Bisphenol A (BPA) in Plastics and Possible Human Health Effects

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Summary

Bisphenol A (BPA) is used to produce certain types of plastic, in thousands of formulations for myriad products. Products made with these plastics may expose people to small amounts of BPA. The most significant source of public exposure is thought to be through food, although other ubiquitous products such as thermal paper coatings, and for some individuals medical devices, such as feeding and breathing tubes, also may contribute significantly to human exposure. Some studies have found that fetal and infant development may be harmed by very small amounts of BPA, but scientists disagree about the amount of BPA that is likely to harm human health.

In the United States and elsewhere, scientific disagreement about the possibility of human health effects that may result from BPA exposure has led to conflicting regulatory decisions by various advisory bodies and regulatory agencies. Controversy has centered on the safety of food containers, especially those intended for use by infants and children. A conclusion by the U.S. Food and Drug Administration (FDA) that BPA use is safe conflicted with earlier findings by a panel of scientific advisers, but other scientists who reviewed that panel's conclusions disagreed. These events prompted some to question FDA's process for the assessment of such health risks, and others to question the agency's fundamental ability to conduct such assessments competently. More recently, FDA expressed concern about possible health effects from BPA exposure and announced that it was conducting new studies on the matter, pending possible changes in its regulatory approach.

The U.S. Environmental Protection Agency (EPA) is responsible for protecting public health and the environment from unreasonable risks associated with production, interstate commerce, and use of industrial chemicals, including BPA, when they are not specifically regulated under other federal laws. In March 2010, EPA released a "chemical action plan" for BPA that proposed to list BPA as a chemical of concern that may present an unreasonable risk to certain aquatic species at concentrations similar to those found in the environment; to consider rulemaking to gather additional data relevant to environmental effects; and to initiate collaborative alternatives assessment activities under its Design for the Environment (DfE) program to encourage reductions in BPA releases and exposures. EPA is evaluating alternatives to BPA for use in paper for thermal printing.

Some food companies, bottle manufacturers, and paper receipt producers have voluntarily changed to BPA-free products. It is reported that some companies are exploring alternatives to BPA-containing food cans. However, others have said that for some types of canned foods, alternatives that preserve the safety and quality of the food currently may not be available.

In the 112th Congress, companion bills, H.R. 432 and S. 136, would ban the use of BPA in food containers. In the 111th Congress, a number of bills (S. 593/H.R. 1523, S. 753/H.R. 4456, H.R. 4341, H.R. 5820) were introduced that would have curtailed uses of BPA in certain products, required labeling of products containing BPA, or required EPA or FDA to reassess risks. None of these bills was enacted.

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Introduction

Bisphenol A (BPA)[1] is a synthetic chemical compound produced in the United States in large quantities, approximately 2.3 billion pounds annually.[2] BPA is not found in nature. Two notable uses are in manufacturing certain forms of plastic: relatively hard, clear polycarbonate (PC), and epoxy resins that are used to line food cans.[3] Under certain conditions, BPA may *migrate* or *leach* (i.e., be released) from PC containers and plastic-lined cans into the food or liquids they contain.

The widespread use of BPA and the potential for human exposure, together with accumulating scientific evidence about possible BPA toxicity, led the National Toxicology Program (NTP) at the National Institutes of Health (NIH) to select BPA for a comprehensive review. NTP released a draft "brief" on BPA in April 2008,[4] and a final monograph in September 2008.[5] NTP's conclusions prompted some to call for federal restrictions on certain BPA uses, and sparked congressional and media interest in the past and current positions of the Food and Drug Administration (FDA). FDA regulates BPA and other chemicals used in food containers, and until recently maintained that current uses of BPA are safe. In August 2008, FDA reiterated this finding in a published risk assessment.[6] The finding prompted criticism from an agency advisory committee and others. FDA is now reviewing its BPA risk assessment for food exposures, and considering exposures from other products it regulates (such as drugs and medical devices), in response to the committee's critique. In January 2010, FDA announced that it is evaluating recent scientific evidence and conducting additional studies.[7] FDA has announced no further subsequent action.

Health Effects

Exposure to large amounts of BPA is acutely toxic to humans and animals, but typical levels of BPA exposure from plastics are low. The possibility of human health effects from exposure to low doses of BPA is controversial,[8] although animal evidence of possible harmful effects has been mounting for about 10 years.

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[1] Bisphenol A also is commonly known as carboxylic acid. It is the single molecule that is chained together (polymerized) to form polycarbonate.

[2] U.S. Department of Health and Human Services (HHS), National Toxicology Program (NTP), Center for the Evaluation of Risks to Human Reproduction (CERHR), "NTP-CERHR Monograph on the Potential Human Reproductive and Developmental Effects of Bisphenol A," NIH Publication No. 08–5994, September 2008, p. 1, http://cerhr.niehs.nih.gov/evals/bisphenol/bisphenol.html, hereafter NTP Monograph on Bisphenol A.

[3] Another BPA use of potential concern is in paper coatings. According to the Environmental Protection Agency (EPA), "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." (EPA, "Bisphenol A Action Plan," March 29, 2010, p. 17, http://www.epa.gov/opptintr/existingchemicals/pubs/actionplans/bpa_action_plan.pdf.)

[4] HHS, NTP, "Draft NTP Brief on Bisphenol A," April 14, 2008.

[5] NTP Monograph.

[6] FDA, "Draft Assessment of Bisphenol A for Use in Food Contact Applications," August 14, 2008, http://www.fda.gov/ohrms/dockets/ac/08/briefing/2008-0038b1_01_00_index.htm.

[7] FDA, "Bisphenol A (BPA), Update on Bisphenol A (BPA) for Use in Food: January 2010," http://www.fda.gov/NewsEvents/PublicHealthFocus/ucm064437.htm.

[8] See, for example, Stephen Musson, "Bisphenol A," *National Geographic Geopedia*, September 18, 2008, (continued...)

