Modeling Exposure to Persistent Chemicals in Hazard and Risk Assessment

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ABSTRACT

Fate and exposure modeling has not thus far been explicitly used in the risk profile documents prepared to evaluate significant adverse effect of candidate chemicals for either the Stockholm Convention or the Convention on Long-Range Transboundary Air Pollution. However, we believe models have considerable potential to improve the risk profiles. Fate and exposure models are already used routinely in other similar regulatory applications to inform decisions, and they have been instrumental in building our current understanding of the fate of POP and PBT chemicals in the environment. The goal of this paper is to motivate the use of fate and exposure models in preparing risk profiles in the POP assessment procedure by providing strategies for incorporating and using models.

The ways that fate and exposure models can be used to improve and inform the development of risk profiles include:

- Benchmarking the ratio of exposure and emissions of candidate chemicals to the same ratio for known POPs, thereby opening the possibility of combining this ratio with the relative emissions and relative toxicity to arrive at a measure of relative risk.
- Directly estimating the exposure of the environment, biota and humans to provide information to complement measurements, or where measurements are not available or are limited.
- To identify the key processes and chemical and/or environmental parameters that determine the exposure; thereby allowing the effective prioritization of research or measurements to improve the risk profile.
- Predicting future time trends including how quickly exposure levels in remote areas would respond to reductions in emissions.

Currently there is no standardized consensus model for use in the risk profile context. Therefore, to choose the appropriate model the risk profile developer must evaluate how appropriate an existing model is for a specific setting and whether the assumptions and input data are relevant in the context of the application.

It is possible to have confidence in the predictions of many of the existing models because of their fundamental physical and chemical mechanistic underpinnings and the extensive work already done to compare model predictions and empirical observations.

The working group recommends that modeling tools be applied for benchmarking PBT/POPs according to exposure-to-emissions relationships, and that modeling tools be used to interpret emissions and monitoring data. The further development of models that couple fate, long-range transport, and bioaccumulation should be fostered, especially models that will allow time trends to be scientifically addressed in the risk profile.

Key words: POPs, PBT, exposure, modeling, risk assessment

INTRODUCTION

There are currently two international, legally-binding agreements that regulate the production, use and release of persistent organic chemicals. These are, 1) the Stockholm Convention on Persistent Organic Pollutants (POPs) (http://chm.pops.int/), and 2) the United Nations Economic Commission for Europe (UNECE) Convention on Long Range Transboundary Air Pollution (CLRTAP) (http://www.unece.org/env/lrtap/). Both of these agreements have provisions for nominating new substances for international regulation, based on "risk profiles" compiled by parties to the agreement. In Annex D of the Stockholm Convention, it is specified that the objective of the risk profile is to provide information to determine whether a nominated substance “is likely, as a result of long-range transport, to lead to *significant adverse effects*, such that global action is warranted”. Similarly, paragraph 2 of the CLRTAP POPs protocol presents the elements of a technical review which include an evaluation of whether the proposed substance “is likely to have *adverse human health and/or environmental effects* as a result of its long-range transboundary atmospheric transport”. The term “adverse effects”, and the process to determine how likely they are, are not specifically defined in either protocol. The dominant legal interpretation of these statements has been that this assessment necessarily involves an analysis of the risks associated with the proposed substance, rather than just determining if the proposed substance is present in the environment. In other words, the evaluation requires determining whether adverse effects are likely based on measured or predicted levels in the environment and knowledge of the toxicity of the chemical at these levels.

Assessing the risk of adverse effects for humans and the environment is a challenging task that must draw upon all available scientific resources. However our review of the existing risk profiles for substances proposed for addition to the Stockholm Convention found that the only evidence used in conducting the exposure component of the assessment of likelihood of significant adverse effects was measured levels in the environment. Models have thus far not played a role in this part of the assessment process.

The objective of this publication is to motivate the use of models in the evaluation of risk of adverse effects under the Stockholm Convention and the UNECE CLRTAP. This is done by illustrating the ways that models have already been used to evaluate the fate and exposure of POPs, presenting the strategies for incorporating models in the assessment, and providing specific guidance.

THE VALUABLE ROLE OF MODELS IN ENVIRONMENTAL SCIENCES

In any environmental system that is complex and dynamic, measurements are rarely, if ever, sufficient as the sole basis for evaluating the behavior of a chemical substance in the system. There is simply not enough time, money, and equipment to collect and analyze a sufficient number of samples to accurately capture the complex relationships among emissions, the characteristics of the environment, and the exposure of humans and ecosystems. This applies to all environmental systems including air basins, lakes, rivers, multimedia systems, ecosystems, indoor environments, and organism pharmacokinetics. Models have a long history of helping to explain scientific phenomena and of predicting outcomes and behavior in settings where empirical observations are limited or not available (NRC, 2007). The use of models has resulted in great advances in scientific understanding and improvements in a wide array of endeavors.

The application of models in environmental science dates back to the late 19th century (NRC, 2007). In the area of transport modeling, Arrhenius’s climate model for assessing the greenhouse effect (Arrhenius, 1896) provided a remarkable level of sophistication and accuracy that illustrated the role of carbon dioxide in trapping heat in the earth’s atmosphere. His model was a seasonal, spatially-disaggregated climate model that relied on a numerical solution to a set of differential equations that represent the surface energy balance. In the middle of the 20th century the observations needed to confirm his model became available, in particular the confirmation of emissions data and the early signals of climate warming. This led to the collection of more measurements to confirm or refute the predictions of global warming and these measurements led in turn to more detailed and reliable models of the greenhouse effect. This is an early and continuing example of the nature and significance of melding models and measurements to build confidence in a scientific hypothesis—in this case the climate warming properties of carbon dioxide.

The complementary nature of models and measurements has also been exploited in the identification and classification of persistent organic pollutants (POPs). The first evidence for long-range transport of these substances came when measurements in animals and the environment of the Arctic revealed the presence of POPs that were never produced or used there. The lack of reliable emissions data led to a number of modeling efforts to explore hypotheses regarding the atmospheric transport and deposition of POPs in the Arctic. For example, Wania and Mackay (1995, 1999a) introduced multimedia global distribution models for persistent organic chemicals with a focus on transport and deposition to the Arctic. Other modelers developed evaluative models to assess global persistence and spatial range as end points in screening level assessments, for example Scheringer (1996, 1997). These models and their results provided key insight both to international agencies, such as the United Nations, and to scientists working independently to make measurements of POP concentrations and how they vary with latitude. These new measurements provided important feedback that made it possible to develop the next generation of models by merging results from both the first generation of models and the new measurements. In the case of POPs the integration of models and measurements offered more insight than either scientific tool used alone.

The US National Research Council (NRC) in its recent study on the use of models in regulation stated that the greatest value of models lies in their ability to synthesize understanding, for example of chemical fate processes, and to facilitate a deepening of that understanding. Furthermore, models have proven to be valuable in assisting decision making by stimulating intuition, illustrating an idea, summarizing data, providing an incentive for improving data quality, and formulating hypotheses for subsequent testing. The NRC correctly points out that although models have provided these valuable insights, they cannot make decisions. Moreover, they note that, while the demand for models has grown, the conceptualization of what a model is has shifted in recent years. In contrast to previous years, models are now viewed less as "truth-generating machines" and much more as tools designed to fulfill specific tasks and purposes (Beck et al. 1997). According to the NRC (2007), as tools, "models serve in the decision-making process as (1) succinctly encoded archives of contemporary knowledge; (2) interpreters of links between health and environmental harm from environmental releases to motivate the making of a regulatory decision or policy; (3) instruments of analysis and prediction to support the making of a decision or policy; (4) devices for communicating scientific notions to a scientifically lay audience; and (5) exploratory vehicles for discovery of our ignorance."

By their very nature, all models are simplifications and approximations of the real world and have inherent limitations. Similarly, measurements have many limitations in that they are always incomplete, sometimes inaccurate, frequently irrelevant to a given hypothesis, and often difficult to interpret. Consequently, an optimum strategy for improving the understanding of environmental fate and exposure of substances, including POPs, has been to rely on both models and measurements.

STRATEGIES FOR USING MODELS WHEN EVALUATING PBTs AND POPs

The goal of an exposure assessment for identifying Persistent, Bioaccumulative and Toxic chemicals (PBTs) is to establish the link between chemical emissions to the environment and exposure in organisms of concern and/or humans. To accomplish this goal, two models are generally needed. First, an environmental fate model is required to describe the fate of the chemical in the physical environment and to predict the concentrations in physical media such as air and water from the emissions. Second, a bioaccumulation model is needed to predict the resulting exposure (i.e., internal concentration in the organism) arising from these concentrations in the physical media (Fig. 1). These two models can either be separate or linked within a modeling package.

In the specific context of preparing a risk profile for a candidate POP, an additional goal is to predict chemical exposure in a remote region as a result of long-range transport. In this case, the model for estimating the long-range transport may be integrated into the physical environmental fate model or it may be a separate model calculation (Fig. 1). Although recently a combination of a global long-range transport model with a human food chain bioaccumulation model was used to identify chemical partitioning properties that result in high exposure/emission ratios in the remote Arctic (Czub et al., 2008), we are currently unaware of any widely available modeling tools which include long-range transport, environmental fate, and bioaccumulation in one modeling system. In the absence of a model to predict the amount of the chemical transported to the remote region of interest, the fraction of emissions transferred to the remote area (e.g., the Arctic) can be estimated using one of the metrics available in the literature

(Scheringer et al., 2000, Wania, 2003, 2006, MacLeod and Mackay, 2004). Once this estimate of the emissions to the remote region is obtained, a fate and bioaccumulation simulation can then be conducted for this region.

Irrespective of the specific models or goals of the modeling approach, we suggest that there are a variety of strategies for the use of exposure models in the evaluation of POPs, and indeed environmental contaminants in general. These strategies are complementary, but they can be applied individually, sequentially, or iteratively:

- Strategy #1: Groundtruthing: Model-based exposure predictions can be compared to existing monitoring data to 1) establish whether these monitoring data and the model's exposure predictions are reasonable, representative and consistent and 2) build confidence in the appropriateness of the model for the chemical under consideration, or discover areas where ignorance about important processes make the model inadequate.
- Strategy #2: Confronting Uncertainty: Sensitivity and uncertainty analysis can bound estimates of exposure, and identify the key information requirements for improving the model's ability to predict both POP-like characteristics and POP exposures.
- Strategy #3: Benchmarking: In the absence of quantitative emission information, a chemical's predicted exposure normalized to a standard emission rate can be compared with that of other substances, including known POPs.
- Strategy #4: Predicting: Models can be used to explicitly predict the exposure of target populations of organisms, including humans, which would be expected based on the known usage of the chemical. However, this is only advisable using a model for which confidence has been built by "Groundtruthing".

