Bisphenol A Action Plan
(CASRN 80-05-7)
[CA Index Name: Phenol, 4,4'-(1-methylethylidene)bis-]

I. Overview

Bisphenol A (BPA) is a high production volume (HPV) chemical widely used in manufacturing polycarbonate plastics and epoxy resins used in many industries. Humans appear to be exposed primarily through food packaging uses of products manufactured using BPA, although those products account for less than 5% of the BPA used in this country. Releases of BPA to the environment exceed one million pounds per year.

EPA intends to consider initiating immediate actions addressing BPA in the environment based on concerns for potential effects in aquatic species. At the same time, EPA will continue to work with the Food and Drug Administration (FDA), the Centers for Disease Control and Prevention (CDC), and the National Institute of Environmental Health Sciences (NIEHS) to better determine and evaluate the human health consequences of BPA exposures. Based on the results of those efforts, EPA will consider whether further action is needed to address human health risks resulting from non-food-packaging uses of BPA.

EPA intends to consider initiating rulemaking under section 5(b)(4) of the Toxic Substances Control Act (TSCA) to identify BPA on the Concern List as a substance that may present an unreasonable risk of injury to the environment on the basis of its potential for long-term adverse effects on growth, reproduction and development in aquatic species at concentrations similar to those found in the environment. A notice of proposed rulemaking is intended to publish in autumn, 2010. In late 2010, EPA intends to consider also initiating rulemaking under section 4(a) of TSCA to develop environmental effects data relevant to a further determination that BPA either does or does not present an unreasonable risk of injury to the environment. Beginning in April 2010, EPA intends to initiate collaborative alternatives assessment activities under its Design for the Environment (DfE) program to encourage reductions in BPA manufacturing and use to facilitate reductions in environmental releases and subsequent exposures. One of these activities will relate to thermal and carbonless paper coatings, including those on cash register receipts, which are uses where alternatives to BPA may be readily available. This DfE environmental and health assessment is expected to be completed in the latter half of 2011. Additionally, EPA intends to conduct alternatives analyses for BPA used in foundry castings since foundries are accountable for large releases of BPA as reported under the Toxic Release Inventory (TRI), and for BPA-based materials lining water and waste water pipes since this application may have a potential for human and environmental exposure.

EPA does not intend to initiate regulatory action under TSCA at this time on the basis of human health. EPA remains committed to protecting human health, but notes that most human exposure, including exposure to children, comes through food packaging materials under the jurisdiction of FDA. Food, food additives, drugs, cosmetics, and medical devices, all regulated by FDA, are specifically excluded from the definition of chemical substance under TSCA. FDA, together with CDC and NIEHS, is investing in important new health studies in both animals and humans to better determine and evaluate the potential health consequences of BPA exposures.

EPA will continue to coordinate closely with FDA, CDC, and NIEHS on this activity. To the extent that FDA may identify health concerns from BPA in food contact materials, EPA will work with FDA to identify and assess potential substitutes. Levels of exposure that may be identified by FDA as being of concern to human health, including children's health, will affect the extent to which EPA would take additional action to address potential risks to human health resulting from uses within TSCA jurisdiction.

Because BPA is a reproductive, developmental, and systemic toxicant in animal studies and is weakly estrogenic, there are questions about its potential impact particularly on children's health and the environment. Studies employing standardized toxicity tests used globally for regulatory decision-making indicate that the levels of BPA in humans and the environment are below levels of potential concern for adverse effects. However, results of some recent studies using novel low-dose approaches and examining different endpoints describe subtle effects in laboratory animals at very low concentrations. Some of these novel low-dose studies in animals are potentially of concern for the environment because the concentration levels identified with effects are similar to some current environmental exposure levels. Regulatory authorities around the world that have reviewed these low-dose studies have generally concluded that they are insufficient for use in risk assessment because of a variety of flaws in some of the study designs, scientific uncertainty concerning the relevance to health and ecological hazard of the reported effects, and the inability of other researchers to reproduce the effects in standardized studies. Although there is disagreement about the interpretation of these low-dose studies, they do raise potential concerns for long-term effects at similar concentrations, and some authorities, including Canada and some U.S. state and county governments, have taken interim risk management action to protect certain sensitive populations, such as infants and toddlers. For example, the Canadian government is taking steps to ban baby bottles that are manufactured with BPA.

II. Introduction

As part of EPA's efforts to enhance the existing chemicals program under the Toxic Substances Control Act (TSCA)[1], the Agency identified an initial list of chemicals, including bisphenol A (BPA), for action plan development based on one or more of the following factors: their presence in human blood; persistent, bioaccumulative, and toxic (PBT)[2] characteristics; use in consumer products; production volume; and other similar factors. This Action Plan is based on and encompasses EPA's initial review of readily available use, exposure, and hazard information[3] on BPA. EPA considered which of the various authorities provided under TSCA and other statutes might be appropriate to address potential concerns with BPA in developing the Action Plan. The Action Plan is intended to describe the courses of action the Agency plans to pursue in the near term to address its concerns. The Action Plan does not constitute a final

[1] 15 U.S.C. §2601 *et seq.*
[2] Information on PBT chemicals can be found on the EPA website at http://www.epa.gov/pbt/.
[3] Information sources customarily employed include Inventory Update Reporting (IUR) submissions; Toxic Release Inventory (TRI) reporting; data submitted to the HPV Challenge Program; existing hazard and risk assessments performed by domestic and international authorities including but not limited to U.S. Federal government agencies, the Organization for Economic Cooperation and Development, the Stockholm Convention on Persistent Organic Pollutants, Health and Environment Canada, the European Union; and others. References to specific sources used in this Action Plan are provided in the individual sections discussing use, exposure, and hazard information.

Agency determination or other final Agency action. Regulatory proceedings indicated by the Action Plan will include appropriate opportunities for public and stakeholder input, including through notice and comment rulemaking processes.

III. Scope of Review

In conducting this review, EPA focused on the two areas with the most potential for environmental releases and exposures: manufacturing and processing. EPA also considered potential human exposures to workers during the manufacturing process and to the general population from the presence of BPA in drinking water sources and systems. Because the principal concern is for potential reproductive and developmental effects in early life stages, EPA considered exposures to children from drinking water and from the use of BPA in consumer products. EPA also examined potential ecological impact from the presence of BPA in the environment.

Although most human exposure appears to come from food packaging materials (e.g., Willhite, 2008), less than 5% of the BPA produced is used in food contact applications. EPA's review addresses the roughly 85-90% of BPA manufactured (includes imports) and used domestically that is subject to TSCA, including the manufacture of non-food-additive, non-medical products.

The FDA has jurisdiction over food additives, which include food contact substances such as food packaging. These substances are not regulated under TSCA. This review does not address potential risks from these food additive uses, which appear to comprise the bulk of human exposure. FDA and NIEHS are doing additional studies on the potential risks from these exposures, and the U.S. Department of Health and Human Services (HHS) has provided recommendations for parents and families to take reasonable steps to reduce exposures, especially for young children.[4]

IV. Uses and Substitutes Summary

Bisphenol A (BPA) is a high production volume chemical with a U.S. volume estimated at 2.4 billion pounds in 2007, and an estimated value of almost $2 billion. It is a monomer used in manufacturing most or all polycarbonate plastics, the majority of epoxy resins, and certain other products such as flame retardants (Mannsville, 2008a). Based on the nature of uses within product areas, EPA judges that the majority (possibly 85% to 90%) of BPA manufactured and used in the United States may fall within TSCA jurisdiction, as shown in Table 1, below.

[4] Recommendations released by HHS on January 15, 2010 can be found at http://www.hhs.gov/safety/bpa/.

