USING MODELS TO SCREEN THE DOMAIN OF INDUSTRIAL CHEMICALS FOR POTENTIAL ENVIRONMENTAL CONTAMINANTS

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Introduction

The ability to identify hitherto unknown environmental contaminants is one of the great challenges of environmental chemistry. The identification of contaminants is important in order to be able to identify substances that could be having a negative impact on the environment or human health. In the past, environmental contaminants have typically been discovered by analytical chemists who observe unknown signals during the trace analysis of environmental matrices[1-4]. The majority of regulated POPs and PBTs have been identified in this manner. However, this approach has a major weakness: it generally only identifies contaminants which are similar to known contaminants because trace analytical methods exclude all chemicals except those similar to the analyte.

To overcome this weakness, a second method has been developed over the last 15 years which is called – amongst other things – effect directed analysis (EDA)[5]. The starting point for this methodology is an observed adverse effect experienced by a biological system. This is commonly an effect in an in-vitro laboratory test system (which may be used as a model for an adverse effect observed in the environment) exposed to a chemical extract of an environmental matrix. The extract is then sub-divided into smaller and smaller fractions based on which fraction causes the same adverse effect in the biological test system until one obtains a fraction that contains so few substances that the chemical causing the effect can be identified. Although the EDA approach sounds very useful in principle, it has proven to be difficult to employ in practice, and to date few new environmental contaminants have been identified in this manner.

The theoretical screening of large numbers of chemicals to identify those with the greatest potential to do harm is a useful and increasingly important regulatory tool[6-7]. An example is the legal requirement to screen the Canadian Domestic Substances List for those that are persistent, bioaccumulative and inherently toxic[8]. Albeit promising, the approaches that have been applied so far tend to address a limited number of screening criteria, and/or do not integrate those criteria into a single measure of potential risk[9-14], and thus they have had limited usefulness in identifying new chemicals of concern. A recent effort by our consortium to apply integrated model elements to screen for chemicals on the basis of expected human exposure[15-16] represented a first step in this direction. It is a stepping stone towards more sophisticated, hierarchical approaches that take into account relative contributions of uncertainty.

With the following work we sought to advance the state of art by a) developing an environmental contaminant screening system with integrated assessment of prediction uncertainty, b) using this screening system to classify more than 10,000 low and high production volume chemicals and for the first time develop a ranking of the chemicals according to their expected concentrations in humans and the environment, and c) verify the utility of the screening system by comparing model predictions with observed concentrations in the environment.

Materials and methods

A rapid throughput method to estimate emissions of organic chemicals in commerce was developed. The method builds upon information in the European Union Technical Guidance Document and utilizes information on quantities in commerce (production and/or import rates), chemical function (use patterns) and physical-chemical properties to estimate emissions to air, soil and water for five stages of the chemical life-cycle[17]. It included estimation of the uncertainty of the emissions estimates.

The emissions predictions were linked to the regional-scale, steady state multimedia mass balance model RAIDAR Ver. 2.0[18]. This model integrates prediction of the environmental fate and transport of organic contaminants with prediction of their bioaccumulation in wildlife and human foodwebs. Uncertainty is considered explicitly for all input parameters and propagated through the model.

A database of 12,619 organic chemicals was compiled including substances with any reported production in Europe, US, Canada, or Japan. This database comprises a broad range of chemical properties and production volumes and is considered to represent much of the diversity of current use organics. The physical chemical properties of the chemicals were estimated using Quantitative Structure Property Relationships (QSPRs) from the United States Environmental Protection Agency's Estimation Program Interface Suite (EPI Suite™) software program. The uncertainties of the calculated property values were also estimated, primarily by using the statistical information from the QSPR training and testing sets[19].

The screening tool was used to predict the expected concentrations of the 12,619 chemicals in a generic environment. This allowed a ranking of the chemicals according to their expected concentrations in different environmental media. The uncertainty of the predicted concentrations in humans was also determined and the major sources of this uncertainty were assessed.

The Baltic Sea, a brackish marginal sea strongly impacted by anthropogenic activity, was selected as the test environment to evaluate the model predictions. Surface sediment samples were collected from 15 remote locations around the Baltic Sea and pooled. Blubber samples were taken from 10 male grey seals aged 1-5 years and pooled. The samples were analyzed for a selection of 38 chemicals from the chemical database.

