PETITION TO ORDER TESTING OF TETRABROMOBISPHENOL A (CAS NO. 79-94-7) UNDER SECTION 4(a) OF THE TOXIC SUBSTANCES CONTROL ACT (DECEMBER 13, 2016)

Via Federal Express & Electronic Mail

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Dear Administrator McCarthy:

Earthjustice,[1] Natural Resources Defense Council (NRDC), [2] Toxic-Free Future (TFF),[3] Safer Chemicals, Healthy Families (SCHF),[4] BlueGreen Alliance (BGA),[5] and Environmental Health Strategy Center (EHSC),[6] submit this Petition to the U.S. Environmental Protection Agency ("EPA"), pursuant to section 21 of the Toxic Substances Control Act ("TSCA"),[7] to

[1] Earthjustice is the nation's largest environmental law organization. Protecting people and the environment from exposure to toxic substances is a key part of its mission. Earthjustice submits this petition on behalf of NRDC, SCHF, TFF, BGA, and EHSC.

[2] NRDC is an international nonprofit environmental organization with more than 2 million members and online activists. Since 1970, our lawyers, scientists, and other environmental specialists have worked to protect the world's natural resources, public health, and the environment. Protecting families and communities from toxic chemicals is a key NRDC goal.

[3] TFF advocates for the use of safer products, chemicals, and practices through advanced research, advocacy, grassroots organizing, and consumer engagement to ensure a healthier tomorrow.

[4] SCHF is a coalition representing over 450 organizations and businesses united by a common concern about toxic chemicals in our homes, places of work, and products we use every day.

[5] BGA unites the largest labor unions in the United States with major environmental organizations to solve environmental challenges in ways that create and maintain quality jobs and build a stronger, fairer economy. A key component of BGA's work is the creation of quality jobs across the country that ensure the health of workers and the environment. Improving job safety by improving the safety of workplace chemicals is a key BGA goal.

[6] EHSC is a public health organization that works nationally for food, water, and products that safer for people and the planet, and for a sustainable economy with justice for all.

[7] 15 U.S.C. § 2620.

issue an order under TSCA section 4,[8] requiring that testing be conducted by manufacturers (which includes importers) and processors on Tetrabromobisphenol A ("TBBPA") (CAS No. 79-94-7).[9] TBBPA is used as a reactive flame retardant in circuit boards; as an additive flame retardant in plastics, paper and textiles; as a plasticizer in coatings and adhesives; and as an intermediate in the synthesis of other flame retardants.[10] The basis for the testing order is laid out below. The specific protocols and methodologies for the development of information that we ask EPA to seek in a TBBPA testing order are set forth in Appendix A hereto.

Pursuant to TSCA section 21(b)(3), we ask EPA to respond to this Petition by issuing the requested test order by March 13, 2017, which is 90 days after the Petition was filed in the principal office of the Administrator of the EPA on December 13, 2016.

[8] 15 U.S.C. § 2603.

[9] TBBPA was the subject of an EPA TSCA Work Plan Chemical Problem Formulation and Initial Assessment, dated August 2015.

[10] Robin E. Dodson et al., *After the PBDE Phase-Out: A Broad Suite of Flame Retardants in Repeat House Dust Samples from California*, 46 Envtl. Sci. & Tech. 13,056, 13,062 (2012), citing Adrian Covaci et al., *Analytical and environmental aspects of the flame retardant tetrabromobisphenol-A and its derivatives*, 1216 J. Chromatography A 346 (2009).

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I. INTRODUCTION

When Congress adopted TSCA in 1976, it stated that "it is the policy of the United States that adequate data should be developed with respect to the effect of chemical substances and mixtures on health and the environment and that the development of such data should be the responsibility of those who manufacture and those who process such chemical substances and mixtures."[11] This congressional statement of national policy has been virtually ignored for several decades.[12] But this state of affairs cannot continue. Due to overall lack of available data or existing data gaps, EPA will be unable to conduct the robust chemical risk evaluations mandated by the reformed TSCA unless it requires manufacturers and processors to develop health and safety information about their chemicals. For the reasons below, we urge EPA to require testing of TBBPA without delay.

Our key reasons for concern about the risks posed by TBBPA include:

- TBBPA has the highest production volume of any brominated flame retardant. In 2011, five companies reported a total of 120 million pounds manufactured or imported.[13] It is used extensively in consumer electronics and other consumer products, *including children's products*.[14] Therefore, the potential for widespread exposure in the population, particularly for sensitive populations such as developing children, is extremely high.

- Reports to the Toxics Release Inventory in 2012 indicated that 52 manufacturing and processing facilities released into the environment or disposed 127,845 pounds of TBBPA.[15] Such widespread release indicated the potential for widespread exposure in the population.

- The presence of TBBPA in people and the environment is established. As EPA noted in its TBBPA Problem Formulation: "TBBPA has been found in humans

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[11] 15 U.S.C. § 2601(b)(1). The reformed TSCA left this statement of policy intact; the only revision changed the term "data" in two places to "information."

[12] U.S. Gen. Accounting Office, GAO-05-458, *Chemical Regulation –Options Exist to Improve EPA's Ability to Assess Health Risks and Manage Its Chemical Review Program* (2005); U.S. Gen. Accounting Office, GAO/RCED-94-103, *Toxic Substances Control Act-Legislative Changes Could Make the Act More Effective* (1994).

[13] Office of Chem. Safety & Pollution Prevention, EPA, Doc. No. 740-R1-4004, *TSCA Work Plan Chemical Problem Formulation and Initial Assessment: Tetrabromobisphenol A and Related Chemicals Cluster Flame Retardants* 10 (2015), https://www.epa.gov/sites/production/files/2015-09/documents/tbbpa_problem_formulation_august_2015.pdf ("TBBPA Problem Formulation").

[14] Problem Formulation at 23-26; *see also* Wash. State Dep't of Ecology, Children's Safe Product Act Reports (last visited Nov. 29, 2016), https://fortress.wa.gov/ecy/cspareporting/Reports/ReportViewer.aspx?ReportName=ChemicalReportByCASNumber [Select Chemical CAS Number 79-94-7]/

[15] TBBPA Problem Formulation at 10.

(blood, breast milk and adipose tissue) and in biota (aquatic and terrestrial animals and plants and in birds). Several studies have also found TBBPA in a variety of environmental media that includes sediment, soil, landfill leachates, sewage sludge, surface water, wastewater and indoor and outdoor air."[16] This indicates that widespread exposure to the population is occurring — from consumer products, environmental release or exposure, or all of the above.

- EPA has long recognized that TBBPA is toxic. In 1999, when EPA added TBBPA to the Toxics Release Inventory ("TRI"), it stated: "EPA considers [TBBPA] to be highly toxic. Since TBBPA is toxic at relatively low concentrations, EPA believes that it causes or can reasonably be anticipated to cause a significant adverse effect on the environment."[17] Given the potential for widespread population exposures, particularly those of young children, the potential health impacts from exposure are of great concern.

Although the available scientific evidence documents the concerns regarding widespread exposure and the potential for adverse health impacts, there is much that remains unknown about the *scope and extent of the risk* posed by TBBPA. At a minimum, testing must be conducted before EPA can undertake a risk evaluation that considers potential risks arising during the full life cycle of TBBPA — from manufacturing, to processing, to distribution, to use, to disposal— and impacts on vulnerable populations from each of these activities, as TSCA requires. [18] EPA's TBBPA Problem Formulation, the likely framework for any future risk evaluation, indicates lack of data for multiple key exposure pathways and toxicity endpoints, including:

- dermal and inhalation exposures; diet and drinking water exposures; exposures to communities near facilities that process TBBPA; exposures to communities near facilities where e-waste is disposed of and recycled; and exposures to the workers in manufacturing, processing, disposal and recycling facilities.

- developmental, reproductive and neurological toxicity, which are hazards of high concern for pregnant women and children.

While these wide-ranging data gaps (which are described in Point III.B below) will prevent EPA from conducting a risk evaluation that fulfills the requirements of TSCA section 6, there is little doubt that the existing information about the risks posed by TBBPA more than satisfy the TSCA section 4 criteria for scenarios where "the Administrator *shall* … require that

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[16] *Id.*

[17] 64 Fed. Reg. 58,666, 58,708 (Oct. 29, 1999).

[18] TSCA section 6(a) requires EPA to "determine[] . . . [whether] the manufacture, processing, distribution in commerce, use, or disposal of a chemical substance or mixture, or that any combination of such activities, presents an unreasonable risk of injury to health or the environment." 15 U.S.C. § 2605(a). Under section 6(b)(4), the purpose of conducting a risk evaluation is to determine whether a substance presents such a risk. In other words, for a risk evaluation to meet the requirements of TSCA, it must consider potential risks arising during the full life cycle of a chemical. And the evaluation must consider risks arising from these activities with a special eye towards impacts on vulnerable populations.

testing be conducted."[19] We therefore urge EPA to issue a section 4 testing order for TBBPA as soon as possible. Because information generated in response to this testing order is likely to be critical to any risk evaluation of TBBPA, we ask EPA not to commence the risk evaluation for TBBPA until data generated to comply with the testing order have been received by EPA.

II. LEGAL CRITERIA FOR ISSUING A TEST ORDER

To facilitate the policy that "adequate information should be developed with respect to the effect of chemical substances and mixtures on health and the environment and that the development of such information should be the responsibility of those who manufacture and those who process such chemical substances and mixtures,"[20] TSCA requires EPA to direct testing on a chemical substance or mixture if it finds the following criteria are met:

> (1) the "manufacture, distribution in commerce, processing, use, or disposal of a chemical substance or mixture, or that any combination of such activities, *may present an unreasonable risk of injury to health or the environment*,"
>
> (2) there is "*insufficient information and experience* upon which the effects of such manufacture, distribution in commerce, processing, use, or disposal of such substance or mixture, or of any combination of such activities on health or the environment can reasonably be determined or predicted," and
>
> (3) "*testing . . . is necessary* to develop such information."[21]

While TSCA reform revised the process for requiring testing, the above-stated criteria for testing under section 4(a)(1) remain essentially unchanged. Thus case law developed under the prior version of section 4 remains applicable here. This case law shows that a mere rational concern about the risks posed by a chemical justifies a testing order.

A. EPA Has Consistently Found the "May Present" Standard Is Satisfied Where There is a More-Than-Theoretical Risk

EPA has previously taken the position that the "may present" finding is satisfied where "the existence of an 'unreasonable risk of injury…' is . . . *more than merely theoretical,*

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[19] 15 U.S.C. § 2603(a) (emphasis added).

[20] 15 U.S.C. § 2601(b)(1).

[21] *Id*. § 2603(a)(1). With the reformed TSCA, EPA can *order* that such testing be conducted rather than proceeding by rulemaking as was required under the prior version of TSCA. *Id.* A section 4 testing order must require that

> testing be conducted … to develop information with respect to the health and environmental effects for which there is an insufficiency of information and experience and which is relevant to a determination that the manufacture, distribution in commerce, processing, use, or disposal of such substance or mixture, or that any combination of such activities, does or does not present an unreasonable risk of injury to health or the environment.