Table 1. BPA U.S. Consumption and Assumed Share Within TSCA Jurisdiction

Product	Percent of BPA U.S. 2007 Consumption[1]	Assumed TSCA share[2]
Polycarbonate resins	74%	62 - 64 %
Epoxy resins	20%	18 - 20 %
Flame retardants; Polyetherimides/ Polyarylates; Polysulfone resins; Unsaturated polyester resins	6%	5 - 6 %
Total	100%	85 - 90 %

[1] Mannsville, 2008a

[2] EPA judgment, based on percentage of BPA consumption for each product area and use believed to fall within EPA jurisdiction under TSCA. Because the available data lack specific detail, these are "ballpark" estimates only and the range may under- or over-estimate the TSCA share.

BPA-based materials are pervasive in the U.S. economy. Apart from food-related uses, they are used in automotive and other transportation equipment, optical media such as DVDs, electrical/electronics equipment, construction, linings inside drinking water pipes, thermal and carbonless paper coatings, foundry casting, and elsewhere. A handful of companies manufacture most BPA, as well as most BPA-based polycarbonate and epoxy resins, but numerous companies process BPA-based materials into final goods.

BPA-based materials tend to be chosen for their performance characteristics. For example, polycarbonates are lightweight and tough compared to glass. In uses subject to FDA jurisdiction, public concern has led industry to move toward non-BPA-based materials in such products as baby bottles, cups, and spoons and adult drink bottles, and to explore alternatives in food can linings. A vast number of other uses are subject to EPA jurisdiction. EPA is aware that substitutes for some of those uses include other epoxies, a wide variety of plastics (some of them blended with polycarbonate), glass, metals, and wood. However, EPA has not assessed the suitability and availability of substitutes for specific uses in this screening-level review.

V. Hazard Identification Summary

Risk assessments for BPA have been conducted by numerous governmental bodies and review panels. OPPT reviewed the following assessments as well as numerous toxicological studies in assessing the hazard of BPA:

- Government Assessments:
  - US (Federal) – Food and Drug Administration (FDA, 2008), National Toxicology Program/Center for Evaluation of Risks to Human Reproduction (NTP-CERHR, 2008)
  - US (State) - California Proposition 65 Developmental and Reproduction Toxicant Identification Committee (DARTIC) (California, 2009a)
  - International – Japan (AIST, 2007), European Union (EU) (EC, 2003, 2008), European Food Safety Administration (EFSA 2006, 2008a-b) and Canada (Canada, 2008)

- Other Reviews: Harvard Panel (Gray et al., 2004; Goodman et al., 2006); Chapel Hill Group (vom Saal et al., 2007; Crain et al., 2007); NSF International (Willhite et al., 2008)

Human Health Hazard Summary

There is general agreement that BPA is a reproductive and developmental toxicant at doses in animal studies of $\geq$ 50 mg/kg-bw/day (delayed puberty in male and female rats and male mice); $\geq$ 235 mg/kg-bw/day (reduced fetal or birth weight or growth early in life, effects on testis of male rats); and $\geq$ 500 mg/kg-bw/day (possible decreased fertility in mice, altered estrous cycling in female rats, and reduced survival of fetuses). Systemic effects (reduction in body weight, changes in relative organ weights, and increases in liver toxicity) were observed at doses above 5 mg/kg-bw/day (identified as a NOAEL; LOAEL of 50 mg/kg-bw/day). There is controversy about whether effects seen at lower doses in animals (less than 1 mg/kg/day) are meaningful and relevant to humans. These low-dose effects are endocrine-related and include effects on puberty and developmental neurotoxicological effects (brain, behavior) at doses in animal studies as low as 2 μg/kg-bw/day.

All of the government BPA assessments reviewed by EPA discuss these low-dose data and virtually all (FDA, 2008; California, 2009a; AIST, 2007; EC, 2003, 2008; EFSA, 2006, 2008a-b) have considered them insufficient for the purposes of hazard evaluation/risk assessment, the exceptions being Canada (Canada, 2008) and the NTP-CERHR (NTP-CERHR, 2008). Canada acknowledged high uncertainty in the data, but took precautionary action to restrict BPA exposures to infants and young children. The NTP-CERHR observed that the uncertainty led to a conclusion of "some concern"[5] for potential effects. New information on these potential low-dose effects has been published on an almost monthly basis over the past year, with some studies supporting the concept and others finding no effects. For example, a recent study performed by EPA scientists comparing BPA with the oral contraceptive ethinyl estradiol (EE) found that low *in utero* doses of EE affected sexual differentiation in female rats, but low *in utero* doses of BPA produced no such effects (Ryan et al., 2010). The same investigators reported results in male rats in an earlier publication, also noting effects in males exposed *in utero* to EE, but not to BPA (Howdeshell et al., 2008). On the other hand, a different study reported that prenatal BPA exposure (again at low doses) in mice leads to adverse effects on the female reproductive tract later in life (Newbold et al., 2009). In addition, the NIEHS recently awarded $30 million dollars in grants for a two-year program of research on these issues (NIEHS, 2009). FDA announced on January 15, 2010 that it shared the perspective of the NTP-CERHR and would undertake additional research in this area. (FDA, 2010).

Given the laboratory animal data, it is important to note that metabolism studies have been performed in multiple species (rats, mice, monkeys, and humans) and show that humans and rodents metabolize BPA differently. Data in all four species indicate metabolism by

[5] NTP's possible levels of concern, from lowest to highest, are negligible concern, minimal concern, some concern, concern, and serious concern. "Some concern" thus represents the mid-point of a five-level scale of concern used by the NTP. In the case of BPA, the NTP stated it "expressed "some concern" for potential exposures to the fetus, infants and children. There are insufficient data from studies in humans to reach a conclusion on reproductive or developmental hazards presented by current exposures to bisphenol A, but there is limited evidence of developmental changes occurring in some animal studies at doses that are experienced by humans. It is uncertain if similar changes would occur in humans, but the possibility of adverse health effects cannot be dismissed."

conjugation in the liver with glucuronic acid to form the metabolite BPA-glucuronide (BPAG). The relative amount of free-BPA and BPAG circulating in mammals is important because free-BPA ("parent") is known to be weakly estrogenic and BPAG is not. Data indicate that BPAG is more prevalent in primates and free-BPA is more prevalent in rodents. These differences in metabolism suggest that rodents may be more sensitive to effects from BPA than humans.

BPA has been found in human biological samples (serum, breast milk, urine, fetal blood, and umbilical cord blood). The literature reporting these results reflects both a variety of analytical techniques and the BPA forms measured (i.e., total BPA , free-BPA and BPAG). In 2008, the CDC reported that BPA was detected in the urine of 93% of the 2,517 people tested in the 2003-4 National Health and Nutrition Examination Survey (NHANES) (Calafat et al., 2008). Recently, urinary BPA concentrations measured in premature infants from two separate intensive care facilities showed that mean urinary concentrations of total BPA were an order of magnitude higher in the infants than in the general population. Over 90% of the BPA found in the urine in that study was in the form of a glucuronide conjugate (Calafat et al., 2009), providing evidence of the ability for neonates to conjugate BPA into its non-estrogenic form. The study authors noted, however, that this metabolic pathway would not be expected to be functional at adult rates until months after birth. The authors also noted that the infants underwent intensive medical intervention, and that some of the BPA exposure may have been attributable to contact with medical devices.

