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The Role of Bioaccumulation in Environmental Risk Assessment: The Aquatic Environment and Related Food Webs

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SUMMARY

In this report the assumptions and equations used to determine bioconcentration and bioaccumulation of substances are reviewed and a possible approach for the integration of these processes into a risk assessment is discussed. The approach has been evaluated with the use of different bioaccumulation models for several representative substances with different properties and use patterns.

A distinction is made between bioconcentration and bioaccumulation. Bioconcentration is defined as the net result of the uptake, distribution, and elimination of a substance in an organism due to water-borne exposure, whereas bioaccumulation includes all routes of exposure (i.e. air, water, soil, food). Biomagnification is defined as accumulation and transfer of substances via the food web. The report describes the critical mechanisms underlying these processes with a brief description of some of their implications of on environmental exposure and effects. It also addresses methods for predicting and determining the potential of substances to bioconcentrate or bioaccumulate.

It was concluded that bioaccumulation of a substance into an organism is not an adverse effect or hazard in itself. Bioconcentration and bioaccumulation may lead to an increase in body burden which may cause toxic effects due to direct (water) and/or indirect (dietary) exposure. Bioaccumulative substances characterised by high persistence and toxicity, negligible metabolism and a log K_{ow} between 5 and 8 may represent a concern when widely dispersed in the environment. Therefore, when appropriate, the potential of a substance to bioaccumulate in the aquatic environment should be included as an exposure related parameter in risk assessment. Biomagnification, resulting in an increase of the internal concentration in organisms at succeeding levels in the trophic chain, is not as widespread as commonly believed; it has only been demonstrated for a very limited number of substances.

The potential of a substance to bioaccumulate is related primarily to its lipophilicity. A surrogate measure of lipophilicity is the n-octanol-water partition coefficient (K_{ow}), which is correlated with bioconcentration potential. Therefore, K_{ow} is often used as predictor in quantitative structure-activity relationships (QSARs) for bioconcentration factors (BCF) of organic non-polar substances. Such QSARs, however, are not universally applicable. While predictions of BCF in aquatic organisms for lipophilic, nonionic substances undergoing minimal metabolism or biotransformation may be satisfactory, there are exceptions, and the equations to predict BCF are best used only within the chemical class for which the QSAR was developed. Substances with a low lipid solubility, substances with a molecular weight well above 700, or substances which are considered as highly lipophilic will not be taken up as predicted from simple QSARs for BCFs. Non-linearity of BCF

versus log K_{ow} for highly lipophilic substances has been demonstrated. Similarly deviations have been reported also for other chemical classes such as surface-active, ionisable and polar substances.

When biotransformation of the substance by the organism occurs, elimination may increase significantly thus reducing bioconcentration. The major drawback of the various models proposed for the prediction of bioconcentration and bioaccumulation is that they assume no active biotransformation. In addition, specific physico-chemical properties of the substance may reduce availability and possibly exclude uptake. Therefore, when available, measured BCF values based on the analysis of parent substance should be used rather than predicted values.

A step-wise approach is recommended to integrate bioaccumulation in an environmental risk assessment scheme for substances which are widely distributed in the environment due to wide dispersive use and effective intermedia transfer, and which potentially can be taken up by biota. Substances which are persistent, bioaccumulative and exhibit negligible metabolism will be selected by this scheme for a more detailed evaluation.

For those substances which reach a steady-state body burden within the organism during the toxicity test, direct effects of bioconcentration are included, and thus the PNEC derived from this testing is appropriate for use in risk assessment. However, for lipophilic substances which are taken up and depurated very slowly by fish, the steady-state body burden may not have been achieved during the test. Hence, environmental effects assessments should consider the "time to reach steady-state" in evaluating PNEC values for these substances. In a preliminary assessment, it is recommended to evaluate the time to reach 95% of steady-state (T_{95}).

It is concluded that dietary uptake by aquatic organisms is significant only if the substance has low water solubility, high lipid solubility and is slowly metabolised or eliminated by the prey organism. Initially, the BCF may be estimated as described above. When the predicted BCF value is above 1,000 (corresponding to a log K_{ow} of 4.3) a PEC/PNEC assessment for predators is made and refined as deemed necessary.

The EU Technical Guidance for environmental risk assessment requires that bioaccumulation and secondary poisoning be assessed when the substance has a log K_{ow} of 3 or more. In this scheme, the approach does not explicitly include the dietary pathway at lower tiers and may underestimate the body burden of prey organisms for substances with higher lipophilicities. The EU method could be overconcerned with substances of little relevance for secondary poisoning, while underestimating actual exposure for substances in the log K_{ow} range of 4.5 to 8 which are potentially the most critical for dietary exposure.