It is clear that BPA is capable of interfering with the action of estrogen, an important regulator of reproduction and development. (Interference with hormonal action is often referred to as *endocrine disruption*.) Therefore, many recent studies have focused on the potential effects of low levels of BPA exposure on fetal or newborn rats or mice. Some of the developmental effects seen among rodents exposed to low doses of BPA include changes in brains and behaviors; precancerous lesions in the prostate and mammary glands; altered prostate and urinary tract development; and early onset of puberty.[9]

These low-dose experiments are difficult to conduct, in part because BPA is ubiquitous in the environment. Thus, different studies have produced different results. Scientists employed by BPA manufacturers and some independent contractors argue that the hundreds of studies conducted so far have produced inconsistent results and are insufficient justification for more stringent BPA regulation.[10] Other scientists maintain that well-designed and executed studies of sufficient statistical power on sensitive strains of laboratory rodents have clearly demonstrated the toxicity of low doses of BPA in mammals, and justify actions to reduce exposure for potentially vulnerable human populations.[11] In 2001, an expert workshop to evaluate the data on low-dose effects of endocrine disruptors concluded that biological effects have been shown to occur in rodents following exposure to some estrogenic compounds at very low levels.[12] The question remains whether those effects would adversely affect rodent health and are a useful predictor of human health impacts.[13]

Some researchers have proposed that low levels of BPA exposure may interfere with functions other than reproduction and development, potentially causing additional types of health effects. The body of research in this area is less extensive than that into BPA's potential effects on reproductive hormones, but this appears to be an active field of investigation. Recent studies using animal models, human cells, or epidemiological data on humans have demonstrated effects on the regulation of insulin or other metabolic hormones, leading authors to posit that environmental BPA exposure may increase susceptibility to obesity and diabetes.[14] Some investigators have called for long-term studies to determine whether high BPA levels are associated with specific health effects later on. Such long-term, prospective studies would provide

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http://ngm.nationalgeographic.com/geopedia/Bisphenol_A.

[9] NTP Monograph on Bisphenol A, pp. 7-8.

[10] U.S, House of Representatives, Committee on Energy and Commerce, Subcommittee on Commerce, Trade, and Consumer Protection, Hearing on the Safety of Phthalates and Bisphenol-A in Everyday Consumer Products, June 10, 2008, testimony of Marian K. Stanley, pp. 81-114, especially page 103.

[11] Martin Scholze and Andreas Kortenkamp, "Statistical Power Considerations Show the Endocrine Disruptor Low-Dose Issue in a New Light," *Environmental Health Perspectives*, 2007, v. 115, Supp. 1, pp. 84-90.

[12] *National Toxicology Program's Report of the Endocrine Disruptors Low Dose Peer Review*, 2001, National Toxicology Program, U.S. Department of Health and Human Services, http://ntp.niehs.nih.gov/ntp/htdocs/liason/LowDosePeerFinalRpt.pdf.

[13] That is, the effects observed are not known to be adverse. For example, at certain very low doses fetal exposure to BPA produces enlarged prostates in male rats, but it is not clear that an enlarged prostate is an adverse health impact.

[14] See, for example, Paloma Alonso-Magdalena et al., "Bisphenol A Exposure During Pregnancy Disrupts Glucose Homeostasis in Mothers and Adult Male Offspring," *Environmental Health Perspectives*, vol. 118, no. 9 (September 2010), pp. 1243-1250; Eric R. Hugo et al., "Bisphenol A at Environmentally Relevant Doses Inhibits Adiponectin Release from Human Adipose Tissue Explants and Adipocytes," *Environmental Health Perspectives*, vol. 116, no. 12 (December 2008), pp. 1642-1647 (both at http://ehp03.niehs.nih.gov); and Iain A. Lang et al., "Association of Urinary Bisphenol A Concentration with Medical Disorders and Laboratory Abnormalities in Adults," *JAMA*, vol. 300, no. 11 (September 17, 2008), pp. 1303-1310.

stronger evidence, one way or the other, regarding a possible causal role of BPA on adverse health effects.

The so-called "low-dose hypothesis" is controversial because it appears to challenge a tenet of toxicology, that "the dose makes the poison." That is, at some low level of exposure, any potentially toxic chemical is innocuous, and conversely, above some other level of exposure, any substance may be toxic. The low-dose hypothesis does not necessarily contradict the traditional tenet, but it states that some chemicals that are known to be toxic at high levels of exposure, and that may have no observable health effect (using traditional toxicological methods), may nonetheless harm health at a still lower level of exposure. In other words, endocrinologists argue, the relationship between the dose and effect is not always in the direction that more exposure is worse.[15]

Moreover, health effects from a low exposure may differ in type from effects observed at a higher dose. For example, some scientists who specialize in the study of hormones say that endocrine-disrupting chemicals like BPA have been shown to cause adverse developmental effects at a level of exposure lower than that at which no adverse effects have been identified using traditional high-dose test methods, particularly when the lower-level exposure occurred at a critical point during fetal development.[16] Such effects are plausible, these scientists argue, because hormones work by regulating or modulating (i.e., by stimulating or dampening) responses of organs so as to maintain optimal physiological conditions that will vary depending on the tissue, dose, and timing in development.[17] Normal responses of endocrine systems sometimes are regulated by very slight changes in hormone levels,[18] and changes in these hormonal systems could be caused by low-dose exposure to external agents such as BPA.[19]

