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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
Total (after duplicates removed)	**22,263**		

*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 EPISuite Version 3.12

Characteristics*	No.	%	Notes
log K_{ow} >5	4239	19%	Indicates tendency to adsorb to sediments and to bioaccumulate
BCF >2000 BCF >5000 BCF >50,000	924 566 19	4.6% 2.8% 0.1%	Bioaccumulation from water exposure – does not include biomagnification
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} ~2-5 and high log K_{oa} ~6-12	2000	10%	Biomagnification in air-breathing organisms (Kelly et al. 2007)

*K_{ow} = octanol water partition coefficient
BCF = bioconcentration factor predicted with EPIsuite 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 BCF > 5000 BCF > 50000	10704 6535 261	6.4% 3.9% 0.16%	4.6% 2.8% 0.09%
AO* half-life > 2 day AO half-life > 10 day	20573 7024	12% 4%	10% 4%
log Kaw > -5 and 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)

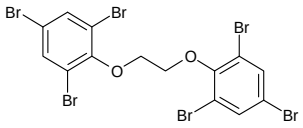
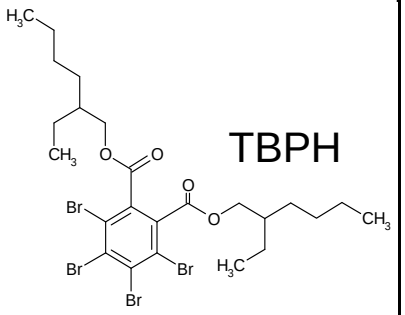
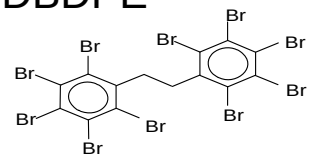
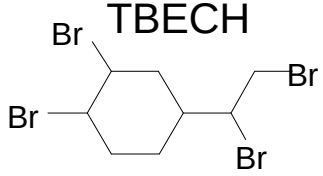
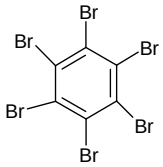
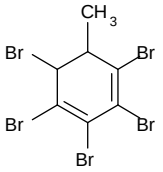
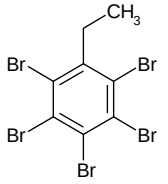
Selection Characteristics	No.	Notes
Predicted BCF: >1000 **Atmospheric Oxidation: >1 day, and Log K_{aw} >-5 and <-1**	105	Using EPIsuite. Mainly chemicals with LRT potential
By chemical class (Br, Cl, F, I, Si, cyclic HCs) and considering biodegradability	505	By expert judgment – includes chemicals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

Information on Measurement and Analyzability of the 610 Substances

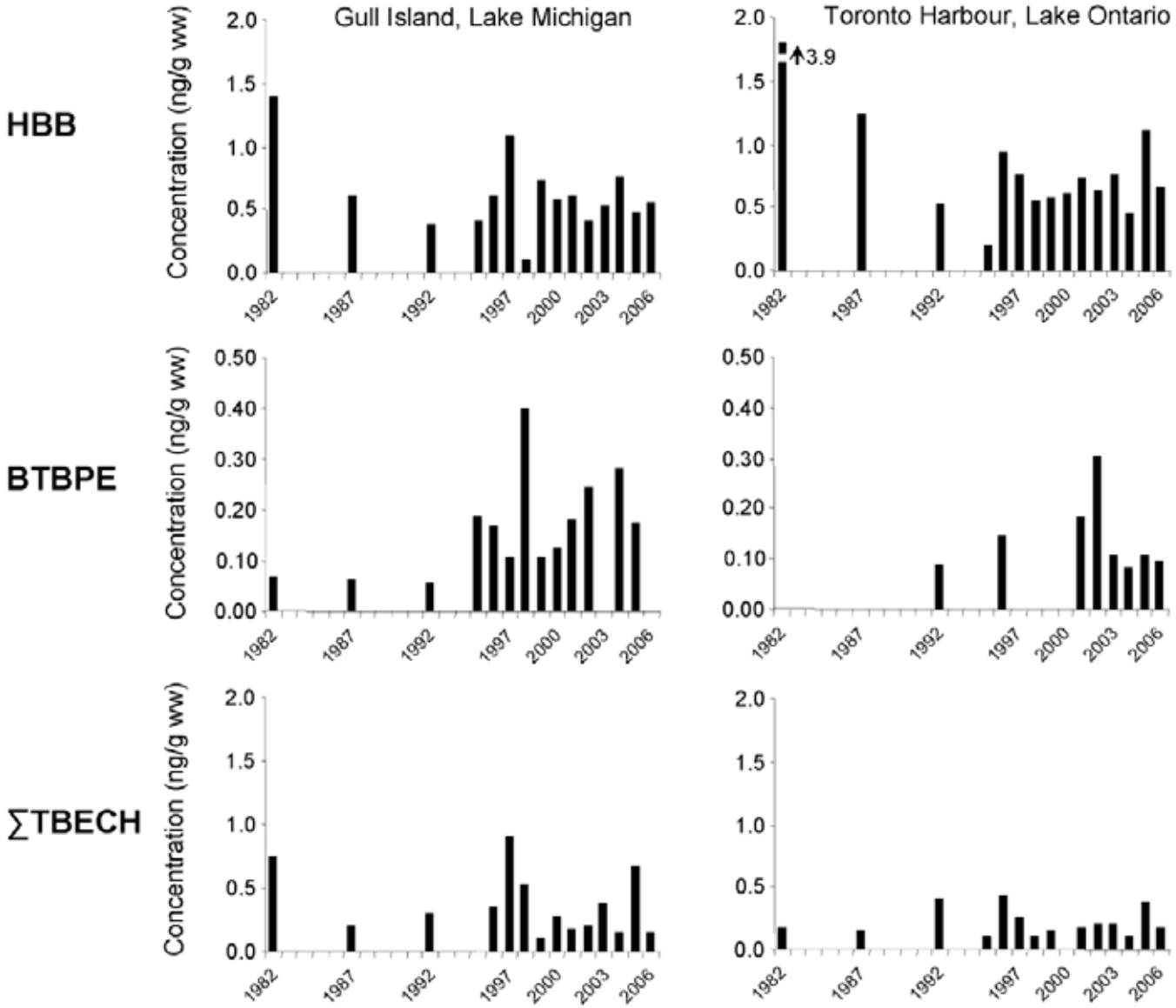
Analysable	Well monitored in the GL region and Arctic (i.e., programs such as IADN, NCP)	Chemicals that may have been analysed in any GL & Arctic measurement studies	Analyzable using existing methods for neutral POPs or other neutrals such as pesticides	Analyzable by LC-MS/MS ESI mode (anionic) or positive CI mode
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