- Strategy #5: Forecasting: Models can be used to provide insight into the implications of existing time trend observations by predicting future trends in concentrations in remote regions.
- Strategy #6: Scenario Testing: In comparing risk management options, models can be invaluable in assessing the potential effectiveness of different measures.

Below, we provide information indicating how each of the strategies can be used to assess exposure to POPs, and contribute to the development of risk profiles.

Strategy #1: Groundtruthing by Comparing Model Results and Monitoring Data

Model results can be used to complement and expand the usefulness of monitoring data and other information used within the context of the risk profile. For example, model results can lend credibility:

- To monitoring data by addressing questions such as: Based on our understanding of chemical fate and bioaccumulation, is it reasonable that a chemical would be present in such quantities in such compartments/organisms?
- To physical chemical properties by addressing questions such as: Based on the observed concentrations in water and sediment, is it reasonable that the chemical is as persistent in sediment as reported?
- To emissions estimates by addressing questions such as: Based on the observed concentrations of the chemical in the major environmental reservoirs and our understanding of the chemical's environmental persistence, is it reasonable that the emissions are as high (or low) as has been estimated?

An important byproduct of comparing model results with monitoring data is the enhancement of model confidence. Since exposure models are only an approximation of the complex reality of the environment, it is essential to have confidence in their ability to predict exposure for the chemical of concern. This confidence is imparted by the physical and chemical principles on which the mechanistic underpinnings of the model are built, by the accumulated evidence from comparing model algorithms for specific processes with empirical observations, and by past experience in applying the models to other similar chemicals (see the case study below and the Appendix).

A fundamental problem that confronts models of open environmental systems is that the model may not fully capture all of the essential details of "reality" needed to accurately predict exposure for a specific scenario. For instance, it may not be possible to include in the fate model all of the vectors of environmental exposure to the endpoint due to limited knowledge or information. Comparing the model to monitoring data can help to discover deficiencies in the model, just as it can help to discover deficiencies in the monitoring data, physical chemical properties, and emissions estimates.

Strategy #2: Confronting Uncertainty

One of the advantages of using exposure models to quantitatively describe the emission source to body burden (i.e., exposure) relationship is that uncertainty and sensitivity analysis of the models can be conducted to identify the processes and parameters that contribute most to uncertainty in the assessment. The results of the uncertainty and/or sensitivity analysis can be especially valuable for improving the quality of the exposure prediction and the risk profile. For example, it can direct the efforts of the assessor to improving the estimates of these key processes and parameters. Furthermore, this information can enable the writing and reviewing of the risk profile to be focused on the most important processes and uncertainties affecting the exposure estimates.

Sensitivity analysis and uncertainty analysis, although closely related, provide different insights into the assessment. Sensitivity normally refers to the percentage change in an output parameter of interest for a small percentage change in a selected input parameter. Highly sensitive parameters are highly influential in determining the value of the output. Uncertainty refers to the range of possible values of a calculated output parameter that result from the range of possible values of inputs. Thus uncertainty provides information about the degree of confidence that can be placed in a given model result and sensitivity analysis identifies key input parameters that should be well characterized in order to reduce uncertainty in the assessment.

There are several possible methods that can be applied to assess uncertainty in model predictions. The most common method is Monte Carlo uncertainty analysis in which input parameters are assigned distributions of possible values that are randomly sampled to assemble a corresponding distribution of outputs. Information about sensitivity of the outputs to each input parameter can be obtained by rank correlation analysis of outputs against inputs for a large number of Monte Carlo realizations. An example application of these techniques is given in the case study.

Strategy #3: Benchmarking of Candidate POPs against Existing POPs

While the quantitative prediction of exposure (see Strategy #4 below) may be the ultimate goal of model-based fate and exposure assessments, in practice there are frequently serious obstacles to reaching this goal. A commonly encountered obstacle is the large uncertainties associated with estimates of historic and current emissions. These uncertainties are – as a rule – linearly translated by the model into uncertainty in the final exposure estimate.

One way to address the problem of uncertainty in emissions is to calculate an exposure metric that is normalized to emissions. An example of such a metric is the quantity of the chemical in an Inuit woman divided by the global emission of the chemical, i.e., the fraction of a unit emission of the chemical that accumulates in a single Inuit woman (Czub et al., 2008). Such an exposure metric provides a pseudo-intrinsic measure of exposure hazard that, for a given receptor, environment, and emission pattern and location, is solely governed by a chemical's properties and thus is independent of the magnitude of chemical emissions (Mackay et al. 2001).

The use of hypothetical unit emission rates also offers a transparent method to compare candidate POPs against existing POPs, in a process called benchmarking. If the environmental fate, transport and bioaccumulation properties of both the candidate POPs and reference POPs are captured in the model in a similar manner, benchmarking also overcomes the problem of inadequate accuracy in the predicted exposure. Although the model may not be able to accurately predict the exposure of the candidate POP, it can nevertheless give a reliable estimate of the fate and exposure of the candidate POP relative to other already identified POP chemicals. Exposure models are frequently very good at predicting the relative behavior of chemicals with similar properties. This can be exploited in chemical exposure assessment for POPs.

A benchmarking procedure was recommended by the OECD expert group charged with developing an approach for assessing whether candidate POPs fulfill the criteria of overall persistence and long-range transport potential (Klasmeier et al., 2006). They recommend that the pseudo-intrinsic chemical properties of overall persistence (Pov) and long-range transport potential (LRTP) for candidate POPs be compared with the Pov and LRTP values for a group of established POPs to determine whether the candidates are similar to established POPs. Using an analogous approach, one could assess whether the exposure to a candidate POP would be similar to the exposure to known POPs, given similar emission rates.

The benchmarking approach can and should also be applied in a risk assessment context. Since contaminant exposure is generally linear with respect to the chemical emissions (i.e., a 10-fold increase in emissions corresponds to a 10-fold increase in exposure), the exposure of a candidate POP relative to existing POPs can be estimated by multiplying the ratio of the pseudo-intrinsic exposure metric by the likely ratio of the emissions of the candidate POP to the known POP. If this is then multiplied by the relative toxicity (hazard) of the candidate POP and the known POP, one obtains an estimate of the relative risk.

$$\text{Relative Risk} = X_{\text{cand}}/X_{\text{known}} \times E_{\text{cand}}/E_{\text{known}} \times T_{\text{cand}}/T_{\text{known}} \qquad (1)$$

where X is the exposure metric (e.g., concentration in mother's milk per unit global emissions), E is global emissions, and T is the toxicity metric. This is a simple and transparent methodology to characterize the relative risk posed by a candidate POP at the screening level.

Strategy #4: Predicting Chemical Exposures from Emissions

By fully quantifying the source-receptor relationship, exposure models that combine chemical fate calculations in the physical environment with computations of food chain bioaccumulation can be used to estimate chemical exposure. In its most sophisticated form, such an assessment relies on well characterized information about emission rates, environmental characteristics, exposure pathways and receptor populations to predict time-variant exposure in a realistic manner. The ultimate goal is to estimate the actual concentrations of the chemical in the environment and in the ecological and human receptors. Whereas this ambition has been largely fulfilled for some well-studied contaminants, such as the polychlorinated biphenyls (Czub and McLachlan, 2004a), the risk profile will in most cases have to be developed using incomplete and limited information about emissions, inventories in the environment, exposure pathways and characteristics of the receptor population.

Strategy #5: Forecasting Exposure in the Future

Models can be especially useful to extrapolate emissions information, physical chemical property information, and monitoring data to forecast future exposure. For example, observations of increasing concentrations over time in remote regions may be of particular concern for the candidate chemical. Models can be used to forecast how much longer these concentrations would be expected to rise in response to various future emissions scenarios (Gouin and Wania, 2007) and thus help to prioritize management options.

One of the key motivations for regulating POPs is the concern that if a key aspect in the hazard assessment is overlooked, then because of the persistence, LRTP, and bioaccumulation properties of the chemical it will take an unacceptably long time to rectify any resulting problems. Simply put, the concentration in target organisms in remote regions will respond too slowly to a reduction in the emissions of the chemical, and damage could persist over very long periods. Given the salient importance of this question in the POP context, non-steady state modeling tools may be required as a component of the risk profile process to predict recovery times of contaminant levels in target organisms. A benchmarking procedure using a characteristic response time for contaminant levels in sentinel organisms in remote regions similar to that proposed for exposure could be a useful framework for classifying chemicals according to this fundamental POP characteristic.

Strategy #6: Scenario Testing of Alternative Risk Management Options

Although not of direct relevance to assembling the risk profile, we note that models can be very useful in the risk management stage of the POP evaluation procedure. The efficacy of different management strategies at reducing the exposure levels in human populations and environmental receptors can be evaluated by running exposure models with different scenarios, i.e., different levels of future emissions, or modified exposure pathways. Models can supply information on not only the magnitude of anticipated changes in exposure but also on the rapidity with which the changes will occur. Examples of scenario testing of different management strategies are provided by Thompson et al. (1999) for Lake Ontario, Canada, and by Davis and co-workers for the San Francisco Bay, USA (Davis, 2004, Conner et al. 2007).

CASE STUDY FOR THE 2006 AND 2007 CANDIDATE POPs

As an illustration of the application of models to calculate human exposure in support of the POP risk profiling process, a case study incorporating the first three of the strategies discussed above is provided here. In the case study, we consider compounds that have been nominated for addition to the Stockholm Convention in 2006 and 2007. First, we apply models to benchmark these candidate POPs against a selection of acknowledged POPs and non-POPs. Then, for one of the candidates, commercial pentabromodiphenyl ether, we present a more detailed analysis that includes emission estimates and comparisons of modeled data against concentrations measured in environmental and exposure media. For this purpose, we have selected one component of the commercial mixture, 2,2',4,4',5-BDE (PBDE-99) to represent the mixture. In these case studies we use the OECD Pov and LRTP Screening Tool (The Tool) (Wegmann et al. 2007) to model long-range atmospheric transport, and the Risk Assessment IDentification And Ranking (RAIDAR) model (Arnot et al. 2006, Arnot and Mackay 2008) to assess regional-scale fate, partitioning, degradation, food web bioaccumulation, far-field exposure, and resulting body burdens in humans.

