Review of Existing Terrestrial Bioaccumulation Models and Terrestrial Bioaccumulation Modeling Needs for Organic Chemicals

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EDITOR’S NOTE:
This paper is 1 of 3 articles resulting from a workshop sponsored by The Health and Environmental Sciences Institute (HESI) held in January 2013 in Miami, Florida, USA. The aim of the workshop was to review current practices, identify data gaps, and provide recommendations to improve current methods and develop new methods supporting both prospective and retrospective environmental assessments of organic chemical bioaccumulation in terrestrial ecosystems.

ABSTRACT
 Protocols for terrestrial bioaccumulation assessments are far less-developed than for aquatic systems. This article reviews modeling approaches that can be used to assess the terrestrial bioaccumulation potential of commercial organic chemicals. Models exist for plant, invertebrate, mammal, and avian species and for entire terrestrial food webs, including some that consider spatial factors. Limitations and gaps in terrestrial bioaccumulation modeling include the lack of QSARs for biotransformation and dietary assimilation efficiencies for terrestrial species; the lack of models and QSARs for important terrestrial species such as insects, amphibians and reptiles; the lack of standardized testing protocols for plants with limited development of plant models; and the limited chemical domain of existing bioaccumulation models and QSARs (e.g., primarily applicable to nonionic organic chemicals). There is an urgent need for high-quality field data sets for validating models and assessing their performance. There is a need to improve coordination among laboratory, field, and modeling efforts on bioaccumulative substances in order to improve the state of the science for challenging substances. Integr Environ Assess Manag 2016;12:123–134. © 2015 The Authors. Integrated Environmental Assessment and Management published by Wiley Periodicals, Inc. on behalf of SETAC.

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INTRODUCTION
Because of concerns over the environmental behavior and health effects of man-made substances (Arnot and Gobas 2006; OECD 2012), a global regulatory initiative has emerged that involves the evaluation of thousands of commercial chemicals. This initiative involves the United Nations (UN) Stockholm Convention on Persistent Organic Pollutants (POPs) (United Nations Environment Program 2006), as legally mandated efforts in Canada (Canadian Environmental Protection Act 1999), the United States of America (USEPA 1976), the European Union (EU) (European Chemicals Agency 2007), and Japan (METI 2011). Although differences exist in the way chemicals are assessed internationally, the approaches are generally similar and include evaluations of the chemical’s persistence (P) and sometimes long-range transport in the environment, its bioaccumulation behavior (B) and its toxicity (T) with the ultimate goal to assess the actual risks of chemicals to human and environmental health.

In most countries, the bioaccumulation behavior of chemicals is assessed by using the first criteria of Annex D of the UN Stockholm Convention on POPs (United Nations Environment Program 2006), that is, the chemical’s Bioconcentration Factor (BCF), Bioaccumulation Factor (BAF), or n-octanol-water partition coefficient (K_{OW}). Annex D of the UN Stockholm Convention on POPs includes 2 additional criteria for the assessment of the bioaccumulation behavior, but these criteria are often not recognized or applied in domestic regulations. The additional criteria are evidence that...
the chemical is bioaccumulative in other species, and monitoring data in biota reveals that the chemical is bioaccumulative. According to the Convention, a chemical is bioaccumulative if any of the 3 criteria is met.

Current assessment methods are of particular relevance to aquatic organisms because the BCF, BAF, and $K_{OW}$ are descriptors of chemical distribution between biota and water (Gobas et al. 2009). Their application to assess the bioaccumulation behavior of chemicals in terrestrial organisms has been questioned, and recent publications have highlighted the importance of assessing bioaccumulation in terrestrial ecosystems (Kelly and Gobas 2001, 2003; Gobas et al. 2003; Kelly et al. 2004). Additionally, 5 of the current 21 chemicals listed as POPs by the UN exhibit a BCF in fish less than 5000 but were considered bioaccumulative by the UN because these substances were found to bioaccumulate in organisms other than fish including terrestrial air-respiring organisms (Kitano 2007). Because of the failure of aquatic organisms to represent the bioaccumulation behavior in air-breathing organisms including mammals, birds, and humans, methods for bioaccumulation assessment need to be improved for terrestrial food chains. This can be accomplished through various means including the application of controlled laboratory tests, field studies, and modeling techniques. This article focuses on the use of models as tools for assessing the bioaccumulation behavior of chemicals in terrestrial food chains. Models are particularly useful for the bioaccumulation assessment of substances having no empirical data.

