

Response to Comments Pertaining to the Notice of Intent to List Bisphenol A as Causing Reproductive Toxicity under Proposition 65

Office of Environmental Health Hazard Assessment California Environmental Protection Agency April 2013

The Office of Environmental Health Hazard Assessment (OEHHA) listed bisphenol A (BPA) as a chemical known to cause developmental toxicity on April 11, 2013. Subsequent to the listing, on April 19, 2013, the Honorable Raymond M. Cadei issued a preliminary injunction requiring OEHHA to delist BPA, pending final resolution of the case, *American Chemistry Council v Office of Environmental Health Hazard Assessment, et al.*, Sacramento County case number 34-2013-00140720. OEHHA is posting these responses to the comments on the Notice of Intent to List BPA in order to complete the record for the April 11, 2013 listing.

On January 25, 2013, OEHHA issued a Notice of Intent to List BPA under Proposition 65¹ as a chemical known to the State to cause reproductive toxicity (developmental endpoint). The action was based on the authoritative bodies provision² of the Proposition 65 implementing regulations. Based on findings by the National Toxicology Program (NTP) in a final report from the NTP Center for the Evaluation of Risks to Human Reproduction (NTP-CERHR) that there is “clear evidence” that BPA causes developmental toxicity at “high” doses (NTP-CERHR, 2008)³, OEHHA found that BPA meets the criteria for listing provided in Title 27, Cal. Code of Regs., section 25306⁴. This document responds to comments on the Notice of Intent to List BPA under Proposition 65.

The conclusions in the 2008 NTP-CERHR report that BPA causes developmental toxicity in laboratory animals at high levels of exposure satisfy the formal identification criteria in the Proposition 65 regulations. NTP found that BPA caused decreases in litter size or number of live pups/litter in rats (Kim et al. 2001, Tyl et al. 2002b) and in mice (Morrissey et al. 1987, Tyl et al. 2002a, NTP, 1985), effects on prenatal or early postnatal growth in rats (Kim et al. 2001, Tyl et al. 2002b) and in mice (Morrissey et al. 1987, Tyl et al. 2002a, Tyl et al. 2008) and delayed puberty in male mice (Tyl et al.

¹ The Safe Drinking Water and Toxic Enforcement Act of 1986 (codified at Health and Safety Code section 25249.5 *et seq.*) hereinafter referred to as Proposition 65 or the Act.

² Title 27, Cal. Code of Regulations, section 25306.

³ See Appendix, Tab 1: National Toxicology Program – Center for the Evaluation of Risks to Human Reproduction (NTP-CERHR, 2008). NTP-CERHR Monograph on the Potential Human Reproductive and Developmental Effects of Bisphenol A. National Toxicology Program, US Department of Health and Human Services, NIH Publication No. 08 – 5994

⁴ All further references are to Title 27, California Code of Regulations unless indicated otherwise.

2008), male rats (Tyl et al. 2002b, Tan et al. 2003) and female rats (Tyl et al. 2002b, Tinwell et al. 2002). The studies NTP cited in making these findings are included in the administrative record for this action.⁵ These studies were reviewed by OEHHA with regard to the sufficiency of evidence criteria in regulation (Section 25306(g)(2)). Information reviewed for each of the cited studies included parameters related to biological plausibility, including adequacy of experimental design, pattern of dosing, route of administration, numbers of test animals, choice of species, choice of dosage levels, and maternal toxicity. On the basis of the studies, effects and species identified above, OEHHA concluded that the sufficiency-of-evidence criteria in the regulation were met.

Comments were submitted on the Notice of Intent to List BPA, on behalf of the following organizations:

- American Coatings Association (ACA)
(submitted by Alexandra Whittaker and Stephen Wieroniey)
- American Chemistry Council (Polycarbonate BPA Group) (ACC)
(submitted by Christian Volz and Stanley Landfair)
- Breast Cancer Fund (BCF)
(submitted by Jeanne Rizzo)
- Can Manufacturers Institute (CMI)
(submitted by Geoffrey Cullen)
- Consumers Union (CU)
(submitted by Urvashi Rangan)
- Grocery Manufacturers Association (GMA)
(submitted by Emilia Lonardo)
- International Formula Council (IFC)
(submitted by Mardi Mountford)
- Natural Resources Defense Council (NRDC)
(submitted by Sarah Janssen and Avinash Kar)
- North American Metal Packaging Alliance (NAMPA)
(submitted by Kathleen Roberts)

An additional two submissions were from individuals:

- U.S. Senator Dianne Feinstein
- Grace Philips

OEHHA reviewed the 11 submissions⁶ in the context of the regulatory criteria for listing chemicals under the authoritative bodies mechanism in Section 25306.

⁵ See Appendix, Tab 2A-2H.

⁶ See Appendix, Tabs 3A-3K

Many comments were similar to those submitted in response to the earlier Request for Relevant Information published on February 12, 2010. OEHHA's responses to those comments⁷ are included in the administrative record and incorporated herein by reference. Comments from the individuals and groups listed above are grouped and numbered by topic, and responses follow below.

1. Developmental and Reproductive Toxicant Identification Committee (DARTIC) Decision on BPA

Comments:

Several commenters objected to the listing of BPA based on the authoritative bodies mechanism because in July 2009, the Proposition 65 Developmental and Reproductive Toxicant Identification Committee (DARTIC) considered listing BPA, but declined to do so (ACA, ACC, CMI, GMA, IFC, NAMPA). One comment further noted that "OEHHA cannot reach exactly the opposite conclusion (as the DARTIC) with regard to the very same studies without egregiously abusing its discretion" (ACC). Some commenters noted that the DARTIC considered the same NTP-CERHR report that served as the basis for the authoritative bodies listing. (ACC, NAMPA).

One comment indicated that the findings of the DARTIC had no bearing because the authoritative bodies listing mechanism is independent of other mechanisms (NRDC).

Response:

Proposition 65 identifies four separate mechanisms for listing chemicals as reproductive toxicants. The two listing mechanisms at issue in the comments are the state's qualified experts mechanism (which provides for the DARTIC to make listing decisions on chemicals), and the authoritative bodies mechanism, which was used for the listing of BPA. Health and Safety Code section 25249.8(b) provides for both as follows:

(b) A chemical is known to the state to cause cancer or reproductive toxicity within the meaning of this chapter if in the opinion of the state's qualified experts it has been clearly shown through scientifically valid testing according to generally accepted principles to cause cancer or reproductive toxicity, **or** if a body considered to be authoritative by such experts has formally identified it as causing cancer or reproductive toxicity..." (emphasis added)

⁷ See Appendix, Tabs 4A1-4R2

The plain wording of the statute indicates that a chemical must be listed if it meets the requirements of either the state's qualified experts or authoritative bodies mechanisms. The only connection in the statute between the two mechanisms is the requirement for the state's qualified experts to identify the authoritative bodies. The statute does not create a hierarchical structure or consensus requirement among each of the listing mechanisms. The DARTIC's July 2009 determination that BPA did not meet the criteria for listing pursuant to the state's qualified experts listing mechanism does not address the entirely separate question of whether BPA meets the criteria for listing pursuant to the authoritative bodies mechanism. Thus, the state's qualified experts cannot preclude consideration and listing of a chemical via the authoritative body process.

The purpose of the authoritative bodies listing mechanism is to conserve the resources including the time and effort of the state's qualified experts. This is because the DARTIC does not need to re-evaluate chemicals for which a thorough scientific evaluation has already been conducted by another respected scientific body. Generally, the chemicals that are brought to the DARTIC are there for a *de novo* review because the chemical has not been considered by an authoritative body. In the case of BPA, the NTP-CERHR report was published during the pendency of BPA's review by the DARTIC. OEHHA could have removed the chemical from DARTIC consideration, but chose not to do so. However, as explained above, OEHHA can and indeed must consider whether BPA meets the authoritative bodies listing criteria, regardless of whether it has been reviewed by the DARTIC.⁸ Nothing in the statute or regulations allows OEHHA to ignore a chemical that may qualify for listing under the authoritative bodies mechanism simply because it has already been considered by the state's qualified experts and not listed. In fact, based on a similar set of facts, OEHHA listed the chemical hexachlorobutadiene as a carcinogen based on essentially the same information the Carcinogen Identification Committee considered in November 2000 and found it did not meet the "clearly shown" standard. OEHHA later listed the chemical in May 2011 by the Authoritative Bodies mechanism based on a US Environmental Protection Agency (US EPA) identification.

⁸ ... [W]hen designating a body as authoritative within the meaning of the statute, the DART Committee determines whether the body uses "the same or substantially the same criteria" set out in regulation 25306(g). Only if it does will it be deemed an "authoritative body." The authoritative body designation thus allows OEHHA to presume that the body made the prescribed findings when it determined a chemical to be a reproductive toxicant: "In effect, there is a presumption that the authoritative body properly applied the criteria." (*Exxon Mobil Corp. v. Office of Environmental Health Hazard Assessment et al.*, 169 Cal.App.4th 1264, 1283; discussing the Final Statement of Reasons for Section 25306, p. 25.) See Appendix, Tab 5

The DARTIC has consistently supported the use of NTP-CERHR reports to make listing decisions, including the listing of BPA. In 2002, the DARTIC designated NTP⁹ as an authoritative body for the listing of reproductive toxicants, with the restriction that it applied “solely as to final reports of the National Toxicology Program’s Center for Evaluation of Risk to Human Reproduction [NTP-CERHR].”¹⁰ In July 2011, the DARTIC unanimously rejected a petition by the Polycarbonate/BPA Global Group of the American Chemistry Council (ACC) to rescind the NTP-CERHR’s designation.¹¹ The ACC’s main argument was that NTP-CERHR reports were unsuitable for making Proposition 65 listing decisions for BPA, as well as other chemicals. In its consideration of the ACC petition, the DARTIC was well aware that OEHHA in 2010 had announced that BPA appeared to meet the criteria for listing under the authoritative bodies mechanism, based on the NTP-CERHR report.

In testimony at the July 2011 DARTIC meeting, Mr. Stanley Landfair, an attorney representing ACC, told the DARTIC¹²:

“Which leads to why did we file the petition?”

“We filed the petition because of the anomaly that came to our attention after the BPA decision two years ago. And as you recall, your Committee voted 7 to nothing, unanimously on all three toxicity endpoints to determine that BPA should not be listed as a reproductive toxin.

“That very day a petition was submitted asking the chemical to be listed versus the authoritative bodies mechanism. And now I don’t know how much you are kept abreast of what’s going on in other – now, the agency is actively considering listing the same chemical under the authoritative bodies mechanism on the basis of the same document that you reviewed so carefully and so thoroughly, with days of testimony talking in person to the people who conducted these studies, to determine whether or not the document, on its face, either concludes that BPA is a developmental toxicant or that it otherwise identifies the chemical as a reproductive toxicant.

“...It’s no insult to NTP and its expertise, but it’s a question of how this document can be used productively, consistently and authoritatively to be served as the

⁹ Title 27, Cal. Code of Regulations, section 25306.

¹⁰ See Appendix, Tab 6. Transcripts. December 4, 2002 Meeting of the Science Advisory Board’s Developmental and Reproductive Toxicant (DART) Identification Committee, see p. 136

¹¹ See Appendix, Tab 7. Transcripts. July 12, 2011 Meeting. State of California Office of Environmental Health Hazard Assessment Proposition 65 Developmental and Reproductive Toxicant Identification Committee. Available online at: http://oehha.ca.gov/prop65/public_meetings/pdf/DARTIC071211trans.pdf

¹² See Appendix, Tab 7. Transcripts. July 12, 2011 DARTIC Meeting, pp. 171-172.

authoritative bodies listing, or conversely, maybe whether it's not, and instead it should be considered by you in a forum where you have the freedom to delve down into the data and make a decision based on the data.”

Nevertheless, the DARTIC unanimously reaffirmed the NTP-CERHR's designation as an authoritative body fully understanding that its action could result in the listing of BPA based on the findings of the NTP-CERHR report.¹³ Further, the DARTIC members were provided with the Notice of Intent to List BPA via the authoritative bodies process and none of the members of the committee, nor the committee as a whole, made any objection to the listing.

OEHHA did not in any way abuse its discretion by listing BPA via the authoritative bodies mechanism. OEHHA was required to list BPA based on the findings of the NTP-CERHR report. The listing reflects the independence of the different listing mechanisms provided in Proposition 65, and is consistent with the DARTIC's decision in 2002 and reaffirmation in 2011 that NTP-CERHR reports can and should be used to list reproductive toxicants.

Comment:

One comment further noted that the DARTIC “specifically considered the NTP document in its deliberations and concluded no risk and determined that BPA should not be listed under Proposition 65” (CMI).

