Prioritising chemicals of emerging concern: some approaches being used in Canada and the USA

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Outline

- The challenge of identifying CECs
  - Screening long lists, categorization and assessment
- Some prioritisation efforts in North America
  - Environment Canada DSL categorization
  - US EPA prioritisation and ToxCast initiatives
  - prioritisation schemes in California
- Howard and Muir categorization & prioritisation scheme
  - selecting P&B chemicals from “industrial” chemicals & pharmaceuticals, and transformation products
- Limitations of inventory screening
- Conclusions – relevance to NORMAN prioritisation initiative

The Universe of Chemicals

Globally

- **73,000,000** organic + inorganic substances (2013)
- Commercially available: **19,184,000**
- inventoried/regulated chemicals: **308,000**
- in commerce in USA, EU, Japan, China **~150,000**
- production > 1 tonne/year **~ 30,000**
- routinely measured in environmental media **- <500**

USA

- Toxic Substances Control Act (TSCA) and TSCA Inventory update originally 62,000 (1976), now **~84,000**
- List of "Industrial" chemicals recently in production or imported is much smaller:
  - **2002 = 13,760 (>10,000 lbs)**
  - **2006 = 6,700 (>25,000 lbs)**
  - **2012 = 7,670 (>25,000 lbs)**
- these numbers include organics and inorganics

Other inventories – Europe and the Asia-Pacific region

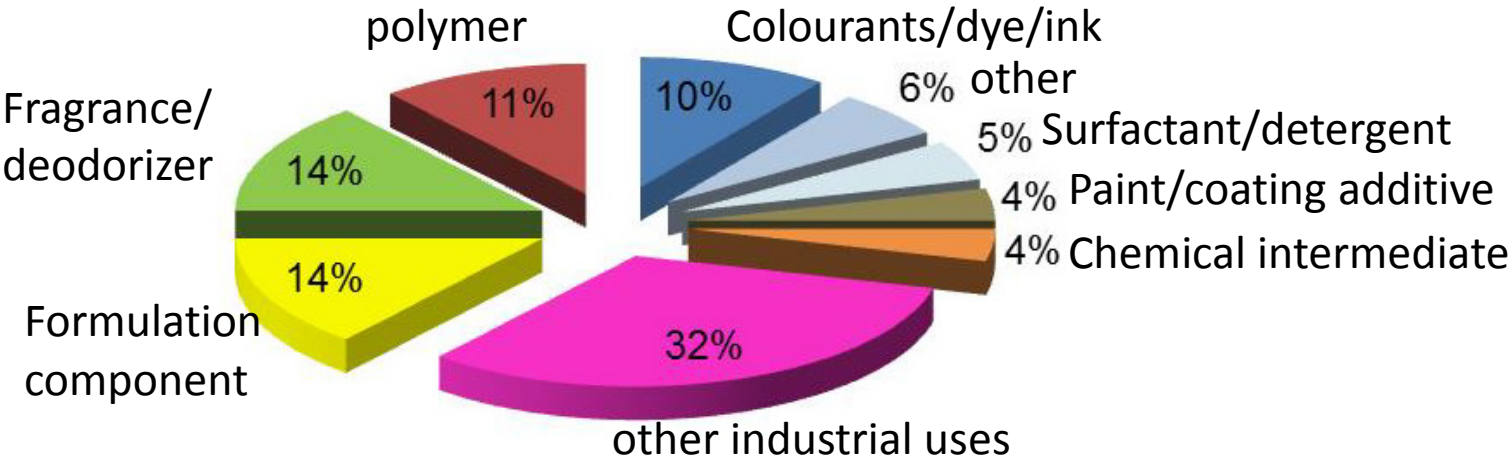
Country/region	Inventory name	Number of substances	Updated?
European Union	REACH	**143,000** **10,500** **~30,000**	• pre-registered as of 09/11 • Registered as of 09/13 • anticipated > 1 t/year
China	IECSC	46,000	•Yes, since 2003
Canada	DSL NDSL	26,000 58,000 (mirrors TSCA)	DSL inventory update underway
Japan	ENCS	20,600 (Existing) ~20,000 “New”	Established 1973 100-800 new substances/year

Also Australia, South Korea, Philippines, Taiwan maintain inventories

Screening and prioritising of chemical inventory lists – the Canadian experience

Environment Canada | Environnement Canada

- 23,000 chemicals – similar to TSCA inventory
- chemicals which were imported or manufactured in Canada at > 100 kg in the period 1984-86
- Screened and categorized organics using a suite of QSPR/QSARs
- For polymers and organometallics used expert judgment

