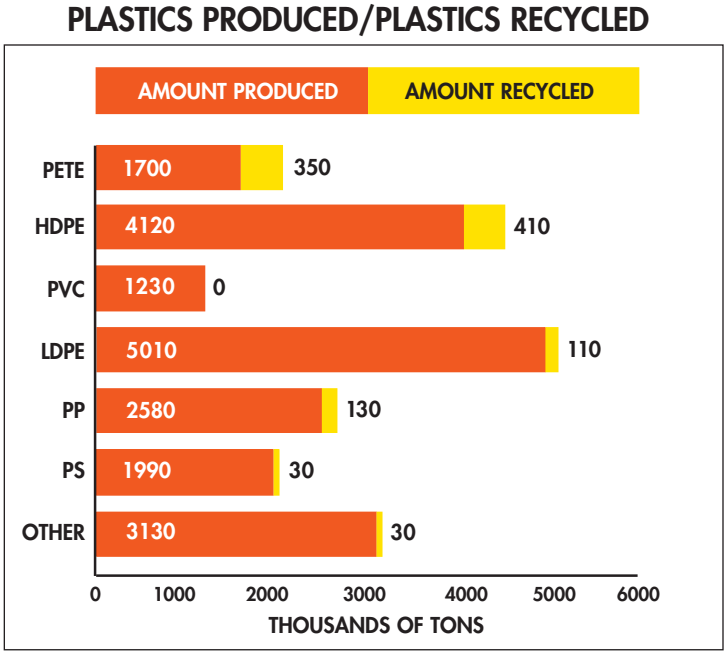

Figure 1. Plastics Produced/Plastics Recycled[37]

Figure 1 conveys a clear picture of recycling failure in our society. PVCs that contain DEHP are simply not recycled. Polycarbonate products are included in the "Other" category, and are not recycled. There are no waste collection provisions for these products, and no recycling programs.

Some recyclable plastics may never be recycled, due to a mixture problem. If plastics labeled #1 (PETE or PET) or #2 (HDPE) become mixed with #3 (PVC plastics), they will be rejected by some plastic recyclers. The PVC and PETE can easily be mixed together because of similar appearance. PVC is difficult to recycle because of its high chlorine content (requiring separation from other non-chlorine-based plastics) and because of the many additives in different vinyl products. If a single bottle of PVC is mixed with PETE bottles, the recycled product may be contaminated, causing the new PETE products to be discolored.[38] Rejected bundles of plastics often end up in landfills or sent overseas,[39] and data on their fate is normally unavailable.

Recycling may extend the life of a plastic product, but it is not a closed recycling loop like glass and aluminum recycling.

In 2006, more U.S. PETE bottles collected for recycling went to export markets than stayed in the U.S.[40] China, where recycling and pollution controls are limited, is the world's largest destination for plastic waste. One investigation tracking the transfer of large amounts of plastic waste from the United Kingdom to a village in China revealed plastic melted without protective measures and plastic waste poured directly into a river.[41] U.S. export costs to China are low as the imbalance of trade often leaves empty space on ships returning to China.

Plastic recycling normally results in a temporary delay before the secondary product is discarded as trash. Even if PETE bottles are recycled, most secondary products, such as polyethylene carpets or fleece jackets, are not recycled again. Plastic food containers cannot be made into new food containers unless the recycled plastic is embedded within layers of virgin plastic, due to concern about chemical contamination from the recycled materials.[42] Recycling may extend the life of a plastic product, but it is not a closed recycling loop like glass and aluminum recycling.

Wasted Plastic

Recycling failure leads to waste and environmental contamination. Most of the 100 million pounds of resins produced each year fabricate single-use products likely to enter the municipal solid waste stream (MSW) to be buried in landfills or incinerated. The amount of plastics in the MSW stream has grown from less than 1 percent of the total amount of MSW in 1960 to about 12% in 2006.[43] Much of the waste is packaging material. Currently, the U.S. disposes about 28 billion pounds of plastic containers and packaging in MSW streams.[44]

An estimated seven billion pounds of PVC materials are discarded every year, and these also end up in landfills or municipal incinerators.[45] PVC is a source of dioxin-forming chlorine, phthalates, lead and cadmium, and is known to contaminate groundwater near landfills.[46, 47]

In coastal regions, plastics that are not recycled, land-filled, or incinerated often find their way into the water and eventually the oceans, where currents concentrate them in a predictable pattern. The North Pacific Subtropical Gyre, a slow-moving clockwise spiral of currents, has developed two large masses of trash, known as the Western Garbage Patch (east of Japan and west of Hawaii) and Eastern Garbage Patch (between Hawaii and California). Together they are known as the Great Pacific Garbage Patch, and their area is estimated to be twice the size of Texas. Although most plastics have limited biodegradability, plastic will photo-degrade, breaking into smaller and smaller pieces over time. These fragments resemble zooplankton and are consumed by jellyfish and other ocean life, thus entering the marine food chain. The mass of plastic particles in the two patches is now estimated to be six times the mass of plankton, and both are consumed by many species of fish. Plastic, by one estimate, now constitutes 90% of all trash floating in the world's oceans.[48]

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Plastics and Petroleum Dependence

Most plastic is produced from fossil fuels, typically natural gas and petroleum. The American Chemistry Council estimated in 2008 that "*plastics production accounts for only 5 percent of the nation's annual consumption of natural gas and petroleum.*"[49] Although 5% sounds like a modest amount, the U.S. consumed 22 trillion cubic feet of natural gas and eight billion barrels of oil in 2005.[50] If the American Chemistry Council is correct, and plastics production depended

The Pacific Institute estimates that more than 17 million barrels of oil are needed just to produce polyethylene (PETE #1) for plastic bottles.[51]

equally on gas and oil, this would mean that the plastics industry consumes nearly 1.1 trillion cubic feet of natural gas and 400 million barrels of oil annually.

The Pacific Institute estimates that more than 17 million barrels of oil are needed just to produce polyethylene (PETE #1) for plastic bottles.[51] Calculating the energy used for pumping and processing, transportation, and refrigeration of bottled water, the Earth Policy Institute estimates the annual fossil fuel footprint of bottled water consumption in the U.S. at over 50 million barrels of oil equivalent.[52]

Some have argued that plastics are a great source of fuel for waste-to-energy plants. When plastics are processed in modern energy recovery facilities, they help other wastes burn more efficiently, producing cleaner emissions and less ash for disposal. Burning plastic might help supply energy for electricity, while reducing the cost of municipal waste disposal and conserving landfill space. Yet it can also release dangerous chemicals to the atmosphere, and some of these include dioxins and mercury that have been propelled by incinerators into global atmospheric circulation, only to rain to earth.

Failure to Regulate

The enormity of the plastics problem grows from government failure to demand that health and environmental effects be fully tested prior to their release to markets. The absence of information regarding the sources, distribution, contamination, human exposure, toxic effects and health loss associated with plastics leaves many with an unfounded impression of safety. The Environmental Protection Agency, the Food and Drug Administration, the Consumer Product Safety Commission and the Occupational Safety and Health Administration have insufficient information to set environmental standards that would assure health and environmental protection. The knowledge may develop in bits and pieces over decades, as exemplified by BPA and DEHP, but no systematic pre-market chemical testing is required.

Despite the absence of regulation, several government institutes have played important roles in identifying the plastics problem. The National Institute for Environmental Health Sciences funded many of the first studies that reported the diversity of health effects described in this report. Similarly, the Centers for Disease Control and Prevention (CDC) provided some of the earliest reports

of widespread human exposures to chemicals that are plastic ingredients in their National Health and Nutrition Examination Survey (NHANES) studies.

BPA and DEHP demonstrate the hormone disruptor problem well, and this problem sits within a much broader chemical testing challenge. Nearly 82,000 chemicals in commerce are listed in the Toxic Substances Control Act (TSCA) Chemical Inventory.[53] When the statute went into effect in 1976, 62,000 of these were listed, but exempted from data submission requirements. Since that time, 45,000 additional chemicals have been introduced to U.S. commerce, yet nearly half of these were added after companies began to manufacture or import and sell them. TSCA does not require EPA to collect and interpret information on chemical toxicity, but the statute does give the Agency the authority to do so. It only requires manufacturers to submit information it already possesses if EPA requests it. The overwhelming majority of chemicals in commerce have *not* been tested to understand their behavior in the environment or their effects on human health. Since 1976, EPA has exercised its authority to require pre-market testing only 200 times. Nearly 90% of "high production volume chemicals"—chemicals produced in volumes of more than one million pounds each year, such as BPA and DEHP—are exempted from review.[54]

The overwhelming majority of chemicals in commerce have not been tested to understand their behavior in the environment or their effects on human health.

Although this report considers health risks associated with only two chemicals, BPA and DEHP, tens of thousands of additional chemicals have yet to be tested to ascertain their effects on normal growth, development, and reproduction.

Summary

The plastics problem is growing in scale and complexity due to a collision of factors, including government neglect of the importance of endocrine disruption; the explosive growth of the U.S. and international plastics industry; the absence of any plastic ingredient and source labeling requirements; nearly complete recycling failure for PVC and polycarbonate plastics; environmental contamination of air, water, soils, oceans, fish and wildlife; nearly universal human exposure to BPA and DEHP from food and beverages in high income nations; the dependence of the plastics industry on petroleum; and government failure to require health and environmental testing prior to chemical production, sale, and disposal. Collectively, these pose a serious challenge to the environment and human health.

BISPHENOL A

Introduction

Bisphenol A (BPA) is the molecular building block for polycarbonate plastics and epoxy resins. U.S. production of BPA grew rapidly from 16 million pounds in 1991 to about 2.3 billion pounds in 2004, making it one of the most produced chemicals in the world.[55]

There are many sources of human exposure to BPA, predominantly because the U.S. Food and Drug Administration (FDA) permits its use in food and beverage packaging, including the interior coating of metal cans and polycarbonate beverage containers including baby bottles. The FDA also permits BPA to be used for dental sealants and other medical devices.[56] The dominant corporations that produce BPA are identified by the National Toxicology Program.[57]

Most BPA-containing plastic products are not recycled and end up in the solid waste stream. BPA is commonly detected in landfill leachate[58] and it is now one of the most frequently detected industrial chemicals in groundwater.[59] It is also often found in surface water, sewage effluents, sludge, and treated wastewater discharge.[60] Its presence in sewage effluent means that it is released to rivers and lakes, where it becomes available to aquatic species, including many different species of fish.