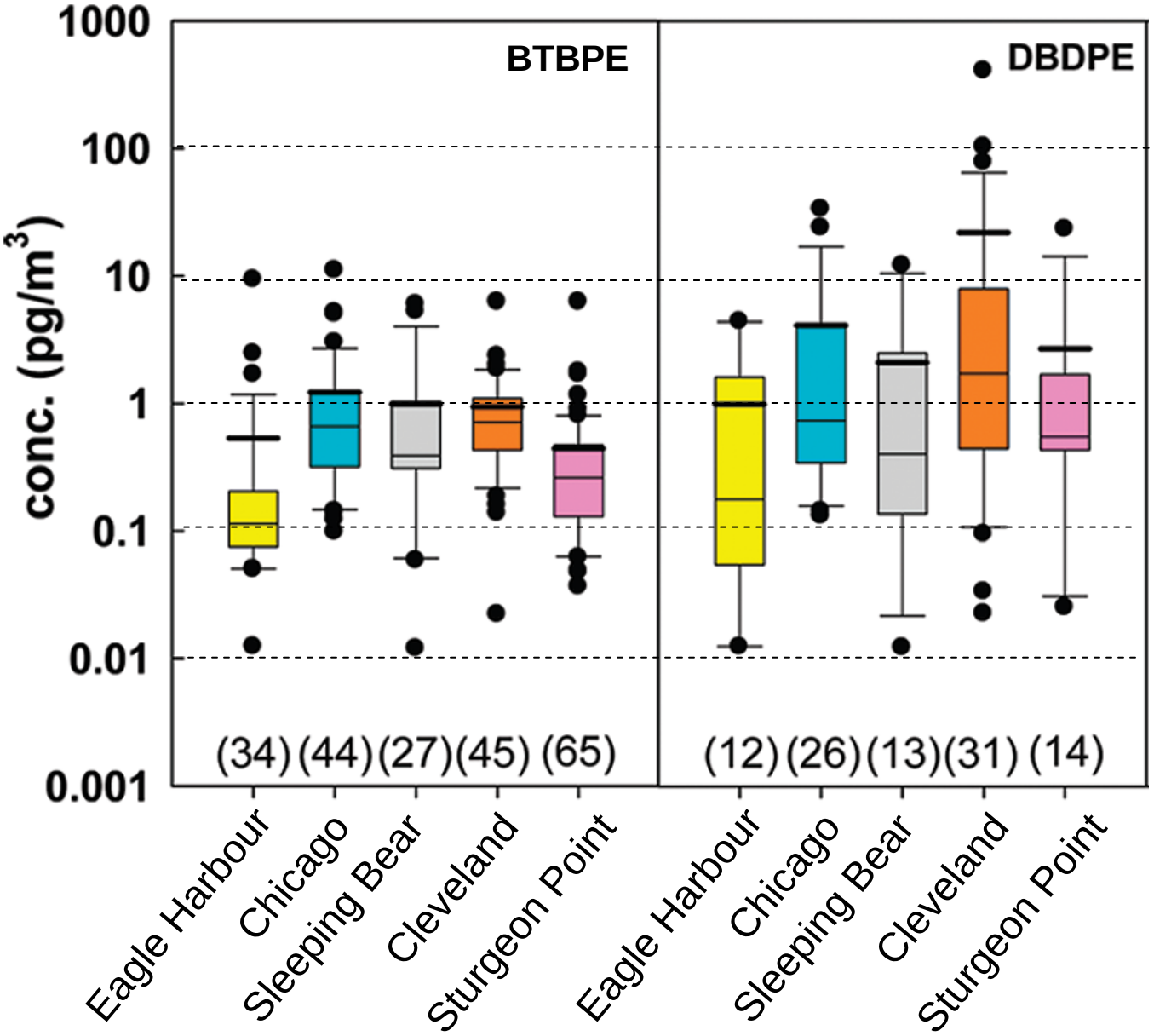
Successes

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

Temporal trends for hexabromobenzene (HBB), 1,2-bis(2,4,6-tribromophenoxy)ethane (BTBPE), and1,2-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 pharmas, CUPs and organometallics

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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/newchems/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