Introduction

• New and existing chemicals are being evaluated to identify persistent, bioaccumulative and toxic (PBT) substances and persistent organic pollutants (POPs) that may pose risks to humans and the environment [1-3].
• Measured chemical property and monitoring data are limited compared to the large number of chemicals requiring assessment; therefore, mass balance models and Quantitative Structure-Activity Relationships (QSARs) are required, at least for screening [4].

Objectives

• Develop a tiered PBT / POP screening system that progresses to reduce the largest contributions to uncertainty.
• Apply screening system to >15,000 organic substances and rank based on far-field human exposure in source (PBT) and remote (POP) environments (Figure 1).
• Evaluate the screening system with monitoring data.
• First stage (this work):
  • Evaluate applicability of existing models and QSARs for rapid screening
  • Identify key sources of uncertainty for screening PBTs / POPs using mass balance models and QSARs.

Methods

• Compile a list of currently produced chemicals (n = 15,000) and structural information (SMILES).
• Apply two screening and ranking methods (Figure 2) (i) RAIDAR v.2.0 [5]
  - Level III mass balance model that can predict human concentrations (CH) in source regions.
  - Requires chemical property information (partitioning, half-life - HL) as input (EPI Suite used [6]).
  - Two sets of output: (1) “hazard-based”; relative exposure potential ranking (assumed equal unit emissions for all chemicals), and (2) “risk-based”; expected exposure ranking based on initial (realistic) emissions and mode-of-entry estimates (EU-TGD default emissions factors used [7]).
  - Uncertainty analysis identifies contribution of variance of model inputs on model output [8] (Figure 3).
(ii) POP-QSAR [9]
  - Screening tool used to identify chemicals with structural similarities to listed POPs.
  - Requires only chemical structure information (SMILES) for direct “hazard-based” ranking.

Results

• RAIDAR CH “risk-based” exposure estimates (upper-bound 97.5 percentile estimates) span >16 orders of magnitude and ~34% exceed a threshold criterion of 1 ng/g-lipid (Figure 4).
• The two methods rank many of the same chemicals high; however, results can be different (Figure 4).
• Emissions and biotransformation half-lives in mammals contribute greatest uncertainty in CH (Figure 3).

Discussion

• Mass balance and QSAR models can be used to rapidly screen large chemical lists for human exposure and POP-like characteristics.
• Merits and limitations with each approach, reasons for large differences (red circles; Figure 4) include different endpoints, the use of expected “realistic” emissions estimates and biotransformation in the mass balance method, etc...
• Combining results of both approaches reduces false positive errors in each and provides first tier guidance for identifying chemicals of concern (blue box; Figure 4).
• Uncertainty analysis identifies key model input parameters contributing greatest uncertainty in predicted CH (emissions, biotransformation half-lives; HL).
• On-going work to improve mass balance model input requirements (i.e. more refined emissions and mode-of-entry information, new QSARs for biotransformation half-lives in fish and mammals, new environmental degradation QSARs, and chemical partitioning QSARs).
• Subsequent tiers will use refined model inputs and more sophisticated models (e.g. CoZMoMan [10]).

References