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# Screening Chemicals in Commerce to Identify Possible Persistent and Bioaccumulative Chemicals: Update March 2009

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# Goals of Our Study

- Develop a North American rather than Canadian or U.S. list of potentially PB&T chemicals
  - Greater relevance to the Great Lakes and trans-boundary long range transport than CMP or CHAMP priorities
- Using Quantitative Structure-Property relationships, and scientific judgment, identify chemicals in commerce that may be P, B and T and have not been previously measured in environmental media
- Assess whether selected chemicals can be analyzed by existing methods in use for POPs and new PB&T chemicals in the Great Lakes and the Arctic
- Analyze use and potential environmental release of new emerging contaminants
- Look for pollution prevention opportunities

## Development of a Combined Canadian and US database of chemicals in commerce (Howard and Meylan 2007; 2008)

Source	No. substances	Reporting threshold	Reporting date
US EPA High production volume (HPV) program and EHPV program*	4049	1,000,000 lbs/yr (454 t/yr)	Post-1990
US EPA TSCA Inventory update rule (IUR) web site**	13,958 organics	>10,000 lbs/yr (4540 kg/yr)	IUR reporting years; 1986 to 2002
Canadian DSL categorization***	11,317 organics	>100 kg	Mid-1980s
UVCBs**** (1400 on the DSL)	3059 organics	>100 kg	Mid-1980s
TSCA IUR update 2006	220	>25,000 lbs/yr	Reporting year 2006
<b>Total (after duplicates removed)</b>	<b>22,263</b>		

\*available from <http://www.epa.gov/HPV/hpvchmlt.htm>

\*\* available from <http://www.epa.gov/oppt/iur>

\*\*\* available from Environment Canada - <http://www.ec.gc.ca/substances/>

\*\*\*\* UVCB = Unknown, of Variable Composition, or of Biological Origin – organic chemicals

## Persistence and Bioaccumulation Characteristics of the 22,263 Chemicals Estimated Using EPI Suite Version 3.12

Characteristics*	No.	%	Notes
$\log K_{ow} > 5$	4239	19%	Indicates tendency to adsorb to sediments and to bioaccumulate
BCF >2000	924	4.6%	Bioaccumulation from water exposure – does not include biomagnification
BCF >5000	566	2.8%	
BCF >50,000	19	0.1%	
AO* half-life >2 days AO half-life >10 days	1973 840	10% 4%	AO half-life indicates stability to atmospheric oxidation and potential long range transport
$\log K_{aw} > -5$ and $\log K_{aw} < -1$	6515	32%	$K_{aw}$ describes air-water partitioning. Compounds with $\log K_{aw} > -5$ & $< -1$ are “hoppers”
$\log K_{ow} \sim 2-5$ and high $\log K_{oa} \sim 6-12$	2000	10%	Biomagnification in air-breathing organisms (Kelly et al. 2007)

\* $K_{ow}$  = octanol water partition coefficient

BCF = bioconcentration factor predicted with EPI suite software

AO = atmospheric oxidation half-life

$K_{aw}$  = air-water partition coefficient

## Persistence and Bioaccumulation Characteristics of the using the Danish QSAR database\* of 166,072 Chemicals

Characteristics**	#	%	Comparison with 22,043 from USEPA/Canada list
log Kow > 5	25781	16%	19%
BCF > 2000	10704	6.4%	4.6%
BCF > 5000	6535	3.9%	2.8%
BCF > 50000	261	0.16%	0.09%
AO* half-life > 2 day	20573	12%	10%
AO half-life > 10 day	7024	4%	4%
log Kaw > -5 <u>and</u> log Kaw < -1	37442	23%	32%
Predicted BCF >1000, Atmospheric Oxidation >1 day, + log Kaw >-5 and <-1	1005	0.61%	0.48%

\* Available via the European Chemical Bureau - <http://ecbqsar.jrc.ec.europa.eu/>

\*\*Kow = octanol water partition coefficient; BCF = bioconcentration factor predicted with EPIsuite software; AO= atmospheric oxidation half-life; Kaw = air-water partition coefficient

## **Comparison with Brown and Wania (ES&T 42, 5202, 2008)**

- used the 105,584 individual chemical database of the EPISuite software
- Screened a list of HPV chemicals (TSCA, EINECS, OECD) and Current use Pesticides (USA, WHO) for structural similarity to Arctic accumulating chemicals
- identified 120 chemicals as potential Arctic contaminants based on persistence, long range transport and bioaccumulation potential

### **Overall good agreement**

- 110 of these are in our 22,263 chemical DSL/IUR database while 10 are Current Use Pesticides which we did not survey
- Of their 110 industrial chemicals, 86 chemicals are in our 610 chemical list
- Most of the 24 in their list that are not in ours are not good potential PBT chemicals due to high reactivity, e.g. alpha-aminonitriles, isocyanates, diesters.