There was a recent report in which a cross-sectional study design was used to suggest an association between BPA levels in humans and a higher risk of diabetes, heart disease, and elevation of certain liver enzyme activities (Lang et al., 2008). The authors examined the human data from the 2003-4 NHANES population. However, this report prompted an immediate review by the European Food Safety Authority (EFSA) (EFSA, 2008b) in late 2008 which concluded that the study did not provide sufficient proof for the stated associations. EPA notes that the same investigative group recently published an online research article repeating their original findings for heart disease but not diabetes on a second NHANES population from 2005-6 (Melzer et al., 2010).

Table 2 below is a list of each major assessment reviewed and the accompanying intake limits chosen in their respective assessments. Some assessments did not derive an intake limit *per se*, but did make hazard/risk decisions:

- The California Proposition 65 Developmental and Reproductive Toxicant Identification Committee (DARTIC) voted on July 15, 2009 not to list BPA as a developmental toxicant, a female reproductive toxicant, or a male reproductive toxicant (each by separate, unanimous votes of 7-0) (California, 2009a).
- Thirty-eight scientists (known as the "Chapel Hill Group"; vom Saal et al., 2007) concluded that: (1) there is relevance of *in vitro* data to *in vivo* effects; (2) ecological studies are consistent with lab animal studies; (3) the low doses in animal studies are relevant to BPA levels found in humans; and (4) life stage is important in pharmacokinetics, exposure, and effects in animals and humans.
- A Harvard Panel (Gray et al., 2004) concluded that the low dose data are not relevant to humans (and reaffirmed this in an update reported in Goodman et al., 2006).

- A National Toxicology Program (NTP) Center for Evaluation of Risks to Human Reproduction (CERHR) Panel (NTP-CERHR, 2008) concluded that rodent studies suggest that BPA causes "...neural and behavioral alterations related to disruptions in normal sex differences in rats and mice (0.01-0.2 mg/kg/day)."

Table 2: BPA Intake Limits for Human Health Assessments

Authors	Intake Limit (mg/kg/day) [1]	Endpoint (Animal dose in mg/kg/day) And Study
USEPA (Integrated Risk Information System; IRIS (1993))	0.05	Reduced body weight (5) NTP 1982 two year cancer study in both rats and mice (as cited in USEPA 1993)
FDA (2008)	0.005	Systemic – reduced body wt and liver effects (5)
	0.05	Irreversible reproductive effects (50)
	0.5	Reversible reproductive effects (50) (All based on both 2-generation mouse study (Tyl et al., 2008) and 3-generation rat study (Tyl et al., 2002))
EFSA (2006, 2008a-b) and EC (2003, 2008)	0.05	Used 5 (lowest value in cited studies) Tyl et al. (2002, 2008)
Japan (AIST, 2004)	0.05 0.5	Body weight (5) Reproduction (50) Tyl et al., (2002, 2008)
	0.046	Liver effects (23) NTP (1985) – continuous breeding study in mice
Canada (2008)	Did not report any	Body weight reduction (5) and dev/repro effects (50) Tyl et al., (2002, 2008) Cited numerous studies with effect levels ranging from 0.010 to 0.100 mg/kg/day for a variety of effects in mice and/or rats including changes in: maternal behavior, gender-specific behaviors; sexual performance; novelty-seeking/impulse behaviors; avoidance response; maze performance.
Willhite,et al. (2008) (NSF International)	0.016	Used 5 (lowest value in cited studies) Tyl et al., (2002, 2008)

[1] Most risk assessments take an exposure value from an animal study (dose in mg/kg-bw/day) and divide it by several uncertainty factors to arrive at an acceptable dose in humans. This value is what is shown here as an "intake limit" and is what is compared to an expected/estimated exposure value in a risk assessment. The uncertainty factors used by the various assessments are: EPA (IRIS) – 1000; FDA – either 1000 (systemic or irreversible effects) or 100 (reversible effects); EFSA/EU – 100; Japan – either 100 or 500; Canada – did not specify; and NSF Int.'l – 300.

Environmental Hazard Summary

Many studies have been conducted to determine potential effects of BPA exposure on invertebrates, fish, amphibians, reptiles, birds, and wild mammals, and a review is provided by Crain et al. (2007). EPA's screening-level ecological hazard review for this Action Plan focused on effects in freshwater aquatic species to provide a framework for determining whether toxicity may warrant further investigation or risk management action.

In general, studies have shown that BPA can affect growth, reproduction and development in aquatic organisms. Among freshwater organisms, fish appear to be the most sensitive species. Evidence of endocrine-related effects in fish, aquatic invertebrates, amphibians and reptiles has been reported at environmentally relevant exposure levels lower than those required for acute toxicity. There is a widespread variation in reported values for endocrine-related effects, but many fall in the range of 1µg/L to 1 mg/L. (Canada, 2008).

The ecological hazard for BPA has been evaluated in three different risk assessments performed by the European Union (EC), Canada, and Japan as summarized below in Table 3. The different methodologies, endpoints and study results used by each country to derive these values highlight the significant uncertainty in the estimated hazard values. Canada used a novel low-dose study (Lahnsteiner et al., 2005) that reported reduced sperm quality and delayed ovulation in brown trout at a very low dose (1.75 µg/L). Other effects such as the induction of intersex (or testes-ova in males and females), decreased spermatogenesis, induction of vitellogenin, delayed or ceased ovulation, or histological liver changes were also reported in other studies referenced in the EU and Japanese hazard evaluations. However, because there were no standardized test guidelines or risk assessment guidance for evaluating some of these endocrine-related effects[6] at the time of these assessments, the EU and Japan set ecotoxicological hazard values based on conventional effects (mortality and reproductive effects) from standardized studies. Canada concluded in its hazard characterization that "[c]onsidered together, the data provide strong evidence that bisphenol A is capable of eliciting adverse effects: (1) following prolonged exposure at levels below those usually seen to elicit effects in standard toxicity tests (i.e., tests based on recognized methods which evaluate endpoints such as survival, reproduction and growth); (2) following brief low-dose exposure, particularly at sensitive developmental stages, with effects apparent later in the life cycle; (3) on filial generations following parental exposure; and (4) using more than one mode of action." (Canada, 2008).

Table 3: Summary of Bisphenol A Ecological Hazard Values

Country	Predicted No Effect Concentrations[1] (µg/L)	Endpoints
European Union	1.5	The predicted no effect concentration (PNEC) for aquatic organisms (derived by using a statistical analysis of data from available data on freshwater and marine aquatic organisms (in this case, 16 different studies, unpublished and published, from 10 different taxonomic groups) to arrive at a value of 7.5 µg/L, which is divided by an uncertainty factor of 5, resulting in a PNEC of 1.5 µg/L (EC, 2008).

[6] As part of its endocrine disruptor screening program, EPA developed a two-tiered approach to implement statutory testing requirements. The purpose of Tier 1 screening is to identify substances that have the potential to interact with the estrogen, androgen, or thyroid hormone systems. The purpose of Tier 2 testing is to identify and establish a dose-response relationship for any adverse effects that might result from the interactions identified through the Tier 1 assays. EPA has established Tier 1 screening test guidelines. Tier 2 test guidelines will be developed after the completion of ongoing validation studies.

Table 3: Summary of Bisphenol A Ecological Hazard Values		
Country	**Predicted No Effect Concentrations[1] (µg/L)**	**Endpoints**
Canada	0.175	This PNEC was derived by using a lowest observed effect concentration (LOEC) of 1.75 µg/L for reduced semen quality and delayed ovulation in a published brown trout study (Lahnsteiner et al, 2005) and applying an uncertainty factor of 10 (Canada, 2008).
Japan	1.6	The PNEC was derived by using the 16 µg/L no effect concentration (NOEC) for egg hatchability in fathead minnows from the unpublished 3 generation study by Sumpter, et al. (2001) multigeneration fish study and dividing by an uncertainty factor of 10 (AIST, 2007).