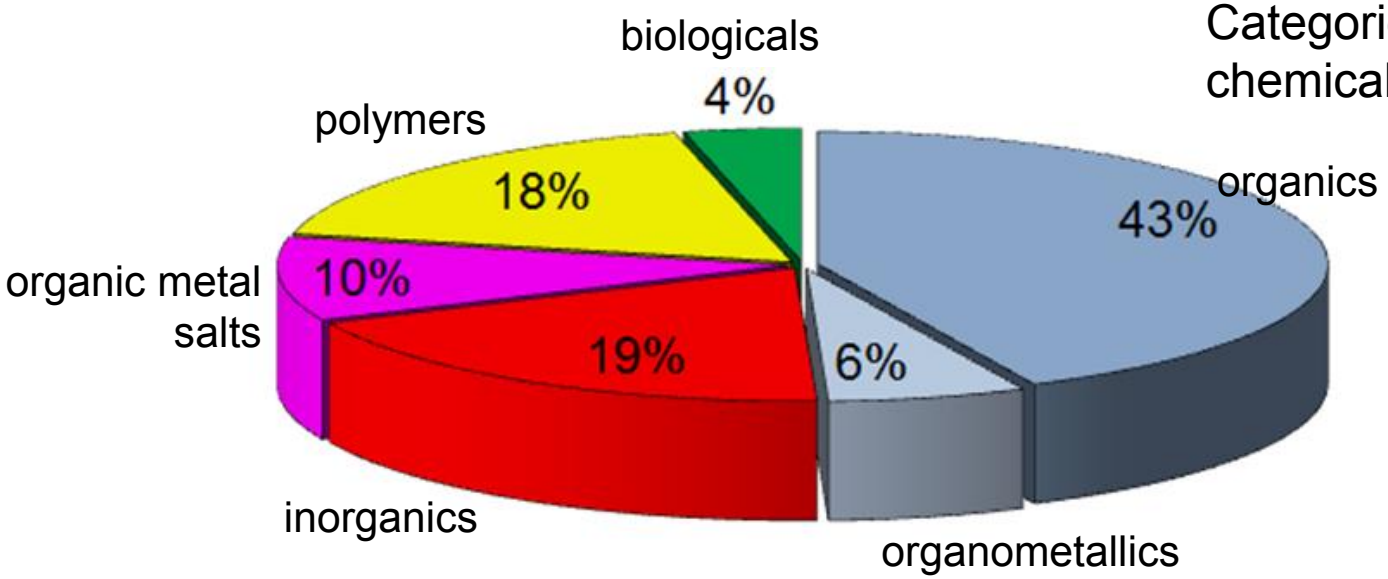


- 3800 chemicals categorized as potential environmental CECs based on persistence, bioaccumulation and/or predicted toxicity