## Further Prioritization Based on Lessons Learned from POPs in the Great Lakes and in the Arctic

1. High bioaccumulation/biomagnification potential – high  $K_{ow}$  can biomagnify.
2. Persistence – sequestered in bottom sediments in the open lakes implying a low rate of biodegradation
3. Long range transport potential (i.e., found in mid-lake, in Lake Superior and remote lakes such as Siskiwit Lake)
4. Quantity in use and potential for emissions (i.e., open use or as an additive vs. as a chemical intermediate)

Selection Characteristics	No.	Notes
<b>Predicted BCF: &gt;1000 Atmospheric Oxidation: &gt;1 day, and Log <math>K_{aw}</math> &gt;-5 and &lt;-1</b>	105	Using EPIsuite. Mainly chemicals with LRT potential
<b>By chemical class (Br, Cl, F, I, Si, cyclic HCs) and considering biodegradability</b>	505	By expert judgment – includes chemicals and their degradation products with low LRT but potential for persisting in sediments and in the water column
<b>Total</b>	610	<b>62% halogenated; 8% siloxanes</b>
<b>Neutral organics</b>	473	Existing QSPRs are more accurate for these substances

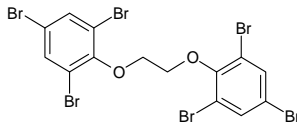
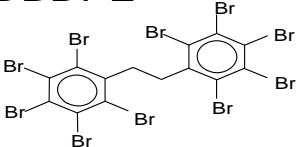
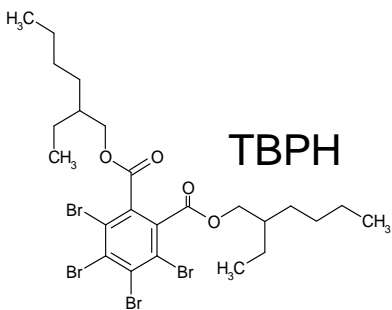
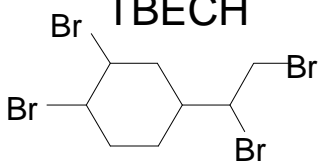
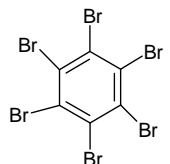
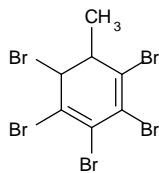
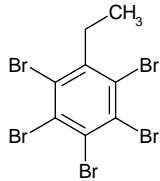
## Information on Measurement and Analyzability of the 610 Substances

<b>Analysable</b>	<b>Well monitored in the GL region and Arctic (i.e., programs such as IADN, NCP)</b>	<b>Chemicals that may have been analysed in any GL &amp; Arctic measurement studies</b>	<b>Analyzable using existing methods for neutral POPs or other neutrals such as pesticides</b>	<b>Analyzable by LC-MS/MS ESI mode (anionic) or positive CI mode</b>
Yes	47	101	404	43
% Yes	7.7	16.5	66.2	7.0
No	563	509	167	
Maybe			39	24