Id.

speculative, or conjectural."[22] Both the D.C. Circuit and Third Circuit Courts of Appeals have deferred to the agency's broad interpretation of its testing authority.[23]

In *Chemical Manufacturers Association v. EPA*, the D.C. Circuit deferred to EPA's expansive interpretation of the "may present" language and upheld a testing rule directed to manufacturers of the chemical 2-ethylhexanoic acid.[24] The court noted that the legislative history of the original TSCA section 4 indicates congressional intent that EPA issue testing rules when unreasonable risk could not yet be "reasonably predicted."[25] The court emphasized that both the statutory wording and legislative history reveal congressional intent for EPA to act on the basis of rational concern even in the absence of "adequate information" relating to the risks of a chemical substance or mixture.[26]

In *Ausimont U.S.A., Inc. v. EPA*, the Third Circuit also deferred to EPA's reading of section 4 and upheld a testing rule directed to manufacturers of fluoroalkenes.[27] Rejecting the chemical industry's arguments, the court noted that Section 4 "focuses on investigating areas of uncertainty as a prelude to regulating harmful substances,"[28] and that "questions broaching the frontiers of scientific knowledge highlight the need for testing," rather than undercutting the conclusion that sufficient probability of risk is present to require testing.[29] The court upheld EPA's reliance on the structure activity relationship between VDF, one of the chemicals subject to the test rule, and vinylidene chloride, a suspected carcinogen, as supporting the need for testing.[30]

B. Courts Have Deferred to EPA's View That the "May Present" Finding Is Satisfied So Long as Evidence of Exposure is More Than Theoretical

In both *Chemical Manufacturers Association* and *Ausimont U.S.A.*, chemical manufacturers argued that EPA's testing rules were improper because evidence of exposure was limited. The courts in these cases deferred to EPA, giving it broad latitude to *infer* exposure. In *Chemical Manufacturers Association*, the chemical industry argued that when industry evidence casts doubt on the existence of exposure, the burden of production shifts to EPA to produce direct evidence documenting actual instances in which exposure has taken place. While EPA agreed that some exposure is a necessary component of "unreasonable risk," it argued that it is permitted to *infer exposure* from the circumstances under which a chemical substance is

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[22] *Chem. Mfrs. Ass'n v. EPA*, 859 F.2d 977, 983-985 (D.C. Cir. 1988).

[23] *Id.*; *see also Ausimont U.S.A., Inc. v. EPA*, 838 F.2d 93 (3d. Cir. 1988).

[24] 859 F.2d at 983-985.

[25] *Id.* at 985.

[26] *Id.*

[27] 838 F.2d at 93.

[28] *Id.* at 96.

[29] *Id.*

[30] *Id.*

manufactured and used.[31] It contended that Section 4 allowed it to issue a test rule so long as it could show a "more-than-theoretical basis for inferring the existence of exposure."[32] The D.C. Circuit deferred to this interpretation, holding: "[w]e conclude that it is reasonable for EPA to rely on inferences in issuing a section 4 test rule, so long as all the evidence - including the industry evidence - indicates a more-than-theoretical probability of exposure."[33] Likewise in *Ausimont U.S.A.*, the industry challengers asserted that exposure to fluoroalkenes was minimal. The court deferred to EPA's concern, finding that it was "not prepared to say that the element of risk is insignificant."[34]

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The clear take-away from court rulings interpreting the scope of EPA's authority to require testing under section 4, is that EPA has broad discretion to require testing based on rational concern that the chemical may present an unreasonable risk.

III. EPA SHOULD ISSUE A SECTION 4 TEST ORDER FOR TBBPA

The standard for issuing a test order is easily met for TBBPA. As a result, EPA "shall … require that testing be conducted."[35]

A. TBBPA "May Present" an Unreasonable Risk

The potential that TBBPA poses an "unreasonable risk of injury" is "more than merely theoretical, speculative, or conjectural."[36] Indeed, it is doubtful that EPA would have added TBBPA to the TSCA Work Plan if the risk of injury it poses were simply theoretical, speculative, or conjectural. Because "[r]isk implicates two concepts – toxicity and exposure,"[37] we address each of these concepts separately below.

1. TBBPA Is Likely Toxic

There is substantial evidence that TBBPA may be toxic:

- The TBBPA Problem Formulation states that TBBPA "can be considered hazardous to the environment"[38] and that "there is some concern" for uterine cancer, hemangiosarcomas, hemangiomas, and developmental effects.[39]

[31] 859 F.2d at 984.

[32] *Id.* at 988.

[33] *Id.* at 989.

[34] 838 F.2d at 97.

[35] 15 U.S.C. § 2603(a)(1)(B).

[36] 859 F.2d at 983-985.

[37] 838 F.2d at 96.

[38] TBBPA Problem Formulation at 31.

[39] *Id.* at 32.

- A recent National Toxicology Program ("NTP") study of TBBPA found "clear evidence of carcinogenic activity in female rats" based on an increased incidence of uterine tumors.[40]

- The California Safer Consumer Products Candidate Chemical list identifies the hazard traits of carcinogenicity, endocrine toxicity, neurotoxicity, and reproductive toxicity for TBBPA based on the following authoritative lists: IARC Carcinogens-2A and CECBP-Priority Chemicals.[41]

- TBBPA has been found to have the following effects during in vitro and animal testing:

    - Endocrine disruption through T3, T4 agonism and estradiol inhibition in vitro;[42]
    - Teratogenic effects for frog embryos,[43]
    - Effects on the reproductive system in experimental animals;[44]
    - Strong T4 agonism;[45]
    - CD25 inhibition in female mice;[46]
    - Decreased T4, increased testis and pituitary weight in orally exposed rats, increased testis weight, testosterone, female gonadal weight in second generation;[47]

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[40] J.K. Dunnick et al., Nat'l Toxicology Program ("NTP"), U.S. Dep't of Health & Human Servs., NTP TR 587, NIH Publication No. 14-5929, *NTP Technical Report on the Toxicology Studies of Tetrabromobisphenol A (CAS NO. 79-94-7) in F344/NTac Rats and B6C3F1/N Mice and Toxicology and Carcinogenesis Studies of Tetrabromobisphenol A in Wistar Han [Crl:WI(Han)] Rats and B6C3F1/N Mice (Gavage Studies)* at 9 (2014), http://ntp.niehs.nih.gov/ntp/htdocs/lt_rpts/tr587_508.pdf.

[41] Cal. Dep't of Toxic Substances Control, *Candidate Chemical Details*, Safer Consumer Products Information Management System (last visited Nov. 29, 2016), https://calsafer.dtsc.ca.gov/chemical/ChemicalDetail.aspx?chemid=22244.

[42] Timo Hamers et al., *In Vitro Profiling of the Endocrine-Disrupting Potency of Brominated Flame Retardants*, 92 Toxicological Sciences 157 (2006).

[43] Huahong Shi et al., *Teratogenic effects of tetrabromobisphenol A on Xenopus tropicalis embryos*, 152 Comp. Biochemistry & Physiology Part C: Toxicology & Pharmacology 62-68 (2010).

[44] Eva Zatecka et al., *Effect of tetrabrombisphenol A on induction of apoptosis in the testes and changes in expression of selected testicular genes in CD1 mice*, 35 Reproductive Toxicology 32 (2013).

[45] Ilonka Meerts et al., *In vitro estrogenicity of polybrominated diphenyl ethers, hydroxylated PDBEs, and polybrominated bisphenol A compounds*, 109 Envtl. Health Persp. 399 (2001).

[46] Sabine Pullen et al., *The flame retardants tetrabromobisphenol A and tetrabromobisphenol A /bisallylether suppress the induction of interleukin-2 receptor a chain (CD25) in murine splenocytes*, 184 Toxicology 11 (2003).

[47] Leo Van der Ven et al., *Endocrine effects of tetrabromobisphenol-A (TBBPA) in Wistar rats as tested in a one-generation reproduction study and a subacute toxicity study*, 245 Toxicology 76 (2008).

- Dopamine and GABA uptake inhibition due to effects on membrane potential in rat brain cells.[48]

In sum, multiple studies have raised significant concern that TBBPA presents a hazard to humans and the environment.

2. Human and Environmental Exposure to TBBPA Is Established

There is also substantial evidence that humans and the environment are exposed to TBBPA. According to the TBBPA Problem Formulation: the "general population may be exposed to TBBPA due to its widespread detection in the indoor and outdoor environment." The TBBPA Problem Formulation notes that TBBPA has been detected in several human and fish biomonitoring studies, and that "the general population may be exposed to TBBPA through oral, inhalation or dermal exposure."[49] In addition, EPA concluded that "there is a potential for exposures to workers" in manufacturing and recycling.[50] A recent study found measurable levels of TBBPA (along with several other flame retardants) emitted from office equipment to indoor air.[51] TBBPA is considered to be persistent and bioaccumulative according to the following authoritative lists: OSPAR Priority Action Part A, US EPA TRI PBTs, and WA PBTs.[52]

3. EPA Has <u>Already Found</u> That TBBPA May Present an Unreasonable Risk

EPA has already determined, *a fortiori*, that TBBPA "may present an unreasonable risk of injury to health or the environment." In 1999, EPA adopted a final rule adding TBBPA to the Toxic Release Inventory ("TRI") established under the Emergency Planning and Community Right to Know Act.[53] The listing of TBBPA on the TRI is, by itself, sufficient indication that TBBPA "may present an unreasonable risk of injury to health or the environment" within the meaning of TSCA section 4. This is because the statutory standard for adding a chemical to the TRI requires a far greater degree of certainty about potential risks than the standard for requiring testing under TSCA section 4.

For EPA to add a chemical to the TRI, it must determine – on the basis of "generally accepted scientific principles," "laboratory tests," or "appropriately designed and conducted … studies" – that there is "sufficient evidence" to establish that the chemical is "known to cause **or** can reasonably be anticipated to cause" at least one of the following:

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[48] Espen Mariussen & Frode Fonnum, *The effect of brominated flame retardants on neurotransmitter uptake into rat brain synaptosomes and vesicles*, 43 Neurochemistry Int'l 533 (2003).

[49] TBBPA Problem Formulation at 30.

[50] *Id.*

[51] Hugo Destaillats et al., *Indoor pollutants emitted by office equipment: A review of reported data and information needs*, 42 Atmospheric Env't 1371 (2008).

[52] *See* Cal. Dep't of Toxic Substances Control, *Candidate Chemical Details*, Safer Consumer Products Information Management System (last visited Nov. 29, 2016), https://calsafer.dtsc.ca.gov/chemical/ChemicalDetail.aspx?chemid=22244.

[53] 64 Fed. Reg. at 58,668 (to be codified at 40 C.F.R. pt. 372).

(A) "significant adverse acute human health effects" at concentrations reasonably likely to exist beyond facility site boundaries; or

(B) (i) cancer or teratogenic effects, or (ii) serious or irreversible reproductive dysfunctions, neurological disorders, heritable genetic mutations, or other chronic health effects; or

(C) "a significant adverse effect on the environment of sufficient seriousness to warrant reporting" because of toxicity, toxicity and persistence, or toxicity and tendency to bioaccumulate in the environment.[54]

EPA added TBBPA to the TRI because of "significant adverse effects on the environment of sufficient seriousness to warrant reporting." The final rule adding TBBPA to the TRI states:

> Based on the available toxicity data, EPA has concluded that *TBBPA is toxic*. It has the potential to kill fish, daphnid, and mysid shrimp, among other adverse effects, based on chemical and/or biological interactions. …. *TBBPA can cause its toxic effects at … relatively low concentrations; therefore, EPA considers it to be highly toxic*. Since TBBPA is toxic at relatively low concentrations, EPA believes that it causes or can reasonably be *anticipated to cause a significant adverse effect on the environment*. In addition, because of the nature of the potential significant adverse effects . . . and the impacts such effects can have on ecological communities and ecosystems, EPA has determined that they are of sufficient seriousness to warrant reporting.[55]

EPA's findings that TBBPA is "highly toxic" and is "*anticipated to cause* a significant adverse effect on the environment" more than satisfy the first criteria under TSCA section 4 that TBBPA "*may present* an unreasonable risk of injury to health or the environment."[56]

B. There Is Insufficient Information To Determine or Predict the Effects of TBBPA During its Full Life Cycle

The TBBPA Problem Formulation provides abundant evidence that there is "insufficient information and experience upon which the effects of [the] manufacture, distribution in commerce, processing, use, or disposal of [a] substance or mixture or of any combination of such activities on health or the environment can reasonably be determined or predicted."[57] In other words, it shows that the second requirement for a testing order is satisfied here.

