A review of bioconcentration factor (BCF) and bioaccumulation factor (BAF) assessments for organic chemicals in aquatic organisms

Jon A. Arnot and Frank A.P.C. Gobas

Abstract: Bioaccumulation assessment is important in the scientific evaluation of risks that chemicals may pose to humans and the environment and is a current focus of regulatory effort. The status of bioaccumulation evaluations for organic chemicals in aquatic systems is reviewed to reduce uncertainty in bioaccumulation measurement, to provide quality data for assessment, and to assist in model development. A review of 392 scientific literature and database sources includes 5317 bioconcentration factor (BCF) and 1656 bioaccumulation factor (BAF) values measured for 842 organic chemicals in 219 aquatic species. A data quality assessment finds that 45% of BCF values are subject to at least one major source of uncertainty and that measurement errors generally result in an underestimation of actual BCF values. A case study of organic chemicals on the Canadian Domestic Substances List indicates that empirical data are available for less than 4% of the chemicals that require evaluation and of these chemicals, 76% have less than three acceptable quality BCF or BAF values. Field BAFs tend to be greater than laboratory BCFs emphasizing the importance of environmental measurement for reliable assessment; however, only 0.2% of current use organic chemicals have BAF measurements. Key parameters influencing uncertainty and variability in BCF and BAF data are discussed using reviewed data and models. A critical evaluation of representative BCF and BAF models in relation to existing measurements and regulatory criteria in Canada indicate the probability of Type II errors, i.e., false negatives or "misses", using BCF models for bioaccumulation assessment may be as high as 70.6% depending on the model. Recommendations for the selection of measured and modelled values used in bioaccumulation assessment are provided, and improvements for the science and regulatory criteria are proposed.

Key words: bioconcentration, bioconcentration factor, bioaccumulation, bioaccumulation factor, octanol–water partition coefficient, fish.

Résumé : L'estimation de la bioaccumulation est importante dans l'évaluation scientifique des risques que les substances chimiques constituent pour les humains et l'environnement, et constitue une préoccupation actuelle des efforts de réglementation. Les auteurs passent en revue des estimations de bioaccumulation de substances organiques dans les systèmes

J.A. Arnot.[1] Canadian Environmental Modelling Centre, 1600 West Bank Drive, Trent University, Peterborough, ON K9J 7B8, Canada.
F.A.P.C. Gobas. The School of Resource and Environmental Management, 8888 University Drive, Simon Fraser University, Burnaby, BC V5A 1S6, Canada.

[1] Corresponding author (e-mail: jonarnot@trentu.ca).

aquatiques, afin de réduire l'incertitude dans la mesure des bioaccumulations, de fournir des données de qualité pour l'évaluation et de contribuer au développement de modèles. Une revue de 392 sources de littérature scientifique et de bases de données comporte 5317 valeurs de facteurs de bioconcentration (BCF), et 1656 valeurs de bioaccumulation (BAF), mesurées pour 842 substances chimiques organiques, chez 219 espèces aquatiques. Une évaluation de la qualité des données montre que 45 % des valeurs BCF font l'objet d'au moins une source d'incertitude et que les erreurs de mesure conduisent généralement à une sous-estimation des valeurs BCF réelles. Une étude de cas, effectuée sur des substances organiques de la Liste canadienne des substances domestiques, indique que des données empiriques ne sont disponibles que pour 4 % des substances qui nécessitent une évaluation, et que de l'ensemble de ces substances chimiques, 76 % comportent moins de 3 valeurs BCF ou BAF de qualité acceptable. Les BAFs venant du terrain ont tendance à être supérieures à celles du laboratoire, ce qui souligne l'importance de mesures environnementales pour une évaluation fiable ; pourtant, seulement 0,2 % des substances chimiques couramment utilisées ont des mesures BAFs. Les auteurs discutent les facteurs clés qui influencent l'incertitude et la variabilité des données BCF et BAF, en utilisant les données et les modèles provenant de leur revue. Une évaluation critique de modèles BCF et BAF représentatifs, en relation avec les mesures existantes et divers critères de réglementation, indique que la probabilité d'erreurs de Type II, i.e., faux négatifs ou absence, en utilisant les modèles BCF pour l'évaluation de la bioaccumulation, pourrait atteindre 70,6 %, selon le modèle. On présente des recommandations pour la sélection des valeurs mesurées et modélisées, utilisées pour l'évaluation de la bioaccumulation, et on propose des amélioration pour les critères scientifiques et réglementaires.

Mots clés : bioconcentration, facteur de bioconcentration, bioaccumulation, facteur de bioaccumulation, coefficient de répartition octanol-eau, poisson.

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Introduction

Relationships between the physical–chemical properties of organic chemicals and physiological responses in organisms have been studied since the late 19th century (Overton 1896; Meyer 1899); however, it was not until the 1960s that the risks of anthropogenic chemicals on human and environmental health drew public attention (e.g., Fox et al. 1991; Carson 1962). Globally, regulatory agencies are developing methods and criteria to assess many of the approximately 100 000 existing chemicals and the 1000–2000 new substances developed each year (USEPA 1976; Government of Canada 1999; European Commission 2001; OECD 2001; UNEP 2001; Walker et al. 2002). For example, The Canadian Environmental Protection Act of 1999 (CEPA 1999) requires that chemicals on the Domestic Substances List (DSL) be subject to a two-phase evaluation (Government of Canada 1999, 2000). The first phase is a hazard assessment in which chemicals are evaluated against persistence (P), bioaccumulation (B), and toxicity (T) endpoint criteria. Hazardous candidates are then subject to more comprehensive evaluations including risk assessment.

Information of high quality is required to reduce uncertainty for hazard and risk assessments. Approaches have been suggested for assessing ecotoxicology data quality (Klimisch et al. 1997; Rufli et al. 1998; OECD 2001); however, no methods or criteria have been explicitly developed for evaluating the quality of bioconcentration and bioaccumulation data. The general lack of empirical information has necessitated the development and application of models (e.g., Environment Canada 2003). Bioconcentration and bioaccumulation endpoints can be estimated using quantitative structure-activity relationships (QSARs) (e.g., USEPA 2004), empirical models (e.g., Neely et al. 1974; Veith et al. 1979; Mackay 1982; Bintein et al. 1993; Meylan et al. 1999; Dimitrov et al. 2005), and mass balance models (e.g., Norstrom et al. 1976; Thomann 1989; Barber et al. 1991; Nichols et al. 1991; Gobas 1993; Campfens and Mackay 1997; Arnot and Gobas 2004).

Table 1. An overview of regulatory bioaccumulation assessment endpoints and criteria.

Regulatory agency	Bioaccumulation endpoint	Criteria (log values)	Program
Environment Canada	K_{OW}	$\geq 100\,000$ (5)	CEPA (1999)[*]
Environment Canada	BCF	$\geq 5\,000$ (3.7)	CEPA (1999)
Environment Canada	BAF	$\geq 5\,000$ (3.7)	CEPA (1999)
European Union 'bioaccumulative'	BCF	$\geq 2\,000$ (3.3)	REACH[†]
European Union 'very bioaccumulative'	BCF	$\geq 5\,000$ (3.7)	REACH
United States 'bioaccumulative'	BCF	$1\,000$ (3)–$5\,000$ (3.7)	TSCA[‡], TRI
United States 'very bioaccumulative'	BCF	$\geq 5\,000$ (3.7)	TSCA, TRI
United Nations Environment Programme	K_{OW}	$\geq 100\,000$ (5)	Stockholm Convention[§]
United Nations Environment Programme	BCF	$\geq 5\,000$ (3.7)	Stockholm Convention

[*]CEPA, Canadian Environmental Protection Act, 1999 (Government of Canada 1999; Government of Canada 2000).
[†]Registration, Evaluation and Authorization of Chemicals (REACH) Annex XII (European Commission 2001).
[‡]Currently being used by the US Environmental Protection Agency in its Toxic Substances Control Act (TSCA) and Toxic Release Inventory (TRI) programs (USEPA 1976).
[§]Stockholom Convention on Persistent Organic Pollutants (UNEP 2001).

In this study, available databases and scientific literature are extensively reviewed for measured bioconcentration and bioaccumulation values for organic chemicals in non-mammalian aquatic organisms, particularly fishes. Key factors that influence uncertainty and variability in bioconcentration and bioaccumulation assessment are described including statistical analyses and case studies of the data. Criteria developed from standard testing guidelines are applied to reduce uncertainty in the measured data and to provide confidence in the quality of the data used for model development and bioaccumulation assessments. Representative models are evaluated with the measured data in the context of the regulatory criteria. Finally, based on this review, recommendations are provided for using available measurements and models in bioaccumulation assessments and for addressing scientific and regulatory needs.

Definitions, assessment endpoints, and regulatory criteria

Bioconcentration, bioaccumulation, and biomagnification are distinct phenomena with unique endpoints and are defined to alleviate confusion as to their context in this review (Barron 1990; Connell 1990; Gobas and Morrison 2000; Mackay and Fraser 2000). Table 1 lists bioaccumulation endpoints and criteria used by regulatory agencies as a part of "P, B, and T", assessment programs. These endpoints are also used for the development of environmental standards, guidelines, and criteria (Walker and Gobas 1999; USEPA 2000).

Bioconcentration

Bioconcentration is the process by which a chemical substance is absorbed by an organism from the ambient environment only through its respiratory and dermal surfaces, i.e., chemical exposure in the diet is not included. It is the net result of competing rates of chemical uptake at the respiratory surface (e.g., gills in fish) and chemical elimination including respiratory exchange, fecal egestion, metabolic biotransformation of the parent compound, and growth dilution. Growth dilution is considered a "pseudo-elimination" process since the chemical is not actually eliminated by the organism but the concentration can be diluted by an increase in the volume of tissue. The degree to which bioconcentration occurs is expressed as the bioconcentration factor (BCF) and can only be measured under controlled laboratory conditions in which dietary intake of the chemical is deliberately not included.

The competing uptake and elimination processes resulting in bioconcentration can be represented mathematically by an organism-water two-compartment model where the organism is considered to be

a single compartment in which the chemical is homogeneously mixed as

[1] $dC_B/dt = (k_1 C_{WD}) - (k_2 + k_E + k_M + k_G)C_B$

where C_B is the chemical concentration in the organism (g·kg^{-1}), t is a unit of time (d^{-1}), k_1 is the chemical uptake rate constant from the water at the respiratory surface (L·kg^{-1}·d^{-1}), C_{WD} is the freely dissolved chemical concentration in the water (g·L^{-1}), and k_2, k_E, k_M, k_G are rate constants (d^{-1}) representing chemical elimination from the organism via the respiratory surface, fecal egestion, metabolic biotransformation, and growth dilution, respectively. When both C_B and C_{WD} no longer vary with exposure duration, i.e., $dC_B/dt = 0$, the system has reached a steady state and eq. [1] can be rearranged to calculate the BCF as

[2] $BCF = C_B/C_{WD} = k_1/(k_2 + k_E + k_M + k_G)$

The BCF can be calculated as the ratio of the chemical concentration in the organism and the chemical concentration in the water at steady state, i.e., $BCF_{SS} = C_B/C_{WD}$. The steady state calculation, also referred to as the "plateau" method, is only valid if a steady state actually occurs (OECD 1996; USEPA 1996a). The BCF can also be determined kinetically as the ratio of the chemical uptake rate constant from water and the total elimination or depuration rate constant k_T (d^{-1}), i.e., $BCF_K = k_1/k_T$, where $k_T = k_2 + k_E + k_M + k_G$.

The total chemical concentration in the bulk water phase C_{WT}, as typically measured by solvent extraction, includes both the freely dissolved chemical concentration in the water, i.e., C_{WD}, and chemical associated or bound to particulate and organic matter. It is believed that only the freely dissolved chemical concentration in water is able to pass through biological membranes and is "bioavailable" for uptake by organisms. In a 'bound' or 'sorbed' state the chemical is considered to be unable to pass through biological membranes. Thus, the fraction of the chemical that is measured in the water that can actually be absorbed is referred to as the bioavailable solute fraction (unitless), i.e., $\phi = C_{WD}/C_{WT}$. The BCF is usually calculated from the measured total water concentration, i.e., $BCF = C_B/C_{WT}$. A more universal bioconcentration endpoint that is independent of the presence of organic matter in the water is expressed in terms of the freely dissolved chemical concentration as $BCF_{fd} = C_B/C_{WD}$; however, accurate measurements of the actual freely dissolved concentration are technically challenging.

The weight of the organism can be expressed on a wet weight (WW), dry weight (DW) or lipid weight (LW) basis. For example, dividing the wet weight chemical concentration by the lipid fraction of the measured sample derives chemical concentrations expressed on a lipid weight basis, referred to as "lipid normalizing", i.e., $BCF_{LW} = BCF_{WW}/lipid\ fraction$. Most commonly, the weight of the organism is presented on a wet weight basis and the units of the BCF are L·kg^{-1}.

Bioaccumulation

Bioaccumulation is a process in which a chemical substance is absorbed in an organism by all routes of exposure as occurs in the natural environment, i.e., dietary and ambient environment sources. Bioaccumulation is the net result of competing processes of chemical uptake into the organism at the respiratory surface and from the diet and chemical elimination from the organism including respiratory exchange, fecal egestion, metabolic biotransformation of the parent compound and growth dilution. Figure 1 summarizes the major routes of chemical uptake and elimination and their associated rate constants in fish. The competing uptake and elimination processes resulting in bioaccumulation can be represented mathematically as

[3] $dC_B/dt = (k_1 C_{WD} + k_D C_D) - (k_2 + k_E + k_M + k_G)C_B$

where k_D is the uptake rate constant for chemical in the diet (kg·kg^{-1}·d^{-1}) and C_D is the chemical concentration in the diet (g·kg^{-1}).

Fig. 1. Major routes and associated rate constants of chemical uptake and elimination in fish.

Metabolic biotransformation; k_M

Gill uptake; k_1

Growth 'dilution'; k_G

Dietary uptake; k_D

Fecal egestion; k_E

Gill elimination; k_2
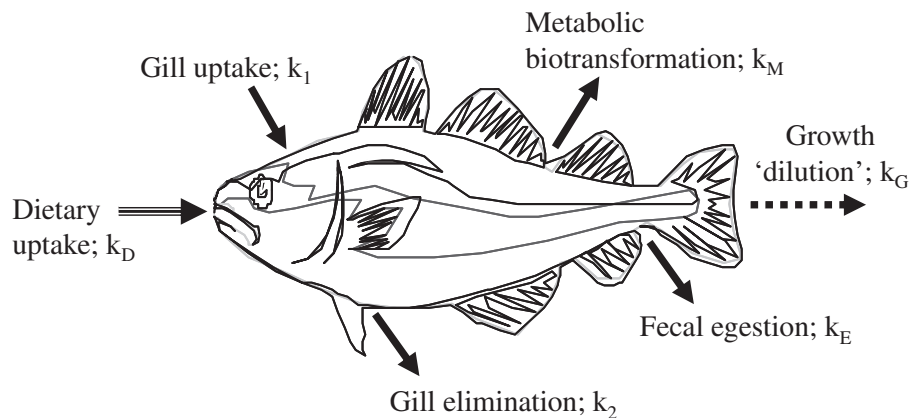
The degree to which bioaccumulation occurs can be expressed as a bioaccumulation factor (BAF) and at steady state, i.e., $dC_B/dt = 0$, the BAF can be calculated as

[4] $BAF = C_B/C_{WD} = \{k_1 + k_D (C_B/C_{WD})\} / (k_2 + k_E + k_M + k_G)$

The BAF is typically measured under field conditions that can include the total chemical concentration in the water phase, i.e., $BAF = C_B/C_{WT}$. Bioavailability should be considered when measuring the BAF since the freely dissolved chemical concentration is affected by site-specific organic matter conditions in the water column. The inherent potential of a chemical substance to bioaccumulate is more appropriately characterized by the endpoint BAF_{fd}, i.e., C_B/C_{WD}, which is independent of site-to-site particulate and dissolved organic matter variability in the water. The BAF can be expressed on wet weight, dry weight, and lipid weight bases. Most commonly, the weight of the organism is presented on a wet weight basis and the units of the BAF are $L \cdot kg^{-1}$. Bioaccumulation is distinct from bioconcentration because chemical exposure in the diet, and therefore potential biomagnification, is included. The BCF and BAF should not be confused and are not interchangeable quantities.