Results and discussion

The predicted concentrations of the 12,619 chemicals in humans are plotted in rank order in Figure 1. These concentrations range over 16 orders of magnitude. This figure also shows the upper and lower bounds of the estimated concentrations. They generally encompass 3-4 orders of magnitude in each direction.

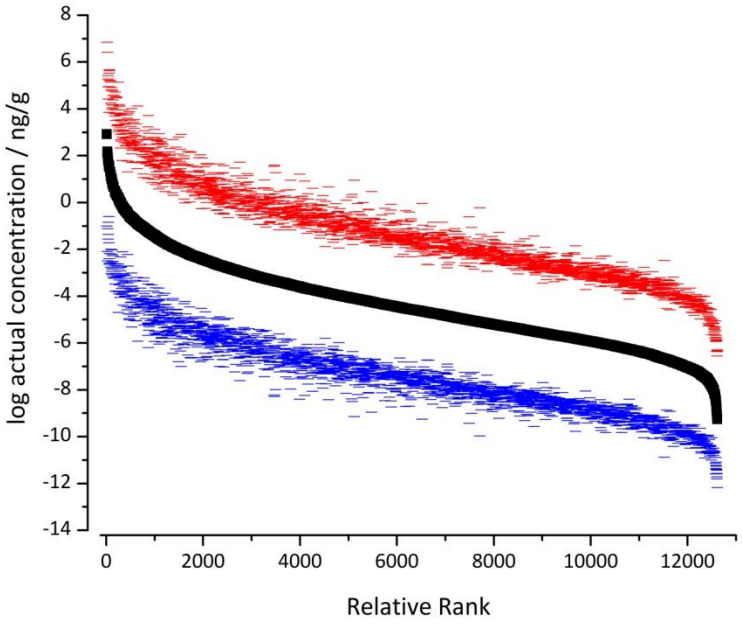

Figure 1: Relative ranking of 12,619 organic substances for far-field human exposure concentrations. Black circles are the median values, the blue bars are the 2.5 percentiles, and the red bars are the 97.5 percentiles.

The contribution of the different model input parameters to the variance in the predicted concentration in humans is illustrated in Figure 2. Approximately three quarters of the uncertainty in the predicted concentration in humans was due to the uncertainty in the prediction of emissions of the chemicals (Ea), which in turn largely reflects the lack of discrete numbers for quantities in commerce as well as a detailed breakdown of chemical function and use. Most of the remaining uncertainty was due to the uncertainty in the prediction of biotransformation of the chemicals in mammals.

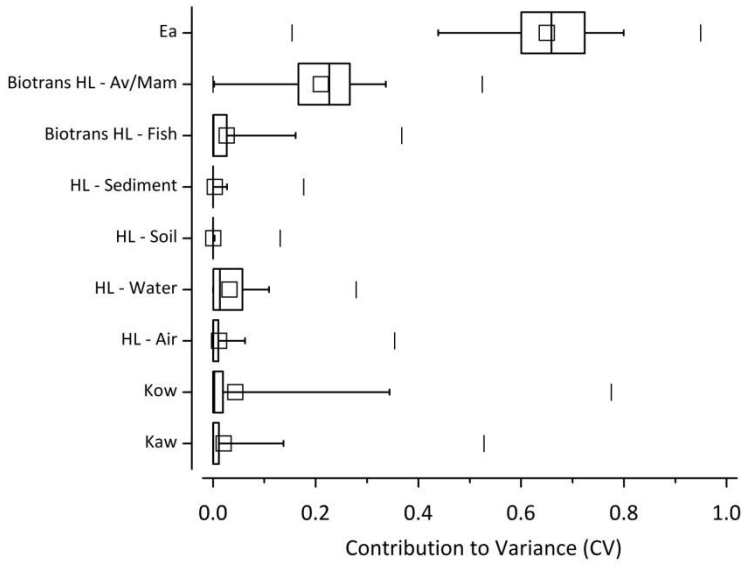

Figure 2: Statistical summary for the contribution of model input parameters to the variance (CV) of the calculated far-field human exposure concentrations for the 12,619 substances. Box plot symbols: × - minima and maxima, whiskers – 5th and 95th percentiles, box – 25th and 75th percentiles, centre line – median, □ – mean. HL refers to half- life.