[1] In Europe, Canada, and Japan, a predicted no effect concentration (PNEC) is compared directly with an exposure value to evaluate risk. If the ratio of environmental concentration to PNEC is less than one, the risk is generally considered acceptable. As noted in the table, countries use different approaches for generating PNECs, and the precise values may differ even when based on the same studies.

VI. Fate Characterization Summary

BPA is a solid at room temperature. It has a low vapor pressure, moderate water solubility, and low volatility (HSDB, 2009). It has low to moderate mobility in soil. It is expected to biodegrade under environmental conditions, although conflicting results have been obtained using biodegradation screening tests. However, the weight of evidence suggests that it is not expected to be persistent in the environment, and degradation is expected to occur. The rate of atmospheric photooxidation is rapid. Hydrolysis is expected to be negligible under environmental conditions since BPA does not contain functional groups that are susceptible to hydrolysis. Based on the criteria set forth in EPA's policy statement on *Category for Persistent, Bioaccumulative, and Toxic New Chemical Substances* (64 Fed. Reg. 60194, November 4, 1999), BPA is expected to have low persistence (P1) and low bioaccumulation potential (B1). (EC, 2003, 2008)

Any residual, unreacted BPA remaining in polycarbonate products and epoxy resins can leach out into food or the environment. Polycarbonate is generally stable, but some BPA can be released from polycarbonate when it is exposed to strongly basic conditions, UV light, or high heat. Epoxy resins made with BPA are stable; only residual BPA is expected to be released from epoxy resins.

VII. Exposure Characterization Summary

BPA is present in the environment as a result of direct releases from manufacturing or processing facilities (USEPA, 2009a). BPA may also be present in the environment as a result of fugitive emissions during processing and handling, or release of unreacted monomer from products (NTP-CERHR, 2008). According to the Toxics Release Inventory (TRI) Database, total

release of BPA in 2007 was 1,132,062 pounds[7], with releases of 122,965 pounds to air, 6,246 pounds to water (direct), 14,972 pounds released on-site to land, and 684,638 pounds transferred off-site to land (USEPA, 2009a). Sources of human exposure to BPA include dietary intake (e.g., migration from food packaging and from repeat-use polycarbonate containers, such as baby bottles), environmental media (ambient air, indoor air, drinking water, soil and dust), and use of consumer products. Given the tendency of young children to put inappropriate objects into their mouths, there is some minor potential for children to be exposed to BPA through their mouthing or accidental ingestion of consumer products. Dietary intake appears to be the primary source of human exposure. However, food packaging and food containers, such as baby bottles, are the purview of the Food and Drug Administration; therefore, OPPT's human and environmental exposure characterization focuses on exposure from manufacturing; processing; industrial uses; commercial uses; selected consumer uses; ingestion of BPA in drinking water, including drinking water contaminated by wastewater releases to surface water, drinking water drawn from ground water contaminated by leachate from landfills, and drinking water distributed through BPA-based water pipes; and incidental ingestion of BPA from contact with consumer products. OPPT used release data, modeling, and information available in peer-reviewed articles and government publications to obtain information on exposure to BPA.

Very little information is available on exposure from consumer products. While noting that the primary intake for children six months and older came through food, Miyamoto and Kotake (2006) also estimated exposure to BPA for Japanese infants from contact with consumer products such as toys. They estimated the mean intake of BPA from toys for male infants 0 to 5 months of age to be 0.026 μg/kg bw per day and the mean intake for infants 6-11 months to be 0.069 μg/kg per day. Current information posted by the HHS indicates that most plastic toys that children put in their mouths do not contain BPA[4]. No studies were identified measuring potential exposures to adults or children from contact with other consumer products.

Limited information is available for BPA concentrations in U.S. water and other environmental media (Table 4, providing values from all of the studies cited in this discussion). Most environmental monitoring results show that the concentrations of BPA in water bodies are lower than 1 μg/L, mainly due to its partitioning and biodegradability properties (Tsai, 2006). BPA was detected at a median concentration of 0.14 μg/L and a maximum concentration of 12 μg/L in 41.2% of 85 samples collected from U.S. streams in 1999 and 2000 (Kolpin et al., 2002). The maximum concentration of 12 μg/L is an outlier; the BPA concentration in other U.S. waters was much lower (as indicated by the median concentration of 0.14 μg/L). In 2001 and 2002, BPA was not detected (< 0.001 μg/L) in effluent from a wastewater treatment plant in Louisiana, and concentrations were not quantifiable in samples collected from surface waters in Louisiana and in drinking water at various stages of treatment at plants in Louisiana (Boyd et al., 2003).

In 2000, the U.S. Geological Survey collected samples from 47 ambient groundwater sites (not drinking water wells) in 18 states and analyzed them for 65 organic wastewater contaminants (Barnes et al., 2008a-b). BPA was detected in 29.8% of the sampled groundwater sites, with a mean detected concentration of 1.78 μg/L and a range of 1.06 to 2.55 μg/L (Barnes

[7] This total does not include off-site water transfer to POTWs (Publicly Owned Treatment Works) wastewater treatment facilities (32,928 pounds) or transfer to incineration (2,759,705 pounds).

et al., 2008b). BPA was among the top five most frequently detected organic compounds (Barnes, et al., 2008a).

In the summer of 2001, the U.S. Geological Survey collected samples from 74 sources of raw, untreated, drinking water in 25 states and Puerto Rico, in areas that were known or suspected to have at least some human and/or animal wastewater sources in upstream or upgradient areas. These sources comprise 25 groundwater and 49 surface water sources of drinking water serving populations ranging from one family to more than 8 million people. BPA was detected in 9.5% of these samples at a reporting level of 1 µg/L. The maximum concentration measured in these samples was 1.9 µg/L (Barnes, et al., 2008a; Focazio et al., 2008).

Landfill leachates from one U.S. study reported maximum BPA concentrations of 1.7 µg/L in landfill leachate and 1.4 µg/L in the receiving groundwater plume at a landfill on Cape Cod that was known to be leaking (Crain et al., 2007). Data for other landfill sites in the United States were not available, and this single point may not be representative of the country. Landfill leachate from other countries contained more than 500 µg/L of BPA, which is on the order of 500 times the BPA concentrations in water bodies (Tsai, 2006). Studies conducted at Japanese landfills resulted in maximum untreated leachate concentrations of 17,200 µg/L and treated leachate concentrations of 5.1 µg/L (Crain et al., 2007).

Soil concentrations reported by NTP-CERHR (2008) were for soil samples taken from outdoor play areas of homes and daycares; BPA concentrations ranged from 4-14 ppb dry weight, with means of 6-7 ppb dry weight. Klecka et al. (2009) reported a median concentration of 0.6 ppb BPA in North American freshwater sediments, including nondetected samples; BPA concentrations in samples from the United States ranged from 1.4 to 140 ppb dry weight. U.S. marine sediments were reported to have a median of 3.5 ppb of BPA and to range from 1.5 to 5 ppb dry weight (Klecka et al., 2009; Tsai, 2006).

