Toxics Use Reduction Institute Science Advisory Board Meeting Minutes
February 29, 2024
Virtual Zoom Meeting
9:30 AM

Members Present: Robin Dodson (Chair), Christine Rioux (Vice Chair), Heather Lynch, Lisa Cashins, Christy Foran, Rich Gurney, Helen Poynton, Denise Kmetzo, Ryan Bouldin, Alicia Timme-Laragy

Members not present: Wendy Heiger-Bernays

Program staff present: Liz Harriman (TURI), Heather Tenney (TURI), Karen Thomas (TURI), Hayley Hudson (TURI), John Raschko (OTA), Kari Sasportas (OTA), Caredwen Foley (OTA), Sandra Baird (MassDEP)

Others present: Katherine Robertson (MCTA), Owen Jappen (ACC), Erin DeSantis (ACC), Laura Spark (Clean Water Action), Carol Holahan (Foley Hoag LLP), Dan Forsythe (Capaccio Engineering)

Welcome & Introductions

The chair noted that this meeting is being conducted remotely, consistent with *An Act Relative to Extending Certain State of Emergency Accommodations* signed by Governor Baker on June 16th, 2022. This allows the extension of the remote meetings under the Open Meeting Law until March 31, 2025. Board members and program staff were introduced, and visitors were asked to put their name and affiliation in the chat.

Approve January Meeting Minutes

There was a motion to review the January meeting minutes and there was a second. The minutes were available for review prior to the meeting. A member pointed out two typos where analogue was spelled incorrectly and 'data' was not referred to as plural. Also, it was requested to have a footnote including the CAS numbers and names for the analogues. There was a roll call vote to approve the minutes with those changes and they were approved with eight members in favor and two abstentions.

Summary Statement for Brominated Phthalates

The last meeting ended in the middle of crafting a summary statement for the brominated phthalates subclass, so it was addressed as the first order of business. Several Board members sent suggestions in the meantime. TURI shared the screen to show the summary statement with all combined suggestions from Board members inserted. The Board discussed and arrived at the following statement:

1. The analogues share the same primary degradation product (tetrabromophthalic acid) so toxic effects of that metabolite would be expected to be shared by the proposed analogues.
2. Persistence – TBPH is persistent and the primary degradation product common to all proposed analogues (and TBPH), tetrabromophthalic acid, is also persistent (EPA, 2015).
3. Bioaccumulation was not reviewed, due to a lack of information for the analogues, including a lack of empirically-based bioaccumulation factors.

Toxicity data on analogues are limited, with some evidence of reproductive and developmental toxicity. However, based on the structural homology and that the differences in each structure does not substantially change the degradation processes of these analogues into the common metabolites of TBPH, similar hazard profiles among TBPH and its analogues are anticipated.

At high temperatures, high pH, and highly aqueous environments occurring during use such as in extinguishing fires the rate of conversion of "analogue 1, 2, 3 & 4" into the common metabolites of TBPH is in fact highly accelerated. The common degradation product, tetrabromophthalic acid, is persistent.

Degradation of TBPH and its analogues is likely given that carboxylesterases, which catalyze the ester bond cleavage in a variety of conditions and play an important role in metabolism, are widely distributed in the environment. Polymerized applications on reacted versions of "analogue 4" will likely have much slower rates of degradation due to lower bioavailability and higher steric hindrance and hydrophobicity in polymeric form.

The analogues are sufficiently similar to TBPH that they would be reasonably anticipated to have similar concerns regarding toxic hazard and persistence.

While conclusions are based upon chemical structure, as toxicity data on analogues are limited, the paucity of data for individual analogues 1, 2, 3 & 4 is not a concern as the structural homology is compelling and the change in each structure does not substantially change the degradation processes of these analogues into the common metabolites of TBPH.