Response:

As a point of clarification, the DARTIC made the hazard identification decision that BPA had not been clearly shown to cause reproductive toxicity. However, it did not conclude that it posed no risk, which would have involved additional considerations outside the scope of the committee's duties.

Comment:

In discussing the 2009 decision of the DARTIC, one commenter stated that “No new information has become available that would change DARTIC's opinion” (GMA).

Response:

The DARTIC has not conducted a review of the literature released since the July 2009 meeting. A large volume of human and animal studies of BPA relevant to the consideration of DART endpoints have been released since then; some of these studies were referred to or sent in by commenters in response to the 2010 Request for Relevant

¹³ Ibid, pp. 123-205.

Information and the 2012 Notice of Intent to List.¹⁴ In anticipation of ongoing research and relevant findings, the DARTIC at its 2009 meeting requested that OEHHA further evaluate the following concerning BPA for discussion at future meetings:¹⁵

- Possible increased susceptibility for developmental toxicity from BPA in subpopulations, for example in those with poor nutritional status for certain nutrients such as folic acid
- Evidence that BPA exposures in utero or pre-conception may lead to precancerous lesions and eventually cancers (e.g., breast and prostate)
- Evidence for BPA-induced developmental- or reproductive-related neurobehavioral effects, as these endpoints are further studied
- Evidence for effects on the immune system resulting from BPA exposures during early development, as new information becomes available
- Evidence of BPA-induced developmental and reproductive effects from epidemiologic studies as new information becomes available.

2. Formal Identification Criteria

2a. NTP-CERHR REPORT COMPARED TO FORMAL IDENTIFICATION CRITERIA

Comment:

Several comments in opposition to the listing stated that NTP's conclusions or the NTP-CERHR document itself did not meet the criteria in Section 25306(d) for formal identification of the chemical as causing reproductive toxicity (ACA, ACC, GMA, NAMPA). In contrast, one commenter indicated that the formal criteria in the regulation were met (NRDC).

Response:

The regulations governing the Proposition 65 authoritative bodies listing mechanism provide the following criteria for "formally identified":

"25306(d). For purposes of this section a chemical is "formally identified" by an authoritative body when the lead agency determines that:

"(1) the chemical has been included on a list of chemicals causing cancer or reproductive toxicity issued by the authoritative body; or is the subject of a report which is published by the authoritative body and which concludes that the

¹⁴ See e.g., Appendix, Tabs 3F, 3H, 4I, and also section 3b below

¹⁵ Appendix, Tab 8, July 15, 2009 DARTIC Meeting synopsis, posted July 23, 2009, also available online at: http://www.oehha.ca.gov/prop65/public_meetings/dart071509synop.html.

chemical causes cancer or reproductive toxicity; or has otherwise been identified as causing cancer or reproductive toxicity by the authoritative body in a document that indicates that such identification is a final action; and
“(2) the list, report, or document specifically and accurately identifies the chemical, and has been:
“(A) Reviewed by an advisory committee in a public meeting, if a public meeting is required, or
“(B) Made subject to public review and comment prior to its issuance, or
“(C) Published by the authoritative body in a publication, such as, but not limited to, the federal register for an authoritative body which is a federal agency, or
“(D) Signed, where required, by the chief administrative officer of the authoritative body or a designee, or
“(E) Adopted as a final rule by the authoritative body, or
“(F) Otherwise set forth in an official document utilized by the authoritative body for regulatory purposes.”

The NTP is designated as an authoritative body for reproductive toxicity “solely as to final reports of the National Toxicology Program’s Center for Evaluation of Risks to Human Reproduction “ (Section 25306(l)(3)). The listing of BPA is based on such a document published by the NTP-CERHR and made subject to public review and comment prior to its issuance. The NTP-CERHR report also was reviewed by an advisory committee in a public meeting. In that document NTP concluded that there was *clear evidence* of adverse effects on development in laboratory animals at “high” doses of BPA. This meets the criteria contained in section 25306(d).

Comment:

Some commenters contended that NTP did not conclude that BPA causes developmental or reproductive toxicity, or that BPA does not qualify for listing because NTP-CERHR does not issue a list of chemicals (NAMPA, ACC).

Response:

Under longstanding case law, listing decisions can be made (and generally are made) based on laboratory-animal data. It is not necessary to cite human data or prove that a chemical causes adverse effects in humans in order for a chemical to be listed.¹⁶

The contention by some commenters that the report does not conclude that BPA causes developmental toxicity is apparently based on misidentification of the relevant

¹⁶ See Appendix, Tab 5, *Exxon Mobil Corp. v. Office of Environmental Health Hazard Assessment et al.*, 169 Cal.App.4th 1264, 87 Cal.Rptr.3d 580; Tab 9, *Western Crop Protection Assn. v. Davis*, 80 Cal.App.4th 741 (2000), 95 Cal.Rptr.2d 631; Tab 10, *AFL-CIO, et al., v. Deukmejian*, 212 Cal.App.3d 425, 260 Cal.Rptr. 479

conclusions in the NTP-CERHR document. For example, the ACC comments point to the following statement in the NTP-CERHR report “...the possibility that bisphenol A may alter human development cannot be dismissed.” OEHHA is not relying on this phrase to list the chemical, though it is relevant to the question whether NTP-CERHR thought the animal studies were relevant to humans (e.g. effects in humans were biologically plausible). As provided for in the regulation, OEHHA is relying on the NTP’s conclusions in the NTP-CERHR report that there is clear evidence that BPA causes developmental toxicity in laboratory animals at high doses.

Specifically, the NTP-CERHR report states:

- “These ‘high’ dose effects of bisphenol A are not considered scientifically controversial and provide **clear evidence of adverse effect on development** in laboratory animals” NTP-CERHR, p.7
- “The NTP finds that there is **clear evidence of adverse developmental effects** at ‘high’ doses of bisphenol A”... NTP-CERHR, p.7
- “High dose developmental toxicity → **Clear evidence of adverse effects**” NTP-CERHR, p.8, Figure 2b
- “The ‘high’ dose effects of bisphenol A that represent **clear evidence for adverse effects on development...**” NTP-CERHR, p.36
(emphasis added throughout)

Thus, the NTP-CERHR report concludes that there is clear evidence of adverse developmental effects in laboratory animals at ‘high’ levels of exposure. These developmental effects include decreases in litter size or number of live pups/litter in rats and mice, effects on prenatal or early postnatal growth in rats and mice, and delayed puberty in male mice and rats of both sexes, in animals exposed prenatally to BPA.

These conclusions by NTP about BPA’s effects at high doses, and the data in the report supporting the conclusions, are the basis for OEHHA’s determination that BPA meets the regulatory criteria for listing, not the NTP’s discussion of levels of concern for current or anticipated levels of human exposure. As noted, the NTP did express some concern for the effects of BPA on humans at current levels of exposure, thus indicating they believed the results of the animal studies were applicable to humans (e.g. effects in humans were biologically plausible).

Thus, the NTP-CERHR report on BPA satisfies the formal identification criteria in 25306(d). The regulatory criteria can be met, as they are here, by a report. NTP need not publish a list of reproductive toxicants.

Comment:

The NTP-CERHR BPA Monograph does not identify BPA as a reproductive toxicant in a final action (NAMPA).

Response:

Identification as causing reproductive toxicity by the authoritative body in a document that indicates that such identification is a final action is only one of three separate criteria in Section 25306(d)(1). As noted above, the parallel criterion that the chemical is the subject of a report which is published by the authoritative body and which concludes that the chemical causes reproductive toxicity has been met for BPA by the NTP-CERHR final report.

Comment:

The 2008 BPA Monograph states that the animal data provide limited evidence that BPA has adverse effects on development (NAMPA).

Response:

As noted above, the NTP-CERHR document states repeatedly that there is *clear evidence* of developmental toxicity in laboratory animals at “high” levels of exposure. This finding qualifies BPA for listing. We consider the statement that there is “clear evidence” to be equivalent to, or stronger than, the statement that there is “sufficient evidence”. As detailed above, NTP made its finding of clear evidence based on a number of positive studies.

Comment:

“OEHHA has fundamentally misinterpreted the National Toxicology Program report on BPA... It clearly and unambiguously identifies BPA as NOT causing developmental toxicity.” (ACC)

Response:

This statement is incorrect. As quoted above, the NTP-CERHR report said repeatedly that there is clear evidence of BPA’s high-dose developmental toxicity in laboratory animals.

Comment:

One comment indicated that “NTP-CERHR did not conclude that BPA causes selective reproductive toxicity.” (GMA)

Response:

Nothing in Proposition 65 or its implementing regulations requires the identification of a chemical as causing “selective reproductive toxicity”. We believe the comment is referring to the co-occurrence of maternal and developmental toxicity. This issue is

discussed in Response 3a below and in responses to comments submitted in the response to the 2010 Request for Response to Relevant Information¹⁷.

2b. CONCLUSIONS IN NTP-CERHR REPORT

Comment:

In arguing that the NTP-CERHR's report on BPA did not formally identify it as causing developmental toxicity, the ACC's comments compared the conclusions of the NTP-CERHR report on BPA to some previous NTP-CERHR reports for different chemicals that were listed under Proposition 65 by the authoritative bodies mechanism. ACC considers the differences in these conclusion statements to be cause for disregarding the conclusions about developmental toxicity in the NTP-CERHR report on BPA. ACC's comments say, "...there is an extremely important, and unavoidable, distinction between BPA and the other eight chemicals. Neither the expert panel report nor the NTP Brief document *any* development hazards for BPA." (emphasis in original)

Response:

One set of statements cited in ACC's comments relate specifically to NTP-CERHR's conclusions regarding the possible reproductive or developmental effects of chemicals on humans. In comments on BPA that focused on low-dose effects, NTP stated that "the possibility that bisphenol A may alter human development cannot be dismissed." ACC contrasted that with statements for some other chemicals that said the chemical may affect human reproduction or development "if exposures are sufficiently high." While it is not surprising that the wording of such statements differs among NTP-CERHR reports, these statements nevertheless do not form the basis for Proposition 65 listing decisions. As stated above, case law from the early years of Proposition 65 requires the listing of chemicals when the evidence in laboratory animals is adequate. Listing decisions do not take into account current exposure conditions and overall risk to humans. Consideration of exposures and risks to humans occurs after listings when businesses determine if they must provide warnings. The NTP-CERHR statements that form the basis for listing decisions are those the NTP makes regarding the weight of evidence that the chemical causes reproductive or developmental effects in laboratory animals or humans.

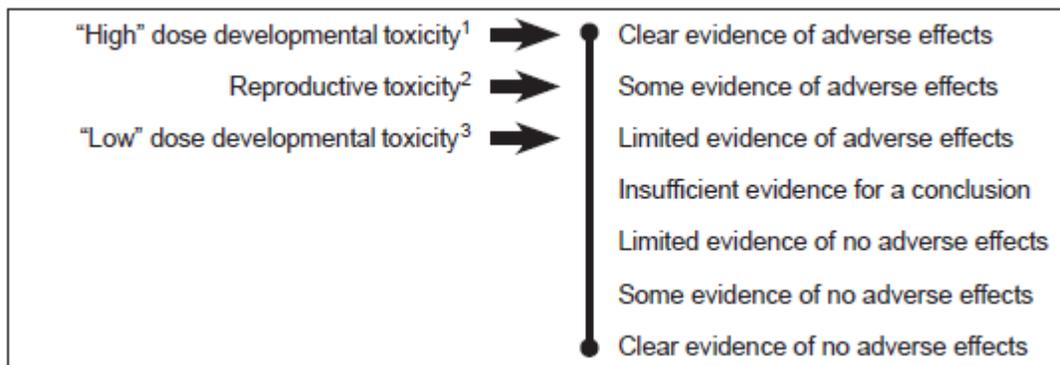
ACC also compared statements on various chemicals made by past expert panels. However, NTP itself is the authoritative body and its weight-of-evidence statements are

¹⁷ See e.g., Appendix, Tab 4E2, OEHHA January 2013 responses to comments of Rochelle W. Tyl, page 7. Also available online at: http://oehha.ca.gov/prop65/CRNR_notices/admin_listing/requests_info/extendedcallinbpa032310.html#comments

instructive. These weight-of-evidence statements are critical to understanding the basis for listing BPA.

Each NTP-CERHR report includes a figure showing NTP's weight-of-evidence conclusions that a given chemical causes adverse developmental and/or reproductive effects in laboratory animals. The specific figure pertaining to BPA¹⁸ is provided below as an example (See labeled "Figure 2b," below). The figure identifies six conclusions that NTP can draw about the evidence for developmental toxicity, reproductive toxicity in males and reproductive toxicity in females. A seventh category is also identified for cases where NTP determines that there is insufficient evidence for a conclusion.