We have outlined below the exposure pathways and hazard endpoints that will be *excluded* from any future risk assessment because of lack of information, according to EPA's TBBPA Problem Formulation.

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[54] 42 U.S.C. § 11023 (d)(2)(A)-(C) (emphasis added).

[55] 64 Fed. Reg. at 58,708.

[56] 15 U.S.C. § 2603(a)(1).

[57] *Id.* § 2603(a)(1)(A)(II).

1) Excluded Dermal and Inhalation Exposure

- "There are *no in vivo toxicokinetics data* via the dermal route for TBBPA."[58]

- *"Data are also lacking* on TBBPA's toxicokinetics after inhalation."[59] "Exposure via directly inhaling TBBPA will not be assessed because no information is available on the toxicity of tetrabromobisphenol A to plants and other wildlife organisms (e.g., birds) exposed via the air."[60]

2) Excluded Exposure From Diet and Drinking Water

- "It is possible that individuals may eat fish or obtain drinking water in areas near WWTPs. *Data on TBBPA concentrations in fish were not located* for areas specifically located near WWTPs. Also, *data on TBBPA concentrations in treated drinking water is not available*. Therefore, EPA/OPPT will not assess these pathways in the current assessment."[61]

- "Although sewage sludge can be applied to agricultural land, risks resulting from this possible scenario are not being considered *for lack of information* on uptake from soil."[62]

- "EPA/OPPT is not proposing to assess the potential for dietary intake from eating crops and livestock around manufacturers for several reasons. Although the EU Risk Assessment…used KOW instead of measured bioconcentration or bioaccumulation factors and Koc values were used to determine uptake to plants and then livestock, more recent data of the uptake of TBBPA by cabbage and radishes from soil showed that a large amount of TBBPA was adsorbed to soil and not available for transfer to plants…. Second, *no data* were found regarding the bioaccumulation of TBBPA into livestock. Third, the evaluation of exposures from food other than fish is the purview of agencies other than EPA."[63]

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[58] TBBPA Problem Formulation at 109 (emphasis added).

[59] *Id* (emphasis added).

[60] *Id.* at 42.

[61] TBBPA Problem Formulation at 45 (emphasis added). EPA did note that "based on information from current published studies on TBBPA in surface waters, risk from TBBPA in drinking water is likely to be of low concern for non-industrial areas." *Id.* This suggests that TBBPA in drinking water could be of concern for people living in industrial areas, inevitably vulnerable populations.

[62] *Id*. (emphasis added).

[63] *Id*. at 42-43 (internal citations omitted) (emphasis added).

3) Excluded Exposure from Manufacturing and Processing

- "US processing sites in sectors other than the plastics and rubber sector have reported . . . stack air releases to TRI. . . However, EPA/OPPT does not propose evaluating these releases . . . because they are only a small proportion of the air emissions from manufacturing sites."[64]

4) Excluded Exposure from Recycling

- "There is significant uncertainty in evaluating the risks from recycling. . . . *Because of these uncertainties,* EPA/OPPT will not evaluate risks from TBBPA present in environmental media surrounding recycling facilities."[65]

- Workers at recycling plants may be exposed to TBBPA particulates. . . . Also, TBBPA concentrations were found in environmental media near e-waste recyclers . . . . [in other countries], and these concentrations could affect the general population living near such facilities. EPA/OPPT is not planning to evaluate risks for workers or the general population given *significant uncertainties* regarding the recycling process in the United States as defined by EPA/ORCR.[66]

5) Excluded Exposure from Disposal

- "[O]nly limited leaching of TBBPA from landfills is likely because TBBPA is expected to adsorb to soil particles. . . . TBBPA has been measured in leachates from landfills in the Netherlands, Finland and Japan. . . . Most often TBBPA concentrations are quite low. Prior to treatment, however, TBBPA may be found at higher concentrations. For the above reasons, EPA/OPPT will not evaluate risks from disposal of final products after use for the environment or humans. Landfills that are no longer in operation or that are out of compliance with regulations limiting releases may result in the potential for exposure. However, an evaluation of these situations is beyond the scope of the proposed assessment."[67]

- "Electronic waste after use is typically sent to landfills. Electronic waste can also be sent to waste-to-energy incinerators…. Products that contain TBBPA can also be sent to municipal incinerators. Furthermore, ash generated from incineration can also be sent to landfills."[68]

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[64] TBBPA Problem Formulation at 43.

[65] *Id.* (emphasis added).

[66] *Id.* (emphasis added).

[67] *Id.* at 44 (internal citations omitted).

[68] *Id.* at 28 (internal citations omitted).

- "EPA/OPPT found only one study measured TBBPA emissions . . . from a mixed household and commercial waste incinerator in Japan. . . . Also, EC/HC (2013) assumed that control devices on incinerators would *limit releases* of TBBPA to air. Therefore, due to *limited data and likely destruction o*f TBBPA during incineration, EPA/OPPT will not calculate risks from incineration of TBBPA-containing products for the environment or humans."[69]

- "Facility waste and final consumer products that contain TBBPA may be sent to WWTPs. Exposure to TBBPA could occur after discharge of effluents from WWTPs to water, where it could remain in surface water or partition to sediments or from generation of sludge that is then applied to agricultural land."[70]

(6) Excluded Exposure to Degradation Byproducts

- "EPA/OPPT concluded that *data on degradation are limited, uncertain or both*. Therefore, EPA/OPPT will not assess risks from TBBPA's degradation products in a risk assessment."[71]

- "EPA/OPPT *doesn't have robust information* on the amount of electronic waste that is incinerated in the United States. Finally, compounds other than TBBPA can result in similar combustion products when incinerated. Therefore, the contribution of TBBPA to combustion byproducts is not possible to determine with enough accuracy to include in EPA/OPPT's proposed risk assessment."[72]

- "TBBPA could be a source of BPA in the environment . . . . Overall, biodegradation data are considered to be *too limited to predict, with confidence, the rate at which TBBPA degrades to BPA in the environment*. This is because the majority of the studies use microorganisms that have been collected from environments contaminated with TBBPA, exposed to TBBPA over extended periods to induce adaptation to degrade the substance and are conducted under laboratory conditions that are not necessarily representative of the environment."[73]

- "TBBPA may photodegrade to form a range of bromophenols and dibromoisopropylphenol derivatives. Overall there appears to be *limited to no human health toxicity data* for dibromophenols. Some ecotoxicity data are available for 2-bromophenol…. Due to uncertainties in extrapolation from

[69] TBBPA Problem Formulation at 44 (emphasis added).

[70] *Id.* at 91.

[71] *Id.* at 91-92 (emphasis added).

[72] *Id.* at 92 (emphasis added).

[73] *Id.* at 92 (internal citation omitted) (emphasis added).

laboratory to the field, it is not certain how much of these products would be formed in the environment…."[74]

7) Excluded Hazard Endpoints

- "The studies evaluating reproductive and developmental toxicity show *a wide variety of results* from no effects up to very high doses to some subclinical effects at low doses. Also, it is not clear whether dosing dams and offspring or just dosing offspring results in effects of TBBPA treatment. Thus, *there is uncertainty* in choosing any developmental toxicity study for evaluation in a quantitative risk assessment of TBBPA."[75]

- "Neurotoxicity and neurobehavioral effects *have not been confirmed*. One study found some potential for hearing loss when dams and newborns were dosed … but *there are questions* about methods and uncertainty about which are the most relevant doses (e.g., both newborns and dams were exposed to TBBPA)."[76]

- "The possible adverse effects of tetrabromobisphenol A exposure on the endocrine system in amphibians have shown *mixed results*. Furthermore, the effect of changes in gene expression is *not clear*. For these reasons, EPA/OPPT has not considered these results further for inclusion in a risk assessment of TBBPA."[77]

In sum, EPA's own TBBPA Problem Formulation plainly demonstrates that EPA has insufficient information on which to conduct the type of full life cycle risk evaluation that TSCA section 6 requires.

C. Testing Is Necessary to Develop This Information

The third criteria for a testing order is also satisfied for TBBPA because "*testing . . . is necessary* to develop [the] information" [78] on the basis of which "the effects of [the] manufacture, distribution in commerce, processing, use, or disposal of [TBBPA] or of any combination of such activities on health or the environment can reasonably be determined or predicted." [79] Appendix A lays out the testing that is necessary to determine the effects of the manufacture, distribution in commerce, processing use, and disposal of TBBPA. Also set out in Appendix A is an explanation of why the EPA is "justifie[d]" in ordering "more advanced testing of potential health or environmental effects or potential exposure without first conducting screening-level testing," pursuant to TSCA section 4(a)(4).

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[74] *Id.* (emphasis added).

[75] *Id.* at 123 (emphasis added).

[76] *Id.* at 32 (emphasis added).

[77] *Id.* at 107 (emphasis added).

[78] 15 U.S.C. § 2603(a)(1)(A)(i)(III).

[79] 15 U.S.C. § 2603(a)(1)(A)(i)(II).

IV. THE TEST ORDER SHOULD BE DIRECTED TO MANUFACTURERS AND PROCESSORS

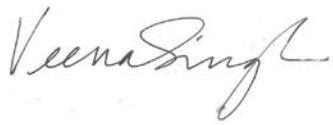
For the reasons above, TBBPA satisfies the criteria for issuing a TSCA section 4 testing rule. Accordingly, EPA "shall . . . require that testing be conducted on [TBBPA] to develop information with respect to the health and environmental effects for which there is an insufficiency of information and experience and which is relevant to a determination [regarding whether TBBPA] does or does not present an unreasonable risk of injury to health or the environment."[80]

We urge EPA to direct the section 4 testing order for TBBPA to all persons who "manufacture[ ] or intend[ ] to manufacture" or "process[ ] or intend[ ] to process" TBBPA.[81,82] The TBBPA Problem Formulation identifies five companies that manufacture or import TBBPA, including one whose name is claimed to be CBI.[83] In addition, the TBBPA Problem Formulation states that four of these five companies also process TBBPA.[84] (The fifth company did not provide information about processing.) At a minimum, the testing order should be directed to these five manufacturers, importers and processors of TBBPA.

V. CONCLUSION

For the reasons above and in Appendix A, we urge EPA to issue a TSCA section 4 testing order to fill the data gaps for TBBPA that EPA has already identified.

Sincerely,



Eve Gartner
Staff Attorney
Earthjustice

Veena Singla
Staff Scientist
Natural Resources Defense Council

cc: Mr. Jim Jones, Assistant Administrator, OCSPP (Jones.Jim@epa.gov)

[80] 15 U.S.C. § 2603(a)(1)(B).

[81] TSCA defines the act of "manufacturing" as importing into the U.S., producing or manufacturing. 15 U.S.C. § 2602(9).

[82] Processor is defined in TSCA section 3 to include anyone who processes a chemical substance, and the action of processing it defined as the "preparation of a chemical substance or mixture, after its manufacture, for distribution in commerce." 15 U.S.C. § 2602(13)-(14).

[83] TBBPA Problem Formulation at 21.

[84] *Id.* at 23.

Appendix A

APPENDIX A

1) Dermal and Inhalation Exposure Toxicity

According to the TBBPA Problem Formulation, "The general population may be exposed to TBBPA through oral, inhalation or dermal exposure."[1] The Problem Formulation also indicates that dermal exposure may be relevant for workers.

However, a significant existing data gap to assess the toxicity of TBBPA via dermal and inhalation exposure pathways is toxicokinetics data.