Other field-based measurement endpoints of bioaccumulation are briefly described. The biota-sediment accumulation factor (BSAF) is the ratio of chemical concentration in an organism to the chemical concentration in the sediment. The food web magnification factor (FWMF) is calculated as the slope of the logarithm of the lipid normalized chemical concentration versus the $\delta N^{15}/N^{14}$ stable isotope ratio and represents the average increase or decrease in lipid normalized chemical concentrations for a unit increase in trophic position (e.g., Fisk et al. 2001; Mackintosh et al. 2004). A FWMF greater than 1 indicates chemical biomagnification occurs in the food web, whereas a value less than 1 indicates trophic dilution. The trophic magnification factor (TMF) is analogous to the FWMF and is also used to identify food web biomagnification (e.g., Tomy et al. 2004). Field based bioaccumulation assessment endpoints generally assume that the system is at steady state or pseudo-steady state.

Biomagnification

Biomagnification is a process in which the thermodynamic activity of the chemical in an organism exceeds that of its diet. Biomagnification can be determined under field conditions and in laboratory feeding experiments. Biomagnification is expressed by a biomagnification factor (BMF), defined as the ratio of the chemical concentration in an organism to that in its diet at steady state, i.e., $BMF = C_B/C_D$. These concentrations can be expressed on a wet weight basis or dry weight basis, i.e., BMF_{WW} or BMF_{DW}; however, it is preferable to express the BMF as a fugacity ratio, i.e., $BMF_f = f_B/f_D$. The fugacity ratio directly expresses the increase in thermodynamic activity of the chemical, i.e., magnification, due to

trophic interaction. For lipophilic substances this can be achieved by expressing chemical concentrations in the organism and its diet on a lipid normalized or lipid weight basis, i.e., $\mathrm{BMF_{LW}} = C_{\mathrm{B(LW)}}/C_{\mathrm{D(LW)}}$. For substances that appear to predominantly accumulate associated with proteins (e.g., perfluorooctane sulfonate or PFOS), concentrations can be expressed on a protein normalized basis or protein weight basis, i.e., $\mathrm{BMF_{PW}} = C_{\mathrm{B(PW)}}/C_{\mathrm{D(PW)}}$.

The bioconcentration and bioaccumulation potential of organic chemicals is often compared to the octanol–water partition coefficient (K_{OW}). K_{OW} represents the lipophilicity and the hydrophobicity of a chemical and how it thermodynamically distributes, i.e., partitions, between aqueous and organic phases. K_{OW} is generally considered to be a reasonable surrogate phase for lipids in biological organisms (e.g., Mackay 1982). The two physical–chemical properties K_{OW} and aqueous solubility (S_{W}) are inversely related and uncertainty of measured and estimated values of K_{OW} generally increases for very hydrophobic chemicals, i.e., log K_{OW} values greater than about 6.

Methods

Measured BCF and BAF data compilation

BCFs and BAFs for organic chemicals measured in a range of aquatic organisms, but primarily fish, were compiled from database sources and the literature shortly following the ratification of CEPA 1999. Empirical data were collected from these sources in two stages beginning in October 1999 and completed in November 2005. The first stage was for the approximately 11 300 organic chemicals on the Canadian DSL to address the legislated mandate of CEPA 1999. The second stage was for organic chemicals not on the Canadian DSL, i.e., non-DSL chemicals, and focused primarily on acceptable quality data studies identified in the first stage from the DSL compilation. Data were obtained from key word searches of the scientific literature and by using several databases to identify the original studies. Data were only considered if the test chemical, test organism and endpoint were clearly identified.

The databases included the United States Environmental Protection Agency's Ecotoxicology (ECO-TOX) database (USEPA 2005), the Syracuse Research Corporation's BCFWIN dataset (SRC 1999), Japan's Chemical Evaluation Research Institute and National Institute of Technology and Evaluation dataset (CERI 1992), the Physical–Chemical Properties and Environmental Fate Handbook (Mackay et al. 1999), the National Library of Medicine's Hazardous Substances Data Bank (National Institutes of Health 2005), and the review "Comparative QSAR: A Comparison of Fish Bioconcentration Models" (Devillers et al. 1998). These databases are summarized in greater detail elsewhere (Weisbrod et al. 2006).

Primary sources reporting original BCF and BAF data were reviewed to document key information regarding the chemical (e.g., chemical abstract service (registration) number (CASN), chemical name, radio-label), the organism (e.g., species, weight, lipid content, tissue analyzed, gender), exposure conditions (e.g., water temperature, pH, organic carbon content, water type, exposure design), and calculation methods (e.g., steady state or kinetic). Repeated values of the same measurement cited from different sources were eliminated from the compiled data. Chemical congeners, i.e., polychlorinated biphenyls (PCBs), and chemical isomers were considered as separate chemicals because they have unique CASNs and distinct physical–chemical properties that influence their bioaccumulation behaviour (e.g., K_{OW}).

Measured laboratory BCF data review

Empirical BCF data were evaluated to review the status of the available values and to provide confidence in the values used for model development and bioaccumulation assessments. Six confidence criteria were developed for the evaluation of the BCF data based on (*i*) Organization for Economic Cooperation and Development (OECD) and US Environmental Protection Agency (USEPA) bioconcentration testing guidelines (OECD 1996; USEPA 1996*a*,1996*b*) and (*ii*) peer reviewed studies on sources of error in BCF experiments (Gobas and Zhang 1992; Devillers et al. 1996; Meylan et al. 1999).

Table 2. Criteria and confidence scoring methods used for the bioconcentration factor (BCF) data quality assessment.

| Criteria	Confidence score		
	1 — High	2 — Moderate	3 — Low
1. Water analysis	Measured	Not reported or uncertain	Not measured or nominal
2. Radio-label	Radio-label not used or corrected for parent compound	N/A	Not corrected for parent compound or analysis not clearly described to ascertain parent compound correction
3. Aqueous solubility	$[C_{WT}] \leq 0.2 S_W$	2A — $0.2 S_W < [C_{WT}] \leq S_W$; 2B — $S_W < [C_{WT}] \leq 5 S_W$; 2C — Not reported or S_W not available	$[C_{WT}] > 5 S_W$
4. Exposure duration	Declared "steady state" or sufficient for 80% steady state or k_1/k_2	Not reported	Insufficient for 80% steady state or reported "not at steady state"
5. Tissue analysis	1A — Whole body and lipid content; 1B — Whole body; no lipid content	Tissue or organ with lipid content reported or muscle tissue using k_1/k_2 or tissue analysis not reported	Tissue or organ without lipid content
6. Other factors considered	N/A	N/A	Details provided in the text

Note: N/A, not applicable; $[C_{WT}]$, exposure concentration; S_W, aqueous solubility of the chemical; k_1/k_2, kinetic methods.

For each criterion, the reported BCF value was scored 1, 2, or 3 for high, moderate, or low confidence, respectively. In some cases these scores were further qualified. Table 2 and Fig. 2 summarize the confidence criteria and scoring methods. Key factors influencing BCF uncertainty are reviewed and provide rationales for the development of the confidence criteria subsequently described. The data confidence assessment is intended to reduce uncertainty in the BCF data but it cannot fully eliminate experimental errors.

Water analysis (criterion 1)

The first criterion recognizes the importance of measuring the chemical concentration in the water during the exposure period in the calculation of the BCF. Guidelines suggest that at least five water samples be collected at the same time as the test organisms during the exposure phase and that the water concentration must be maintained within 20% of the mean measured values during the uptake phase for a BCF test to be valid. BCF measurement errors are introduced when the chemical concentration in the water is not appropriately measured or maintained. Deviations between the intended, or nominal,

Fig. 2. A flow chart illustrating the application of the bioconcentration factor (BCF) data confidence scoring criteria used to identify low confidence values and to provide measured BCF data considered to be of acceptable confidence for bioaccumulation assessment and model development.
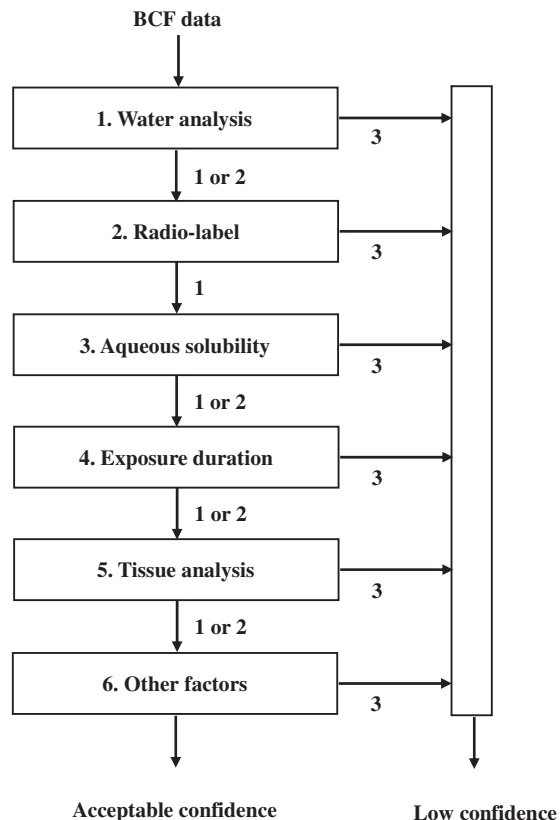
and actual exposure concentrations can result from errors in preparation and delivery of the chemical to the exposure media. A chemical may be adsorbed to surfaces of testing equipment and by organic matter in the water phase. For chemicals with higher Henry's Law constants the substance may also partition into the air. Chemical absorption by the organism may also reduce the concentration in the water, particularly at the onset of the experiment when initial chemical concentrations in the organism are low. These errors may be exacerbated in static test designs where the chemical is not regularly renewed.

BCF calculations that assume or do not measure water concentrations generally result in an underestimate of the actual BCF because the actual exposure concentration is less than the intended value. Therefore, if chemical concentrations in the water were measured during the exposure period, then confidence in the BCF was considered high and the value received a score of 1. If the chemical concentrations in the water were not measured during exposure or were reported as nominal, then the BCF was considered to be of low confidence and assigned a score of 3. If water concentrations were not reported or were not clearly documented, then the value was assumed to be of moderate confidence and assigned a score of 2.

Accurate BCF measurements require that the chemical concentration in the water remains constant during the test (Gobas and Zhang 1992; Devillers et al. 1998; Meylan et al. 1999). This requirement can be difficult to satisfy, particularly at the onset of the experiment when net uptake rates of chemical from water to organism are high and for chemicals with low water solubility in which there is both a low concentration and mass of chemical in the experimental system. Fluctuations in the water concentration

during exposure can lead to either over- or under-estimates in the actual BCF by about one order of magnitude (Gobas and Zhang 1992). Some methods including nonlinear regression and iterative numerical integration can correct for errors associated with fluctuating chemical concentrations in the water, but they are generally not applied. Since time course data were only available for a few of the studies reviewed, it is important to recognize that significant errors may still remain even in the data considered to be of high confidence.

Radio-labelled chemicals (criterion 2)

The second criterion addresses the uncertainty that may arise from studies that use radio-labelled substances to quantify the amount of chemical present in the water and test organism. Guidelines state that BCF determinations should be based on the concentration of parent compound and not upon the total radio-labelled signals that may include metabolites. Uncertainty in the determination of the actual BCF arises when radio-labelled test chemicals are used to quantify chemical concentrations without distinguishing between radio-labelled parent compound and radio-labelled biotransformation products and impurities. The use of radio-labelled substances may result in overestimations of the actual BCF if the parent compound is transformed and the metabolite with the radio-label is not eliminated from the organism. For example, the gall bladder contains high concentrations of radio-labelled metabolites as a result of excretion from the liver to the gall bladder in fish that are not fed during the experiment (Wakabayashi et al. 1987; Goodrich et al. 1991; Toshima et al. 1992). Conversely, if the radio-labelled metabolite is returned to the water there can be an overestimate of the "apparent" test compound in the water resulting in an underestimation of the actual BCF. Transformation of the chemical in the water phase may also contribute to errors in calculating the BCF for non-corrected radio-labelled compounds, especially if the metabolite has different bioconcentration characteristics than the parent substance.

BCF data were considered to be of high confidence if a clear method was described to separate the signals from parent compound and metabolites in both the water and the organism resulting in a score of 1. Studies that did not use radio-labels also scored 1 by default for this criterion. If radio-labelled chemicals were used without corrections for parent compounds in either the water or the organism or a clear method of correction was not described, confidence in the BCF value was low and scored 3.

Aqueous solubility (criterion 3)

The third criterion assesses the chemical concentration in the water in relation to the aqueous solubility of the chemical. If the chemical concentration in the water is greater than the chemical's aqueous solubility, then the chemical concentration is likely to overestimate the concentration that can be absorbed via the respiratory route resulting in underestimates of the actual BCF. Solvents, dispersants, and solubilizing agents ("solubilizers") are sometimes used to facilitate dissolution of relatively insoluble chemicals, i.e., typically hydrophobic chemicals. Solubilizers are not recommended by protocol guidelines and the use of these agents was not common in the reviewed literature.

For many chemicals measurements and estimates of the aqueous solubility are uncertain. For example, empirical water solubility values for chlorpyrifos and hexachlorobenzene range by a factor of approximately 6 and 10, respectively (Mackay et al. 1999). Therefore, an uncertainty factor of 5 was applied to selected measured and estimated aqueous solubility values for assessing this criterion. If the reported average chemical concentration in the water was less than or equal to one-fifth of the selected aqueous solubility, i.e., 20%, confidence in the BCF value was considered high and scored 1. If the reported average chemical concentration in the water was above the aqueous solubility by a factor of 5, confidence in the BCF value was considered low and scored 3. If the reported average chemical concentration in the water was less than or equal to the aqueous solubility but greater than 20% of the aqueous solubility, the BCF value confidence was considered moderate and scored 2A. If the reported average chemical concentration in the water was greater than the aqueous solubility but within a factor of 5, the BCF value confidence was also considered moderate and scored 2B. Finally, if the exposure

concentration was not reported or aqueous solubility data were not available, the BCF value was considered of moderate confidence with a score of 2C. Since there is uncertainty in the actual value of a chemical's aqueous solubility there may still be errors in the evaluated data.

Exposure duration (criterion 4)

The fourth criterion addresses the exposure period in relation to the kinetics of chemical uptake and elimination. A key characteristic of the BCF endpoint is that it applies at steady state. Protocols recommend that organisms be exposed during the uptake phase for 28 d or until steady state is achieved. Steady state is considered when mean fish concentrations are not significantly different between three sequential sampling periods during the uptake phase with a consistent aqueous exposure concentration. Hence, if the BCF is calculated using the steady state or "plateau" method, i.e., $BCF_{SS} = C_B/C_W$, the exposure duration of the experiment must be sufficiently long to reach steady state or pseudo-steady state for the calculation to be valid. A 20% fluctuation from steady state is considered acceptable by testing guidelines. Since a 20% fluctuation in the mean water exposure concentrations is also considered acceptable by testing guidelines, 80% of steady state was determined to be a reasonable level of uncertainty for this data confidence assessment.

