

November 27, 2007

Ms. Cynthia Oshita
Office of Environmental Health Hazard Assessment
Proposition 65 Implementation
P.O. Box 401
1001 I Street, 19th Floor
Sacramento, CA 95812-4010

Dear Ms. Oshita:

The Environmental Working Group (EWG) strongly supports the Office of Environmental Health Hazard Assessment's (OEHHA) request for a priority review of Bisphenol A (BPA). Over the last decade, a growing body of science has provided substantial evidence of the developmental and reproductive toxicity of BPA in lab animals at low, environmentally relevant doses and has demonstrated widespread exposures among the public. In addition, many of the diseases and health conditions linked to BPA in animal studies are common among the US population. This gives us great concern that BPA exposures for pregnant women and children may pose significant health risks.

In particular, the following finding on BPA toxicity and human exposures demonstrate why this priority review of this chemical by OEHHA is so important and relevant:

- Developmental and reproductive toxicity of BPA is demonstrated in multiple animal studies
- Studies demonstrate widespread exposure to BPA among the public at levels that have been shown to cause adverse effects in numerous lab studies
- Health effects linked to BPA in lab studies are common among the public
- A recent federal Center for the Evaluation of Risk to Human Reproduction (CERHR) review of BPA contains fundamental errors that support the need for an independent review by OEHHA; and

- Findings of an independent BPA expert panel, including their concerns about potential adverse effects in humans, support the need for priority review by OEHHA

Each of these points is detailed further below:

Developmental and Reproductive Toxicity: In the last decade, numerous animal studies have shown that exposure to BPA results in developmental and reproductive toxicity in exposed animals and their offspring. In 1993, OEHHA published a list of criteria that need to be met in order for a chemical to be listed as a reproductive toxin (OEHHA 1993). Earlier this year, OEHHA compiled a list of 63 studies that meet these established criteria for developmental or reproductive toxicity from BPA exposure (OEHHA 2007). These studies reported toxic effects that included:

- persistent changes to breast tissue that predispose cells to carcinogenesis in the offspring of exposed animals
- neurobehavioral changes in offspring of exposed animals
- germ cell damage in offspring of exposed animals
- persistent changes to prostate tissue that predispose cells to carcinogenesis in the offspring of exposed animals; and
- adverse effects on fertility and reproductive system of exposed animals

OEHHA had also outlined in the 1993 document that “effects should occur in multiple studies or multiple species for a substance to be recommended for listing”; the 63 studies that OEHHA reviewed confirms the reproducibility of findings that illustrate the low dose toxicity of this chemical.

Widespread Exposure: We want to call your attention to a very recent publication in Environmental Health Perspectives in which the national Centers for Disease Control and Prevention (CDC) detected BPA in 93% of people age 6 and older. CDC tested the urine of 2,517 people who are representative of the US population for BPA and found children ages 6 and older had higher concentrations than adolescents, who in turn had higher concentrations than adults. Women, non-Hispanic blacks, and lower income adults were also sub-groups with higher concentrations (Calafat et

al 2007). Because BPA has a short half-life in the body, this study confirms daily, sustained exposures among the general public.

In addition, BPA has also been found in breast milk, amniotic fluid, and cord blood, indicating exposure to the developing fetus and neonates (CERHR 2006). The widespread exposure demonstrated by these studies is consistent with the many sources of exposure to BPA from a variety of consumer products. BPA ranks in the top two percent of high production volume chemicals in the US, with annual production exceeding a billion pounds per year. It is used as plasticizer in a variety of commonly used consumer products and is so ubiquitous that it pollutes not only people but also rivers, estuaries, sediment, and house dust.

Earlier this year, EWG spearheaded a study in which an independent laboratory tested 97 cans of name-brand fruit, vegetables, soda, and other commonly eaten canned foods for the presence of BPA (EWG 2007a). Canned foods represent a major source of exposure to BPA for the general public and Japanese manufacturers voluntarily decreased the use of the chemical in their products beginning in 1997 for the benefit of their customers (Matsumoto 2003).

EWG's tests found the following:

- BPA was detected in 56% of samples
- Of all foods tested, chicken soup, infant formula, and ravioli had BPA levels of highest concern. Just one to three servings of foods with these concentrations could expose a pregnant woman or child to BPA at levels that caused serious adverse effects in animal tests (2.0 ug/kg/day linked to permanent damage of the reproductive system and aggressive behavior- Nagel et al 1997, Kawai et al 2003)
- For women of childbearing age who routinely eat canned food, chronic exposure levels throughout pregnancy can exceed safe doses. For example, the BPA dose for one-quarter of all women eating 2 servings of canned food daily would fall within a margin of safety of 10 from levels linked to increases in anogenital distance in both genders and early puberty in studies of *in utero* exposures (2.4 ug/kg/day- Howdeshell et al 1999, Honma et al 2002)

EWG also included tests of liquid infant formula in this study and combined this information with FDA tests of liquid infant formula in 1996 (EWG 2007b). EWG analysis of these results revealed the following:

- One of every 16 infants fed ready-to-eat canned formula would be exposed to BPA at doses exceeding those that altered testosterone levels, affected neurodevelopment, and caused other permanent damage to male and female reproductive systems (2.4 ug/kg/day- Howdeshell et al 1999, Honma et al 2002)
- At the highest BPA levels found in formula (17 parts per billion), nearly two-thirds of all infants fed ready-to-eat formula would be exposed above doses that proved harmful in animal tests (2.4 ug/kg/day- Howdeshell et al 1999, Honma et al 2002)

This EWG study provides the most comprehensive U.S. based examination of BPA in canned food available and confirms widespread contamination of these foods by BPA. Because of its ubiquity in foods that are commonly eaten by the public, this study provides strong evidence that significant numbers of pregnant women, formula fed infants, and young children may be exposed to BPA on a daily basis at levels that have been found to be harmful in lab animals.

