MA Flame Retardants Law, 2020

An Act to Protect Children, Families and Firefighters from Harmful Flame Retardants

Mass. Gen. Laws Ch 21A, Section 28

TURI
TOXICS USE REDUCTION INSTITUTE
UMASS LOWELL

Differences between TURA and FR law

Provision	MA TURA	MA FR Law
Who does it affect?	Users (manufacturers and distributors) in certain SIC codes, >10 workers	Retailers, importers, and users (manufacturers, distributors)
Which chemicals?	List of over 1500 chemicals, above thresholds	11 chemicals and **chemical analogues** of the 11, above 1000 ppm for any component
What do they have to do?	Report and plan	**This is a ban.**
What end products?	All	Bedding, carpeting, children's products, residential upholstered furniture or window treatments

SAB Responsibilities – ADVISE DEP

- Specified in the law
- 3 initial questions – CAS, Isomers, Analogues
- Advice/summary statement can be provided with any qualifiers or explanation necessary. No vote required.
- Broad goal is always (and especially in the case of FRs) to avoid regrettable substitution.

Review of September meeting outcomes for FRs

Summary statement for DEP regarding brominated diphenyl ethers (BDE):

"Deca- to di-bromodiphenyl ether are reasonably anticipated to have similar concerns regarding toxicity hazard, persistence, and bioaccumulation to the original flame retardants (octa- and penta-bromodiphenyl ether) in the Massachusetts Flame Retardant Law. Mono-bromodiphenyl ether shows ecotoxicity concerns but likely has lower persistence and bioaccumulation. Also, mono-bromodiphenyl ether is likely to have higher brominated isomers in the mixture."

Current Advice Requested by DEP

Q3b: Is each proposed **analogue** sufficiently similar to at least one chemical identified in the law such that the proposed analogue would be reasonably anticipated to have similar concerns re: toxic hazard, persistence, bioaccumulation?

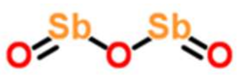
Today we will discuss:

Subclass 7: Inorganics (Antimony)
Subclass 4: Polyhalogenated Phthalates/Benzoates/Imides
Subclass 5: Polyhalogenated Bisphenol Aliphatics

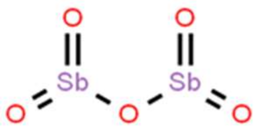
TURI Approach to preparing EHS materials

- Identification of relevant endpoints through various hazard info sources (PubChem, Pharos, ChemHat)
- Literature search for studies of relevant endpoints (preferably review of many studies)
- Policies/programs/statements about the category as a whole
- Explored EPA tools
  - **CompTox** – experimental and predicted physical properties, bioactivity (ToxCast), list of FRs (797)
  - **GenRA** - read-across predictions of in vivo toxicity and in vitro bioactivity
  - **Cheminformatics** - chemical structures, experimental and predicted physicochemical properties, environmental fate and transport information, and appropriately linked toxicity data (using QSAR and empirical)

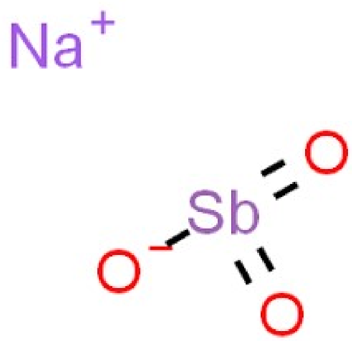
Subclass 7 - Inorganics



Antimony trioxide



Antimony pentoxide



Sodium antimonate

Relevant endpoints: chronic aquatic toxicity, persistence, other health effects

Antimony information provided

- EHS Summary of Antimony by TURI
- ATSDR 2019 Tox Profile
- CompTox physical and chemical properties
- Cheminformatics
- ECOTOX
- 3 research papers about ecological effects

Antimony overview

- "Antimony compounds" are one category under EPA TRI, EPA air toxics (they are HAPs), TURA, WA and VT states Chemicals of High Concern to Children

- Most common oxidation states +3, +5

- Oxidation state can change under environmental conditions & in biota - Most dissolved antimony in natural waters under aerobic conditions is present in the pentavalent oxidation state as antimonate species. Anthropogenic emissions commonly contain antimony in the trivalent oxidation state; however, it is unclear how quickly antimonite oxidizes to antimonate under natural conditions. Under anoxic reducing conditions, trivalent species are the most thermodynamically stable forms of antimony. Antimony can be reduced and methylated by microorganisms in anaerobic sediment, releasing volatile methylated antimony compounds into the water. Multiple microorganisms have been found to methylate antimony in the soil and water and some anoxic or poorly oxygenated environments (ASTDR 2019)