BPA Health Effects

BPA was first recognized to have estrogenic activity as a synthetic drug in 1936,[61, 62] long before it was used to form polycarbonate plastic and resins in the early 1950s. Interest and concern about the health effects of BPA have been growing, following reports that the health effects seen in exposed animals are also on the rise in humans. These include breast and prostate cancer, regional decline in sperm counts, abnormal penile/urethra development in males, early sexual maturation in females, increasing neurobehavioral problems, increasing prevalence of obesity and type 2 diabetes, and immune system effects.[63]

Interest and concern about the health effects of BPA have been growing, following reports that the health effects seen in exposed animals are also on the rise in humans.

Low-Dose Effects

Most BPA health effect studies prior to 1997 were conducted on laboratory animals at doses close to or higher than the level EPA set as a "reference dose" (RfD), a benchmark of maximum acceptable daily exposure. EPA chose the lowest dose tested (50 mg/kg/day) as a Lowest Observed Adverse Effect Level (LOAEL). In 1988 the Agency then divided this dose by a 1,000-fold safety factor to calculate the maximum concentration it believed would be health-protective (50 µg/kg/day), even if experienced daily over a lifetime. This choice was based upon "high dose experiments" conducted by the U.S. National Toxicology Program in 1982.[64] A 1,000-fold safety factor would normally provide an ample margin of protection against adverse health effects, if the experiments had thoroughly explored whether effects occur at lower doses. They did not.

Since 1997, more than 100 additional peer-reviewed studies have reported health effects in animals from BPA doses beneath the EPA Reference Dose (RfD), which has remained unchanged since 1988.[65] For the purposes of this report, "low-dose" is defined as exposures beneath the EPA RfD. Many scientists have reported diverse abnormal endocrine effects in both terrestrial and aquatic animals at doses far lower than the LOAEL used to set the EPA RfD. And BPA has been detected circulating in human blood in parts per billion (ppb) concentrations that would not be explained if exposures were occurring at the EPA RfD.

Scientists now believe that there are are at least two mechanisms by which BPA disrupts normal endocrine function.

Scientists now believe that there are at least two mechanisms by which BPA disrupts normal endocrine function. BPA can act as a weak estrogen, binding to the estrogen receptor. Alternatively, BPA can block the effect of stronger natural estrogens, inhibiting estrogen function. They are commonly assumed to act through the estrogen receptors in the cell nucleus that regulate gene expression. Several other mechanisms of BPA action are thought to be relevant to its biological effect. BPA may bind to the recently discovered membrane estrogen receptor. Activation of these receptors regulates cell signaling and influences gene expression. In addition, BPA produces changes in DNA structure by adding methyl groups to DNA, silencing their expression. These later two mechanisms do not respond in the same way to BPA as the classic receptors, and may have very different response to low doses of BPA. These latter effects have been reported at exceptionally low part per trillion doses, nearly 1,000 times lower than the effect level used to establish the current EPA RfD.[66]

Types of Effects Found in Animals at Low Doses

- *Female Reproductive Tract:* Studies have noted abnormalities in the female reproductive tract from low dose neonatal exposure, including abnormalities in the ovaries and reproductive tracts of aged female mice[67] and early vaginal opening.[68] In utero exposure in rats to low levels of BPA has been found to promote uterine disruption in rat offspring[69] and to alter vaginal morphology of postpubertal offspring.[70]

- *Male Reproductive System*: BPA has been associated with rat reproductive system changes,[71, 72] reduced daily sperm production,[73] reduced mice testis weight,[74] and enhanced anogenital distance.[75]

- *Early Puberty*: Several studies report early onset of sexual maturation in female mice occurring at low maternal doses.[76, 77]

- *Meiotic Failure*: Mice exposed to low BPA doses had high rates of meiotic failure, specifically an increase in aneuploid eggs and embryos.[78]

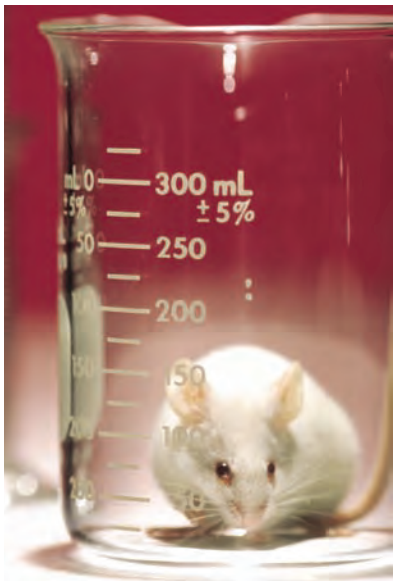
- *Reduced Sperm Count*: Low-dose developmental or adult exposure reduced daily sperm production and fertility in males in rat and mouse studies.[79]

- *Mammary Gland Development*: Low-dose BPA exposure stimulated mammary gland development in mice in several studies.[80] Fetal BPA exposure was reported to induce the development of pre-neoplastic and neoplastic lesions in the mammary gland.[81]

- *Prostate disease and cancer*: Low-dose maternal[82, 83] and fetal[84] exposure to BPA increased prostate size in male mouse offspring. Neonatal exposure to low doses of BPA increased susceptibility to precancerous prostatic lesions in rats as they aged and sensitized the prostate gland to adult-induced hormonal carcinogenesis.[85] Low dose BPA exposure for a few days after birth predisposed male rats to develop prostate cancer in adulthood.[86]

- *Diabetes and Obesity*: Low-level chronic exposure to BPA induced insulin resistance in adult mice.[87] Insulin resistance is associated with type 2 diabetes, hypertension and cardiovascular disease. Low-dose BPA produced insulin resistance in male mice.[88] Continuous exposure of mice to BPA before and shortly after birth caused the development of obesity and hyperlipidemia.[89] Scientists at the National Institute of Environmental Health Sciences (NIEHS) concluded that brief exposure early in life to environmental endocrine-disrupting chemicals, especially those with estrogenic activity like BPA, can increase body weight as mice age.[90]

- *Impaired Immune Function*: Several studies show altered immune function occurring in mice at low BPA doses.[91]



Low-level chronic exposure to BPA induced insulin resistance in adult mice.[88]

Substantial animal evidence exists to demonstrate that exposure to BPA before and shortly after birth may lead to adverse health effects later in life.

- *Behavioral Changes:* Behavioral effects noted in animals following low BPA exposure include hyperactivity;[92] increased aggression;[93] changes in response to painful or fear-provoking stimuli;[94] elimination of sex differences in behavior;[95] changes in maternal behavior (e.g., reductions in time spent nursing, increases in time resting away from offspring, and increases in time spent out of the nest);[96] and altered socio-sexual behaviors.[97]

- *Brain Effects*: BPA has been shown to inhibit the activity of estrogen in the rat brain, which normally increases the growth and regulates the viability of connections between neurons, impairing learning and memory among rats.[98] In several studies, low-dose exposure to BPA caused changes in the reproductive system and social behaviors.[99]

Life Stage Effects: Low-Dose Perinatal Animal Exposure

A DES-like effect on the reproductive tracts of mice exposed to low doses of BPA prior to or shortly after birth is a concern. BPA and other estrogen mimics may have a dual mechanism of action. At higher doses they may work as weak estrogens, and predictably would have little effect when one looks at typical human exposure and typical estrogen-induced changes. However, a number of animal studies show that BPA actions are mediated through effects on gene methylation or chromosomal integrity; methylation causes lasting changes in gene expression. These changes may be especially important during pregnancy and shortly after birth when the effects of BPA can result in abnormal development of female reproductive organs and the inability to function normally as an adult.

Substantial animal evidence exists to demonstrate that exposure to BPA before and shortly after birth may lead to adverse health effects later in life, supporting the "developmental origins of adult health and disease" hypothesis. A review of the published literature on animal studies by a National Institute of Environmental Health Sciences (NIEHS) panel of experts concluded that exposure to low levels of BPA (below 50 ug/kg/day) during the prenatal and neonatal period can cause a variety of male and female reproductive effects, behavioral effects, increased body weight, and thyroid and immune system effects.[100] These perinatal studies are summarized in the table that follows, and references include multiple citations for those who wish to explore further.

Table 2. Effects Following Low-Dose Perinatal Exposure to BPA in Animals

Male Reproductive Effects
Reproductive system changes[101, 102]
Reduced daily sperm production[103]
Reduced testis weight[104]
Enhanced anogenital distance[105]
Increased prostate size[106, 107]
Predisposition of prostate to disease[108]
Precancerous prostatic lesions in aged animals[109]
Female Reproductive Effects
Female reproductive system anomalies [110, 111, 112, 113, 114]
Reproductive tract alterations[115]
Adult uterine diseases[116]
Changes in early meiotic events[117, 118]
Accelerated growth and puberty[119]
Altered development of mammary gland[120, 121, 122, 123]
Increased risk of mammary cancer[124, 125]
Other Health Effects
Changes in behavior[126, 127]
Disruption of sexual differentiation in brain[128, 129, 130, 131]
Changes in behavior into adulthood[132, 133, 134, 135]
Changes in brain development[136]
Masculinization of female behavior[137]
Depression[138, 139]
Hyperactivity[140]
Behavioral Effects
Increased body weight, obesity[141]
Impaired thyroid hormone action[142]
Effects on the immune system[143, 144, 145]

Human and animal development of organ systems continues well after the perinatal period through adolescence and puberty.

Effects Following Adult and Young Animal Exposure

Human and animal development of organ systems continues well after the perinatal period through adolescence and puberty. Young and adult rodents exposed to low BPA doses in laboratory studies have demonstrated health effects including impaired male reproduction and fertility,[146] interference with cognitive function and development,[147] induced insulin resistance (predicts type 2 diabetes),[148] and obesity.[149, 150]

Many changes in aging adults could make them susceptible to endocrine disruptors, including BPA. Adults lose certain cell and enzyme repair capacity, and they can accumulate exposures that may contribute to cancer risk. Metabolic activity normally declines with age, and this could slow the elimination of BPA from the body. All of these possibilities deserve further exploration.