Table 4: U.S. Reported Environmental Concentrations of BPA

Location	Mean or Range of Means (ppb)	Range (ppb)
Surface Water	0.012 to 0.14	0.0009 to 12
Groundwater	0.0041 to 1.9	0.006 to 2.55
Drinking Water	0.005 to <0.1	<0.1 to 0.42
Wastewater	<0.1	0.0036 to 50
Soils	6 to 7	4 to 14
Sediment, Fresh	0.6*†	1.4 to 140†
Sediment, Marine	3.5*	1.5 to 5.0

***** Value is median; mean values not reported

† median value includes nondetected values below the MDL, while the reported range includes only detected values

E-FAST2[8] modeling of BPA releases in the 2007 TRI showed the most conservative estimates of the potential acute dose rate for ingestion of BPA in drinking water by children ages 1-2 ranged from 0.0000531 to 16.5 µg/kg/day, and the most conservative estimates of the surface water concentration ranged from 0.000574 to 232 µg/L. The E-FAST2 model is intended to be used for screening level exposure characterization. E-FAST2 is based on numerous assumptions that are designed to be conservative; for example, E-FAST2 does not account for the half life of a chemical in surface water. The inputs selected for the E-FAST2 modeling of BPA were also selected to be conservative; for example, the bioconcentration factor was selected to be at the high end of the range of values reported for BPA in the literature.

FDA estimated exposure to BPA from food contact uses to be 0.185 µg/kg bw/day for adults. The highest estimate by FDA is 2.42 µg/kg bw/day for female infants, 1-2 months of age (FDA, 2008). Human exposures from food contact uses are consistently estimated by researchers to be higher than exposures from all other sources (e.g., Willhite, 2008).

Workers may be exposed to BPA by inhalation or skin contact during the manufacture of BPA and BPA-containing products. No data were available for dermal exposures, and limited data were available for inhalation exposures. Table 5 summarizes EPA's estimates for occupational exposures that may occur during manufacturing. These estimates were derived using models developed by EPA/OPPT for use in preparing screening-level exposure assessments of chemicals. These models do not take into account the effect of any personal protective equipment that may be used.

Table 5. Inhalation and Dermal Exposure Estimates to BPA During BPA Lifecycle Stages

Lifecycle Stage	Exposure Type	BPA Exposure Dose (mg/day)
Manufacturing	Inhalation	0 – 9.6
	Dermal (liquids and solids)	882 – 3,100 [a]
USE 1: Polycarbonates	Inhalation	0.7 – 2.7 [b]
	Dermal (solids)	0.31 – 3,100 [c]
USE 2: Epoxy Resins	Inhalation	0 – 28
	Dermal (solids)	3,100 [c]
USE 3: Flame Retardants	Inhalation	0 [d]
	Dermal (solids)	3,100 [c]

a – Exposure is in milligrams per event. Events can include sampling of solutions containing BPA or solid BPA and loading/unloading of BPA from containers.
b – Exposure is to polycarbonate dust.
c – Exposure is in milligrams per loading/unloading of BPA from containers, which is the only identified potential exposure during this stage of the lifecycle.
d – Inhalation exposure to BPA during the production of flame retardants is not expected.

VIII. Risk Management Considerations

BPA has been evaluated as a chemical of potential concern by some U.S. agencies and other countries since the early 1980's.

[8] Information on E-FAST2 can be found at http://www.epa.gov/opptintr/exposure/pubs/efastdl.htm.

U.S. EPA and State/Local Regulatory Reviews and Actions

BPA was included in the initial proposal of the Toxics Release Inventory (TRI) list published in 1987 (52 Fed. Reg. 21001, June 4, 1987). That initial list was mandated by the Emergency Planning & Community Right-to-Know Act (EPCRA) section 313(c), 42 U.S.C. § 11023(c), to include the substances specified by the Senate Environment and Public Works Committee Print 99-169, so there was no separate discussion of the justification for placing BPA on the initial TRI list.

In 2009, the EPA Office of Water considered BPA during its development of the third Candidate Contaminant List (CCL3) of substances that might be appropriate candidates for future regulation. Although BPA appeared on the potential CCL (PCCL) list used during the screening process, BPA did not meet the combined screening criteria of potential to occur in public water systems and potential for public health concern because its measured presence in water was well below potential effect levels in guideline studies, and thus did not appear on the final CCL3 list. The notice publishing the final CCL3 list (74 Fed. Reg. 51850, October 8, 2009) does not specifically address BPA, but supporting materials available on the EPA website describe the process and criteria used in the development of the list, including the information on BPA (USEPA, 2009b).

Connecticut, Minnesota, Wisconsin, Washington, Chicago and Suffolk County, N.Y., have banned the sale of polycarbonate baby bottles, food containers and cups that contain BPA. The Connecticut ban also applies to infant formula cans and all reusable food and beverage containers. The Suffolk County ban (County of Suffolk, 2009) went into effect in July 2009. The Minnesota ban (Minnesota, 2009) went into effect on 1/1/2010, and the Chicago ban (Chicago, 2009) on 1/31/2010. The Wisconsin ban (Wisconsin 2010) will go into effect on 6/15/2010, and the Connecticut ban (Connecticut, 2009) will take effect on 10/1/2011. The Washington state ban (Washington, 2010) will take effect on 7/1/2010 concerning food and drink containers for children three years old and under, and will ban BPA in sports water bottles effective 7/1/2012. Similar bills banning BPA in children's food and drink containers passed both houses in Maryland (Maryland, 2010) in February 2010, and if they are signed into law by the governor, would take effect on 1/1/2012. California bill (California, 2009) to ban the use of BPA in baby bottles and cups and infant formula cans failed to pass in September 2009 and was moved to the inactive file. A similar bill failed to pass in Oregon (Oregon, 2010) in February 2010.

International Regulatory Reviews and Actions

Numerous foreign governmental bodies and review panels have conducted human health risk assessments for BPA in the recent past. Japan (AIST, 2007), the European Union (EC, 2008), and the European Food Safety Administration (EFSA, 2008) all concluded within the past three years that the novel studies indicating low dose, endocrine-related effects were insufficient for the purposes of hazard evaluation/risk assessment. Using hazard values derived by dividing the doses used in standardized animal studies by the respective uncertainty factors applied by the different regulatory bodies, these regulatory bodies concluded that expected exposures even from

food contact uses, the largest expected source of exposure, did not present concern for risk to human health.

In contrast, on June 26, 2009, Canada became the first country to take regulatory action against BPA. Canada announced that it was moving forward with proposed regulations to prohibit the advertisement, sale and importation of polycarbonate plastic baby bottles that contain BPA, to reduce newborn and infant exposure to this substance. In announcing this decision, Canada noted "The Government has concluded that exposure levels for newborns and infants up to 18 months of age are below those that could cause health effects. However, due to the uncertainty raised in some studies relating to the potential effects of low levels of BPA, the Government wants to further limit exposure." (Canada, 2009).

Ecological risk for BPA has been evaluated by the European Union (EC, 2008), Canada (Canada, 2008), and Japan (AIST, 2007). Japan concluded that "the current exposure levels of BPA will not pose unacceptable risks to the local populations of aquatic life, particularly fish." The EU concluded that although the predicted exposure concentrations were significantly below its hazard values, there was a need for further information and/or testing on such organisms as freshwater snails. Based on a novel low-dose study (Lahnsteiner et al., 2005), Canada concluded that BPA concentrations in water have the potential to cause adverse effects on populations of pelagic organisms in Canada and concentrations in biota have the potential to cause adverse effects in populations of wildlife in Canada, but that there is a low risk of direct adverse effects to sediment organisms and to avian wildlife species in Canada. In the conclusion of its risk assessment, Canada stated that it is considered appropriate to apply a precautionary approach when characterizing risk, observing "it is concluded that bisphenol A is entering the environment in a quantity or concentration or under conditions that have or may have an immediate or long-term harmful effect on the environment or its biological diversity."

In August 2009, Taiwan designated BPA as a Class 4 toxic substance under the Toxic Chemical Substances Control Act (Taiwan, 2009). A Class 4 toxic substance is defined as a substance for which there is concern of pollution of the environment or the endangerment of human health. Handlers of Class 4 substances are required to keep and report records of the toxicity, production, release, and use of those chemicals, but the chemicals are not subject to other restrictions on handling, transportation, or use (Taiwan, 2007). Class 4 is the lowest designation for a toxic substance in Taiwan.