The time to steady state is controlled by the total elimination or depuration rate of the chemical. The slower the elimination rate or the longer the half-life ($t_{1/2}$), the longer the exposure period must be for the organism to reach steady state. For chemicals that have very long half-lives, the period of exposure to calculate the BCF using the plateau method may be greater than 28 d. Conversely, chemicals with short half-lives may reach a steady state during an exposure period less than 28 d. Assuming first-order kinetics, the BCF can also be calculated using ratios of the uptake and elimination rate constants, i.e., $BCF_K = k_1/k_T$. The estimated time to reach 80% of a steady state value can then be calculated as $t_{80} = 1.6/k_T$ (OECD 1996) where $k_T = k_2 + k_E + k_G + k_M$.

The BCF values from studies that did not explicitly declare steady state information were assessed using a BCF model (Arnot and Gobas 2004) to estimate the exposure time required to achieve 80% steady state using parameters reported from the individual studies. If organism mass, lipid content, and exposure temperature were not reported the model used the median values from the reviewed data. The model and defaults are summarized in Table 3. If measured total elimination rates were reported they were used to confirm that the exposure duration was sufficient for at least 80% steady state.

Studies that reported "steady state" or that calculated the BCF using a kinetic method were considered of high confidence. Thus, BCF values were considered to be of high confidence and scored 1 if (*i*) it was clearly stated or documented that the organism had reached "steady state", or (*ii*) kinetic methods were used to calculate the BCF, or (*iii*) the model estimated that 80% of steady state was achieved. Low confidence and a score of 3 was assigned to BCF values if (*i*) it was clearly stated or documented that the organism was "not at steady state" or (*ii*) the model estimated there was insufficient exposure duration to reach 80% of steady state. If the exposure duration was not reported the study was considered of moderate confidence and scored 2.

It is important to consider that uncertainty in the evaluated data still remains despite this method for assessing this criterion. For example, an error using the kinetic method to calculate the BCF, i.e., BCF_K, can occur if experimental periods are too short for the induction of metabolizing enzymes to occur, i.e., minutes or only a few hours (e.g., de Maagd et al. 1998; Baussant et al. 2001). Also, since the default model calculations used to estimate the time required to reach 80% steady state do not include metabolic biotransformation rates, the calculated elimination rate constant may overestimate actual values for substances that are appreciably metabolized, particularly for more hydrophobic chemicals, i.e., log $K_{OW} > 5$. In these instances the time estimated to 80% steady state may be too long. In an effort to balance the conservatism introduced by applying the model, professional judgment was also used for chemicals with a high likelihood of metabolic biotransformation potential (e.g., esters).

Table 3. The bioconcentration model and default parameters based on values selected from the reviewed data (Arnot and Gobas 2004).

Symbol	Units	Parameter	Equation or default value
BCF	$L \cdot kg^{-1}$	Bioconcentration factor	$(k_1\phi)/(k_2 + k_E + k_G + k_M)$
k_1	$L \cdot d^{-1} \cdot kg^{-1}$	Gill uptake rate constant	$E_W G_V / W$
E_W	unitless	Gill chemical transfer efficiency	If $\log K_{OW} \geq 0 = (1.85 + 155/K_{OW})^{-1}$
			If $\log K_{OW} < 0 = 0.006$
K_{OW}	unitless	Octanol–water partition coefficient	See supplementary information
G_V	$L \cdot d^{-1}$	Gill ventilation rate	$(980W^{0.65})/(D_{OX})$
W	kg	Median fish whole body wet weight	0.002
D_{OX}	$mg \cdot L^{-1}$	Median dissolved oxygen concentration	7.1
ϕ	unitless	Bioavailable solute fraction	$(1 + 0.35\chi_{POC}K_{OW} + 0.08\chi_{DOC}K_{OW})^{-1}$
χ_{POC}	$kg \cdot L^{-1}$	Concentration of particulate organic carbon	0
χ_{DOC}	$kg \cdot L^{-1}$	Concentration of dissolved organic carbon	10^{-6}
k_2	d^{-1}	Gill elimination rate constant	$k_1/(L_B K_{OW} + NLOM_B K_{OW}\beta + WC_B)$
L_B	fraction	Median fish whole body lipid content	0.05
$NLOM_B$	fraction	Nonlipid organic matter of organism	0.20
WC_B	fraction	Water content of organism	$1 - (L_B + NLOM_B)$
β	$L \cdot kg^{-1}$	Non-lipid organic matter – octanol proportionality constant	0.035
k_E	d^{-1}	Fecal egestion rate constant	$G_F E_D K_{GB}/W$
$G_F{}^*$	$kg \cdot d^{-1}$	Fecal egestion rate	$0.5 G_D$
G_D	$kg \cdot d^{-1} \cdot kg^{-1}$	Feeding rate (assumed 1.5% body weight d^{-1})	$0.015W$
E_D	unitless	Gut chemical transfer efficiency	$(3.0 \times 10^{-7} K_{OW} + 2)^{-1}$
K_{GB}	$kg \cdot kg^{-1}$	Gut-biota partition coefficient	$(L_G K_{OW} + NLOM_G \beta K_{OW} + WC_G)/(L_B K_{OW} + NLOM_B \beta K_{OW} + WC_B)$
$L_G{}^*$	fraction	Lipid content of gut	0.012
$NLOM_G{}^*$	fraction	Nonlipid organic matter of gut	0.24
$WC_G{}^*$	fraction	Water content of gut	0.74
$k_G{}^\dagger$	d^{-1}	Growth rate constant	$0.00586(1.113)^{T-20} \times (1000W)^{-0.2}$
T	°C	Median water temperature	21
k_M	d^{-1}	Metabolic biotransformation rate constant	0

[*]Based on dry fish food composed of 15% lipid, 60% protein and 12% water, and lipid, nonlipid organic matter and water assimilation efficiencies for the fish food of 92%, 60%, and 15%, respectively.
[†](Gewurtz et al. 2006).

Tissue analysis (criterion 5)

The fifth criterion recognizes that the BCF is defined as the ratio of the chemical concentrations in the whole organism and the water. BCF testing guidelines recommend the whole body of the organism is used to determine the chemical concentration and that the whole body lipid content is measured. The distribution of the chemical among the different tissues of an organism can also be influenced by the lipid

contents of the tissues as well as tissue specific perfusion rates and blood–tissue partition coefficients (Nichols et al. 1990). There is strong evidence that hydrophobic substances reach equilibrium in the lipid fraction of different tissues of an organism (Bertelsen et al. 1998; Tietge et al. 1998; Gobas et al. 1999). If the chemical concentration in the organism was derived from a specific tissue and the lipid content of that tissue was reported, then a lipid normalized tissue concentration can be determined. An assumed whole body wet weight BCF can be estimated from a lipid normalized tissue BCF as the product of the lipid normalized tissue BCF and the whole body lipid content, i.e., lipid normalized tissue BCF $\times L_B$. This estimate can then be compared with whole body wet weight BCF values and criteria. If whole body lipid contents were not reported a value of 5% can be used as a first approximation of a whole body lipid content i.e., lipid normalized tissue BCF $\times$ 5%.

BCFs calculated using whole body concentrations were considered to be of high confidence and scored 1. If the whole body lipid content was also reported, the score was further qualified as 1A, if the whole body lipid content was not reported, the score was 1B. BCF data derived from either (*i*) specific tissues and a reported tissue specific lipid content or (*ii*) from muscle tissue using kinetic methods were considered to be of moderate confidence and scored 2. For bivalves (e.g., mussels, clams), if the "edible" or "soft tissue" was analyzed this was considered to be a whole body measurement. If the tissue analyzed was not reported nor clearly stated, a moderate confidence was assumed and the study scored 2. If only a specific organ or tissue of the organism was measured (e.g., gall bladder, liver, skin, viscera) and a lipid content for that organ or tissue was not reported, the value was considered to be of low confidence and scored 3. This criterion was intended to exploit available BCF data derived from tissue samples but recognizes that uncertainty still remains.

The "Banerjee method" for calculating the BCF only measures the loss of chemical in the water and assumes an uptake rate constant into the organism (Banerjee et al. 1984). Tissues are not actually measured. This method may be appropriate for some chemicals, particularly those that are not metabolized, not overly hydrophobic and stable in the water; however, because of the uncertainty that can arise from this method these BCF values were considered to have low confidence.

Other factors considered (criterion 6)

A sixth criterion addresses data confidence concerns for reasons other than those previously described in criteria 1–5. In absence of sufficient detail in the reported studies to evaluate information in each of the previously described criteria it was generally assumed that the criteria were met but BCFs were of moderate confidence, i.e., scored 2. However, if only chemical identification, species, and endpoint were reported or if other experimental problems were identified, the data were considered of low confidence, i.e., scored 3.

Toxicity

Guidelines suggest the chemical concentration in the water of bioconcentration tests be less than 1% of the acute asymptotic median lethal concentration, i.e., LC_{50} (OECD 1996). Toxic effects may alter normal physiological functions of the impacted organism, i.e., respiration rates, which can generate uncertainty in the BCF. For many chemicals maintaining and measuring water concentrations at this level may be difficult and reliable LC_{50} and toxicity data were not available for all chemicals; therefore, only studies reporting obvious impairment to the organism were considered to be of low confidence.

Water quality and temperature

Guidelines recommend that the natural particle content as well as total organic carbon be as low as possible to avoid adsorption and decreased bioavailability. Studies that included particulate material in the exposure vessels (e.g., sand, sediment, and soils) do not conform to standard BCF guidelines. In such studies, it is possible that ingestion of contaminated particles occurs, causing uptake from the

water to no longer be the only exposure route. Studies that used or reported high levels of organic carbon in the water column, i.e., greater than 2 mg·L^{-1}, and did not attempt to correct for the freely dissolved fraction were considered of low confidence. According to guidelines, water temperature variation must be no greater than ±2 °C during a test for it to be considered valid and temperatures are recommended for certain species (e.g., OECD 1996). A criterion was not included to address this potential source of uncertainty; however, temperature limits were set for data to be considered acceptable for assessments. Testing exposure temperatures greater than 30 °C and less than 3 °C were considered to be extreme and not indicative of typical environmental exposures and were considered to be of low confidence.

Physical–chemical properties

Reliable K_{OW} values are not available for 16 chemicals for which BCF data are available and reviewed in this study, including certain dyes, pigments, and perfluorinated chemicals. The 44 BCF values for these substances could not be assessed according to all of the confidence criteria. If other confidence criteria were met the BCFs of these substances were considered of moderate confidence, i.e., score 2.

Measured field BAF data review

Presently, there are no criteria with regards to the reporting of BAF values. The criteria derived earlier for the BCF are, in most cases, not applicable. For example, aqueous chemical concentrations in the field are generally far below the solubility of the chemical and the organisms are exposed throughout their lifetime, causing concentrations in the organism to be near their steady state values. In addition, environmental conditions cannot be controlled in the field. The most relevant experimental factors that determine the quality of reported BAF data include the analytical rigor applied throughout the sampling and analytical process and the statistical design of the study. There is ample information in the literature on criteria for environmental analysis including the usage of "blanks" and reference materials, quality assurance and quality control (QA/QC) protocols, and criteria for good laboratory practice (GLP) (e.g., OECD 1998). This literature was referred in order to provide guidance in the evaluation of the quality of collected BAFs. It should be acknowledged that older studies generally contain less information from which to evaluate the analytical rigor as QA/QC procedures were less developed at the time these studies were conducted.

Microcosm, mesocosm, and model ecosystem studies attempt to simulate environmental exposure under controlled conditions, i.e., in the lab or in situ. These studies are not controlled bioconcentration tests and they are not true field BAF studies, since many ecosystem processes may not be well characterized and study periods are generally not long. Presumably these studies would include dietary routes of exposure; however, the times required for the system, the diet, and the organism to approach pseudo-steady state are highly uncertain. There are no standard methods for assessing the quality of data from these "model ecosystem" studies. These "BAF" values were included as a part of this review but were considered of low confidence, i.e., scored 3.

BCF and BAF models

All models have certain merits and limitations and comprehensive reviews for empirical bioconcentration models (e.g., Devillers et al. 1996), mechanistic bioconcentration models (Barber 2003), and food web bioaccumulation models (Burkhard 1998; Gobas and Morrison 2000; Mackay and Fraser 2000) are available. Estimates of the BCF are usually derived from linear regression between empirical BCF data and K_{OW} (e.g., Mackay 1982). Regression models typically provide "average" or "best-of-fit" values. Mass balance BCF and BAF models calculate rates of chemical uptake and elimination. Most food web BAF models require site-specific information for parameterization. A semi-empirical

BAF model has been developed that calibrates a mass balance model to empirical BAF data of selected trophic levels and requires only K_{OW} to estimate BAFs (Arnot and Gobas 2003).

Representative BCF models and a BAF model were selected to compare predicted BCF and BAF values for fish to evaluated empirical data. The models include the Mackay BCF regression model (Mackay 1982), BCFWIN (Meylan et al. 1999), and the Arnot–Gobas BCF and BAF models (Arnot and Gobas 2003). The Arnot–Gobas BCF estimates used the default parameters outlined in Table 3. The Arnot–Gobas BAF was calibrated to empirical BAF data for upper trophic level fish species by minimizing the residual errors in the model predictions, i.e., 50% of the empirical upper trophic level BAF data was underestimated by the model and 50% of the empirical BAF data was overestimated by the model. Biotransformation rate estimates can be included in the mass balance models for substances subject to metabolic biotransformation; however, the Arnot–Gobas BCF and BAF predictions assume no metabolic biotransformation by default.

Physical–chemical property data and statistical analyses

Physical–chemical property data were needed to evaluate confidence in the empirical data and K_{OW} values were required as input for the models. Empirical physical–chemical property data obtained from temperatures between 10 and 30 °C were provided by Environment Canada and from database and literature sources (e.g., Staples et al. 1997; Mackay et al. 1999; Cousins and Mackay 2000). In the absence of empirical data, estimates were obtained from Estimation Programs Interface (EPI) Suite (USEPA 2004). When necessary, limits were established for estimated physical–chemical property data (e.g., minimum log $K_{OW} = -4$; maximum log $K_{OW} = 10$, unitless, and minimum log water solubility $= -5$; maximum log water solubility $= 6$, units mg·L^{-1}). Statistical analyses were conducted using JMP$_{IN}$ (SAS Institute Inc. 2000).

Results and discussion

Measured laboratory BCF data review

Figure 3 illustrates the distribution of 5317 unique BCF values reviewed for 822 chemicals in 186 aquatic species. The data are from 380 sources published between 1966 and 2005 with approximately 70% of the data generated between 1995 and 2005. The data are comprised of 60 different ECOSAR chemical class or chemical class combination domains and approximately 47% of the data are classified as "neutral organics" (USEPA 2004). The molar mass of the chemicals ranges from 53 to 1356 g·mol^{-1} with 97% of the data for chemicals with a molar mass less than 500 g·mol^{-1}. Empirical log K_{OW} values range from -2.61 to 8.68 and are available for 535 of the chemicals and 4406 of the BCF values. The reviewed BCF data, including compiled study parameters and primary reference information, are available in the supplementary information[2]. The BCF data that do not have reliable K_{OW} values are not included in the figures or regression statistics.