Bioconcentration and bioaccumulation models will generally overestimate the potential for bioaccumulation and therefore may trigger unjustifiable concerns about transfer of substances up the food web. Additional work is needed to provide further insights into the limitations and uncertainties of QSARs used at the screening stage in the bioaccumulation assessment. Validation and/or reformulation of these QSARs for a wider range of chemical classes is needed if these QSARs are to be used with confidence in the risk assessment process. Furthermore, additional work is needed to incorporate both knowledge and prediction of metabolic processes to account for its influence on bioaccumulation. The development of empirical QSARs for metabolism would aid in the prioritisation, assessment and regulation of apparently persistent and bioaccumulative substances.

1. INTRODUCTION

The development of environmental risk assessment procedures for substances has received considerable attention from regulators, academia and industry (EEC, 1992a; EEC 1993a; ECETOC 1993; OECD 1994a). An iterative and tiered approach in data gathering, evaluation, and decision making has been generally adopted (EEC, 1993b; EEC, 1994; OECD, 1994a). The risk assessment process essentially consists of a stepwise and iterative comparison of the Predicted Environmental Concentration (PEC) with the Predicted No Effect Concentration (PNEC) for the substance and compartment of interest, with each iteration improving the PEC and PNEC estimates.

The environmental exposure can be estimated if it is known how and in what quantity a substance enters the environment and how it is subsequently distributed and transformed in these receiving compartments (i.e. air, water, soil). The effect of transport and transformation processes on the distribution and concentration of substances in the different environmental compartments may be predicted by using mathematical models (OECD, 1989a; OECD, 1991; Braat *et al*, 1991; ECETOC, 1992; ECETOC, 1994c; RIVM, VROM, WVC 1994), assessed in experimental laboratory simulation models, or measured in actual environmental compartments if specific analytical techniques are developed for the substance of interest. An environmental exposure assessment typically yields predicted or measured concentrations on the local or regional scale.

The potential for environmental effects due to exposure to a substance can be estimated if the intrinsic hazardous properties of the substance have been determined, and if it is known how these effects can be extrapolated to the field, i.e. how populations, communities or ecosystems are affected (ECETOC, 1993; OECD, 1994a). It is important to account for potential effects on biota which may be expressed only after some time.

The properties of certain substances - resistance to biotic or abiotic degradation resulting in high persistence, lack of metabolism by organisms and tendency to accumulate in lipid - have led to their widespread dispersion in the environment and elevated concentrations in aquatic organisms. Some substances, such as DDT/DDE (causing egg-shell thinning) and co-planar PCBs (causing mink reproductive failure) have elicited unexpectedly subtle forms of toxicity. The challenge facing industry and regulators is to screen for the potential of other substances to bioconcentrate and/or bioaccumulate and elicit toxic effects after prolonged exposure.

Bioconcentration and bioaccumulation may therefore be of concern for lipophilic substances as both direct and indirect (secondary poisoning) toxic effects may be observed upon chronic exposure. Bioconcentration is defined as the net result of the uptake, distribution, and elimination of a

substance in an organism due to water-borne exposure, whereas bioaccumulation includes all routes of exposure (i.e. air, water, soil, food). Biomagnification is defined as accumulation and transfer of substances via food webs, resulting in an increase of the fat-adjusted internal concentration in organisms at succeeding levels in the trophic chain.

It is generally assumed that the potential to bioaccumulate is related primarily to lipophilicity. A surrogate measure of lipophilicity is the n-octanol-water partition coefficient (K_{ow}), which can be correlated with bioconcentration (Mackay, 1982; Chiou, 1985). Therefore K_{ow} is often used as a predictor in Quantitative Structure Activity Relationships (QSARs) for bioconcentration factors (BCF) of organic non-polar substances. Since most BCF QSARs are based on K_{ow}, regulatory trigger values to determine the potential for bioaccumulation are primarily derived from this single property. It has been proposed that values of log K_{ow} greater than or equal to 3 indicate that a substance has the potential for significant bioaccumulation (EEC, 1993b), triggering the requirement for a determination of a so-called secondary poisoning assessment.