BPA Studies in Humans

Very few human studies have explored possible associations between BPA exposures and adverse health effects. Several studies have explored the relationship between health effects in humans and animals, but these have been small and criticized by manufacturing interests such as the American Chemistry Council (ACC). The ACC notes that human studies that relate levels of chemicals in the body to a health effect cannot prove a causal effect.[151] The following human health studies demonstrate that scientists are just beginning to examine the relationship between the health effects seen in animals exposed to BPA and similar effects that are on the rise in human populations.

Obesity: A Japanese study found significantly higher BPA blood levels in obese women.[152] These data are quite limited, but they are consistent with those of scientists at the NIEHS.[153] Additional research in this area seems especially important because of recent trends in bodyweight in the U.S. Nearly 20% of adults are clinically obese, an additional 30% are overweight, and the prevalence of overweight among adolescents has nearly tripled in the past two decades.[154]

Miscarriage: A study in 2005 reported an association between BPA exposure and recurrent miscarriages.[155] The study was small and preliminary, but suggests that further research of the effects of BPA on human reproduction is important, particularly since researchers demonstrated that daily oral dosing with the compound causes meiotic aneuploidy in female mice,[156] and 40–70% of sporadic spontaneous abortions are linked to chromosomal abnormalities, especially aneuploidy.[157]

Endometrial and Ovarian disease: A study of Japanese women in 2004 found that lower BPA serum levels are associated with complex endometrial hyperplasia in women.[158] Another Japanese study found an association between higher BPA blood levels and polycystic ovarian disease.[159] Some support for this hypothesis can be found in the animal literature. A recent study of mice reported an association between low-level neonatal BPA exposure and ovarian and reproductive tract abnormalities in middle-aged mice.[160]

Breast Cancer: Normal human breast cells exposed to low, environmentally relevant, levels of BPA expressed genes characteristic of aggressive breast cancer cells. The journal *Cancer Research* recently reported findings from a study that tested non-cancerous cells from women with a high risk of breast cancer or its recurrence. The cells were treated with low levels of BPA in the lab and analyzed. The scientists then screened 40,000 genes in these cells and found an increase in the sets of genes that promote cell division, increase cell metabolism, and increase resistance to drugs that usually kill cancer cells. Breast cancer patients with this type of gene expression have a higher recurrence than other patients and a lower survival rate.[161]

Very few human studies have explored possible associations between BPA exposures and adverse health effects.

Conflicting Expert Panels

During 2007, two scientific panels, both funded by the U.S. National Institutes of Health (NIH), reached conflicting conclusions about low-dose health effects of BPA on women and children.[162] Both groups reviewed over 500 published studies.

The National Institutes of Health's Center for the Evaluation of Risks to Human Reproduction (CERHR) concluded that, for pregnant women, fetuses, infants and children, there is "some concern" that exposure to BPA

There is chronic, low level exposure of virtually everyone in developed countries to BPA...[166]

causes neural and behavioral effects and "minimal concern" for reproductive effects.[163] The CERHR panel was criticized for its lack of BPA-specific expertise, and because background papers were prepared by a consulting firm that had financial ties to the BPA industry. CERHR fired this panel prior to the meeting. The 12-member panel stressed the need for more data:

"The lack of reproducibility of the low dose effects, the absence of toxicity in those low-dose-affected tissues at high doses, and the uncertain adversity of the reported effects led the panel to express 'minimal' concern for reproductive effects."[164]

Another panel of 38 scientists also sponsored by NIEHS (the "Chapel Hill" panel) signaled a stronger warning about the health effects of BPA. The Chapel Hill panel included many of the most prominent scientists working specifically on BPA health effects, and concluded:

"Recent trends in human diseases relate to adverse effects observed in experimental animals exposed to low doses of BPA. Specific examples include: the increase in prostate and breast cancer, uro-genital abnormalities in male babies, a decline in semen quality in men, early onset of puberty in girls, metabolic disorders including insulin resistant (type 2) diabetes and obesity, and neurobehavioral problems such as attention-deficit hyperactivity disorder (ADHD)."[165]

"There is chronic, low level exposure of virtually everyone in developed countries to BPA.... The published scientific literature on human and animal exposure to low doses of BPA in relation to in vitro mechanistic studies reveals that human exposure to BPA is within the range that is predicted to be biologically active in over 95% of people sampled. The wide range of adverse effects of low doses of BPA in laboratory animals exposed both during development and in adulthood is a great cause for concern with regard to the potential for similar adverse effects in humans."[166]

Why did the panels reach such different conclusions? First, the CERHR panel reviewed a smaller set of studies, while the Chapel Hill panel reviewed nearly 700 studies, including those that found effects at very low doses. Second, the CERHR panel received a different charge, so that it avoided the study of cancer risk. Third, The CERHR panel concluded that only exposure via ingestion would be considered, whereas many of the low-dose studies found effects following a variety of dosing methods.[167]

Human Exposure

The widespread use of BPA in consumer products and its presence in environmental media have led to the detection of BPA in human urine, serum, breast milk[168] (in higher concentrations than in blood serum),[169] maternal and fetal plasma, amniotic fluid, and placental tissue at birth.[170] According to a nationally representative study of BPA in the U.S. population, higher concentrations of BPA in children may be partially explained by children's higher food consumption and air inhalation rates in relation to their bodyweight. Females also had significantly higher concentrations of BPA than males, and participants in the low household income category had significantly higher concentrations than participants in the high household income category.[171]

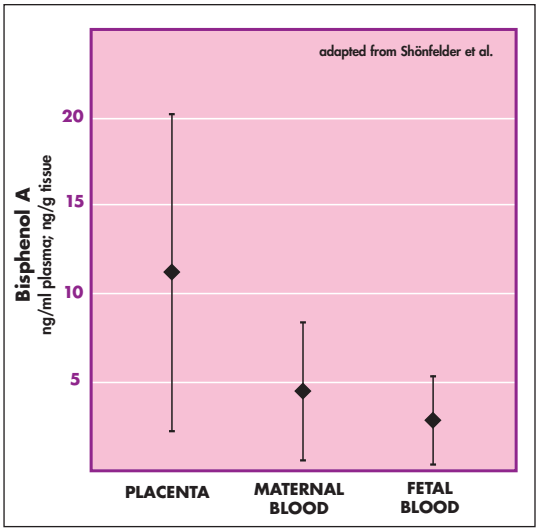


Figure 2. Levels of BPA in Blood and Placenta[179]

The CDC found that 95% of urine samples from people in the U.S. have measurable BPA levels,[172] consistent with studies from other countries.[173] Of particular importance is the finding that children have higher concentrations of BPA in their urine than adolescents and adults.[174] Research indicating that BPA is rapidly metabolized in humans and excreted in urine[175] suggests that exposure to BPA is likely continuous and from multiple sources.

BPA accumulation in fetuses suggests significant prenatal exposure.[176] Additional research found rapid absorption and distribution of BPA in maternal organs and fetuses through the placenta.[177] Exposure levels of BPA in women and fetuses were similar to those found to be toxic to reproductive organs of male and female offspring in animal studies.[178]

Children are exposed to low doses of BPA from a number of sources, primarily from ingesting foods and beverages that have been in contact with epoxy resin coatings or polycarbonate containers.[180] An observational study of preschool children in North Carolina and Ohio concluded that dietary exposure accounted for 99% of the children's exposure to BPA.[181] A recent Japanese study found that the main source of human exposure to BPA is food from some cans with linings that contain BPA.[182] The following is a review of some of the primary sources of BPA for children.

Children are exposed to low doses of BPA from a number of sources, primarily from ingesting foods and beverages....[180]

Products commonly consumed by children, including chicken soup, infant formula, and ravioli, had the highest levels of BPA tested, according to one public interest group.[190]

Canned Food

BPA-based epoxy resins are used as linings in cans for food and beverages[183] and residual BPA can migrate from these resins into the liquid in the can.[184] Canned food makes up an estimated 17% of the U.S. diet.[185] Since the early 1990s, it has been documented that epoxy compounds can be detected in foods packed in cans lined with epoxy resins.[186, 187] Substances such as caffeine, sodium chloride, vegetable oils, and glucose can increase BPA migration with rising temperatures.[188]

The Environmental Working Group (EWG) tested nearly 100 cans of foods and beverages and found that the BPA levels varied, but were as high as 385 ppb.[189] Products commonly consumed by children, including chicken soup, infant formula, and ravioli, had the highest levels of BPA tested, according to one public interest group.[190]

Are the levels detected unsafe? The Food and Drug Administration does not restrict levels of BPA in food. A 2007 letter on the FDA's position states:

"The dietary exposure to BPA from all food contact materials is thousands of times lower than the levels that showed no adverse effects in animals…(the) FDA has confidence that no safety concern exists for BPA in regulated food contact materials... FDA has determined that the use of polycarbonate-based baby bottles and BPA-based epoxy coated cans used to hold infant formula is safe."[191]

As a result of concerns about BPA in cans of foods and beverages, some Japanese manufacturers voluntarily found BPA substitutes in the 1990s. A Japanese study of urinary BPA levels in a sample of students before and after the reduction in BPA use in cans found that levels of BPA were positively correlated with coffee and tea consumption before the reduction, but not after. The authors hypothesize that reduction in the use of BPA in cans of coffee and tea in Japan explain these findings.[192]

Baby Bottles, Sippy Cups and Water Bottles

Most clear, hard plastic baby bottles, toddler drinking cups, and water bottles are made of plastics containing BPA. Manufacturers of polycarbonate baby bottles and water bottles claim that their products are safe, despite the levels of BPA that may leach from their products.[193, 194] Other groups disagree: *Parenting* Magazine posts a warning on its website to avoid polycarbonate baby bottles made of BPA;[195] Whole Foods Markets has stopped selling polycarbonate baby bottles and child drinking cups; and a billion-dollar class action law suit has been filed against five leading manufacturers of baby bottles on behalf of babies in California, who may have been injured by drinking out of plastic bottles that contain BPA.[196]

The controversy over the safety of BPA in baby bottles is due in part to insufficient data on how much BPA leaches from polycarbonate baby bottles and what level of BPA exposure may be harmful to a child. Few studies have been conducted on BPA leaching from baby bottles in the last ten years, and most have been small. Available studies studies have used varying detection limits, migration scenarios, and other assumptions, and have reached inconsistent conclusions.