Our case study considers two fate and exposure scenarios. The first scenario describes emissions to air and calculates the body burden in a representative human living in the source region. This scenario is a useful complement to PBT hazard assessments aimed at identifying substances that are of concern due to local or regional scale exposure of humans living in the source region. The second scenario describes emissions to air in a source region followed by long-range atmospheric transport to a remote region, and exposure of a representative human living in the remote region. This type of assessment provides information about the levels of exposure due to long-range transport, and is most relevant for assessing the need for international regulatory action, especially under the Stockholm Convention. The exposure information derived from either scenario can be combined with information about effect levels to provide a screening level risk assessment.

As discussed above, models can be applied to benchmark candidate substances against acknowledged POPs and non-POP substances. For our case study, we have selected a set of reference chemicals recommended by the OECD expert group on Pov and LRTP assessment that includes acknowledged POPs and non-POPs (Klasmeier et al. 2006). It is important to recognize that the role of the benchmark substances is to provide a comparative context for understanding the model results for the candidate substances. The model results for the benchmark substances should not be interpreted as defining "bright line" boundaries between POP-like and non-POP-like substances.

We collected physical-chemical property data and estimates of degradation half-lives in environmental compartments for the candidate POPs from the risk profile documents prepared for the Persistent Organic Pollutant Review Committee (POPRC 2006), from reports on persistence and long-range transport modeling of the substances (Scheringer et al. 2006, Wegmann et al. 2007), and from data compilations and QSPR models (Mackay et al. 2006, U.S. EPA 2007, Schenker et al. 2005, Arnot et al. 2005) (Table 1). In addition, we have included screening level biotransformation half-life estimates for fish, birds and mammals for all substances. Biotransformation in food webs and in humans has not been explicitly modeled in far-field exposure assessments until very recently. Therefore, for both scenarios considered here we present two sets of results. The first case assumes negligible biotransformation in fish, birds and mammals in the food chain (half-life; HL_N = 30,000 d), and the second case includes biotransformation half-lives as specified in Table 1. Details for the selection of degradation half-life estimates are provided in the Appendix at the end of the paper.

Benchmarking the POP Candidates against Acknowledged POPs and Non-POP Substances

This benchmarking exercise is based on results from two models. First, RAIDAR Ver. 2.0 (Arnot and Mackay 2008) is used to estimate the body burden of contaminant in a representative individual in an evaluative regional environment for a steady-state unit emission rate of 1 kg/h. The calculated body burden is an estimate for humans living in the source region receiving emissions to air. Second, the OECD Tool (Wegmann et al. 2007) is used to calculate the characteristic travel distance (CTD, km) of each substance in air. The CTD is an estimate of the distance at which the concentration of a chemical in a moving parcel of air that interacts with the surface falls to (1/e) or 37% of its initial value (Bennett et al. 1998). The potential for human exposure in a remote region is assessed using the CTD to estimate an effective emission rate into the remote region as a result of long-range transport in air from a source region 2500 km away. In this illustrative case study only atmospheric transport to the remote region is considered and not transport in oceans or river water. The estimated body burden in RAIDAR is directly proportional to the assumed emission rate, thus the body burden in the remote region is calculated by scaling the body burden in the source region by the fraction of the chemical that is transported to the remote region. For this illustrative example we use identical generic environmental conditions (e.g., temperature, surface coverage of water, soil and vegetation) and exposure pathways (e.g., dietary selection) to describe both the source and remote regions.

Figure 2 shows the calculated human body burden in the region of emission for a unit release rate of each of the candidate POP substances compared to benchmark substances representing acknowledged POPs and non-POPs. It is apparent from inspection of Figure 2 that the results for the non-POP benchmark chemicals are strongly dependent on whether or not biotransformation in the food web is considered in the model assessment. For example, when biotransformation in the food web is neglected, the modeled body burden of atrazine is comparable to body burdens for some of the POP benchmark substances; however, the atrazine body burden is considerably lower when biotransformation is considered. The estimated body burdens for *p*-cresol and biphenyl are also sensitive to the inclusion or exclusion of biotransformation in the food web. It is thus apparent that assessments neglecting biotransformation may be overly conservative for certain substances, and will reduce the effectiveness of model assessments used to identify those substances that have the greatest potential to cause high exposures in the human population.

The results when biotransformation is considered show a marked difference in calculated body burdens between the acknowledged POP and non-POP benchmark substances. All of the POP candidate substances lie within the range of calculated body burdens defined by the POP benchmark substances indicating that the POP candidates have similar human exposure potential in the source region as the acknowledged POP benchmark substances.

In such a benchmarking exercise it is important to remember that the benchmark substances do not define “bright-line” criteria, but are only useful for providing a context to interpret model results. In this particular case, the candidate POPs have been nominated for addition to the Stockholm Convention because of concern about their potential to have significant adverse effects on humans and the environment due to long-range transport to remote regions. Therefore the assessment of potential for exposure in the source region does not fully address concerns that motivated the nominations of these substances as POP candidates. Potential for long-range transport and exposure in a remote region is addressed in the following paragraphs.

Figure 3 shows the modeled fraction of emissions to air that reach a remote region 2500 km away, calculated from the CTD for emissions to air from The OECD Tool. This is a metric of the atmospheric LRTP of the substances. All of the acknowledged POP benchmark substances have high LRTP, and the effective emissions to air in the remote region are estimated to be less than a factor of 10 lower than in the source region. The same is true for all of the candidate POP substances except chlordecone, for which the effective emission rate to the remote region is 3% of the emission rate in the source region. Among the non-POP benchmarks, carbon tetrachloride has a very high LRTP as it is volatile and resistant to degradation in the atmosphere, and biphenyl is predicted to have potential for transport to the remote region that is comparable to the candidate POPs and the POP benchmark substances.

Figure 4 shows the calculated human body burdens in a remote region based on a unit emission in the source region. The data in Figure 4 are calculated as the product of the body burdens in the region of emission shown in Figure 2 and the efficiency of atmospheric transport to the remote region shown in Figure 3. The benchmarking exercise demonstrates that the majority of the candidate POP substances have calculated body burdens in the remote region that are comparable to those of the acknowledged POP benchmark substances, and these values are several orders of magnitude higher than any of the non-POP benchmarks. Thus our analysis supports the case that the candidate POPs may have potential to cause adverse effects in human populations as a result of long-range transport.

Among the candidate POPs, chlordecone has the lowest calculated body burden in the remote region. This is a consequence of relatively low efficiency of long-range atmospheric transport from the source region compared with other candidate POPs and the POP benchmark substances.

Among the non-POP benchmarks two factors can limit the body burden in the remote environment. Atrazine has a calculated body burden in the source region that is comparable to many of the POP benchmarks when biotransformation estimates are not included, but it has very low LRTP in air and exposures to higher trophic level organisms are mitigated by biotransformation in food webs. Thus the body burdens calculated in the remote region are low, particularly when biotransformation is included in the assessment. In contrast, carbon tetrachloride is very efficiently transported to the remote region; however, it has low potential for accumulation in aquatic and terrestrial food chains and has low calculated body burdens in both the region of emission and the remote region. Insights such as these into the important processes that control environmental and human exposure for each substance illustrate the potential added value of applying exposure assessment models as a complement to PBT and POPs assessment.

Combining Modeling with Monitoring Data

In this section PBDE-99 is used to illustrate how model results can be combined with monitoring data in PBT and POPs assessment. Models can play an important role by establishing that the monitoring data are reasonable, representative and consistent; by providing a means to extrapolate a data set to fill gaps in the measurements; and, by identifying which data gaps require the greatest attention. In turn, assessments that combine modeling with monitoring data can help to identify shortcomings in the modeling approach for the particular case under consideration and thus provide guidance for model improvement. In this illustrative case study we rely primarily on information that is summarized in the risk profile for commercial pentabromodiphenyl ethers adopted by the Persistent Organic Pollutant Review Committee (POPRC, 2006).

A practical obstacle when making direct comparisons between model estimates and monitoring data is making a representative estimate of the actual emission rate into the environment (Breivik et al. 2006). Emissions of PBDE-99 are dominated by volatilization from in-use products (POPRC, 2006). Palm et al. (2002) estimated a “worst case” emission rate of about 4.7 mg PBDE-99/(capita year) in industrialized countries. However emission estimates made in subsequent studies imply higher emissions than the estimate by Palm et al. Jones-Otazo et al. (2005) estimated emissions of 20 – 80 mg/(capita year) for PBDE-47 and PBDE-99 in Toronto, Canada. Denier van der Gon et al. (2007) estimated approximately 110 mg/(capita year) of commercial pentabromodiphenyl ether emission in Europe in the year 2000. The Persistent Organic Pollutant Review Committee (POPRC, 2006) estimated a median value of 820 tonnes/year for global emissions of commercial pentabromodiphenyl ether, which corresponds to 124 mg/(capita year) for a global population of 6.6 billion (ca. 2000). In a controlled experiment, Wilford et al. (2003) determined that 17% of the mass of commercial pentabromodiphenyl ether mixture that volatilized from treated foam was PBDE-99. Applying this factor to the emission estimates for commercial pentabromodiphenyl ether made by Denier van der Gon et al. and POPRC implies emissions of 18.7 and 21.1 mg PBDE-99/(capita year) respectively, where the first estimate applies to Europe, and the second to the entire global population. Assuming that 20% of the emissions estimated by Jones-Otazo et al. are PBDE-99 implies emissions of 4 – 16 mg PBDE-99/(capita year) in Toronto, Canada. Based on this information, we selected an emission rate of 15 mg PBDE-99/(capita year) as input to our modeling study. The RAIDAR evaluative model describes a regional environment of 100,000 km^2 with an assumed population of approximately 8,000,000 people. Thus, the estimated emission rate to the model region is 120 kg PBDE-99/year, or 13.7 g PBDE-99/hour.

A second complicating factor in comparing modeling and monitoring data is interpreting the model results in a way that allows meaningful comparison with monitoring data that may represent a different spatial and temporal scale (Armitage et al. 2007). The primary source of PBDE-99 monitoring data used in this comparison is from the United Kingdom over the period 2000 – 2004; however, other monitoring data from different regions are also included, particularly for fish, wildlife and humans.

