Introduction to Special Series: Science-Based Guidance and Framework for the Evaluation and Identification of PBTs and POPs

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ABSTRACT

There is a growing sense of urgency among scientists and environmental policy-makers concerning the need for improving the scientific foundation supporting international regulations for identifying and evaluating persistent, bioaccumulative, and toxic (PBT) substances and persistent organic pollutants (POPs) in the environment. The current national and international regulations define PBTs and POPs in terms of fairly strict criteria that are based on the state of the science in the late 1970s and early 1980s. Since then, an evolution in the state of the science has produced new insights into PBT substances and an array of new methods to identify PBT chemicals. The development of regulatory criteria has not kept up with the rapid development in environmental chemistry and toxicology, and as a result, scientists often find themselves in the situation where guidance on PBT and POPs criteria is limited and, in some respects, out of date. With this background, a Society of Environmental Toxicology and Chemistry (SETAC) Pellston Workshop brought together experts from academia, government, and industry to reach consensus on the significance of advancements in our understanding of the behavior and potential impact of POPs and PBTs in the environment, the current understanding of the state of the science, as well as recommendations for policy-makers to improve and coordinate national and international regulations on this issue. The workshop builds on the outcome of a previous Pellston workshop, held in 1998, which focused on the evaluation of persistence and long-range transport of organic chemicals in the environment, and is linked to other recent Pellston workshops, among them the Tissue Residue Approach for Toxicity Assessment workshop held in 2007. The results of this workshop are conveyed in a series of 9 articles, published in this issue of *Integrated Environmental Assessment and Management*, and describe the coordination of science, regulation, and management needed to more effectively achieve a common goal of managing chemicals on our planet.

Keywords: Persistent organic pollutants Persistent, bioaccumulative, and toxic substances Risk assessment Long-range transport Significant adverse effects

INTRODUCTION

Several national regulations and regional or global conventions aim to identify and prioritize hazardous substances, including the Canadian Environmental Protection Act (CEPA), the European Union (EU), Existing Chemicals and Registration Evaluation Authorization of Chemicals (REACH) programs, the US Toxic Substances Control Act (TSCA) and the Toxics Release Inventory (TRI) under the Emergency Planning and Community Right to Know Act (EPCRA), the United Nations Economic Commission for Europe (UNECE) Convention on Long-Range Transboundary Air Pollution (LRTAP), and the United Nations Environment Programme (UNEP) Stockholm Convention on persistent organic pollutants (POPs). The criteria for evaluating persistent, bioaccumulative, and toxic (PBT) characteristics of substances under the various regulations are not harmonized but show large similarities.

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Regulations focusing on PBT chemicals and POPs are generally supplementary to existing regulations covering other chemicals. Their aim is to identify substances that may cause unexpected problems, such as those that persist and bioaccumulate and that may ultimately lead to adverse effects in organisms, particularly in remote areas where the substances are not directly emitted or used.

The current regulations define candidate PBT substances and POPs in terms of fairly strict criteria that are based on the state of the science established in the late 1970s and early 1980s. During most of the past 2 decades, the evolution in environmental and analytical chemistry, computational chemistry, information technology, and environmental toxicology has produced new insights into the persistence, bioaccumulation, and toxicity of chemical substances and an array of new methods to identify PBT chemicals. The development of regulatory criteria has not kept up with the rapid development in environmental chemistry and toxicology. As a result, businesses, regulators, and academics find themselves in situations where guidance on PBT substances and POPs criteria is available but often too limited and sometimes out of date. These limitations have produced some major challenges. One key challenge is the interpretation of substance information in the form in which it is usually provided in assessment documents with respect to PBT criteria as they are formulated in the various regulations. Very often, these do not match. Another challenge is to identify PBT chemicals and POPs at an early stage, sometimes, when information is still limited. Equally challenging is the need for accuracy in the process of identification: False-negatives may cause environmental problems when impacts are discovered at a late stage, whereas false-positives may cause significant business and societal consequences and may unduly deny society beneficial products. Overall it is of key importance that current legislation is applied effectively, taking advantage of the current state of the science.

WORKSHOP PURPOSE AND GOALS

To foster the advancement of a sound scientific foundation for identifying and evaluating PBT chemicals and POPs, an international workshop, sponsored by the Society of Environmental Toxicology and Chemistry (SETAC), was held in Pensacola, FL, USA, on 28–31 January 2008, to address scientific issues related to persistence, long-range transport, bioaccumulation, environmental toxicity, and the potential for significant adverse effects. The workshop had broad, tripartite participation from academia, government, and industry.