"Figure 2b. The weight of evidence that bisphenol A causes adverse developmental or reproductive effects in laboratory animals." (Figure with footnotes reproduced from NTP-CERHR, 2008)



¹Based on reduced survival in fetuses or newborns (≥ 500 mg/kg bw/day) (36 – 40), reduced fetal or birth weight or growth of offspring early in life (≥ 300 mg/kg bw/day) (36, 37, 41), and delayed puberty in female rats (≥ 50 mg/kg bw/day) and male rats and mice (≥ 50 mg/kg bw/day) (37, 41 – 43).

²Based on possible decreased fertility in mice (≥ 875 mg/kg bw/day) (40); altered estrous cycling in female rats (≥ 600 mg/kg bw/day) (110), and cellular effects on the testis of male rats (235 mg/kg bw/day) (111).

³Based a variety of effects related to neural and behavior alterations (≥ 10 μ g/kg bw/day) (44 – 50), lesions in the prostate (10 μ g/kg bw/day) (51) and mammary glands (0.0025 – 1 mg/kg bw/day) (52, 53); altered prostate gland and urinary tract development (10 μ g/kg bw/day) (54), and early onset of puberty (2.4 and 200 μ g/kg bw/day) (48, 55).

This figure clearly shows that if "insufficient evidence for a conclusion" is not selected, the other choices are necessarily conclusions based on the weight of the evidence. In addition, OEHHA does not just rely on the words from this figure for its finding that BPA

¹⁸ From the NTP-CERHR report, page 8. Available in Appendix Tab 1 and online at <http://ntp.niehs.nih.gov/ntp/ohat/bisphenol/bisphenol.pdf>

has been formally identified as causing developmental toxicity. As noted above, this conclusion is discussed and reiterated throughout the NTP report. Further, the NTP-CERHR report cites as the basis for this conclusion a number of developmental effects, as cited in Footnote 1 of Figure 2b (reproduced above).

Below is a table that includes language that satisfies the formal identification criteria specified in Section 25306(d) extracted from the NTP-CERHR BPA report, as well as from eight other NTP-CERHR reports on chemicals listed under Proposition 65 as causing reproductive toxicity via the authoritative bodies process¹⁹.

CHEMICAL (year listed under Proposition 65)	LANGUAGE FROM NTP-CERHR REPORT
Bisphenol A ²⁰ NTP-CERHR, 2008 (listed in 2013)	<p>“High’ dose developmental toxicity¹ → Clear evidence of adverse effects” (p. 8, Figure 2b)</p> <p>“... studies with laboratory rodents show that exposure to high dose levels of bisphenol A during pregnancy and/or lactation can reduce survival, birth weight, and growth of offspring early in life, and delay the onset of puberty in males and females. These effects were seen at the same dose levels that also produced some weight loss in pregnant animals (“dams”). These “high” dose effects of bisphenol A are not considered scientifically controversial and provide clear evidence of adverse effects on development in laboratory animals.” (pp. 6-7)</p> <p>“The NTP finds that there is clear evidence of adverse developmental effects at ‘high’ doses of bisphenol A...” (p.7)</p> <p>“The ‘high’ dose effects of bisphenol A that represent clear evidence for adverse effects on development...” (p. 36)</p> <p>“These [animal] studies provide clear evidence for adverse effects on development, but occur at exposure levels far in excess of those experienced by humans.” (p. 39) [emphasis added throughout]</p> <hr/> <p>¹ Based on reduced survival in fetuses or newborns (≥ 500 mg/kg bw/day) (36 – 40), reduced fetal or birth weight or growth of offspring early in life (≥ 300 mg/kg bw/day) (36, 37, 41), and delayed puberty in female rats (≥ 50 mg/kg bw/day) and male rats and mice (≥ 50 mg/kg bw/day) (37, 41 – 43)”.</p>

¹⁹ These chemicals were the subject of Tables 1 and 2 of the ACC comments submitted on the Notice of Intent to List BPA, which is in the Appendix, Tab 3B.

²⁰ See Appendix, Tab 1 pp. 1-39.

<p>Acrylamide²¹ NTP-CERHR, 2005 (listed in 2011)</p>	<p>“Developmental and reproductive toxicity² → Clear evidence of adverse effects” (p. 2, Figure 2) “...studies reviewed by the expert panel show that oral exposure of laboratory animals to high amounts of acrylamide can adversely affect reproduction and development (Figure 2).” (p. 2) “In this case, recognizing the absence of human data and clear evidence of adverse effects [on development and reproduction] in laboratory animals (Figure 2), the NTP judges the scientific evidence sufficient to conclude that acrylamide may adversely affect human development and/or reproduction if exposures are sufficiently high.” (pp. 2-3) [emphasis added throughout] . ² Reproductive effects in male mice and rats.”</p>
<p>1-Bromopropane²² NTP-CERHR, 2003 (listed in 2004)</p>	<p>“Developmental and reproductive toxicity → Clear evidence of adverse effects” (p. 2, Figure 2) “...studies reviewed by the expert panel and more recent studies in rats show that exposure to 1-BP can adversely affect reproduction and development (Fig. 2).” (p.2) “...the NTP judges the scientific evidence of effects in laboratory animals sufficient to conclude that 1-BP may adversely affect human development and reproduction if exposures are sufficiently high.” (p. 2) [emphasis added throughout]</p>

²¹ See Appendix, Tab 11A, NTP-CERHR, 2005. NTP-CERHR Monograph on the Potential Human Reproductive and Developmental Effects of Acrylamide. NIH Publication No. 05 – 4472, available online at http://ntp.niehs.nih.gov/ntp/ohat/acrylamide/Acrylamide_Monograph.pdf

²² Appendix, Tab 11B, NTP-CERHR, 2003. NTP-CERHR Monograph on the Potential Human Reproductive and Developmental Effects of 1-Bromopropane. NIH Publication No. 04 – 4479, available online at http://ntp.niehs.nih.gov/ntp/ohat/bromopropanes/1-bromopropane/1BP_monograph.pdf

<p>2-Bromopropane²³ NTP-CERHR, 2003 (listed in 2005)</p>	<p>“Reproductive toxicity (> 100 ppm) → Clear evidence of adverse effects” (p. 2, Figure 2) “There is evidence that human exposure to 2-BP causes reproductive toxicity in both males and females. However, the small number of exposed individuals and uncertainties in exposure levels preclude a definitive answer. Studies reviewed by the expert panel and more recent studies clearly show that exposure to 2-BP can adversely affect the reproductive system of rodents (Figure 2).” (p. 1) “Studies reviewed by the expert panel and more recent studies clearly show that exposure to 2-BP can adversely affect the reproductive system of rodents (Figure 2).” (p. 1) “Recognizing the limited evidence of reproductive effects in occupationally exposed humans and clear evidence of effects in laboratory animals, the NTP judges the scientific evidence sufficient to conclude that 2-BP may adversely affect human reproduction if exposures are sufficiently high.” (p. 1) [emphasis added throughout]</p>
<p>Butyl Benzyl phthalate²⁴ (BBP) NTP-CERHR, 2003 (listed in 2005)</p>	<p>“Developmental toxicity→Clear evidence of adverse effects” (p. 2, Figure 2) “Although there is no direct evidence that exposure of people to BBP adversely affects reproduction or development, studies reviewed by the expert panel and subsequently published studies with laboratory rodents show that exposure to BBP can adversely affect development, including development of the male reproductive tract. (Fig. 2)” (p. 2) [emphasis added throughout]</p>

²³ See Appendix, Tab 11C, NTP-CERHR, 2003. NTP-CERHR Monograph on the Potential Human Reproductive and Developmental Effects of 2-Bromopropane. NIH Publication No. 04 – 4480, available online at http://ntp.niehs.nih.gov/ntp/ohat/bromopropanes/2-bromopropane/2BP_Monograph.pdf

²⁴ Appendix, Tab 11D, NTP-CERHR, 2003. NTP-CERHR Monograph on the Potential Human Reproductive and Developmental Effects of Butyl Benzyl Phthalate. NIH Publication No. 03-4487, available online at http://ntp.niehs.nih.gov/ntp/ohat/phthalates/bb-phthalate/BBP_Monograph_Final.pdf, pp. 1-5

<p>Di-n-butyl phthalate (DBP)²⁵ NTP-CERHR, 2003 (listed in 2005)</p>	<p>“Developmental and reproductive toxicity → Clear evidence of adverse effects” (p. 2, Figure 2) “Although there is no direct evidence that exposure of people to DBP adversely affects reproduction or development, studies with laboratory rodents show that exposure to DBP can cause adverse effects (Fig. 2).” (p. 2) “In this case, recognizing the lack of human data and the clear evidence of effects in laboratory animals (Fig. 2), the NTP judges the scientific evidence sufficient to conclude that DBP may adversely affect human reproduction or development if exposures are sufficiently high.” (p. 2) [emphasis added throughout]</p>
<p>Di-n-hexyl phthalate (DnHP)²⁶ NTP-CERHR, 2003 (listed in 2005)</p>	<p>“Reproductive Toxicity→Clear evidence of adverse effects” (p. 2, Figure 2) “Although there is no direct evidence that exposure of people to DnHP adversely affects reproduction or development, a few studies with mice and rats show that exposure to DnHP can cause adverse developmental and reproductive effects. (Fig. 2)” (p. 1) [emphasis added throughout]</p>
<p>Di-isodecyl phthalate (DIDP)²⁷ NTP-CERHR, 2003 (listed in 2007)</p>	<p>“Developmental Toxicity → Clear evidence of adverse effects” (p. 2, Figure 2) “Although there is no direct evidence that exposure of people to DIDP adversely affects reproduction or development, studies with rats have shown that exposure to DIDP can cause adverse developmental effects, but it does not affect reproduction. (Fig. 2)” (p. 1) [emphasis added throughout]</p>

²⁵ See Appendix, Tab 11E, NTP-CERHR, 2003. NTP-CERHR Monograph on the Potential Human Reproductive and Developmental Effects of Di-n-Butyl Phthalate, available online at http://ntp.niehs.nih.gov/ntp/ohat/phthalates/dbp/DBP_Monograph_Final.pdf.

²⁶ See Appendix, Tab 11F, NTP-CERHR, 2003. NTP-CERHR Monograph on the Potential Human Reproductive and Developmental Effects of Di-n-Hexyl-Phthalate, NIH Publication No. 03-4489, available online at http://ntp.niehs.nih.gov/ntp/ohat/phthalates/dnhp/DnHP_Monograph_Final.pdf

²⁷ See Appendix, 11G, NTP-CERHR, 2003. NTP-CERHR Monograph on the Potential Human Reproductive and Developmental Effects of Di-Isodecyl Phthalate (DIDP). NIH Publication No. 03-4485, pp 1-5, available online at http://ntp.niehs.nih.gov/ntp/ohat/phthalates/didp/DIDP_Monograph_Final.pdf

Methanol ²⁸ NTP-CERHR, 2003 (listed in 2012)	<p>“Developmental Toxicity → Clear evidence of adverse effects” (p. 2, Figure 2)</p> <p>“Laboratory animal studies reviewed by the expert panel, and an additional published study using cultured mouse embryos, show that methanol can adversely affect development (Figure 2).” (p. 2)</p> <p>“In this case, recognizing the lack of human data and the clear evidence of laboratory animal effects (Figure 2), the NTP judges the scientific evidence sufficient to conclude that methanol may adversely affect human development if exposures are sufficiently high.” (p. 2) [emphasis added throughout]</p>
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In the case of BPA, NTP made different weight-of-evidence conclusions for “high” dose and “low” dose effects for developmental toxicity. For 2-bromopropane (a chemical listed under Proposition 65 in 2005 based on an NTP-CERHR report), NTP found clear evidence of reproductive toxicity at air concentrations above 100 parts per million. For several other chemicals, NTP made “clear evidence” findings without any qualifying statements about dose levels or air concentrations. As discussed above, OEHHA considers the weight-of-evidence conclusions in the BPA document to be functionally identical to those in other NTP-CERHR documents used as the basis for listing other chemicals under Proposition 65.

Comment:

ACC identifies the level-of-concern for human exposures conclusions contained in Figure 3 on page 8 of the NTP-CERHR report as the only conclusions of the report. Other commenters also stated that NTP-CERHR does not provide a conclusion or determination of developmental toxicity but instead expresses levels of concern (NAMPA, GMA), as stated in Figure 3. They say the level of concern does not meet the criterion for formal identification.