Figure 5 compares modeled concentrations with monitoring data for abiotic environmental media. The modeled concentrations in these compartments are within the ranges of values detected in the environment from different global regions (Hites 2004, POPRC 2006, SFEI 2008, Lorber 2008). The modeled concentrations in air are in very good agreement with the median estimate from monitoring data. The monitoring data for water are limited and the lower modeled estimate may be attributable to our assumption that all emissions are to air, when it is likely there are some releases to water and land. Further, the monitoring data do not reflect the occurrence of non-detects that may lower the range of values depicted in the figure, and this may be of particular relevance for soils and sediments. Another possible explanation for the underestimation of soil concentrations by the model is underestimation of the biodegradation half-life of PBDE-99 in soils used as input to the model.

Figure 6 compares modeled concentrations of PBDE-99 in ecological receptors, agricultural products, and humans with monitoring data from various global regions (Huwe et al. 2002, Ohta et al. 2002, Hites 2004, FSAI 2004, POPRC 2006, Darnerud et al. 2006, SFEI 2008, Binelli et al. 2008, Lorber 2008). The modeled concentrations are generally within a factor of three to five of the median measured values, with the notable exception of certain root vegetables (e.g., potatoes, carrots).

In light of the assumptions used in this case study we view the agreement between the model estimates and the monitoring data as exceptionally good. Other studies that have compared modeling results with monitoring data have not generally resulted in such close agreement (see the Appendix for details).

Sensitivity and Uncertainty Analysis

Sensitivity and uncertainty analysis of the model can provide guidance for identifying process descriptions and input parameters that dictate the overall uncertainty in modeled exposure. We have conducted a sensitivity and uncertainty analysis of the modeled relationship between emissions to air and human body burden of PBDE-99. The sensitivity and contribution to uncertainty of model inputs describing the chemical (partitioning and half-live values listed in Table 1) on model output (total human body burden) are illustrated for PBDE-99 in Figure 7. We have characterized uncertainties in all chemical property input parameters by assuming possible values are log-normally distributed and using confidence factors (*Cf*) to quantify the degree of uncertainty, where 95% of possible values are expected to lie between the median value divided by *Cf* and the median value multiplied by *Cf* (MacLeod et al. 2002a). Higher *Cf* values thus reflect greater uncertainty and variability in the parameter. The partitioning properties were assigned *Cf*s of 3.2 and primary transformation half-lives in air, fish, and birds/mammals were assigned *Cf*s of 5.6 and the half-lives in water, soil and sediment were assigned *Cf*s of 10.

The biotransformation half-lives in fish and birds/mammals are the most sensitive selected chemical property parameters and are most influential in determining the modeled human body burden. The human body burden estimates are expected to be sensitive to biotransformation rate estimates since other chemical elimination processes are very low for hydrophobic non-ionic chemicals and biotransformation rates thus largely influence the biological residence time. This analysis suggests that improving knowledge for these chemical parameters may reduce uncertainty in modeled human body burden of PBDE-99, recognizing that biotransformation rates are expected to be highly variable in a range of species.

The present uncertainty analysis did not include the uncertainty in model parameters describing the environment and the food webs and uncertainty in the estimated emission rate. Uncertainty in the emission rate is often a dominant source of uncertainty in exposure assessments based on models. For example, it is reasonable to assign a *Cf* of 10 to the estimated emission rate implying 95% confidence that the actual emission rate of PBDE-99 to the atmosphere is between 12 and 1,200 kg/y in the regional environment. Under this assumption, the uncertainty analysis indicates that the estimated emission rate is the most sensitive parameter (S = 1), and has the greatest contribution to variance in calculated human body burden (65% of the total). Thus it is clear that accurate estimation of emission rates is a prerequisite to obtaining accurate estimates of exposures and risks in a model-based assessment.

Findings from the Case Study

In summary, this simple case study illustrated several of the contributions that modeling can make to the development of a risk profile in the POP review process:

a) The benchmarking exercise provided clear evidence that PBDE-99 and the other POP candidate substances are – from an exposure perspective – similar to acknowledged POPs. The ratios of emissions: tissue levels in humans are comparable to that of known POPs, providing evidence that the POP candidates fulfill the persistence, long-range transport, and bioaccumulation POP criteria.

b) The comparison of monitoring data and model predictions showed very good agreement for most of the matrices, including – most importantly for the risk profile – humans and top predators. This builds confidence in the ability of the model to predict the behavior of PBDE-99 and lends further credibility to the results of the benchmarking exercise.

c) The comparison of monitoring data and modeling predictions revealed an inconsistency between calculated concentration in soils and observations of levels in the environment. This inconsistency may be due to overestimation of the rate at which PBDE-99 is degraded in soils. This provides important information to the review process, as it indicates that the residence time of PBDE-99 in the environment may be much longer than otherwise would have been expected. This may lengthen the recovery time of the environment to reductions in emissions, adding to the "POP concern" for this chemical.

d) The sensitivity/uncertainty analysis revealed that the biotransformation half lives were the largest source of chemical property uncertainty in the estimation of human exposure in the source regions, thus directing the team preparing / evaluating the risk profile to return to and critically review the evidence for these parameters.

This simple case study has incorporated the first three of the strategies for employing models proposed above. The good agreement between the monitoring data and the model predictions indicates that Strategy #4 could also be pursued for this chemical, for example by employing the model to directly predict human tissue levels in the context of a risk assessment. At the risk management stage of the POP review process, this risk assessment could be repeated for different emissions scenarios to evaluate e.g., if there are some uses of PBDE-99 that can be permitted (Strategy #6). Although the Strategy #5, predicting exposure in the future, was not utilized in this example analysis, the identification of the possible inconsistency in the biodegradation rate constants in soil and sediment already provides important information for future extension of this evaluation. In summary, the case study clearly illustrates that models are available that allow quantitative tracking of the emissions-to-exposure relationship for humans and ecological receptors and that they can contribute to the development of a risk profile in many ways.

GUIDANCE ON CHOOSING AND USING MODELING TOOLS WHEN EVALUATING POPs

As the previous discussion and the case study have illustrated, using fate and exposure models in developing the risk profile for PBTs and POPs would be very beneficial. A model selection decision is required because there is no “universal” model that is appropriate for assessing all aspects of chemical behavior in the environment. Depending on the properties of the chemical, the properties of the environment, and the question that needs to be addressed, different models with different levels of complexity may be appropriate. The model selection decision must have a logical basis and adequate documentation, particularly with regard to those reviewing the assessment.

The complexity of the environment makes simplification imperative in exposure assessment models. As features and capabilities are added to a model, making it more complex, the cumulative effect on model performance needs to be evaluated carefully. Increasing the complexity of models without adequate consideration of the impact of this complexity can decrease the potential for a model to be transparent and accessible to users and reviewers. It is often preferable to omit complexities that do not improve model performance substantially. Even more problematic are models that accrue substantial uncertainties because they contain more parameters than can be estimated or calibrated with available observations. Thus, the best model is the simplest model which nevertheless captures the key processes that have a major influence on exposure.

Two characteristics of POPs are their high degree of persistence and their susceptibility to long-range transport. These properties both contribute to a leveling of spatial gradients in the environment. While chemicals which are rapidly degraded in the environment or which do not move from their point of emission tend to show strong spatial gradients around the emissions sources, this propensity is reduced for POPs. As a consequence, box models, which assume uniform concentrations of the chemical in a given environmental medium in a given region, are often appropriate for modeling POPs (Wania and Mackay, 1999b). Secondly, within a given environmental medium (e.g., water, air), it is appropriate to assume equilibrium partitioning. Given that POPs are also by definition bioaccumulative and hence have low rates of metabolism, equilibrium can also be assumed within organisms. Hence, in selecting modeling tools for POP exposure assessment, one should have few qualms about choosing models that make these simplifications. Indeed, most POP models are based on these assumptions (Wania and Mackay, 1999b).

Criteria to Consider in Choosing Models

When choosing a model or models for the fate and exposure assessment, a primary criterion to consider should be the similarity of the chemical to be evaluated to those that were used to develop empirical relationships coded into the model. Most exposure assessment models incorporate empirical relationships to express certain chemical fate processes. Examples are regressions that relate laboratory- or QSPR-derived physical-chemical properties (such as K_{OW}) to distribution coefficients between environmentally relevant phases (such as K_{OC}) or to kinetic terms (such as those related to uptake/excretion in biota). A consequence of the use of such expressions in models is that they are strictly only applicable to substances for which these relationships hold. Very rarely are such relationships applicable to all chemicals of interest. They are most likely to be valid for substances that are similar to those that were used in their derivation. For example, because the relationships between K_{OC} and K_{OW} were derived using neutral organic chemicals, they may not be particularly effective at describing the sorption behavior of charged chemical species. Similarly, relationships to describe bioaccumulation based on hydrophobicity (e.g., K_{OW}) will not apply to PFOA and PFOS, which bioaccumulate according to different mechanisms.

Another related criterion that should be considered in the choice of model is whether the fate processes included in the model are applicable to the chemical of interest. Models only tend to include processes that are relevant for the chemicals for which they were designed. For example, a model developed for the assessment of exposure to persistent hydrophobic chemicals may ignore exposure pathways that are of no concern for such chemicals, such as inhalation exposure or exposure through drinking water, and models designed for persistent chemicals may ignore metabolic elimination. However these processes may be important for the chemical of interest.

One should also assess whether the model is valid for the region of interest. For example, a model that has been developed for a sub-tropical region may not be appropriate for a polar region. The model should capture both the central features of the physical environment (e.g., ratio of land to water, climate) and the biological environment (e.g., food web structure, exposure endpoints) in an appropriate manner. Some of the available models can be re-parameterized to better reflect the study area of interest.

A further concern can be whether the model has as output the kind of exposure endpoint desired. Some models calculate external exposure, while other models can predict internal exposure metrics such as tissue concentrations or body burden. The choice can depend on the information available for and/or desires for the significant adverse effects assessment.

Similarly, the ability of the model to handle the mode and timing of emission of a chemical may, in some cases, influence model selection. If, for instance, the emissions are highly seasonal and there is evidence that this strongly influences the fate (e.g., due to seasonality in climatic conditions), it may be appropriate to choose a model which allows this aspect of the emissions to be included.