The main objectives of this article are to 1) review the current state of the science on modeling the bioaccumulation of organic chemicals in terrestrial food chains, 2) identify the limitations of the existing models, and 3) provide research recommendations for improving terrestrial bioaccumulation models. The work was carried out as part of a Human and Environmental Sciences Institute (HESI)-sponsored workshop on terrestrial bioaccumulation held in January 2013 in Miami, Florida. The ultimate goal of the workshop and its reports is to contribute toward the development of a framework for the assessment of bioaccumulation in terrestrial food chains.

### TERRESTRIAL BIOACCUMULATION METRICS

Bioaccumulation is defined as “a process by which chemicals are taken up by an organism either directly from exposure to a contaminated medium or by consumption of food containing the chemical” (USEPA 2010). Bioaccumulation metrics in the terrestrial environment are often expressed using concentration ratios from laboratory or field studies. For comparability across studies, these metrics should be derived for steady-state conditions and, in the case of field studies, minimize the effect of confounding factors regarding spatial and temporal exposure concentrations. Frequently used terrestrial bioaccumulation metrics are presented in Table 1 and are briefly described in the Supplemental Data.

### EXISTING MODELS DESIGNED TO ESTIMATE TERRESTRIAL BIOACCUMULATION

Strategies for modeling the bioaccumulation behavior of chemicals in terrestrial ecosystems include models for individual species and for complete food webs (Supplemental Data; Figure S1). The following review starts with modeling approaches for individual species at the base of the food chain, proceeds to models for mammals and birds, and then, transitions to models consisting of multiple species and pathways that describe a complete food web.

| Table 1. Terrestrial bioaccumulation metrics |
|--------------------------------------------|
| Metric | Applicable taxa | Uptake route | Definition/description |
| BAF ($kg_{soil} \times kg^{-1}_{worm}$) | Terrestrial invertebrates (usually earthworms); mammals | Diverse (skin adsorption and food ingestion) | Concentration ratio between organism and surrounding medium; Kelly and Gobas (2003) defines as ratio of chemical concentrations in the organism and air; for plants, BAF is concentration ratio between plant and soil |
| BSAF ($kg_{soc} \times kg^{-1}_{lipid}$) | Soil-linked food web organisms (earthworms, insects, birds, mammals) | Exposure through soil | Concentration ratio between an organism (lipid basis) and soil (organic C basis) |
| BCF (L/kg$_{worm}$) | Plants, terrestrial invertebrates (usually earthworms) | Exposure through soil | Concentration ratio between organism (plant) and soil porewater; often lipid normalized |
| BMF ($kg_{prey/diet} \times kg^{-1}_{lipid, predator}$ or $kg_{lipid, predator} \times kg^{-1}_{prey/diet}$) | Terrestrial food webs | Exposure through diet | Concentration ratio between a predator and its prey or diet; for nonionic and ionic organics, concentrations are on a lipid and wet basis, respectively |
| TMF ($kg_{prey/diet} \times kg^{-1}_{lipid, predator}$ or $kg_{lipid, predator} \times kg^{-1}_{prey/diet}$) | Have not been widely applied to terrestrial systems | Multiple | Average BMF per trophic level over the whole food chain (or a substantial part); antilog of the slope of the regression model developed between the log-transformed concentrations of chemical in organisms and trophic level; for nonionic and ionic organics, concentrations are on a lipid and wet basis, respectively |

BAF = bioaccumulation factor; BCF = bioconcentration factor; BMF = biomagnification factor; BSAF = biota-to-soil accumulation factor; TMF = trophic magnification factor.
Plant models

Plants play an important role in the exchange of chemicals from air and soil to herbivores and play an integral role in the bioaccumulation of chemicals in terrestrial food webs (Collins et al. 2006). Organic contaminants can directly contact aboveground plant tissues (shoots) through vapor and particle deposition or below ground tissues via the roots (Collins et al. 2011). Most plant uptake models have focused on uptake either from the atmosphere (McLachlan 2011) or soil (Travis and Arms 1998) although several models have been developed that incorporate both pathways (Trapp 2007). In addition, models have been developed to specifically predict the foliar uptake and translocation of organic crop protection chemicals intentionally applied to plants, often with various formulations designed to enhance cuticle contact or penetration (Satchivi 2014). This specific model application will not be addressed in this review.

