



Oregon Department of Environmental Quality

Compilation of ATSAC Responses to TEFs & Brominated Analogues Email on 11-1-2023

Copy of DEQ Email

From: GOECKNER Apollonia * DEQ

Sent: Wednesday, November 1, 2023 11:30 AM

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Subject: Application of toxic equivalency factors (TEFs) for dioxins, furans, and dioxin-like PCB congeners to their brominated analogues

Dear ATSAC,

It has been a little over a month since our last communication with you. We hope you are well and had a good summer (or winter as per your relevant hemisphere).

We are still months away from scheduling a meeting for formal review of our Toxicity Reference Value (TRV) updates; however, we have come across a question that we would like your input on before we finalize these updates. This question is more open-ended than we expect most of our questions for you to be. We hope to get your input on this issue via email without an actual meeting, although we could host a meeting to discuss if you feel this is too complicated to do via email.

The attached review paper, as we understand it, proposes to apply the toxic equivalency factors (TEFs) designed for assessing risk from polychlorinated dibenzo-p-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs), and dioxin-like polychlorinated biphenyls (PCBs) to their *brominated* analogues.

Our questions to you are:

1. Do we correctly understand what they are recommending?
 2. Is the reasoning applied by the authors of this review sound?
3. Does this paper provide a sufficiently robust evidence base to adopt their proposal?
4. Do you know of other studies/papers that either support or argue against these authors' proposal?
5. As far as we know, no other government agencies have implemented this proposal. Do you know of any?
6. In light of all of the above, would you recommend that we apply existing TEFs for dioxins, furans, and dioxin-like PCBs to their brominated analogues when calculating toxic equivalency quotients (TEQs) at facilities in Oregon?
7. Do you think we need to have a virtual meeting about this?

Here is some additional Oregon-specific context if it helps you think through this:

- Oregon has permitted facilities that may emit these substances – e.g., incinerators, scrap metal foundries using electric arc furnaces.
- The Cleaner Air Oregon program looks closely at all emissions from sources and in many cases requires source testing to obtain representative emissions data – there are current methods used for sampling the chlorine-substituted compounds that could be used for analyzing the bromine-substituted molecules.
- DEQ is committed to understanding potential health risks from toxic air contaminants and needs to ensure we are not excluding a potentially significant source of health risk.

If you could please get us your responses to these questions by **January 5, 2024** we would really appreciate it. Please reply all via email, and note that your responses will be part of the public record.

Please let us know if you have any additional questions or concerns.

Thank you!

-ATSAC Governance Team

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State of Oregon
Department of Environmental Quality

ATSAC Responses

ATSAC Member	ATSAC Member Responses
<p data-bbox="110 268 483 310">Dr. John Vendenberg</p> <p data-bbox="110 331 230 363">1-5-2024</p>	<p data-bbox="516 268 1453 598">Question 1: The authors (van den berg et. al., 2013¹) are recommending that Toxic Equivalency Factors be applied for brominated -dioxin, -furan and -biphenyl compounds in the same fashion as is generally done for chlorinated -dioxin, -furan and -biphenyl compounds. This is based on emerging, but limited, information available on the presence and mode of action of these brominated compounds and the similarity in many aspects to the chlorinated compounds.</p> <p data-bbox="516 619 1510 730">¹ van den berg, M et al., Polybrominated dibenzo-p-dioxins, dibenzofurans, and biphenyls: inclusion in the Toxicity Equivalency Factor concept for dioxin-like compounds. Toxicological Sciences 133(2), 197-208 (2013).</p> <p data-bbox="516 772 1510 1066">Question 2: The authors are internationally renowned toxicology experts and they have carefully considered and documented the rationale underlying their recommendations. Their discussion of available information on kinetics, metabolism and toxicity is sound and the alignment in Figure 1 of the paper of the relative potency factors for PXDDs, PXDFs and dl-PXBs is very informative. I find their reasoning to be sound.</p> <p data-bbox="516 1108 1510 1486">Question 3: I think this paper is part of the evidence base but to me a single paper is not typically sufficient to adopt a proposal. To adopt a proposal the body of relevant literature needs to be considered, with an understanding of the strengths and limitations of the totality of evidence. That said, the summary and evaluation of evidence described in van den berg (2013) for PBDD/PBDFs appears sufficient to conclude that the use of TEFs is now warranted (see also my response to questions 4 and 6). I'm not certain the evidence is sufficient for the dioxin-like PBBs.</p> <p data-bbox="516 1528 1510 1986">Question 4: A limited search of the literature published since the 2013 publication by van den berg et al (2013) found there have been many studies published that evaluate the potential exposures to these brominated compounds. A literature search of peer reviewed publications based just on the keyword "PBDD" returned over 460 references from a wide range of journals. Based on my limited review of some of this literature I find most provide information on formation and occurrence/exposure of the compounds and relatively few on the mechanism of action that support the author's proposal. For example, the study by Budin et al, Chemosphere 263(2021) provides relevant new information on the mechanism of action of these compounds and</p>