The distribution of the BCF data for individual chemicals is not uniform. There are only one or two BCF values for 69% of the chemicals and there are five or fewer reported BCF values for 83% of the chemicals. Three to five BCFs exist for 143 chemicals, six to ten reported values exist for 54 chemicals, and there are more than 11 observations for 92 chemicals. A few chemicals have a large number of reported BCF values. For example, there are 249 values for hexachlorobenzene, 149 for γ-hexachlorocyclohexane (γ-HCH or lindane), and between 130 and 135 for each of diazinon, chlorpyrifos, pentachlorophenol, and 1,1-(2,2,2-trichloroethylidene)bis(4-chlorobenzene) (p,p'-DDT).

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[2] Supplementary data for this article are available on the journal Web site (http://er.nrc.ca) or may be purchased from the Depository of Unpublished Data, Document Delivery, CISTI, National Research Council Canada, Building M-55, 1200 Montreal Road, Ottawa, ON K1A 0R6, Canada. DUD 5109. For more information on obtaining material refer to http://cisti-icist.nrc-cnrc.gc.ca/irm/unpub_e.shtml.

Fig. 3. Frequency of the total bioconcentration factor (BCF) data reviewed from different organism classes for chemicals of varying octanol–water partition coefficients (K_{OW}).
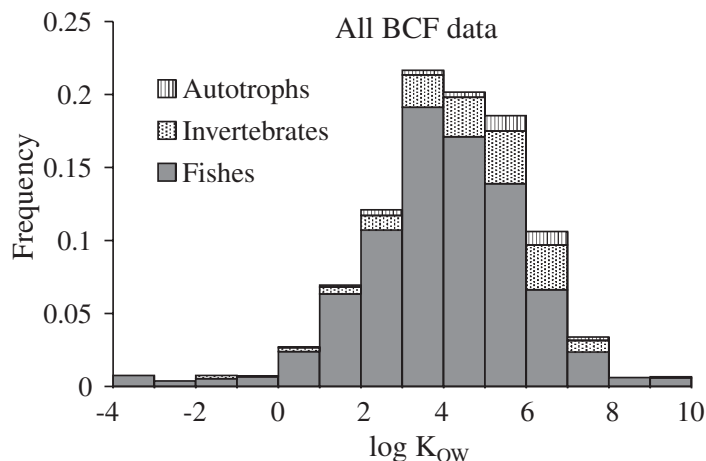

Figure 4a illustrates 186 BCF observations for 123 discrete substances from various autotrophic species, i.e., algae and phytoplankton, as a function of chemical K_{OW}. The data are from laboratory, field, and modelled ecosystem studies. These organisms do not ingest food therefore all values are BCFs reflecting uptake from ambient water only. Figure 5a shows 764 BCF values for 53 chemicals from 109 aquatic invertebrate species as a function of K_{OW}. Figure 6a shows the 4323 BCF and BCF_{fd} values reviewed for 770 chemicals in 65 fish species as a function of K_{OW}. The invertebrate and fish data are from laboratory studies only.

The data confidence assessment provides 2925 BCF values (55%) for 711 chemicals that are considered of acceptable quality for assessing bioconcentration. Figure 4b shows the 136 BCF data for 107 chemicals from autotrophic species that are acceptable. Figure 5b illustrates 218 acceptable BCF values for 22 chemicals in aquatic invertebrates. Figure 6b shows the 2527 empirical fish BCF data and BCF_{fd} for 646 chemicals that are acceptable. Accordingly, 2392 of the total empirical BCF data from all species (45%) are subject to at least one major source of experimental error identified by the criteria. There is uncertainty in the actual BCF from these estimates and they are considered of low confidence, i.e., BCF values with a score of 3 in at least one of the data confidence criteria (see Fig. 2).

Figures 4–6 indicate general trends in the data and a statistical analysis is provided in Table 4. There is no apparent relationship between log BCF and log K_{OW} for chemicals with log K_{OW} less than zero. This supports the partitioning theory that bioconcentration of these chemicals is controlled by organism tissue components other than the lipids. There are strong statistically significant positive correlations of log BCF with log K_{OW} for substances with log K_{OW} greater than zero. The coefficients of determination (r^2) increase in the acceptable datasets compared to the total datasets. For autotrophs, invertebrates, and fishes respectively, approximately 88, 61, and 52% of the total variation in log BCF is accounted for by log K_{OW}. The lower r^2 values in higher order organisms may be a result of the greater potential for metabolic biotransformation by these species or may be a result of the larger number of observations and chemical classes. The regression coefficients, i.e., slopes, increase in the acceptable BCF datasets compared to the total datasets. The increase in the regression coefficients and lower Y intercepts in the acceptable datasets compared to the total datasets suggests that many sources of uncertainty in the reviewed data tend to underestimate the actual BCF.

Table 5 summarizes the effect of the data confidence analysis on fish BCFs for five representative chemicals with log K_{OW} values between 3.30 and 7.73. In all cases, the evaluation considerably reduced the range of reported values. For example, for naphthalene and p,p'-DDT, the range of all reviewed BCF values spans approximately 4 orders of magnitude while the data considered to be acceptable as a result

Fig. 4. Measured bioconcentration factor (BCF) data in aquatic autotrophic species, i.e., algae and phytoplankton, as a function of the octanol–water partition coefficient (K_{OW}) for (*a*) the total data reviewed and (*b*) the acceptable confidence data (see Table 4 for regression summaries).
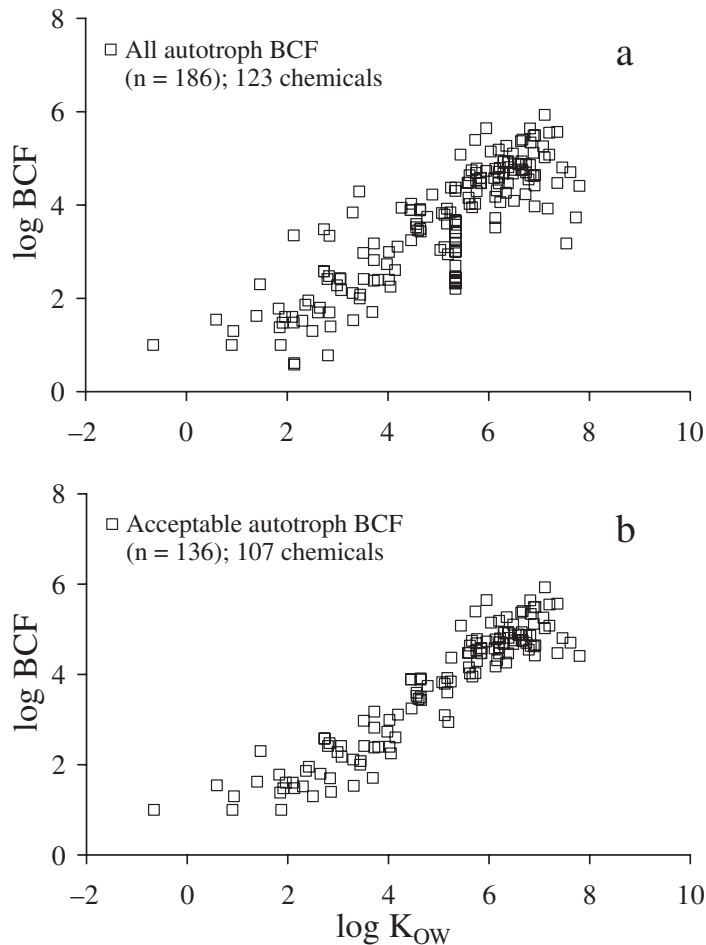

of the confidence evaluation reduces this range to approximately 1.5 orders of magnitude and less than 1 order of magnitude, respectively. Median values for individual chemicals are greater in the acceptable BCF datasets compared to the total BCF datasets. The geometric means of acceptable BCF data for individual chemicals are greater than the geometric means from the total BCF dataset. The coefficient of variation of log BCF values is reduced by a factor of about 2 for naphthalene (41.4 to 19.3) and by as much as a factor of about 5 for 1,2-benzenedicarboxylic acid, bis(2-ethylhexyl) ester (DEHP) (35.0 to 6.5). This analysis supports the finding that most errors in the measurement of the BCF underestimate the actual value of the BCF.

BCFs are generally difficult to measure and tests are most valid when following recommended guidelines and for stable organic chemicals with log K_{OW} range 1.5–6.0 (OECD 1996). BCF tests are applied to more hydrophobic chemicals for which the propensity for uncertainty generally increases. The BCF data confidence criteria attempt to reduce the uncertainty in the BCF data due to measurement errors. In consideration of the difficulty measuring BCFs and the generally limited documentation of key study parameters, the data confidence assessment cannot remove all of the uncertainty in actual BCF values. Inherent variability in the BCF for a particular chemical also occurs and is explicitly different from uncertainty. Key sources of uncertainty and variability in BCF measurements are reviewed below.

Fig. 5. Measured bioconcentration factor (BCF) and bioaccumulation factor (BAF) data in aquatic invertebrate species, e.g., bivalves, oligochaetes, insects, as a function of the octanol–water partition coefficient (K_{OW}) for (*a*) the total data reviewed and (*b*) the acceptable confidence data (see Table 4 for regression summaries).
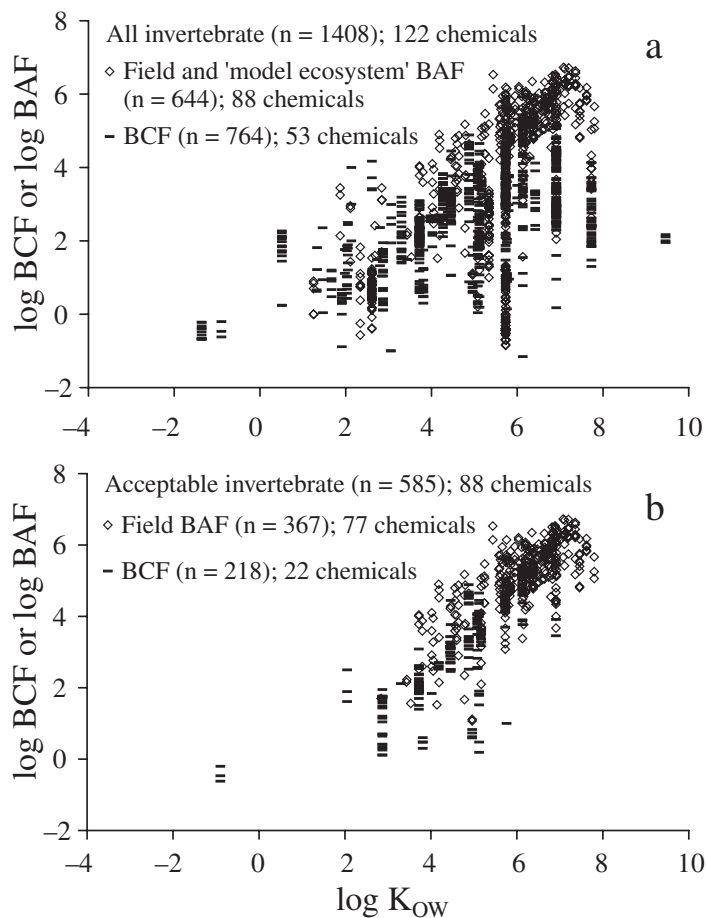

BCF uncertainty

Table 6 summarizes the frequency of errors in fish BCFs as identified by the criteria for both DSL and non-DSL chemicals combined. Table 7 summarizes the errors identified by the confidence criteria for fish BCFs from the DSL subset of data only. BCFs for non-DSL chemicals were included after a preliminary review of BCF data for DSL chemicals, i.e., acceptable studies were revisited to obtain BCF values for non-DSL chemicals. Thus, the DSL values (Table 7) are more likely reflective of sources of uncertainty in the "true" population of BCF values.

Much of the uncertainty in the BCF data is attributable to exposure durations that are insufficient to reach at least 80% of steady state, i.e., criterion 4, and to the use of radio-labelled compounds without adequately correcting for the parent signal, i.e., criterion 2. Based on model calculations, i.e., Table 3, and reported steady state information, about 19% of fish BCFs for DSL chemicals are derived under conditions in which the exposure duration is reported as not reaching steady state or the BCF calculation is estimated to be less than 80% of steady state (Table 7). Test exposure durations in the reviewed fish data range from 10 min to 735 d, with a median exposure duration of 14.0 d. About 58% of the fish BCF data are derived from exposure periods less than the guideline recommendations of 28 d (OECD 1996).

Fig. 6. Measured bioconcentration factor (BCF) data in fishes as a function of the octanol–water partition coefficient (K_{OW}) for (*a*) the total data reviewed and (*b*) the acceptable confidence data (see Table 4 for regression summaries). A BCF calculated from measured freely dissolved water concentrations (log BCF_{fd} = 5.44) is compared to a BCF calculated from measured total water concentrations (log BCF = 3.92) for decachlorobiphenyl (DCB).
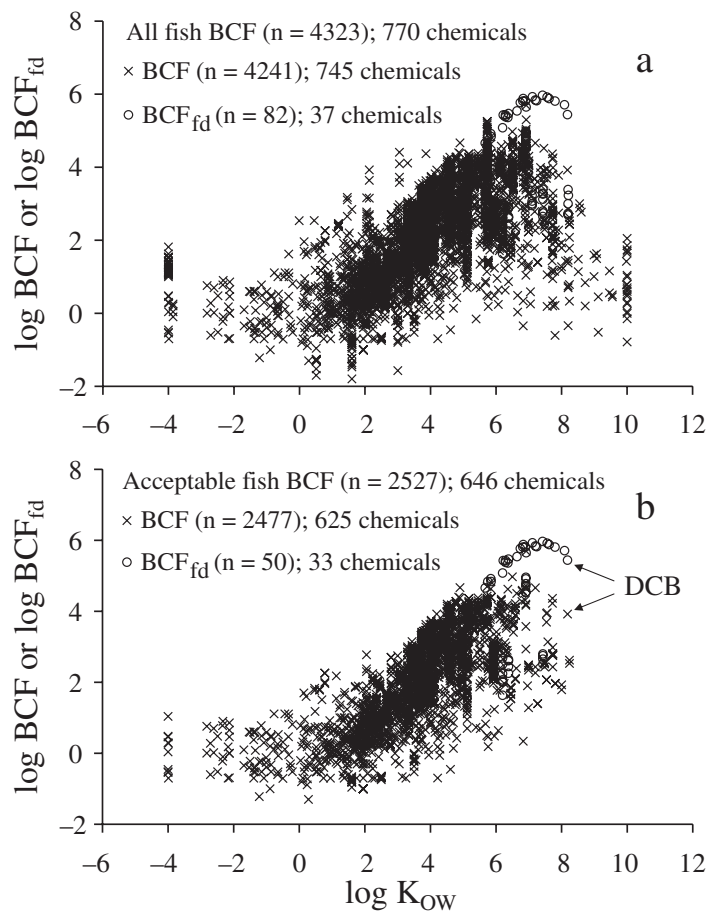
Approximately 42% of the fish BCFs are calculated after exposure periods equal to or less than 1 week, and 16% are derived after exposure periods equal to or less than 24 h. About 29% of the BCF data are derived using radio-labelled compounds. Only 33% of these data clearly documented corrections for radio-labelled metabolites and are considered acceptable for use in bioaccumulation assessments. Thus, approximately 20% of reported BCFs are derived from radioactivity measurements that include signals from parent substance and biotransformation products.

Analytical methods for chemical concentrations in the organism and the water can result in uncertainty in the whole body BCF. Approximately 14% of the total fish BCFs are derived from tissues or organs without providing a means to express the BCF on a whole body wet weight basis, i.e., criterion 5. About 32% of the data are from whole body analyses that also included measurements of whole body lipid contents. It is estimated that about 8% of BCF data do not include at least one measurement of the chemical concentration in the water, i.e., criterion 1. The actual occurrence of this error in the literature may be more frequent since the methods assume water concentrations are measured if this information is not explicitly documented.