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[15] Note that this hypothesis is not consistent with the hypothesis that a threshold of exposure to an endocrine disruptor exists below which there is no adverse health effect. This is because naturally occurring hormones already are above threshold levels, and the processes that they regulate are ongoing. According to the low-dose hypothesis, a physical response may be stimulated at virtually any dose, while a higher dose might inhibit the same response, or different responses might be triggered or suppressed, depending on the dose, timing, and tissue involved. Proponents of the low-dose hypothesis argue that endocrine systems are complex, involving multiple tissues and cell types that maintain system stability (homeostasis) by responding to small changes in hormone secretions as well as to external chemicals to which they are exposed. They suggest that even low-level exposures to certain chemicals in the environment might upset that stability and lead to adverse health effects. See, for example, the Prague Declaration on Endocrine Disruption at http://ehp.niehs.nih.gov/docs/2007/10517/suppl.pdf, a consensus statement agreed to by many scientists actively engaged in research in the field of endocrine disruption (Andreas Kortenkamp, 2007, "Introduction: Endocrine Disruptors—Exposure Assessment, Novel End Points, and Low-Dose and Mixture Effects," *Environmental Health Perspectives*, v. 115, p. 7, http://ehp03.niehs.nih.gov/article/fetchArticle.action?articleURI=info%3Adoi%2F10.1289%2Fehp.10517). Those who are skeptical regarding the low-dose hypothesis find the scientific evidence to be inconsistent and unconvincing. See, for example, Calvin C. Willhite, Gwendolyn L. Ball, and Clifton J. McLellan, "Derivation of a Bisphenol A Oral Reference Dose (RfD) and Drinking-Water Equivalent Concentration," *Journal of Toxicology and Environmental Health, Part B*, (2008) v. 11, pp. 69-146.

[16] Frederick S. vom Saal, B.T. AkFingbemi, S.M. Belcher et al. "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," *Reproductive Toxicology:* v. 24, pp. 131-138. Also, Frederick S. vom Saal, personal communication, March 29, 2011.

[17] Henry M. Kronenberg, Shlomo Melmed, Kenneth S. Polonsky, and P. Reed Larsen, *Williams Textbook of Endocrinology*, 11th ed., 2008, pp. 5-6.

[18] Ibid., pp. 6, 8-9.

[19] Frederick S. vom Saal, personal communication, April 6, 2011.

Human Exposure

Bisphenol A exposure in the general population comes primarily from consumption of food and beverages.[20] The latest national survey by the Centers for Disease Control and Prevention (CDC) found BPA in the urine of more than 90% of the people studied, which included children six years of age and older and adults.[21] Among these people, the highest average concentrations were found in children.[22] The NTP monograph estimates that the highest daily intakes of BPA occur in infants and children.[23] BPA has been found in human breast milk; however, the NTP monograph estimates that infants who are formula-fed have higher daily BPA intake levels than those who are breast-fed,[24] because there is more BPA in infant formula than in breast milk, and because BPA may increase when PC baby bottles are used for formula feeding, especially if the bottles are heated. These BPA exposure levels in humans "are similar to levels of [BPA] associated with several 'low' dose laboratory animal findings of effects on the brain and behavior, prostate and mammary gland development, and early onset of puberty in females," according to the NTP monograph.[25]

More recently, some scientists have concluded that sources of exposure other than food may be important.[26] For example, there have been calls for assessments of human exposure from other FDA-regulated products such as drugs and medical devices.[27] Some are especially concerned about medical devices, such as feeding and breathing tubes, that could leach the chemical into tissues, and, in particular, the possible health effects of such exposures in premature or critically ill infants, in whom such products may be used for long periods of time.[28] Other potential sources of exposure are regulated by the Environmental Protection Agency (EPA). For example, in July 2010, several studies indicated that skin contact with BPA in thermal paper coatings (for example, the paper used for cash register receipts) may contribute significantly to human exposure.[29]

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[20] Ruthann A. Rudel, Janet M. Gray, Connie L. Engel et al., 2011, "Food Packaging and Bisphenol A and Bis(2-Ethylhexyl) Phthalate Exposure: Findings from a Dietary Intervention," *Environmental Health Perspectives*: March 30, 2011, http://ehp03.niehs.nih.gov/article/info%3Adoi%2F10.1289%2Fehp.1003170.

[21] Centers for Disease Control and Prevention (CDC), National Center for Environmental Health, *Fourth National Report on Human Exposure to Environmental Chemicals*, Executive Summary, Atlanta, GA, 2009, p. 3, http://www.cdc.gov/exposurereport/.

[22] Ibid.

[23] Certain occupational groups are estimated to have the highest human exposure levels. NTP Monograph on Bisphenol A, p. 2. A recent study of Chinese factory workers with high levels of BPA exposure found a correlation between urinary BPA levels and sperm abnormalities. De-Kun Li et al., "Urine Bisphenol-A (BPA) Level in Relation to Semen Quality," *Fertility and Sterility*, published online October 29, 2010, http://www.fertstert.org/home.

[24] NTP Monograph on Bisphenol A, p. 3.

[25] Ibid., pp. 7-8.

[26] Kellyn S. Betts, "Body of Proof: Biomonitoring Data Reveal Widespread Bisphenol A Exposures," *Environmental Health Perspectives*, v. 118, no. 8 (August 2010), pp. a353-a353; and Tanya Tillett, "Bisphenol A, Chapter 2: New Data Shed Light on Exposure, Potential Bioaccumulation," *Environmental Health Perspectives*, v. 117, no. 5 (May 2009), pp. A210-A210, both at http://ehp03.niehs.nih.gov.

[27] See, for example, Representative Rosa L. DeLauro, "DeLauro Presses for Expanded FDA Inquiry of BPA Health Risks," press release, June 16, 2008, http://www.house.gov/delauro/news.html.

[28] For example, one study found urine BPA levels in infants receiving neonatal intensive care that substantially exceeded levels found in young children in the CDC national exposure survey (footnote 21). Antonia M. Calafat et al., "Exposure to Bisphenol A and Other Phenols in Neonatal Intensive Care Unit Premature Infants," *Environmental Health Perspectives*, vol. 117, no. 4 (April 2009), pp. 639-644.

[29] Janet Raloff, "Cashiers May Face Special Risks from BPA," *Science News*, August 2, 2010, (continued...)