Ongoing Activities and Issues

The primary issue with regard to risk management approaches to BPA is the uncertainty surrounding the actual determination of risk, particularly from low dose exposures. There is agreement among international regulatory authorities using generally accepted approaches to human health assessment that human exposures to BPA are below levels that would be associated with health effects, leading to determinations that current uses of BPA do not present human health risks warranting further regulatory controls. Similarly, environmental concentrations of BPA, apart from isolated hot spots, are estimated generally to be lower than the levels associated with effects in standardized toxicological studies done according to established guidelines. The complicating factor, however, is the uncertainty surrounding the meaning and

relevance both to humans and the environment of the effects seen in some novel low-dose studies, because some concentrations are similar to levels associated with observed effects reported in those studies.

Reproductive and developmental toxicity are the most sensitive effects observed in the guideline studies, and some novel studies suggest the potential for endocrine-related effects at much lower levels than the effect levels identified in the standardized studies. Accordingly, BPA exposures raise particular questions concerning children's health. Children may be exposed to BPA before birth through their mothers' exposures, and directly through the use of BPA in food packaging materials and child feeding products (such as baby bottles, sippy cups, and spoons) within FDA jurisdiction. FDA is conducting further studies on potential health risks to both children and adults from exposure to BPA in food contact materials (FDA, 2010), and HHS has provided recommendations on how parents and families can reduce their potential exposure to BPA while this investigation continues[4]. Children and adults may also be exposed to a lesser extent through contact with other consumer products and through contact with environmental media (e.g., air and water). Children's exposures are greater than adults' due to increased intakes of food, water, and air per pound of body weight.

On October 28, 2009, the National Institute of Environmental Health Sciences (NIEHS), part of the National Institutes of Health under the U.S. Department of Health and Human Services, announced the award of $14 million in Recovery Act funds to support two-year research grants into the potential effects of BPA on human health (NIEHS, 2009). Including these Recovery Act funds, NIEHS is investing approximately $30 million over two years on BPA research. The new two-year animal and human studies will focus on either developmental exposure or adult chronic exposures to low doses of BPA. Researchers will be looking at a number of health effects including behavior, obesity, diabetes, reproductive disorders, development of prostate, breast and uterine cancer, asthma, cardiovascular diseases and transgenerational or epigenetic effects.

Given that human exposures from TSCA uses of BPA are minor compared with human exposures from uses under FDA jurisdiction, EPA considers that FDA has the lead in making human health judgments on BPA. EPA does not consider that action under TSCA would be warranted at this time on the basis of potential human health concerns from exposures through TSCA uses of BPA.

EPA has jurisdiction over environmental exposures to BPA. Although there is disagreement in interpreting the novel low-dose studies and some of the effects observed in the many aquatic toxicity studies performed thus far with BPA, a comparison of the range of predicted no effect concentration (PNEC) values used in the three international regulatory risk assessments (0.175 to 1.6 µg/L, Table 3) with measured concentrations in U.S. waters and sediments, which included values as high as 12 µg/L (surface water), 2.55 µg/L (ground water), and 140 µg/kg sediment (freshwater sediment) (Table 4), raises concern about possible risk of injury to aquatic organisms. However, limited information is available for BPA concentrations in U.S. water, and most available environmental monitoring results show that the concentrations of BPA in water bodies are lower than 1 µg/L (median concentration of 0.14 µg/L, below any calculated PNEC). These environmental measurements represent only isolated snapshots in time

and do not provide an indication of how many areas may exceed PNEC values or concentrations of concern, how often or how long such concentrations may be exceeded, or the pathways leading to BPA presence in the environment from manufacturing, processing, distribution in commerce, use, or disposal. Additional information would help to resolve these uncertainties.

IX. Next Steps

In conducting this review of bisphenol A, EPA considered a number of potential actions, including regulatory actions under TSCA sections 4, 5 and 6; cooperative activities with other federal agencies; and voluntary actions through such programs as Design for the Environment (DfE).

Based on EPA's screening-level review of hazard and exposure information, including the uncertainties surrounding the low-dose studies, EPA intends to:

1. Consider initiating rulemaking under section 5(b)(4) of the Toxic Substances Control Act (TSCA) to identify BPA on the Concern List as a substance that may present an unreasonable risk of injury to the environment on the basis of its potential for long-term adverse effects on growth, reproduction and development in aquatic species at concentrations similar to those found in the environment. A notice of proposed rulemaking is intended to publish in autumn, 2010.

2. Consider initiating rulemaking under section 4(a) of TSCA to develop data with respect to environmental effects relevant to a further determination that BPA either does or does not present an unreasonable risk of injury to the environment. This may include testing or monitoring data in the vicinity of landfills, manufacturing facilities, or similar locations to determine the potential for BPA to enter the environment, including surface water, ground water, and drinking water, at levels of potential concern particularly for environmental organisms, pregnant women, and children. EPA anticipates publishing an advance notice of proposed rulemaking in late 2010.

3. Initiate collaborative alternatives assessment activities under its Design for the Environment (DfE) program to encourage reductions in BPA manufacturing and use to facilitate reductions in environmental releases and subsequent exposures. One of these activities, intended to be initiated in April 2010, will address thermal and carbonless paper coatings, a use where preferable alternatives to BPA may be readily available. This DfE alternatives assessment is expected to be completed in the latter half of 2011. Paper coatings are not a major use of BPA, but thermal paper has been reported to contain free BPA, which would be expected to be more available for exposure than BPA bound into resin or plastic. Popular uses of this paper include airline tickets, event and cinema tickets, labels, and point of sale applications (receipts). While there is little concern for dermal absorption of BPA, free BPA can readily be transferred to skin and residues on hands can be ingested. Use of BPA in paper also may contribute to the presence of BPA in the stream of recycled paper used in toilet paper, paper tableware, and other products, and may contribute to the presence of BPA in landfills since paper products are a major solid waste stream. Additionally, EPA intends to initiate alternatives analyses for BPA used in foundry castings since foundries are accountable for large releases of BPA as reported under TRI, and for BPA-based materials lining water and waste water pipes since this application may have a potential for human and environmental exposure.

EPA does not intend to initiate regulatory action under TSCA at this time on the basis of human health. EPA remains committed to protecting human health, but notes that most human exposure, including exposure to children, comes through food packaging materials under the jurisdiction of the Food and Drug Administration (FDA). FDA, together with the Centers for Disease Control and Prevention (CDC) and the National Institute of Environmental Health Sciences (NIEHS), is investing in important new health studies in both animals and humans to better determine and evaluate the potential health consequences of BPA exposures. EPA will continue to coordinate closely with FDA, CDC, and NIEHS on this activity. To the extent that FDA may identify health concerns from BPA in food contact materials, EPA will work with FDA to identify and assess potential substitutes. Levels of exposure that may be identified by the ongoing review as being of concern to human health, including children's health, will affect the extent to which EPA would take additional action to address potential risks to human health resulting from uses within TSCA jurisdiction.

As part of the Agency's efforts to address BPA, EPA also intends to evaluate the potential for disproportionate impact on children and other sub-populations through exposure from TSCA uses.

X. References

AIST (Japan's National Institute of Advanced Industrial Science and Technology). 2007. AIST Risk Assessment Document Series 4. Bisphenol A.

Barnes, K.K., Kolpin, D.W., Furlong, E.T., Zaugg, S.D., Meyer, M.T., and Barber, L.B. 2008. A national reconnaissance of pharmaceuticals and other organic wastewater contaminants in the United States—I) Groundwater. Science of the Total Environment, v. 402, no. 2–3, p. 192–200.