Response:

Since NTP’s level-of-concern conclusions related to humans take into account what is known about current or anticipated levels of human exposure, not just the weight-of-evidence for reproductive and developmental toxicity, they are not relevant to formal identification for listing a chemical under the Proposition 65 authoritative bodies mechanism. Levels of human exposure are, of course, important. Human exposures can be considered under Section 25821 to determine whether or not a given exposure

²⁸ Appendix, Tab 11H, NTP-CERHR, 2003. NTP-CERHR Monograph on the Potential Human Reproductive and Developmental Effects of Methanol. NIH Publication No. 03-4478, available online at http://ntp.niehs.nih.gov/ntp/ohat/methanol/Methanol_Monograph.pdf

requires a warning. In fact, OEHHA had already proposed a “safe harbor” level for BPA for adoption into Section 25805 to assist businesses in determining which exposures may require a Proposition 65 warning.²⁹ That rulemaking has been temporarily withdrawn pending the outcome of the *American Chemistry Council v Office of Environmental Health Hazard Assessment, et al.*, (Sacramento County case number 34-2013-00140720) challenge to the listing of BPA.

The contention that the only conclusions of the NTP-CERHR documents relate to levels of concern is not consistent with NTP’s own statements about its evaluation process. In a presentation to the DARTIC on July 12, 2011, Dr. John Bucher, Associate Director of NTP, described two phases of the NTP-CERHR process, each of which results in conclusions:³⁰

“CERHR evaluated selected chemicals, agents, mixtures, or exposure circumstances based on production volume, the potential for human exposure and the extent of public concern, and the extent of available literature with data that were applicable to an evaluation of reproductive and developmental hazard.”

“These have been published as NTP-CERHR monographs that assess the evidence, whether the environmental substance causes adverse effects on reproduction and development, which as you heard earlier, is the Phase 1, the hazard identification phase of the document.”

“And secondly, the second phase is to provide an opinion on whether these substances may be of concern, given what is known about current human exposure levels. And these are the levels of concern statements that are developed...”

“As you saw in one of the slides previously, the hazard identification portion of this used a seven point hazard identification scale, weighting the evidence from both human and experimental animal data. And these were considered ***independently***. And then the conclusions are reached on a case-by-case basis.” (emphasis added)

²⁹ See Appendix, Tab 12A-12B, Notice of Proposed Rulemaking and Initial Statement of Reasons to establish a maximum allowable dose level for Bisphenol A.

³⁰ See Appendix, Tab 7, pp. 142-143. Transcripts. July 12, 2011 Meeting. State of California Office of Environmental Health Hazard Assessment Proposition 65 Developmental and Reproductive Toxicant Identification Committee, Available online at: http://oehha.ca.gov/prop65/public_meetings/pdf/DARTIC071211trans.pdf

This seven-point hazard identification scale allows NTP to choose from a range of options including a finding that there is “insufficient evidence for a conclusion”. Each of the other options, ranging from “clear evidence of adverse effects” to “clear evidence of no adverse effects” represents a determination by NTP that there is sufficient information to draw a conclusion about the weight of the evidence. The statement that there is “clear evidence of adverse effects” for high-dose developmental toxicity of BPA constitutes NTP’s conclusion about the weight of the evidence of the hazard presented by the chemical, and meets the requirements of Section 25306(d)(1). In addition, when NTP presented the BPA report to the NTP Board of Scientific Counselors for peer review on June 11, 2008³¹, it included in the presentation a figure essentially identical to Figure 2b in the final NTP report, with the same hazard conclusion in the narrative. That figure and the summary minutes reflect NTP’s conclusion concerning the weight of evidence for each relevant endpoint, including clear evidence of adverse effects for “high” dose developmental toxicity. This was explicitly presented as NTP’s conclusions about the weight of evidence.

Comment:

The lack of definitive conclusions in the NTP-CERHR reports was identified by the DARTIC in 2002 when they initially deliberated as to whether NTP-CERHR should be considered an authoritative body (NAMPA).

Response:

At its December 4, 2002 meeting, the DARTIC discussed several aspects of the process followed by NTP-CERHR, the content of the documents prepared by NTP-CERHR and the applicability of the findings in those documents to the authoritative bodies listing mechanism³². Following that discussion, the DARTIC voted unanimously to designate NTP as an authoritative body solely as to final reports of the NTP-CERHR. In a meeting of the DARTIC on July 12, 2011, the Committee considered a petition to rescind the designation of NTP-CERHR as an authoritative body, because of the proposed listing of BPA via that report. After extensive discussion of the relevant issues, including the conclusions drawn in the NTP-CERHR final reports, the DARTIC voted unanimously to retain NTP as an authoritative body, solely as to final reports of the NTP-CERHR³³.

³¹ See Appendix, Tab 13, Documents related to the NTP Board of Scientific Counselors peer review of Bisphenol A at their June 11, 2008 meeting, including summary minutes for the June 11 meeting and presentations.

³² See Appendix, Tab 6, Transcripts. December 4, 2002 Meeting of the Science Advisory Board’s Developmental and Reproductive Toxicant (DART) Identification Committee, pp. 100-136.

³³ See Appendix, Tab 7, Transcripts. July 12, 2011 Meeting, pp. 128-205. State of California Office of Environmental Health Hazard Assessment Proposition 65 Developmental and Reproductive Toxicant

Comment:

The statement of “clear evidence” of the high-dose developmental toxicity of BPA in Figure 2b of the NTP-CERHR is not a conclusion on BPA’s hazards, but instead is simply a summary of the data contained in the individual studies reviewed by NTP-CERHR’s expert panel (ACC). “Extracting isolated statements from one part of the Monograph without the context and detail provided by the full Monograph is inappropriate,” ACC said in its comments.

Response:

The NTP-CERHR report identifies its “clear evidence” statement as a determination made by the agency, and provides no basis for the commenter’s assertion that it is merely a summary of available data. As indicated above, Figure 2b³⁴ is entitled, “**The weight of evidence** that bisphenol A causes adverse developmental or reproductive effects in laboratory animals” (emphasis added). “Weight of evidence” is a long-established and well-understood term in epidemiology and toxicology. In a weight of evidence evaluation, scientists attempt to reach conclusions as to whether a chemical may cause a given health effect by evaluating and considering (or, in other words, weighing) the available scientific data suggesting that a chemical does or does not cause that health effect. The NTP-CERHR report supports this common meaning of the term on page 9 by stating, “Scientific decisions concerning health risks are generally based on what is known as the ‘weight of evidence’.” In the pages following that statement, the NTP-CERHR report discusses the strengths, weaknesses and limitations of various BPA studies, as typically occurs during a weight of evidence evaluation.

Given its preeminence in toxicology and its explicit acknowledgment of the significance of “weight of evidence”, NTP-CERHR simply could not have used that term in the title of Figure 2b unless the statements in the figure reflected the agency’s conclusions following a careful evaluation of all the data taken together.

2c. EXPERT PANEL REPORT

Comment:

One commenter stated it based its conclusion that NTP did not formally identify BPA as a reproductive toxicant “in part on the Expert Panel Report that is appended to the NTP monograph, and which does not conclude that there is clear evidence of developmental toxicity.” The commenter also argued that the NTP-CERHR report is a “shorter

Identification Committee, Available online at:
http://oehha.ca.gov/prop65/public_meetings/pdf/DARTIC071211trans.pdf

³⁴ NTP-CERHR (2008), page 8, see Appendix, Tab 1.

summary document” of the expert panel report and is “specifically designed” to follow the expert panel report (ACC).

Response:

With regard to the ACC’s contention, it is explicitly NTP and not the expert panel that is designated as the authoritative body. The expert panel report contains a specific disclaimer regarding the relationship between the conclusions by the expert panel and those of NTP, as follows:

“The findings and conclusions of this report are those of the Expert Panel and should not be construed to represent the views of the National Toxicology Program. Members of this panel participated in the evaluation of bisphenol A as independent scientists. The findings and conclusions in this report are those of the authors and do not necessarily represent the views of their employers.”

It should also be noted that designation of the Expert Panel as the authoritative body was specifically considered and rejected in 2002 by the DARTIC when it designated “the National Toxicology Program solely as to final reports of the National Toxicology Program’s Center for Evaluation of Risks to Human Reproduction” as an authoritative body. This is illustrated by excerpts from the transcript of the DARTIC meeting of December 4, 2002:³⁵

Dr. Burk: “...it sort of makes sense to pick the Center rather than the expert panel” (page 127)

Dr. Miller: “...the expert panel produces the draft report, and they’re not the Center, because the expert panel changes from chemical review to chemical review. I think we’re approving the final report from NTP/CERHR.” (page 132)

Dr. Denton (OEHHA Director and Executive Secretary to the DARTIC): “...is there a motion to designate NTP as an authoritative body, but only as to final reports of the CERHR?” (page 136)

The DARTIC voted unanimously on the motion to approve NTP-CERHR, rather than the Expert Panel, as a Proposition 65 authoritative body for reproductive toxicity.

Lastly, the NTP-CERHR report explicitly says that it is not merely a summary document of the expert panel report. In the Introduction section, NTP-CERHR says the report “is based on information about bisphenol A provided in the expert panel report, public comments, comments from peer reviewers and additional scientific information available since the expert panel meeting.”³⁶ Thus, the NTP-CERHR report is clear that the expert

³⁵ Appendix, tab 6, 2002 DARTIC meeting transcripts, pp. 127, 132, 136

³⁶ NTP-CERHR, 2008, p. ix, see Appendix, Tab 1

panel report is not the only source of information considered by NTP-CERHR, and that the NTP-CERHR report does not simply summarize the expert panel report.

3. Sufficiency of evidence

Several commenters in opposition to the listing stated that the scientific criteria for listing via the authoritative bodies mechanism in Section 25306(g) as causing reproductive toxicity were not met by the NTP-CERHR report (ACC, GMA, CMI). One commenter stated that the scientific criteria in regulation were met (NRDC). These comments are further discussed below.

3a. MATERNAL TOXICITY

Comment:

Some commenters argued that the high-dose findings of reproductive toxicity in the studies serving as the basis for NTP's conclusions were due to maternal toxicity, and were not likely indicative of reproductive or developmental toxicity (CMI, ACC, GMA). For example, GMA refers to a statement by Dr. Tyl that "Reproductive or developmental effects occur only at very high BPA doses in the presence of profound maternal toxicity. ... it is apparent that maternal toxicity is the most likely critical determinant of embryo-fetal/offspring toxicity..."

ACC presented several quotes concerning maternal toxicity from previous comments submitted in 2010 in response to OEHHA's Request for Relevant Information by Drs. Tyl, Scialli, Kimmel and Lamb and appended a January 2012 letter to OEHHA from Drs. Tyl, Scialli, Kimmel and Lamb.³⁷ These comments stated:

"OEHHA's selection of the NTP-CERHR statement that "there is clear evidence of adverse developmental effects at 'high doses' of BPA' in the form of fetal death, decreased litter size..." does not account for the maternal toxicity seen at these high dose levels."

GMA stated that "BPA is not a selective reproductive or developmental toxicant" and referenced comments by Dr. Tyl submitted in the 2010 request for relevant information.³⁸

³⁷ See Appendix, Tab 3B1.

³⁸ See Appendix, Tab 4E1.

Response:

The regulations governing the Proposition 65 authoritative bodies listing mechanism provide the following criteria for “as causing reproductive toxicity”:

“25306 (g) For purposes of this section, “as causing reproductive toxicity” means that either of the following criteria have been satisfied:

“(1) Studies in humans indicate that there is a causal relationship between the chemical and reproductive toxicity, or

“(2) 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, numbers 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.”

However, the chemical is not listed if scientifically valid data which were not considered by the authoritative body clearly establish that the sufficiency of evidence criteria were not met (Section 25306(h)).

OEHHA carefully considered the comments provided by Drs. Tyl, Scialli, Kimmel and Lamb in 2010 and 2012 on maternal toxicity in considering the sufficiency of evidence in the NTP-CERHR report before listing the chemical. As stated in OEHHA’s January 2013 responses to comments on the Request for Relevant Information on BPA³⁹ and discussed below, OEHHA has determined that this information was not persuasive on this point.

As noted in the GMA comment, Dr. Tyl’s discussion was intended to support her conclusions that BPA is not a “selective developmental toxicant” and that “developmental toxicity occurs only at very high oral BPA doses in the presence of profound maternal toxicity”⁴⁰. Drs. Kimmel and Lamb also phrased their analysis in terms of “specific or selective developmental toxicity”. However, Proposition 65 requires the listing of chemicals that cause developmental toxicity, and is not limited to “selective developmental toxicants”.