1A) DERMAL

Assessment of available information

While no *in vivo* toxicokinetics data via the dermal route were available prior to the release of the TBBPA problem formulation, at least two relevant studies have since been published. The first study estimated percutaneous uptake of TBBPA in humans from *in vivo* rodent (female Wistar Han rats) toxicokinetics data and human and rat skin *in vitro* data, reported penetrated, absorbed, and unabsorbed fractions for two doses (100 and 1000 nmol/cm^2, and concluded that up to 6% of dermally applied TBBPA may be bioavailable to humans exposed to TBBPA.[2] The second study, which evaluated absorption and excretion of TBBPA following subchronic dermal exposures to male Wistar rats, demonstrated that, dependent on dosing regimen, 3.31-11.21% of tetrabromobisphenol A was absorbed dermally.[3] These studies indicate that, contrary to the assumption in the Problem Formulation,[4] dermal exposures may be significant. Because at present no validated alternative methods completely cover absorption, distribution, metabolism, and excretion, further *in vivo* testing is needed in order to generate the toxicokinetic data needed for quantitative assessment.

While *in vivo* testing is required for toxicokinetic data, the dermal absorption parameters are of particular interest and novel *in vitro* models for absorption may also provide additional data for assessment. These models have been widely used in pharmacological studies, and are now being used for environmental exposures as well. A recent study of commercially available 3D human skin-equivalents demonstrated these to be comparable to fresh human *ex-vivo* skin samples for

[1] TBBPA Problem Formulation at 30.

[2] Knudsen, G. A., Hughes, M. F., McIntosh, K. L., Sanders, J. M., & Birnbaum, L. S. (2015). Estimation of tetrabromobisphenol A (TBBPA) percutaneous uptake in humans using the parallelogram method. *Toxicology and Applied Pharmacology, 289*(2), 323-329. https://doi.org/10.1016/j.taap.2015.09.012

[3] Yu, Y., Xiang, M., Gao, D., Ye, H., Wang, Q., Zhang, Y., ... & Li, H. (2016). Absorption and excretion of Tetrabromobisphenol A in male Wistar rats following subchronic dermal exposure. *Chemosphere, 146*, 189-194. https://doi.org/10.1016/j.chemosphere.2015.12.027

[4] TBBPA Problem Formulation at 109 ("…the compound will have limited absorption through the skin").

measuring dermal absorption of brominated flame retardants, including TBBPA.[5] However, it is important to note that such models do not account for potential differences in absorption by life-stage, which is particularly relevant for vulnerable populations such as infants and young children.

Testing requested

In vivo study will generate the most informative and appropriate toxicokinetic data for risk assessment, due to the intact physiological and metabolic systems present in test animals. The **Organization for Economic Cooperation and Development (OECD) guidelines for toxicokinetics (OECD 417),**[6] with references as directed to the earlier **OECD guidelines for skin absorption: in vivo absorption (OECD 427)**,[7] provide an appropriate approach to generate further *in vivo* toxicokinetics data via the dermal route for TBBPA. Under these guidelines, TBBPA is administered to the selected test species, typically a rodent, with at least 4 animals of each sex for each dose, although a larger sample size should be used to evaluate low dose effects. The exposure occurs either in a single dose or repeated doses with 6 or 24 hours between application and removal of test substance by skin washing, based on expected human exposure scenarios. The 24 hour exposure period should be used for residential exposure scenarios as U.S. dust testing data indicates widespread presence of TBBPA in indoor environments.[8] At least two concentrations, chosen based on the results of the Knudsen and Yu studies cited above, should be tested. TBBPA and its metabolites are then determined in body fluids, tissues and waste products. The guideline further recommends that metabolites present at concentrations at least 5% of the administered dose should be identified, which provides additional information needed for assessment of toxicity of TBBPA via the dermal pathway.

1B) INHALATION

Assessment of available information

The Problem Formulation noted only one study with inhalation exposure, a 14-day toxicity study in rats, which lacked toxicokinetic data.[9] The Problem Formulation also noted that the EU

[5] Abdallah, M. A. E., Pawar, G., & Harrad, S. (2015). Evaluation of 3D-human skin equivalents for assessment of human dermal absorption of some brominated flame retardants. *Environment International, 84*, 64-70. https://doi.org/10.1016/j.envint.2015.07.015

[6] OECD (2010). Test No 417: Toxicokinetics. Guideline for the testing of chemicals. In *OECD Guidelines for the Testing of Chemicals, Section 4: Health Effects*. OECD Publishing, Paris.

[7] OECD (2004). Test No. 427: Skin Absorption: In Vivo Method. In *OECD Guidelines for the Testing of Chemicals, Section 4: Health Effects*. OECD Publishing, Paris.

[8] Mitro, S. D., Dodson, R. E., Singla, V., Adamkiewicz, G., Elmi, A. F., Tilly, M. K., & Zota, A. R. (2016). Consumer product chemicals in indoor dust: a quantitative meta-analysis of US studies. *Environmental Science & Technology, 50*(19), 10661-10672. https://doi.org/10.1021/acs.est.6b05530

[9] International Research and Development Corporation (1975). *Fourteen-Day Inhalation Toxicity Study in Rats*. Unpublished manuscript (as cited in European Commission (2006). *European Union Risk Assessment Report for TBBP-A Part II – Human Health, CAS No. 79-94-7, EINECS No. 201-236-9. 4th Priority List, Volume: 63, EUR22161 EN*. Institute for Health and Consumer Protection, Joint Research Centre, Luxembourg).

approximates 5% of inhaled particulates will be absorbed directly into the lungs,[10] indicating that inhalation exposures may be significant.

While *in vitro* models may provide some toxicokinetic information, particularly as regards absorption, which are increasingly used in analogous pharmacological studies,[11,12] no national or international authority has yet validated such an alternative testing strategy for risk assessment purposes. *In vivo* study remains the most informative for risk assessment, representing an intact physiological and metabolic system and further *in vivo* testing is needed in order to generate the toxicokinetic data needed for quantitative assessment.

Testing requested

The **OECD guidelines for toxicokinetics (OECD 417)** via the inhalation route are the most widely accepted guidance and should be implemented with a standard mammalian species and an additional avian species, given potential for toxicity to wildlife following ecologic exposure. Species selection in this methodology is for a rodent model by default, but species determination should take into consideration models used in existing toxicity studies. Under the OECD 417 guidelines, TBBPA is administered using a "nose-cone" or "head-only" apparatus to prevent absorption by alternate routes of exposure. A single exposure over a defined period, typically 4 to 6 hours in duration, should be used for each group of subjects. Subsequent to exposure, TBBPA and its metabolites are determined in body fluids, tissues and waste products. The guideline recommends that metabolites present at concentrations of at least 5% of the administered dose should be identified, which provides information needed for assessment of toxicity of TBBPA via the inhalation pathway.

In addition to the paucity of toxicokinetics data following inhalation exposure to TBBPA, the rationale presented in the Problem Statement for not assessing exposure via direct inhalation of TBBPA is that no information is available on toxicity to plants and other wildlife organisms (e.g., birds) exposed via the air.[13] Rather than exclude exposure through inhalation, testing should be ordered, as validated methods exist both for testing toxicity to plants exposed via the air, and to wildlife organisms exposed via the air.

For plants, EPA's **Early Seedling Growth Toxicity Test (OCSPP 850.4230 guideline)**[14] is designed to screen a test substance to determine its potential to cause phytotoxicity in an early

[10] TBBPA Problem Formulation at 109.

[11] Nahar, K., Gupta, N., Gauvin, R., Absar, S., Patel, B., Gupta, V., ... & Ahsan, F. (2013). In vitro, in vivo and ex vivo models for studying particle deposition and drug absorption of inhaled pharmaceuticals. *European Journal of Pharmaceutical Sciences*, *49*(5), 805-818. https://doi.org/10.1016/j.ejps.2013.06.004

[12] Sarmento, B. (2015). *Concepts and Models for Drug Permeability Studies: Cell and Tissue Based in Vitro Culture Models*. Woodhead Publishing.

[13] TBBPA Problem Formulation at 42.

[14] EPA Office of Chemical Safety and Pollution Prevention (2012). *OCSPP 850.4230: Early Seedling Growth Toxicity Test*. Retrieved from https://www.regulations.gov/document?D=EPA-HQ-OPPT-2009-0154-0025.

growth stage in terrestrial plants, mainly using commercially important crop species. Surface deposition is the anticipated mode of terrestrial plant exposure to TBBPA from air; thus the foliar exposure pathway in the testing method should be used.

For wildlife, an avian surrogate might be evaluated for toxicokinetics, as mentioned in the preceding paragraph, and also acute toxicity following exposure via inhalation. As quantitative data is needed to inform risk assessment, it is appropriate to start with an acute inhalation toxicity study, such as the protocol described in **EPA's OPPTS 870.1300 guidelines.**[15] This protocol is already adaptable for non-rodent mammalian species, and can be modified to accommodate a standard avian model, such as quail, with which other studies of TBBPA have been conducted. Such an acute inhalation toxicity study is the initial step in evaluation, providing information on health hazards likely to arise from short-term exposure via inhalation.

2) Diet and Drinking Water Exposures

2A) DIET

Assessment of available information

Experimental data and models for plant bioaccumulation of organic contaminants such as TBBPA have a role in assessing potential human and ecological risks. TBBPA has been found in a number of foods beyond fish, including dairy products such as milk and cheese as reported in European studies.[16,17] Asian studies, including the Fourth Total Diet Survey in China, have reported TBBPA concentrations in powdered milks, produce, meat, eggs, and aquatic foods including shellfish.[18,19,20] Further, a recent analytical method study conducted in the United States detected TBBPA in commercial baby food products.[21] Testing is warranted because lack

[15] EPA Office of Prevention, Pesticides and Toxic Substances (1998). *OPPTS 870.1300: Acute Inhalation Toxicity*. Retrieved from https://www.regulations.gov/document?D=EPA-HQ-OPPT-2009-0156-0005

[16] Thomsen, C., Leknes, H., Lundanes, E., & Becher, G. (2002). A new method for determination of halogenated flame retardants in human milk using solid-phase extraction. *Journal of Analytical Toxicology, 26*(3), 129-137. https://doi.org/10.1093/jat/26.3.129

[17] de Winter-Sorkina, R., Bakker, M. I., Van Donkersgoed, G., & Van Klaveren, J. D. (2003). *Dietary intake of brominated flame retardants by the Dutch population.* RIVM report 31305001/2003. RIVM – Netherlands Institute of Public Health and the Environment.

[18] Murata, S., Nakagawa, R., Ashizuka, Y., Hori, T., Yasutake, D., Tobiishi, K., & Sasaki, K. (2007). Brominated flame retardants (HBCD, TBBPA and ΣPBDEs) in market basket food samples of Northern Kyushu district in Japan. *Organohalogen Compd, 69*, 1985-1988.

[19] Shi, Z. X., Wu, Y. N., Li, J. G., Zhao, Y. F., & Feng, J. F. (2009). Dietary exposure assessment of Chinese adults and nursing infants to tetrabromobisphenol-A and hexabromocyclododecanes: occurrence measurements in foods and human milk. *Environmental Science & Technology, 43*(12), 4314-4319. https://doi.org/10.1021/es8035626

[20] Nakao, T., Kakutani, H., Akiyama, E., & Ohta, S. (2013). Levels of tetrabromobisphenol A and its related compounds in infant foods in Japan. *Organohalogen Compd, 75*, 169-172.

[21] Allen, K. M. (2016). *Analysis of tetrabromobisphenol-A in baby food by gas chromatography-mass spectrometry and liquid chromatography-mass spectrometry*. (Unpublished thesis). University of Colorado, Colorado Springs.

of information on uptake from soil is preventing consideration of risks resulting from multiple scenarios, including surface deposition from air releases from manufacturing facilities and application of sewage sludge containing TBBPA to agricultural land, and subsequent potential for entry into the food chain.