Risk assessment of the selected chemicals – the Canadian experience

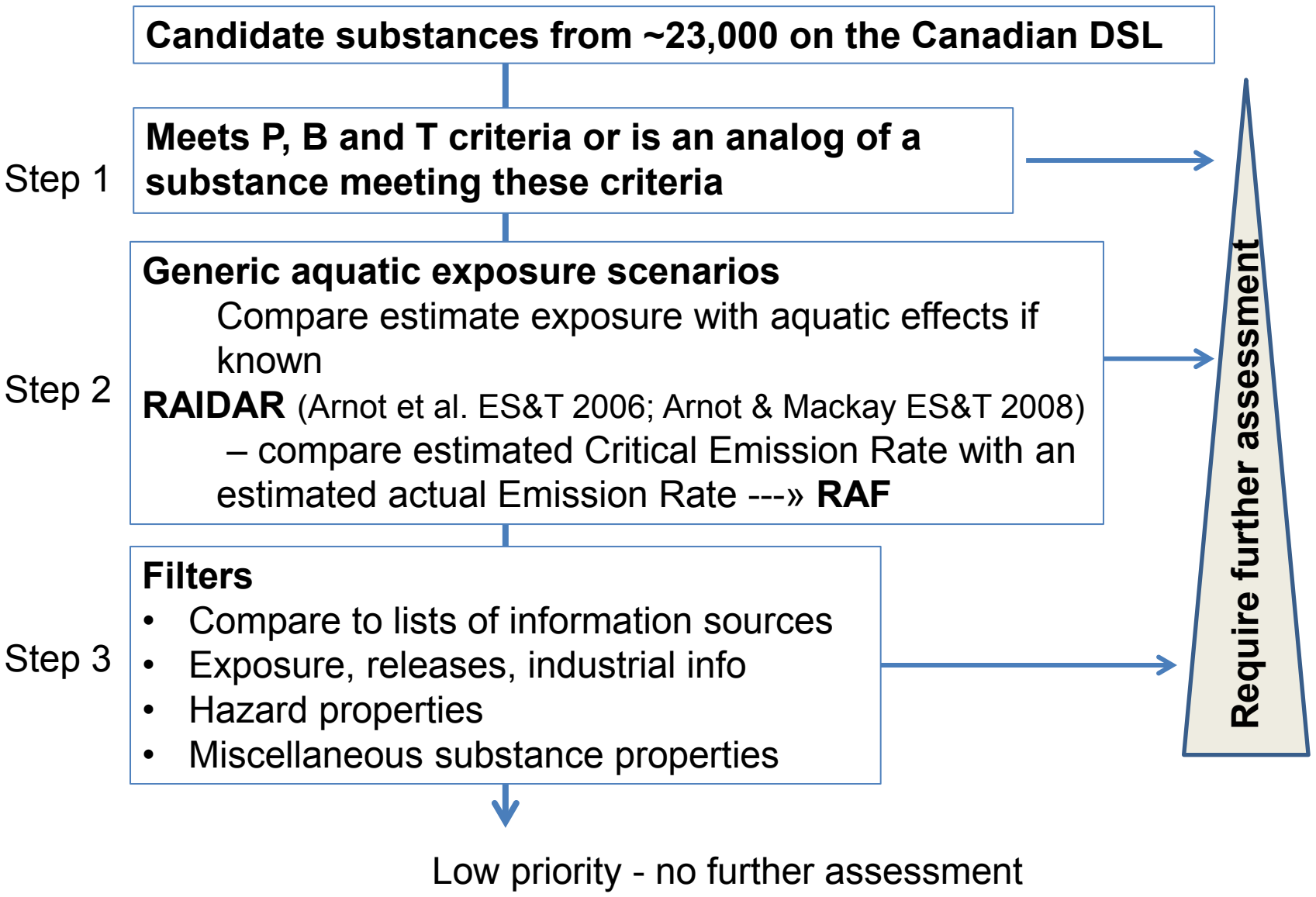
Environment Canada | Environnement Canada

- 3,800 chemicals originally selected for assessment in 2006
- 500 have been assessed (persistence, bioaccumulation and ecotox)
  - by requesting data from industry
  - Supporting research and monitoring
  - 3300 currently under review to be completed by 2020



- Canada is the first country to try to fully assess its chemical inventory list

Rapid screening approach for substances not P and/or B & T



Current priorities for eco-risk assessment in Canada (Chemicals Management Plan)

Grouping *	# individuals
Replacement BFRs	8
Phosphate based FRs	9
Aromatic, aliphatic and alicyclic esters	45
Benzothiazole and benzotriazoles	16
Hindered phenols (antioxidants)	20
Inorganics/metals: Lanthanides, PGEs, Bi, Tl	~30
Musks	10
Phthalates	10
Resin and Rosin Acids/esters	34
Substituted phenyl and diphenyl amines	~50

*** + 23 other groups of lower priority**

US EPA Activities related to prioritisation

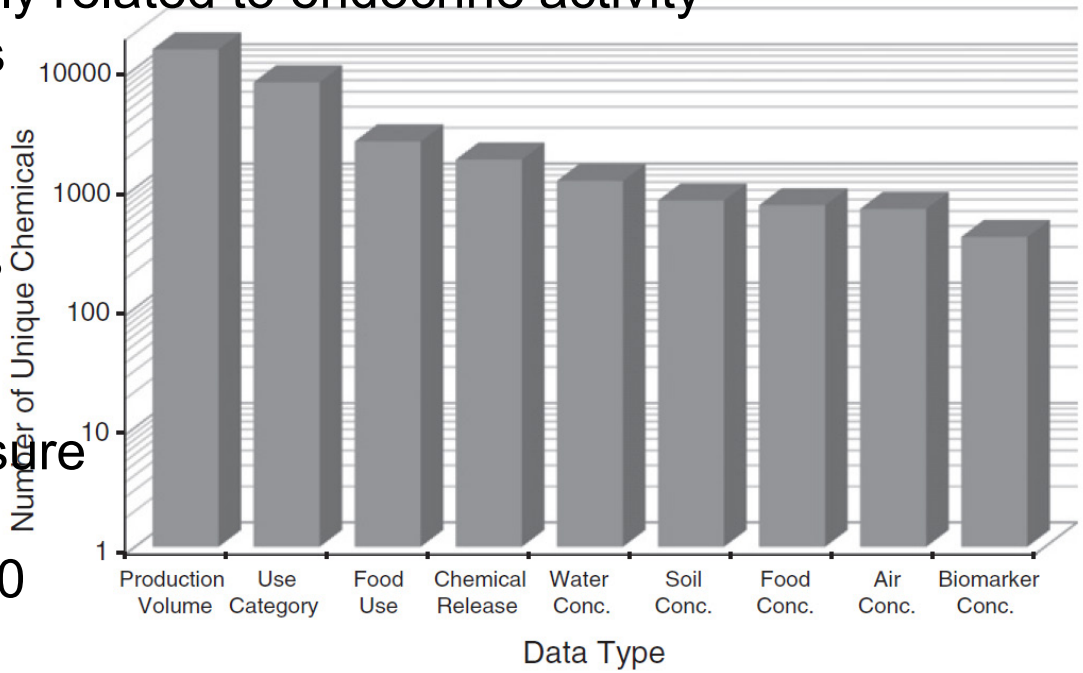
- 83 chemicals selected for prioritisation under TSCA Workplan (2012-13)
  - ~5 chemicals per year
- Development of ToxCast and the ACToR database