Boyd GR, Reemtsma H, Grimm DA, Mitra S. 2003. Pharmaceuticals and personal care products (PPCPs) in surface and treated waters of Louisiana, U.S.A. and Ontario, Canada. Sci Total Environ 311: 135-149.

Calafat, A. M., Weuve, J., Ye, X., Jia, L. T., Hu, H., Ringer, S., Huttner, K. and R. Hauser. 2009. Exposure to Bisphenol A and Other Phenols in Neonatal Intensive Care Unit Premature Infants. *Environ. Health Persp.* 117(4): 639-644.

Calafat, AM, X Ye, Y-L Wong, JA Reidy, and LL Needham. 2008. Exposure of the U.S. Population to Bisphenol A and 4-tertiary-Octylphenol: 2003–2004 *Environ Health Perspect* 116:39–44 (2008).

California. 2009a. California Proposition 65 Committee (see presentations/meeting materials for DARTIC decision meeting on July 15, 2009 http://www.oehha.ca.gov/prop65/public_meetings/dart071509ag.html)

California. 2009b. California Legislature Legislative Index. SB-797 Senate Bill History. Accessed at http://www.leginfo.ca.gov/pub/09-10/bill/sen/sb_0751-0800/sb_797_bill_20090911_history.html. (Text of bill as amended in Assembly July 15, 2009 accessed at http://www.leginfo.ca.gov/pub/09-10/bill/sen/sb_0751-0800/sb_797_bill_20090715_amended_asm_v97.html.)

Canada. 2008. Environment Canada, Health Canada. *Screening Assessment for the Challenge Phenol, 4,4' (1-methylethylidene)bis- (Bisphenol A) CAS 80-05-7*. October 2008 http://www.ec.gc.ca/substances/ese/eng/challenge/batch2/batch2_80-05-7_en.pdf

Canada. 2009. Government of Canada Acts to Protect Newborns and Infants from Bisphenol A in Polycarbonate Plastic Baby Bottles. Accessed at http://hc-sc.gc.ca/ahc-asc/media/nr-cp/_2009/2009_106-eng.php.

Caunter, J.E., Williams, T.D., Hetheridge, M.J., and Evans, M.R. 2000. Bisphenol A: Multigeneration study with the fathead minnow (*Pimephales promelas*). Brixham Environmental Laboratory, AstraZeneca UK Limited (unpublished).

Chicago. 2009. Substitute Ordinance. Municipal Code of Chicago, Section 7-28-637, BPA-Free Kids Ordinance. Accessed at http://egov.cityofchicago.org/webportal/COCWebPortal/COC_EDITORIAL/bpaordinance.pdf.
Connecticut. 2009. Public Act No. 09-103, An Act Concerning Banning Bisphenol-A in Children's Products and Food Products. Accessed at http://www.cga.ct.gov/2009/ACT/PA/2009PA-00103-R00HB-06572-PA.htm.

County of Suffolk. 2009. Resolution No. 154-2009, Adopting Local Law No. 6-2009, A Local Law Establishing the Toxin Free Toddlers and Babies Act. Accessed at http://legis.suffolkcountyny.gov/clerk/legal_notices/2009/ln051409.pdf.

Crain, D.A., Eriksen, M., Iguchi, T., Jobling, S., Laufer, H., LeBlanc, G.A. and L.J. Guillette, Jr. 2007. An ecological assessment of Bisphenol A: evidence from comparative biology. Reprod. Toxicology (24): 225-239.

EPP. 2008. EPP Rapid Research. "Rehabilitating Home Water Pipes with Epoxy Coatings." December 2008. Accessed October, 2009, at http://www.pprc.org/research/epp/Epoxy-Lined_Pipes.pdf.

EU. 2003. *European Union Risk Assessment Report. Bisphenol A, CAS No: 80-05-7*. Institute for Health and Consumer Protection, European Chemicals Bureau, European Commission Joint Research Centre, 3rd Priority List, Luxembourg: Office for Official Publications of the European Communities.

EU. 2008. *European Union Updated Risk Assessment Report. Bisphenol A, CAS No: 80-05-7*. Institute for Health and Consumer Protection, European Chemicals Bureau, European Commission Joint Research Centre, 3rd Priority List, Luxembourg: Office for Official Publications of the European Communities.

European Food and Safety Authority (EFSA). 2006. Scientific Panel on Food Additives, Flavourings, Processing Aids and Materials in Contact with Food . Summary Opinion of the Scientific Panel on food additives, flavourings, processing aids and materials in contact with food (AFC) related to 2,2-BIS(4-HYDROXYPHENYL) PROPANE. Question number EFSA-Q-2005-100 November.

European Food and Safety Authority (EFSA). 2008a. Scientific Opinion of the Panel on Food additives, Flavourings, Processing aids and Materials in Contact with Food (AFC) on a request from the Commission on the toxicokinetics of Bisphenol A. *The EFSA Journal* (2008) 759, 1-10.

European Food and Safety Authority (EFSA). 2008b. Statement of EFSA prepared by the Unit on food contact materials, enzymes, flavourings and processing aids (CEF) and the Unit on Assessment Methodology (AMU) on a study associating bisphenol A with medical disorders. *The EFSA Journal* (2008) 838, 1-3.

Focazio, M.J., Kolpin, D.W., Barnes, K.K., Furlong, E.T., Meyer, M.T., Zaugg, S.D., Barber, L.B., and Thurman, E.M. 2008. A national reconnaissance for pharmaceuticals and other organic wastewater contaminants in the United States—II) Untreated drinking water sources. Science of the Total Environment, v. 402, no. 2–3, p. 201–216.

Gray, G. M., Joshua T. Cohen, Gerald Cunha, Claude Hughes, Ernest E.McConnell, Lorenz Rhomberg, I. Glenn Sipes, and Donald Mattison. 2004. Weight of the Evidence Evaluation of Low-Dose Reproductive and Developmental Effects of Bisphenol A. *Human and Ecological Risk Assessment*, 10: 875–921.

Goodman JE, McConnell EE, Sipes IG, Witorsch RJ, Slayton TM, Yu CJ, Lewis AS, Rhomberg LR. 2006. An updated weight of the evidence evaluation of reproductive and developmental effects of low doses of bisphenol A. *Crit Rev Toxicol* 36:387–457.

Howdeshell KL, Furr J, Lambright CR, Wilson VS, Ryan BC and Gray LE. 2008. Gestational and lactational exposure to ethinyl estradiol, but not bisphenol A, decreases androgen-dependent reproductive organ weights and epididymal sperm abundance in the male Long Evans hooded rat. *Tox. Sci*. (102)(2): 371-382.

HSDB. 2009. Hazardous Substance Databank. National Library of Medicine. Available from: http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB as of June 22, 2009.

ICIS. 2009. ISIS Chemical business, "Chemical Profile: Epoxy Resins," July 13, 2009, page 35.

Kirk-Othmer. 1996. Kirk-Othmer Encyclopedia of Chemical Technology, 4th Edition, "Polycarbonates," 1996 (pages 584-608).

Klecka GM, Staples CA, Clark KE, van der Hoeven N, Thomas DE, Hentges SG. 2009. Exposure Analysis of Bisphenol A in Surface Water Systems in North America and Europe. Environ Sci Technol 43(16):6145-6150.

Kolpin DW, Furlong ET, Meyer MT, Thurman EM, Zaugg SD, Barber LB, Buxton HT. 2002. Pharmaceuticals, hormones, and other organic wastewater contaminants in U.S. streams, 1999–2000: a national survey. Environ Sci Technol 36:1202–1211.