	<p>concludes "like PCDD/Fs, PBDD/PBDFs are potent activators of the human AhR".</p> <p>I did not conduct a systematic review of the literature and recommend that a more thorough evaluation focused on the available toxicological science be considered.</p> <p>Question 5: I'm not aware of any other agencies having implemented this proposal. I serve on the Secretary's Science Advisory Board for the State of North Carolina and to my knowledge there are no NC standards or guidelines for PBDD/Fs. I do not find these brominated compounds listed as hazardous air pollutants under the current amendments to the Clean Air Act.</p> <p>Question 6: I am inclined to conclude that the evidence is sufficient to apply TEFs for dioxins, furans and dioxin-like PCBs to their brominated analogues when calculating toxic equivalency quotients (TEQs) at facilities in Oregon, but I would prefer to have a discussion of this approach and hear from the other members of the ATSAC prior to making a final recommendation.</p> <p>Question 7: Yes. A discussion as to what constitutes sufficient evidence to make a recommendation, and the specific information available on the brominated analogues to the chlorinated dioxins, furans and dioxin-like PCBs, would be useful.</p>
<p>Dr. Susan Tilton 1-2-2024</p>	<p>Question 1: Yes, as I understand it, this is still the current recommendation for polybrominated dibenzodioxins and dibenzofurans due to lack of data for brominated compounds.</p> <p>Questions 2 & 3: The rationale for use of TEFs for polybrominated dioxin-like compounds is because these compounds were found to function through the aryl hydrocarbon receptor to mediate toxicity similar to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) and so can be compared to TCDD with a TEF = 1. Polychlorinated and polybrominated compounds also result in similar adverse outcomes. This is a reasonable approach in the absence of data for brominated analogues.</p> <p>Question 4: In addition to the paper provided, there are papers that support use based on common mechanisms, common biological and toxic effects and similar potencies based on limited in vivo and in vitro data, but also some reports that note significant gaps observed in relative potencies between certain chlorinated and brominated dioxin congeners with substitutions at the same position. The WHO justifies use of TEFs based on the fact that any differences are likely within the</p>

	<p>assumed uncertainty of one order of magnitude for mammalian TEFs of chlorinated congeners. Therefore, using TEFs is worthwhile in the short-term so these compounds are included. In the long-term, values specific for brominated dioxins, furans and biphenyls should be developed.</p> <p>Hornung MW et al (1996) Toxic equivalency factors of polybrominated dibenzo-p-dioxin, dibenzofuran, biphenyl, and polyhalogenated diphenyl ether congeners based on rainbow trout early life stage mortality. <i>Toxicol. Appl. Pharmacol.</i> 140, 227–234.</p> <p>Nakayama K et al (2022) Determination of the relative potencies of brominated dioxins for risk assessment in aquatic environments using the early-life stage of Japanese medaka. <i>Ecotoxicol Environ Safety.</i> 247:114227.</p> <p>Olsman H et al (2009) Relative differences in aryl hydrocarbon receptor-mediated response for 18 polybrominated and mixed halogenated dibenzo-P-dioxins and -furans in cell lines from four different species. <i>Environ Toxicol Chem.</i> 26(11):2448-2454.</p> <p>Suzuki et al (2017) Dioxin-like activity of brominated dioxins as individual compounds or mixtures in in vitro reporter gene assays with rat and mouse hepatoma cell lines. <i>Toxicol In Vitro.</i> 44:134-141.</p> <p>Wall RJ et al (2015) Characterisation of chlorinated, brominated and mixed halogenated dioxins, furans and biphenyls as potent and as partial agonists of the Aryl hydrocarbon receptor. <i>Environ Intl,</i> 76:49-56.</p> <p>Question 5: I am not the best to answer this question.</p> <p>Question 6: Yes, given the prevalence of brominated analogues, I support the current recommendations to use TEFs for calculating TEQs so that these compounds are included. As new data comes available, the use of TEFs should be re-evaluated.</p> <p>Question 7: No.</p>
<p>Dr. Qiaoxiang (Daisy) Dong 11-28-2023</p>	<p>Question 1: Yes, van den Berg et al. 2013 proposed to use the TEF values of chlorinated congeners for their brominated analogues. Although the paper stated that these are interim TEF values and there are limited studies for PBDDs/PBDFs when compared with</p>

PCDDs/PCDFs, the paper provides strong scientific evidence to use similar TEF values for brominated congeners.

Question 2: Yes.

Question 3: Yes, the evidence is strong based on available literature at the time the paper was published.

Question 4: An earlier study by Shaw et al. 2013 used TEFs of PCDD/Fs to calculate the risk of PBDD/Fs for firefighters. More recently, Budin et al., 2020 used this approach to assess the risk of PBDD/Fs contained in plastic toys for children. See below for the references and I also attached the PDF files of these two papers in the email.

Susan D. Shaw, Michelle L. Berger, Jennifer H. Harris, Se Hun Yun, Qian Wu, Chunyang Liao, Arlene Blum, Anthony Stefani, Kurunthachalam Kannan, Persistent organic pollutants including polychlorinated and polybrominated dibenzo-p-dioxins and dibenzofurans in firefighters from Northern California, *Chemosphere*, Volume 91, Issue 10, 2013, Pages 1386-1394, ISSN 0045-6535, <https://doi.org/10.1016/j.chemosphere.2012.12.070>.

Clémence Budin, Jindrich Petrlik, Jitka Strakova, Stephan Hamm, Bjorn Beeler, Peter Behnisch, Harrie Besselink, Bart van der Burg, Abraham Brouwer, Detection of high PBDD/Fs levels and dioxin-like activity in toys using a combination of GC-HRMS, rat-based and human-based DR CALUX® reporter gene assays, *Chemosphere*, Volume 251, 2020, 126579, ISSN 0045-6535, <https://doi.org/10.1016/j.chemosphere.2020.126579>.

Question 5: I am not aware of any government agencies implementing this proposal.

Question 6: Yes, I would recommend applying existing TEFs to brominated analogues.

Question 7: Unless there are disagreements among ATSAC members, there is no need to have a virtual meeting.

Contact

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