Testing requested

As plants are receptor organisms and potential vectors for chemical exposures to all other organisms, the most critical data in this scenario is potential for plant uptake of TBBPA. The most appropriate test is **EPA's Plant Uptake and Translocation (OCSPP 850.4800)**,[22] which outlines procedures for conducting a mass balance study of the distribution of a chemical in environmental matrices and different components of the plant under either root or foliar exposure for use in determining human and livestock food safety. Foliar exposure is of particular use for scenarios in which the anticipated mode of exposure to plants is surface deposition, as would be the case with stack releases of TBBPA to the air from production sites. Root exposure would be appropriate for releases to water, and in the scenario of sewage sludge application to agricultural fields. When implemented following the guidelines, the Plant Uptake and Translocation test generates data on the quantity of a substance incorporated in plant tissues, which allows for consideration of quantitative plant uptake and bioaccumulation and further informs the potential for entry into food chains, which also addresses the paucity of data regarding livestock.

Food products most susceptible to TBBPA bioaccumulation, including animal and plant products, could also be tested; methods could be adapted from existing monitoring studies for similar chemical contaminants, outside of routine pesticide residue assessments conducted by the Food & Drug Administration (FDA). For example, FDA published a strategy on monitoring and method development for dioxin and PCB contaminants.[23] Although FDA's existing Drug & Chemical Residues Methods, as publically available, do not include a method for TBBPA or closely related compounds, analytical methods could also be adapted from existing peer-reviewed literature, such as those used in the studies cited in the previous subsection of Section 2A, if sufficient according to existing FDA guidelines for validation of chemical methods.[24]

2B) DRINKING WATER

Assessment of available information

According to the TBBPA Problem Formulation, there is no data on the presence of TBBPA in ground water or drinking water in the U.S.[25] However, the Problem Formulation also states that TBBPA is expected to be persistent in water and is reported in surface water and waste water, indicating that drinking water is a likely source of TBBPA exposure. We are requesting testing so that the contribution of drinking water to TBBPA exposure can be better quantified.

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[22] EPA OCSPP (2012). *OCSPP 850.4800: Plant Uptake and Translocation Test*. Retrieved from https://www.regulations.gov/document?D=EPA-HQ-OPPT-2009-0154-0006

[23] FDA (2002, Feb. 7). *DIOXINS: FDA Strategy for Monitoring, Method Development, and Reducing Human Exposure*. Retrieved from http://www.fda.gov/Food/FoodborneIllnessContaminants/ChemicalContaminants/ucm077432.htm

[24] FDA (2015). *Guidelines for the Validation of Chemical Methods for the FDA FVM Program* (2nd ed.). Retrieved from http://www.fda.gov/downloads/ScienceResearch/FieldScience/UCM273418.pdf

[25] TBBPA Problem Formulation at 45.

Testing requested
To fully understand the potential for TBBPA exposure from ground water and drinking water in the United States, a study design must include sampling of waters in the vicinity of representative manufacturing and processing facilities known to discharge TBBPA to the environment. EPA has extensive guidelines for sampling strategies and study designs which guide development of new studies. EPA's **Guidance for Data Useability in Risk Assessment (Part A)**,[26] for example, presents an extensive discussion of possible sampling strategies, sampling methods, and analytical methods.

Appropriate locations for TBBPA testing can be identified from existing data sources, including TRI. Waters in the vicinity of representative disposal facilities, such as municipal landfills and e-waste recycling plants, should also be identified for testing.

As to sampling for TBBPA in such waters, EPA has guidelines specific to sampling studies of chemical contaminants in treated drinking water and in drinking water sources for those contaminants within the scope of current regulatory monitoring, but also including guidance for chemicals outside of this scope, such as **Sampling Guidance for Unknown Contaminants in Drinking Water**.[27] These guidelines can be applied in development of testing for TBBPA in representative waters. Generally, for a sampling approach, grab samples would be expected to provide a reasonable snap-shot view of the environment, and should be appropriate for this purpose, so long as sufficient repeat surveys are conducted under different conditions, to ensure the sampling locations are as representative as is reasonably possible. Quality assurance and control protocols including blank and duplicate samples will depend on final study design, but must be taken into consideration as well, in compliance with EPA's **Guidance on Choosing a Sampling Design for Environmental Data Collection**.[28] In development of testing protocols, existing sample handling and storage procedures currently utilized for similar organic compounds under regulatory monitoring can be applied to TBBPA.

Though existing sampling approaches can be applied for testing of TBBPA, a sensitive and specific analytical method for determination and quantification of TBBPA in sampled waters is still required. EPA has not recommended an analytical method for analysis of TBBPA. Further, the interagency National Environment Methods Index (NEMI) does not list any analytical method for analysis of TBBPA. However, there are a number of peer reviewed, published methods for determination and quantification of TBBPA in a variety of environmental media. This includes several optimized for environmental water samples, such as the two mass-

[26] EPA Office of Research and Development (1991). *Guidance for Data Useability in Risk Assessment (Part A).* Retrieved from https://rais.ornl.gov/documents/USERISKA.pdf

[27] EPA Office of Water (2008). *Sampling Guidance for Unknown Contaminants in Drinking Water*. Retrieved from https://www.epa.gov/sites/production/files/2015-08/documents/2008_12_31_watersecurity_pubs_guide_watersecurity_samplingforunknown.pdf

[28] EPA Office of Environmental Information (2002). *Guidance on Choosing a Sampling Design for Environmental Data Collection*. Retrieved from https://www.epa.gov/sites/production/files/2015-06/documents/g5s-final.pdf

spectrometry based methods described in Labadie et al. (2010)[29] and Yang et al. (2014),[30] which could be adopted and validated for testing purposes, in lieu of novel method development.

3) Exposure from Manufacturing and Processing

3A) COMMUNITIES

Assessment of available information

As ecological and human communities in the vicinity of manufacturing and processing facilities may experience exposure to TBBPA, environmental media should be assessed or monitored for TBBPA and TBBPA-specific degradates. Because the European Commission risk assessment[31] found that facility risks may differ based on whether TBBPA is used reactively or additively, testing should be carried out separately for both types of processing facilities: those that use TBBPA reactively and those that use TBBPA additively.

Testing requested

Given a paucity of data regarding concentrations of TBBPA in ecological and human communities, sampling studies to determine environmental contaminations are necessary to estimate exposures.

No single method applies to all monitoring and assessment needs. For a multimedia environmental assessment of TBBPA in communities in the vicinity of processing and manufacturing facilities, media-specific approaches must be employed. At a minimum, media including air, soil, and water should be included in the overarching assessment strategy; however, media evaluated will necessarily be specific to each site assessed. Representative sampling sites should be based on available data for sources of TBBPA, including TRI reporting, and also take into consideration properties of TBBPA and relevant exposure pathways for communities of interest.

As possible, existing EPA guidance for similar compounds in respective media should be utilized for sampling strategy design and protocols, and comply with EPA's Guidance on Choosing a Sampling Design for Environmental Data Collection.[32] However, for analytical determination

[29] Labadie, P., Tlili, K., Alliot, F., Bourges, C., Desportes, A., & Chevreuil, M. (2010). Development of analytical procedures for trace-level determination of polybrominated diphenyl ethers and tetrabromobisphenol A in river water and sediment. *Analytical and Bioanalytical Chemistry*, *396*(2), 865-875. https://doi.org/10.1007/s00216-009-3267-x

[30] Yang, Y., Lu, L., Zhang, J., Yang, Y., Wu, Y., & Shao, B. (2014). Simultaneous determination of seven bisphenols in environmental water and solid samples by liquid chromatography–electrospray tandem mass spectrometry. *Journal of Chromatography A*, *1328*, 26-34. https://doi.org/10.1016/j.chroma.2013.12.074

[31] European Commission (2008). *Risk Assessment of 2,2',6,6-Tetrabromo-4,4'-Isopropylidene Diphenol (Tetrabromobisphenol-A)L Final Environmental Rar of February 2008.* Rapporteur: United Kingdom. Retrieved from http://echa.europa.eu/documents/10162/17c7379e-f47b-4a76-aa43-060da5830c07

[32] EPA Office of Environmental Information (2002). *Guidance on Choosing a Sampling Design for Environmental Data Collection*. Retrieved from https://www.epa.gov/sites/production/files/2015-06/documents/g5s-final.pdf

and quantification, existing agency methods will require modification or, alternatively, substitution with existing peer-reviewed, published methods, as EPA has not recommended an analytical method for analysis of TBBPA. Further, the interagency National Environment Methods Index (NEMI) does not list any analytical method for analysis of TBBPA.

Air

For assessment of TBBPA in ambient air, a high-volume air sampling approach, such as that of **EPA Air Method Toxic Organics-9A** (TO-9A, Determination Of Polychlorinated, Polybrominated And Brominated/Chlorinated Dibenzo-p-Dioxins And Dibenzofurans In Ambient Air),[33] should be employed. High-volume air sampling approaches for semi-volatile chemicals are expected to provide sufficient analyte for detection limits with shorter sampling periods.[34] Although originally designed for dioxins and furans in ambient air, the approach described can be implemented for other semivolatile organic compounds with similar properties. This method uses a high-volume air sampler equipped with a quartz-fiber filter and polyurethane foam (PUF) adsorbent cartridge for sampling 325 to 400 m^2 ambient air over a 24-hour sampling period, with sample analysis based on high resolution gas chromatography-high resolution mass spectrometry. This detection method should be further modified for TBBPA; modifications could readily be made to the analytical method based on existing peer-reviewed sampling studies of TBBPA in air using PUF-based sampling media.[35,36]

Soil

Sampling of soils or sediment will vary based on the type of material present, but should follow considerations for screening sampling such as are discussed in guidances like **Preparation of Soil Sampling Protocols** (EPA/600/R-92/128),[37] which provides methods, techniques, and procedures for designing a variety of soil measurement programs, or field assessment guides like **Description and Sampling of Contaminated Soils** (EPA/625/12-91/002).[38] Existing EPA analytical methods, such as **Method 8270**,

[33] EPA Office of Research and Development (1999). *Compendium Method TO-9A: Determination Of Polychlorinated, Polybrominated And Brominated/Chlorinated Dibenzo-p-Dioxins And Dibenzofurans In Ambient Air*. Retrieved from https://www3.epa.gov/ttnamti1/files/ambient/airtox/to-9arr.pdf

[34] Longer sampling periods could reasonably use either a passive air sampling approach or a low-volume air sampling approach, such as that of EPA Air Method Toxic Organics-10A (TO-10A, Determination of Pesticides and Polychlorinated Biphenyls in Ambient Air Using Low Volume Polyurethane Foam (PUF) Sampling Followed by Gas Chromatographic/Multi-Detector Detection (GC/MD)).

[35] Takigami, H., Suzuki, G., Hirai, Y., Ishikawa, Y., Sunami, M., & Sakai, S. I. (2009). Flame retardants in indoor dust and air of a hotel in Japan. *Environment International*, *35*(4), 688-693. https://doi.org/10.1016/j.envint.2008.12.007

[36] Tollbäck, J., Crescenzi, C., & Dyremark, E. (2006). Determination of the flame retardant tetrabromobisphenol A in air samples by liquid chromatography-mass spectrometry. *Journal of Chromatography A*, *1104*(1), 106-112. https://doi.org/10.1016/j.chroma.2005.11.067

[37] Mason, B. J. (1992). *Preparation of Soil Sampling Protocols: Sampling Techniques and Strategies.* EPA Office of Research and Development Environmental Monitoring Systems Laboratory, Las Vegas.