Table 4. A summary of regression statistics for different organism classes before and after the confidence assessment on the reviewed data. Regressions are for chemicals with a $K_{OW} > 1$, except where noted.

Figure	Dataset	Linear regression (standard errors)	n	r^2	p-value
4a	All autotroph	$\log BCF = 0.40\ (0.16) + 0.63$ $(0.03) \log K_{OW}$	185	0.70	<0.0001
4b	Acceptable autotroph	$\log BCF = 0.21\ (0.12) + 0.71$ $(0.02) \log K_{OW}$	135	0.88	<0.0001
5a	All invertebrate BCF	$\log BCF = 0.98\ (0.12) + 0.35$ $(0.02) \log K_{OW}$	749	0.23	<0.0001
5b	Acceptable invertebrate BCF	$\log BCF = -1.67\ (0.26) + 1.02$ $(0.06) \log K_{OW}$	215	0.61	<0.0001
5a	All invertebrate BAF	$\log BAF = -1.45\ (0.27) + 0.92$ $(0.05) \log K_{OW}$	644	0.38	<0.0001
5b	Acceptable invertebrate BAF	$\log BAF = 0.09\ (0.24) + 0.82$ $(0.04) \log K_{OW}$	367	0.55	<0.0001
6a	All fish BCF	$\log BCF = 0.27\ (0.04) + 0.46$ $(0.01) \log K_{OW}$	4119	0.38	<0.0001
6b	Acceptable fish BCF	$\log BCF = -0.23\ (0.05) + 0.60$ $(0.01) \log K_{OW}$	2393	0.52	<0.0001
6b	Acceptable fish BCF; $K_{OW} \leq 1$	$\log BCF = 0.06\ (0.11) + 0.0006$ $(0.05) \log K_{OW}$	84	0.00	0.99
11a	All fish BAF	$\log BAF = -0.75\ (0.17) + 0.98$ $(0.03) \log K_{OW}$	1012	0.55	<0.0001
11b	Acceptable fish BAF	$\log BAF = 0.12\ (0.17) + 0.86$ $(0.03) \log K_{OW}$	912	0.55	<0.0001

Figure 7a demonstrates lower "apparent" measured BCF values when the exposure concentration exceeds the aqueous solubility, i.e., criterion 3. This example for DEHP is for data that are of acceptable confidence with the exception of water concentrations exceeding the aqueous solubility. Exposure to a chemical 1 order of magnitude greater than its aqueous solubility will result in approximately a 1 order of magnitude underestimation in the actual BCF. Figure 7b illustrates the results of a method to correct for this error by re-calculating the BCF values that are derived for water concentrations above the solubility limit as

$$[5] \qquad BCF_{corrected} = BCF_{measured}\ (C_W / S_W)$$

where C_W is the measured exposure water concentration and S_W is the chemical's aqueous solubility with the same units. This correction method should be approached cautiously with a full awareness of the accuracy of the aqueous solubility value and other potential errors in the BCF. Three percent of the DSL fish BCF data are reported under conditions in which the exposure concentration exceeds the aqueous solubility by at least a factor of 5. Approximately 7% of the BCF data are from measured water concentrations that are close to the aqueous solubility, i.e., within a factor of 5. Greater certainty in aqueous solubility values would provide greater certainty in the actual BCF.

Sources of uncertainty included in the data review ascribed to the "general" sixth criterion identify about 10% of the fish BCF data for DSL chemicals as low confidence (e.g., notable adverse toxic effects, extreme exposure temperatures). There are other possible sources of measurement uncertainty not considered in the applied data confidence criteria because, in general, the parameters are not regularly documented and criteria are more difficult to define. These are briefly discussed below.

Table 5. Summary statistics of bioconcentration factor (BCF) values from the total data reviewed and from the acceptable dataset for five case study chemicals.

Chemical	Log K_{OW}	n	Range log BCF (SD)	Median log BCF	Mean log BCF (SE)	CV
Naphthalene (total)	3.30	75	0.00–4.11 (0.82)	2.11	1.98 (0.09)	41.4%
Naphthalene (acceptable)	3.30	14	1.51–3.00 (0.47)	2.54	2.44 (0.13)	19.3%
Lindane (total)	3.72	83	0.52–3.32 (0.67)	2.45	2.32 (0.07)	28.9%
Lindane (acceptable)	3.72	33	2.16–3.32 (0.35)	2.84	2.80 (0.06)	12.5%
Hexachlorobenzene (total)	5.73	178	1.81–5.26 (0.78)	4.08	3.87 (0.06)	20.2%
Hexachlorobenzene (acceptable)	5.73	21	3.57–4.70 (0.32)	4.26	4.12 (0.07)	7.8%
p,p'-DDT (total)	6.91	22	1.04–5.00 (0.83)	4.44	4.23 (0.18)	19.6%
p,p'-DDT (acceptable)	6.91	5	4.17–4.72 (0.27)	4.65	4.48 (0.12)	6.0%
DEHP (total)	7.73	33	0.20–3.81 (0.78)	2.39	2.23 (0.13)	35.0%
DEHP (acceptable)	7.73	6	2.43–2.98 (0.18)	2.79	2.76 (0.07)	6.5%

Note: n, number of observations; SD, standard deviation; SE, standard error of the mean; CV, coefficient of variation; p,p'-DDT, 1,1-(2,2,2-trichloroethylidene)bis(4-chlorobenzene); DEHP, 1,2-benzenedicarboxylic acid, bis(2-ethylhexyl) ester.

Table 6. The number of reported bioconcentration factor (BCF) observations for all chemicals in fish (and percentage of the total 4367) identified by the data confidence criteria. BCF counts are listed with percentages rounded to nearest whole number in brackets.

Category	Number of counts for each confidence score		
	1 — High	2 — Moderate	3 — Low
1. Water analysis	4054 (93%)	75 (2%)	238 (5%)
2. Radio-label	3729 (85%)	N/A	638 (15%)
3. Aqueous solubility	3766 (86%)	2A — 172 (4%)	134 (3%)
		2B — 118 (3%)	
		2C — 177 (4%)	
4. Exposure duration	3385 (78%)	58 (1%)	924 (21%)
5. Tissue analysis	1A — 1940 (44%)	375 (9%)	430 (10%)
	1B — 1622 (37%)		
6. Other factors considered	4029 (92%)	N/A	338 (8%)

Analytical methods

The chemical should be extracted from biotic and abiotic samples, identified and quantified by acceptable methods and further verified with appropriate QA/QC protocols according to GLP (OECD 1998). There are no broadly applicable standards to assess analytical methods, percentage recovery, and measures of uncertainty and these parameters are not consistently documented. Chemical purity should not be a significant source of uncertainty in the BCF if chemical concentration in both water and test organisms are measured. There is a general lack of well-documented QA/QC. Acknowledgment of adherence to GLP is essentially non-existent in the reviewed literature. Many journals now include supporting information sections where these data and other information relevant to the BCF measurement can be provided.

Table 7. The number of reported bioconcentration factor (BCF) observations for Canadian Domestic Substances List (DSL) chemicals in fish (and percentage of the total 2672) identified by the data confidence criteria. BCF counts are listed with percentages rounded to nearest whole number in brackets.

Category	Number of counts for each confidence score		
	1 — High	2 — Moderate	3 — Low
1. Water analysis	2389 (89%)	75 (3%)	208 (8%)
2. Radio-label	2150 (80%)	N/A	522 (20%)
3. Aqueous solubility	2280 (85%)	2A — 117 (4%)	88 (3%)
		2B — 83 (3%)	
		2C — 104 (4%)	
4. Exposure duration	2142 (80%)	19 (1%)	511 (19%)
5. Tissue analysis	1A — 843 (32%)	304 (11%)	368 (14%)
	1B — 1157 (43%)		
6. Other factors considered	2407 (90%)	N/A	265 (10%)

Two exposure concentrations

Guidelines suggest that the organism be exposed to at least two different concentrations of test substance, which requires experimental resources be doubled. In theory, the BCF is a net result of competing rates of uptake and elimination and therefore should not be affected by the exposure concentration unless the concentration impacts the organism in some physiological manner (e.g., enzyme saturation or toxic effects). The "two different exposure concentration" protocol is not regularly observed in the reviewed data.

Feeding regimes and growth rates

Guidelines recommend feeding test organisms a maintenance diet of known lipid and protein content that does not include any test chemical during the experiment at a rate of 1%–2% body weight per day. Remnants of food should be siphoned directly after feeding to avoid chemical sorption from the water reducing bioavailability and providing a source for dietary uptake. Feeding should not promote high growth rates and lipid accumulation. Higher growth rates can lead to lower "apparent" BCFs via dilution. Fecal egestion is an important loss route, particularly for more hydrophobic chemicals and inconsistent feeding methods will result in uncertain assessments. Metabolic biotransformation may also be affected by different feeding regimes. Feeding regimes are not always reported but it is estimated that fish are fed in approximately 70% of reviewed BCF values. Growth rates are very rarely documented, i.e., less than 5%, but should also be reported, particularly if longer exposure and elimination durations are required.

Oxygen

Guidelines suggest that the dissolved oxygen concentration must not fall below 60% of saturation. Decreased oxygen concentrations ranging from 2.5 to 9.0 mg·L^{-1} do not appear to affect the steady state BCF for chlorobenzenes (Opperhuizen and Schrap 1987). Dissolved oxygen concentrations are not regularly documented but generally range from 4.1 to 9.2 mg·L^{-1}, with both mean and median values estimated as 7.1.

Experimental design

Guidelines recommend a "flow-through" method since static and renewal designs cannot maintain a constant exposure concentration. For all fish BCF data, about 82% are derived from flow-through experimental designs and 16% are from static, semi-static or renewal methods, and those remaining

Fig. 7. An illustration of the lower "apparent" bioconcentration factors (BCF) derived from water exposure concentrations greater than the chemical's aqueous solubility (dotted vertical line; 2.5 μg/L) for 1,2-benzenedicarboxylic acid, bis(2-ethylhexyl) ester (DEHP). Confidence scoring values are also shown, i.e., 1, 2A, 2B, 3, as summarized in Table 2. BCF values (*a*) below, near, and above the limit and (*b*) "corrected" BCF estimates derived from eq. [5].
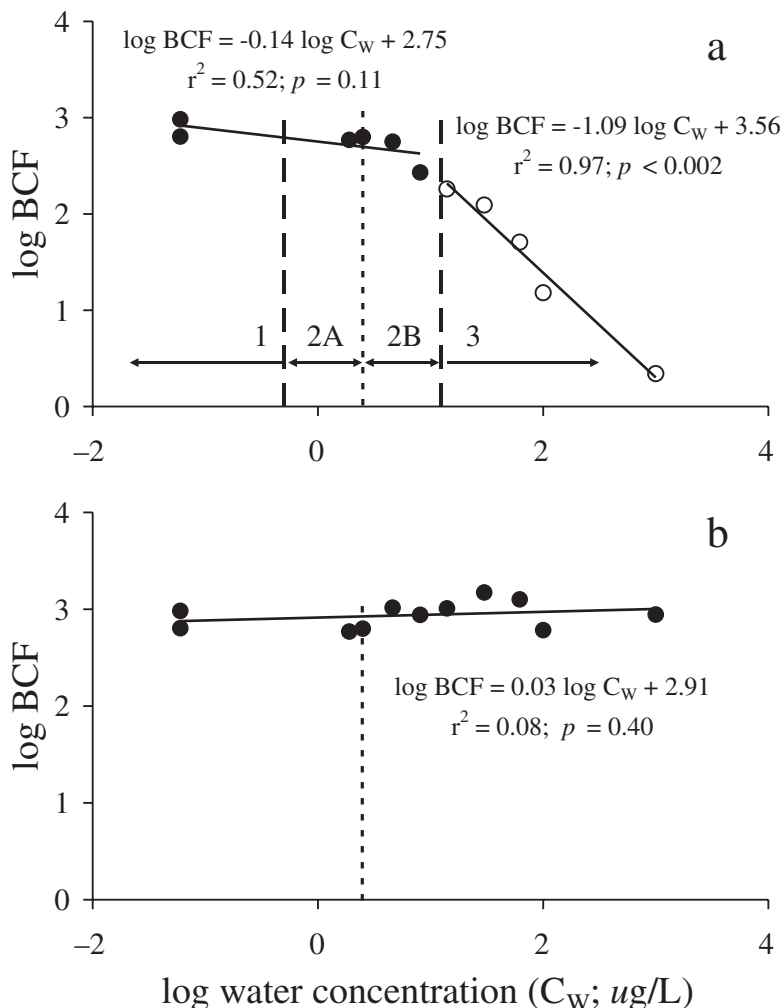
are not clearly documented. Currently, there are no standards to compare BCFs derived from different exposure systems.

Salinity

Approximately 90% of the BCFs are derived in fresh water and about 10% are in salt water. An increase in the salinity of the water (presence of electrolytes) reduces the aqueous solubility of organic chemicals. This "salting out" effect on the water solubility can be corrected using Setschenow constants. The water solubility of various organic chemicals is estimated to be reduced by a factor of about 1.36 under typical natural and artificial seawater salinity, i.e., 30%–35% (Xie et al. 1997), but there are no standards for comparing BCF data.

Molecular size

Steric hindrance, an attribute related to the cross section of the molecule, has been investigated in few studies (e.g., Opperhuizen et al. 1985; Gobas et al. 1989). A bioavailability cut-off for chemicals with minimal internal cross section of 0.95 nm or greater has been proposed; however, studies show that chemicals with greater minimal internal cross sections are available to fish via the gills and are reported in tissues (e.g., Muir et al. 1986; Gobas et al. 1989; Stapleton et al. 2004). In general, concentrations of molecules of this size and of high molar mass are technically difficult to measure, particularly in water since they are often sparingly soluble. Absorption efficiencies may be low; however, bioconcentration and bioaccumulation are dependent on relative rates of uptake and elimination; therefore, even low efficiencies may result in significant bioaccumulation at steady state, i.e., slow absorption may imply slow desorption. Molecular size and molar mass and their relationship to chemical accumulation can typically be characterized by K_{OW}.

BCF variability

The confidence criteria attempt to separate measurement uncertainty from natural variability. While the evaluated data still contains sources of error, it is important to acknowledge there are also sources of inherent variability. Some possible sources resulting in observed variability in the BCF for individual chemicals among experiments are reviewed below.

Lipid content

Lipids are the predominant media in biota to which hydrophobic substances partition (Mackay 1982; Thomann 1989; Geyer et al. 1994; OECD 1996). Variability in the BCF can, in some cases, be explained by differences in whole body lipid contents among the test animals or species investigated. For example, Fig. 8 shows the variability attributable to lipid content in acceptable BCF values for fenthion derived from different studies at similar temperatures and for fish of similar size. A two-fold increase in the lipid content results in an approximate two-fold increase in the BCF. Variability and fluctuations in lipid content are influenced by feeding regime and may affect the BCF, especially in experiments with long exposure durations and for substances with slow elimination rates. Lipid content is also an important parameter for determining the time to steady state. Lipid normalization may allow for reduced variability in inter-individual, inter-species, and inter-study comparisons. Despite the significant influence of whole body lipid content on the BCF this parameter is reported for only 36% of the total fish BCF data and 42% of the DSL data reviewed. The whole body fish lipid contents range from 0.67% to 15%, with median and mean values of 5.0% and 5.5%, respectively.