The specific objectives of the workshop were to discuss, reach consensus, and develop guidance on how to evaluate substances that may fulfill PBT substance or POP criteria using scientific information, such as experimental data, monitoring data, and computer models. The PBT and POP criteria are intended here in the broadest sense, including criteria defined in regulations around the world, as well as recommendations for new criteria. Workshop participants, representing broad international perspectives and recognized expertise in environmental chemistry, toxicology, multimedia modeling, and risk assessment, addressed the information required to provide a weight of evidence for substance evaluation under these criteria. After thorough discussions of each criterion and an evaluation of several case studies, the participants derived a framework with detailed guidance and recommendations on how to interpret substance-specific scientific information related to such PBT substance and POP criteria.

From the intensive science and regulatory policy deliberations that occurred during the meeting, nine technical documents were prepared for publication as a special series in the peer-reviewed journal *Integrated Environmental Assessment and Management* that convey the key elements of the new state of the science, the evolution of scientific understanding, and the challenges for future worldwide regulation of PBT chemicals and POPs. Each publication contributes to shaping a new framework for future coordinated environmental action.

Building on the results of a previous Pellston workshop, Boethling et al. (2009) address recent advances in the evaluation of the persistence of organic compounds in environmental media in terms of their single-medium degradation half-lives. Scheringer et al. (2009) discuss how information on partitioning and degradation can be used in conjunction with multimedia models to derive overall persistence and long-range transport potentials. Because of recent advances in the state of the science, a series of 3 articles address methods for the evaluation of bioaccumulation potential. Nichols et al. (2009) discuss the importance of adsorption, distribution, metabolism, and elimination processes and describe current work on the development of in vitro techniques. Weisbrod et al. (2009) present methods for evaluating bioaccumulation potential using in vivo laboratory and field studies. Gobas et al. (2009) revisit the criteria used in POP and PBT assessments and discuss differences in assessing bioaccumulation potentials in air- and water-breathing animals. The assessment of exposure is presented in a series of articles. Swackhamer et al. (2009) discuss the use of measurement data in evaluating exposure of humans and wildlife to POP substances and PBTs, and Cowan-Ellsberry et al. (2009) present ways that fate and exposure models can be used to improve and inform the development of risk profiles. Solomon et al. (2009) describe the use of ecotoxicity information for screening and classification of adverse effects of compounds. In the final document, van Wijk et al. (2009) present an integrated approach to PBT substance and POP prioritization and risk assessment.

CONCLUSIONS FOR THE IDENTIFICATION AND ASSESSMENT OF PBT AND POP SUBSTANCES

Many of the regulatory programs for the identification and assessment of PBT and POP substances consist of an initial priority-setting phase, followed by a more in-depth phase assessing the properties of prioritized substances and their potential for adverse effects. The ultimate basis for decisions about whether a substance is a PBT or POP, and whether risk management decisions are required, will depend on the goal and mandate of the initiative. For example, under the Stockholm Convention, decisions about potential POPs are based on "whether the chemical is likely, as a result of its long-range environmental transport, to lead to significant adverse human health and/or environmental effects, such that global action is warranted." The existing frameworks for evaluating POP chemicals and PBTs provide adequate flexibility to introduce additional, new, and emerging scientific evidence into the processes.

In assessing any of the properties associated with potential PBT chemicals or POPs (persistence, bioaccumulation, toxicity, long-range transport [LRT], significant adverse effects [SAE]), a range of approaches, including the use of empirically derived and model-derived information, can be considered and applied as appropriate. In so doing, both quantitative and qualitative lines of evidence can be used, but the reporting of results should recognize and communicate uncertainties associated with both of these. Although this workshop concentrated on scientific issues, it is important to note that views of the public and other stakeholders, plus legislation in force in different national jurisdictions will also influence the way in which PBT chemicals and POPs are evaluated, as will the particular requirements of those commissioning the evaluation. For example, there is a fundamental difference in the methods used to rank and prioritize chemicals for PBT or POP properties when compared with detailed PBT or POP assessment of chemicals that have already been prioritized. In the former case, well-defined prioritization criteria are used, at first, to filter out substances that are likely neither PBT substances nor POPs or to identify substances with potential for being PBT chemicals or POPs (e.g., Canadian Domestic Substances List Categorization, US New Chemicals PBT modeling, and EU PBT work group). In this first, priority-setting phase, rapid and efficient approaches should be used and, generally, will be developed to minimize the probability of false-negative results. Substances that are identified as priorities or as potential PBT or POP substances by this process need to be assessed in more detail in a second assessment phase by collating empirical and other robust data. The use of more specific models, consideration of data for analogous chemicals, and weight-of-evidence approaches, are recommended for the assessment phase.