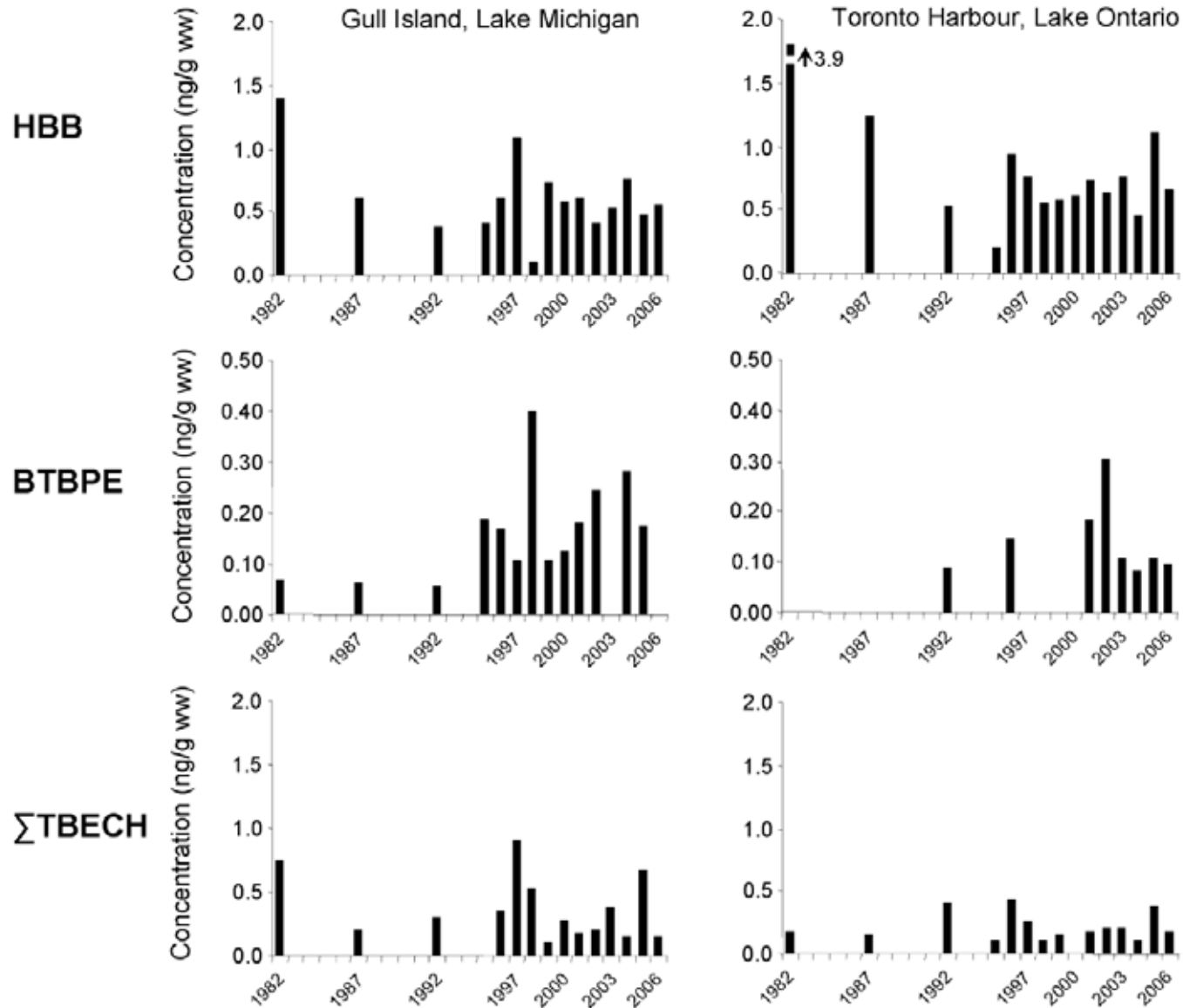
### Conclusion:

**Most could be analysed with existing methods if standards were available**

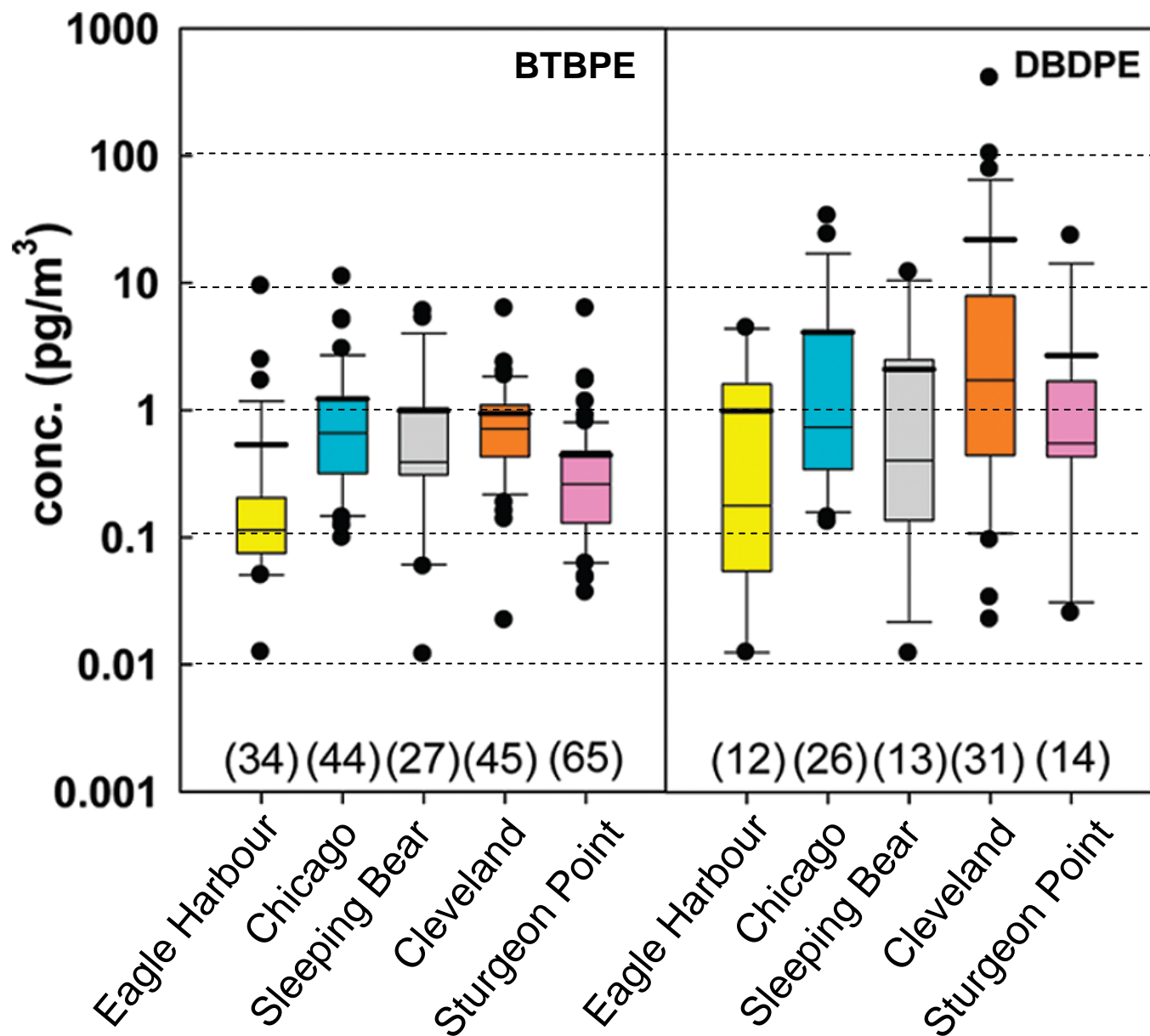
## Successes

<p>Stapleton et al. <i>ES&amp;T</i> 2008</p> <p>Quantified several PBDE replacements in house dust: BTBPE, DBDPE, 2-ethylhexyl 2,3,4,5-tetrabromobenzoate(TBB) and bis(2-ethylhexyl)-tetrabromophthalate(TBPH)</p>	<p><b>BTBPE</b></p>  <p><b>DBDPE</b></p>  <p><b>TBPH</b></p> 
<p>Tomy et al. <i>ES&amp;T</i> 2008</p> <p>TBECH(1,2-dibromo-4-(1,2-dibromoethyl) Cyclohexane) in arctic beluga whales</p>	<p><b>TBECH</b></p> 
<p>Gauthier et al. <i>ES&amp;T</i> 2009</p> <p>BTBPE, DBDPE, TBECH, HBB (and others tentatively confirmed)</p>	<p><b>HBB</b></p> 
<p>Gouteux et al. <i>ES&amp;T</i> 2008</p> <p>Pentabromotoluene (PBT<sub>o</sub>), pentabromoethyl benzene (PBEB), HBB in GL air</p>	<p><b>PBT<sub>o</sub></b></p>  <p><b>PBEB</b></p> 
<p>Venier and Hites <i>ES&amp;T</i> 2008</p> <p>BTBPE, DBDPE in GL air (all US IADN sites)</p>	

Temporal trends for hexabromobenzene (HBB), 1,2-bis(2,4,6-tribromophenoxy)ethane (BTBPE), and 1,2-dibromo-4-(1,2-dibromoethyl)-cyclohexane (TBECH) at two GL herring gull colonies (Gauthier et al. 2009)



# Bis(tribromophenoxy) ethane and decabromodiphenyl ethane in GL air, 2005-2006 (Venier and Hites ES&T 2008)



## Toxicity Estimates of Priority Chemicals:

1. AIM tool to identify analogs with measured toxicity information
2. OncoLogic – identification of substances with potential to cause cancer

QSAR	Number of chemicals tested or within model domain	Endpoints	Results	Number	%
AIM tool	429	close analogs that have measured toxicity data	Included in 45 classes	277	65
OncoLogic	146	Cancer potential	High High-moderate Moderate Low-Moderate Marginal Low	0 10 24 34 29 49	0 6.8 16 23 20 34