ToxCast

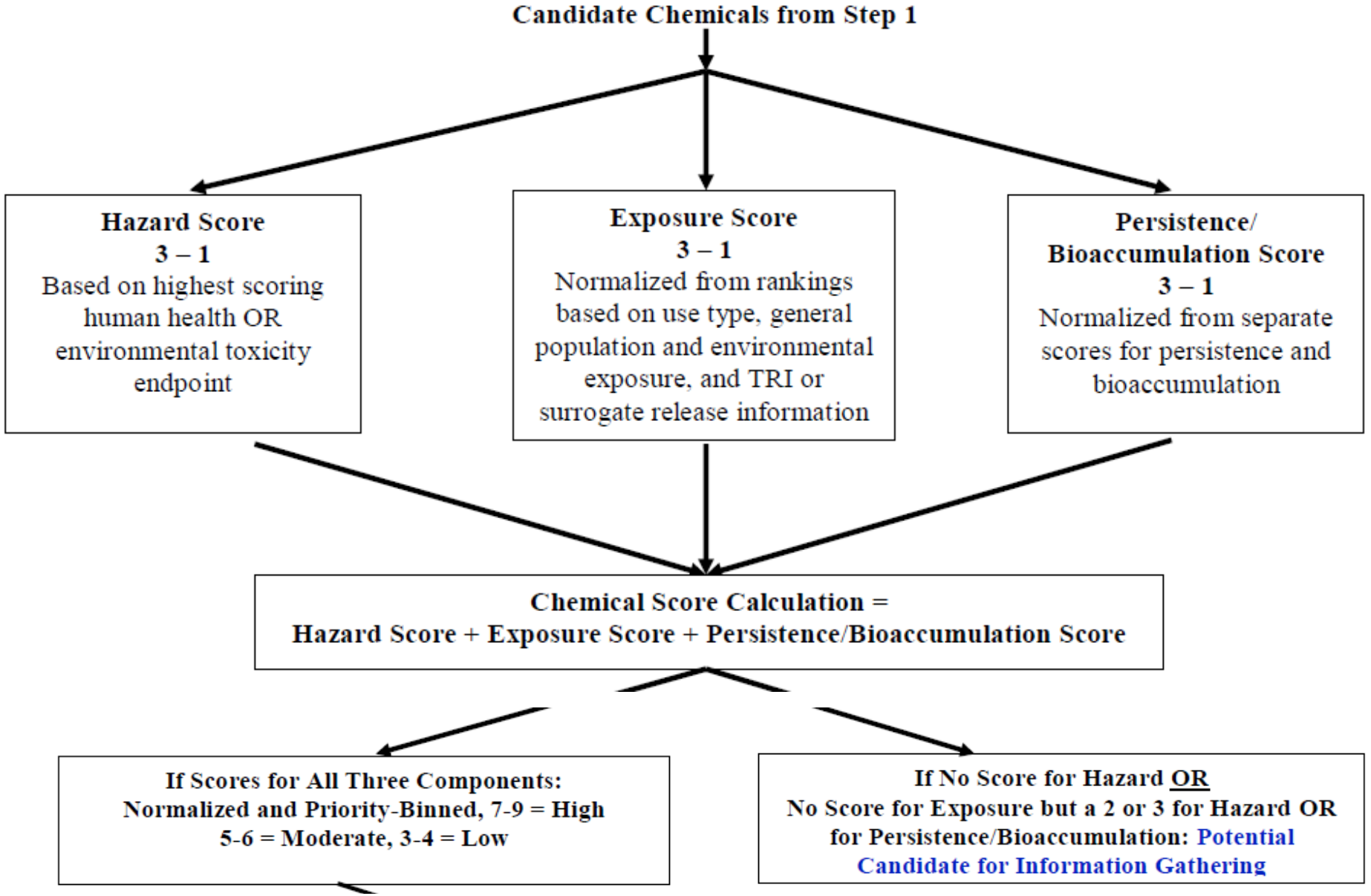
- 1860 unique compounds as of 2013
- High throughput screening, high-content screening and genomics techniques
- 767 test chemicals (e.g., pesticides, industrial chemicals, drugs, food additives, fragrances, etc.)
- 800 unique chemicals specifically related to endocrine activity
- 135 "failed pharma" compounds