Of the 38 chemicals analyzed, 16 were measured above the LOQ in sediment and 12 in seal blubber. The remaining chemicals were present between the LOD and the LOQ with one exception. For those chemicals below the LOQ, the LOQ was used for the model evaluation.

In the left panel of Figure 3 the rank of the predicted concentration of the chemical in the sediment (for all 12,619 chemicals) is plotted against the rank of the measured concentrations (for the 38 chemicals), while the right panel shows the same plot for seal blubber. There is no correlation between the predicted and observed rank for either matrix. This indicates that the screening tool was not able to predict the rank of chemical concentrations in the Baltic Sea environment.

Figure 1 provides an explanation for the performance of the screening system ranking compared with the monitoring data ranking. The lower bound of the predicted concentration for the chemical ranked about #20 is 0.01 ng/g. This is equal to the upper bound of the predicted concentration for the chemical ranked #8000. Excluding the first 20 chemicals in the data set, this means that the chemical with the next highest concentration in humans could be nearly any one of the 7980 chemicals with a rank between 21 and 8000.

This very large ranking uncertainty is due to the uncertainty in the model predictions. The only way to improve the ability of models to prioritize chemicals based on their expected environmental concentrations is to reduce the uncertainty in the predicted concentrations. The dominant source of this uncertainty is the prediction of emissions and the prediction of the biotransformation rates in mammals. Without large reductions in the uncertainties in the prediction of these parameters, most particularly emissions, models will be of little value for the prioritization of chemicals according to their expected concentrations in the environment.

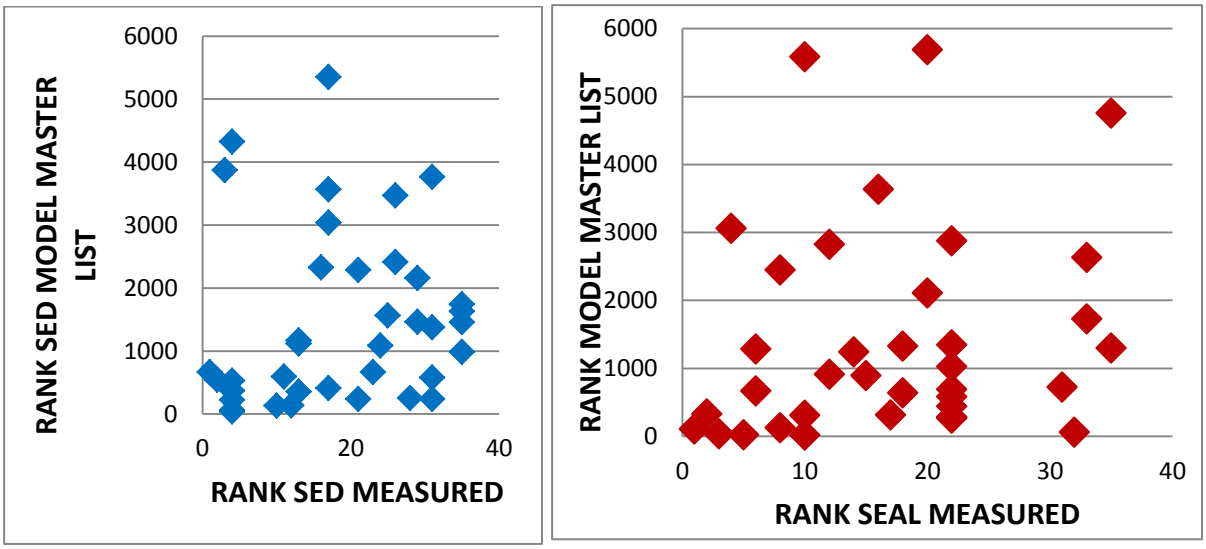

Figure 3: Rank of the modeled concentrations versus rank of the measured concentrations for sediment (left) and seal blubber (right).

This work illustrates the key importance of uncertainty analysis when using models to address environmental contamination. It must be recognized that screening and prioritization uncertainty also exists in other screening methods (i.e., PBT categorization)[13].

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