Current Federal BPA Regulation

Depending on its use, BPA is potentially regulated by various regulatory agencies, including the Consumer Product Safety Commission (CPSC), the Occupational Safety and Health Administration (OSHA), EPA, and FDA.[30]

EPA is responsible for protecting public health and the environment from unreasonable risks associated with production, interstate commerce, and use of industrial chemicals, including BPA, when they are not specifically regulated under other federal laws, such as those covering alcohol, food, drugs, or consumer products. EPA has made BPA the focus of a "chemical action plan" to gather information and possibly to regulate the chemical. The plan was released in March 2010.[31] It proposes to include BPA on a list of chemicals of concern, a list created under the authority of the Toxic Substances Control Act (TSCA), section 5(b)(4), "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." [32] A chemical of concern is "a substance that may present an unreasonable risk of injury to the environment." Listed chemicals may be subject to additional rulemaking.[33]

In addition, EPA sent an advance notice of proposed rulemaking to the White House Office of Management and Budget in December 2010.[34] The notice requests comment on whether it should initiate rulemaking under section 4(a) of TSCA to develop data with respect to effects on the environment. Specifically, EPA intends

> to request comment on requiring toxicity testing to determine the potential for BPA to cause endocrine-related adverse effects in environmental organisms at low concentrations. The ANPRM will also seek comment on requiring sampling and monitoring of surface water, ground water, drinking water, soil, sediment, sludge, and landfill leachate in the vicinity of expected BPA releases to determine whether potentially sensitive organisms may currently be exposed to concentrations of BPA in the environment that are at or above levels of concern for adverse effects, including endocrine-related effects.

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http://www.sciencenews.org/index/generic/activity/view/id/61740/title/Cashiers_may_face_special_risks_from_BPA.

[30] Neither the Consumer Product Safety Commission (CPSC) nor the Occupational Safety and Health Administration (OSHA) is discussed in this report.

[31] U.S. Environmental Protection Agency, "Bisphenol A (BPA) Action Plan Summary," April 15, 2010, http://www.epa.gov/opptintr/existingchemicals/pubs/actionplans/bpa.html.

[32] CRS Report RL31905, *The Toxic Substances Control Act (TSCA): A Summary of the Act and Its Major Requirements*, by (name redacted).

[33] For example, EPA has stated, "In prescribing a rule which lists any chemical substance, the Administrator shall also identify those uses, if any, which the Administrator determines, by rule, would constitute a significant new use of the substance … If a chemical substance is subject to a rule promulgated under TSCA section 5(b)(4), EPA can, by rule, require a small manufacturer or processor of that chemical to submit reports … from which small businesses are otherwise exempt. Also, anyone who exports or intends to export a chemical substance that is the subject of a proposed TSCA section 5(b)(4) rule are subject to the export notification provisions...." See EPA's website "TSCA Section 5(b)(4) Concern List" at http://www.epa.gov/oppt/existingchemicals/pubs/sect5b4.html. For more information about TSCA, see CRS Report RL31905, *The Toxic Substances Control Act (TSCA): A Summary of the Act and Its Major Requirements*, by (name redacted).

[34] EPA, "Testing of Bisphenol A (BPA)," Rulemaking Gateway, March 29, 2011, http://yosemite.epa.gov/opei/RuleGate.nsf/byRIN/2070-Aj83?opendocument.

Finally, EPA has initiated "collaborative alternatives assessment activities" under its Design for the Environment (DfE) program. These activities aim to reduce BPA releases and environmental exposures. The first partnership is searching for alternatives to BPA in thermal paper.[35]

The safety of most foods, thought to be the primary source of human exposure to BPA, is the responsibility of FDA. Current BPA-containing PC polymers and epoxy resins used in food containers—such as baby bottles and infant formula cans, respectively—are regulated by FDA as food additives, based on approvals issued more than 40 years ago. Under this approach, any manufacturer may use BPA-containing packaging without notifying FDA of that use. In its January 2010 announcement, FDA said that it is considering regulating BPA-containing substances under its newer and more rigorous food contact notification program, under which manufacturers advise FDA of specific uses, giving the agency an opportunity to review and consider safety information.[36] FDA also announced that its National Center for Toxicological Research was conducting additional studies on the effects of low-dose BPA exposure, to guide future regulatory efforts. FDA plans to complete a draft technical report on its research before the end of 2011. A final report is expected to be issued in 2012.[37]

FDA is also responsible for the safety of drugs and medical devices. In October 2008, FDA issued a request for information regarding BPA in all types of products it regulates.[38] Subsequently, FDA has asked its Science Board, which advises the Commissioner, to review the agency's proposals to study the possible effects of exposure to BPA from drugs and medical devices, noting that there is limited information available at this time with which to balance possible BPA exposure risks against the therapeutic benefits provided by the drugs and devices.[39]

Events Surrounding the Current Controversy

Although BPA has been in use in food contact substances and other applications for several decades, the debate among scientists, consumers, and government authorities about the safety of the chemical has escalated in recent years. **Table 1** below provides a brief chronology of events, which are discussed in additional detail in this section.

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[35] EPA, Design for the Environment, BPA Alternatives in Thermal Paper Partnership, http://www.epa.gov/dfe/pubs/projects/bpa/index.htm.

[36] FDA, "Bisphenol A (BPA), Update on Bisphenol A (BPA) for Use in Food: January 2010," February 19, 2010, http://www.fda.gov/NewsEvents/PublicHealthFocus/ucm064437.htm. See also FDA's Food Contact Substance Notification Program, at http://www.fda.gov/Food/FoodIngredientsPackaging/FoodContactSubstancesFCS/default.htm.

[37] FDA, About FDA, FDA-TRACK NCTR Research Divisions Dashboard–FY 2010, Program Measures, Division of Biochemical Toxicology, D. "Bisphenol A (BPA) Data Gap Analysis," http://www.fda.gov/AboutFDA/Transparency/track/ucm242846.htm.