Organism size

Figure 9 demonstrates an example of the BCF variability that can be attributable to organism size for acceptable quality lipid normalized fish BCFs for two chemicals (1,2,4-trichlorobenzene and hexachlorobenzene) from different studies conducted at similar temperatures. A two-fold increase in fish wet weight results in an approximate 15%–25% increase in the lipid normalized BCFs for these chemicals. Organism size has previously been identified as an influencing factor in the bioaccumulation of organic chemicals (Hendriks et al. 2001). Organism weight is documented for approximately 58% of the total BCF fish data and 48% of the DSL data. The wet weights from reviewed fish data range from 1.9 mg to 3.7 kg with a median value of 2.0 g.

Metabolic biotransformation

Metabolic biotransformation rates are influenced by several factors such as species and the health status, gender and life stage of the animals in the test. For example, certain life-stages have greater bioaccumulation potential than others, presumably as a result of kinetic differences and in particular

Fig. 8. An illustration of the influence of lipid content on acceptable wet weight bioconcentration factor (BCF_{WW}) values for fenthion in fishes.
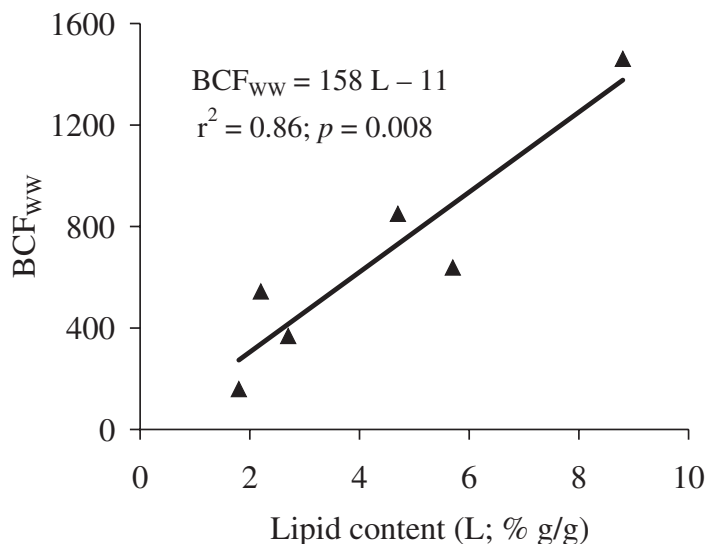
metabolic biotransformation potential. For example, the biological half-life of *p*-dichlorobenzene in rainbow trout (*Oncorhynchus mykiss*) eggs is approximately 2 orders of magnitude greater than it is in yolk-sac fry, or alevins (Galassi et al. 1982). Most of the BCF data reviewed are for juvenile and adult fish. Figure 10*a* illustrates the sensitivity of metabolic biotransformation rates on the BCF as a function of K_{OW} using the Arnot and Gobas (2004) model as described with model input parameters specified in Table 3. The BCF is more sensitive to metabolic biotransformation for higher K_{OW} chemicals because the other rates of chemical elimination, i.e., respiratory, are slower for high K_{OW} substances than for low K_{OW} substances. Even significant rates of chemical elimination via metabolic biotransformation have only minimal impacts on the steady state BCF for less hydrophobic chemicals because other loss rates are also fast, i.e., respiratory exchange.

Organic carbon in water

Higher concentrations of particulate and dissolved organic carbon in the water reduce bioavailability and the actual BCF if calculated from total water concentrations (McCarthy 1983; McCarthy and Jimenez 1985; McCarthy et al. 1985; Gobas et al. 1989; Haitzer et al. 1998). Figure 10*b* demonstrates the influence of different forms and fractions of organic carbon on the BCF for very hydrophobic substances, i.e., log K_{OW} > 6, using a model (Table 3). Figure 6*b* compares a log BCF_{fd} value of 5.44 from a freely dissolved chemical concentration to a log BCF value of 3.92 from a total water concentration for decachlorobiphenyl (log K_{OW} = 8.18). The organic carbon content in the water and the BCF_{fd} are not regularly reported in the literature.

Temperature

Opperhuizen et al. (1988) have illustrated a general trend for increasing BCF values for chlorinated benzenes with increased water temperature. Their data suggest an approximate 35%–40% increase in the BCF over a range of about 20 °C. Temperature may also affect bioenergetics and metabolic biotransformation activity, i.e., reduced activity at lower temperatures (e.g., Buckman et al. 2004). Recommended temperature ranges for BCF tests are species specific and range from 13 to 25 °C with the majority of species recommended for testing at temperatures between 20 and 25 °C, i.e., room

Fig. 9. An illustration of the influence of fish wet weight (ww) on acceptable lipid weight bioconcentration factor (BCF_{LW}) values for (*a*) 1,2,4-trichlorobenzene and (*b*) hexachlorobenzene.
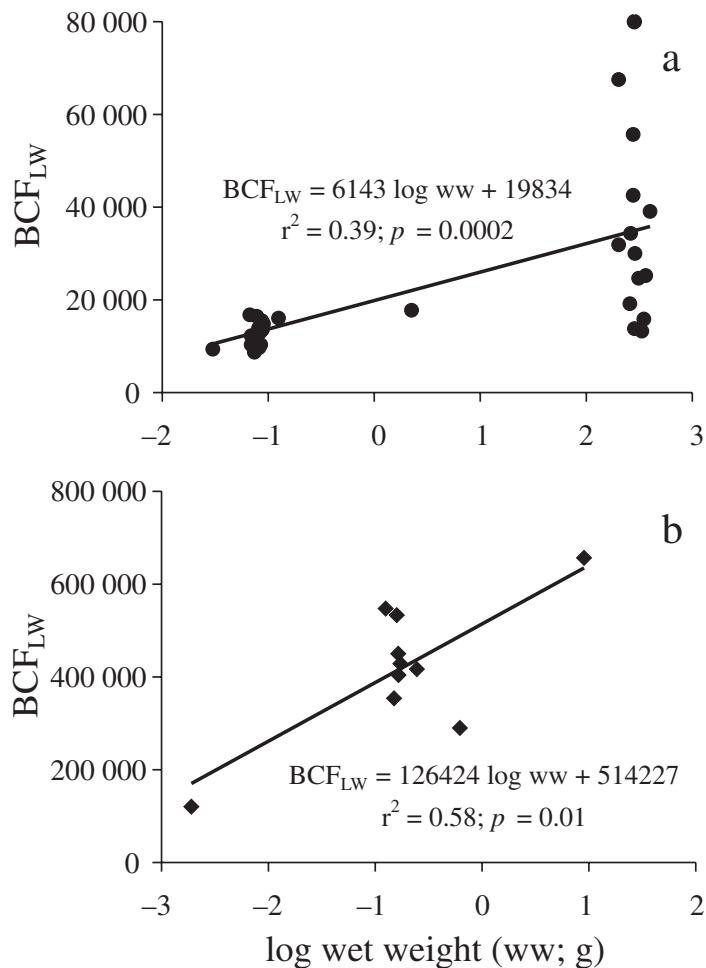

temperature and not typical environmental temperatures (OECD 1996). There are no standard methods for comparisons of BCFs measured at different temperatures. The temperature of the water is measured for approximately 68% of all reported BCF values and ranges from 4 to 35 °C with a median value of 21.0 °C.

pH

In general, but with notable exceptions (i.e., Kobayashi and Kishino 1980; Saarikoski and Viluksela 1982; Spehar et al. 1985; Stehly and Hayton 1990; McKim and Erickson 1991; Tolls et al. 1994; Martin et al. 2003), chemicals with ionization potential at relevant pH are not well studied or documented. It has been suggested that only the neutral species of the chemical is able to diffuse across biological membranes; however, evidence suggests this assumption is not always valid and measured BCFs are greater than expected from the fraction of neutral species in the water alone (McKim and Erickson 1991; Martin et al. 2003; Erickson et al. 2006*a*, 2006*b*). The pH of the water is reported for about 38% of all the BCFs and ranges from 4 to 9 with a median value of 7.4. Approximately 20% of the total BCFs reviewed are for chemicals that have the potential for ionization and the pH of the water is reported for less than 40% of these chemicals.

Fig. 10. Illustration of the effect of (*a*) metabolic biotransformation rates (k_M, d^{-1}) in fish and (*b*) concentrations of dissolved organic carbon (DOC) and particulate organic carbon (POC) in the water, on the bioconcentration factor (BCF) as a function of the octanol–water partition coefficient (K_{OW}).
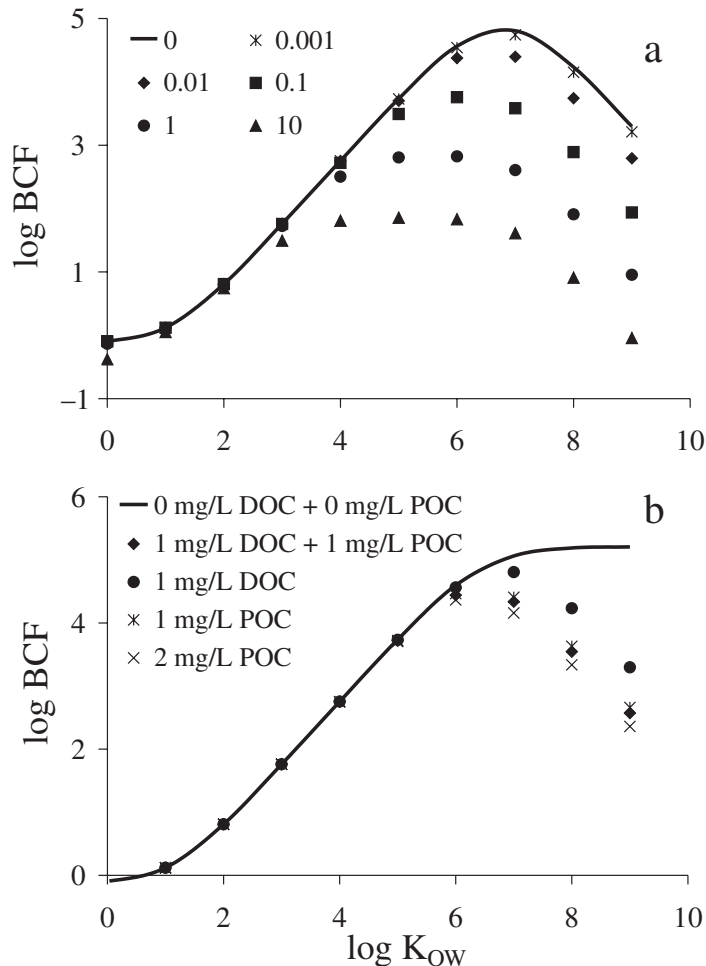

Many surfactants, or surface-active chemicals, have the potential to ionize. Bioconcentration data have been critically reviewed for 22 of these substances (Tolls et al. 1994). In general, surfactant BCF testing appears to follow a one-compartment first-order model and all classes of surfactants are readily taken up across the gill, i.e., nonionic, anionic, cationic (Bishop and Maki 1980; Tolls et al. 1994). Reliable surfactant BCF values also require a chemical concentration in the water below the critical micelle concentration to avoid micelle formation resulting in a loss of bioavailability and thus an underestimate of the actual BCF. Bioconcentration generally increases with increasing alkyl chain length, i.e., increasing K_{OW}, for the same chemical class from comparable studies (Tolls et al. 1994).

Measured field BAF data review

Figure 11 illustrates the distribution for a total of 1656 unique BAF values for 121 substances in 73 aquatic species reviewed from 39 primary literature sources. Most of these BAF data are for chemicals with a log K_{OW} range of approximately 5 to 7 and for legacy pollutants, many of which are currently subject to regulation (e.g., PCBs). Various field studies from a range of locations including

Fig. 11. Frequency of the total bioaccumulation factor (BAF) data reviewed from different organism classes for chemicals of varying octanol–water partition coefficients (K_{OW}).
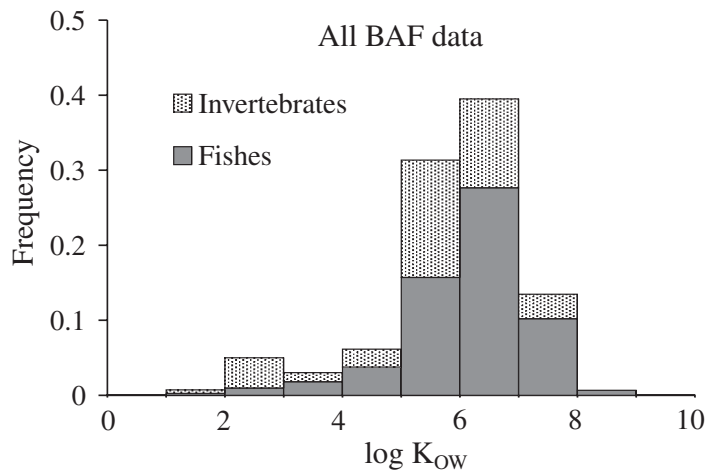
many different species have been conducted to include tissue samples; however, the number of associated BAFs is low due to a lack of concomitant sampling of the chemical concentrations in the water. Other key information relevant to bioaccumulation assessment criteria (e.g., trophic status information) is also generally not included. The reviewed BAF data, including compiled study parameters and primary reference information, are available in the supplementary information[2].

Figure 5*a* illustrates 585 BAF values reviewed for 88 chemicals from 38 invertebrate species as a function of K_{OW}. Figure 5*b* illustrates 367 invertebrate BAF values evaluated to be of acceptable confidence for 77 chemicals as a function of K_{OW}. Figure 12*a* illustrates the 1012 BAF values reviewed for 108 chemicals from 39 species of fish as a function of K_{OW}. Figure 12*b* illustrates the 912 acceptable fish BAF values for 92 chemicals as a function of K_{OW}. The BAF data considered of low confidence are usually derived from "model ecosystem" studies, many of which also use radio-labelled chemicals, or enclosure studies where organisms are subject to brief exposure periods. A strong relationship of increasing log BAF with increasing log K_{OW} is apparent in all datasets as supported by the regression statistics summarized in Table 4.

BAF uncertainty and variability

Figure 13 provides an example of the uncertainty typical in BAF measurements. These data represent fish of two general trophic levels from the same ecosystem. The 95% confidence intervals encompass approximately 4 orders of magnitude. Many of the same sources of variability in the BCF are also sources of variability in the BAF, i.e., lipid content, organism size, and temperature. Unique factors influencing BAF assessment include species and ecosystem characteristics, steady state assumptions related to spatial and temporal variability in exposure concentration, sample size, and analytical limitations.