ACToR database

- ~500,000 individual compounds
- Screened with EPISuite 4.1
  - BCF/BAF, BIOWIN
- Limited information use & exposure info for most chemicals
  Eg production volume ~ 14,000
- *Egeghy et al STOTEN 2012*



Process to Identify the TSCA Workplan Chemicals



Howard and Muir (ES&T 2010, 2011, 2012) screening industrial organics and pharmaceuticals

Source	No. substances	Reporting threshold	Reporting date
US EPA High Production Volume (HPV) programs	4049	454 tonnes/yr	Post-1990
US EPA TSCA Inventory Update Rule (IUR)	13,958	4540 kg/yr	IUR reporting years; 1986 to 2002
Canadian DSL categorization	11,317	>100 kg	Mid-1980s
UVCBs*	3059	>100 kg	Mid-1980s
TSCA IUR update 2006	220	11,400 kg/yr	Reporting year 2006
Total "industrial" organics (after duplicates removed)	**22,263**		
Pharmaceuticals	**2584**	All with known molecular structures	April 2011

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

Results of industrial organics and pharmaceutical screening

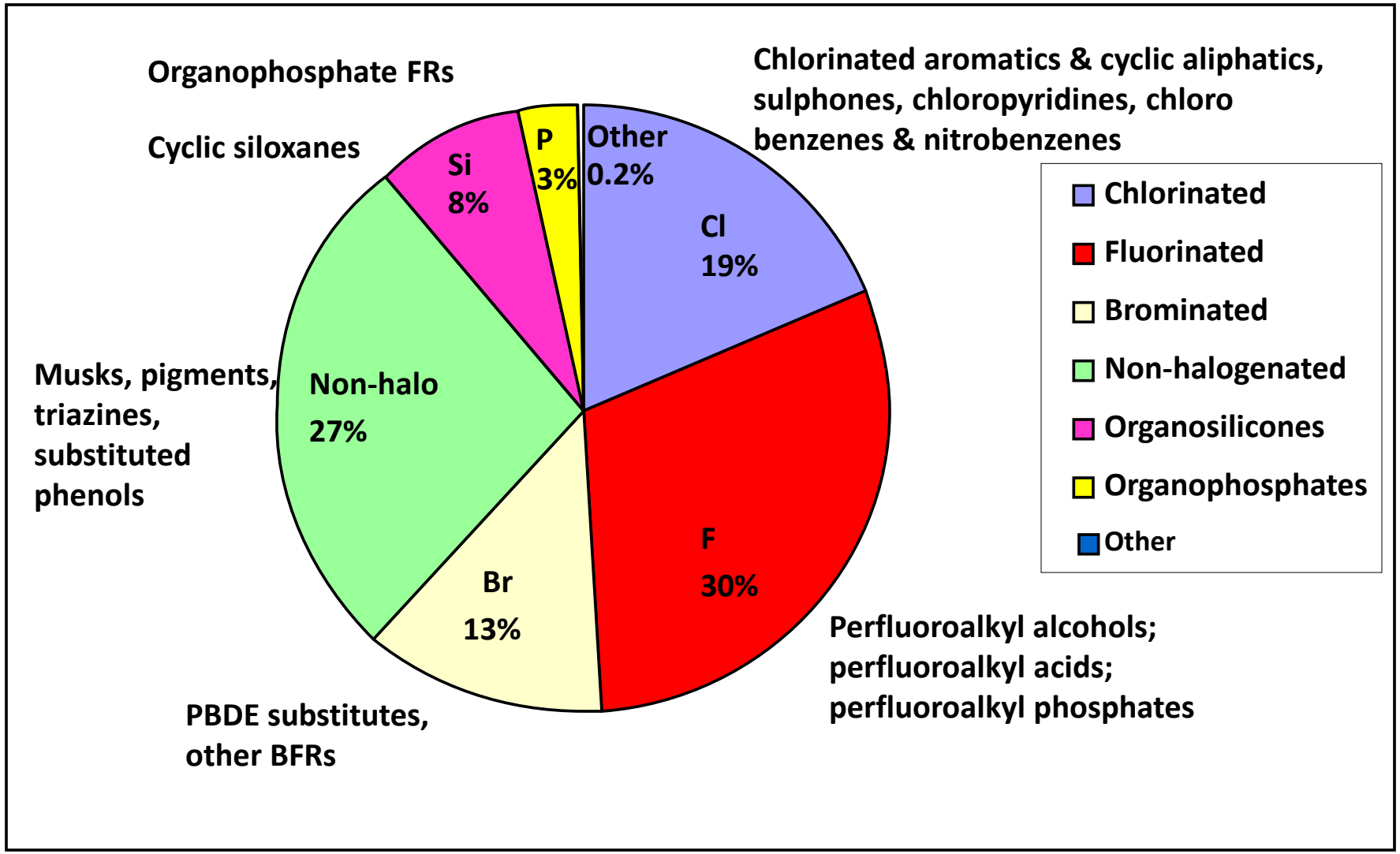
Industrial organics

Category	Screening/assessment Criteria	Prioritisation approach	#
22,263	• **Predicted BCF: >1000** • **Atmospheric Oxidation: >1 day** • **Log $K_{air\text{-}water}$ >-5 and <-1**	Predicted with EPISuite Exceeds Threshold for all 3 criteria	105
	• **Analogs** • **Chemical class (Br, Cl, F, I, Si, cyclic HCs)** • **Biodegradability**	Exceed threshold for 1 or more criteria "Rules of Thumb" for biodegradability	505