A 1997 FDA study did not detect BPA from intact bottles, but detected a small amount (1 ppb) in cut strips of bottles in vials containing infant formula.[197] Another study found that older bottles leach more BPA than new bottles, and that extremely worn bottles leach even more.[198] The most recent study published by Environment California Research and Policy Center found that BPA leached from five brands of polycarbonate baby bottles at levels found to cause health effects in laboratory studies (up to 10 ppb).[199] These findings are similar to a 2003 Norwegian study that detected 8 ppb in the liquid from polycarbonate baby bottles.[200]

Most clear, hard plastic baby bottles, toddler drinking cups, and water bottles are made of plastics containing BPA.

Table 3. BPA Measured in Polycarbonate Baby Bottles

Year	Finding	Author Affiliation	Limitation	Max BPA Detected (ppb)
1997	*No BPA detected following normal sterilization practices.*[201]	*Peer reviewed Government, UK*	*24 brands tested; detection limit 0.03 mg/kg*	*ND*
1998	*Cut strips of bottles in vials containing infant formula simulant leached about 1 ppb BPA. No BPA detected from intact bottles.*[202]	*Peer reviewed FDA, USA*	*Bottles not heated with liquid inside.*	*1*
1999	*Heating plastic from bottles leached BPA into simulated infant formula. Babies who drank formula sterilized by heating bottles could be exposed to BPA at doses 40 times higher than the conservative definition of safety.*[203]	*Consumer Advocacy, USA*	*6 bottles tested*	*NR*
2001	*BPA detected in a food-simulating liquid at 1.2 ppb.*[204]	*Peer reviewed University, Argentina*		*1.2*
2003	*Migration testing detected an increase in migration of BPA with use (demonstrated by no dishwashing, dishwashing 51 times, and dishwashing 169 times).*[205]	*Peer reviewed Norway*	*12 bottles tested*	*>8*
2005	*BPA detected in 19 of 28 bottles between 4.01 and 141 mg/kg, using food-simulating solvents and high temperatures.*[206]	*Peer reviewed Government, Singapore*	*28 bottles tested*	*0.1*
2007	*Five types of polycarbonate bottles leached BPA "at levels found to cause harm in numerous laboratory animal studies."*[207]	*Advocacy group/ independent laboratory USA*	*Small study*	*10*
2008	*Temperature crucial factor for migration of BPA from plastic to water.*[208]	*Peer reviewed University, Greece*	*31 bottles tested*	*≤14.3* microg kg(-1)

Like the controversy over the safety of polycarbonate baby bottles, debate surrounds the safety of polycarbonate water bottles. Nalge Nunc International cites the FDA, EPA, and American Plastics Council in their claims that their products are safe.[209] But concerns about the safety of BPA in polycarbonate bottles led Patagonia Inc. to pull polycarbonate water bottles from its stores worldwide in 2005 and a major Canadian retailer removed Nalgene and other polycarbonate plastic containers from store shelves in 2007.

There have been even fewer studies conducted on the amount of BPA leaching from polycarbonate water bottles than from baby bottles. In FDA's 1997 study,[210] BPA was found to migrate at room temperature from polycarbonate water containers into bottled water at levels as high as 4.7 ng/g. BPA migration levels increased with time. One very recent study found that BPA migrated from polycarbonate water bottles at rates ranging from 0.20 ng/h to 0.79 ng/h and that exposure to boiling water increased the rate of BPA migration by up to 55-fold,[211] suggesting the potential for higher BPA levels in hot beverages served in nalgene containers, such as coffee or tea made in polycarbonate brewers.

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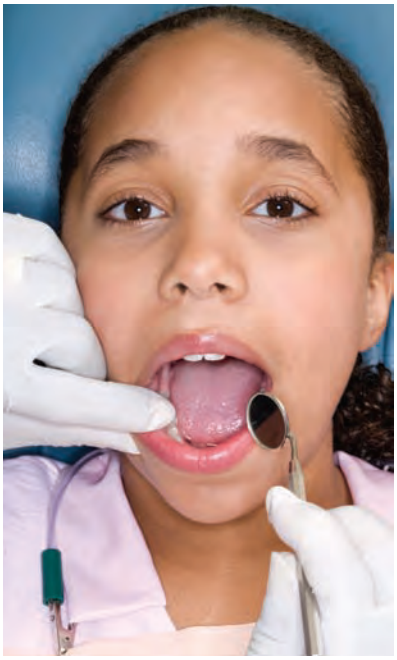

Very little research has been conducted on leaching of BPA from medical and dental products.

Medical and Dental Materials

BPA is used in the manufacture of a variety of medical equipment (e.g., incubators, kidney dialyzers, blood oxygenators, drug infusion units, labware, and flexible medical tubing)[212] and in the manufacture of materials found in some dental sealants, resin-based composites[213] and polycarbonate orthodontic brackets.[214] Very little research has been conducted on leaching of BPA from medical and dental products. Most of the research on exposure to BPA via medical and dental equipment has focused on dental materials, primarily dental sealants[215] (where it can make up to 50% of sealants).[216] More than ten years ago, researchers speculated that the use of sealants in children contributes to human exposure to xenoestrogens (i.e., man-made chemicals that act like estrogen in the human body)[217] and studies have found that dental sealants may be a source for low-level BPA exposure at levels that show health effects in rodents.[218]

Several recent studies have investigated the changes in BPA concentration in saliva after restoration with composite resins. One reported BPA in saliva after teeth were filled with a composite resin and found that it can be removed with sufficient gargling.[219] Another study concluded that sealants may result in exposure levels that show health effects in rodents. The study, which measured BPA in saliva and urine samples in 14 men exposed to "clinically appropriate" amounts of one of two sealants, found that one leached BPA at concentrations similar to those used in lab animal testing.[220]

A 2002 position statement by the American Dental Association (ADA) stated that none of the 12 dental sealants that carry the ADA Seal released BPA,[221] but a more recent statement (March 2007) issued by the ADA acknowledges that, while BPA is not an ingredient in sealants or composites, some dental products may contribute to low-level BPA exposure. While the ADA states that there is "no cause for concern" regarding BPA exposure from composites or sealants, it supports "additional research into how much BPA people are actually exposed to and at what levels of exposure health effects start to occur."[222] The National Toxicology Program's (NTP) Center for the Evaluation of Risks to Human Reproduction (CERHR) reported that exposure to BPA through dental sealants is an "acute and infrequent event with little relevance to estimating general population exposures."[223]

Hard Plastic Toys

Toys that babies put into their mouths may contain BPA, but peer-reviewed studies could not be found on the amount of BPA leaching from toys. Since toys are not labeled, it is difficult or impossible to know which toys contain BPA. The *San Francisco Chronicle* tested some children's products and detected BPA in a rattle, teething ring, waterproof books designed for babies, a doll's face and a My Little Pony toy.[224] The National Institute of Environmental Health Sciences at the National Institutes of Health recommends that consumers concerned about BPA look for toys that are labeled BPA-free.[225] Since there is no "ingredient labeling" requirement for toys, this is not realistic.

Since toys are not labeled, it is difficult or impossible to know which toys contain BPA.

Other Consumer Products

Many products manufactured throughout the world contain BPA but do not have the clear, hard plastic appearance of polycarbonate. These include the following products demonstrated in recent studies to leach BPA: non-stick-coated cookware (UK),[226] PVC stretch film used for food packaging (Spain),[227] recycled paperboard food boxes (Japan),[228] and clothing treated with flame retardants. Tetrabromobisphenol-A, for example, is the most commonly used flame retardant, and it has increased in blood serum since the 1970s, reaching concentrations 3 1/2 times higher in children under age four than in adults by 2002.[229]

Regulating BPA

Bisphenol A has been "Generally Regarded as Safe" (GRAS) as an "indirect food additive" for food and beverage packaging and containment, by many of the world's higher-income nations. Note that all of the regulations listed below were established prior to the publication of literature described above regarding low-dose effects.

BPA is permitted in products used by children in the U.S. and Europe. Resins added to plastics used for food packaging are regulated by FDA's requirements for indirect food additives. The FDA approved BPA for use in food and beverage containers in the 1960s using the standard that BPA was Generally Regarded as Safe (GRAS), since there was no evidence for harm. The agency stated that it believes there is no reason to ban BPA.[231]

Several states have introduced bills banning the sale of certain products containing BPA. California, Maryland, Massachusetts, Maine, Minnesota and New York have proposed bills proposing that BPA be banned. Some of these bills have been defeated and some states are working on new legislation to introduce in 2008.

Table 4. Global Food Contact Regulations Specific to Polycarbonate Resin[230]

Country	Applicable Regulations
USA	Food and Drug Administration - 21 Code of Federal Regulations Part 177.1580
Japan	Self-restrictive Requirements on Food-Contact Articles (JHOSPA) Section 2-24 Polycarbonate (March 1996)
European Union	EU Directive 90/128/EEC of 2/23/90, as amended
Germany	(BgVV) Lebensmittel-und Bedarfsgegenstandegesetz of 7/8/93 Bedarfsgegenstandeverordnung of 4/10/92, as amended BgVV Recommendation XI (Status of 12/1/96)
Netherlands	Food Packaging and Utensils Decree of 10/1/79, as amended, Chapter 1
France	Min. Decree of 9/14/92 Brochure 1227 (January 1994)
Italy	Min. Decree of 3/21/73, as amended, Min. Decree No. 220 of 4/26/93
Spain	Royal Decree 211/1992 of 3/6/92, Royal Decree 1769/1993 of 10/8/93
Belgium	Royal Decree of 5/11/92, as amended
United Kingdom	The Materials and Articles in Contact with Food Regulations 1987 (S.I. No. 1523). The Plastic Materials and Articles in Contact with Food Regulations 1992 (S.I. No. 3145), as amended.

In June 2006, San Francisco banned BPA in children's products, but the following October the ordinance was subjected to a lawsuit claiming that the ordinance was "flawed and scientifically unsound."[232] In April 2007, the San Francisco Board of Supervisors passed amendments to repeal the ban on products containing BPA, but urged the State of California to prohibit or restrict the sale of children's products containing BPA.[233]

Summary

In summary, BPA is neglected by most U.S. environmental laws, with the exception of the Food, Drug, and Cosmetic Act. The Food and Drug Administration (FDA) has approved its use for food packaging and beverage containment and this has become the dominant source of human exposure. The FDA considers the chemical to be "generally regarded as safe (GRAS)."

