



March 27, 2013

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

Re: NOIL-Bisphenol A

Dear Ms. Oshita:

On behalf of the Natural Resources Defense Council (NRDC), which has 1.3 million members and activists, 250,000 of whom are Californians, we write in strong support of OEHHA's Notice of Intent to list the chemical Bisphenol A (BPA) as a reproductive and developmental toxicant, via the "authoritative bodies" mechanism (22 CCR § 12306).

On July 15, 2009, NRDC filed a petition to OEHHA requesting this listing. As NRDC's petition demonstrated and as OEHHA recognized in proposing listing, BPA meets the requirements for listing under the Authoritative Bodies listing mechanism¹ as it has been formally identified by an authoritative body recognized by the State of California as causing reproductive toxicity. Our comments in response to the Request for Relevant Information laid out in detail why BPA should be listed on the Proposition 65 list pursuant to the Authoritative Bodies listing. As we pointed out, the authoritative mechanism for listing chemicals under Proposition 65 is independent of other mechanisms, and a prior decision by the State Developmental Reproductive Toxicity Identification Committee (DART IC) on BPA has no bearing on the listing decision currently before OEHHA pursuant to the Authoritative Bodies mechanism. We also demonstrated that the 2008 report by the National Toxicology Program's Center for the Evaluation of Risks to Human Reproduction met all the requirements for listing pursuant to the Authoritative Bodies mechanism. We attach our previous comments here and add further comment below, elaborating on some of the points we previously raised.

NTP's findings about BPA's reproductive toxicity are supported by both "high dose" and "low dose" studies

OEHHA's regulations lay out the requirements for listing of a reproductive toxin under the Authoritative Bodies mechanism. They require listing by OEHHA if a chemical has "been formally identified by an authoritative body as causing . . . reproductive toxicity." 27 Cal. Code Regs. § 25306(c). A chemical is "formally identified" by an authoritative

¹ Section 25306(c) of Title 27 of the California Code of Regulations

body when the “lead agency,” i.e. OEHHA, determines that the chemical has been included on a list of chemicals causing reproductive toxicity issued by the authoritative body or is the subject of a report concluding that chemical causes reproductive toxicity or has otherwise been identified as causing reproductive toxicity by the authoritative body in a final document. *Id.* § 25306(d)(1). The Proposition 65 regulations define how a chemical is identified “as causing reproductive toxicity” for purposes of the Authoritative Bodies listing mechanism. A chemical “causes” reproductive toxicity if:

Studies in experimental animals indicate that there are sufficient data, taking into account, the adequacy of the experimental design and other parameters such as, but not limited to, route of administration, frequency and duration of exposure, number of test animals, choice of species, choice of dosage levels, and consideration of maternal toxicity, indicating that an association between adverse reproductive effects in humans and the toxic agent in question is biologically plausible.

27 Cal. Code Regs. § 25306(g)(2) (emphasis added). Therefore, “[t]o list a chemical pursuant to regulation 25306 . . . OEHHA must conclude that an authoritative body has determined that the chemical is a reproductive toxicant—i.e., that the experimental animal data are sufficient to support a conclusion that adverse effects in humans are biologically plausible.” *Exxon Mobil v. OEHHA*, 169 Cal. App. 4th 1264, 1280 (2009). Moreover, the authoritative body need not state directly in the “Conclusions” section that BPA is a reproductive toxicant in humans and the precise categorization of the form of the monograph is immaterial. *See id.* at 1281-82 (“We do not agree . . . that the authoritative body’s report is the only permissible evidence that the authoritative body made the regulatory findings. . . . So long as OEHHA can conclude, on the basis of the entire record before it, that the authoritative body made the regulation 25306(g) findings, it may list a chemical pursuant to the authoritative body provision of the statute.”).

These criteria have been met for BPA on the basis of both “high dose” and “low dose” animal studies.

First, the National Toxicology Program (NTP) Center for the Evaluation of Risks to Human Reproduction (CERHR) is an authoritative body for the listing of reproductive toxins under Proposition 65. 27 Cal. Code Regs. § 25306(l)(3). The DART IC unanimously rejected a request by the American Chemistry Council to remove the NTP CERHR as an authoritative body.² While, the body no longer formally exists, reports issued by the body still constitute findings of a recognized authoritative body.