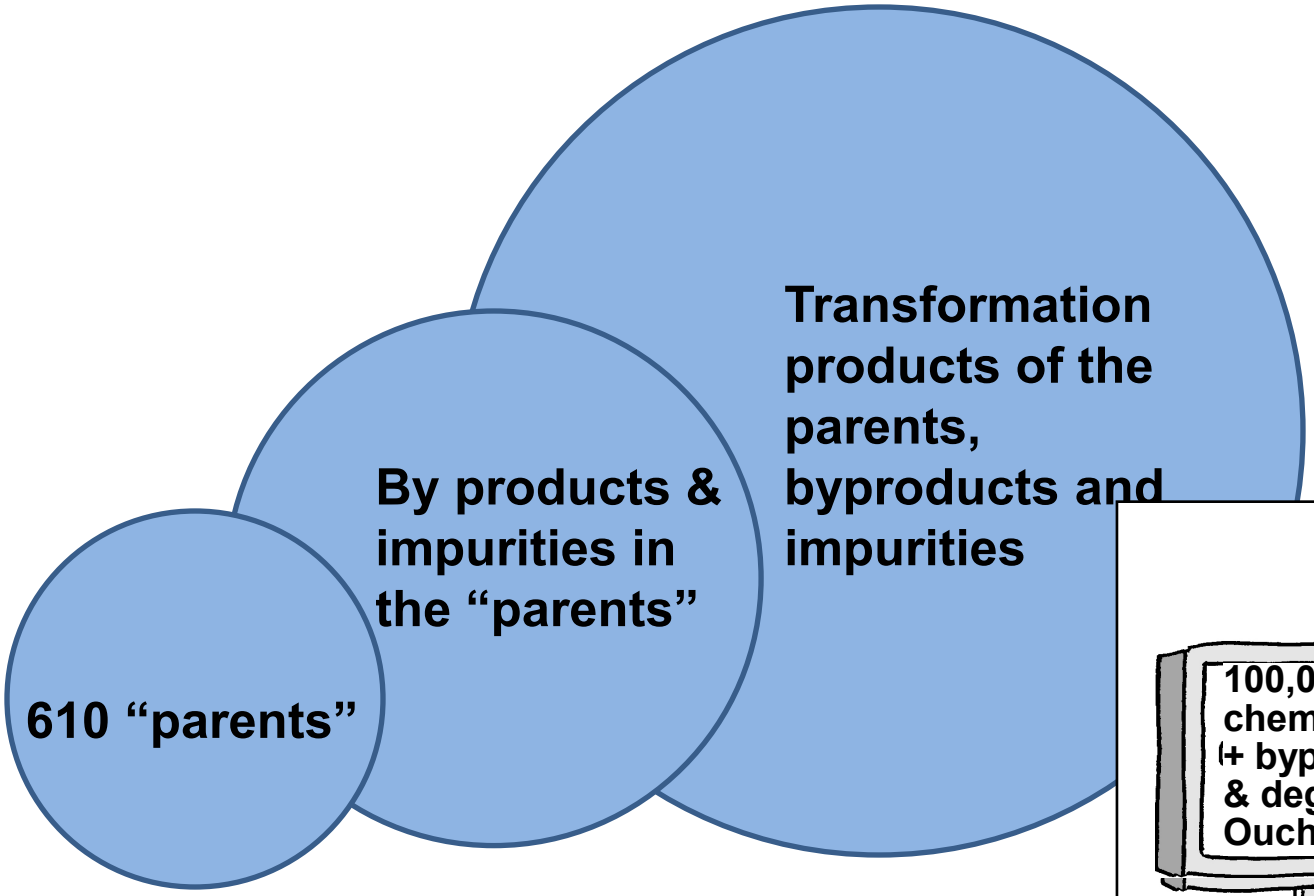
Pharmaceuticals

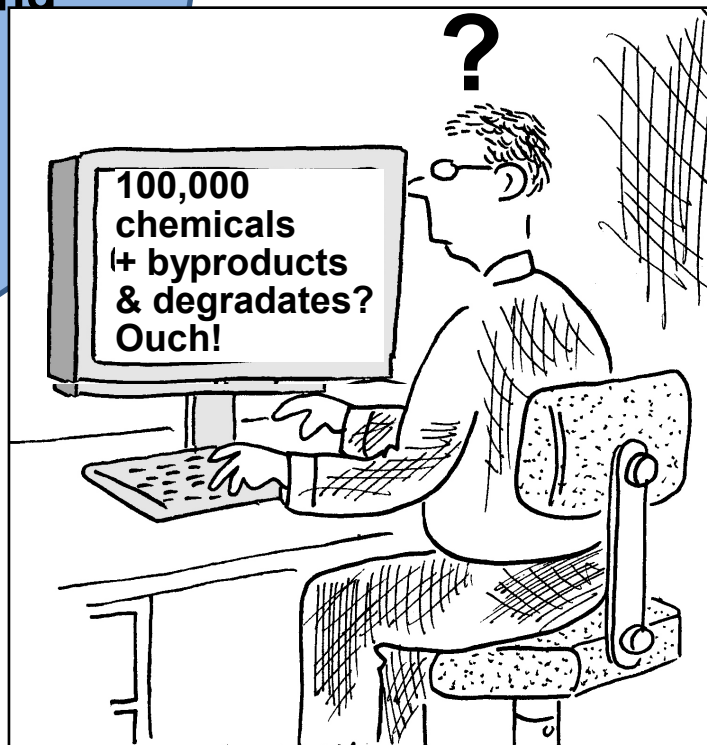
Detected	• **Detection in environmental media**	Detection	275
297 HPV pharmas	• **Predicted BCF: >100 (neutral species)** • **BIOWIN1 or BIOWIN5 probability <0.5** • **Recalcitrant structural group**	Exceeds Threshold for P & B "Rules of Thumb" for biodegradability	58