[38] See FDA's request for information regarding other routes of exposure at FDA, "FDA-Regulated Products that Contain Bisphenol-A: Request for Information," 73 *Federal Register* 61135-61136, October 15, 2008. In response, an organization representing companies that manufacture medical devices provided information from a membership survey, listing adult and pediatric medical devices that contain BPA. Comment and accompanying attachment, "Medical Devices and Articles Used in Product Manufacturing Containing Bisphenol-A Related Materials," from Advanced Medical Technology Association (AdvaMed) to FDA, docket number FDA-2008-N-0523, December 22, 2008, http://www.regulations.gov.

[39] See, for example, FDA, "Safety Assessment of BPA in Medical Products, August 7, 2009," Briefing Information for the August 17, 2009 Meeting of the Science Board to the FDA, http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/ScienceBoardtotheFoodandDrugAdministration/default.htm.

Table 1. Chronology

1970	FDA approves BPA for food-contact uses
November 2007	NTP expert panel reports "some concern" for potential neurological effects of BPA exposure for fetuses and infants
April 2008	FDA forms task force to review BPA risk
	Canada publishes risk assessment on infant BPA exposure
June 2008	NTP Board of Scientific Counselors notes "some concern" for neurological and prostate effects
August 2008	FDA issues draft risk assessment for food contact applications of BPA
September 2008	NTP issues final brief and Monograph
October 2008	FDA Science Board Subcommittee report criticizes FDA's draft risk assessment
March 2009	Large manufacturers of baby bottles stop sale of bottles containing BPA
July 2009	U.S. House approves H.R. 2749, requiring that FDA determine safety of BPA for approved uses (this provision was not enacted by the 111th Congress)
January 2010	FDA announces "some concern" for neurological and prostate effects in fetuses, infants, and young children; begins to plan study and to take steps to reduce exposure
March 2010	Canada bans use of BPA in baby bottles
September 2010	European Food Safety Authority scientists announce they found "no convincing evidence" of neurological effects
October 2010	Canada designates BPA a toxic substance
November 2010	World Health Organization declares Canada's BPA ban to be premature
Late January/early February 2011	S. 136/H.R. 432 are introduced in the 112th Congress

National Toxicology Program

In early 2007, NTP convened an expert panel to conduct a comprehensive review of the scientific literature on BPA. The panel met during 2007 and issued its report on November 26, 2007.[40] It concluded that animal studies were sufficient to elicit "some concern" about possible effects of BPA exposure on the neurological development of human fetuses and newborns, but "minimal concern" about effects on the early onset of puberty or development of mammary or prostate cancer. (The expression of "some concern" is midway in a qualitative scale used by NTP. In order, from greatest to least, the levels of concern are serious concern, concern, some concern, minimal concern, and negligible concern.) Some other scientists who reviewed the panel's conclusions disagreed.

NTP's own scientists reviewed the panel report, as well as numerous studies that were not considered by the panel, many that were completed or published in late 2007 and early 2008. NTP then issued its draft BPA "brief" on April 14, 2008, which largely agreed with the panel report, but expressed a higher level of concern with respect to early puberty and effects on the mammary and prostate glands. The draft report concluded, "the possibility that [BPA] may alter

[40] HHS, NTP, "Expert Panel Report on the Reproductive and Developmental Toxicity of Bisphenol A," November 26, 2007, http://cerhr.niehs.nih.gov/evals/bisphenol/bisphenol.html.

human development cannot be dismissed."[41] Specifically, the NTP report concluded that there is "some concern" for neural and behavioral effects in fetuses, infants, and children at current levels of human exposure, and "some concern" in those same groups for effects on the prostate gland, mammary gland, and on earlier age of puberty in females. Public comment on the draft brief was invited through May 23, 2008.[42]

On June 11, 2008, the NTP Board of Scientific Counselors met to review the draft report and public comments. The board voted to lower the level of concern for BPA's effects on the mammary gland and on the onset of puberty in females.[43] This vote is reflected in the final version of the NTP brief, which was included in the NTP Monograph issued in September 2008.[44] Thus, the official NTP view is that current levels of human exposure to BPA warrant "some concern" for possible effects on the brain, behavior, and prostate gland in fetuses, infants, and children; "minimal concern" for effects on the mammary gland and an earlier age for puberty in female fetuses, infants, and children, and for workers exposed occupationally; and "negligible concern" for all other current exposures and reproductive or developmental effects.

Food and Drug Administration

During the week of April 14, 2008, in response to the release of the NTP draft BPA brief, FDA formed an agency-wide task force to review current information regarding BPA in all FDA-regulated products. In June 2008, FDA asked its Science Board, the advisory board to the FDA Commissioner, to establish a subcommittee to review research on BPA and exposures from food containers, and deliver its findings to the board's annual meeting that fall.[45]

On August 14, 2008, FDA published a draft risk assessment of BPA in food contact applications, saying, "FDA has concluded that an adequate margin of safety exists for BPA at current levels of exposure from food contact uses. At a later date, FDA will publish a separate document that provides a safety assessment of BPA exposure from other FDA-regulated products."[46] Consumer groups and some Members of Congress questioned the finding, which appeared to contradict earlier findings by the NTP. Among other things, concerns were raised about whether FDA relied too heavily on industry-sponsored studies, and whether the agency should have considered more recent evidence of health effects other than the reproductive and developmental effects on which it focused.[47] FDA said that it relied heavily on the industry-sponsored studies because they

[41] HHS, NTP, "Draft NTP Brief on Bisphenol A," April 14, 2008, p. 9.

[42] National Institute of Environmental Health Sciences, "Since You Asked - Bisphenol A," http://www.niehs.nih.gov/news/media/questions/sya-bpa.cfm.

[43] National Institute of Environmental Health Sciences, "Actions on the Draft NTP Brief on Bisphenol A by the NTP Board of Scientific Counselors (BSC), June 11, 2008," http://ntp.niehs.nih.gov/files/BSCactionsBPA_508.pdf.

[44] NTP Monograph on Bisphenol A, p. vii.

[45] FDA, "FDA's Chief Scientist Asks Science Board Subcommittee to Review Research on Bisphenol-A," press release, June 6, 2008, http://www.fda.gov/opacom/hpnews.html.