Second, it is a generally accepted toxicological assumption that a chemical that causes developmental harm in experimental animals will cause similar harm in humans. *See Exxon Mobil*, 169 Cal. App. 4th at 1288-89 (citing EPA guidance and NTP practice, and referring to the record in the case). Unless experimental animals and humans differ from

² Meeting Synopsis and Slide Presentations, Developmental and Reproductive Toxicant Identification Committee Meeting Held on July 12 and 13, 2011. Available at: http://www.oehha.org/prop65/public_meetings/2011DARTsynop.html.

one another in physiologically significant ways, extrapolation to humans from animal studies is appropriate. *Id.* at 1289. The simple fact that animals might have been exposed at higher doses than humans are normally exposed is not sufficient to preclude listing under Proposition 65, contrary to arguments previously put forward by the American Chemistry Council. In *Exxon Mobil*, the court expressly rejected the contention that issues of level of exposure could preclude listing. There, the court accepted OEHHA's argument that "whatever the *probability* that humans are actually exposed through ingestion to levels high enough to cause developmental toxicity, or even to require warnings about such exposures, these data establish unequivocally that such exposures are *possible*" and that "[i]f rats can ingest food contaminated with high levels of DIDP, humans can do the same." *Id.* at 1291 (emphasis in original). More importantly, the court also affirmed OEHHA's argument that the level of human exposure are not relevant to the determination of whether a chemical should be listed under Proposition 65 and should be addressed post-listing "if and when [an entity] seeks to prove that it is exempt from the Proposition 65 requirements because a specific exposure that it causes is below the warning threshold." *Id.* at 1291-92.

Third, the NTP CERHR made the requisite determination that BPA is a reproductive toxicant. The NTP's final Monograph on BPA found "clear evidence of development effects at high doses" in animal studies. NTP Monograph, NTP Brief on Bisphenol A at 6-7, NIH Publication No. 08-5994 (September 2008). It also relied on animal studies, including both high- and low-dose studies, to reach an explicit "conclusion" regarding the "possibility that human development or reproduction might be effected by exposure to bisphenol A"—stating that the "NTP has some concern for effects on the brain, behavior, and prostate gland in fetuses, infants, and children at current human exposures to bisphenol A." *Id.* at 7-8, 38. The NTP Monograph relied on both the high-dose and low-dose studies as evidence supporting the conclusion that BPA can "possibly" affect "human development and reproduction," thus explicitly recognizing the biological plausibility of adverse effects in humans from BPA. *Id.* at 6-7, 34. Specifically, the Monograph states: "When considered together [both high dose and low dose studies], these laboratory animal findings provide limited evidence that bisphenol A has adverse effects on development," leading the NTP to conclude that "the possibility that human development may be altered by bisphenol A at current exposure levels cannot be dismissed." *Id.* at 34. These findings easily meet the requirements for listing under *Exxon Mobil*. Therefore, OEHHA should find that the NTP-CERHR, an authoritative body, has determined that the chemical is a reproductive toxicant based on both high and low dose animal studies, and should list BPA under Proposition 65.

New studies since the NTP Monograph was published support NTP's findings

Since the NTP Monograph was published, additional studies in both animals and humans have found evidence of reproductive toxicity.

Recent findings from an American Chemistry Council-sponsored BPA study confirmed body weight reductions at 50 and 130 mg/kg-d (for gestation and lactation) (Stump 2010). A 2010 study of BPA gestational and perinatal exposures in mice found a decrease

in the cumulative number of pups, and a decline in fertility and fecundity over time in female mice exposed peri-natally to BPA (Cabaton et al. 2011).

Human studies published since the NTP report of 2008 have also found evidence of BPA exposure causing adverse birth outcomes. A study published in Taiwan found women with higher levels of BPA had babies with lower birth weight or babies that were small for gestational age (Chou et al. 2011). The Generation R study, just published in Environmental Health Perspectives found that prenatal exposure to BPA results in diminished fetal growth (Cabatan et al. 2011). When adjusted for creatinine, higher levels of BPA in maternal urine were associated with lower growth rates for fetal weight and head circumference (Snijder et al. 2013). Other studies have found similar results of decreased birth weight (Miao et al. 2011).

The body of research continues to find consistent evidence of low dose effects of BPA on reproduction and development. Recent research finds low levels of BPA exposure causes harm in the mammary gland (Ayyanan 2011), prostate tissue (Prins et al. 2011), and brain (McCaffrey et al. 2013). This is consistent with previous research in multiple studies which have linked BPA exposure to a predisposition to mammary (breast) cancer, prostate cancer, and changes in behavior (Rubin 2011; Golub et al. 2010). In addition, human studies continue to find links between BPA and cardiovascular disease (Melzer et al. 2012), obesity (Carwile and Michels 2011) and metabolic changes affecting insulin levels (Soriano et al. 2012) which could lead to diabetes.

Thus, there is a robust body of science that supports the listing of BPA as a chemical that may pose risks to human reproduction and development.

Conclusion

In conclusion, NTP-CERHR's formal identification of BPA as a reproductive toxicant, based on both high-dose and low-dose studies, requires OEHHA to list BPA under Proposition 65.

Thank you for considering these comments.

Sincerely,


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Senior Scientist


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Attachments:

Cited studies, in alphabetical order by lead author
NRDC-EWG Comments on Request for Relevant Information