CMI states that high-dose effects are indicative of maternal toxicity rather than developmental toxicity. OEHHA relies on generally accepted scientific principles

³⁹ See Appendix, Tab 4 Also available online at http://www.oehha.ca.gov/prop65/CRNR_notices/admin_listing/requests_info/extendedcallinbpa032310.html

⁴⁰ ACC comments, page 17. See Appendix, Tab 3B.

including scientific guidelines published by authoritative organizations like US EPA. The topic of the relationship between maternal and developmental toxicity has been carefully considered by regulatory agencies and broadly discussed in the peer-reviewed literature, as reviewed by OEHHA in its January 2013 response to Dr. Tyl's comments.⁴¹

Examples of discussion of these scientific principles from authoritative scientific agencies:

“Agents that produce developmental toxicity at a dose that is not toxic to the maternal animal are especially of concern because the developing organism is affected but toxicity is not apparent in the adult. However, the more common situation is when adverse developmental effects are produced only at doses that cause minimal maternal toxicity; in these cases, the developmental effects are still considered to represent developmental toxicity and should not be discounted as being secondary to maternal toxicity. At doses causing excessive maternal toxicity (that is, significantly greater than the minimal toxic dose [defined elsewhere in the guidelines to be marginal but significantly reduced body weight, reduced weight gain, or specific organ toxicity, and at the most no more than 10% mortality]), information on developmental effects may be difficult to interpret and of limited value. Current information is inadequate to assume that developmental effects at maternally toxic doses result only from maternal toxicity; rather, when the LOAEL is the same for the adult and developing organisms, it may simply indicate that both are sensitive to that dose level. Moreover, whether developmental effects are secondary to maternal toxicity or not, the maternal effects may be reversible while effects on the offspring may be permanent.” US EPA (1991) Guidelines for Developmental Toxicity Risk Assessment.⁴²

“Developmental effects, which occur even in the presence of maternal toxicity are considered to be evidence of developmental toxicity, unless it can be unequivocally demonstrated on a case by case basis that the developmental effects are secondary to maternal toxicity.” United Nations Economic Commission for Europe Globally Harmonized System of Classification and Labeling of Chemicals (Section 3.7.2.4.2, 2011)⁴³

An example from a scientific expert in the peer-reviewed literature:

⁴¹ See Appendix, Tab 4E2.

⁴² See Appendix Tab 14, U.S. Environmental Protection Agency, Guidelines for Developmental Toxicity Risk Assessment, EPA/600/FR-91/001, December 1991,

⁴³ See Appendix, Tab 15, UN Economic Commission for Europe Globally Harmonized System of Classification and Labeling of Chemicals, Part 3, Health Hazards, section 3.7.2.4.2. p. 176, also available online at: http://www.unece.org/fileadmin/DAM/trans/danger/publi/ghs/ghs_rev04/English/ST-SG-AC10-30-Rev4e.pdf

“There currently remains a considerable burden of proof lying with the investigator if developmental effects are suspected to be secondary to altered maternal physiology. This burden is justifiable in that maternal toxicity is not always associated with developmental toxicity. Thus a cause and effect relationship between the two is not automatic.” Carney, 1997.⁴⁴

Quote from Dr. John Bucher, associate director of NTP:

“I think when the literature are initially [e]valuated by the expert panel and by the NTP, we take into consideration maternal toxicity, in essence weighing the influence that the outcome would have on the overall determination. So I don’t think that we have a statement anywhere that specifies exactly how one would utilize information with maternal toxicity but is taken into consideration.....I’m sympathetic with the problems that maternal toxicity presents in interpreting these studies. And all I can say is that we recognize this. When we designed the evaluation criteria for our own NTP developmental and reproductive toxicity studies, we have, in fact, taken into consideration how maternal toxicity might figure into an overall evaluation.”⁴⁵

OEHHA included all the generally-accepted endpoints in its consideration of maternal toxicity in reviewing the NTP-CERHR report and the studies cited in the report. The following list of endpoints considered by OEHHA is drawn from the U.S. EPA (1991) Guidelines for Developmental Toxicity Risk Assessment (pp 8-9)⁴⁶:

- Mortality
- Mating index [(no. with seminal plugs or sperm/no. mated) × 100]
- Fertility index [(no. with implants/no. of matings) × 100]
- Gestation length (useful when animals are allowed to deliver pups)
- Body weight
 - Day 0
 - During gestation
 - Day of necropsy
- Body weight change
 - Throughout gestation
 - During treatment (including increments of time within treatment period)
 - Post-treatment to sacrifice
 - Corrected maternal (body weight change throughout gestation minus gravid

⁴⁴ See Appendix, Tab 16, Carney, E. (1997). Maternal physiological disruption. Drug Toxicity in Embryonic Development. Kavlock RJ and Daston GP. New York, Springer. 1: 573-594.

⁴⁵ See Appendix, Tab 7, Transcripts. July 12, 2011 DARTIC Meeting. , pp 153-155, also available online at http://www.oehha.ca.gov/prop65/public_meetings/pdf/DARTIC071211trans.pdf

⁴⁶ See Appendix, Tab 14, US EPA Guideline for Developmental Toxicity Risk Assessment, 1991

- uterine weight or litter weight at sacrifice)
- Organ weights (in cases of suspected target organ toxicity and especially when supported by adverse histopathology findings)
 - Absolute
 - Relative to body weight
 - Relative to brain weight
- Food and water consumption (where relevant)
- Clinical evaluations
 - Types, incidence, degree, and duration of clinical signs
 - Enzyme markers
 - Clinical chemistries
- Gross necropsy and histopathology

No factual information demonstrating that the developmental effects in the high-dose studies utilized by NTP-CERHR were secondary to maternal toxicity was submitted to OEHHA by any commenter. OEHHA has completed a determination of sufficiency of evidence including “consideration of maternal toxicity”, and has determined that the maternal toxicity occurring in this case is not sufficient to discount the chemical’s effects on the fetus. OEHHA recognizes the qualifications of the experts who submitted their scientific judgments and interpretations of the data relied upon by NTP. However, OEHHA is required by the regulations and case law to accept the scientific judgment of the authoritative body unless there is factual information which demonstrates that the regulatory criteria have not been met.

3b. SCIENTIFICALLY VALID DATA NOT CONSIDERED BY THE AUTHORITATIVE BODY

Comment:

Section 25306(h) says a chemical may not be listed via the authoritative bodies mechanism “if scientifically valid data which were not considered by the authoritative body clearly establish that the chemical does not satisfy” the sufficiency criteria. It was also stated that recent studies of BPA pharmacokinetics establish the lack of biological plausibility for its effects in humans (GMA). Comments refer to studies on BPA pharmacokinetics and physiological differences between rodents and primates.

In contrast, another commenter provided citations to several human studies published since the 2008 NTP-CERHR report that found evidence of BPA exposure causing adverse birth outcomes (NRDC). In an attachment, the commenter also refers to a 2010

study in animals consistent with NTP-CERHR's conclusion of developmental toxicity at "high" doses (NRDC).

Response:

The relevant regulatory provision, Section 25306(h) states:

"(h) The lead agency shall find that a chemical does not satisfy the definition of "as causing reproductive toxicity" if scientifically valid data which were not considered by the authoritative body **clearly establish** that the chemical does not satisfy the criteria of subsection (g), paragraph (1) or subsection (g), paragraph (2)." (emphasis added)

Scientific data concerning BPA's developmental toxicity continue to appear in the literature. There have been a number of recent human studies reporting reproductive toxicity endpoints with positive findings. Some were submitted in response to the Notice of Intent to List.⁴⁷ Pharmacokinetic and developmental toxicity studies described as "FDA" studies published are discussed by GMA and used as support for their statement that there is a lack of biological plausibility between BPA exposure and adverse reproductive outcomes⁴⁸.

Studies of most relevance to the authoritative bodies findings in the NTP-CERHR report are those conducted at the "high doses" described by NTP-CERHR in their identification of BPA as a developmental toxicant. The direct relevance of the low-dose studies as "valid data not considered by the authoritative body" is limited. This applies in particular to the developmental toxicity study described by Dr. Hentges on p. 3 of his September 2011 letter to Dr. Alexeeff. This study was conducted at doses of 0, 2.5 or 25 µg/kg-d in rats as opposed to doses ≥ 50 mg/kg-d characterized as "high" in the NTP-CERHR report.

⁴⁷ See Appendix, Tab 3H2-3H14.

⁴⁸ See Appendix, Tab 17 for GMA cited references of Doerge and colleagues:

Doerge, D. R., M. Vanlandingham, N. C. Twaddle and K. B. Delclos (2010). "Lactational transfer of bisphenol A in Sprague-Dawley rats." Toxicol Lett **199**(3): 372-376.

Doerge, D. R., N. C. Twaddle, M. Vanlandingham, R. P. Brown and J. W. Fisher (2011). "Distribution of bisphenol A into tissues of adult, neonatal, and fetal Sprague-Dawley rats." Toxicol Appl Pharmacol **255**(3): 261-270.

Doerge, D. R., N. C. Twaddle, K. A. Woodling and J. W. Fisher (2010). "Pharmacokinetics of bisphenol A in neonatal and adult rhesus monkeys." Toxicol Appl Pharmacol **248**(1): 1-11.

Doerge, D. R., N. C. Twaddle, M. Vanlandingham and J. W. Fisher (2010). "Pharmacokinetics of bisphenol A in neonatal and adult Sprague-Dawley rats." Toxicol Appl Pharmacol **247**(2): 158-165.

OEHHA has reviewed the four pharmacokinetic studies cited by GMA and also six additional BPA pharmacokinetic studies from the same research group⁴⁹. OEHHA has concluded that these studies do not demonstrate a lack of biological plausibility as described in Proposition 65 regulations. The studies demonstrate that BPA is rapidly distributed and metabolized after oral exposure, but that un-metabolized BPA reaches the fetal circulation and tissues when administered to pregnant rodents. Studies of fetal exposure to BPA after oral administration to pregnant monkeys were not conducted. Studies with intravenous exposure of pregnant monkeys to BPA showed distribution to the fetal circulation and fetal tissues.

The conclusions of these studies involve “interpretation of blood monitoring studies,” an issue highlighted by NTP in Appendix A in its report⁵⁰ along with the issue of species differences between rats and humans in enterohepatic circulation of BPA.

In the recent pharmacokinetic studies, data were gathered making it possible to compare metabolism of BPA in rats, mice and nonhuman primates. The authors⁵¹ conclude:

Despite major differences in BPA metabolism and disposition between rodents (enterohepatic recirculation and extensive fecal excretion of unconjugated BPA) and primates (extensive urinary excretion of conjugated BPA), internal exposures to unconjugated BPA following oral administration are similarly low.....for adults of all

⁴⁹ See Appendix, Tab 18 for additional pharmacokinetic studies by Doerge and colleagues, retrieved and reviewed by OEHHA:

Doerge, D. R., N. C. Twaddle, M. Vanlandingham and J. W. Fisher (2011). "Pharmacokinetics of bisphenol A in neonatal and adult CD-1 mice: inter-species comparisons with Sprague-Dawley rats and rhesus monkeys." *Toxicol Lett* **207**(3): 298-305.

Doerge, D. R., N. C. Twaddle, M. Vanlandingham and J. W. Fisher (2012). "Pharmacokinetics of bisphenol A in serum and adipose tissue following intravenous administration to adult female CD-1 mice." *Toxicol Lett* **211**(2): 114-119.

Fisher, J. W., N. C. Twaddle, M. Vanlandingham and D. R. Doerge (2011). "Pharmacokinetic modeling: prediction and evaluation of route dependent dosimetry of bisphenol A in monkeys with extrapolation to humans." *Toxicol Appl Pharmacol* **257**(1): 122-136.

Patterson, T. A., N. C. Twaddle, C. S. Roegge, R. J. Callicott, J. W. Fisher and D. R. Doerge (2013). "Concurrent determination of bisphenol A pharmacokinetics in maternal and fetal rhesus monkeys." *Toxicol Appl Pharmacol* **267**(1): 41-48.

Teegarden, J. G., A. M. Calafat, X. Ye, D. R. Doerge, M. I. Churchwell, R. Gunawan and M. K. Graham (2011). "Twenty-four hour human urine and serum profiles of bisphenol a during high-dietary exposure." *Toxicol Sci* **123**(1): 48-57.

Twaddle, N. C., M. I. Churchwell, M. Vanlandingham and D. R. Doerge (2010). "Quantification of deuterated bisphenol A in serum, tissues, and excreta from adult Sprague-Dawley rats using liquid chromatography with tandem mass spectrometry." *Rapid Commun Mass Spectrom* **24**(20): 3011-3020.