[38] EPA Center for Environmental Research Information (1991). *Description and Sampling of Contaminated Soils: A Field Pocket Guide.* Retrieved from https://www.epa.gov/nscep.

for semivolatile organics do not include TBBPA, but outline sample preparation and gas chromatography/mass spectrometry-based analysis of semivolatile organic pollutants in multiple matrices, including solid waste and soil.[39] Such methods could be adapted to include TBBPA, or more specific extraction and mass spectrometry-based analytical methods as described in recent peer-reviewed soil/sediment/sludge sampling studies of TBBPA could be adopted.[40, 41, 42]

Water

Approaches for sampling studies of TBBPA in water will vary based on the type of water; drinking water, surface water, and ground water require different considerations, but each have sampling strategies for similar compounds recommended by EPA which could be utilized for sampling for TBBPA. In terms of analysis of collected water samples, a number of peer reviewed, published methods optimized for environmental water samples, exist. As described above, these include two mass-spectrometry based methods described in Labadie et al. (2010)[43] and Yang et al. (2014),[44] which could be adopted and validated for testing purposes.

3B) MANUFACTURING- WORKERS

Assessment of available information

According to the Problem Formulation, current estimates of TBBPA dust concentrations in manufacturing plants are based off of data for PNOR (particulates not otherwise regulated).[45]

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[39] EPA (2014). *Publication SW-846, Method 8270D: Semivolatile Organic Compounds by Gas Chromatography/Mass Spectrometry (GC/MS)*. Retrieved from https://www.epa.gov/hw-sw846/sw-846-compendium.

[40] Chu, S., Haffner, G. D., & Letcher, R. J. (2005). Simultaneous determination of tetrabromobisphenol A, tetrachlorobisphenol A, bisphenol A and other halogenated analogues in sediment and sludge by high performance liquid chromatography-electrospray tandem mass spectrometry. *Journal of Chromatography A*, *1097*(1), 25-32. https://doi.org/10.1016/j.chroma.2005.08.007

[41] Gorga, M., Martínez, E., Ginebreda, A., Eljarrat, E., & Barceló, D. (2013). Determination of PBDEs, HBB, PBEB, DBDPE, HBCD, TBBPA and related compounds in sewage sludge from Catalonia (Spain). *Science of the Total Environment*, *444*, 51-59. https://doi.org/10.1016/j.scitotenv.2012.11.066

[42] Qu, G., Liu, A., Hu, L., Liu, S., Shi, J., & Jiang, G. (2016). Recent advances in the analysis of TBBPA/TBBPS, TBBPA/TBBPS derivatives and their transformation products. *TrAC Trends in Analytical Chemistry*, *83*, 14-24. https://doi.org/10.1016/j.trac.2016.06.021

[43] Labadie, P., Tlili, K., Alliot, F., Bourges, C., Desportes, A., & Chevreuil, M. (2010). Development of analytical procedures for trace-level determination of polybrominated diphenyl ethers and tetrabromobisphenol A in river water and sediment. *Analytical and BioanalyticalBchemistry*, *396*(2), 865-875. https://doi.org/10.1007/s00216-009-3267-x

[44] Yang, Y., Lu, L., Zhang, J., Yang, Y., Wu, Y., & Shao, B. (2014). Simultaneous determination of seven bisphenols in environmental water and solid samples by liquid chromatography–electrospray tandem mass spectrometry. *Journal of Chromatography A*, *1328*, 26-34. https://doi.org/10.1016/j.chroma.2013.12.074

[45] OSHA (2015). *Chemical Exposure Health Data*. United States Department of Labor, Washington, DC.

An occupational assessment including biological and environmental monitoring, should be conducted in representative manufacturing facilities.

Testing requested
Representative sites should be determined using existing data sources, including TRI. Testing of TBBPA in air and dust inside plants requires a sampling strategy that minimizes the differences between measured proxies and actual exposure levels. The approaches used should keep with those recommended by OSHA as published in the Technical Manual,[46] with sampling and analytical methods that have been validated by either OSHA or the National Institute for Occupational Safety and Health (NIOSH) used whenever possible.

Air sampling: There is a publically available, although only partially validated OSHA sampling/analytical method for TBBPA, in which air samples are collected by drawing a known volume of air through a glass fiber filter on site, which is subsequently extracted in the laboratory by 85:10:5 sooctane/isoproponal/methanol and analyzed by high performance liquid chromatography (HPLC) using an ultraviolet (UV) detector. However, this analytical method is out of date, less sensitive and less specific than more recently published, peer reviewed methods such as the stable isotope dilution liquid chromatography–mass spectrometry protocol developed for determination of TBBPA and other phenols by Inoue et al. (2006).[47] Using this method, the quantification limit for TBBPA in the air samples tested was 0.l ng/m^2. Unless OSHA or NIOSH have a validated analytical method that is as sensitive and specific, this approach, or one similar, should be adopted for occupational air sampling. This method uses the same principles, in which a known volume of air (in the published method, 7 L / min for 24 hours) is drawn from the surroundings by a mechanical pump to a glass filter and solid phase disc in a cartridge, with subsequent extraction to elute retained compounds of interest prior to instrumental analysis. For this type of indoor air sampling, either area or personal sampling devices may be used, with area sampling devices preferable for longer periods of sampling.

As TBBPA-containing particle size and composition may vary in these occupational environments, to best evaluate occupational exposures of TBBPA, sampling that allows for separation and collection of respirable and inhalable dust fractions should be conducted in addition to total air sampling. These fractions can also be analyzed by the instrumental methods for total air sampling, although extraction from the sampling media or dust matrix will be dependent on collection method used. The recommended OSHA approach involves use of a cyclone apparatus to separate and capture those particles in defined size ranges, for which many devices are commercially available. There are, however, alternative designs that meet OSHA air particulate sampling criteria and allow for collection of these fractions, such as the commercially available personal sampling device used in a recent peer reviewed study of TBBPA and other

[46] OSHA (n.d.). *OSHA Technical Manual, OSHA Instruction TED 01-00-015*. Retrieved from https://www.osha.gov/dts/osta/otm/index.html.

[47] Inoue, K., Yoshida, S., Nakayama, S., Ito, R., Okanouchi, N., & Nakazawa, H. (2006). Development of stable isotope dilution quantification liquid chromatography–mass spectrometry method for estimation of exposure levels of bisphenol A, 4-tert-octylphenol, 4-nonylphenol, tetrabromobisphenol A, and pentachlorophenol in indoor air. *Archives of Environmental Contamination and Toxicology, 51*(4), 503-508.

halogenated flame retardants in respirable and inhalable particulates, settled dust, and polyurethane foam.[48]

Dust sampling: In addition to air sampling approaches, settled dust sampling should be conducted to assess the presence of TBBPA on surfaces that may lead to worker exposure, either through direct dermal exposure, transfer to foodstuffs and accidental ingestion, or surface agitation causing particles to resuspend in air, resulting in additional inhalation exposure. Bulk dust sampling and surface wipe sampling approaches should both be utilized. Quantitative surface wipe sampling, in which an area of specified size is wiped, should be used as it is necessary to determine the concentration of a contaminant on a surface and subsequently estimate the amount of contamination to which workers are potentially exposed. According to the OSHA Technical Manual (OSHA Instruction TED 01-00-015 [TED 1-0.15A]) the standard surface area to be wiped is a 10 cm x 10 cm square, as it approximates the surface area of a worker's palm.[49] Bulk dust sampling is conducted on a larger scale, typically with a vacuum, for which there are methods for a wide range of compounds and surfaces, although not all are applicable to occupational settings.[50] However, in addition to gathering bulk dust for analysis, these methods are also useful when sampling very large surface areas or surface areas that are porous or irregular, where it is impractical to use wipes. Extraction methods exist for similar compounds from standard wipes and from dust as a matrix, which would be followed by an instrumental analysis as previously described.

Biomonitoring: Biological monitoring should follow the protocols of the current study, **Assessment of Occupational Exposure to Flame Retardants**, conducted by NIOSH for NTP.[51] In this study, exposure to PBDEs and nine alternative flame retardants including TBBPA are assessed through air, urine, and sera samples from workers for a variety of occupations (workers in construction, plastic goods manufacturing, gymnasium workers, and firefighters).[52] Dermal exposure should also be considered for manufacturing, processing and recycling workers.

3C) PROCESSING- WORKERS

Assessment of available information

[48] La Guardia, M. J., & Hale, R. C. (2015). Halogenated flame-retardant concentrations in settled dust, respirable and inhalable particulates and polyurethane foam at gymnastic training facilities and residences. *Environment International*, *79*, 106-114. https://doi.org/10.1016/j.envint.2015.02.014

[49] OSHA (n.d.). *OSHA Technical Manual, OSHA Instruction TED 01-00-015*. Retrieved from https://www.osha.gov/dts/osta/otm/index.html

[50] Creek, K. L., Whitney, G., & Ashley, K. (2006). Vacuum sampling techniques for industrial hygienists, with emphasis on beryllium dust sampling. *Journal of Environmental Monitoring*, *8*(6), 612-618. https://doi.org/10.1039/b601572g

[51] National Toxicology Program (2015). NTP at NIOSH: Comprehensive Assessment of Occupationally Relevant Exposures. In *2015 Annual Report*. Retrieved from https://ntp.niehs.nih.gov/annualreport/2015/partners/niosh_comprehensive/index.html

[52] National Institute of Occupational Safety & Health (2014). *Update on NIOSH Projects*. Retrieved from https://ntp.niehs.nih.gov/ntp/about_ntp/bsc/2014/dec/nioshupdate_508.pdf

According to the Problem Formulation, only one of the dust monitoring studies in TBBPA processing plants was specific to TBBPA, and this study was not carried out in a US facility.[53] An occupational assessment, including biological and environmental monitoring, should be conducted in representative processing facilities. Because the European Commission risk assessment found that facility risks may differ based on whether TBBPA is used reactively or additively, testing should be carried out separately for both types of processing facilities: those that use TBBPA reactively and those that use TBBPA additively.

Testing requested
Air testing, dust testing, surface wipe testing and worker biomonitoring as described above in Section 3B: Manufacturing Workers should be carried out for facilities that process TBBPA reactively and for facilities that process TBBPA additively.

4) Exposure from Recycling

Assessment of available information
According to the Problem Formulation, there is currently no information on the levels of TBBPA or its by-products in U.S. facilities that recycle e-waste. Studies in electronics dismantling facilities in other countries indicate potential for inhalation and dermal exposures to TBBPA for workers.[54] It is clear that workers may be exposed by recycling processes, and that testing is warranted to estimate TBBPA exposures from recycling facilities in the U.S.

Testing requested
4A) COMMUNITIES
As ecological and human communities in the vicinity of recycling facilities may experience exposure to TBBPA, environmental media should be assessed or monitored for TBBPA and TBBPA-specific degradates.

Assessments of representative recycling facilities which include air, soil and water testing should be carried out as described in Section 3A: Communities above.

4B) WORKERS
Air testing, dust testing, surface wipe testing and worker biomonitoring as described above in Section 3B: Manufacturing Workers should be carried out for representative recycling facilities.

5) Exposure from Disposal

5A) LANDFILLS, WASTEWATER TREATMENT PLANTS, AND SEWAGE SLUDGE

[53] European Commission (2008). *Risk Assessment of 2,2',6,6-Tetrabromo-4,4'-Isopropylidene Diphenol (Tetrabromobisphenol-A)L Final Environmental Rar of February 2008.* Rapporteur: United Kingdom. Retrieved from http://echa.europa.eu/documents/10162/17c7379e-f47b-4a76-aa43-060da5830c07

[54] Mäkinen, M. S., Mäkinen, M. R., Koistinen, J. T., Pasanen, A. L., Pasanen, P. O., Kalliokoski, P. J., & Korpi, A. M. (2009). Respiratory and dermal exposure to organophosphorus flame retardants and tetrabromobisphenol A at five work environments. *Environmental Science & Technology, 43*(3), 941-947. https://doi.org/10.1021/es802593t

Assessment of available information
Given the decades of TBBPA product use and disposal, consideration of TBBPA exposure from landfills should be based on quantifiable data as to the potential for occurrence.