The gender, reproductive status, life-stage or age, size, and lipid content of an organism can influence the BAF (e.g., Nichols et al. 1998; Russell et al. 1999). Organisms with higher lipid contents have a greater capacity to store hydrophobic organic chemicals and therefore can exhibit a higher BAF. Larger organisms have slower elimination rates and may feed at higher trophic levels. Trophic position is a key factor influencing the BAF as observed for legacy pollutants (e.g., Connolly and Pedersen 1988; Oliver and Niimi 1988). General trends related to trophic position such as food web biomagnification or trophic dilution may be detectable if spatial and temporal constraints from the same system are considered. For chemicals that biomagnify in the food web, the highest BAFs are observed in the highest trophic level species. Food web magnification factor studies in aquatic systems show that for chemicals that

Fig. 12. Measured bioaccumulation factor (BAF) data in fishes as a function of the octanol–water partition coefficient (K_{OW}) for (*a*) the total data reviewed and (*b*) the acceptable confidence data (see Table 4 for regression summaries).
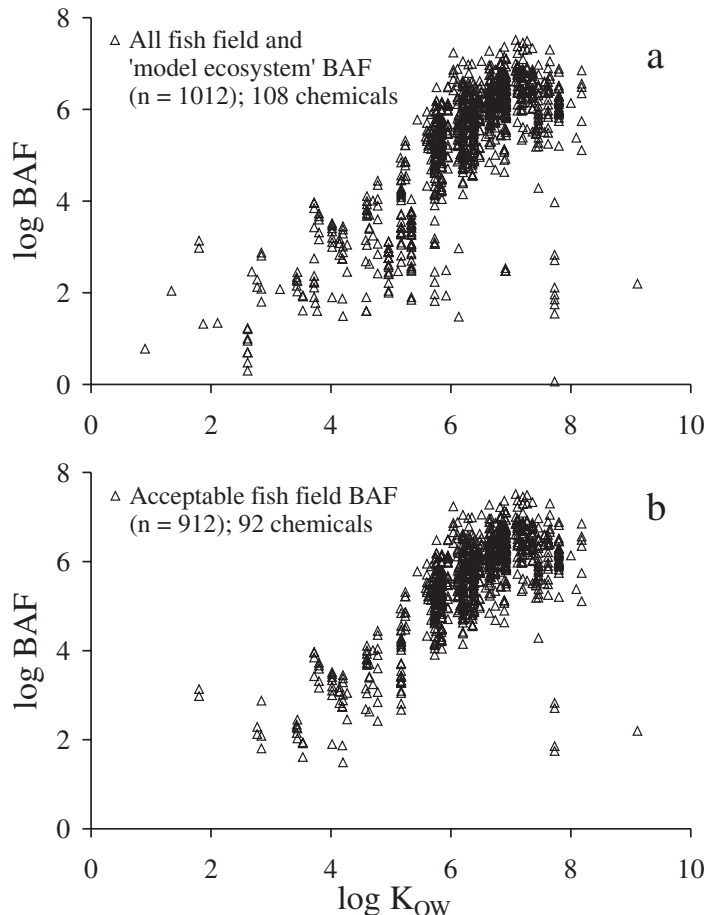

are not metabolized the average increase in lipid normalized concentrations ranges between a factor of 2 and 6.5 for each trophic position (e.g., Mackintosh et al. 2004). This can result in upper trophic level BAFs that are several times greater than lower trophic level organisms. If higher trophic level organisms possess the ability to metabolize a substance that lower level organisms do not, then trophic dilution can occur and the lower level organisms tend to have the highest BAFs.

It is difficult to compare BAFs from one food web to another because each ecosystem has unique characteristics such as water column depth, dietary preference, primary production and organic matter, trophic structure, temperature, and varying degrees of benthic interaction with the sediment (Burkhard 2003; Gobas and Maclean 2003). The degree of sediment–water disequilibria is typically variable and can produce different relationships between the BAF and trophic position among ecosystems. Burkhard (2003) provides a comprehensive analysis of field assessments outlining key influencing factors on the BAF from mass-balance model simulations. Borga et al. (2004, 2005) illustrate and discuss factors affecting the bioaccumulation and trophic transfer of persistent organic chemicals in arctic marine and fresh water food webs with analyses of empirical data.

BAF assessments assume that sampled organisms are at, or near, steady state with the ambient water; however, the natural environment is dynamic and highly variable. An obvious difficulty in obtaining

Fig. 13. Measured lipid normalized bioaccumulation factors (BAFs) in fishes (black circles; error bars are 95% confidence intervals) and Arnot–Gobas semi-empirical BAF model predictions as a function of the octanol–water partition coefficient (K_{OW}); (*a*) various upper trophic level species and (*b*) various middle trophic level species. Empirical data from (Oliver and Niimi 1988) model from (Arnot and Gobas 2003).
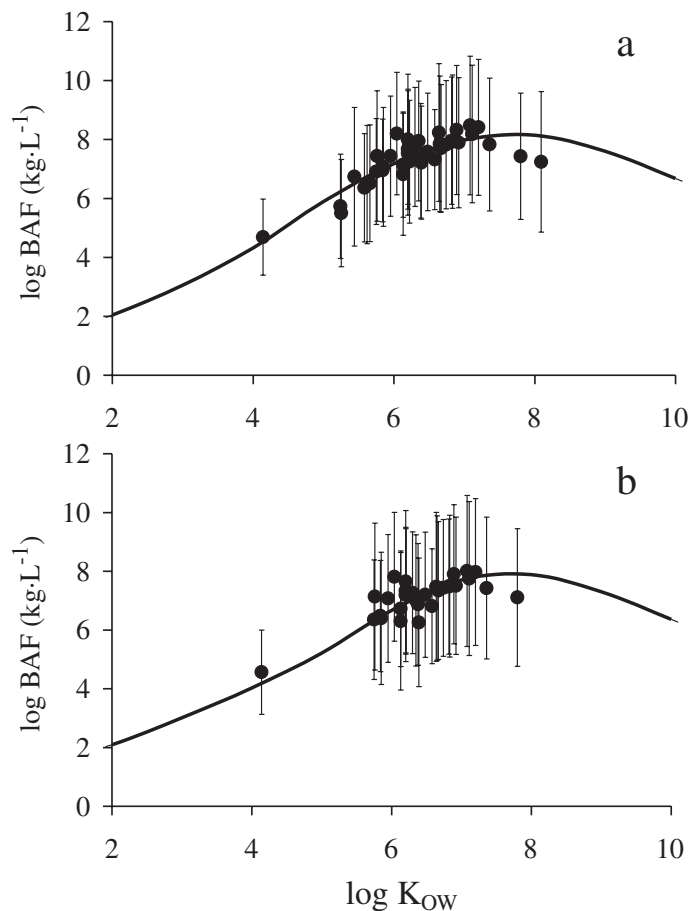
reliable bioaccumulation information from field data relates to the spatial and temporal variability associated with sampling. Organisms that are mobile may be exposed to a wide range of chemical concentrations from both the water and their diet. Variability from seasonal and geographical conditions can also occur. For example, the time of year influences lipid storage in many organisms and is also important for the general availability of food. Following periods of increased primary production there is a subsequent abundance of organic matter flowing through the food web, which results in growth and increased lipid storage. Conversely, during periods of diminished primary production, the storage capacity for hydrophobic substances may decline. Consequently, the BAF is observed to increase and decrease seasonally following the trends in storage capacity for certain chemicals.

Sample size is often limited and may not be representative of the study area or ecosystem. Sufficient statistical power and true random sampling are difficult to obtain and economic and ecological costs may be high. A collection of environmental samples that provide long-term average conditions for the area in question are recommended to obtain a representative assessment of bioaccumulation and these methods have been reviewed (USEPA 2000; Burkhard 2003). Spatial–temporal variability will contribute inherent uncertainty to the BAF assessment and thus steady state assumptions may not always be appropriate.

Table 8. A case study comparison of acceptable fish bioconcentration factor (BCF) and bioaccumulation factor (BAF) values for 5 chemicals.

Chemical (endpoint)	Log K_{OW}	n	Range log values (SD)	Median log value	Mean log value (SE)
Chlorobenzene (BCF)	2.84	2	1.13–1.34 (0.15)	1.24	1.24 (0.11)
Chlorobenzene (BAF)	2.84	3	1.81–2.88 (0.55)	2.09	2.26 (0.32)
Lindane (BCF)	3.72	33	2.16–3.32 (0.35)	2.84	2.80 (0.06)
Lindane (BAF)	3.72	4	3.43–3.97 (0.25)	3.90	3.80 (0.13)
Hexachlorobenzene (BCF)	5.73	21	3.57–4.70 (0.32)	4.26	4.12 (0.07)
Hexachlorobenzene (BAF)	5.73	26	3.91–5.74 (0.48)	4.75	4.74 (0.09)
p,p'-DDT (BCF)	6.91	5	4.17–4.72 (0.27)	4.65	4.48 (0.12)
p,p'-DDT (BAF)	6.91	7	5.84–6.62 (0.27)	6.33	6.31 (0.10)
DEHP (BCF)	7.73	6	2.43–2.98 (0.18)	2.79	2.76 (0.07)
DEHP (BAF)	7.73	2	1.86–2.83 (0.69)	2.35	2.35 (0.49)

Note: n, number of observations; SD, standard deviation; SE, standard error of the mean; p,p'-DDT, 1,1-(2,2,2-trichloroethylidene)bis(4-chlorobenzene); DEHP, 1,2-Benzenedicarboxylic acid, bis(2-ethylhexyl) ester.

In general, environmental samples in which the chemical concentration is below the analytical detection limits are generally referred to as "non-detects". There is uncertainty as to whether the chemical is actually present in these samples or if the concentration is too low to be quantified by the analytical method. The statistical treatment selected to address "non-detect" samples can have substantial effects on the derivation of the BAF. A key uncertainty for BAF assessments can be the measurement of the water concentration, which in many cases is close to the analytical detection limit. For example, to detect and measure the chemical concentration in the water 1000 L or more are often required. Different filtration methods may result in different measurements and errors are also associated with the bioavailable fraction of the chemical. BAFs reported using total water concentrations or operationally defined freely dissolved water concentrations, i.e., $<0.7~\mu$m, tend to overestimate the bioavailable concentration in the water and underestimate the actual BAF.

BCF and BAF data comparison

There are 27 chemicals included in this review with two or more acceptable BCF and BAF data to compare laboratory and field measurements of bioaccumulation. Table 8 lists summary statistics for five chemicals selected as a case study to compare BCFs and BAFs for the same chemical in fish species. For chemicals that are known to biomagnify in food webs, field BAFs can be up to almost 2 orders of magnitude greater than the BCFs from laboratory experiments that do not include dietary exposure. For example, mean BAF values for p,p'-DDT are almost 100 times greater than mean BCF values. For chemicals that are metabolically biotransformed at significant rates such differences between the BCF and the BAF are not observed. For example, the BCF and BAF values for the phthalate ester DEHP are comparable. Interestingly, certain chemicals that are not expected to biomagnify in the environment because of lower log K_{OW} values, i.e., <5, are observed to have greater BAFs than BCFs. For example, γ-HCH and chlorobenzene have field BAFs that are about 10 times greater than laboratory derived BCFs. This is believed to be a result of environmental processes increasing chemical levels in the sediment and pore water beyond thermodynamic equilibrium with the overlying water (Gobas 1993; Burkhard 2003; Gobas and Maclean 2003; Mackintosh et al. 2004). This evidence suggests that BCF values derived from the laboratory can underestimate BAFs in the environment by approximately 1–2 orders of magnitude for a range of chemicals.

Measured data and the Canadian DSL

The Canadian DSL includes approximately 11 300 discrete organic chemicals and provides a case study to review empirical bioaccumulation data for the assessment of commercial organic chemicals. Fish are typically used for the assessment of bioaccumulation (Environment Canada 2003). Included in the supplementary information[2] are 2672 BCFs for 415 DSL chemicals and 223 BAFs for 38 DSL chemicals resulting in a total of 2895 empirical BCF and BAF values from 81 fish species for 423 DSL chemicals. Thus, from all of the data reviewed there are measured fish bioconcentration and bioaccumulation data for 3.7% of the organic chemicals on the DSL suggesting that about 96% of commercial chemicals have not been measured for bioaccumulative properties in aquatic organisms. Approximately 64% of the chemicals that have been measured have two or fewer BCF and BAF measurements and 75% of the data are for chemicals with a log K_{OW} less than 5.1.

The data confidence criteria provide 1441 acceptable BCFs for 344 DSL chemicals and 130 acceptable BAFs for 23 DSL chemicals resulting in a total of 1571 BCF and BAF measurements for 350 DSL chemicals, i.e., 3.1% of the organic chemicals on the DSL. Assuming that the DSL is representative of the "universe" of current use commercial chemicals, suggests that acceptable quality empirical BCF and field BAF data are available for 3.0% and 0.2% of organic chemicals that require assessment, respectively. Approximately 76% of these 350 chemicals have two or fewer BCF and BAF measurements and 75% of the data are for chemicals with a log K_{OW} less than 5. There are only 325 acceptable BCF measurements in fish for 58 chemicals from the DSL with a log $K_{OW} > 5$, i.e., 0.5% of commercial chemicals.

Eighteen of the 350 organic chemicals identified in this review, or about 5.1%, exceed the Environment Canada BCF and BAF criteria, i.e., $\geq$5000 (Government of Canada 1999, 2000). Assuming that the chemicals that have been measured are random samples of the organic chemicals on the DSL, then approximately 600 organic chemicals on the DSL are expected to be bioaccumulative in aquatic systems according to the criteria used by Environment Canada.

BCF and BAF models

Figure 14 illustrates predictions from three representative BCF models and a BAF model as a function of K_{OW}. The Mackay linear BCF model represents thermodynamic equilibrium between the water and a 4.8% lipid content aquatic organism. BCFWIN is a bi-linear regression model, which incorporates correction factors for certain classes of chemicals (corrections are not included in the figure). The parabolic relationship between the mass-balance model BCF estimates (Arnot–Gobas BCF) and K_{OW} is a result of various processes. In the absence of metabolic biotransformation, BCFs increase from about log K_{OW} 1 to 5 as a result of chemical partitioning from the water phase to the lipid of the organism via uptake and elimination at the gills. For more hydrophobic chemicals, growth dilution and fecal egestion become more influential on the BCF as gill elimination rates are reduced. BCFs calculated from total water concentrations, as depicted in Fig. 14, also decrease with increasing log K_{OW}, i.e., >6, as a result of reduced bioavailability. BCFs calculated from freely dissolved water concentrations, or in the complete absence of organic carbon as depicted in Fig. 10*b*, do not decrease with increasing log K_{OW}, i.e., >6, unless the chemical is biotransformed.

Figure 14 illustrates that Arnot–Gobas BAF predictions for upper trophic level fish species are greater than the BCF predictions as a result of calibrating the model to empirical BAF data for poorly metabolized chemicals in upper trophic level fish. Naturally occurring processes such as dietary uptake and trophic interactions that result in BAFs being greater than BCFs are reflected in the model predictions of bioaccumulation potential. Figure 13 further demonstrates the applicability of the Arnot–Gobas BAF model calibrated to two different fish trophic levels of BAF data. There are very few BAF data available for the super hydrophobic chemicals, i.e., log $K_{OW} > 7.5$. The BAF model predictions are at steady state, which may not be reached for all super hydrophobic chemicals in all organisms in the environment.

Fig. 14. A comparison of measured and modelled bioconcentration factor (BCF) and bioaccumulation factor (BAF) values as a function of the octanol–water partition coefficient (K_{OW}) in comparison to regulatory criteria. Dotted, dashed and solid black lines correspond to the BCF and BAF criteria of 1000, 2000, and 5000, respectively.
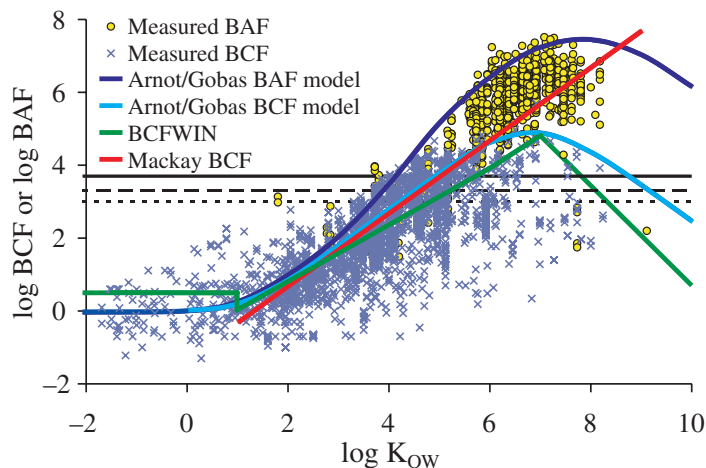
Measurements, models, and the regulatory context

Figure 14 includes the acceptable empirical fish BCF and BAF data and model estimates in relation to various regulatory criteria. Figure 14 illustrates that measured BAFs in the environment are generally greater than BCFs measured in the laboratory. This is due to dietary uptake and magnification, trophic transfer, and sediment–water disequilibra, which are represented in the BAF but not in the BCF. This means that decisions regarding the bioaccumulative nature could be influenced by the selection of the bioaccumulation descriptor, i.e., BCF or BAF.