The setting of log K_{ow}, BCF and BAF (= bioaccumulation factor) trigger values to determine the potential for bioconcentration, bioaccumulation and particularly biomagnification must be based on scientific evidence to ensure that the 'real' problem substances are tackled and unnecessary animal testing is avoided. Bioconcentration and bioaccumulation have generally been considered in a risk assessment based on specific "cut-off" values (e.g. log $K_{ow} > 3$), but were not integrated in an overall tiered risk assessment scheme. These approaches do not consider factors including actual release pattern, distribution and fate of substances in the environment and their potential to be metabolised by aquatic organisms.

To further explore when and how bioaccumulation should be incorporated into a risk assessment, the European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOC) formed a Task Force with the following Terms of Reference:

- discuss the processes involved in bioaccumulation and describe the methods for its measurement and prediction on the basis of physico-chemical properties;
- assess the importance of bioaccumulation in environmental risk assessment of aquatic ecosystems and recommend possible physico-chemical and bioconcentration trigger values to be used in consideration of additional work, and
- recommend alternative approaches to assess bioaccumulation for substances which cannot be addressed by the generic regulatory approach.

The objective of the Task Force was to review the assumptions and equations used to determine bioconcentration and bioaccumulation of substances and to recommend some practical approaches to the use of this information in risk assessments.

The potential of a substance to bioconcentrate and bioaccumulate should be assessed and, when appropriate, accounted for in a risk assessment. The critical mechanisms underlying bioconcentration and bioaccumulation will be summarised in Section 3, with a brief description of some of the implications of the processes on environmental exposure and effects. Section 4 will discuss methods for determining the potential to bioconcentrate and bioaccumulate, both from measurement and prediction. Section 5 will provide guidance and suggestions in the assessment and interpretation of the Predicted No Effect Concentration (PNEC) when prolonged exposure may possibly elicit true effects. In addition, guidance is provided in Section 5 for the assessment and interpretation of the potential increasing Predicted Environmental Concentrations (PEC). Finally, conclusions and recommendations are summarised in Section 6.

2. BACKGROUND

On 30th April 1992 the European Council adopted the 7th Amendment of Directive 67/548/EEC (EEC, 1992a). This came into force on 31st October 1993. Article 3.2. of this Council Directive requires that risk assessment be carried out in accordance with principles laid down in a Commission Directive on Risk Assessment of New Substances (93/67/EEC). The specific guidance on how to conduct an exposure and effect assessment, and risk characterisation is described in Technical Guidance Documents (EEC, 1993b). This guidance is to be used in conjunction with the Risk Assessment Directive (93/67/EEC).

The purpose of these Technical Guidance Documents is to assist the notifier and assessor in the risk characterisation and, if necessary, in deciding on what further testing would be required and its timing. The Guidance Documents for New Chemicals call for a classification of "Indication of Bioaccumulation Potential" when a substance:

- has a log K_{ow} > 3; or
- is highly adsorptive; or
- generates a surface tension of < 50 mN/m at a concentration < 1 g/l in water; or
- belongs to a class of substances known to have a potential to accumulate in living organisms; or
- there are indications from structural features;
- and there are no mitigating properties, e.g. hydrolysis or fast biodegradation.

If the K_{ow} cannot be experimentally determined, it has been suggested that this value be calculated from the chemical structure in order to estimate a bioconcentration factor (BCF). The Technical Guidance documents point out that log K_{ow} - BCF QSARs do not account for phenomena of active transport, non-linear uptake and depuration kinetics, metabolism in organisms, changes in the behaviour of diffusion through cell membranes, affinity due to specific interactions with tissue components and special structural properties (e.g. amphiphilic substances or dissociating substances that may lead to multiple equilibrium processes) (EEC, 1993b). In the absence of specific information on the above processes, the well-established regression equations based on log K_{ow} (i.e.

Mackay, 1982) will be used for conservative estimates of the potential for bioconcentration and bioaccumulation.

Depending on the intrinsic toxicity of substances classified as exhibiting a bioaccumulation potential, further testing and evaluation for secondary poisoning will be requested.

Similarly, the EC Council Regulation 793/93/EEC on the evaluation and control of the environmental risks of existing substances requires competent authorities to evaluate the risks to man and environment of existing substances (EEC, 1993a). This regulation was adopted on March 23rd 1993, and came into force on 4th June 1993. It was amended by a Commission Regulation (No. 1488/94) describing the principles of risk assessment of Existing Substances to man and the environment and by another set of Technical Guidance documents (EEC, 1994). This Directive refers to a large extent to the Commission Directive on Risk Assessment of New Substances and its respective Technical Guidance documents.