Lahnsteiner, F., B. Berger, M. Kletzl and T. Weismann. 2005. Effect of Bisphenol A on Maturation and Quality of Semen and Eggs in the Brown Trout, *Salmo trutta f. fario*. Aquatic Tox. 75: 213-224.

Lang, I., Galloway, T., Scarlet, A., Henley, W., Depledge, M., Wallace R. and Melzer, D. 2008. Association of Urinary Bisphenol A Concentration With Medical Disorders and Laboratory Abnormalities in Adults. Journal of the American Medical Association. 2008; 300(11):1303-1310

Mannsville. 2006. Chemical Products Synopsis: Epoxy Resins, Mannsville Chemical Products Corp., August 2006.

Mannsville. 2008a. Chemical Products Synopsis: Bisphenol A, Mannsville Chemical Products Corp., January 2008.

Mannsville. 2008b. Chemical Products Synopsis: Polycarbonate Resins, Mannsville Chemical Products Corp., January 2008.

Maryland, 2010. History of Maryland Senate Bill 213, cross-filed with House Bill 33, entitled Child Care Articles Containing Bisphenol A – Prohibition. Accessed at http://mlis.state.md.us/2010rs/billfile/sb0213.htm.

Melzer, D., Rice, N.E., Lewis, C. Henley, W.E., and Galloway, T.S. (2010). Association of Urinary Bisphenol A Concentration with Heart Disease: Evidence from NHANES 2003/06, PLoS One. Accessed at http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0008673. January 2010.

Minnesota. 2009. Minnesota Session Laws, 2009, Regular Session, Chapter 40--S.F.No. 247, An act relating to public health; protecting the health of children; prohibiting bisphenol-A in products for young children. Office of the Revisor of Statutes. Accessed at https://www.revisor.mn.gov/laws/?id=40&doctype=chapter&year=2009&type=0.

Miyamoto, K. and Kotake, M. 2006. Estimation of Daily Bisphenol A Intake of Japanese Individuals with Emphasis on Uncertainty and Variability, *Environmental Sciences*, 13, 1 (2006) 015-029.

Newbold, R, Jefferson W.N. and Padilla-Banks, E.. 2009. Prenatal Exposure to Bisphenol A at Environmentally Relevant Doses Adversely Affects the Murine Female Reproductive Tract Later in Life *Env Health Persp* (117)(6) 879-885.

NIEHS. 2009. NIEHS Awards Recovery Act Funds to Address Bisphenol A Research Gaps. Accessed at http://www.niehs.nih.gov/news/releases/2009/bisphenol-research.cfm.

NTP/CERHR. 2008. NTP-CERHR Monograph on the Potential Human Reproductive and Developmental Effects of Bisphenol A. US Department of Health and Human Services. National Toxicology Program. Center for the Evaluation of Risks to Human Reproduction. http://cerhr.niehs.nih.gov/chemicals/bisphenol/bisphenol.pdf.

Oregon. 2010. Oregon Senate Bill 1032 Relating to Containers Made with BPA, Measure Activity. Accessed at http://gov.oregonlive.com/bill/sb1032/.

PlasticsEurope. 2009. American Chemistry Council, PlasticsEurope, and Japan Chemical Industry Assoc. Available at http://www.bisphenol-a.org.

Ryan, B.C., Hotchkiss, A.K., Crofton, K.M., and Gray Jr., L.E. 2010. In Utero and Lactational Exposure to Bisphenol A, in contrast to Ethinyl Estradiol, Does not Alter Sexually Dimorphic Behavior, Puberty, Fertility and Anatomy of Female LE Rats. *Toxicological Sciences* 114(1), 133-148 (2010).

Sohoni, P., C.R. Tyler, K. Hurd, J. Caunter, M. Hetheridge, T. Williams, C. Woods, M. Evans, R. Toy, M. Gargas, and J.P. Sumpter. 2001. Reproductive Effects of Long-Term Exposure to Bisphenol A in the Fathead Minnow (*Pimephales promelas*). Env. Sci. Technol. 35: 2917-2925.

Sumpter, J. P., Tyler, C.R. and Sherazi A. 2001. Bisphenol-A: Multigeneration study with the fathead minnow (*Pimephales promelas*). Brunel University (unpublished).

Taiwan. 2007. Toxic Chemical Substances Control Act. Accessed at http://law.epa.gov.tw/en/laws/788537580.html.

Taiwan. 2009. Bisphenol A Added to List of Toxic Chemicals; New Restrictions on Mercury, Asbestos, and Dioxane. Environmental Protection Administration. Accessed at http://www.epa.gov.tw/en/NewsContent.aspx?NewsID=1417&path=426.

Tsai, W. 2006. Human Health Risk on Environmental Exposure to Bisphenol-A: A Review. Journal of Environmental Science and Health Part C, 24:225-255.

Tyl, R.W., Myers, C.B., Marr, M.C., Sloan, C.S., Castillo, N.P., Veselica, M.M., Seely, J.C., Dimond, S.S., Van Miller, J.P., Shiotsuka, R.N., Beyer, D., Hentges, S.G., Waechter, J.M.,Jr.. 2008. Two-generation reproductive toxicity study of dietary bisphenol A (BPA) in CD-1 (Swiss) mice. *Toxicological Sciences* 104(2): 362-384.

USEPA. 1993. Integrated Risk Information System (IRIS) (1993). Accessed at http://www.epa.gov/ncea/iris/subst/0356.htm.

USEPA. 2009a. Toxic Release Inventory. 2007 Public Data Release, Released March 14, 2009. http://www.epa.gov/tri/tridata/index.htm#pdr

USEPA. 2009b. Drinking Water Contaminant Candidate List and Regulatory Determinations, Contaminant Candidate List 3, Accessed at http://www.epa.gov/ogwdw000/ccl/ccl3.html.

US FDA. 2008. U. S. Food and Drug Administration http://www.fda.gov/Food/FoodIngredientsPackaging/ucm166145.htm.

US FDA. 2010. U.S. Food and Drug Administration. Update on Bisphenol A for Use in Food Contact Applications: January 2010. Accessed at http://www.fda.gov/NewsEvents/PublicHealthFocus/ucm197739.htm.

USGS. 2008. US Geological Survey. Water-Quality Data for Pharmaceuticals and Other Organic Wastewater Contaminants in Ground Water and in Untreated Drinking Water Sources in the United States, 2000-01. http://pubs.usgs.gov/of/2008/1293/.

vom Saal FS, Akingbemi BT, Belcher SM, Birnbaum LS, Crain DA, Eriksen M, et al. 2007. Chapel Hill bisphenol A expert panel consensus statement: integration of mechanisms, effects in animals and potential to impact human health at current levels of exposure. *Reprod Toxicol* 24(2):131–138.

Waechter JM. 2002. Three-generation reproductive toxicity study of dietary bisphenol A in CD Sprague-Dawley rats. *Toxicological Sciences* 68(1): 121-146.

Washington. 2010. History of Bill SB 6248 - 2009-10, Concerning the use of bisphenol A. Accessed at http://apps.leg.wa.gov/billinfo/summary.aspx?bill=6248.

Willhite, C.C., G.L. Ball and C.J. McLellan. 2008. Derivation of a bisphenol A oral reference dose (RfD) and drinking-water equivalent concentration. *J. Toxicol. Environ. Health B Crit. Rev.* 11: 69-146.

Wisconsin. 2010. History of Senate Bill 271. Accessed at http://www.legis.state.wi.us/2009/data/SB271hst.html. Text of Act 145 accessed at http://www.legis.state.wi.us/2009/data/acts/09Act145.pdf.