The FDA's definition of acceptable exposure, its reference dose, or RfD, is based upon animal studies that are now two decades old, and which did not consider or test the effects resulting from low-dose exposures. Nor did the FDA have the benefit of the U.S. Centers for Disease Control and Prevention's (CDC) National Health and Nutrition Examination Survey (NHANES) studies that found BPA present in the tissues of nearly everyone tested. Exposure is widespread and chronic. Recent studies cited above report effects at doses nearly 1,000-fold smaller than that used to establish the reference dose. Many state laws have been proposed to control childhood exposure to BPA, but at the time of this writing, none have been adopted. The landscape of regulations is continuously changing, but currently it is a patchwork of voluntary actions by some manufacturers, retailers and hospitals, as well as some local and state governments.

DEHP

Introduction

Phthalates[234] are "plasticizers" used to produce diverse products, including food and beverage packaging materials, medical devices and products, flexible tubing, electrical conduits, building products, lubricants, perfumes, hairsprays, cosmetics, construction materials, wood-finishers, and adhesives. Phthalates are additives that give plastics like polyvinyl chloride (PVC) properties such as flexibility and stress resistance. Six phthalates are in common use (see Table 5). However, di(2-ethylhexyl) phthalate, commonly known as DEHP, has received the most regulatory and scientific attention due to the strength of evidence demonstrating its testosterone-blocking potential in males.[235]

Nearly 240 million pounds of DEHP were produced in 2002, a figure that represents a quarter of all plasticizers produced.[236] Most DEHP is added to PVC plastics produced from vinyl chloride. It is often mixed with plasticizers (softeners), heat stabilizers such as lead, cadmium, zinc, and tin, as well as lubricants, and other additives that affect both mechanical and physical properties. Some vinyl contains 40% DEHP.[237] DEHP is the focus of this section of our report, because it has the greatest potential for endocrine disruption among all phthalates, and has received the greatest attention of all the phthalates due to the strength of evidence of its potential to disrupt health in laboratory studies.

Nearly 15 billion pounds of PVC plastics are produced each year. The chemical complexity and diversity of PVC plastics make them difficult and expensive to sort and recover. The effect is that a very small proportion (0.1–0.5%) are recovered through recycling efforts.[238]

Recovery failure, in turn, means that the majority is released to the environment in landfills or via incineration. If placed in landfills, the chemical often leaches into groundwater. If burned, a variety of highly toxic chemicals is produced and often released to the atmosphere. These include polychlorinated dibenzodioxins (PCDD), and polychlorinated dibenzofurans (PCDF), both well recognized for their hazard to human health. These chemicals are often released from incinerators, and also from accidental fires that burn materials containing PVC plastics, such as vinyl flooring, paints, wall coverings, electrical wiring, and vinyl siding.

The enormous volume of PVC in consumer and industrial products, its persistence, and its routine disposal to the environment help to explain why human exposure to DEHP is nearly ubiquitous. DEHP has been found in human blood, seminal fluid, amniotic fluid, breast milk, and saliva.[239] Our focus on DEHP is explained by the strength of evidence of human exposure and the relative clarity of animal evidence of health hazard in comparison with other phthalates, briefly summarized in Table 5.

Table 5. Phthalate Toxicity Concerns by Type, National Toxicology Program (NTP), U.S. DHHS

DEHP	*DEHP causes reproductive and developmental damage in animal studies. These studies are plausibly relevant to humans, especially male infants, children, and pregnant and lactating women.*[240]
BBP	*Studies report reproductive toxicity in adult rats and developmental toxicity in rats and mice are assumed relevant to humans.*[241]
DBP	*Studies report developmental toxicity among exposed rats and mice.*[242]
DINP	*Child exposure via children's products is common and children may be exposed to 10- to 100-fold higher levels than adults by mouthing toys and other articles containing DINP. Quality of toxicological evidence is weaker than for DEHP.*[243]
DNOP	*Data are limited or inadequate.*[244]
DIDP	*Children may have higher levels of exposure than adults if they mouth toys and other objects that contain DIDP.*[245]

Studies have found that male rodents exposed to DEHP before or shortly after birth exhibit a variety of developmental and reproductive abnormalities.

DEHP Health Effects

- The EPA derived a chronic oral RfD of 0.02 mg/kg/day for DEHP in 1986, based on a "lowest observed adverse effect level" (LOAEL) of 19 mg/kg/day for hepatic effects in guinea pigs noted in a 1953 study,[246] and supplemented by studies from the early 1980s.[247] This RfD was derived before studies were published reporting malformations of the reproductive tract,[248] low-dose health effects,[249] and health effects due to inhalation exposure.[250]

- Most early studies on the health effects of DEHP experimented with doses administered to animals above ranges encountered by most people. In the 1970s, DEHP toxicological studies noted that prenatal exposure of rats to DEHP resulted in skeletal malformations, cleft palate, and a decreased number of live fetuses at birth.[251] Several toxicological studies in the 1980s reported that prenatal, suckling, and adult rats exposed to DEHP experienced reduced hepatic enzyme activity.[252] By 1999, researchers established that DEHP alters sexual differentiation in male rats in an anti-androgenic manner, producing malformations of the reproductive tract.[253] Numerous studies on animals subsequently reported DEHP association with diminished testicular function and developmental processes dependent upon androgen. Studies have found that male rodents exposed to DEHP before or shortly after birth exhibit a variety of developmental and reproductive abnormalities, including undescended testicles, reduced anogenital distance, hypospadias, female-like areolas/nipples in infant male rats and other anatomical differences,[254] as well as decreased sperm production[255] and testosterone levels.[256]

- Other than a few scattered studies on the potential for female reproductive health effects of DEHP, most of the reproductive studies conducted on DEHP have focused on males. However, a 1994 study reported that female adult rats exposed to high doses of DEHP had suppressed ovulation and polycystic ovaries.[257]

- A recent study has noted that prenatal DEHP exposure resulted in adverse effects on rat lung tissue development.[258]

Low-Dose Effects

- In the last several years, scientists have noted health effects in animals given low, environmentally relevant doses of DEHP. A brief summary of the types of effects found in animals at low doses is provided below.

- *Male Reproductive Toxicity*: Prenatal and lactational DEHP exposure reduced daily sperm production and induced reproductive abnormalities in male offspring rats. The LOAELs for these effects were 15 and 5 mg/kg/day, respectively.[259]

- *Brain Development*: A 2006 study reported that rats exposed to DEHP at low doses during fetal and neonatal development show changes in the function of a brain enzyme (aromatase) that controls estrogen availability.[260] One study noted that low DEHP doses caused larger effects than higher doses: lower doses of DEHP suppress the activity of aromatase, necessary for masculinization of the male brain of rats, while higher doses increase the enzyme's activity.

- *Early onset of puberty in males*: A study of low environmentally relevant DEHP levels on testicular function reported that "low levels of DEHP may shift the body's hormonal equilibrium to a higher level as the endocrine system struggles to overcome the anti-androgenic propensities of the chemical. The overall increase in circulating testosterone is sufficient to speed the onset of puberty in male rats."[261]

- *Delayed/Advanced puberty in females*: A 2006 study of female rats reported that in utero and lactational exposure to DEHP at 15 mg/kg/day and above delayed puberty in female offspring.[262] Another 2006 study reported that DEHP inhaled at higher doses by pre-pubertal female rats advanced the onset of puberty and altered post-pubertal reproductive functions.[263]

- *Allergies*: DEHP enhanced atopic dermatitis-like skin lesions in mice at hundred-fold lower levels than the "No Observable Adverse Effect Level (NOAEL)," based upon histologic changes in rodent livers.[264]

The study noted that low DEHP doses caused larger effects than higher doses: lower doses of DEHP suppress the activity of aromatase, necessary for masculinization of the male brain of rats, while higher doses increase the enzyme's activity.

Several studies reported an association between phthalate exposure and sperm damage in men.

Human Studies

- *Male Reproductive Malformations*: Researchers in 2005 reported a relationship between exposure to phthalates during pregnancy and anogenital distance in young boys.[265] The mother's prenatal urinary concentrations of several phthalates were measured and compared to anogenital distance of their infant sons. A shorter distance was reported in boys exposed to higher levels of phthalates during pregnancy. Shorter distances were also associated with an increased proportion of boys with incompletely descended testicles and small genital size, suggesting an anti-virilizing effect of phthalates in infants.[266] The 2005 study showed an effect for all phthalates, but did not reach statistical significance for the individual compound DEHP and its metabolite, mono-2-ethylhexyl phthalate (MEHP).

- *Sperm Damage*: Several studies reported an association between phthalate exposure and sperm damage in men. In 2003, researchers from Harvard and the CDC found that men with low sperm counts and impaired sperm quality are more likely to have higher phthalate levels. Highest phthalate concentrations were found in men with the lowest sperm counts.[267] The same investigators in 2007 found human sperm DNA damage was associated with DEHP metabolites. Urinary levels of phthalate metabolites among men in this study were similar to those reported for the U.S. general population.[268]

- *Asthma*: Several recent studies report an association between DEHP and respiratory illness, including asthma. Others suggest that DEHP may contribute to allergic reactions in people.[269] Phthalates have been measured in residential air and are common components of air and house dust. A Swedish study found a positive association between allergic asthma in children and DEHP in house dust, noting that DEHP in house dust correlated with the amount of PVC in flooring.[270] Another study related the risk of asthma to the presence of plastic wall materials (which can contain 40% DEHP).[271] One study suggests that development of lung problems in the first two years of life may be linked to exposure to plastic interior surfaces.[272]

This finding is consistent with other epidemiologic studies in children living in Norway, Finland, Sweden, and Russia.[273, 274] A survey of asthmatics found that 30% of people with asthma reported that air fresheners caused breathing difficulties.[275] Preterm infants exposed to DEHP from respiratory tubing have been reported to have a higher risk of bronchial asthma.[276]

- *Early puberty in girls*: A study of Puerto Rican girls found that girls with premature sexual development had higher levels of phthalates measured in their blood. High levels of phthalates were found in more than two-thirds of the girls with premature sexual development, compared to only about one in five of the subjects with normal puberty. Levels of DEHP were found at concentrations seven times greater in girls with premature breast development (girls with an average age of 31 months) than in the control group.[277] This study has been criticized for possible failure to control laboratory contribution of DEHP to reported tissue concentrations.