Although many of the approaches and methods discussed at this workshop are most appropriate for application in the assessment phase of this framework, there was some discussion of approaches for the rapid prioritization for persistence, bioaccumulation, toxicity, and LRT through the use of QSARs and software programs, such as the Organisation for Economic Co-operation and Development (OECD) Toolbox or the OECD Long-Range Transport Tool. It should be noted that Annex D of the Stockholm Convention on POPs discusses "screening criteria," which partly overlap with the approaches proposed for the priority-setting phase of this framework. However, the Stockholm Convention screening criteria also provide for consideration of empirical data from experimental and monitoring studies, which generally might better apply in the assessment phase of the proposed framework.

Several conclusions from the workshop are relevant for the screening or priority-setting phase of substance identification. Reliable data from empirical studies should carry more weight in any assessment than the results from predictive tools or estimates. However, empirical data may be unavailable for many substances, so reliance on modeling is usually inevitable during priority setting. When using predictive tools (e.g., QSARs), the advantages and disadvantages of predictive approaches need to be understood by the users, which includes consideration of the domain of applicability (boundary conditions), so that application in assessment regimes is informed.

In current legislation, persistence is often assessed against criteria for single-media half-lives for the most relevant environmental compartments. However, it is important to note that uncertainty ranges for estimates of chemical half-life based on QSARs and degradation studies may vary by a factor of 5 to 10. Further, some structure–activity approaches can overlook important features of chemicals that undergo redistribution in a multimedia environment. Chemicals should, therefore, also be assessed with respect to their overall environmental persistence (P_{ov}) in an evaluative, multimedia, regional, or global environment. Tools, such as the OECD P_{ov} and LRTP Screening Tool, are available for performing this type of evaluation. For volatile and semivolatile compounds, atmospheric transport is usually the primary mode for conveying persistent substances to remote areas. The UNEP and UNECE criterion of a half-life in air of >2 d is an appropriate threshold for prioritizing these compounds.

In the screening phase, bioconcentration and bioaccumulation potentials are often assessed by examining the partitioning characteristics of the substance. Non-ionizable, nonpolar organic chemicals with a log $K_{ow} < 4$ do not normally biomagnify in aquatic food webs via enrichment in fat tissues, and there is no evidence that these substances exhibit bioconcentration factors (BCFs) >5000. In terrestrial food webs, with air-breathing organisms, chemicals with a log $K_{oa} < 5$ are not expected to biomagnify. Further, if molecules of a substance are larger than 1.5 nm, they are not likely to exceed a BCF of 5000. However, this observation is context specific; no size threshold can be defined for the ability to biomagnify through dietary uptake.

When toxicological data are limited, a variety of approaches can be used to assess a chemical, including the use of SARs (e.g., OECD Toolbox) and consideration of the mode of toxic action. Various QSARs have been developed and tested for a variety of chemical and organism classes. Furthermore, understanding the mode of action of a chemical enables a reasonable extrapolation of potential sensitivity and effect responses across taxonomically diverse groups of organisms.

Other conclusions from the workshop address the use of more detailed tools and empirical approaches in the assessment phase of substance evaluation. For the evaluation of persistence, studies of the environmental fate of a chemical should be conducted under relevant environmental conditions with respect to temperature, pH, substance concentrations, etc. It is important to understand the mechanisms by which degradation or distribution of the parent material or intermediate degradation products occurs. No single half-life value can adequately describe degradation in the environment or any environmental compartment. Typically, where multiple degradation studies have been conducted, there is a range of observed half-lives, all of which might be considered when degradation in the relevant compartment is assessed. In such cases, it is not appropriate to use the slowest or most conservative half-life; instead, care should be taken when such data are compiled. Partitioning properties should be checked for internal consistency, and outliers should be identified and not taken into consideration. The results of higher-tier biodegradation (simulation) studies can also be difficult to interpret because of the different mechanisms involved in removal and distribution of the parent compound. One critical issue for sediments and soils is whether residues are bound in a way that might reduce their bioavailability. Another critical issue for water–sediment simulation studies is the unrealistic ratio between water and sediment in the test vessels compared with that in natural water bodies.