Analogues:
#1: 2-(2- hydroxyethoxy)ethyl-2- hyroxypropyl-3,4,5,6- tetrabromo phthalate, CAS 20566-35-2
#2: 2-(2- hydroxyethoxy)ethyl-2- hyroxypropyl-3,4,5,6- tetrabromo phthalate mixed esters with diethylene and propylene glycol, CAS 77098-07-8
#3: Tetrabromophthalic acid dimethyl ester, CAS 55481- 60-2
#4: Diallyl tetrabromophthalate, CAS 49693-09-6

Polyhalogenated Alicycles

The Polyhalogenated Alicycles subclass consists of three chemicals, one named in the law and two analogues. The chemical named in the law is the widely known and commonly used Hexabromocyclododecane (HBCDD). Analogue #1 is Hexabromocyclodecane (HBCyD), which has numerous examples of misspellings in the literature due to its name similarity to HBCDD. It is almost always the dodecane (HBCDD) they are referring to, so hazard information is minimal. Analogue #2 is 1,2,3,4,5-Pentabromo-6-chlorocyclohexane (PBCC) and there was limited literature on this chemical as well. HBCDD is on the TURA List but has never been reported. It is also included in the 2015 Stockholm Convention phase out. TURI summarized the general information for HBCDD and the two analogues and then opened it up for discussion from the Board.

A Board member reviewed the log K_{ow} values for the bioconcentration factor (BCF) data from the 1985 EPA paper which summarized the health and environmental effects of PBCC. The more the BCF model

has been studied the more information we have about which chemicals will likely fall off the regression lines. They explained that they think the chemicals that are being talked about here will follow the pattern of other hydrophobic chemicals and this is likely a good prediction. Very high molecular weight compounds and high log Kow (above seven) is when these relationships start to fall apart. Based on the table in the paper the log BCF for PBCC is probably between three and five, which is similar to HBCDD which has a log BCF of five.

There was discussion around the Cheminformatics summary table at the bottom of the EHS Summary. There are several categories with incomplete data, but the ecotoxicity data appear concerning for the analogues with very high ratings for aquatic toxicity. The bioaccumulation data in the Cheminformatics table are different compared to the 1985 EPA paper just discussed. It was noted that the data from Cheminformatics were modeled using QSAR, rather than experimental.

A Board member stated that the three structures look different enough that if the physiological effects are specific receptor-based effects (e.g., endocrine effects), they might be different. If the mechanism is something more overarching, like liver damage, kidney effects, etc, that don't necessarily work through specific receptor-based mechanisms, they could have very similar effects.

Visitor Comments/Questions

There was an opportunity for visitor comments and there was one question from OTA in the chat: Is the issue of similar degradation products or metabolites of the analogues to those of HBCDD relevant to this subclass?

Summary Statement

The Board had extensive discussion around the draft summary statement and agreed on the following points.

- The strongest empirical evidence regarding the similarity of the analogues to HBCDD pertains to bioaccumulation. Based on hydrophobicity and modeled BCF values, PBCC and HBCyD are expected to be bioaccumulative to highly bioaccumulative. Experimental data also confirm the high bioaccumulation for PBCC.
- It appears that the analogues to HBCDD have similar concerns regarding acute and chronic aquatic toxicity based upon predicted Cheminformatics values. Acute aquatic toxicity for PBCC is greater than HBCD, based upon limited experimental data (Usenko 2016).
- There is a general lack of human toxicity and persistence data for these analogues. There is no empirical - only predicted - information on analogue 1 (HBCyD).
- PBCC has suggestive evidence of carcinogenic potential (based on one study, EPA 1985), an effect that has not been seen in HBCDD. Note PBCC is noted as a “less close” analogue to HBCDD.

Polyhalogenated Bisphenol Aliphatics

It was suggested to add the following statement to the previously agreed upon summary statement for polyhalogenated bisphenol aliphatics: All (above) analogues are sufficiently similar to TBBPA that they

would be reasonably anticipated to have similar concerns regarding toxic hazard, persistence, or bioaccumulation. There was discussion about specific language.