2221 non HPVs	• **Same as for HPV pharmas**	Same as for HPVs	364

Classes of the 610 Priority Chemicals



Screening for transformation products could present a major challenge given all possible pathways and products





Main selection criteria

B: Use predicted Log Kow or log BCF = >3

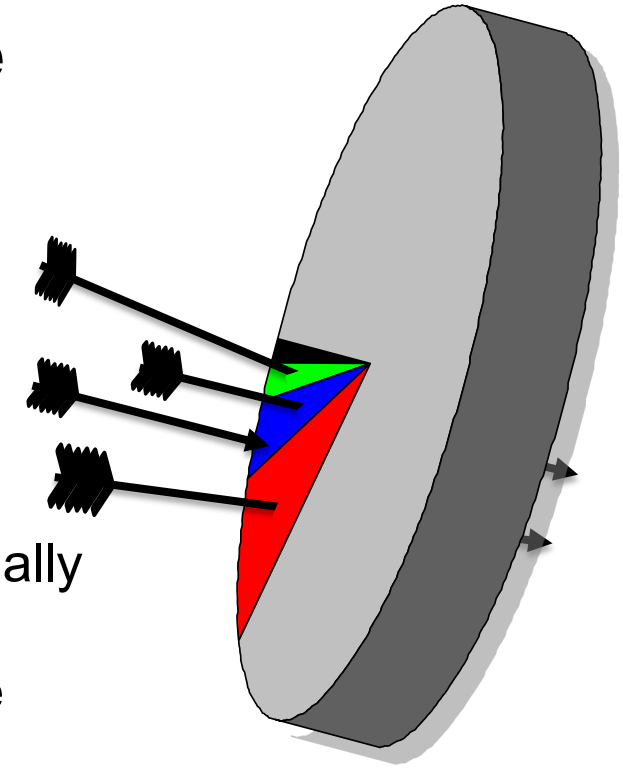
P: Use BIOWIN1 and BIOWIN5 (probability <0.5)