The assessment of bioaccumulation potential can be improved substantially by consideration of the adsorption, distribution, metabolism, and elimination (ADME) of the substance. Methods for estimating these properties from in vitro studies are developing rapidly. The mechanistic nature of more recent in silico models makes them more transparent and interpretable and affords the opportunity to incorporate in vitro–derived ADME information. According to recent findings, the most relevant bioaccumulation criterion is the trophic magnification factor (TMF), and the most conclusive evidence to demonstrate that a chemical substance biomagnifies is a TMF >1. The TMF is derived from a correlation between appropriately normalized chemical concentration in biota and trophic position. It is crucial for the characterization of TMF that both aquatic and terrestrial food webs are considered. Such consideration is important because chemicals can exhibit fundamentally different TMFs in aquatic and terrestrial food webs because of differences in the bioaccumulation mechanisms between water- and air-breathing organisms. However, a high BCF is also a strong indicator for a high bioaccumulation potential of a chemical, including secondary poisoning effects in food webs.

The recommended matrix for monitoring and assessing human exposure to POPs is blood or its components, such as serum or plasma. Human breast milk may also be used in some jurisdictions. Diet-based or tissue-based approaches are direct, accurate, and site-specific methods for assessing the risks to top predators from secondary poisoning by PBT chemicals and POPs. The method uses diet to estimate the ingestion of POPs by predators. The advantage of this approach is that the only requirements for exposure assessment are samples of the predator's diet, realistic estimates of dietary composition, ingestion rates, and measured concentrations in the prey. Even more direct is the tissue-based approach, which uses measurements of PBT or POP concentrations in the tissues of receptor species (top predators) to determine internal exposure directly and compares this exposure concentration to tissue-based effect concentrations ("toxicity threshold values") to determine risk. The advantage of this approach is that estimates of PBT or POP transfer to top predators from lower trophic levels, which often have high uncertainty, are not required. In practice, availability of dose–response and internal exposure–response relationships is limited for PBT substances and POPs in top predators, so dose–response relationships for surrogate species must often be used. Ideally, these data from surrogate species are supported by field biomarker data on PBT or POP exposure and biological responses in the receptor species of interest.

In developing guidance for global environmental monitoring of legacy POPs, UNEP Guidance for a Global Monitoring Programme recommends focusing on air, human milk, or blood, as well as widely measured biota (mussels, marine mammals, bird eggs, and fish) as the most appropriate types of samples because of past extensive studies. This is also the most appropriate approach for new candidate POPs. The overall recommendation for assessing exposure in humans and top predators is to use or obtain direct measurements of the compound of concern from a significantly and uniquely exposed population (indigenous populations or remote populations), as well as data demonstrating biomagnification and time trends, if possible.

Detection of a chemical in a remote area is not evidence, per se, of persistence and long-range transport potential. Detection in remote environments needs to be assessed in the context of amounts and patterns of usage and emission and the sensitivity of the analytical methods. Among the recommendations of the workshop is the need for development of a consensus modeling tool for benchmarking a PBT–POPs exposure-to-emissions metric. This model or modeling system should 1) have the ability to couple models describing environmental fate, bioaccumulation, and LRT potential; 2) incorporate the ability to include metabolic loss and transformation of the chemical at all trophic levels; 3) allow for incorporation of new partitioning mechanisms, such as those observed for ionizable chemicals; and 4) include the ability to model non–steady-state conditions to allow time-trend concerns to be scientifically addressed in a risk profile. Such model development should build on the consensus approach used in developing and gaining acceptance for the current LRT models.

Risk characterization, defined in existing risk assessment frameworks and paradigms as an integration of exposure and effects assessments, is a useful model in assessing PBT chemicals and in evaluating the potential for significant adverse effects resulting from long-range transport in POPs assessments. Although risk profiles or assessments of PBT substances or POPs may not necessarily be fully quantitative risk assessments, inclusion of information on risks and uncertainties is desirable at the assessment phase, notably in helping producers, importers, and users of chemicals or regulatory authorities (such as the Stockholm Convention POP Review Committee, the Conference of the Parties, or national authorities) to set priorities and make decisions. Lack of scientific certainty about currently available approaches and tools (such as models) should not prevent their use in providing an integrated risk characterization that considers the weight of multiple lines of evidence and associated uncertainties.

Ultimately, the goal of the workshop was to provide timely input into national and international assessments of PBT chemicals and POPs. We believe that the 9 articles in this special issue provide a scientific consensus on tools and approaches and an excellent framework for future national and international assessments of chemicals regarding their persistence, bioaccumulation, environmental toxicity, long-range transport, and potential for significant adverse effects. In addition to this special issue, the Executive Summary is available on the SETAC Website (http://www.setac.org/node/265), and the workshop results have been communicated to the scientific community and to policy makers.

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