[46] FDA, "Draft Assessment of Bisphenol A for Use in Food Contact Applications," August 14, 2008, p. 2, http://www.fda.gov/ohrms/dockets/ac/08/briefing/2008-0038b1_01_00_index.htm. FDA's definition of safety in this context is that "there is a reasonable certainty in the minds of competent scientists that the substance is not harmful under the intended conditions of use." 21 CFR § 170.3(i).

[47] See, for example, Jennifer C. Smith, "Lawmakers, Consumer Groups Question FDA's BPA Summary," *InsideHealhPolicy.com*, September 23, 2008.

followed the agency's guidance for good laboratory practices (GLPs) and constituted robust evidence for that reason, but that other studies were also considered.

On October 15, 2008, FDA issued a notice in the *Federal Register* requesting information regarding types of FDA-regulated products that contain BPA, and any information relating to the leaching of BPA from packaging into a product, and/or leaching from a product during its use in humans.[48] FDA said that its agency-wide task force had completed the assessment of the potential exposure to BPA from food-contact materials (published in August), and was interested in additional information on other types of products, specifically medical devices, biological products (including blood, blood products, vaccines, and cell and gene therapies), and drugs.

On October 31, 2008, the BPA Subcommittee of the FDA Science Board released its review of FDA's draft risk assessment. The subcommittee concurred with FDA's focus on food exposures and exposures in children. It differed with the agency on several other matters, however, urging, among other things, more emphasis on cumulative exposures; non-food exposures (especially in neonates); and evidence from non-GLP studies. Overall, the subcommittee determined that "Coupling together the available qualitative and quantitative information (including application of uncertainty factors) provides a sufficient scientific basis to conclude that the Margins of Safety defined by FDA as 'adequate' are, in fact, inadequate."[49]

On December 3, 2008, FDA provided an initial response to the subcommittee in a letter, saying that it generally agreed with the subcommittee's concerns and planned further assessments, including expanding its work to consider sources of exposure other than food.[50]

One year later, in January 2010, FDA announced,

> on the basis of results from recent studies using novel approaches to test for subtle effects, both the National Toxicology Program at the National Institutes of Health and FDA have some concern about the potential effects of BPA on the brain, behavior, and prostate gland in fetuses, infants, and young children. In cooperation with the National Toxicology Program, FDA's National Center for Toxicological Research is carrying out in-depth studies to answer key questions and clarify uncertainties about the risks of BPA.

While awaiting research results, FDA is "taking reasonable steps to reduce human exposure to BPA in the food supply," and adopting "a more robust regulatory framework for oversight of BPA."[51]

FDA's struggles with BPA regulation would seem to illustrate a number of charges of systemic problems within the agency made by the FDA Science Board. In November 2007, the board issued a highly critical report finding that FDA's regulatory mission was severely compromised

[48] FDA, "FDA-Regulated Products that Contain Bisphenol-A: Request for Information," 73 *Federal Register* 61135-61136, October 15, 2008.

[49] FDA Science Board Subcommittee on Bisphenol A, *Scientific Peer Review of the Draft Assessment of Bisphenol A for Use in Food Contact Applications (Draft)*, October 31, 2008, http://www.fda.gov/ohrms/dockets/ac/08/briefing/2008-4386b1-05.pdf. The subcommittee considered scientific evidence that included presentations made at a public meeting on September 16, 2008.

[50] Letter from Norris Alderson, FDA Associate Commissioner for Science, to Barbara J. McNeil, Chair, FDA Science Board, December 3, 2008.

[51] FDA, "Bisphenol A (BPA): Update on Bisphenol A (BPA) for Use in Food: January 2010," http://www.fda.gov/NewsEvents/PublicHealthFocus/ucm064437.htm.

by inadequate and eroding scientific and technical resources, including the size and capability of its workforce, and its processes for risk assessment and related activities.[52] The board said that the agency's food safety program, in particular, was "in a state of crisis" as a result of a constellation of problems that flowed from increasing scientific, technical, and regulatory demands, coupled with inadequate resources.[53] Subsequently, Congress provided a 45% increase in FDA's food safety budget from FY2008 ($577 million) to FY2011 ($837 million).[54] FDA has not announced any new findings or changes in its regulatory approach to BPA since its January 2010 announcement, although it has issued an information sheet aimed at parents of young children.[55]

State Government Actions

Many states have considered or are considering legislation to restrict use of BPA in products intended for use by infants and children. Connecticut, Maryland, Massachusetts, Minnesota, New York, Vermont, Washington, and Wisconsin have enacted such legislation. North Carolina and New Mexico have authorized studies. Delaware stated its support for efforts to develop alternatives, and Pennsylvania passed legislation that "[u]rges the Congress of the United States and the Food and Drug Administration to encourage the use of reduced bisphenol-A in the manufacture of plastic food containers and bottles."[56] Legislation introduced to ban BPA in children's products has failed to advance in several other states.

Selected International Actions

As with U.S. federal agencies and advisory boards and with the states, foreign governments and international advisory bodies have reached different conclusions and taken different approaches regarding the safety of low-level exposures to BPA.

On October 13, 2010, Canada became the first country to designate BPA as a toxic substance.[57] According to the Canadian government, this enables the Minister of the Environment to propose a regulation or other instrument to manage human health and environmental risk posed by a listed chemical under the Canadian Environmental Protection Act. Officials may also choose to develop non-regulatory approaches to manage these risks. Canada has taken numerous intervening actions with respect to BPA.[58] For example, in April 2008, it published a risk assessment finding that "the

[52] FDA Science Board, Subcommittee on Science and Technology, *FDA Science and Mission at Risk*, November 2007, http://www.fda.gov/ohrms/dockets/ac/07/briefing/2007-4329b_02_01_FDA%20Report%20on%20Science%20and%20Technology.pdf.

[53] Ibid., pp. 4 and 22.