UM-Biocatalysis/Biodegradation Pathway Prediction

Problems with this screening approach

- Focussing on registered chemicals ignores low volume chemicals that could be toxic to aquatic life
  - e.g. synthetic estrogen is low volume but an important EDC in surface waters
  - other pharmaceuticals with endocrine disruption, antimicrobial or other unique biological activity
- Many “industrial chemicals” may never be released to the environment
  - many low volume chemicals are designed to be released e.g. in personal care products, pesticides
- Screening of chemical inventory lists doesn’t capture degradation products or byproducts
- Many chemicals are difficult to assess with current science
  - Can be acids or organometallics
  - These may constitute up to 2/3 of registered chemical lists

A more targeted approach is possible with pharmaceuticals, pesticides and personal care products



Screening based on properties and use

- Generally chemical structures and important physical-chemical properties are known
- Some chronic toxicity information available especially for pesticides
- Quantities in use and use area (for pesticides) are known

Screening based on environmental occurrence in surface waters

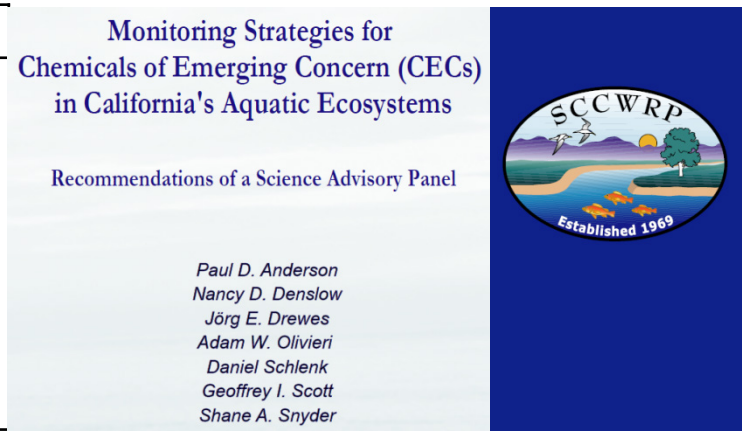
- ~ 300 pharmaceuticals have been detected
- ~ 140 pesticides routinely measured
- ~ 45 personal care product chemicals widely measured

- Total of 1150 chemicals measured in water out of the 500,000 in the ACToR database

Chemical Prioritization in California

- Science Advisory Panel for “Monitoring CECs in California’s Aquatic Ecosystems” (2012)
- Selected 82 chemicals for initial screening based on
  - Focussing on occurrence, toxicity and methods
    - published lists and availability of toxicological information
    - Availability of analytical methods and commercial labs
- Used three representative receiving water scenarios - recommended 15 chemicals for State-Wide monitoring

Industrial/personal care	Pharmaceutical	Pesticides
Bis(2-ethylhexyl) phthalate	Estrone	Bifenthrin
Butylbenzyl phthalate	Ibuprofen	Permethrin
Bisphenol A	17-beta estradiol	Chlorpyrifos
p-Nonylphenol	Diclofenac	
Galaxolide (HHCB)	Triclosan	
PBDE -47 and 99		
PFOS		



Conclusions and Future Directions

- This presentation mainly addresses the development of a list of potential new or data poor “emerging” chemicals of concern
- Compatible with NORMAN data gathering and gaps identification
- Main application is for non-target screening e.g. using high res MS and/or bioanalytical screening
- Many challenges to the screening approach
  - Robust QSPR/QSARs work well but only for a limited range of organic chemicals
  - Ionizable organics and organometallics together represent high proportion of commercial chemicals and are poorly modelled
  - Emissions, uses, transformation products/rates often unknown thus high uncertainty in risk assessment/PEC modelling phase
- We don’t just need a “harmonised European approach to prioritisation” but one that is harmonised globally

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