Some models calculate chemical fate and exposure assuming that the chemical is at steady state, while others are non-steady state models. This can be an important criterion when the objective of the assessment includes comparing model predictions with monitoring data for POPs. Steady state models assume that all properties in the environment including emissions are constant over time, while non-steady state models allow variability in chemical emissions and, frequently, environmental parameters as well. Steady state models are simpler, and they are generally easier to use, two factors which speak for their selection. However, due to their high persistence in the environment, POPs are seldom close to steady state. Under conditions of constant emissions it can take decades or centuries until the concentrations in the major storage reservoirs in the environment stabilize. Steady state models would therefore greatly over-predict the concentrations in these reservoirs for a candidate POP which has been in use for a much shorter period. Furthermore, in reality emissions of candidate POPs have seldom been constant over long periods of time, and hence the fundamental assumption behind a steady state model is violated. As a consequence, non-steady state models should be preferred when comparing model predictions with monitoring data for POPs.

Depending on the focus and objectives of the assessment, another consideration in choosing a model may be the inability of most existing exposure assessment models to directly assess exposure to products of degradation reactions in the environment or metabolic conversions within an organism. Only recently have multimedia models been developed and used that directly quantify exposure to secondary pollutants (Schenker et al. 2008a, b; Cahill et al. 2003).

The model selection criteria mentioned above can all be subsumed under the umbrella of maximizing confidence in the model. This should be the primary guiding principle in model selection. Confidence is grounded first on the validity of the underlying theoretical concepts; aspects of this were addressed above. Model confidence can be further heightened, as mentioned previously, by conducting evaluation exercises where the results of the model are compared with reality. Consequently, one criterion for model selection is that the model should have been applied successfully to similar chemicals before. There are many studies in the literature in which model results have been compared against monitored concentrations. Some of these confidence building studies are referenced in the annex.

Using multiple models has the advantage of providing insights into how sensitive results are to different modeling choices and levels of complexity. When multiple models are run and compared to appropriate monitoring data, the assessor also gains information about how much trust can be put in results from any one model. However, this approach involves substantially more effort and time than selecting one model at the beginning of the assessment process.

In practical terms, when choosing a model or models there is unlikely to be an ideal model; therefore, trade-offs must be considered including (adopted from NRC 2007):

- *The need to get the correct answer* – This refers to the need to choose a model capable of generating accurate as well as consistent and reproducible predictions of current or future fate and exposure.
- *The need to get the correct answer for the correct reason* – This refers to the need to choose a model that reproduces the spatial and temporal detail of the system's workings. For example, simple process and empirical models can be "trained" to mimic a system of interest based on an initial set of observations; however, if the model fails to capture all the important system processes, the model could fail to behave correctly for an observation outside the limited range of "training" observations.
- *Transparency* – This refers to the need to choose a model based on the transparency of the essential workings of the model that can be understood by peer reviewers as well as informed but scientifically lay stakeholders and members of the public. This need will tend to drive models toward less detail. Transparency can also be enhanced by ensuring that reviewers, stakeholders and the public comprehend the procedures followed in developing, evaluating, and applying a model, even if they do not fully understand the basic science behind the models.

Specific characteristics to evaluate these three trade-offs are given in Table 4.1 of NRC (2007).

Practical Considerations in Using Models

Exposure assessment models require information on a chemical's partitioning properties, transformation kinetics, and emissions to the environment. That information may not be available at all, or, more likely, may only be available in part but with considerable uncertainty. This may often constitute the major obstacle to the use of exposure assessment models in the preparation of risk profiles. Some chemical properties, such as partitioning properties, environmental degradation half lives and even metabolism rate constants, may be estimated from molecular structure using a variety of QSPRs or by analogy with related substances, but again such information may be highly uncertain.

Sensitivity analyses, as discussed above, may indicate whether such uncertainty can be tolerated or has a major impact on the results of the exposure assessment. For example, Czub and McLachlan (2004b) noted that within fairly large ranges of the chemical partitioning space, the Environmental Bioaccumulation Potential (EBAP) of various organisms including humans is relatively insensitive to the magnitude of the chemical's partitioning properties, which suggests that even very approximate knowledge of those properties may be acceptable. On the other hand, metabolism rate constants are often the decisive factor controlling levels in higher organisms and thus would need to be known with reasonable accuracy for a credible exposure assessment.

If emission information is missing, some limited assessment is still possible. In particular, as discussed above, the properties of a substance can be compared with those of benchmark chemicals. In other words, even though it is not possible to make statements on the risk associated with the use of a substance in the absence of quantitative emission information, it should still be possible to establish whether a compound has POP-like characteristics.

CONCLUSIONS AND RECOMMENDATIONS

Models have proven very useful in understanding the fate of many chemicals including PBT and POPs chemicals. Thus, not surprisingly, they can be used in a variety of ways to make valuable contributions to the development of risk profiles. An assessor can have confidence in using existing models to inform and improve the risk profiles that are currently developed for the Stockholm and LRTAP protocols. The choice of the model to use and the confidence in the predictions made can be informed by the given criteria and by appropriate documentation of how the model or models chosen meet these criteria.

To foster the use of models in this regulatory context, we propose the development of a model benchmarking tool for human and wildlife exposure in remote regions along the lines of the assessment done in this paper. This tool would be analogous to the benchmarking tool for persistence and LRT developed for stage 1 of the POP review process. Such a tool would allow a non-expert to do a model-based exposure assessment with confidence, and would contribute to lowering the barriers to exploiting the potential of models.

Furthermore, we suggest the development of a second model benchmarking tool for the recovery time of remote environments following the cessation of chemical emissions. Such a tool would provide transparent, readily comprehensible information that addresses a key motivation for our concern about POPs, namely that if we misclassify a chemical as safe due to oversight or insufficient understanding and it becomes a risk, then will it be possible to reduce that risk in a reasonable period of time.

Finally, we would like to emphasize the importance of the further development of existing models and the exploration of new modeling concepts to address the identified weaknesses and limitations of existing models. This should be coupled with concerted model evaluation exercises to further build model confidence and identify as yet unknown weaknesses in the models. Only in this way will it be possible to expand the range of applicability of the models such that they can be applied to the diverse chemicals now coming under scrutiny as potential POPs or PBT chemicals.

APPENDIX: DO THE MODELS WORK? EXAMPLES OF MODEL EVALUATIONS

An essential prerequisite for using models is confidence in their ability to approximate the reality that the model is intended to simulate. In the context of multimedia fate and bioaccumulation modeling of organic contaminants, this confidence is garnered from a variety of sources.

One source of confidence is the validity of the fundamental physical and chemical principles that form the basis for the model algorithms. Thus, models that are largely constructed of mechanistically based descriptions of the fate and bioaccumulation processes are generally considered to be more robust and more reliable than models that employ largely non-mechanistic process descriptions, e.g., correlations.

A second source of confidence is the agreement between the predictions of the model and empirical observations for specific processes. Most often the algorithms used to describe a process in a multimedia fate model or a bioaccumulation model have been derived from a large set of empirical observations for that particular process. The model's description of this process is thus associated with a high degree of confidence as long as the model is applied in a manner that does not depart far from the conditions under which the empirical data were created or the range of validity of the fundamental physical and chemical processes.

Perhaps the most convincing source of confidence is the agreement between the predictions of the entire model (e.g., from emissions to endpoint) versus monitoring data. Such evaluations are more complex as they involve several process descriptions (although it is important to note that typically only a small sub-set of the process descriptions in a model is tested in any given simulation, namely those that have the dominant influence on the fate and bioaccumulation of the given chemical in the given situation). Full model evaluations are also typically more difficult to conduct as the empirical data are seldom consistent with regards to space and time, the choice of model parameterization is difficult, and key input data such as emissions are often lacking. As a result, evaluation exercises of this kind are seldom conducted. Note that, paradoxically, although a full emissions-to-endpoint simulation may seem to be the most important form of confidence building for models, the uncertainty in the model predictions, and hence in any conclusions about good agreement with empirical observations, is typically greatest in this kind of model evaluation due to the difficulties mentioned above. Note that the opposite is also true: for an uncertain model evaluation, poor agreement between model predictions and empirical observations may not allow any conclusions to be drawn about deficits in either the model or the empirical observations. The uncertainties are frequently greatest in the predicted concentrations, as these are directly linked to many uncertain factors such as the emission rates. It can be more instructive to evaluate models by comparing other metrics such as the ratios of concentrations in connected environmental media (e.g., air and water), time trends in concentrations, or spatial gradients in concentrations (Bakker et al. 2003, Lee et al. 2004, Armitage et al. 2007, Daly et al. 2007).

In the context of employing models for assembling the risk profile, it is essential that the models are already furnished with a high degree of confidence. While this confidence should, if possible, be heightened while assembling the risk profile by comparing model predictions with empirical data for the chemical of interest (as outlined in the paper), it should already be high in the models chosen. Due to the multitude of theoretical considerations and process descriptions in the model, it is not feasible to summarize the confidence building evidence at the theoretical or process levels. Suffice it to say that the evidence is considerable, and that most of the models use similar algorithms for the process descriptions as a broad consensus has been reached on their validity. In the following we will restrict ourselves to summarizing model evaluation exercises in which “multiple process” modeling outputs were compared with monitoring data. Examples for modeling chemical fate at the global scale, chemical fate at the regional scale, and bioaccumulation are given. All of the examples address identified or candidate POPs.

Chemical Fate at the Global Scale

A global model with 10 different climate zones has been used to simulate the fate of α-HCH (Wania et al., 1999). On the basis of historical global emissions estimates covering the years 1947-1997 and the physical chemical properties of the chemical, the concentrations in the atmosphere and seawater over time and space were calculated. The predictions were within an order of magnitude of measured concentrations of this chemical, correctly reproducing the spatial trends in the world’s oceans as well as the temporal trends observed in both the atmosphere and in seawater. Of particular note was the models ability to correctly simulate the consequences of the strong reduction in usage during the 1980s, namely the rapid decline of the concentrations in the atmosphere and in seawater with the exception of the Arctic Ocean, where both the model and monitoring data indicated that the concentrations in seawater remained high.

