

Chemical Selection Planning

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Presentation to Scientific Guidance Panel

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Purpose of agenda item

- ▶ Follow-up on panel recommendations from November 2010 meeting
- ▶ Propose an approach for screening possible candidates for designation to bring to SGP
- ▶ Illustrate the approach with the example of non-halogenated organophosphate flame retardants (PFRs)
- ▶ Obtain Panel input on both the approach and the example

Issues for the Panel to consider

- ▶ Usefulness of proposed screening approach
 - Are there elements you would add or delete?
 - Is this enough information for the Panel to choose possible candidates for designation?
- ▶ For the example of PFRs,
 - Are there specific chemicals the Program should consider bringing back for potential designation?
 - Should the Program consider preparing a document on a class of PFRs?

Screening approach

- ▶ Search for data on extent and type of use, including trend
- ▶ For chemicals with evidence of significant use, brief search of literature & secondary sources for:
 - Indicators of:
 - Environmental persistence
 - Bioaccumulation
 - Toxicity
 - Past environmental sampling and biomonitoring studies
- ❖ Panel reviews summary of above information and advises on possible candidates

Example Screening Table

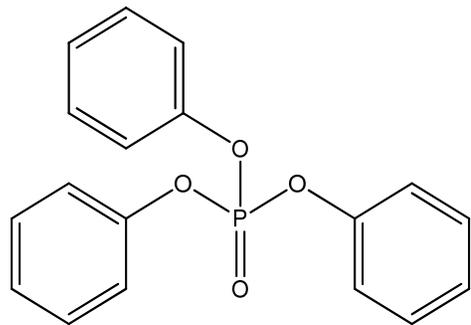
Chem	Type of use	Vol [Trend]	Persistence (P) Bioaccumulation (B)		Tox	Environ Sample	Biota Sample	Biomon Study
			P US EPA	B LogK _{ow}				
XYZ	consumer product	1-10 M [↑]	++	5.0	✓	house dust	bird eggs	urine; blood

Non-halogenated organophosphate flame retardants (PFRs)

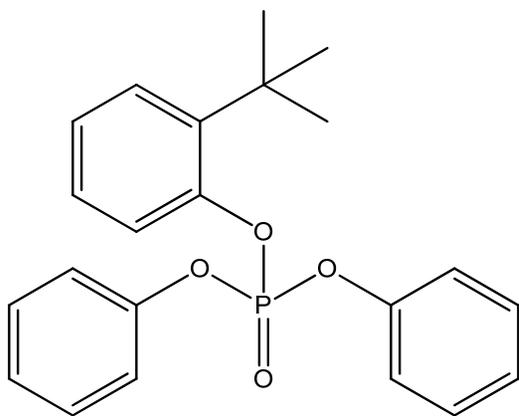
Uses

- ▶ Flame retardants
- ▶ Plasticizers
- ▶ Other: anti-foaming agents, wetting agents, anti-wear additives
- ▶ Example applications:
 - Computers and household electronics
 - Polyurethane foam and textiles
 - Artificial leather and synthetic rubber
 - Floor polish
 - Hydraulic fluids

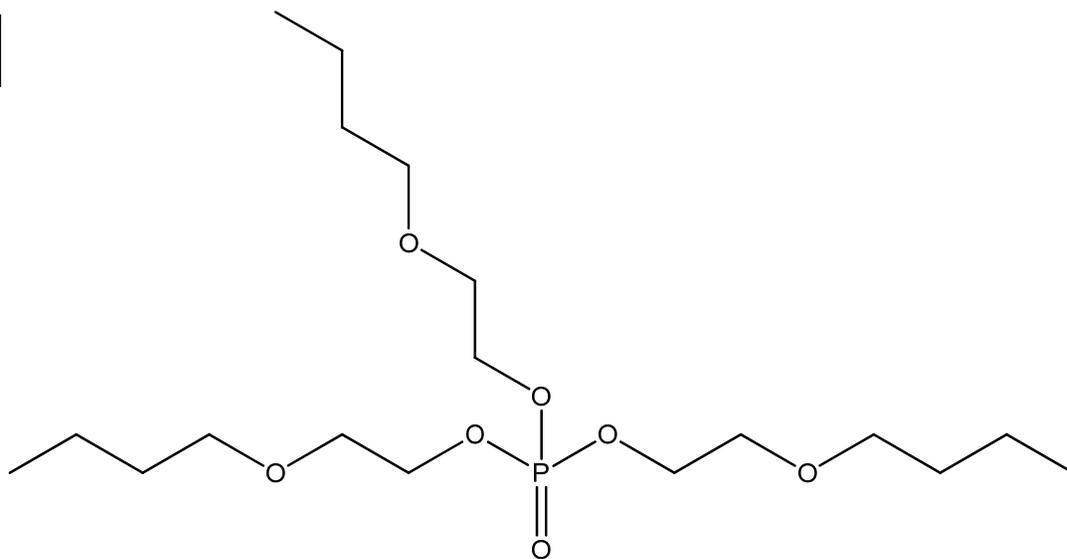
Examples of PFRs



Triphenyl phosphate



t-Butylphenyl diphenyl phosphate (one isomer)