Testing requested
Testing, such as described in **EPA's 835.1240 guideline, Leaching Studies**,[55] although originally intended to support pesticide assessment, is suitable for TBBPA. Such studies, which assess the mobility of a substance through columns packed with various soils, could be used to predict leaching potential of TBBPA and TBBPA degradates through a variety of soil profiles representative of US landfills.

Testing should also be performed to evaluate potential fate of TBBPA following disposal of wastes containing TBBPA via WWTPs, as both facility waste and final consumer products containing TBBPA may be sent to WWTPs. Simulation testing, such as outlined in **EPA-OPPTS 835.3280, Simulation Tests to Assess the Primary and Ultimate Biodegradability of Chemicals Discharged to Wastewater**,[56] is the most relevant approach. Based on OECD test guideline 413, this method consists of five simulation tests including treated effluent in the mixing zone of surface water and untreated wastewater that is directly discharged to surface water. These tests are appropriate for episodic and continuous releases to wastewater, and are designed to measure rates of primary biodegradation and mineralization as well as determine major transformation products.

Additional testing is also needed to allow for consideration of the bioavailability of TBBPA in resultant sewage sludge, given potential application to agricultural land. As described above in Section 2A- Diet, an appropriate test is **EPA's Plant Uptake and Translocation (OCSPP 850.4800)**.[57] Root exposure is appropriate for testing the scenario of sewage sludge application to agricultural fields.

5B) INCINERATION
Assessment of available information
There is currently no information on the levels of TBBPA or its by-products in U.S. facilities that dispose of TBBPA-containing products. TBBPA is used in products that are known to undergo disposal through incineration. As such, additional data is required to assess risk of TBBPA exposure from disposal through incineration, especially given known combustion products hazardous to health including PAHs, PBDDs, and PBDFs (see section 6C below). In addition to the further combustion testing of TBBPA described in Section 6C Combustion By-Products below, site assessments of representative facilities and occupational assessments of workers in representative facilities are warranted. Because disposal by incineration produces toxic

[55] EPA Office of Prevention, Pesticides and Toxic Substances (2008). *OPPTS 835.1240, Leaching Studies*. Retrieved from https://www.regulations.gov/document?D=EPA-HQ-OPPT-2009-0152-0007

[56] EPA OPPTS (2008). *OPPTS 835.3280, Simulation Tests to Assess the Primary and Ultimate Biodegradability of Chemicals Discharged to Wastewater*. Retrieved from https://www.regulations.gov/document?D=EPA-HQ-OPPT-2009-0152-0036

[57] EPA OCSPP (2012). *OCSPP 850.4800: Plant Uptake and Translocation Test*. Retrieved from https://www.regulations.gov/document?D=EPA-HQ-OPPT-2009-0154-0006

combustion by-products, site and occupational assessments should include testing for TBBPA *and* its combustion by-products PAHs, PBDFs, and PBDDs.

Testing requested
Assessments of representative disposal facilities which include air, soil and water testing for TBBPA and its combustion products should be carried out as described in Section 3A: Communities above.

Air testing, dust testing, surface wipe testing and worker biomonitoring for TBBPA and its combustion products as described above in Section 3B: Manufacturing Workers should be carried out for representative disposal facilities.

6) Exposure to Degradation By-Products

6A) DEGRADATION IN WATER OR SOIL
Assessment of available information
TBBPA has been found in diverse environments that include anaerobic and aerobic conditions; as such, a range of degradation processes can be expected to occur. That data on degradation are limited, uncertain or both, is insufficient to exclude assessment of risks from TBBPA's degradation products. Rather, this warrants testing to provide information sufficient to evaluate TBBPA's rates of transformation and degradation products. Such testing must be specific to likely environmental scenarios or a degradation process of concern, and should take into account existing data.

Photodegradation of TBBPA, which may result in formation of a range of bromophenols and dibromoisopropylphenol derivatives is one process that should be tested further. Though photolysis may occur in air, it is unlikely to occur given the properties of TBBPA, so evaluation should be limited to photolysis in water and at soil surface, both of which are relevant media for environmental fate. EPA and OECD guidelines for testing exist for photolysis in both of these, and data generated should be readily interpretable for risk assessment.

Testing requested
EPA-OPPTS guideline 835.2240 describes tiered testing for photodegradation in water, including determination of direct photolysis rate constants and half-life in water and sunlight as well as the products likely to be produced in this process.[58] **EPA-OPPTS guideline 835.5270**, for indirect photolysis in waters containing dissolved humic substance, describes studies that quantify a reaction resulting from chemical or electronic excitation transfer from light-absorbing humic species rather than direct sunlight.[59] This latter test is relevant as, while TBBPA generally is of low to moderate solubility, dissolved organic matter, such as may be found in wastewater treatment plants or natural waters, can increase solubility. The **OPPTS guideline 835.2410**

[58] EPA OPPTS (2008). *OPPTS 835.2240, Photodegradation in Water*. Retrieved from https://www.regulations.gov/document?D=EPA-HQ-OPPT-2009-0152-0012

[59] EPA OPPTS (1998). *OPPTS 835.5270, Indirect Photolysis Screening Test.* Retrieved from https://www.regulations.gov/document?D=EPA-HQ-OPPT-2009-0152-0031

describes testing for photolysis in soil, which, while intended to meet data requirements for pesticides under FIFRA, is reasonable for other substances.[60] 835.2410 describes studies of soil surface-catalyzed photolysis that provide sufficient information to enable determination of stability of a chemical and its photoproducts when exposed to sunlight, and prediction of persistence.

6B) MICROBIAL DEGRADATION

Assessment of available information

In addition to such abiotic processes, microbial degradation has been demonstrated for TBBPA, and requires consideration. The exclusion of existing data from studies conducted with exposed microbes in calculation of TBBPA degradation rates to BPA is inappropriate, as it is most likely that TBBPA degradation will take place by organisms in contaminated sites. Further, additional studies have been published since the Problem Statement was finalized, including a study of degradation in sludge-amended soil[61] but also, of greater relevance given expressed concerns, a study characterizing the effect of TBBPA on microbial community structure.[62] In this study, of the start-up phase of a bench-scale anaerobic sludge reactor, introduction of TBBPA significantly shifted only a small proportion of the taxa present, including some species already known to be dehalogenating bacteria. Additionally, this study demonstrated that TBBPA was nearly completely transformed to BPA by reductive debromination in 55 days. Even with this latest data, supplemental biodegradation testing should be ordered, rather than exclude microbial degradants from assessment.

Testing requested

A suite of OECD guidelines exist for biodegradation tests, with the most applicable in this situation, especially given concerns about data extrapolation, falling under the category of simulation tests. Such tests exist for a variety of environments, with aerobic and anaerobic conditions. One relevant test, as described in **OECD 307**, the Aerobic and Anaerobic Transformation in Soil,[63] uses representative soil preparations (such as silty loam) rather than potentially pre-exposed samples from relevant locations, to determine the rate of transformation and transformation products. Additionally, although limited to terrestrial soil-plant ecosystems, one study that could provide information readily interpretable by EPA is **EPA-OCSPP's Terrestrial Soil-Core Microcosm Test (OCSPP 850.4900)**.[64] The soil-microcosm test utilizes soil cores with soil and plants/crops typical of a region of interest, but not previously exposed.

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[60] EPA OPPTS (2008). *OPPTS 835.2410, Photodegradation in Soil.* Retrieved from https://www.regulations.gov/document?D=EPA-HQ-OPPT-2009-0152-0015

[61] Yang, C. W., Chen, W. Z., & Chang, B. V. (2016). Biodegradation of tetrabromobisphenol-A in sludge-amended soil. *Ecological Engineering*, *91*, 143-147. https://doi.org/10.1016/j.ecoleng.2016.02.037

[62] Lefevre, E., Cooper, E., Stapleton, H. M., & Gunsch, C. K. (2016). Characterization and Adaptation of Anaerobic Sludge Microbial Communities Exposed to Tetrabromobisphenol A. *PloS one*, *11*(7), e0157622. https://doi.org/10.1371/journal.pone.0157622

[63] OECD (2002). Test No. 307: Aerobic and Anaerobic Transformation in Soil. In *OECD Guidelines for the Testing of Chemicals, Section 3: Degradation and Accumulation.* OECD Publishing, Paris.

[64] EPA OCSPP (2012). *OCSPP 850.4900: Terrestrial Soil-Core Microcosm Test*. Retrieved from https://www.regulations.gov/document?D=EPA-HQ-OPPT-2009-0154-0007

These biota are exposed and monitored for a minimum 12 week period with subsequent analysis of leachate, soil, and plant samples to determine the environmental fate of the test substance. This test also allows for determination of ecological effects.

As to further testing that should be ordered for biodegradation in aquatic environments relevant to TBBPA, implementation of studies following two simulation test guidelines should provide sufficient information. The first, **EPA-OPPTS's Aerobic Mineralization in Surface Water-Simulation Biodegradation Test**, first provides data for the basis of degradation kinetics, but also identification of transformation products, and quantification of concentrations as possible.[65] The second, **EPA-OPPTS 835.3280, Simulation Tests to Assess the Primary and Ultimate Biodegradability of Chemicals Discharged to Wastewater** is relevant not only for potential deposition of TBBPA, but for end-of-life disposal.[66] Based on OECD test guideline 413, this method consists of five simulation tests including treated effluent in the mixing zone of surface water and untreated wastewater that is directly discharged to surface water. These tests are appropriate for episodic and continuous releases to wastewater, and are designed to measure rates of primary biodegradation and mineralization as well as determine major transformation products.

6C) COMBUSTION PRODUCTS

Assessment of available information

According to the Problem Formulation, incineration of TBBPA releases polycyclic aromatic hydrocarbons (PAHs), polybrominated dibenzo-p-dioxins (PBDDs) and polybrominated dibenzofurans (PBDFS): "A recent study found that PBDDs, PBDFs and PAHs were emitted from incineration of TBBPA epoxy laminates. PAHs were emitted at higher levels from this laminate than from non-flame retardant laminates (Sidhu et al., 2013). In another study, Wichmann et al. (2002) found that PBDDs and PBDFs were emitted at similar magnitudes when comparing emissions from TBBPA used in reactive applications to those in additive flame retardant applications with PBDFs released in higher amounts than PBDDs."[67]

PAHs, PBDDs and PBDFs are known chemicals of concern. A more recent study of thermal degradation of TBBPA at varying temperatures and atmospheric conditions identified over 100 semivolatile combustion products of TBBPA, including levels of brominated dioxins and furans in the parts per million (ppm) range.[68] This study further observed maximum formation of PAHs at the higher temperature scenario of 800 degrees. Further, there is data to support that thermal destruction of TBBPA is not efficient even at high temperatures, with one study reporting an

[65] EPA OPPTS (2008). *OPPTS 835.3190, Aerobic Mineralization in Surface Water - Simulation Biodegradation Test.* Retrieved from https://www.regulations.gov/document?D=EPA-HQ-OPPT-2009-0152-0032

[66] EPA OPPTS (2008). *OPPTS 835.3280, Simulation Tests to Assess the Primary and Ultimate Biodegradability of Chemicals Discharged to Wastewater*. Retrieved from https://www.regulations.gov/document?D=EPA-HQ-OPPT-2009-0152-0036

[67] TBBPA Problem Formulation at 91.