Antimony health effects in both the +3/+5 oxidation state

- Antimony trioxide is reasonably anticipated to be a human carcinogen based on sufficient evidence from animals and mechanistic studies (NTP RoC, 2021) mechanism in vivo for +3 = DNA/micronucleas damage, for +5 = oxidative stress
- Antimony trioxide, IARC 2A (updated 2022), inhalation, "For pentavalent antimony, evidence regarding cancer in humans and cancer in experimental animals was "inadequate" since no data were available to the Working Group."
- The most sensitive targets appear to be the respiratory tract, heart, gastrointestinal tract, serum glucose, and developing animal (ATSDR 2019)
  - Respiratory effects are a **presumed** health effect for humans (inhalation, +3)
  - Myocardial effects and EKG alterations are a **suspected** health effect for humans (injection, +3/+5)
  - Gastrointestinal effects are a **presumed** health effect for humans (oral and inhalation)
  - Developmental effects are a **suspected** health effect for humans (oral, +3/+5)
  - Alterations in blood glucose levels are a **suspected** health effect for humans (+3/+5)

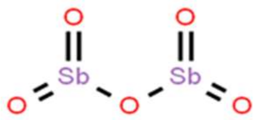
Antimony compounds: properties and tox values

Name	Water solubility, mol/L	Octanol water coefficient, LogKow	NOEC, mg/L	LOEC, mg/L
Antimony trioxide	**2.26e-7 (p)**	**6.23 (p)**	**<1 (EcoTox)**	**<1 (ECHA IUCLID)**
Antimony pentoxide	1.32e-7 (p)	6.23 (p)		<1 (ECHA IUCLID)
Sodium antimonate	slight' 2.46e-3 from PubChem/MSDS	no data		<1 (ECHA IUCLID)

Data from CompTox and Cheminformatics unless noted otherwise
NOEC – no observed effect concentration
LOEC – lowest observed effect concentration
ECOTOX – EPA – provides environmental toxicity data on aquatic and terrestrial species
ECHA – European Chemicals Agency
IUCLID – International Uniform Chemical Information Database for chemical data

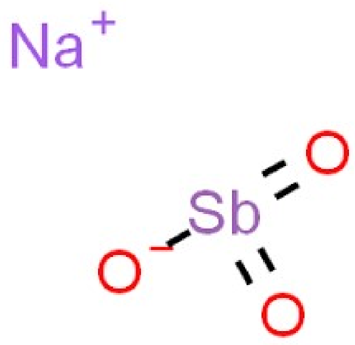
Current Question before the Board

Antimony trioxide



Antimony pentoxide

Q3b: Is each proposed **analogue (antimony pentoxide, sodium antimonate)** sufficiently similar to at least one chemical identified in the law (antimony trioxide) such that the proposed analogue would be reasonably anticipated to have similar concerns re: toxic hazard, persistence, bioaccumulation?

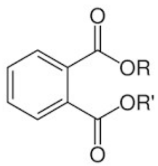


Sodium antimonate

Subclass 4 – TBPH and Subclass 5 –TBBPA Similarities

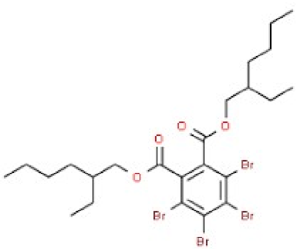
- Offered as less hazardous alternatives to PBDEs
- Complex chemistries with many analogues
- Complex toxicologies – backbone + brominated phenyl groups
- Identified initially for aquatic toxicities
- Later identified for various adverse human health outcomes
- Found to be ubiquitous in biomonitoring studies
- Reassessed for their potential persistence and bioaccumulative properties
- Well-studied (though only as a mixture for TBPH)
- Analogues do not have much tox data except for predicted value based on structural similarities

Subclass 4 – Polyhalogenated Phthalates, Benzoates, Imides



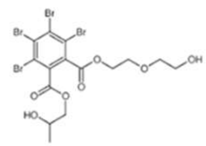
Dialkyl ortho-phthalates; a phenyl ring with two extended acetate groups

Base of TBPH is DEHP



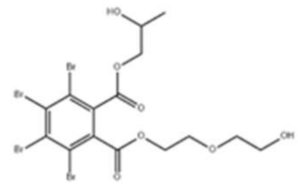
Bis(2-Ethylhexyl)-3,4,5,6-tetrabromophthalate (TBPH)