It was agreed that the following will be added to the summary statement for polyhalogenated bisphenol aliphatics: *All (above) analogues are sufficiently similar to TBBPA that they would be reasonably anticipated to have similar concerns regarding toxic hazard. Analogue 1, 3, and 4 would be reasonably anticipated to have similar concerns regarding persistence.*

Future Projects

At the next meeting, planned for late April or early May, the plan is to review some of the tools that TURI has been looking at while collecting flame retardant data (such as QSAR and GenRA) and what was learned in the process. TURI will also investigate the methodology of Cheminformatics and why it might be predicting dissimilar values.

TURI presented introductory information on the last two subgroups - Subclass 1: Polyhalogenated Organophosphates and Subclass 6: Polyhalogenated Aliphatic Chains (Paraffins).

The phosphates are a very complex and large group. There are three named chemicals in the law, and TURI chose three analogues. One analogue is based off one of the named chemicals in the law and the other two are based off another named chemical. Toxicity information has been emerging for this class. EPA's full flame-retardant inventory includes roughly 797 chemicals, 101 of which are phosphates. This is also the largest subclass that NAS named, and it consists of 22 substances. . Two of these phosphates (Tris(2-chloroethyl) phosphate, Tris(1,3-dichloro-2-propyl) phosphate) were added to the TURA list in the fall with reports due in 2025. A board member commented that phosphates will likely have a similar structural homology and degradation products as we saw for brominated phthalates.

The last subclass is the Paraffins. Short chain chlorinated paraffins with 10-13 carbons are included in the law. There are also medium and long chain chlorinated paraffins. Most are commonly found as a mix of chain lengths. EPA has a 2009 Action Plan for the short chain chlorinated paraffins. Short chains were on the Stockholm Convention POPs list as of 2017 and medium chains were recommended for 2023 and are currently under evaluation.

These two subclasses will be discussed at the next meeting.

Next Meeting

Heather will put out a When2Meet for late April early May.

There was a motion to adjourn and there was a second.

Handouts:
DRAFT January Meeting Minutes
Updated Proposed FR CAS Numbers, isomers, and Analogues for SAB
FR Questions and Definitions

CPSC 2024: Organohalogen Flame Retardant Scope Document: Polyhalogenated Alicycle Subclass
EHS Summary for Alicycles
Cheminformatics for HBCDD and Analogues
Physical and Bioactivity Data for HBCDD and Analogues
EHS Summary for Brominated Phthalates
Cheminformatics for Brominated Phthalates
Physical and Bioactivity Data for Phthalates
ACC-NAFRA Comments MA TURA SAB

Relevant Comments from Chat

11:00:08 From Helen Poynton (she/her) to Everyone:
Based on hydrophobicity and modeled BCF values, PBCC and HBCyD are expected to be bioaccumulative to highly bioaccumulative. Experimental data also confirm the high bioaccumulation for PBCC as well as acute toxicity.

11:10:23 From Lisa Cashins MA Consultation to Everyone:
Penta - there is "suggestive evidence of carcinogenic potential: CPSC 2024

11:19:07 From Rich Gurney (Simmons U) to Everyone:
Does our summary statement include the information adequately from the Usenko paper (by saying LC50 pent more toxic) - "Although it was one of the most toxic BFRs identified in the current work PBCC is, historically, the least studied. PBCC has not been extensively used as a flame retardant, nor has its toxicity been evaluated in other model systems, to our knowledge. In addition to inducing mortality in the low ppm range, exposure to 2.5 ppm PBCC induced the greatest increase in GST activity [oxidative stress marker]. Further characterization of PBCC-induced toxicity maybe warranted if production and use increase." [Which is unlikely as it is now banned correct?]

11:33:13 From Ryan Bouldin (he/him) - Bentley University to Everyone:
Can we say "we have additional concerns about carcinogenicity for PBCC (EPA 1985)" and leave it

11:38:38 From John Raschko to Everyone:
Is the issue of similar degradation products or metabolites of the analogs to those of HBCDD relevant to this subclass?

12:03:12 From Sandra Baird (MassDEP) to Everyone:
Thank you!!!