- *Female Reproductive Tract Disease*: Several studies report an association between DEHP levels and endometriosis: women with endometriosis had higher blood levels of DEHP in Italy[278] and India.[279] Women with uterine fibromatosis showed significantly lower blood MEHP concentrations.[280]

- *Premature delivery*: Investigators have determined that pregnancy complications such as low birth weight and shorter pregnancy duration[281] correlate with DEHP exposure. A 2003 study found phthalates and their breakdown products in the blood of newborn infants, with higher levels associated with a higher incidence of premature delivery.[282]

- *Thyroid Effects:* A recent study reported that men with higher levels of the DEHP metabolite MEHP in their urine had lower levels of two major thyroid hormones in their blood.[283] Thyroid hormones influence many body functions in people, such as cell growth and brain development in children.

A survey of asthmatics found that 30% of people with asthma reported that air fresheners caused breathing difficulties.[275]

Male infants exposed to high DEHP concentrations through medical procedures are at greatest risk…

Interpretations of the Data

A scientific panel convened by the U.S. National Toxicology Program (NTP) reviewed the health effects of DEHP, and concluded that exposure can present a risk to the development of the reproductive tract of male infants (Table 6). Male infants exposed to high DEHP concentrations through medical procedures are at the greatest risk. The panel concluded that male infants may also be at risk from reproductive effects of DEHP from non-medical exposures, noting that infants may be exposed through their diet or mouthing DEHP-containing objects. The panel also acknowledged *some concern* about reproductive tract abnormalities in male offspring of women who were exposed to DEHP from non-medical sources.[284]

Table 6. Center for the Evaluation of Risk to Human Reproduction (CERHR), Level of Concern for DEHP Exposure

CERHR Level of Concern	Population Sub-group	Type of Exposure
Serious Concern	*Male infants*	*Medical procedures*
Concern	*Male offspring*	*Pregnant and breastfeeding women undergoing some medical procedures*
	Male infants less than one year	*Diet or mouthing DEHP-containing objects*
Some Concern	*Male infants over one year*	*Diet or mouthing DEHP-containing objects*
	Male offspring	*Women exposed to DEHP from non-medical sources*

Production, Disposal, and Environmental Contamination

In 2002, U.S. manufacturers produced an estimated 260 million pounds of DEHP.[285] Ninety to 95% of the chemical produced in the U.S. is used to make PVC. Medical devices account for approximately 25% of DEHP manufacturer use.[286, 287] In the U.S., PVC consumption has been increasing steadily since the 1960s. There are about 260 facilities that produce, process or use DEHP in 40 different states.[288, 289]

When DEHP (either as a commercial chemical product or chemical intermediate) becomes a waste, its disposal is regulated under the Resource Conservation and Recovery Act (RCRA). In 1998, EPA estimated that about one million pounds of waste DEHP were transported from production facilities or points of usage for disposal, including publicly owned treatment works.[290]

No data were located regarding quantity or trends in disposal of DEHP.[291] It is unclear what happens to the DEHP when disposed of in landfills, but a Japanese study of endocrine-disrupting chemicals in landfill leachate found that not only was DEHP the most abundant of the substances measured, but aeration, biological treatment, coagulation and sedimentation removed only a small amount of DEHP.[292]

In the U.S., PVC consumption has been increasing steadily since the 1960s.

Table 7. Environmental DEHP Concentrations Found in the U.S.[293]

Medium	Mean concentration	Median concentration (range)
Surface water, µg/L	0.21	0.05 (<0.002–137)
Ground water, µg/L	15.7	15.7 (not detected–470)
Drinking water, µg/L	0.55	0.55 (0.16–170)
Sediments, µg/kg	1.4	0.16 (0.00027–218)
Soil, µg/kg	0.03	median not available (0.03–1280)
Outdoor air, ng/m^3	5.0	2.3 (<0.4–65)
Indoor air, ng/m^3	109.0	55 (20–240)
Dust, g/kg	3.24	median not available (2.38–4.10)
Wastewater, µg/L	27.0	8.3 (0.01–4400)
Sludge, g/kg	0.301	median not available (0.000420–58.3)
Rainwater, µg/L	0.17	0.17 (0.004–0.68)

From Clark, et al.

Fetal exposure to DEHP has been shown to be closely related to maternal exposure.[302]

Human Exposures to DEHP

The U.S. Centers for Disease Control and Prevention (CDC) studied human tissue to understand patterns of human exposure. These studies document that childhood exposure to phthalates is widespread.[294] The CDC found that children aged 6-11 years excrete higher concentrations of phthalate metabolites than older age groups.[295] Younger children appear to have higher concentrations of DEHP, possibly due to higher food consumption related to body weight, mouthing behavior, and/or playing near the ground[296] (i.e., coming into closer contact with PVC-type flooring products). The DEHP dose taken up by nursery school children was found to be about twice as high as the dose taken up by adults.[297] The total intake of DEHP, excluding non-dietary ingestion, is higher in all children younger than 19 years than in adults, but the highest exposure is in children six months to four years old.[298] In addition to an increased risk of exposure to DEHP, research on its metabolite, MEHP, indicates that it may have a longer half-life in the body of young infants.[299]

Women of childbearing age were found to have significantly higher phthalate exposures than other adults.[300] A study measuring levels of phthalates in personal air samples collected from pregnant women in New York and Poland found DEHP in 100% of air and urine samples.[301] Fetal exposure to DEHP has been shown to be closely related to maternal exposure.[302]

A German study of DEHP daily intake found that nearly one-third of the men and women in the study exceeded the U.S. EPA RfD limit for DEHP.[303] Another study correlated DEHP intake with the intensive use of DEHP in plastics. In a recent Taiwanese study, 85% of the study participants exceeded the U.S. RfD for DEHP, and the authors concluded that the body burden of DEHP for Taiwanese reflects the intensive use of plastic materials.[304] Similarly, a 2007 German study reported a correlation of the daily intake of DEHP in university students with the regional industrial production of DEHP.[305] DEHP is in many

products that children are exposed to, including foods packaged in some plastics, indoor air (from vinyl flooring, wallpaper, furniture and paints), and soft PVC toys and pacifiers. Childhood exposure to DEHP is a concern because of its heavy production, common presence as an environmental contaminant, leaching potential, and hormonal activity. Children may be exposed to DEHP by mouthing plastic toys or pacifiers, eating foods contaminated with DEHP from packaging or during manufacturing, breathing contaminated air inside homes, or receiving medical care in hospitals.

The migration of phthalates from packaging materials to foods, particularly fatty foods, is a well known source of food contamination.[308]

Packaged Food and Beverages

The major source of exposure to DEHP for most children is food (Table 8).[306] DEHP has been detected in many foods common in a child's diet, including milk, cheese, meat, margarine, eggs, cereal products, baby food, infant formula, and fish.[307] The migration of phthalates from packaging materials to foods, particularly fatty foods, is a well known source of food contamination.[308] FDA allows the use of DEHP in can coatings,[309] adhesives,[310] paper manufacturing,[311] single and repeated use containers,[312] cellophane,[313] and as a metal foil lubricant.[314] Processing equipment, including plastic tubing, surface

Table 8. Estimated Daily Intake of DEHP (µg/kg of Body Weight per Day)[318]

AGE	0–6 mos.	6 mos.–4 yrs.	5–11 yrs.	12–19 yrs.	20–70 yrs.
Indoor air	0.86	0.99	1.2	0.95	0.85
Drinking water	0.13–0.38	0.06–0.18	0.03–0.10	0.02–0.07	0.02–0.06
Food	7.9	18	13	7.2	4.9
Soil	0.000064	0.000042	0.000014	0.000004	0.000003
Total estimated intake	8.9–9.1	19	14	8.2	5.8

A study conducted by the Consumers Union nearly 10 years ago found moderate levels of DEHP in cheeses wrapped in plastic wrap, although the plastic wrap itself did not contain DEHP.

coatings and gaskets used in the food industry in contact with foods may also contain DEHP.[315] DEHP is considered an indirect additive in packaged foods due to its use in plastic wraps, heat seal coatings for metal foils, closure seals for containers, and printing inks for food wrappers and containers.[316] It is known to migrate into food from plastics during processing and storage.[317]

In a 2006 study published by the World Wildlife Fund, 16 of 21 European food items analyzed contained DEHP, including meat and dairy products (butter and particularly cheeses). The highest level of DEHP (and total phthalates) was detected in olive oil (24,000 ng/g).[319] Several other studies show that DEHP is widely found in dairy products. One source of DEHP in milk is the plastic tubing in milk transferring systems. Since DEHP has been found in dairy products in countries where DEHP no longer is allowed for use in transfer tubing, the presence of DEHP in milk may originate from environmental sources.[320]

A study conducted by the Consumers Union nearly 10 years ago found moderate levels of DEHP in cheeses wrapped in plastic wrap, although the plastic wrap itself did not contain DEHP. Potential sources of DEHP identified included the glues and inks used on the printed labels, or background environmental contamination of the cheese.[321]

Bottled water has also been found to contain DEHP. The NRDC detected DEHP in several types of bottled water tested. The level detected is just below the EPA tap water standard for this chemical, though there is no bottled water standard.[322]

Much of the literature on DEHP contamination of food has been conducted outside the U.S., and it is uncertain how applicable this information is to U.S. exposures. Examples of migration studies that have been conducted are shown in Table 9.