The current reference dose for BPA of 50 ug/kg/day was derived from traditional toxicological studies and does not take into account the large body of work from the last ten years that shows that BPA is biologically active at much lower doses (vom Saal and Hughes 2005). In fact, there are many studies that show harm to lab animals at BPA doses that are well below the reference dose (Nagel et al 1997, Kawai et al 2003, Howdeshell et al 1999, Honma et al 2002). The low doses that have been found to be harmful to animals are similar to levels that are found in people.

BPA and Human Health Trends: BPA has been linked to a variety of medical conditions that are prevalent and taking a major toll on our collective health. Diseases like breast cancer, prostate cancer, polycystic ovarian syndrome, and insulin resistance have all been associated with BPA exposure in lab studies (vom Saal and Hughes 2005, Maffini 2006). In many of these studies, exposure occurs *in utero* and these conditions develop in exposed offspring long after birth. Many of the adverse health effects of BPA arise from its ability to mimic estrogen. What is most worrisome about these studies is that the doses of BPA that are being used are extremely low and in the range of the levels that have been found in people.

A few studies have reported on potential effects of exposure to BPA in humans. OEHHA's study summary of BPA included a study in which Japanese scientists found that women with polycystic ovarian syndrome (PCOS) had higher serum levels of BPA relative to women with normal ovarian function, and that there were positive correlations between BPA concentrations and androgen levels (Takeuchi et al 2006). Polycystic ovarian syndrome is one of the most common causes of female infertility in the U.S. and affects 5 to 10% of American women.

Another study of women with a history of recurrent miscarriages found they had higher serum BPA levels when compared with women with normal pregnancies, leading the authors of the study to conclude that "exposure to bisphenol A is associated with recurrent miscarriage" (Sugiura-Ogasawara et al. 2005). Recurrent miscarriages affect one percent of American couples trying to conceive (Rai 2006).

OEHHA's study summary did not include a study of men with occupational exposure to plastics that contain BPA that found that they had decreased secretion of follicle stimulating hormone (FSH) when compared with men without occupational exposure to epoxy resins (Hanaoka et al 2002). FSH is critical to sperm formation. Abnormal secretion of this hormone in men can result in reduced sperm concentration and infertility.

Federal Review Flawed: The recent review of BPA by the federal CERHR found "some concern" with respect to neural and behavior effects from *in utero* exposure but disregarded the substantial number of studies linking fetal exposure to BPA to breast and prostate cancers and reproductive problems. This review had been plagued by many issues, including charges leveled by the House Oversight and Government Reform Committee of the potential conflict of interest on the part of the subcontractor that conducted the initial literature search and prepared the first draft. The subcontractor, Sciences International, was subsequently fired but the document they prepared continued to be used by the expert panel. It should also be noted that the CERHR panel lacked BPA experts and their final draft was found to contain significant numbers of errors of omission and fact upon review by scientists with BPA expertise (Vandenberg et al 2007).

This failure on the part of the federal panel to make a decision that is fully protective of public health, in addition to the fundamentally flawed process by which they reached their decision, underscores the need for a fair and unbiased reassessment of the public health risks posed by this chemical. OEHHA is in a position to make just such an assessment.

BPA Experts Release Consensus Statement: In August of this year, a group of 38 independent scientists who research BPA toxicity released a consensus statement in which they concluded that BPA represents a clear risk to human health (vom Saal et al 2007). This group of scientists published a series of four articles in the journal Reproductive Toxicology that outlined their conclusions drawn from their review of over 700 scientific articles related to BPA. In this consensus statement, these scientists wrote:

“The wide range of adverse effects of low doses of BPA in laboratory animals exposed both during development and in adulthood is a great cause for concern with regard to the potential for similar adverse effects in humans. Recent trends in human disease relate to adverse effects observed in experimental animals exposed to low doses of BPA.”

Given the flaws in the process that lead to the federal CERHR decision on BPA, OEHHA has an opportunity to reevaluate the reproductive and developmental toxicity of this chemical in a fair and unbiased way that takes into account the substantial body of work that has been published over the last decade. We hope that OEHHA can quickly address the pressing public health issues posed by widespread human exposures to this chemical that has demonstrated extremely low dose toxicity in scores of laboratory studies.

Environmental Working Group strongly supports OEHHA’s decision to prioritize a review of BPA under Prop 65 as a reproductive toxicant.

Sincerely,

Anila Jacob, M.D., M.P.H.
Senior Scientist
Environmental Working Group.

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