⁵⁰ See Appendix, Tab 1, pp. 40-45, NTP-CERHR, 2008, "Appendix A – Interpretation of Blood Biomonitoring Results"

⁵¹ See Appendix, Tab 18A, Doerge, D.R., Twaddle, N.C., Vanlandingham, M., Fisher, J.W. 2011. Pharmacokinetics of bisphenol A in neonatal and adult CD-1 mice: inter-species comparisons with Sprague-Dawley rats and rhesus monkeys. *Toxicology Letters* 207 (3):p.303.

three species. This commonality reflects the dominant role of presystemic Phase II metabolism in the GI tract and liver,

Thus, these studies taken together do not support metabolic differences between species that preclude biological plausibility of toxic effects in humans.

In conclusion, OEHHA finds that there are no scientifically valid data not considered by the authoritative body that clearly establish that the chemical does not satisfy the scientific criteria for listing in 25306(g).

3c. PROFESSIONAL JUDGMENTS OF EXPERTS

Comment:

The ACC and the ACA argue that 23 eminent scientists (CERHR Expert Panel, the four scientists cited by ACC, and the members of the DARTIC present at the July 15, 2009 meeting) all concluded that BPA does not cause developmental toxicity. ACC commented, “Dismissing the professional judgment of these 23 highly qualified experts, collectively with many **centuries** of highly relevant experience, is arbitrary, capricious and an egregious abuse of discretion” (emphasis in original).

In contrast, the Consumers Union referred to a consensus statement of 38 independent scientific experts funded by the National Institutes of Health regarding potential impacts of BPA on reproductive endpoints.

“They cited several studies of adverse health effects in animals exposed to low doses of BPA --effects consistent with recent trends in human disease, such as increases in prostate and breast cancer, uro-genital abnormalities in male babies, a decline in semen quality in men, early onset of puberty in girls, metabolic disorders including insulin resistant (type 2) diabetes and obesity, and neurobehavioral problems such as attention deficit hyperactivity disorder (ADHD)”.

Consumers Union also referred to a position by the Endocrine Society⁵² with similar concerns.

NRDC, in providing its earlier 2010 submission, noted the 2010 US EPA Action Plan⁵³ states that BPA is a reproductive and developmental toxicant in animal studies and contains a quote detailing the high dose levels at which reproductive and developmental

⁵² Appendix, Tab 19, E Diamanti-Kandarakis, J Bourguignon, LC. Giudice, R Hauser, G Prins, AM Soto, RT Zoeller, and AC Gore, 2009. “Endocrine-Disrupting Chemicals: An Endocrine Society Scientific Statement.” *Endocrine Reviews* 30(4):293-342.

⁵³ Appendix, Tab 20, US Environmental Protection Agency, Bisphenol A Action Plan, March 29, 2010.

outcomes were observed. They also referred to the European Chemical Bureau's classification of BPA as a substance that causes concern:

“European Chemicals Bureau (ECB) has classified Bisphenol A as a Category 3 reproductive toxicant; that is a substance which causes concern for human fertility based on sufficient evidence of reproductive toxicity in experimental animals (ECB 2003).”

Response:

OEHHA acknowledges that a number of experts and expert groups have made varying conclusions about the reproductive toxicity of BPA. Proposition 65 is very specific as to how listing decisions can be made. The statute requires the listing of chemicals identified as animal or human reproductive toxicants by authoritative bodies designated by the DARTIC. The fact that ACC can cite 23 scientists in arguing against the listing of BPA is not relevant as to whether BPA meets the regulatory criteria for a Proposition 65 listing. OEHHA's decision to list a chemical that has been identified by NTP-CERHR as causing reproductive toxicity where the scientific basis for the NTP's conclusion meets the sufficiency of evidence criteria in section 25306(g) is entirely consistent with the regulation and is indeed required.⁵⁴

As stated in response to Comment 1, the DARTIC's 2009 decision to not list BPA cannot overrule OEHHA's decision that BPA meets the regulatory criteria for listing via the authoritative bodies mechanism. The DARTIC exercises its own independent judgment based on the criteria of the statute. OEHHA, on the other hand must defer to the scientific judgment of the NTP when it made its conclusions regarding the clear evidence of developmental toxicity of BPA in determining whether the criteria in section 25306 had been met. Further, when the DARTIC in 2011 unanimously rejected ACC's petition to rescind the designation of NTP-CERHR as an authoritative body, it did so with full knowledge that its action could allow the listing of BPA based on the NTP-CERHR report.

As noted in the response to Comment 2c, the NTP-CERHR expert panel is not a separate Proposition 65 authoritative body, and the Expert Panel Report explicitly states, “The findings and conclusions of this report are those of the Expert Panel and should not be construed to represent the views of the National Toxicology Program”⁵⁵ (p. iii). The NTP-CERHR report is not merely a summary of the expert panel's report, but is its own document that also relies on additional sources of information, including

⁵⁴ Appendix, Tab 5, *Exxon Mobil Corp. v. Office of Environmental Health Hazard Assessment et al.*, 169 Cal.App.4th 1264

⁵⁵ Appendix Tab 21, NTP-CERHR, 2008, Appendix 1, 3rd page (Chapin et al. Birth Defects Research (Part B) 83:158, 2008)

expert scientific peer reviewers. Further, OEHHA may consider the entire record and apply its knowledge concerning the authoritative bodies' process when determining whether a chemical has been identified as a reproductive or developmental toxicant.⁵⁶

Clearly BPA's toxicity is a topic of concern and discussion not only here in California, but also nationally and internationally. In addition to the 23 experts noted in the ACC comments, many other individuals and groups have offered conclusions of different types and in different forums concerning BPA's reproductive and developmental toxicity. For example, the CU in its comments described the previously cited consensus statement by 38 scientific experts indicating reproductive and developmental endpoints⁵⁷, and a statement by US EPA that BPA exhibits high dose reproductive and developmental toxicity,

A recent report published by the United Nations Environment Programme and World Health Organization⁵⁸ used BPA as an example of a chemical with exposure in early development leading to alterations in endocrine gland development.

In summary, there is a range of opinion in the scientific community about the level of severity of the reproductive and developmental hazards of BPA. Under Proposition 65, authoritative bodies listing decisions are based on the conclusions of the relevant body. OEHHA does not second-guess the scientific conclusions of the experts who created the report. OEHHA listed BPA after determining that the NTP-CERHR's identification of BPA as a high-dose developmental toxicant in laboratory animals met the regulatory criteria for listing under the authoritative bodies mechanism.

Comment:

In OEHHA's responses to the earlier comments, OEHHA unfairly rejected the opinions of four eminent scientists in favor of its own scientific expertise⁵⁹ (ACC).

⁵⁶ "... OEHHA properly can conclude that the authoritative body made the necessary findings based on OEHHA's review of the scientific literature on which the authoritative body relied and its knowledge of the authoritative body's methodology. 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." (*Exxon Mobil Corp. v. Office of Environmental Health Hazard Assessment et al.*, 169 Cal.App.4th 1264, 1282.) See Appendix, Tab 5.

⁵⁷ Appendix Tab 22, Vom Saal FS, Akingbemi BT, Belcher SM, 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.

⁵⁸ Appendix Tab 23, State of the Science of Endocrine Disrupting Chemicals. Summary for Decision Makers. Edited by A Bergman, JJ Heindel, S Jobling, KA Kidd, RT Zoeller. United Nations Environment Programme and the World Health Organization, 2012. Available at www.unep.org/pdf/EDCs_Summary_for_DMs%20_Jan24.pdf

⁵⁹ See Appendix, Tabs 4C, 4D, 4E.

Response:

A detailed explanation of OEHHA's consideration of the information provided by the four experts in connection with its "sufficiency of evidence" analysis is provided in OEHHA's previous responses to comments received during the "Request for Relevant Information" public comment period.⁶⁰ In the current NOIL comments, no further information relevant to consideration of maternal toxicity was provided. Rather, the ACC comment provides extensive argument that OEHHA scientists must accept the scientific judgments of the four ACC experts (Drs. Tyl, Lamb, Scialli, and Kimmel) and determine that BPA does not meet the regulatory criteria for listing. This approach would not comply with the requirements of the regulations.

The Final Statement of Reasons for Section 25306(g) notes that "It is not the intention of the Agency [OEHHA] to substitute its scientific judgment for that of the authoritative body. The Agency's inquiry will be limited to whether the authoritative body relied upon scientific data in an amount sufficient to conclude that the chemical causes reproductive toxicity." Although the scientific judgment of the experts who commented on ACC's behalf differs from that of the authoritative body, OEHHA neither agrees with the judgment of those commenters nor has any regulatory authority allowing it to substitute their judgment for that of the authoritative body.⁶¹

Comment:

A letter signed by the ACC experts and provided as an Appendix to the ACC comments stated:

"As Dr. Kimmel emphasized in our meetings in OEHHA's offices on December 5, 2011, it appears that OEHHA is misinterpreting EPA's DT guidelines with their position that less than 10% maternal mortality defines "minimal maternal toxicity"."

Response:

The relevant section of the U.S. EPA's Guidelines for Developmental Toxicity Risk Assessment states:

"The high dose is selected to produce some minimal maternal or adult toxicity (i.e., a level that at the least produces marginal but significantly reduced body weight, reduced weight gain, or specific organ toxicity, and at the most produces no more than 10% mortality)"...

⁶⁰ See Appendix, Tab 4 for the full record of comments submitted in response to the 2010 request for information and OEHHA's responses to them.

⁶¹ Appendix Tab 5, *Exxon Mobil Corp. v. Office of Environmental Health Hazard Assessment et al.*, 169 Cal.App.4th 1264

While 10% maternal mortality does not, in and of itself, define minimal maternal toxicity, it is one of the parameters identified by U.S. EPA in the context of identifying a dose level that causes minimal maternal toxicity. OEHHA has used this parameter in that regard.

The relationship between maternal and developmental toxicity is important to review. The US EPA Guidelines are important to consider in reviewing the data related to the relationship. This approach is consistently used in the OEHHA process for evaluating “sufficiency of evidence”.

4. Risk Assessments and Actions by other Organizations and Governments

Comments:

Several comments discussed conclusions of other agencies regarding actions other states have taken to control exposures to BPA, or statements that BPA did or did not pose a risk to humans. For example, these comments noted the 2007 consensus statement (see comment 3a above) on the potential health effects of BPA by 38 scientific experts convened by the National Institutes of Health, and concerns expressed by US NTP and the Endocrine Society (CU); and approaches by the US EPA, Canadian government and European Union to treat BPA as a chemical of concern (NRDC attachment⁶²).

CMI stated that while other government bodies have all concluded that there is a lack of scientific support for purported low-dose effects, the conclusions regarding high-dose effects are consistent with those of other government bodies.

On the other hand, the IFC noted in December 2011, the European Food Safety Authority (EFSA) upheld its 2006 Tolerable Daily Intake for BPA of 0.05 mg/kg body weight and its assessments to date imply that BPA does not pose a risk to human health. It also noted a November 2010 conclusion by the World Health Organization that the “initiation of public health measures [to address BPA] would be premature, and Health Canada has conducted numerous surveys of BPA in foods and beverages, including infant formula, and repeatedly stated: “The current dietary exposure to BPA through food packaging is not expected to pose a health risk to the general population, including infants and young children.”

⁶² See Appendix Tab 3H1

Response:

These comments do not address whether or not the NTP-CERHR report formally identified BPA as a developmental toxicant using scientific evidence that meets the criteria in the Proposition 65 regulations. OEHHA acknowledges various state, federal and international governments and agencies have evaluated information on the toxicity of and human exposure to BPA and have taken actions to limit exposures and have made statements regarding BPA risks or levels of concern for human exposures to the chemical.

In regards to the IFC comments, the level of exposure at which BPA may pose a risk of developmental effects is more relevant to the proposed Maximum Allowable Dose Level (MADL) for BPA that OEHHA released for public comment in January 2013⁶³.

Businesses that cause BPA exposures below the MADL (previously proposed at 290 micrograms per day) would not be required to provide Proposition 65 warnings.

Regarding statements or actions taken by regulatory agencies in the United States:

- The U.S. Food and Drug Administration (FDA) no longer permits the use of BPA in polycarbonate plastic bottles and infant sippy cups for the U.S. market and is facilitating the development of alternatives to BPA for the linings of infant formula cans.
- US EPA developed an action plan out of concern for human exposures to BPA in regards to reproductive and developmental toxicity, among other endpoints of concern.⁶⁴ U.S. EPA is considering initiating rulemaking under section 4(a) of the Toxic Substances Control Act to develop data with respect to environmental effects relevant to a future evaluation as to whether BPA presents an unreasonable risk of injury to the environment.