Tris(2-butoxyethyl) phosphate

Screen of aromatic PFRs, 10–50 mil lbs (2006)

Aromatic PFR [trend]	Persistence (P) Bioaccumulation (B)		Tox	Environ Sample	Biota Sample	Biomon Study
	P US EPA	B LogK _{ow}				
Triphenyl phosphate	+	4.59	✓	house dust, computers	dolphins, bird eggs	urine; plasma, breast milk
Isopropylated triphenyl phosphate [↑ Nordic]	++	5.44	✓			
t-Butylated triphenyl phosphate [↑ US]	++	4.85	?			
Bisphenol A bis(diphenylphosphate) (rxn products) [↑ US]	<i>(High concern)</i>					

Screen of aromatic PFRs, 1–10 mil lbs (2006)

Aromatic PFR [trend]	Persistence (P) Bioaccumulation (B)		Tox	Environ Sample	Biota Sample	Biomon Study
	P US EPA	B LogK _{ow}				
Tricresyl phosphate	++	5.11	✓	house dust		not found (urine)
2-Ethylhexyl diphenyl phosphate	+	5.73			bottom-dwelling fish	breast milk
Isodecyl diphenyl phosphate	++	5.44				

Screen of non-aromatic PFRs, 1–10 mil lbs (2006)

Non-aromatic PFR [trend]	Persistence (P) Bioaccumulation (B)		Tox	Environ Sample	Biota Sample	Biomon Study
	P US EPA	B LogK _{ow}				
Tris(2-butoxyethyl) phosphate [↓US , Nordic]	—	3.75	✓	dust, computer drinking water indoor air	bird eggs	breast milk, adipose tissue
Tri-n-butyl phosphate	+	4.00	✓	indoor air		breast milk
Triethyl phosphate [↑Nordic]	—	0.8		indoor air		
Bis(2-ethylhexyl) phosphate	+					

Examples of toxicity information

- ▶ Triphenyl phosphate
 - Associated with decreased fertility and hormone alterations in men
- ▶ Isopropylated triphenyl phosphate
 - Neurotoxic in hens
- ▶ *t*-Butylated triphenyl phosphate (tBuTPP)
 - Lubricant oil containing 3% tBuTPP neurotoxic in hens

Toxicity: Data gaps for PFRs

- ▶ Consumer Product Safety Commission nominated representative aromatic PFRs to National Toxicology Program (NTP) for testing:
 - t-Butylphenyl diphenyl phosphate
 - 2-Ethylhexyl diphenyl phosphate
 - Isodecyl diphenyl phosphate
 - Isopropylated triphenyl phosphate
 - Tricresyl phosphate
 - Triphenyl phosphate

Toxicity: NTP research on PFRs

- ▶ Short-term screening evaluation of aromatic PFRs as a class
 - Effect of structure
 - Toxicity of mixtures
 - Endpoints include: neurotoxicity, reproductive toxicity, steroidogenesis, liver enzymes
- ▶ In-depth testing of two aromatic PFRs:
 - Developmental toxicity studies
 - Two-year carcinogenicity studies
 - Adult exposure in mice
 - Perinatal exposure in rats

Questions?

Limitations of screening approach

- ▶ Volume does not reliably indicate extent of use
 - US volume information is out of date
 - Chemicals in imported products not included
- ▶ Difficult to represent subtlety of information in tabular form
 - Mixtures vs. specific isomer
 - Checkmark (✓) for toxicity
 - Environmental sampling results
- ▶ Brief search may miss important information

Questions for Panel

- ▶ Is this a useful screening approach for identifying possible candidates for designation?
- ▶ Are there elements you would add or delete?
- ▶ Would a summary table be enough information for the Panel to choose possible candidates for designation?

Questions for Panel (cont.)

- ▶ For the specific example of PFRs,
 - Does the Panel want to see particular PFRs brought back for potential designation?
 - Does the Panel want to see a group of chemicals (e.g., aromatic PFRs)?