[54] See CRS Report R40792, *Food and Drug Administration Appropriations for FY2010*, by (name redacted); the FDA section of CRS Report R41737, *Public Health Service (PHS) Agencies: Overview and Funding, FY2010-FY2012*, coordinated by (name redacted) and (name redacted); and Department of Defense and Full-Year Continuing Appropriations Act, 2011 (P.L. 112-10, Sec. 1269).

[55] U.S. Department of Health and Human Services, "Bisphenol A (BPA) Information for Parents," http://www.hhs.gov/safety/bpa/.

[56] State legislation is cataloged by the National Conference of State Legislators and may be searched at http://www.ncsl.org/default.aspx?tabid=13223 for statutes or at http://www.ncsl.org/?tabid=17322 for recent legislation.

[57] Canada Gazette, "Order Adding a Toxic Substance to Schedule 1 to the Canadian Environmental Protection Act, 1999," vol. 144, no. 21, October 13, 2010, http://gazette.gc.ca/rp-pr/p2/2010/2010-10-13/html/sor-dors194-eng.html.

[58] See Government of Canada, Chemical Substances, "Bisphenol A: Risk Management Action Milestones," (continued...)

main source of exposure [to BPA] for newborns and infants is through the use of polycarbonate baby bottles when they are exposed to high temperatures and the migration of [BPA] from cans into infant formula…. [BPA] exposure to newborns and infants is below levels that may pose a risk, however, the gap between exposure and effect is not large enough."[59] The Canadian government said, in essence, that although exposure levels are below those that could cause health effects, they are close enough to those levels that the government wanted to be prudent and reduce exposures further. The government banned PC baby bottles in March 2010, saying, "Given that toxicokinetic and metabolism data indicate potential sensitivity to newborns and infants, it is considered appropriate to apply a precautionary approach when characterizing risk."[60]

The European Food Safety Authority (EFSA), a component of the European Union, has consistently reached a different conclusion regarding the safety of low-level BPA exposures. Most recently, on September 30, 2010, a panel of EFSA scientists announced that after a comprehensive scientific review, they could not identify any new evidence that would lead them to revise the current Tolerable Daily Intake (TDI) level for BPA, which the agency established in 2006. Reviewers stated that they

> acknowledge that some recent studies report adverse effects on animals exposed to BPA during development at doses well below those used to determine the current TDI. These studies show biochemical changes in the central nervous system, effects on the immune system and enhanced susceptibility to breast cancer. However, these studies have many shortcomings. At present the relevance of these findings for human health cannot be assessed....[61]

In addition, according to the panel, available data on BPA do not provide "convincing evidence that BPA has any adverse effects on aspects of behavior, such as learning and memory."[62]

In November 2010, the World Health Organization (WHO), in conjunction with the U.N. Food and Agriculture Organization (FAO), held an expert meeting to assess the safety of BPA. The expert panel included representatives from the EFSA, Health Canada, and the U.S. National Institute of Environmental Health Sciences (NIEHS) and FDA.[63] The experts concluded that:

- There is insufficient evidence on which to judge the carcinogenic potential of BPA.[64]
- There are no specific long-term toxicity studies with BPA other than those to examine carcinogenicity.

(...continued)

http://www.chemicalsubstanceschimiques.gc.ca/challenge-defi/batch-lot-2/bisphenol-a/bpa-risk_hazard-eng.php.

[59] Health Canada, "Government of Canada Takes Action on Another Chemical of Concern: Bisphenol A," press release, April 18, 2008, http://www.hc-sc.gc.ca/ahc-asc/media/nr-cp/_2008/2008_59-eng.php.

[60] Canada Gazette, "Order Amending Schedule I to the Hazardous Products Act (bisphenol A)," vol. 144, no. 7, March 31, 2010, http://www.gazette.gc.ca/rp-pr/p2/2010/2010-03-31/html/sor-dors53-eng.html.

[61] European Food Safety Authority, "EFSA Updates Advice on Bisphenol A," press release, September 30, 2010, http://www.efsa.europa.eu/en/press/news/cef100930.htm, with link to the full report.

[62] Ibid.

[63] WHO, "Joint FAO/WHO Expert Meeting to Review Toxicological and Health Aspects of Bisphenol A, Summary Report," November 1-5, 2010, Ottawa, Canada, http://www.who.int/foodsafety/chem/chemicals/BPA_Summary2010.pdf.

[64] Ibid., Executive Summary, p. ix.

- There is considerable uncertainty as to whether BPA has any effect in rodents on conventional reproductive or developmental endpoints at very low doses by the oral or injected routes of exposure, or potential effects in humans at current exposure levels.[65]
- Further investigation is necessary to address uncertainty regarding possible neurobehavioral effects of BPA exposure.
- Ongoing studies may clarify the effect of BPA on cardiovascular function and metabolic syndrome and diabetes.
- Existing animal studies are inadequate for human health risk assessment.[66]

Nevertheless, the European Union announced that it would ban the use of BPA in plastic baby bottles early in 2011.[67] Reportedly, this decision was "the result of months of discussion and exchange of views between the [European] Commission's services, the EFSA, the member states and the industry."[68] China and Malaysia reportedly have imposed similar bans.[69]

Private Sector Actions

In April 2008, concerns raised by the NTP draft brief about the health effects of BPA prompted Wal-Mart, Playtex Infant Care, and Nalgene, among other companies, to stop allowing BPA in the beverage bottles they produce or sell.[70] At the same time, the American Chemistry Council (ACC), which represents chemical manufacturing companies, called on FDA to update its review of the safety of BPA in food contact applications, saying, "The extensive body of scientific study regarding [BPA] is well documented and well reviewed. Nevertheless, recent media reports have raised concerns about the safety and use of polycarbonate plastic and epoxy resins, unnecessarily confusing and frightening the public."[71]

In March 2009, the six largest manufacturers of baby bottles announced that they would stop selling BPA-containing bottles in the United States, partly in response to growing numbers of retailers that would no longer carry the products.[72] Noting the announcement, the ACC reiterated FDA's assessment, at that time, that currently approved uses of BPA were safe.[73]

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[65] Ibid., p. x.