BCF models are derived from BCF data and sources of error in BCF data can be incorporated into BCF models. The Mackay linear regression, BCFWIN (including correction factors) and Arnot–Gobas BCF models underestimate 36.2, 45.8, and 28.2% of the acceptable empirical fish BCF data, respectively. It is apparent from Fig. 14 that BCF models underestimate the large majority of available BAF data. The BCF models are not expected to estimate BAFs or to estimate field bioaccumulation potential very well because they have not been developed for that purpose.

Figure 14 shows that models vary substantially in their identification of chemicals with bioaccumulation potential as characterized by K_{OW}. This is detailed in Table 9 which lists the types of chemicals, as characterized by their K_{OW}, that are assessed to be bioaccumulative by the representative models according to various bioaccumulation criteria. Measured BCF and BAF data indicate that chemicals with a log K_{OW} between approximately 3.7 and 8.2 can exceed the bioaccumulation criteria of 5000. The Mackay BCF model identifies chemicals with a log K_{OW} greater than or equal to 5 to have bioaccumulation potential and the BCFWIN model (correction factors not included) identifies chemicals with log K_{OW} values between approximately 5.7 and 7.8 as having bioaccumulation potential according to the BCF criterion of 5000. The Arnot–Gobas BCF model identifies chemicals with log K_{OW} values between approximately 4.9 and 8.8 as having bioaccumulation potential and the Arnot–Gobas BAF model identifies chemicals with log K_{OW} values between 4.1 and 12.5 as having bioaccumulation potential according to the BAF criterion of 5000. This demonstrates that different models will assess different chemicals as potentially bioaccumulative according to the same criteria.

Errors can occur when using either measured or modelled values in the assessment of bioaccumulation potential. Type II errors, or false negatives, occur when a chemical is not identified as being bioaccumulative when in fact it is actually bioaccumulative according to selected criteria. Type I errors,

Table 9. Regulatory bioconcentration factor (BCF) and bioaccumulation factor (BAF) criteria and the approximate range of logarithms of the octanol–water partition coefficient (log K_{OW}) for chemicals identified to exceed the criteria from laboratory and field measurements and from various models.

BCF or BAF criteria (log values)	Log K_{OW} range of BCF or BAF values exceeding criteria				
	BCF or BAF measured	Mackay BCF model	BCFWIN model	Arnot–Gobas BCF model	Arnot–Gobas BAF model
≥1000 (3.0)	1.8–8.2	≥4.3	4.8–8.3	4.2–9.4	3.7–13.2
≥2000 (3.3)	3.5–8.2	≥4.6	5.2–8.1	4.5–9.1	3.9–12.9
≥5000 (3.7)	3.7–8.2	≥5.0	5.7–7.8	4.9–8.8	4.1–12.5

Table 10. Estimated probabilities of generating Type II errors in the bioaccumulation assessment of organic chemicals on the Canadian Domestic Substances List (DSL) based on available empirical data and Environment Canada bioconcentration factor (BCF) and bioaccumulation factor (BAF) criteria. Type II errors are false negatives or "misses", i.e., chemicals that have measured log BCF or log BAF values greater than or equal to 3.7, but that are not identified as bioaccumulative by the listed models.

BCF or BAF criteria (log values)	Percent probability of Type II error				
	BCF or BAF measured	Mackay BCF model	BCFWIN model	Arnot–Gobas BCF model	Arnot–Gobas BAF model
≥5000 (3.7)	0%	35.3%	70.6%	35.3%	5.6%

or false positives, occur when a chemical is identified as being bioaccumulative when in fact it is not actually bioaccumulative. Table 10 summarizes the probabilities of generating Type II errors using the different representative models according to measured acceptable BCF and BAF data included in this review for the DSL and the Canadian and Stockholm Convention BCF and BAF criteria of 5000. The likelihood of making Type II errors using the Mackay linear regression, BCFWIN (including correction factors) and Arnot–Gobas BCF models are about 35.3, 70.6, and 35.3%, respectively. The Arnot–Gobas semi-empirical BAF model can be calibrated to a selected probability of a Type II error occurrence based on available measured BAF data. According to the BCF and BAF criteria of 5000 and existing empirical data for the DSL, the likelihood of making a Type II error as a result of calibrating the BAF model to empirical BAF data of upper trophic level fish is about 5.6%. Figure 14 and Tables 9 and 10 indicate that BCF models may make a large number of Type II errors according to various regulatory criteria. In general, this review shows that the uncertainty of assessing bioaccumulation potential with BCF models is substantial.

Figure 14 further illustrates that there are chemicals (e.g., γ-HCH and hexachlorobutadiene) that have a log $K_{OW} < 5$ but a BAF ≥5000. This suggests that caution should be applied when selecting a log K_{OW} value as the only predictor of bioaccumulation potential in the absence of BCF or BAF data and models.

Recommendations

Bioaccumulation assessment

More than four decades of research and regulatory deliberation have resulted in the development of criteria and assessment methods that are now being applied to commercial chemicals at a global scale. To assist in this global assessment of commercial chemicals, this review can offer some observations and recommendations.

First, given that the bioaccumulative behaviour in the environment has been measured for so few chemicals implies that a precautionary approach is warranted in the preliminary stages of bioaccumulation assessment. This approach will minimize the likelihood of Type II errors, or "misses". Of course minimizing Type II errors increases the probability of Type I errors. Type I errors can be reduced after an initial assessment for bioaccumulation potential by bioaccumulation and biotransformation testing in the field and the laboratory and by applying professional judgment or a "weight-of-evidence" approach in assessing bioaccumulation related information.

Secondly, since current regulatory criteria strive to identify the potential of chemicals to biomagnify in food webs as a result of feeding interactions, it is important to realize that the BAF is the only current regulatory measure of bioaccumulation included in the criteria that provides direct information on the chemical's ability to biomagnify in food webs. If acceptable quality empirical BAF data are available these should be the primary source of information for the identification of bioaccumulative chemicals and for estimating exposure levels for risk assessment. The BCF is a poor descriptor of biomagnification in food webs because it is derived from laboratory experiments and does not include dietary exposure. This review shows that BAFs can be at least 1 order of magnitude greater than acceptable BCFs across a wide range of K_{OW}, i.e., log K_{OW} 1.8–8.2. Hence, BCF data should be used judiciously and should not be used as a sole predictor of bioaccumulation potential and for exposure estimates in risk assessment. BCF data can be used to estimate metabolic biotransformation rates that can then be incorporated into BAF models (Fisk et al. 2000; van der Linde et al. 2001; Arnot and Gobas 2003). For example, chemicals with metabolic biotransformation rates in fish that are greater than about 0.1 to 0.2 d^{-1} do not appear to biomagnify in aquatic food webs (Arnot and Gobas 2003). Other measures of bioaccumulation such as the BMF and the FWMF should be considered by regulatory agencies, as they are the most direct measures of the bioaccumulative capacity of chemical substances.

Thirdly, given that acceptable measured BAF data are not available for most chemicals, estimation methods must be used for bioaccumulation assessments. We recommend that BAF based QSARs are used. This review article documents a database for the development of such QSARs and includes a model algorithm, i.e., Arnot–Gobas BAF, which can be applied to the database under various levels of precaution as set by an "acceptable" probability for Type II errors.

Finally, Table 9 summarizes a series of QSARs based on available empirical knowledge useful for identifying possible bioaccumulative substances according to various regulatory jurisdictions. For example, based on Canadian and Stockholm Convention criteria, i.e., BCF or BAF $\geq$ 5000, chemicals with a log K_{OW} between approximately 3.7 and 8.2 are potentially bioaccumulative. There are very few measured BCF or BAF values for chemicals with a log K_{OW} greater than about 7.5 and it is possible that chemicals with log K_{OW} values greater than 8.2 have bioaccumulation potential in aquatic systems. There are only two chemicals with acceptable BAF measurements for chemicals with a log K_{OW} greater than 8.2 and there are few BAF measurements for chemicals with log K_{OW} values less than 5. If the log K_{OW} ranges derived from available empirical BAF data are used to assess the bioaccumulation potential of organic chemicals it is expected that the occurrence of potential Type II errors will be minimized.

Science

Paramount to reducing uncertainty in bioaccumulation measurements and improving scientific knowledge is stricter adherence to standard protocols and better documentation of the key experimental parameters as discussed in this review. There is a need to further standardize BCF testing for key influencing parameters (e.g., water temperature, feeding and growth rates, organism size and lipid content). These efforts should result in a better understanding of bioaccumulation processes and better quantification of key factors contributing to variability. More research is required for certain chemical classes, i.e., ionizable and fluorinated substances that do not predominantly partition to lipids, to better understand their partitioning behaviour and to ascertain the factors controlling their uptake and elimination.

Metabolic biotransformation rate information is vital for hazard and risk assessment. These measurements in fish and other taxa will be challenging but this science should be advanced. The development and standardization of methods and models for extrapolating in vitro rate estimates to in vivo values could provide cost and time effective means to address uncertainty and address inter-species variability as well as reduce the number of animals required for BCF tests.

The propensity for field BAFs to be greater than laboratory BCFs and the fact that there are very few comprehensive field studies for high production volume commercial chemicals warrants more field research. There is a need to develop standard guidelines for conducting and assessing field data and to critically review the endpoints obtained from bioaccumulation field studies as to the quality of the data they provide in the context of both hazard and risk assessment. BAF data for different chemical classes over a wide range of K_{OW} are critically needed. Concomitant sampling of water and sediment concentrations with tissue monitoring programs would provide more BAF data and improve understanding of field-based bioaccumulation. FWMFs can provide critical information on whether a chemical concentration is increasing or decreasing throughout the food web, and unlike BCFs and BAFs, FWMFs are not sensitive to uncertainty in measurements of the chemical concentration in the water.

Models require high quality data and better models can be developed if uncertainty in the data is reduced and if the domain of chemicals with reliable empirical data is expanded. BCF measurements of low quality should not be used for bioaccumulation assessment and model development. Currently, bio-concentration and bioaccumulation models may not adequately characterize certain chemicals, such as perfluorinated substances. Reliable physical–chemical properties for estimating partitioning behaviour, evaluating the data, and using the models are also required.

Integrating regulatory needs with scientific research should focus efforts on reducing key uncertainties in an efficient manner. Improving the knowledge of key parameters leading to higher bioaccumulation in the environment will improve the ability of regulations to effectively assess chemical hazards and potential risks.

Regulations

A complete evaluation of regulatory criteria for assessing bioaccumulation is beyond the scope of this review; however, a few key points are noteworthy. Regulations need to consider conditions that are indicative of the natural environment since this is where the risks from chemical exposure exist. For both hazard and risk assessment reliable field-based data are preferable (e.g., BAF). The BCF is not capable of meeting environmental objectives because dietary exposure and other key environmental processes that may lead to higher chemical concentrations are not included. Despite the substantial sources of uncertainty in using the BCF for assessing bioaccumulation potential it is consistently referred to by regulatory agencies (e.g., Table 1). The BCF endpoint ostensibly exists as a result of BCF data being more readily available compared to other endpoints. Since less than about 4% of the "universe of organic chemicals" have been subject to BCF evaluations, there should be serious consideration for the exploration of alternative and more robust criteria.

Criteria for bioaccumulative substances were developed to identify those chemicals that are highly bioaccumulative, i.e., have the capacity to biomagnify in food webs. High levels of bioaccumulation are generally the net result of slow depuration rates. Criteria based on the characterization of depuration rate constants (e.g., Niimi 1987) should therefore be considered. Test organisms could be exposed via the water for less hydrophobic chemicals and exposed via the diet for more hydrophobic chemicals or both and then transferred to clean water tanks to measure the rate of depuration. These measurements are subject to less experimental problems and hence are more reliable (especially for very hydrophobic chemicals). Organism size and lipid content will affect the depuration rate and other factors will also be important and would require standardization or normalization. Using depuration rates as bioaccumulation criteria may also allow chemicals that do not fit the K_{OW} paradigm very well, i.e., perfluorinated

chemicals, to be evaluated along with legacy pollutants. Controlled laboratory biomagnification factor studies should also be considered, perhaps in concert with depuration rate estimates. FWMFs may provide more conclusive empirical evidence of biomagnification and trophic dilution phenomena in the field than BAFs (Fisk et al. 2001; Hoekstra et al. 2003; Mackintosh et al. 2004); however, the development of FWMF hazard criteria requires clarification as to whether values greater than 1 should apply to the entire food web or to a sub-class (e.g., benthic invertebrates), since metabolic biotransformation rates are variable among organism classes.

Inherent variability attributed to bioaccumulation endpoints requires consideration in regulatory criteria. Variability observed in the empirical data as a result of the influence of certain key parameters (e.g., lipid content, weight, and temperature) require a means for standardization of BCF and BAF criteria. Standard scaling factors and models should be developed to an established benchmark (e.g., 2 g, 5% lipid content fish). Standards should be developed that are more representative of fish species in the environment rather than those in the laboratory, specifically those that are most likely to have higher bioaccumulative properties and that are actually consumed by humans (e.g., 2 kg, 15% lipid content). It is possible that larger, fatter organisms, other than those typically used for testing, will have greater bioaccumulation potential. Because of the large variability associated with BCF and BAF values the selection of an appropriate statistical endpoint to compare to the criteria requires consideration (e.g., mean, median, confidence limits). Discrepancies between the criteria also need further review. Figure 14 and Table 9 highlight that measured BCF and BAF values exceed criteria whereas the K_{OW} values do not for certain chemicals.

Regulations need to consider organisms other than aquatic species for hazard and risk assessment. All current criteria are based on endpoints obtained from aquatic species while many deleterious effects attributable to high levels of chemical bioaccumulation are observed in non-aquatic organisms (e.g., birds, mammals). For chemicals with low K_{OW} but high K_{OA}, aquatic organisms have a greater capacity for elimination of these chemicals than air-breathing organisms. Such chemicals have been observed to biomagnify in certain terrestrial food webs while showing no biomagnification in aquatic food webs (Kelly and Gobas 2001, 2003; Czub and McLachlan 2004). In absence of metabolic biotransformation, approximately 40% of commercial chemicals that do not biomagnify in aquatic systems have the potential to biomagnify in terrestrial food webs (Gobas et al. 2003). The main source of contamination to higher trophic level receptors is via the diet. While some of the aquatic based criteria may be able to indirectly identify bioaccumulative hazards to non-aquatic species, current criteria do not explicitly account for these inherent differences between aquatic and terrestrial organisms.

Hazard identification is an important aspect of chemical assessment, but risk is the fundamental issue regarding the quality of the environment and human health. Risk includes the quantity of chemical released to the environment, fate and transport, and toxicity as well as bioaccumulation. Pressing potential regulatory action could benefit from prioritizing scientific research for assessing those chemicals that pose the greatest risk (e.g., Arnot et al. 2006). The uncertainty in chemical risk assessment would then be reduced in concert with an improved understanding of key factors regarding bioaccumulation potential and hazard assessment.

Acknowledgement

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