The performance of a similar zonally averaged global model to reproduce the global distribution of dichlorodiphenyltrichloroethane (DDT), and its degradation products dichlorodiphenyldichloroethylene (DDE), and dichlorodiphenyldichloroethane (DDD) based on a realistic DDT emission scenario covering the period from 1940 to 2005 was evaluated by

Schenker et al. (2008a). A qualitative and quantitative comparison of model-predicted concentrations in air and soil with measurements suggested good agreement, in particular with respect to time trends.

The evaluation of BETR-Global, a model which offers a much higher spatial resolution (288 multimedia regions on a 15° grid) than the two models discussed in the preceding paragraphs and which relies on real climate data, focused on the ability to reproduce 479 individual observations of atmospheric PCB concentrations at 11 long-term monitoring stations in the Northern Hemisphere (MacLeod et al., 2005). Using historical emission estimates for seven individual PCB congeners over a 70 year period it was found that the variability in measured air concentrations that was not explained by the model is less than 1 order of magnitude for 96 % of the data.

Chemical Fate at the Regional Scale

Models that have been evaluated in terms of their capability to predict environmental fate of POP-like contaminants on a continental to regional scale range from fairly complex, continental scale models (Macleod et al., 2002b) to dynamic regional models with moderate spatial and temporal resolution (Breivik and Wania, 2002, MacLeod et al., 2007) to very simple steady-state box models with no spatial resolution (Macleod and Mackay, 1999, Kawamoto et al., 2001, Wiberg et al., 2007).

Breivik and Wania (2002) evaluated the ability of a non-steady-state mass balance model of the Baltic Sea environment for its ability to simulate the fate of α- and γ-hexachlorocyclohexane isomers from 1970 to 2000. Agreement was found with respect to absolute concentration levels in a variety of environmental media, and with respect to geographical and temporal trends. Levels in air, seawater, marine sediments, and needles were predicted well within an order of magnitude, often even within a factor of 2. Model and observations indicated relatively uniform seawater concentrations of both HCH isomers across the Baltic Sea, as well as similar declining time trends of α-HCH in air, seawater, freshwater fish, and marine fish.

Faced with a lack of reliable emission data, Lee et al. (2004) evaluated the ability of the spatially unresolved, dynamic multimedia fate model POPsME to describe the environmental behavior of 12 polycyclic aromatic hydrocarbons in the region of Seoul, Korea, by comparing ratios of concentrations (using soil as the reference medium) rather than absolute concentration values. Predictions were found to generally agree within an order of magnitude with monitoring data for aerosol, water, sediment and foliage. The performance of the relatively simple, steady-state CalTOX model to predict concentrations of six tetra- through octa-chlorinated dioxin and furan congeners in media relevant for human exposure (meat, milk, fish, egg) was evaluated by Wiberg et al. (2007). Also not able to rely on actual emission estimates, this study used generic scenarios, in which emission rates were tuned to yield agreement between calculated air and soil concentrations with average levels measured at background sites in southern Sweden. Modeled concentrations of chlorinated dioxin and furan congeners in soil, vegetation, surface water, eggs, dairy products and meat were generally found to be within a factor of 4 of observed values. Modeled concentrations in fish were underestimated by the default model algorithms that only consider bioconcentration, but were brought into agreement by estimating bioaccumulation through the food web.

Bioaccumulation

A model for hydrophobic organic chemical bioaccumulation in aquatic food webs was evaluated on the basis of 1,019 measured data points (35 species, 64 chemicals) from three different freshwater ecosystems (Arnot and Gobas, 2004). The model predicts chemical concentrations, and bioconcentration and bioaccumulation factors (BAFs) on the basis of information on chemical properties, chemical concentrations in water and sediment, and the characteristics of the organisms in the foodweb. The model evaluation showed that 60% and 95% of the model predicted bioaccumulation factors (BAFs) for aquatic invertebrates were within a factor of 2 and 10 of the observed BAFs, respectively. For fish, 60% and 98% of the model predicted BAFs were within a factor of 2 and 10 of the observed BAFs, respectively.

Czub and McLachlan (2004a) tested the ability of a model of human food chain accumulation from air, water, and soil via marine and agricultural food chains, to reproduce polychlorinated biphenyl (PCB) concentrations in fish, milk, beef, and human tissue measured in southern Sweden. Using historical scenarios of concentrations in air, water, and soil, and dynamic and mechanistic descriptions of all relevant processes, the resulting model predictions agreed well with the measurements.

Table A-1. Selected values and various source estimates for primary degradation half-life (HL; days) in water. Half-life values in soil were assumed to be 1.5x the water estimate, and values in sediment were assumed to be 6x the water estimate.

CASRN	Chemical name	HL in water (d)	Source 1	Source 2	Source 3
118741	Hexachlorobenzene (HCB)	1000	365	676	2292
25569806	PCB 28	300	360	72	229
32598100	PCB 101	1200	1200	246	2292
35065271	PCB 180	2200	2200	873	2292
92524	Biphenyl	15	15	14	7
106445	*p*-cresol	5	1	14	1
1912249	Atrazine	50	40	143	N/A
56235	Carbon tetrachloride	150	250	118	71
319846	α-hexachlorocyclohexane	440	360	237	708
58899	γ-hexachlorocyclohexane	400	25	237	708
319857	β-hexachlorocyclohexane	900	1825	237	708
608935	Pentachlorobenzene	500	365	355	708
N/A	Short chain chlorinated paraffins (SCCP)[1]	400	365	745	N/A
32536520	Octabromodiphenyl ethers	1800	600	4235	N/A
32534819	2,2',4,4',5-pentabromodiphenyl ether (PBDE 99)	850	850	472	N/A

CASRN	Chemical name	HL in water (d)	Source 1	Source 2	Source 3
36355018	Hexabromobiphenyl congeners	1800	600	847	N/A
143500	Chlordecone	900	730	219491	N/A

[1] SMILES notation used for SCCP: ClC(C(Cl)C(Cl)C(Cl)C(Cl)CC(C)Cl)C(C)Cl

Source 1: POPRC, 2006, Scheringer et al., 2006, Wegmann et al., 2007

Source 2: U.S. EPA 2007 EPI suite estimates calibrated to empirical estimates as described in Arnot et al., 2005

Source 3: Mackay et al., 2006

Table A-2. Selected values and various source estimates for primary degradation half-life (HL; days) in air.

CASRN	Chemical name	HL in air (d)	Source 1	Source 2	Source 3
118741	Hexachlorobenzene (HCB)	650	N/A	650	708.3
25569806	PCB 28	6	N/A	4	7.1
32598100	PCB 101	20	N/A	14	70.8
35065271	PCB 180	80	N/A	65	229.2
92524	Biphenyl	3	3	2	2.3
106445	*p*-cresol	0.3	0.3	0.3	0.2
1912249	Atrazine	0.4	0.4	0.4	0.2
56235	Carbon tetrachloride	900	20000	1000	708.3
319846	α-hexachlorocyclohexane	50	115	20	N/A
58899	γ-hexachlorocyclohexane	50	96	20	7.1
319857	β-hexachlorocyclohexane	50	10	20	N/A
608935	Pentachlorobenzene	230	275	200	229.2
N/A	Short chain chlorinated paraffins (SCCP)[1]	5	4	6	N/A
32536520	Octabromodiphenyl ethers	80	76	95	N/A
32534819	2,2',4,4',5-pentabromodiphenyl ether (PBDE 99)	20	N/A	20	N/A
36355018	Hexabromobiphenyl congeners	40	N/A	40	N/A

CASRN	Chemical name	HL in air (d)	Source 1	Source 2	Source 3
143500	Chlordecone	900	N/A	1000	N/A

[1] SMILES notation used for SCCP: ClC(C(Cl)C(Cl)C(Cl)C(Cl)CC(C)Cl)C(C)Cl

Source 1: POPRC, 2006, Scheringer et al., 2006, Wegmann et al., 2007

Source 2: U.S. EPA 2007

Source 3: Mackay et al., 2006

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LIST OF FIGURES

Fig. 1 Modeling steps involved in the exposure assessment of P and B substances and POPs.

Fig. 2 Modeled human body burden (mmol/kg wet weight) per unit emission to air (1 kg/hr) in the source region for benchmark POPs and non-POPs, and candidate POP substances assuming (A) no biotransformation in the food web, and (B) biotransformation as indicated in Table 1.

Fig. 3 Modeled fraction of emissions to air that reach a remote region 2500 km away by long-range atmospheric transport for benchmark POPs and non-POPs, and candidate POP substances.

Fig. 4 Modeled human body burden (mmol/kg wet weight) per unit emission to air in a remote region 2500 km from the source region for benchmark POPs and non-POPs, and candidate POP substances assuming (A) no biotransformation in the food web, and (B) biotransformation as indicated in Table 1.

Fig. 5 Comparison of model estimates (×) with monitoring data (O) for concentrations of PBDE-99 in bulk physical environmental compartments. Point estimates are median values and error bars approximate the range of detectable values.

Fig. 6 A comparison of model estimates (×) with monitoring data (O) for PBDE-99 concentrations in various biological compartments and humans. Point estimates are median values and error bars approximate the range of detectable values. wwt: wet weight, lwt: lipid weight.

Fig. 7 Sensitivity (*S*; blue) and contribution to variance (*CV*; red) of model input parameters (I_j; Table 1) on modeled source region human body burden (*HBB*) of PBDE-99 where $S_{I_j} = \dfrac{\delta HBB / HBB}{\delta I_j / I_j}$ and $CV_j = \dfrac{(\ln Cf_{I_j})^2 S_{I_j}^2}{\sum_{k=1}^{n} (\ln Cf_{I_k})^2 S_{I_k}^2}$ (MacLeod et al. 2002); $t_{1/2}$ bio – primary biotransformation half-life; $t_{1/2}$ deg – primary degradation half-life; K_{OW} – octanol-water partition coefficient; K_{AW} – air-water partition coefficient;

Table 1: Physical chemical properties of candidate POPs and benchmark chemicals at 25°C. Biotransformation half-lives (HL_N) in biota are listed normalized to 1 kg body size and scaled to mass (M_i; kg) specific values (HL_i) for different species in the model as $HL_i = HL_N \times (M_i/1)^{-0.25}$. Unless otherwise noted estimates for fish are from a database (Arnot et al., 2008) or a model (Arnot 2008) and HL values for higher order vertebrates are assumed ~1/3 of fish HL values.