The comments note actions or risk statements by entities outside of the United States. Other actions that have been taken on BPA based on concern about reproductive and developmental toxicity include:

- In January 2011, the European Commission adopted Directive 2011/8/EU, prohibiting the use of BPA for the manufacture of polycarbonate infant feeding bottles.⁶⁵

⁶³ See Appendix Tabs 12

⁶⁴ See Appendix, Tab 20, US EPA Bisphenol A (BPA) Action Plan March 29, 2010, available at: http://www.epa.gov/opptintr/existingchemicals/pubs/actionplans/bpa_action_plan.pdf

⁶⁵ See Appendix, Tab 24, Commission Directive 2011/8/EU of 28 January 2011 amending Directive 2002/72/EC as regards the restriction of use of Bisphenol A in plastic infant feeding bottles. Available online at <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2011:026:0011:0014:EN:PDF>

- Canada banned BPA in baby bottles in August 2008.⁶⁶
- The French government (Agency for Food, Environmental and Occupational Health & Safety) released a report on March 25, 2013 stating, “In the current state of knowledge and on the basis of the methodology adopted, these conclusions identify risk situations for the unborn child, associated with exposure to BPA during pregnancy. The risks identified for the unborn child relate to the mammary gland and may be characterised by an increase in the number of undifferentiated epithelial structures associated with an increased susceptibility of the mammary gland to tumour transformation. The risks potentially affect children of both sexes.” They made a number of recommendations to reduce exposure to BPA.⁶⁷
- The French National Assembly subsequently passed a bill that bans the sale of any food packaging container and food material containing BPA by January 1, 2014.⁶⁸

A number of states in the US have taken actions:

- California has enacted the Toxin-Free Infants and Toddlers Act (Chapter 467, Statutes of 2011). The law will, beginning on July 1, 2013, prohibit the manufacture, sale or distribution of any bottle or cup designed for consumption of food or beverages by children age 3 or younger that contains detectable levels of BPA of more than 0.1 parts per billion. The prohibition will not apply to medical devices or to food and beverage containers designed primarily for consumption by the general population.⁶⁹
- The website for the National Conference of State Legislatures⁷⁰ lists various actions taken by Connecticut, Delaware, Maine, Maryland, Massachusetts, Minnesota, New York, Vermont, Washington, Wisconsin and the District of Columbia.

⁶⁶ See Appendix Tab 25, Order Amending Schedule I to the Hazardous Products Act (bisphenol A). Canada Gazette vol. 144, No. 7, March 31, 2010. <http://www.gazette.gc.ca/rp-pr/p2/2010/2010-03-31/html/sor-dors53-eng.html>

⁶⁷ Appendix Tab 26, Opinion of the French Agency for Food, Environmental and Occupational Health & Safety on the assessment of the risks associated with bisphenol A for human health, and on toxicological data and data on the use of bisphenols S, F, M, B, AP, AF and BADGE. March 25, 2013. ANSES Opinions Request no. 2009-SA-0331 and no. 2010-SA-0197

⁶⁸ Appendix, Tab 27, French National Assembly adoption on November 28, 2012 of a bill prohibiting the sale of food packaging containers and food material containing BPA, available at <http://www.assemblee-nationale.fr/14/ta/ta0050.asp>

⁶⁹ Appendix, Tab 28, California Health and Safety Code, Division 104, Chapter 12, Section 108940, Bisphenol A. Toxin-Free Infants and Toddlers Act. Also Available at online http://leginfo.legislature.ca.gov/faces/codes_displayexpandedbranch.xhtml

⁷⁰ Appendix, Tab 29, National Conference of State Legislatures (NCSL) Policy Update: State Restrictions on Bisphenol A (BPA) in Consumer Products, available at: <http://www.ncsl.org/issues-research/env-res/policy-update-on-state-restrictions-on-bisphenol-a.aspx>

OEHHA acknowledges that these entities are not Proposition 65 authoritative bodies; however, the statements and actions of the various state, national and international entities cited in this response support and do not contradict the conclusions drawn in the NTP-CERHR report.

5. Product Labeling

Comments:

One commenter (Grace Phillips, private individual) requested that OEHHA require disclosures of BPA in all products that contain the chemical in their packaging or bottling, or that have contact with edibles.

Another commenter (IFC) expressed concern that listing would result in mandatory labeling which would cause confusion for the consumer and create an undue burden on manufacturers and retailers.

Response:

Whether a business will eventually be required to provide a warning for exposure to BPA from its product is not part of the criteria for listing the chemical. The Proposition 65 warning requirement for BPA would have taken effect in April 2014; however the recent court order in *American Chemistry Council v Office of Environmental Health Hazard Assessment, et al.*, (Sacramento County case number 34-2013-00140720) has resulted in the de-listing of BPA. Warnings for exposures to BPA will only be required if the chemical is eventually re-listed and the exposure exceeds the maximum allowable dose level (MADL), which OEHHA previously proposed to set at 290 micrograms per day. Exposures to BPA from many products are likely to be below the MADL.⁷¹ During the one year “grace period” following listing, before the warning requirement takes effect, businesses are free to determine whether they wish to provide a warning,

⁷¹ Health and Safety Code section 25249.10. Exemptions from Warning Requirement. Section 25249.6 shall not apply to any of the following:

- (a) An exposure for which federal law governs warning in a manner that preempts state authority.
- (b) An exposure that takes place less than twelve months subsequent to the listing of the chemical in question on the list required to be published under subdivision (a) of Section 25249.8.
- (c) An exposure for which the person responsible can show that the exposure poses no significant risk assuming lifetime exposure at the level in question for substances known to the state to cause cancer, and that the exposure will have no observable effect assuming exposure at one thousand (1000) times the level in question for substances known to the state to cause reproductive toxicity, based on evidence and standards of comparable scientific validity to the evidence and standards which form the scientific basis for the listing of such chemical pursuant to subdivision (a) of Section 25249.8. In any action brought to enforce Section 25249.6, the burden of showing that an exposure meets the criteria of this subdivision shall be on the defendant.

remove the chemical from their products, or otherwise reduce exposures to below the MADL.

6. Support for listing BPA on Proposition 65

Comments:

Four comments were received supporting the listing of BPA

Senator Dianne Feinstein supported the listing and the use of scientific evidence in the listing process. Senator Feinstein called on OEHHA to give every consideration to all the available scientific evidence regarding this chemical and the health risks it presents.

Grace Phillips (private individual), BCF, NRDC and CU made general statements in support of the listing.

Response:

OEHHA acknowledges the submissions of support for listing BPA under Proposition 65.

Appendix to

Response to Comments Pertaining to the Notice of Intent to List Bisphenol A as Causing Reproductive Toxicity under Proposition 65

Office of Environmental Health Hazard Assessment California Environmental Protection Agency April 2013

Tab	Subtab	Document
1		National Toxicology Program – Center for the Evaluation of Risks to Human Reproduction (NTP-CERHR, 2008). NTP-CERHR Monograph on the Potential Human Reproductive and Developmental Effects of Bisphenol A. National Toxicology Program, US Department of Health and Human Services, NIH Publication No. 08 – 5994
2		Studies of developmental toxicity relied upon by the NTP for its finding of clear evidence:
	2A	Kim JC, Shin HC, Cha SW, Koh WS, Chung MK, Han SS (2001) Evaluation of developmental toxicity in rats exposed to the environmental estrogen bisphenol A during pregnancy. <i>Life Sci.</i> 69: 2611 – 2625.
	2B	Morrissey RE, George JD, Price CJ, Tyl RW, Marr MC, Kimmel CA (1987) The Developmental Toxicity of bisphenol A in Rats and Mice. <i>Fundam Appl Toxicol.</i> 8: 571 – 582.
	2C	NTP (1985) Bisphenol A: reproduction and fertility assessment in CD-1 mice when administered in the feed. NTP-85-192. Research Triangle Park, NC.
	2D	Tan BL, Kassim NM, Mohd MA (2003) Assessment of pubertal development in juvenile male rats after sub-acute exposure to bisphenol A and nonylphenol. <i>Toxicol Lett.</i> 143:261 – 270.
	2E	Tinwell H, Haseman J, Lefevre PA, Wallis N, Ashby J (2002) Normal sexual development of two strains of rat exposed in utero to low doses of bisphenol A. <i>Toxicol Sci.</i> 68:339 – 348.
	2F	Tyl RW, Myers CB, Marr MC, Sloan CS, Castillo NP, Veselica MM, Seely JC, Dimond SS, Van Miller JP, Shiotsuka RN, Beyer D, Hentges SG, Waechter JM, Jr. (2008) Two-generation reproductive toxicity study of dietary bisphenol A (Bisphenol A) in CD-1(R) (Swiss) mice. <i>Toxicol Sci.</i> 104:362 – 384.
	2G	Tyl R, Myers CB, Marr MC. Abbreviated one-generation study of dietary bisphenol A (Bisphenol A) in CD-1® (Swiss) mice (2002a). In. Research Triangle Park, NC: RTI (sponsored by the Society of the Plastics Industry, Inc.).
	2H	Tyl RW, Myers CB, Marr MC, Thomas BF, Keimowitz AR, Brine DR, Veselica MM, Fail PA, Chang TY, Seely JC, Joiner RL, Butala JH, Dimond SS, Cagen SZ, Shiotsuka RN, Stropp GD, Waechter JM (2002b) Three-generation reproductive toxicity study of dietary bisphenol A in CD Sprague-Dawley rats.

3	Submissions on the January 25, 2013 Notice of Intent to List by:
3A	American Coatings Association (ACA) (submitted by Alexandra Whittaker and Stephen Wieroniey)
3B	American Chemistry Council (Polycarbonate BPA Group) (ACC) (submitted by Christian Volz and Stanley Landfair)
3B1	Attachment to ACC submission: January 13, 2012 letter from J Lamb, C Kimmel, A Scialli, R Tyl to G Alexeeff
3B2	Incorporated by reference in 3B1: NTP 1985. Bisphenol A: Reproduction and fertility assessment in CD-1 mice when administered in the feed. NTP 85-192 (same as tab 2C)
3B3	Incorporated by reference in 3B1: NTP 1985. Teratologic evaluation of bisphenol A (Cas No. 80-05-7) administered to CD-1 rats on gestational days 6 through 15. Final study report. NTP-85-089
3B4	Incorporated by reference in 3B1: Teratologic evaluation of bisphenol A (Cas No. 80-05-7) administered to CD-1 mice on gestational days 6 through 15. Final Study Report. NTP-85-088
3C	Breast Cancer Fund (BCF) (submitted by Jeanne Rizzo)
3D	Can Manufacturers Institute (CMI) (submitted by Geoffrey Cullen)
3E	Consumers Union (CU) (submitted by Urvashi Rangan)
3F	Grocery Manufacturers Association (GMA) (submitted by Emilia Lonardo)
3G	International Formula Council (IFC) (submitted by Mardi Mountford)
3H	Natural Resources Defense Council (NRDC) (submitted by Sarah Janssen and Avinash Kar)
3H1	Attachment to NRDC Submission: May 13, 2010 letter responding to the 2010 Request for Relevant Information
3H2	Attachment to NRDC Submission: Ayyanan et al. 2011. Perinatal exposure to bisphenol A increases adult mammary gland progesterone response and cell number
3H3	Attachment to NRDC Submission: Cabaton et al. 2011. Perinatal exposure to environmentally relevant levels of bisphenol A decreases fertility and fundity in CD-1 mice
3H4	Attachment to NRDC Submission: Carwile and Michels 2011. Urinary bisphenol A and obesity: NHANES 2003-2006
3H5	Attachment to NRDC Submission: Chou et al. 2011. Biomonitoring of bisphenol A concentrations in maternal and umbilical cord blood in regard to birth outcomes and adipokine expression: a birth cohort study in Taiwan
3H6	Attachment to NRDC Submission: Golub et al. 2010. Bisphenol A; Developmental toxicity from early prenatal exposure
3H7	Attachment to NRDC Submission: McCaffrey et al. 2013. Sex specific impact of perinatal bisphenol A (BPA) exposure over a range of orally administered doses on rat hypothalamic sexual differentiation
3H8	Attachment to NRDC Submission: Melzer et al. 2012. Urinary bisphenol