Analogue #1



2-(2-hydroxyethoxy)ethyl-2-hyroxypropyl-3,4,5,6-tetrabromo phthalate

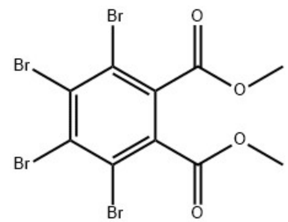
Analogue #2



2-(2-hydroxyethoxy)ethyl-2-hyroxypropyl-3,4,5,6-tetrabromo phthalate mixed esters with diethylene and propylene glycol

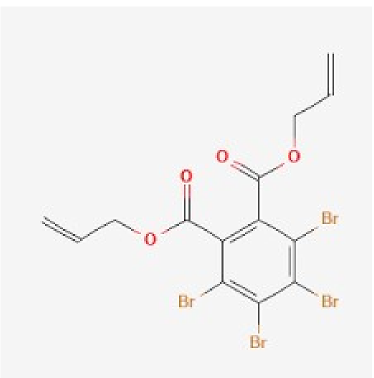
Relevant endpoints:
PBT(dev & aquatic)

Analogue #3



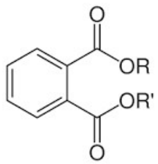
Tetrabromophthalic acid dimethyl ester

Analogue #4



Diallyl tetrabromophthalate

Regulatory history of phthalate esters (non-brominated)



- 1986 voluntary discontinuation of phthalates in bottle nipples and pacifiers due to hormonally active agent properties with the most sensitive system being the immature male reproductive tract.
- CWA, CERCLA, CAA, SDWA – restrictions on certain phthalate esters
- 2008 US prohibited 8 phthalates >0.1% by wt in childcare articles; 2017 in toys
- 2012-now EPA TSCA Action Plan, Work Plan, Risk Eval – focus on a few (5-8) and note 'phthalate syndrome effects' (fetal dev of the repro system) in a wider group
- **2015 TSCA Work Plan for Brominated phthalates cluster (FRs)**

TURA and phthalate esters

- “Phthalate esters" category on TURA list due to presence on CERCLA list (aquatic tox issues from CWA)
- Some phthalate esters listed individually on TURA (not brominated)
- Current DEP policy has exempted reporting of this category
- SAB spent 3 years defining the category for DEP (2016 report)
- Concluded that C4-C7 members had significant evidence of adverse effects in animals on: endocrine pathways, liver, thyroid
- **By definition the brominated phthalate esters used as FRs could be part of this category**

Challenges of this subclass (as FRs)

- Lack of data for individual chemicals
- Mixtures – most data is for Firemaster 550 which is a mixture of TBPH/TBB/TPP/IPTPP
- Ubiquitousness proven – EPA first said not persistent/bioaccum, now proving false due to it being found in air, surface and water sediment and in remote areas.

Information provided

- EHS Summary by TURI
- Cheminformatics
- Physical and chemical data from CompTox
- Bioactivity data from CompTox (TBPH only, no data for analogues)

Physical Chemical Properties of TBPH and analogues

CAS	Name	Vapor pressure, mmHg	Soil adsorption coeff (Koc), L/kg	Water solubility, mol/L	Octanol water coefficient, LogKow	Biodeg. Half-Life, days	Fish Biotrans. Half-Life (Km)	bioconcentration factor, L/kg	MW (g/mol)	Approx carbon chain length
26040-51-7	**bis(2-ethylhexyl)-3,4,5,6-tetrabromophthalate (TBPH)**	**1.16e-13 to 1.50e-8**	**8.91E+04**	**2.81e-15 to 6.17e-6**	**7.55 to 11.9**	**16.2**	**2.75**	**102**	**706**	**6**
20566-35-2	2-(2-hydroxyethoxy)ethyl-2hydroxypropyl-3,4,5,6-tetrabromo phthalate) (Analogue 1)	3.59e-15 to 9.79e-10	95.5	4.82e-6 to 2.70e-4	1.15 to 3.61	3.55	0.191	4.37	627.9	6
77098-07-8	2-(2-hydroxyethoxy)ethyl-2-hyroxypropyl-3,4,5,6-tetrabromo phthalate mixed esters with diethylene and propylene glycol (Analogue 2)	no data due to no definite structure							663.9	6
55481-60-2	Tetrabromophthalic acid dimethyl ester (Analogue 3)	0 to 1.23e-5	3.16E+03	6.61e-7 to 31.9	4.23 to 7	6.17	0.676	93.3	509.8	1
49693-09-6	Diallyl tetrabromophthalate (Analogue 4)	1.35e-10 to 2.09e-7	2.14E+03	6.31e-10 to 5.70e-6	4.67 to 6.91	4.68	0.427	245	561.8	3