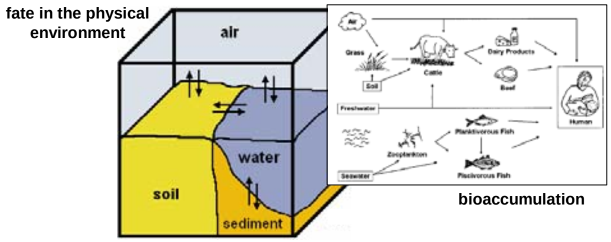
Status	**Substance name**	**log K_{OW}**	**log K_{AW}**	**log K_{OA}**	**Primary transformation half-life (d) in:**					
					Air	**Water**	**Soil**	**Sediment**	**Fish**	**Avian / Mammals**
POP	Hexachlorobenzene (HCB)	5.50	-1.52	7.02	650	1000	1500	9000	860	290
POP	PCB 28	5.66	-1.91	7.57	6	300	450	2700	190	8.3[a]
POP	PCB 101	6.33	-2.01	8.34	20	1200	1800	10800	370	44 [a]
POP	PCB 180	7.16	-2.48	9.64	80	2200	3300	19800	1100	29000 [a]
NonPOP	Biphenyl	4.06	-1.96	6.02	3	15	22.5	135	5.2	0.2 [a]
NonPOP	*p*-cresol	1.97	-4.26	6.23	0.3	5	7.5	45	0.35	0.2
NonPOP	Atrazine	2.73	-6.84	9.57	0.4	50	75	450	0.3	0.2
NonPOP	Carbon tetrachloride	2.83	0.19	2.64	900	150	225	1350	0.2	0.2
Candidate	α-hexachlorocyclohexane	3.94	-3.53	7.47	50	440	660	3960	55	20
Candidate	γ-hexachlorocyclohexane	3.72	-4.05	7.77	50	400	600	3600	120	40
Candidate	β-hexachlorocyclohexane	3.78	-4.33	8.11	50	900	1350	8100	90	30

Status	**Substance name**	**log K_{OW}**	**log K_{AW}**	**log K_{OA}**	**Primary transformation half-life (d) in:**					
					Air	**Water**	**Soil**	**Sediment**	**Fish**	**Avian / Mammals**
Candidate	Pentachlorobenzene	5.00	-1.47	6.47	230	500	750	4500	240	80
Candidate	Short chain chlorinated paraffins	6.20	-2.40	8.60	5	400	600	3600	55 [b]	20
Candidate	Octabromodiphenyl ethers	7.90	-4.50	13.61	80	1800	2700	16200	730	120 [c]
Candidate	PentaBDE 99	6.76	-3.67	11.26	20	850	1275	7650	285	95
Candidate	Hexabromobiphenyl congeners	6.90	-4.62	11.52	40	1800	2700	16200	1440	480
Candidate	Chlordecone	5.00	-6.69	11.69	900	900	1350	8100	42	20

[a] Brown, 1994, [b] Fisk et al., 2000, [c] Thuresson et al., 2006.

Fig. 1

Exposure assessment for P and B substances



Exposure assessment for POPs (P, B, and LRT)

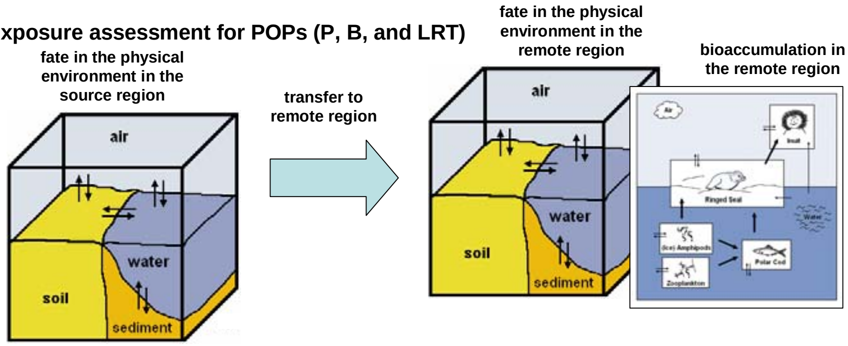


Fig. 2

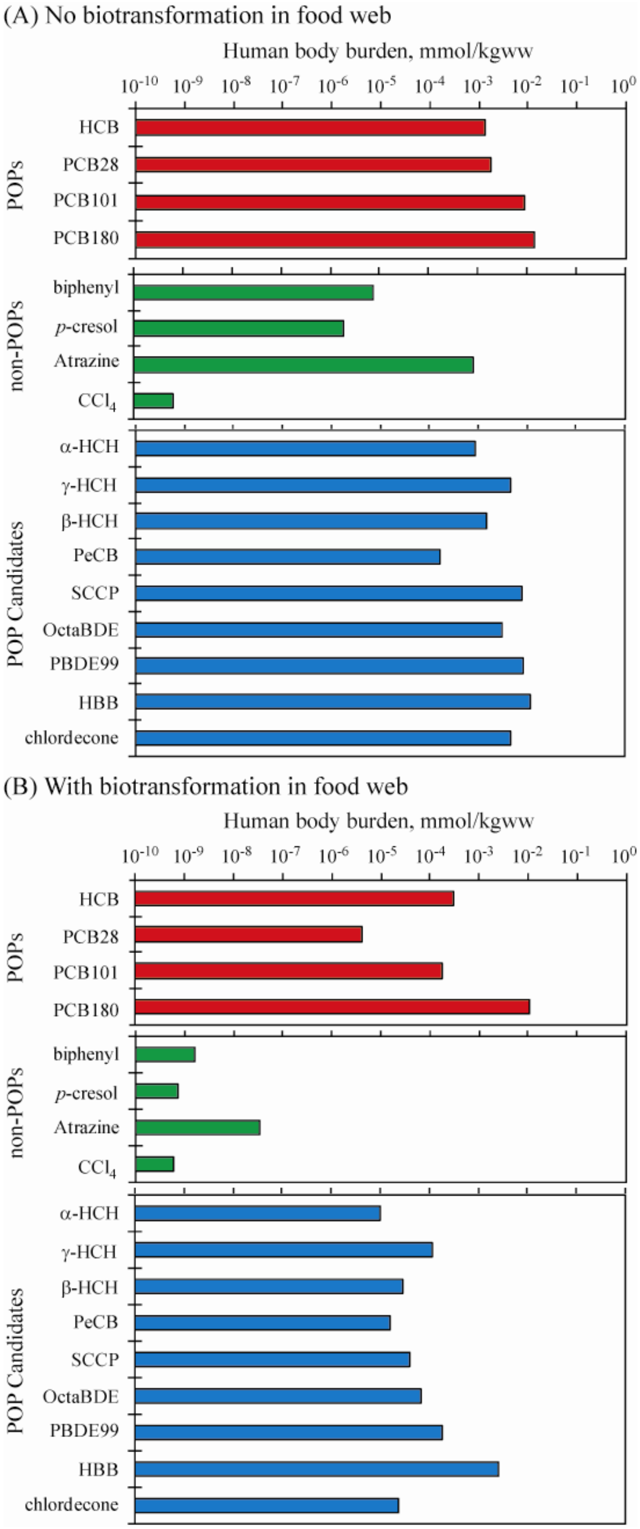
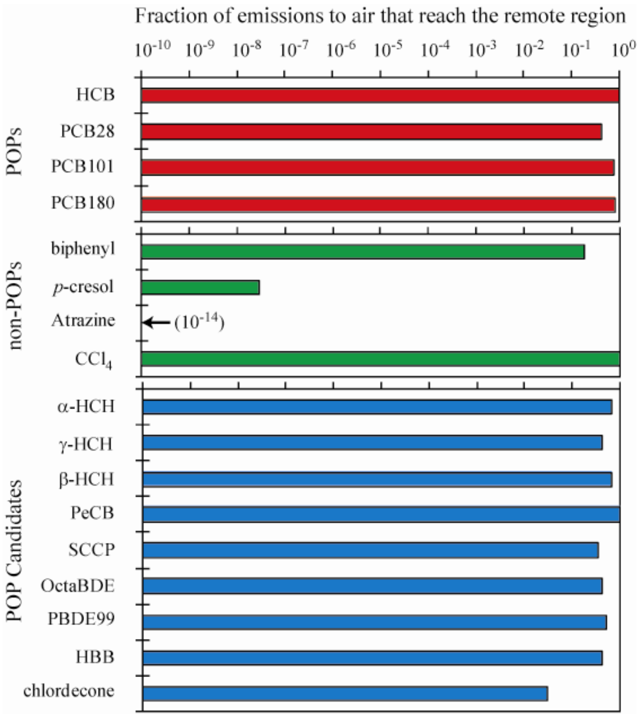

(A) No biotransformation in food web
Human body burden, mmol/kgww
10^{-10} 10^{-9} 10^{-8} 10^{-7} 10^{-6} 10^{-5} 10^{-4} 10^{-3} 10^{-2} 10^{-1} 10^{0}
POPs
HCB
PCB28
PCB101
PCB180
non-POPs
biphenyl
p-cresol
Atrazine
CCl_4
POP Candidates
α-HCH
γ-HCH
β-HCH
PeCB
SCCP
OctaBDE
PBDE99
HBB
chlordecone
(B) With biotransformation in food web
Human body burden, mmol/kgww
10^{-10} 10^{-9} 10^{-8} 10^{-7} 10^{-6} 10^{-5} 10^{-4} 10^{-3} 10^{-2} 10^{-1} 10^{0}
POPs
HCB
PCB28
PCB101
PCB180
non-POPs
biphenyl
p-cresol
Atrazine
CCl_4
POP Candidates
α-HCH
γ-HCH
β-HCH
PeCB
SCCP
OctaBDE
PBDE99
HBB
chlordecone