[68] Ortuño, N., Moltó, J., Conesa, J. A., & Font, R. (2014). Formation of brominated pollutants during the pyrolysis and combustion of tetrabromobisphenol A at different temperatures. *Environmental Pollution, 191,* 31-37. https://doi.org/10.1016/j.envpol.2014.04.006

organic halogen residual ratio of 7,159 ug g^{-1} following combustion at 600 °C and subsequent gas combustion at 800 °C, as compared to 718 ug g^{-1} for DBDE.[69] That EPA/ OCSPP does not have robust information on the amount of electronic waste that is incinerated in the United States is not sufficient to exclude combustion products of TBBPA. TBBPA is used in products that are known to undergo disposal through incineration, whether in an e-waste recycling process or in municipal incineration facilities, and therefore it is necessary to collect data to estimate the magnitude of these exposure scenarios.

Testing requested
While there is not an EPA-OCSSP guideline for pyrolysis, combustion testing of products, such as was conducted with TBBPA-based laminate as part of the EPA-industry partnership "Alternatives Assessment: Partnership to Evaluate Flame Retardants in Printed Circuit Boards,"[70] could provide data for possible source apportionment combined with even a limited survey of product types at typical municipal incineration facilities and e-waste recycling operations with incineration capacity.

6D) TOXICITY OF DEGRADATION PRODUCTS
Assessment of available information
Little to no toxicity data are available for many of the known degradation products of TBBPA (such as the bromophenols and dibromoisopropylphenol derivatives). For these and other TBBPA degradation products with limited or no data for evaluation, testing to determine properties and toxicity is warranted to inform risk assessment.

Testing requested
Physical and chemical properties should be determined using the EPA Series 830 Group B testing guidelines,[71] as these are intended to meet testing requirements under FIFRA and TSCA. These results will provide information as to potential risk and further direct selection of subsequent toxicity tests.

Screening for potential toxicity using high throughput assays, such as EPA's ToxCast program, may generate initial toxicity information for such products. However, due to significant limitations of these methods,[72,73] as well as their almost exclusive focus on human health

[69] Takata, M., Watanabe, N., & Yamamoto, S. (2015). Destruction of organic Cl and Br compounds through incineration enhanced by alkali and alumina addition. *Journal of Material Cycles and Waste Management, 17*(2), 282-289. https://doi.org/10.1007/s10163-015-0359-x

[70] EPA (2015). *Alternatives Assessment: Partnership to Evaluate Flame Retardants in Printed Circuit Boards.* Retrieved from https://www.epa.gov/saferchoice/alternatives-assessment-partnership-evaluate-flame-retardants-printed-circuit-boards

[71] EPA (n.d.). *Series 830 - Product Properties Test Guidelines.* Retrieved from https://www.epa.gov/test-guidelines-pesticides-and-toxic-substances/series-830-product-properties-test-guidelines

[72] Pham, N., Iyer, S., Hackett, E., Lock, B. H., Sandy, M., Zeise, L., ... & Marty, M. (2016). Using ToxCast to Explore Chemical Activities and Hazard Traits: A Case Study with Ortho-Phthalates. *Toxicological Sciences, 151*(2), 286-301. https://doi.org/10.1093/toxsci/kfw049

[73] Silva, M., Pham, N., Lewis, C., Iyer, S., Kwok, E., Solomon, G., & Zeise, L. (2015). A Comparison of ToxCast Test Results with In Vivo and Other In Vitro Endpoints for Neuro, Endocrine, and

endpoints, high throughput testing alone is not sufficient. Based on the results of property testing, human health tests could be prioritized from EPA's **Health Effects Test Guidelines** (EPA Series 870).[74] In addition to testing potential for human health effects, potential for ecological effects must also be considered. While degradation and bioconcentration potential of TBBPA degradation products may be estimated from chemical and physical properties, toxicity to aquatic or terrestrial biota must tested. Although testing will necessarily be prioritized not only by relevant properties of the degradates but the degradation method, and environment, through which they are produced from TBBPA, relevant methods such as those provided in EPA's **Ecological Effects Test Guidelines** (EPA Series 850) should be used, as these were designed to meet ecotoxicity testing requirements under TSCA.[75]

7) Hazard Endpoints

7A) REPRODUCTIVE, DEVELOPMENTAL AND NEUROTOXICITY

Assessment of available information

Additional data is required to mitigate the previously described uncertainty in choosing any of the reviewed developmental toxicity studies, with a stated wide variety of results, for evaluation in a quantitative risk assessment of TBBPA. Given criticism of existing studies, a more definitive reproductive and developmental toxicity study should be ordered, with inclusion of doses in the range for which subclinical effects have been reported. Although there are three *in vitro* assays validated for embryo toxicity by the European Union Reference Laboratory for alternatives to animal testing (EURL-ECVAM), no national nor international validation authority has yet validated a non-animal method or alternative testing strategy for fully assessing reproductive and developmental toxicity, or for endpoints of concern such as neurotoxicity, so an *in vivo* test method is essential to adequately evaluate these outcomes.

Testing Requested

The selected approach should be modified to allow for cross-fostering of a subset of offspring between exposure and control groups to address concerns about whether dosing dams and offspring or just dosing offspring results in effects of TBBPA treatment.

An *in vivo* developmental toxicity screening test, such as the **OECD 421**,[76] a typical test recommended by EPA, could be ordered. This test administers a test substance in graduated dose to male and female animals, typically rats, with females dosed throughout the study, and provides sufficient screening data for assessment, with results including clinical observations, oestrous cycle monitoring, thyroid hormone measurement, as well as gross necropsy and

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Developmental Toxicities: A Case Study Using Endosulfan and Methidathion. *Birth Defects Research Part B: Developmental and Reproductive Toxicology, 104*(2), 71-89. https://doi.org/10.1002/bdrb.21140

[74] EPA (n.d.). *Series 870 – Health Effects Test Guidelines.* Retrieved from https://www.epa.gov/test-guidelines-pesticides-and-toxic-substances/series-870-health-effects-test-guidelines

[75] EPA (n.d.). *Series 850 – Ecological Effects Test Guidelines.* Retrieved from https://www.epa.gov/test-guidelines-pesticides-and-toxic-substances/series-850-ecological-effects-test-guidelines

[76] OECD (2015). OECD Test No. 421: Reproduction/Developmental Toxicity Screening Test. In *OECD Guidelines for the Testing of Chemicals, Section 4: Health Effects*. OECD Publishing, Paris.

histopathology. However, it may not be sufficiently informative of certain endpoints of concern which are supported by existing data, such as neurodevelopmental effects. That Lilienthal et al. (2008)[77] demonstrated potential for neurotoxicity in an underpowered study, even given a less ideal animal model for which there are questions about methods and uncertainty about which are the most relevant doses (e.g., both newborns and dams were exposed to TBBPA), indicates that further data is needed to assess neurotoxic and neurobehavioral effects. As such potential neurotoxic effects have not been confirmed, utilizing the TG 421 approach for developmental toxicity would require a supplemental study, or additional study arm, in order to assess developmental neurotoxicity. The ideal supplement to OECD TG 421 would be **OECD 426**,[78] the Developmental Neurotoxicity Study. This test guideline, according to OECD experts reviewing implementation of the guideline, is the best available science for assessment of developmental neurotoxicity.[79] The TG 426 protocol involves daily dosing of at least 60 pregnant rats from implantation through lactation and evaluates neurologic and behavioral abnormalities in offspring, with neuropathology assessed through adulthood at multiple time points.

An alternative to a combined TG 421/426 approach, and a truly definitive test that could be ordered for reproductive and developmental toxicity, including developmental neurotoxicity endpoints, would be the **NTP Modified One Generation Study, or MOG**.[80] The MOG approach involves exposure of pregnant females throughout gestation, lifetime exposure of the F1 and generation of two cohorts of F2 animals. The study design uses fewer animals than a classical two-generation study, but allows for full evaluation of first generation offspring animals following pre- and postnatal chemical exposure. At weaning, offspring are assigned to a number of different cohorts,[81] with endpoint inclusion informed by existing data, and which for TBBPA should include a developmental neurotoxicity cohort.[82]

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[77] Lilienthal, H., C. M. Verwer, L. T. van der Ven, A. H. Piersma, and J. G. Vos. 2008. Exposure to Tetrabromobisphenol A (TBBPA) in Wistar Rats: Neurobehavioral Effects in Offspring from a One-Generation Reproduction Study. *Toxicology, 246*(1), 45-54. https://doi.org/10.1016/j.tox.2008.01.007

[78] OECD (2007). *Test No. 426: Developmental Neurotoxicity Study*. In *OECD Guidelines for the Testing of Chemicals, Section 4: Health Effects*. OECD Publishing, Paris.

[79] Makris, S. L., Raffaele, K., Allen, S., Bowers, W. J., Hass, U., Alleva, E., ... & Crofton, K. M. (2009). A retrospective performance assessment of the developmental neurotoxicity study in support of OECD test guideline 426. *Environmental Health Perspectives*, *117*(1), 17-25. https://doi.org/10.1289/ehp.11447 ("The OECD DNT guideline represents the best available science for assessing the potential for DNT in human health risk assessment, and data generated with this protocol are relevant and reliable for the assessment of these end points.")

[80] National Toxicology Program (n.d.). *Modified One-Generation Studies*. Retrieved from https://ntp.niehs.nih.gov/testing/types/mog/index.html

[81] The standard cohorts include: a prechronic toxicity cohort (analogous to a standard 90-day study) for evaluating clinical pathology and target organ toxicity and pathology; a teratology cohort for evaluating prenatal development; and another cohort to evaluate breeding and littering for potential examination of the subsequent generation.

[82] National Toxicology Program (n.d.). *Guidance Document for the Developmental neurotoxicity arm of the MOG Study*. Retrieved from https://ntp.niehs.nih.gov/ntp/test_info/mog_guidance_508.pdf

The OECD Extended One Generation Reproductive Toxicity Study, EOGRTS, (OECD TG 443) is similar, but there are a number of weaknesses and complexities as compared to the MOG, which have been discussed elsewhere.[83, 84]

7B) AMPHIBIAN ENDOCRINE SYSTEM

Assessment of available information

The studies that demonstrated mixed results of TBBPA on the endocrine system in amphibians, including the changes in thyroid-mediated gene expression, for which the effect is not clear, do not constitute a complete screening battery for such effects. It is not surprising to see varied results from studies using differing model organisms, routes of administration, dosing and other design considerations. However, these results suggest the potential for TBBPA to interact with thyroid hormone systems, indicating that additional data is required to make an assessment.

Testing requested

Additional testing should prioritize thyroid endpoints for evaluation of adverse effects. A single testing protocol may be sufficient to address these mixed results, the **Larval Amphibian Growth and Development Assay (LAGDA) (OCSPP 890.2300**).[85] The LAGDA, which is included as a Tier 2 assay in the Endocrine Disruptor Screening Program, is based on amphibian metamorphosis, a well-studied thyroid-dependent process. When implemented following OCSPP guidelines, the LAGDA can detect perturbations of normal function of the hypothalamic-pituitary-thyroid (HPT) system and also of reproductive development through hypothalamic-pituitary-gonadal (HPG) axis interference. Testing under this protocol in a model amphibian such as *Xenopus laevis*, as a validated approach designed to inform the risk assessment process, would identify adverse endocrine-related effects of TBBPA and establish a quantitative relationship between dose and effects.

[83] Foster, P. M. (2014). Regulatory Forum Opinion Piece New Testing Paradigms for Reproductive and Developmental Toxicity—The NTP Modified One Generation Study and OECD 443. *Toxicologic Pathology*, *42*(8), 1165-1167. https://doi.org/10.1177/0192623314534920

[84] Foster, P. M. (2016). Influence of Study Design on Developmental and Reproductive Toxicology Study Outcomes. *Toxicologic Pathology*, 0192623316671608. https://doi.org/10.1177/0192623316671608

[85] EPA OCSPP (2015). *OCSPP 890.2300, Larval Amphibian Growth and Development Assay (LAGDA).* Retrieved from https://www.regulations.gov/document?D=EPA-HQ-OPPT-2009-0576-0018