## Toxicity Estimates of Priority Chemicals:

### 3. ECOSAR – estimates of aquatic toxicity – 96 hr EC-50's and other endpoints\*

QSAR	Number of chemicals tested	Endpoints	Results	Number	%
ECOSAR	603	Predicted 96 hr EC50 in freshwater fish or in mysid shrimp	<0.001 ug/L = >0.001 – 1 ug/L = >1-1000 ug/L = >1000 ug/L =	60 107 282 155	10 18 47 26

- Chemicals with log Kow > 7 were generally not within model domain
- This represents 27% (165) of 603 chemicals with structures in our list of 610

## Conclusions re toxicity screening

- Many of the chemicals, particularly neutral organics with high log Kows, were outside the model domain which is generally  $\log Kow = <5$  to 7 for ECOSAR's 96 hr acute toxicity test.
- ~10% of the 610 chemicals had relatively high predicted aquatic toxicity based on low 96 h LC50s ( $<0.001$  ug/L) in either mysids or fish
- Offers an alternative method for identifying chemicals of concern from P & B criteria
- screening substances with intermediate or low log Kow by toxicity first might be an approach for prioritizing chemicals of concern which may not meet P and B criteria but are *pseudo-persistent*

## Limitations of our screening approach

- Degradation products not fully assessed
  - some chemicals were selected because they probably had stable degradation products – with F, Br, Cl groups
- TSCA IUR chemicals with CBI not included
- Chemicals *within* imported products, e.g. DBDPE, not captured
- QSPR/QSAR model “domains” were often exceeded e.g. ECOSAR, BCFWIN
- Information on uses and releases is unknown or very limited
  - critical to proper assessment and prioritization
- pollution prevention evaluation e.g. identifying alternatives for flame retardants, plasticizers etc has not been done

## Current screening activities (by SRC for USEPA GLNPO)

- (1) identification of the chlorinated chemicals to assess their use and potential release;
  - There are 126 chlorinated chemicals in our list of 610. Many are intermediates e.g. chlorinated cyclopentanes
  - Bis(chlorophenyl) sulfone is possibly the most interesting potential P and B chemical in this group
- (2) review of the European chemical Substances Information System (ESIS) list of 127 PBT chemicals
  - 98 ESIS PBT chemicals are in the DSL/IUR 22,263 database
  - 27 ESIS PBT chemicals are in our list of 610
  - Conclusion: a few potential additional chemicals
- (3) screening of the chemicals unique to the 2006 TSCA IUR.
  - 10 chemicals unique to the 2006 IUR added to our list
- (4) Completion of AIM and OncoLogic screening of 181 chemicals added to the original 429 substances

## What we could look at

- Pharmaceuticals (human and veterinary)
- Current use pesticides
- Cosmetics – some ingredients are on the TSCA e.g. siloxanes, parabens
- Food additives
- Organometallic substances
- Polymers – some containing perfluorinated or brominated moieties are in the 22,263

*Difference screening approaches may be required since many of the above are ionic e.g. many pharma, CUPs and organometallics*

# Acknowledgements

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# ECOSAR

- ECOSAR is a computerized program for aquatic toxicity estimates that is currently used by EPA's Office of Pollution Prevention and Toxics (OPPT)
- Part of the EPISuite™ software – provides estimates of potential for aquatic toxicity based up  $K_{ow}$  and chemical class
- To date, over 150 SARs have been developed for more than 50 chemical classes
- This analysis involves the application of SARs (Structure Activity Relationships) to predict the aquatic toxicity of chemicals ( $LC_{50}$ ,  $EC_{50}$ , chronic, etc.) for various aquatic organisms (fish, daphnid, algae, etc.)

# AIM

- EPA is currently developing the AIM tool to identify close analogs that have measured data
- Designed to help identify publicly available, experimental toxicity data on closely related chemical structures
- AIM database contains 31,031 potential analogs with publicly available toxicity data
- Experimental data sources Indexed
  - On-Line Databases
    - TSCATS, HSDB, IRIS
  - U.S. Government Documents
    - NTP, ATSDR, HPV Challenge Program
  - Other Sources
    - DSSTox, RTECS, IUCLID, AEGLS

# OncoLogic

- Available from:  
<http://www.epa.gov/oppt/newchemicals/tools/oncologic.htm>
- The OncoLogic program was run on each chemical that a structure was available for in the program
- The program assigns a baseline concern level from high to low for a chemical to have the potential to cause cancer
- The chemical analog structure activity method was used with some standard exposure scenarios selected