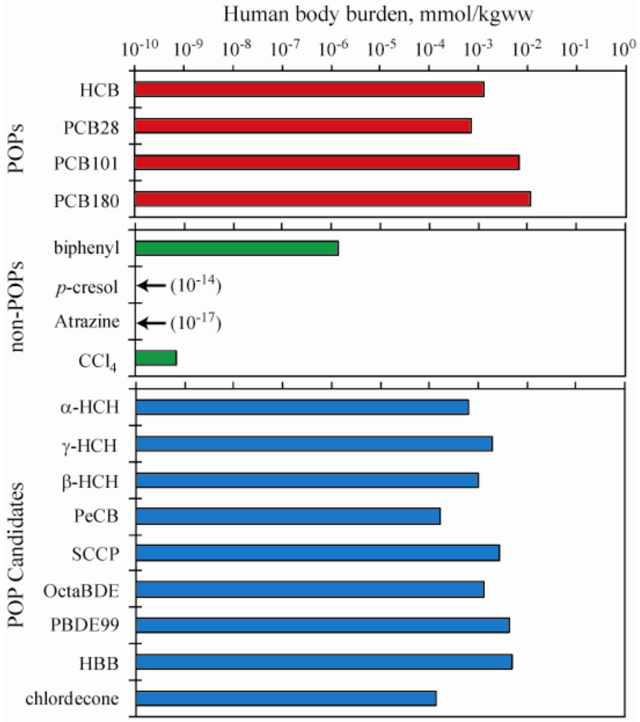
Fig. 3



Fraction of emissions to air that reach the remote region
10^{-10} 10^{-9} 10^{-8} 10^{-7} 10^{-6} 10^{-5} 10^{-4} 10^{-3} 10^{-2} 10^{-1} 10^{0}
POPs
HCB
PCB28
PCB101
PCB180
non-POPs
biphenyl
p-cresol
Atrazine
(10^{-14})
CCl_4
POP Candidates
α-HCH
γ-HCH
β-HCH
PeCB
SCCP
OctaBDE
PBDE99
HBB
chlordecone

Fig. 4

(A) No biotransformation in food web



(B) With biotransformation in food web

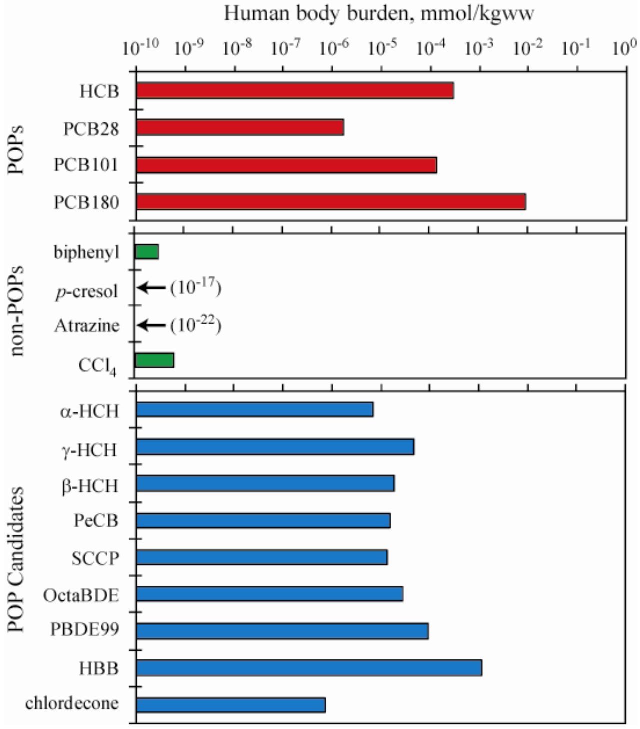
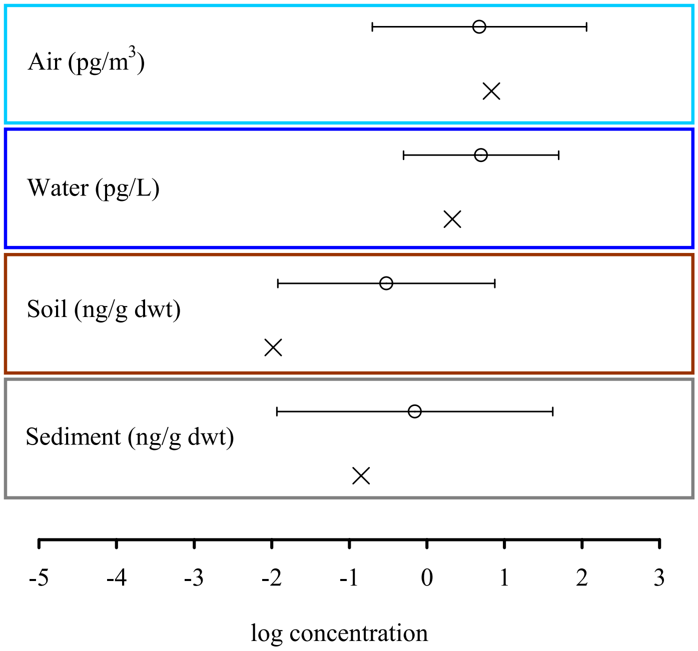
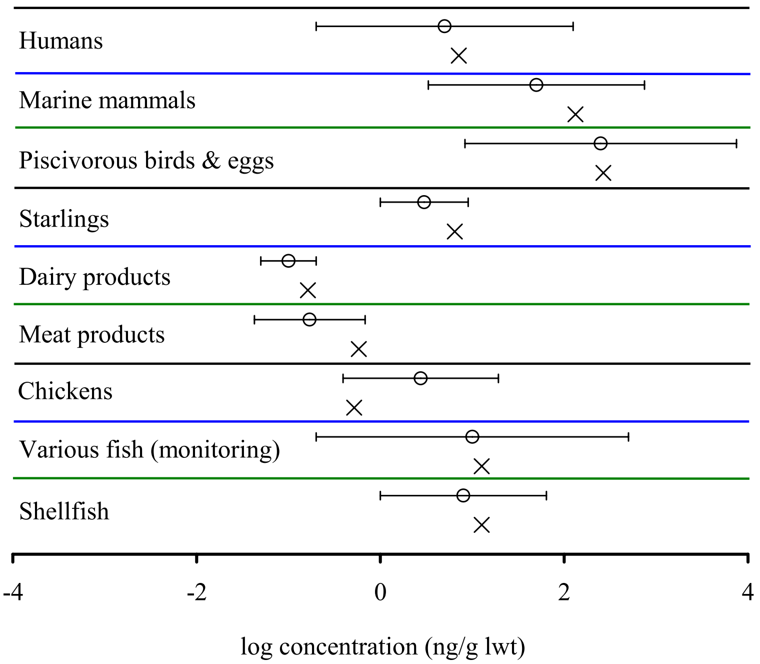


Fig. 5



Air (pg/m^3)
Water (pg/L)
Soil (ng/g dwt)
Sediment (ng/g dwt)
-5
-4
-3
-2
-1
0
1
2
3
log concentration

Fig. 6


Humans
Marine mammals
Piscivorous birds & eggs
Starlings
Dairy products
Meat products
Chickens
Various fish (monitoring)
Shellfish
-4
-2
0
2
4
log concentration (ng/g lwt)

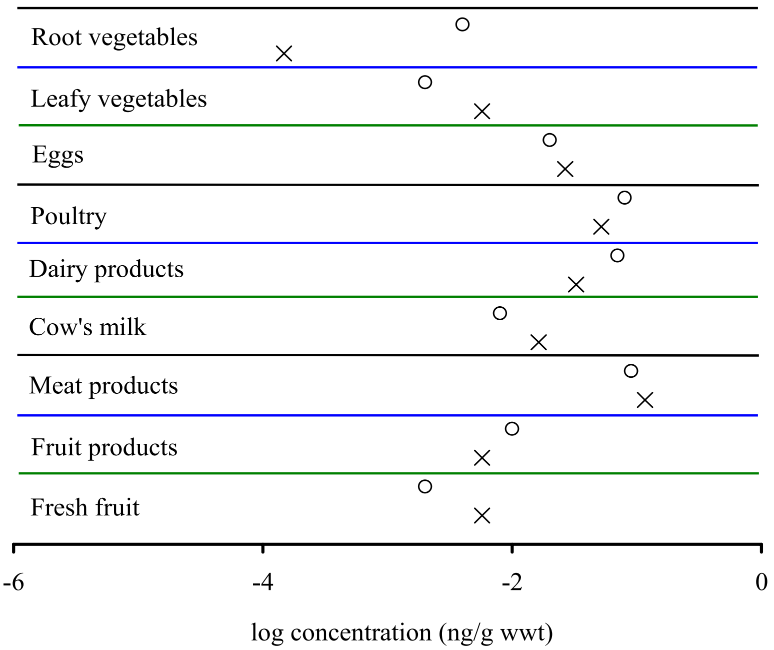
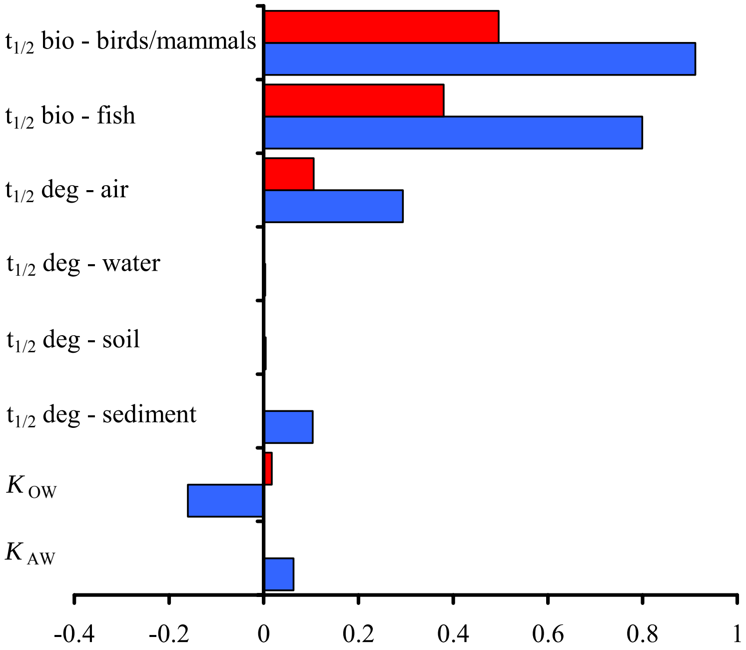

Root vegetables
Leafy vegetables
Eggs
Poultry
Dairy products
Cow's milk
Meat products
Fruit products
Fresh fruit
-6
-4
-2
0
log concentration (ng/g wwt)

Fig. 7



$t_{1/2}$ bio - birds/mammals
$t_{1/2}$ bio - fish
$t_{1/2}$ deg - air
$t_{1/2}$ deg - water
$t_{1/2}$ deg - soil
$t_{1/2}$ deg - sediment
K_{OW}
K_{AW}
-0.4
-0.2
0
0.2
0.4
0.6
0.8
1