All data from CompTox and are predicted

Persistence and Bioaccumulation data summary of TBPH

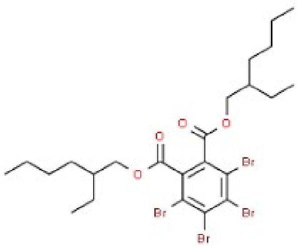
		Persistence			Bioaccumulation		
		Cheminformatics Biowin3 (EpiSuite)	**EPA 2015 Hazard Assessment 1/2 Life (PBT Profiler est)**	**REACH 2022 SVHC Determination**	**EPA 2015 Hazard Assessment Bioaccumulation**	**REACH 2022 SVHC Determination**	**REACH 2022 SVHC Determination**
26040-51	**bis(2-ethylhexyl)-3,4,5,6-tetrabromophthalate (TBPH)**	1.97 1.75 <= Biowin 3 Score <= 2.25 days	120 days	7% degradation in 28 days (OECD Guideline 302C)	the persistence of TBPH and its detection in many species from different habitats and trophic levels indicates potential for a high bioaccumulation designation in aquatic or terrestrial species.	BCF>5000 in fish laboratory studies	vB for aquatic organisms based on logKow = 10.2
20566-35-	2-(2-hydroxyethoxy)ethyl-2hydroxypropyl-3,4,5,6-tetrabromo phthalate) (Analogue 1)	1.86 1.75 <= Biowin 3 Score <= 2.25 days					
77098-07-	2-(2-hydroxyethoxy)ethyl-2-hyroxypropyl-3,4,5,6-tetrabromo phthalate mixed esters with diethylene and propylene glycol (Analogue 2)	1.86					
55481-60-	Tetrabromophthalic aciddimethyl ester (Analogue 3)	1.81					
49693-09-	Diallyl tetrabromophthalate (Analogue 4)	1.69					

BIOWIN3 provide an indication of the time needed for complete biodegradation (mineralization) in the aquatic environment as a value between 1 and 5, where 5 = hours, 4 = days, 3 = weeks, 2 = months and 1> months.

Summary of TBPH data

- PB – vPvB (REACH 2022, SVHC; EPA 2015 Hazard Summary)
- Developmental - EPA classified TBPH as a moderate hazard for reproductive, developmental, neurological, and repeated dose toxicities based on rodent toxicity of commercial mixtures, structurally similar chemicals, and professional judgement. Data in EPA Hazard Summary.
- Aquatic toxicity – FishChV <0.001 mg/L exceeds solubility (ref. ECOSAR v1.11)
  (37 data points on ECOTOX for TBHP, none for analogues)

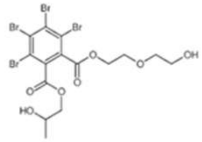
Current Advice Requested by DEP



Bis(2-Ethylhexyl)-3,4,5,6-tetrabromophthalate (TBPH)

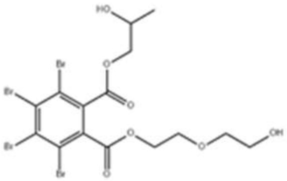
Q3b: Is each proposed **analogue (#1,2,3,4)** sufficiently similar to at least one chemical identified in the law (TBPH) such that the proposed analogue would be reasonably anticipated to have similar concerns re: toxic hazard, persistence, bioaccumulation?

Analogue #1



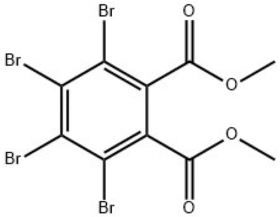
2-(2-hydroxyethoxy)ethyl-2-hyroxypropyl-3,4,5,6-tetrabromo phthalate

Analogue #2



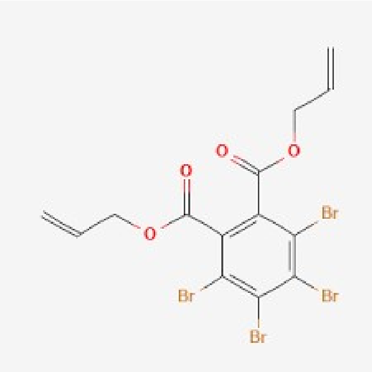
2-(2-hydroxyethoxy)ethyl-2-hyroxypropyl-3,4,5,6-tetrabromo phthalate mixed esters with diethylene and propylene glycol

Analogue #3



Tetrabromophthalic acid dimethyl ester

Analogue #4



Diallyl tetrabromophthalate