[66] Ibid., pp. x-xi.

[67] Europa, Press releases RAPID, "Bisphenol A: EU Ban on Use in Baby Bottles Enters into Force Next Week," February 25, 2011, http://europa.eu/rapid/pressReleasesAction.do?reference=IP/11/229&format=HTML&aged=0&language=%20EN&guiLanguage=en.

[68] EurActiv.com, "EU to ban Bisphenol A in baby bottles in 2011," http://www.euractiv.com/en/food/eu-ban-bisphenol-a-baby-bottles-2011-news-500052.

[69] Jonathan Bardelline, "China, Malaysia Become Latest Nations to Ban BPA," http://www.greenbiz.com/news/2011/03/14/china-malaysia-latest-nations-ban-bpa.

[70] See, for example, "Companies Move to Curb Risk From Chemical BPA," *Associated Press*, April 21, 2008.

[71] American Chemistry Council, "ACC Calls on FDA to Update Review of Bisphenol A," press release, April 17, 2008, http://www.americanchemistry.com/s_acc/index.asp.

[72] Lyndsey Layton, "No BPA For Baby Bottles In U.S.," *The Washington Post*, March 6, 2009.

[73] American Chemistry Council, "ACC Statement on Manufacturers Decision not to Use Bisphenol A in Baby Bottles," press release, March 6, 2009, http://www.americanchemistry.com/s_acc/index.asp.

The market's response to concerns about BPA was apparently easier for plastic bottles, for which BPA-free alternatives are available, than for other types of containers. Although it is reported that many food companies are considering a switch to other forms of BPA-free food packaging, manufacturers of cans represented by the North American Metal Packaging Alliance maintain that suitable alternatives to BPA are not available, and in almost all cases are not likely to become available in the immediate future.[74] Until alternatives for all uses are developed, they argue that BPA-containing linings will be necessary to ensure a tight seal on cans and lids, and thus to prevent food spoilage and food poisoning risks to consumers.

In September 2010, a "green" capital management company published its second annual report ranking companies that market packaged foods on their efforts to use BPA-free packaging.[75] The authors report that "notable progress has been made towards commercializing substitutes to BPA epoxy can linings."[76]

However, in 2009, Consumers Union found measurable amounts of BPA in two food brands labeled "BPA-free." This prompted one of the manufacturers to suggest that the chemical may be ubiquitous, and could not be completely eliminated from the food supply.[77]

Congressional Actions

In the 112th Congress, companion bills, H.R. 432 and S. 136, would ban the use of BPA in food containers.

The 111th Congress considered several bills that addressed BPA, but none was enacted. Companion bills (S. 593/H.R. 1523) would have prohibited the use of BPA in food and beverage containers regulated by the FDA. A second pair of bills (S. 753/H.R. 4456) would have required the CPSC to prohibit BPA use in children's food and beverage containers under the Federal Hazardous Substances Act. Another bill (H.R. 4341) would have required a warning label on any food container containing BPA.

Another bill in the 111th Congress, H.R. 5820, would have placed BPA on a priority list of chemicals for which EPA would assess safety, authorize specific uses, and impose conditions under the Toxic Substances Control Act (TSCA).[78] Activities under H.R. 5820 would have been required to ensure that a chemical would meet a stringent standard of safety, namely that the authorized use of the chemical under the conditions imposed "is not reasonably anticipated to present a risk of injury to health or the environment, … provides a reasonable certainty of no harm, including to vulnerable populations," taking into account aggregate and cumulative

[74] John Rost and Kathleen Roberts, personal communication, April 15, 2010. See also Lyndsey Layton, "Replacing BPA in Cans Gives Foodmakers Fits; FDA Safety Concerns Prompt Scramble to Remove the Chemical," *The Washington Post*, February 23, 2010.

[75] Green Century Capital Management, *Seeking Safer Packaging 2010*, Ranking Packaged Food Companies on BPA, 2010, http://www.greencentury.com/bpareport.

[76] Ibid., Executive Summary.

[77] See Lyndsey Layton, "Replacing BPA in Cans Gives Foodmakers Fits; FDA Safety Concerns Prompt Scramble to Remove the Chemical," *The Washington Post*, February 23, 2010.

[78] For more information about TSCA and H.R. 5820, see CRS Report R41335, *Proposed Amendments to the Toxic Substances Control Act (TSCA): Senate and House Bills Compared with Current Law*, by (name redacted).

exposure to the chemical, and "protects the public welfare from adverse effects, including effects on the environment." For uses of BPA when no substitute was available, the bill would have allowed continued BPA use provided that conditions were imposed to reduce risk "to the greatest extent feasible."

The House acted on another approach to BPA regulation on July 30, 2009, when it amended and approved H.R. 2749, the Food Safety Enhancement Act of 2009. Section 215 of the bill would have required FDA to determine whether there was "a reasonable certainty of no harm for infants, young children, pregnant women, and adults, for approved uses of polycarbonate plastic and epoxy resin made with bisphenol A in food and beverage containers ... under the conditions of use prescribed in current [FDA] regulations." FDA would have been required to notify Congress about any uses of BPA for which such a determination could not be made and how the agency would regulate such use to protect the public health. The Senate did not act on this bill.

Senator Dianne Feinstein sought to amend comprehensive food safety legislation in the Senate (S. 510) with an amendment that would have banned the use of BPA in baby bottles and sippy cups, but facing substantial opposition, she abandoned that effort prior to the final vote on the bill on November 30, 2010.[79]

Conclusion

There is scientific consensus that exposure to high levels of BPA can cause adverse reproductive effects in mammals. There is growing concern among the public, and among many scientists, about low-dose BPA exposures, sharpened by the fact that such exposures within the general population are, without question, highest in infants. The scientific debate about the safety of BPA is likely to continue, and further reaction in the policy, regulatory, and commercial arenas, as well as in Congress, is expected.

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[79] *Congressional Record*, November 17, 2010, pp. S7940-S7942.