	A concentration and risk of future coronary artery disease in apparently healthy men and women
3H9	Attachment to NRDC Submission: Miao et al. 2011. In utero exposure to bisphenol-A and its effect on birth weight of offspring
3H10	Attachment to NRDC Submission: Prins et al. 2011. Serum bisphenol A pharmacokinetics and prostate neoplastic responses following oral and subcutaneous exposures in neonatal Sprague-Dawley rats
3H11	Attachment to NRDC Submission: Rubin 2011. Bisphenol A; An endocrine disruptor with widespread exposure and multiple effects
3H12	Attachment to NRDC Submission: Snijder et al. 2012. Fetal Growth and Prenatal Exposure to Bisphenol A: The Generation R Study
3H13	Attachment to NRDC Submission: Soriano et al. 2012. Rapid insulinotropic action of low doses of bisphenol-A on mouse and human islets of Langerhans: Role of estrogen receptor β
3H14	Attachment to NRDC Submission: Stump et al. 2010. Developmental neurotoxicity study of dietary bisphenol A in Sprague Dawley rats
3I	North American Metal Packaging Alliance (NAMPA) (submitted by Kathleen Roberts)
3J	US Senator Dianne Feinstein
3K	Grace Phillips (email)
4	Comments on the 2010 Request for Relevant Information on the Possible Listing of Bisphenol A under Proposition 65, and OEHHA responses:
4A1	Advanced Medical Technology Association comment (submitted by Thomas Tremble)
4A2	OEHHA response to Advanced Medical Technology Association
4B1	American Chemistry Council Comment 1 submitted by Steven Hentges of the ACC Polycarbonate Bisphenol A Global Group
4B2	OEHHA response to American Chemistry Council Comment 1 submitted by Steven Hentges
4C1	American Chemistry Council Comment 2 submitted by James C Lamb, IV, and Carole A. Kimmel of Exponent
4C2	OEHHA response to American Chemistry Council Comment 2 submitted by James C Lamb, IV, and Carole A. Kimmel of Exponent
4D1	American Chemistry Council Comment 3 submitted by Anthony R Scialli of Tetra Tech Sciences
4D2	OEHHA response to American Chemistry Council Comment 3 submitted by Anthony R Scialli of Tetra Tech Sciences
4E1	American Chemistry Council Comment 4 submitted by Rochelle W Tyl of RTI International
4E2	OEHHA response to American Chemistry Council Comment 4 submitted by Rochelle W Tyl of RTI International
4F1	California Dental Association (CDA) comment submitted by Lisa Halko, Greenberg Traurig LLP
4F2	OEHHA response to CDA comment
4G1	California Society of Pediatric Dentistry (CSPD) comment submitted by David Rothman and Paul Reggiardo
4G2	OEHHA response to CSPD comment

4H1	Can Manufacturing Institute (CMI) comments submitted by Geoff Cullen
4H2	OEHHA response to CMI comments
4I1	Dr. Leon Earl Gray Jr.
4I1A	Attachment to Dr. Gray's submission: Sharpe RM. (2010) Is It Time to End Concerns over the Estrogenic Effects of Bisphenol A? <i>Toxicol. Sci.</i> Mar;114 (1): 1-4
4I1B	Attachment to Dr. Gray's submission: Howdeshell KL, Furr J, Lambright CR, Wilson VS, Ryan BC, Gray LE Jr (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. <i>Toxicol. Sci.</i> ; Apr;102(2):371-382
4I1C	Attachment to Dr. Gray's submission: Ryan BC, Hotchkiss AK, Crofton KM, Gray LE Jr (2009) 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. <i>Toxicol. Sci.</i> Mar;114(1):133-48
4I2	OEHHA response to Dr. Gray
4J1	Grocery Manufacturers Association (GMA) comments submitted by Michele B. Corash, Morrison and Foerster
4J2	OEHHA response to GMA comments
4K1	Healthy Building Network (HBN) comments submitted by Julie Silas and Tom Lent
4K2	OEHHA response to HBN
4L1	Institute for Liberty individuals (SE Gerrard and 3000+ others via email)
4L2	OEHHA response to Institute for Liberty submissions
4M1	Dr. Donald O. Lyman, Chief, Division of Chronic Disease and Injury Control, California Department of Public Health
4M2	OEHHA response to Dr. Lyman
4N1	Mead Johnson Nutrition submitted by Hugh N. Tucker
4N2	OEHHA response to Mead Johnson Nutrition
4O1	Motion Picture Association of America (MPAA) comments submitted by Sharon Rubalcalva of Alston & Bird, LLP
4O2	OEHHA response to MPAA
4P1	Natural Resources Defense Council (NRDC) (Sarah Janssen and Avinsah Kar) and Environmental Working Group (EWG) (Renee Sharp) comments
4P2	OEHHA response to NRDC and EWG comments
4Q1	North American Metal Packaging Alliance (NAMPA) comments submitted by John M. Rost
4Q2	OEHHA response to NAMPA comments
4R1	Comments from a group of 13 Non-Governmental Organizations (NGOs)
4R2	OEHHA response to NGO comments
5	<i>Exxon Mobil Corp. v. Office of Environmental Health Hazard Assessment et al.</i> , 169 Cal.App.4th 1264, 1283
6	Transcripts. December 4, 2002 Meeting of the Science Advisory Board's Developmental and Reproductive Toxicant (DART) Identification Committee, pp.100-136

7	Transcripts. July 12, 2011 Meeting. State of California Office of Environmental Health Hazard Assessment Proposition 65 Developmental and Reproductive Toxicant (DART) Identification Committee, pp. 123-205
8	Posted July 23, 2009 Meeting synopsis and slide presentations. Developmental and Reproductive Toxicant (DART) Identification Committee Meeting Held on July 15, 2009
9	Western Crop Protection Assn. v. Davis, 80 Cal.App.4 th 741 (2000), 95 Cal.Rptr.2d 631
10	AFL-CIO, et al., v. Deukmejian, 212 Cal.App.3d 425, 260 Cal.Rptr. 479
11	
11A	NTP-CERHR, 2005. NTP-CERHR Monograph on the Potential Human Reproductive and Developmental Effects of Acrylamide. NIH Publication No. 05 – 4472
11B	NTP-CERHR, 2003. NTP-CERHR Monograph on the Potential Human Reproductive and Developmental Effects of 1-Bromopropane. NIH Publication No. 04 – 4479
11C	NTP-CERHR, 2003. NTP-CERHR Monograph on the Potential Human Reproductive and Developmental Effects of 2-Bromopropane. NIH Publication No. 04 – 4480
11D	NTP-CERHR, 2003. NTP-CERHR Monograph on the Potential Human Reproductive and Developmental Effects of Butyl Benzyl Phthalate. NIH Publication No. 03-4487
11E	NTP-CERHR, 2003. NTP-CERHR Monograph on the Potential Human Reproductive and Developmental Effects of Di-n-Butyl Phthalate.
11F	NTP-CERHR, 2003. NTP-CERHR Monograph on the Potential Human Reproductive and Developmental Effects of Di-n-Hexyl-Phthalate, NIH Publication No. 03-4489.
11G	NTP-CERHR, 2003. NTP-CERHR Monograph on the Potential Human Reproductive and Developmental Effects of Di-Isodecyl Phthalate (DIDP). NIH Publication No. 03-4485
11H	NTP-CERHR, 2003. NTP-CERHR Monograph on the Potential Human Reproductive and Developmental Effects of Methanol. NIH Publication No. 03-4478
12	Proposed MADL for BPA:
12A	Notice of Proposed Rulemaking, Title 27, California Code of Regulations, Amendment To Section 25805, January 25, 2013
12B	Initial Statement of Reasons, Proposed Amendment to Section 25805(b), Maximum Allowable Dose Level for Bisphenol A
13	NTP Board of Scientific Counselors, Summary Minutes for the June 11, 2008 meeting and webpage for BPA on the NTP website
14	U.S. Environmental Protection Agency (1991) Guidelines for Developmental Toxicity Risk Assessment, EPA/600/FR-91/001, December 1991.
15	UN Economic Commission for Europe Globally Harmonized System of Classification and Labeling of Chemicals, Part 3, Health Hazards, section 3.7.2.4.2. p. 176
16	Carney, E (1997). Maternal physiological disruption. Drug Toxicity in Embryonic Development. Kavlock RJ and Daston GP. New York, Springer. 1: 573-594

17	Studies by Doerge, et al., cited by Grocery Manufacturers Association in their letter of March 27, 2013 (Tab 3F):
17A	Doerge, D. R., N. C. Twaddle, M. Vanlandingham and J. W. Fisher (2010). "Pharmacokinetics of bisphenol A in neonatal and adult Sprague-Dawley rats." <i>Toxicol Appl Pharmacol</i> 247(2): 158-165.
17B	Doerge, D. R., M. Vanlandingham, N. C. Twaddle and K. B. Delclos (2010). "Lactational transfer of bisphenol A in Sprague-Dawley rats." <i>Toxicol Lett</i> 199(3): 372-376.
17C	Doerge, D. R., N. C. Twaddle, M. Vanlandingham, R. P. Brown and J. W. Fisher (2011). "Distribution of bisphenol A into tissues of adult, neonatal, and fetal Sprague-Dawley rats." <i>Toxicol Appl Pharmacol</i> 255(3): 261-270.
17D	Doerge, D. R., N. C. Twaddle, K. A. Woodling and J. W. Fisher (2010). "Pharmacokinetics of bisphenol A in neonatal and adult rhesus monkeys." <i>Toxicol Appl Pharmacol</i> 248(1): 1-11.
18	Additional pharmacokinetic studies by the Doerge group, retrieved and reviewed by OEHHA:
18A	Doerge, D. R., N. C. Twaddle, M. Vanlandingham and J. W. Fisher (2011). "Pharmacokinetics of bisphenol A in neonatal and adult CD-1 mice: inter-species comparisons with Sprague-Dawley rats and rhesus monkeys." <i>Toxicol Lett</i> 207(3): 298-305.
18B	Doerge, D. R., N. C. Twaddle, M. Vanlandingham and J. W. Fisher (2012). "Pharmacokinetics of bisphenol A in serum and adipose tissue following intravenous administration to adult female CD-1 mice." <i>Toxicol Lett</i> 211(2): 114-119.
18C	Fisher, J. W., N. C. Twaddle, M. Vanlandingham and D. R. Doerge (2011). "Pharmacokinetic modeling: prediction and evaluation of route dependent dosimetry of bisphenol A in monkeys with extrapolation to humans." <i>Toxicol Appl Pharmacol</i> 257(1): 122-136.
18D	Patterson, T. A., N. C. Twaddle, C. S. Roegge, R. J. Callicott, J. W. Fisher and D. R. Doerge (2013). "Concurrent determination of bisphenol A pharmacokinetics in maternal and fetal rhesus monkeys." <i>Toxicol Appl Pharmacol</i> 267(1): 41-48.
18E	Teegarden, J. G., A. M. Calafat, X. Ye, D. R. Doerge, M. I. Churchwell, R. Gunawan and M. K. Graham (2011). "Twenty-four hour human urine and serum profiles of bisphenol a during high-dietary exposure." <i>Toxicol Sci</i> 123(1): 48-57.
18F	Twaddle, N.C., M.I. Churchwell, M. Vanlandingham, and D.R. Doerge (2010). "Quantification of deuterated bisphenol A in serum, tissues, and excreta from adult Sprague-Dawley rats using liquid chromatography with tandem mass spectrometry." <i>Rapid Commun Mass Spectrom</i> 24(20): 3011-3020.
19	Diamanti-Kandarakis E, Bourguignon J, Giudice IC, Hauser R, Prins G, Soto AM, Zoeller RT, Gore AC. 2009. Endocrine-Disrupting Chemicals: An Endocrine Society Scientific Statement. <i>Endocrine Reviews</i> 30(4):293-342.
20	US Environmental Protection Agency, Bisphenol A Action Plan, March 29, 2010.
21	NTP-CERHR, 2008, Appendix 1, 3 rd page (Chapin et al. <i>Birth Defects Research (Part B)</i> 83:158, 2008)
22	Vom Saal FS, Akingbemi BT, Belcher SM, 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. <i>Reprod Toxicol</i> 24(2):131-138.
23	State of the Science of Endocrine Disrupting Chemicals. Summary for Decision Makers. Edited by A Bergman, JJ Heindel, S Jobling, KA Kidd, RT Zoeller. United Nations Environment Programme and the World Health Organization, 2012.
24	Commission Directive 2011/8/EU of 28 January 2011 amending Directive 2002/72/EC as regards the restriction of use of Bisphenol A in plastic infant feeding bottles
25	Order Amending Schedule I to the Hazardous Products Act (bisphenol A). Canada Gazette vol. 144, No. 7, March 31, 2010.
26	Opinion of the French Agency for Food, Environmental and Occupational Health & Safety on the assessment of the risks associated with bisphenol A for human health, and on toxicological data and data on the use of bisphenols S, F, M, B, AP, AF and BADGE. March 25, 2013. ANSES Opinions Request no. 2009-SA-0331 and no. 2010-SA-0197
27	French National Assembly adoption on November 28, 2012 of a bill prohibiting the sale of food packaging containers and food material containing BPA
28	California Health and Safety Code, Division 104, Chapter 12, Section 108940, Bisphenol A. Toxin-Free Infants and Toddlers Act.
29	National Conference of State Legislatures (NCSL) Policy Update: State Restrictions on Bisphenol A (BPA) in Consumer Products