Table 9. DEHP Non-Medical Migration Studies

Product Tested	Country	Finding	Year
PVC gloves to prepared food	*Japan*	*Content of packed lunches exceeded 1.85 mg DEHP, the EU TDI for a person of 50 kg body weight.*	2001[323]
Bottled water	*U.S. NRDC*	*Detected DEHP in bottled water at levels exceeding 6 ppb (tap water standard — there is no standard for DEHP in bottled water).*	1999[324]
Bottled mineral water	*U.S. New Jersey*	*Detected DEHP in three imported bottled mineral waters above 6 ppb, New Jersey's maximum contaminant level (MCL) for DEHP in bottled water.*	2006[325]
PET bottles, yogurt drinks	*Iran*	*Temperature (45°C) and storage (over 70 days) increased DEHP migration.*	2007[326]
Cap-sealing for bottled foods	*Japan*	*DEHP migrated from cap-sealing into food; shaking bottles increased migration of DEHP into foods.*	2002[327, 328]
Milk Processing	*Germany*	*Migration of DEHP during milk processing and storage.*	2000[329]
Soft PVC Toys	*Netherlands*	*DEHP migration exceeded the SCTEE guidance release value of 1.7 microg min(-1) 10 cm(-2).*	2002[330]
PVC tubes used in food preparation	*Japan*	*DEHP migrated from PVC tubes; tubes considered unsuitable for direct contact with oils, fats or oily foods.*	2002[331]
Infant Products	*U.S. California*	*12 infant products (including waterproof books, teething ring, and bath toys) contained DEHP.*	2007[332]
PVC films	*Taiwan*	*Food covered with PVC films and microwaved for 3 minutes had significant increases in DEHP levels.*	2007[333]

Phthalates, including DEHP, have been detected in baby food in studies from several countries.[334, 335]

Baby Food, Infant Formula, and Breast Milk

Phthalates, including DEHP, have been detected in baby food in studies from several countries.[334, 335] DEHP was the most frequently detected phthalate in a 2000 Danish study of baby food and baby formula. The survey found that mixed baby food with meatballs had the highest level of DEHP—up to 34% of the Tolerable Daily Intake (TDI) from a single jar of food.[336] The TDI is an estimate of the amount of a chemical contaminant in food or water that can be ingested daily over a lifetime without posing a significant risk to health. The study was small, but demonstrates that baby food and infant formula can be an important source of exposure to DEHP for infants and young children. A Japanese study found high concentrations of DEHP (5990 ng/g) in baby food and identified the source of contamination as the PVC tube used during food production.[337]

The presence of phthalates in infant formula[338] and human breast milk samples from the U.S.,[339] Canada,[340] Germany,[341] and Finland and Denmark[342] is well documented. Since DEHP can migrate into fat, and phthalates have been shown in animal studies to cross the placenta and pass into breast milk,[343] its presence in human breast milk is not surprising.

Indoor Air Exposure: Building Materials and Furnishings

Phthalate esters have been recognized as major indoor pollutants in homes and schools.[344] DEHP is widely used in building and furniture materials, including furniture upholstery, mattresses, wall coverings, floor tiles, and vinyl flooring. While industry representatives have indicated that most U.S. wall covering manufacturers do not use DEHP, products from international manufacturers may,[345] and many other indoor vinyl products are imported. These indoor polyvinyl chloride (PVC) products, a potentially large source of DEHP exposure, include shower curtains, automobile interiors, and vinyl flooring. Indoor air can have higher levels of DEHP than outdoor air, particularly after a room is painted or flooring installed. One study estimates the typical home indoor air median concentration of DEHP at 77 $\mu g/m^3$ [346] — greater than the concentration estimated to provide a protective level for

DEHP carcinogenic effects (0.42 µg/m^3). This level represents the estimated probable risk of producing one additional cancer case in a million people if they were to continuously breathe air with this concentration over a lifetime.[347]

Table 10 shows that indoor air in a room with PVC flooring may contribute significantly to DEHP exposure levels.

A child's mattress or waterproof mattress cover may also contain DEHP, since many mattresses contain or are covered by waterproof PVC coatings. The amount of DEHP a newborn infant may be breathing as he or she sleeps has not been calculated. Since a baby may spend 10-12 hours per day on a mattress, the release of volatile compounds, including DEHP, could represent a significant proportion of total exposure.[349]

Table 10. Potential Non-Medical Sources of DEHP Exposures[348]

Source	Daily Exposure (mg/day)
Air, in cars at 25°C	<0.07
Air, indoor room with PVC flooring	1–6
Air, outdoor urban	0.0005–0.016
Drinking water	<0.06
Food	0.27–2.0

Studies have documented the release of DEHP from toys from mouthing behavior.[353]

Indoor Air Exposure: Fragrances

DEHP is often used in cosmetics and personal care products to carry fragrances. Under current law, phthalates can simply be listed as "fragrance" on the label, even if they are a large component of the product.

DEHP is found in many products that have fragrances, such as laundry detergents, dryer sheets, colognes, scented candles and air fresheners. Phthalates are used to extend the life of perfumes, and to enhance the penetration of skin lotions.

Children living in homes that are heavily fragranced may have higher exposures to DEHP. The Consumers Union recently tested eight fragrances for phthalates,[350] some of which were advertised to be free of phthalates, and all contained DEHP.[351] The Cosmetic, Toiletry and Fragrance Association claims that cosmetic companies do not use DEHP in their perfume formulas and that DEHP may have leached into the fragrance from their plastic containers.[352]

Toys and Infant Supplies

Soft plastic products intended to be in the mouths of infants and young children, including toys, pacifiers, teethers, and nipples, may contain DEHP. Soft PVC children's products are usually plasticized with phthalates, and children who suck and chew on toys can extract and ingest these plasticizers. Studies have documented the release of DEHP from toys from mouthing behavior.[353]

DEHP was the most common plasticizer used in soft PVC products intended for children in the U.S. until the early 1980s, when U.S. manufacturers and the Consumer Product Safety Commission (CPSC) reached a voluntary agreement to remove it from toys intended for mouthing: nipples, teethers, pacifiers, and rattles.[354] But DEHP is still

found in toys intended for young children in the U.S. and abroad. Since about 80% of toys sold in the U.S. are made in China,[355] and China has no restrictions on the use of DEHP in toys, the presence of DEHP would be expected in the U.S. toy market.

Medical Equipment

DEHP is the most commonly used phthalate in medical devices, and phthalates have been used in medical equipment since the 1950s. DEHP is used to soften PVC products, such as medical tubing and blood storage bags, and can be found in blood and intravenous bags containing fluids used in neonatal care units, pediatric wards, and throughout hospitals.

Newborns and infants undergoing particular medical procedures may have 100 to 1,000 times the exposure experienced by the general population.[356] Quantitative evidence confirms that newborns who undergo intensive medical interventions are exposed to higher concentrations of DEHP than the general population.[357]

The FDA has identified the male fetus, male neonate, and peripubertal male as high-risk groups for health risks from medical exposure to DEHP.[358] The American Academy of Pediatrics agrees that pediatric medical exposure to DEHP is a health concern.[359] The Academy reported that DEHP has been documented to be toxic to the male reproductive tract in laboratory animals at doses close to those resulting from intensive medical procedures in humans.[360] More recently, CERHR concluded that exposure of critically ill neonates to DEHP represents a "serious concern."[361]

Despite the consensus in the medial community that medical exposure to DEHP is a health concern, the FDA does not restrict DEHP or require medical device manufacturers to label products that contain DEHP.[362]

Newborns and infants undergoing particular medical procedures may have 100 to 1,000 times the exposure experienced by the general population.[356]

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Regulating DEHP

Children's Products

The U.S. is one of the few developed countries with no government limits on DEHP in children's products. Two decades ago, the Consumer Product Safety Commission and U.S. toy manufactures came to a voluntary agreement to remove DEHP from children's pacifiers, teethers, and rattles, restricting concentrations of DEHP to three percent.[363] Many other countries have government-mandated restrictions on the use of DEHP in children's products.

The European Union (EU) restricts the use of DEHP in toys and childcare articles, and is conducting an investigation that may lead to legislation restricting its use in medical devices.[364] Initially, the EU prohibited DEHP and five other phthalates[365] from soft PVC toys[366] intended to be placed in the mouth by children under three,[367] noting specifically concern about testicular damage caused by DEHP. The EU broadened the ban to include other childcare articles, including any product intended to facilitate sleep, relaxation, hygiene, the feeding of children, or any item intended for sucking by children.[368]

The EU noted, "Young children are also exposed to phthalates from sources other than PVC toys and childcare articles, but the level of exposure due to these sources cannot…be quantified because of lack of sufficient data…the Commission considers that toys and childcare articles for young children made of soft PVC-containing phthalates are liable to present a serious and immediate risk to health."[369]

Health Canada has proposed to "…prohibit the sale, advertisement, and importation of toys for children under three years of age and products for children under three years of age that are likely to be mouthed" that contain DEHP.[370] Argentina, Austria, Cyprus, the Czech Republic, Denmark, Fiji, Finland, Germany, Greece, Italy, Japan, Mexico, Norway, and Sweden have restricted phthalates in children's toys.[371]

Despite government restriction and voluntary efforts, many toys intended to be mouthed by young children still contain DEHP. Although the U.S. does not test toys for DEHP, other governments and organizations have done so. While tests conducted by the Canadian Government in 1998 and 2006 found a decline in the use of DEHP in these products, the 2006 tests found DEHP in other products intended for young children.[372] Tests conducted by Environment California and the Public Interest Research Group found that 15 out of 18 products tested contained one or another of the six phthalates banned in the EU and 12 products designed for children contained DEHP.[373]

The National Environmental Trust tested 60 teethers, bath and squeeze toys and dolls for phthalates in 1998 and 1999 and found that one toy in each of these three categories contained DEHP in concentrations well in excess of three percent.[374] DEHP was recently found in toys in Europe, despite more aggressive regulations in the EU than in the U.S. Products included an inflatable rubber ring and raft made in China (noted to contain 26.8% and 30% by weight of DEHP), a child's bib made in Slovakia, a changing mat and a stuffed teddy bear of unknown origin.[375]

Table 11. Examples of National PVC Childcare Restrictions[376]

Country	Year	National Restrictions
Austria	1999	Ban on the sale of phthalate plasticizers in toys for children under age three.
Denmark	1999	Ban on phthalate plasticizers in toys and childcare articles for infants under age three.
Argentina	1999	Covers all toys and baby articles containing phthalates that could be chewed by children under three.
Greece	1999	Bans the import and sale of PVC toys containing phthalates for children under three years old.
Norway	1999	Bans production, distribution, import and export of toys and other products aimed at children under three years old and containing phthalate plasticizers.
European Union	1999	Ban on six toxic softeners found in soft PVC toys marketed for teething. In 2000 increased restriction to reduce maximum allowed concentration of phthalates in PVC to 0.05 percent instead of 0.1 percent, and bans any PVC toys containing perfumes, such as fruit flavors, which tempt children to suck them.
Cyprus	2000	Ban on baby toys made of PVC.
Fiji Islands	2000	Ban on the sale of children's items made of PVC, including soft PVC toys intended for children's mouths, and other articles such as stroller covers and mattress covers.
Tunisia	2000	Ban on the importation, selling and distribution of all PVC toys and childcare articles intended for children under the age of three and which contain more than 0.1% of one of the six mentioned categories of phthalates (DINP, DEHP, DNOP, DIDP, BBP, DBP).
Czech Republic	2001	Ban on phthalates in PVC toys.
Japan	2001	Ordinance: In the production of resin toys, PVC containing DEHP should not be used.

Medical Products

The FDA has not restricted DEHP use in medical equipment, nor has it required that medical equipment containing the chemical be labeled. The American Medical Association (AMA) has urged the FDA to require labeling of all medical products containing DEHP.[377] The FDA published a public health notification in 2002 recommending alternatives to PVC devices containing DEHP for medical procedures that might expose newborn boys, women pregnant with boys, and boys entering puberty.[378]

Food Packaging

PVC packaging, which may or may not contain DEHP, has been either banned or restricted in a number of countries, including Canada, Spain, South Korea and the Czech Republic.[379] The FDA approved DEHP as a plasticizer for use in packaging material of foods with high water content[380] even though it migrates into bottled water, but neither FDA nor EPA set limits for DEHP in bottled water. Some states, such as New Jersey, have established a "maximum contaminant limit" (MCL) for DEHP. In a "spot check" of bottled water in New Jersey, three types of imported mineral water exceeded New Jersey's MCL for DEHP and were banned from sale.[381] DEHP-contaminated bottled water products may legally be sold or distributed in those states that have not established their own MCL for DEHP.

Although detected in both bottled water and tap water, DEHP is only regulated under EPA tap water rules, not FDA's bottled water rules. A report by the Natural Resources Defense Council (NRDC) notes: "Some bottlers and members of the plastics manufacturing industry vigorously opposed a phthalate standard, arguing that it would cause some bottled water to be in violation after storage for long periods.… As one company put it, "bottled water tested immediately after packaging would meet the 6 ppb [FDA proposed] limit but with storage it is possible that levels might exceed this requirement…[so] the proposed amendment… [would] effectively ban the use of DEHP in closure sealants for bottled water.…" The NRDC claims this to be in violation of the Federal Food, Drug and Cosmetic Act, which requires bottled water rules to be at least as stringent as EPA's tap water rules.[382]

Although detected in both bottled water and tap water, DEHP is only regulated under EPA tap water rules, not FDA's bottled water rules.

Consumers in the U.S. will remain confused, and our youngest will continue to be exposed, until the federal government adopts and implements a national standard that is protective of children's health.

State Efforts

California listed DEHP on Proposition 65[383] in 2003 due to concerns about developmental and male reproductive health effects[384] and recently became the first state in the country to ban the use of certain phthalates, including DEHP, in some children's products because of health concerns. Beginning in 2009, the state will prohibit the manufacture, sale, or distribution of certain toys and child-care articles if they contain DEHP in concentrations greater than 0.1%.[385]

Municipal and Private Sector Efforts

In 2007, San Francisco became the first government in the U.S. to prohibit the sale or distribution of toys, child-care products, or child feeding products made with DEHP exceeding 0.1 percent.[386] Efforts to regulate PVCs by several other municipalities demonstrate concerns about all PVC plastics. Rahway, New Jersey,[387] prohibits the use of PVC (and polystyrene) by retail food vendors located within the city and requires them to use degradable packaging. Glen Cove, New York banned city retail food establishments from selling, giving or providing eating utensils or food containers composed of polystyrene or PVC.[388] In Spain, over 60 municipalities have approved PVC phase-out measures.[389]

Some industries, retailers, and hospitals in the U.S. have made commitments to stop using phthalates in products ranging from teethers to medical tubing. Other companies have made more general commitments to the phase-out of PVC in plastics. As of the completion of this report, the U.S. government has neither regulated nor banned the use of DEHP in products designed for infants and children. Their only protection results from a checkerboard of voluntary actions by some manufacturers, retailers, and hospitals.

Summary

The State of California is the only state in the nation to have adopted a law that limits the concentration of DEHP in products intended for infants and children to 0.1%, yet even it will not begin to take effect until 2009. Many other states have attempted similar reforms, but have been overwhelmed by industry lobbying efforts. The European Union has adopted even more stringent regulations than California, limiting concentrations to 0.05% DEHP. Consumers in the U.S. will remain confused, and our youngest will continue to be exposed, until the federal government adopts and implements a national standard that is protective of children's health.

Table 12. Examples of Voluntary Efforts to Reduce Phthalates (Constantly Changing)

Manufacturers	*Chicco, Little Tikes, Disney, Mattel (Fisher-Price ARCOTOYS, Tyco Preschool), Evenflo, Safety 1st, The First Years, Sassy, Gerber, Shelcore Toys, and Hasbro*	*Stopped using phthalates in teethers and rattles in early 1999.*[390]
Retailers	*Toys-R-Us, Walmart, Sears, Target, K-Mart, ShopKo Stores, Inc., and Warner Brothers Studio Stores*	*Removed phthalate-containing teethers, rattles, pacifiers, and bottle nipples from their product lines.*[391]
Hospitals	*Kaiser Permanente*	*Switch to non-DEHP products for three NICU devices: umbilical vessel catheters, PICC lines, and enteral feeding products.*[392]

Table 13. Examples of Corporate PVC Phase-Out Policies (Constantly Changing)

Athletic Shoemakers	*Adidas, Asics, Nike, Puma*
Automobile Interiors	*Daimler Benz, Ford, General Motors, Honda, Toyota, Volkswagen, Volvo*
Building Materials & Furnishings	*Carnegie Fabrics (wall covering, upholstery), Firestone Building Products (roofing membranes), Herman Miller (office furniture), Milliken (carpet), Shaw (carpet)*
Consumer Products & Packaging	*Aveda, Body Shop, Bristol Myers, Crabtree & Evelyn, Helene Curtis, Hennes & Mauritz (H&M), Honest Teas, IKEA, Johnson & Johnson, Victoria's Secret, Bath & Body Works, Microsoft, SC Johnson, Wal-Mart (private brands)*
Electronics	*Apple, Hewlett Packard, Samsung, Sharp, Sony*
Food Packaging	*Dean Milk Chug Brand, Eagle Brand Cremora Brand, Federated Groups*
Healthcare	*Kaiser Permanente, Catholic Healthcare West (IV bags), Consorta*
Toys	*Big Toys (playgrounds), Brio, Chicco, Early Start, First Years, Lamaze Infant Development, Lego Group, Little Tykes, Mattel*

Source: Center for Health, Environment and Justice. PVC Corporate Policies.

RECOMMENDATIONS

Recommendations for the Federal Government

- ***Product Bans:*** The federal government should ban the use of BPA and DEHP in all plastic products specifically intended for use and contact by children below the age of three.

- ***Labeling:*** The federal government should mandate that all plastic products be labeled to indicate their chemical ingredients and country of origin. This would require a new coding system that would permit the consumer to easily associate ingredients with codes. This coding system should be different from the current numerical recycling code.

- ***Warnings:*** The federal government should warn pregnant women, and women intending to become pregnant, to avoid consuming food or beverages from containers made from BPA or DEHP.

- ***Fragrances:*** The federal government should require labeling to disclose the phthalate ingredients in fragrances, air fresheners, scented candles, dryer sheets, and other consumer products that are commonly found in children's environments.

- ***Reference Dose (RfD) Periodic Review:*** The EPA and FDA should review their acceptable exposure limits (RfDs) for DEHP and BPA ingredients in plastics at least every five years. RfDs for both BPA and DEHP are more than 15 years old, yet relatively recent peer-reviewed scientific reports show that low-dose exposures are becoming increasingly important. When establishing acceptable exposure limits for packaging ingredients in foods, the FDA should continue to employ a 1,000-fold uncertainty factor to judge acceptable human exposure.

- ***Certification:*** The federal government should develop and require a Plastics Certification System modeled after the Food Production Act of 1990 that establishes an accurate labeling system that identifies plastics free from BPA, DEHP, lead and other potentially hazardous compounds.

- ***Biomonitoring:*** The U.S. Centers for Disease Control and Prevention should expand its human tissue-sampling program (NHANES) to test for plastic ingredients in human tissues every two years within individual states.

RECOMMENDATIONS

Recommendations for the State Government

- States should prohibit the sale of baby bottles that contain BPA.
- States should work together to require the federal government to ban the use of BPA and DEHP in all plastic products specifically intended for use by children beneath the age of three. In lieu of federal action, states should pass such legislation.
- States should work together to encourage the federal government to mandate that all plastic products be labeled to indicate their chemical ingredients and country of origin.
- States should pass a "Bottle Bill" that would place a deposit on all plastic bottles and thus improve their recovery rate and reduce their disposal in landfills and incinerator plants.
- States should test underground aquifers that provide drinking water for chemical contaminants from plastics.

Recommendations for Local Governments

- Towns and cities should provide curbside recycling for all plastics.
- Local health departments should encourage schools to reduce their use of plastics.
- Local health Departments should encourage parents to use glass bottles when feeding infants.

RECOMMENDATIONS

Recommendations for Schools, Hospitals, and Institutions

- Schools, hospitals, and other institutions should reduce their use of plastics. Their purchasing departments should try to avoid buying PVC and polycarbonate plastics.
- Hospitals should use medical equipment that is DEHP-free.
- Maternity departments should encourage new parents to use glass bottles when feeding their infants.

Recommendations for Individuals

- Use glass baby bottles when feeding infants.
- Avoid using plastic containers and plastic wraps in microwave ovens.
- Avoid the use of scented candles, air fresheners, dryer sheets, and other heavily scented products, as many contain phthalates.
- Avoid exposure to BPA and DEHP during pregnancy.
- Do not store plastic water bottles under conditions of extreme heat. Heat may cause some plastic ingredients to leach out of the plastic at a faster rate.
- Ask your dentist if BPA is in the dental sealants. If so, ask for BPA-free sealants.
- Teach children not to drink water directly from garden hoses, since many hoses are plastic and contain DEHP.
- Reduce your consumption of plastics. Average consumers purchase more than 200 pounds per year. Purchase materials that are recyclable or biodegradable.

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