Like aquatic systems, both empirical and mechanistic bioaccumulation models have been developed. The root uptake of most xenobiotic organic compounds is passive and driven by transpiration (McFarlane 1994). Once the chemical passes through the root membrane it can be transported to other parts of the plant via xylem and phloem channels depending on its properties. Xylem channels unidirectionally conduct water and nutrients from roots to the photosynthetic sections of the plant, whereas phloem is the bidirectional flow that distributes sugars and other photosynthetic products throughout the plant (Marschner and Marschner 2012). However, within the xylem, lateral movement to adjacent cells occurs and may provide a pathway for contaminants to partition into the phloem (McFarlane 1994; Hendrix 2002; Marschner and Marschner 2012). Xylem transport rates are on the order of 10 cm/min whereas phloem transport rates are much slower, approximately 1 cm/min (Lang 1990). The contact of organics with aboveground vegetation (shoot) occurs through gas exchange and wet and dry deposition with the dominant pathway dependent on the properties of the chemical and the environmental conditions (Riederer 1990; Barber et al. 2004; McLachlan 2011). Gas exchange is thought to be most important for relatively volatile organic chemicals and faster than deposition. Dry deposition is important when the chemical in the atmosphere is sorbed to aerosols and the climate is relatively dry. Wet deposition is important for more water-soluble compounds and when aerosol sorbed compounds are trapped in precipitation (McLachlan 2011). After contact through gas exchange and deposition, the lipophilic cuticle is thought to be the main plant component governing air to shoot transfer although the stomatal route of entry might be important for some gas phase chemicals (Barber et al. 2004). Chemicals that accumulate in aboveground tissues during periods of high atmospheric concentration can be released when concentrations decrease (McLachlan 2011). Plant models can be divided into 3 categories.

**Empirical plant–soil models.** Empirical data describing chemical uptake by plant roots are generally expressed as ratios of chemical concentrations in the plant compartment of interest (e.g., shoots, roots, xylem sap) to that in the exposure medium, (soil, soil porewater, hydroponic solution) measured at the time the samples are collected (Doucette et al. 2011). These ratios, that may not reflect equilibrium or steady state, are generally referred to as BCFs or bioconcentration ratios (McKone and Maddalena 2007) but have also been named for the specific plant tissue analyzed such as root concentration factor (Briggs et al. 1982, 1983; Topp et al. 1986) and stem concentration factor (Garbarini and Lion 1986; Severtson and Banerjee 1996; Mackay and Gschwend 2000; Trapp et al. 2001; Ma and Burken 2003) or transpiration stream (xylem sap) concentration factor (Shone and Wood 1974; Briggs et al. 1982; Dettenmaier et al. 2009). Plant–soil BCF values have been used directly as models to provide estimates of plant tissue concentrations from measured exposure concentrations and have also been used as input into mechanistic models and in risk assessments. In addition, specific plant tissue BCFs have been further subdivided into fractions like lignin for wood-water BCF (Ma and Burken 2002) or the polymeric lipid fraction (cutin) shown by Chen et al. (2008) to be the dominant sorptive fraction for naphthalene and 1-naphthol on tomato and apple cuticles. Normalizing plant concentrations to an operationally defined amount of lipid has been used to account for species differences (Collins et al. 2006). However, the success of this simple approach has been varied and is limited by the lack of available plant tissue lipid data (Collins et al. 2006) and the potential influence of various other lipid-like components that exhibit varying affinities for organic contaminants (Barber et al. 2004; Chen et al. 2008). Correlations between the various plant BCFs and log $K_{OW}$ have also been developed and used to estimate plant BCF values (Travis and Arms 1988; McKone and Maddalena 2007; Inui et al. 2008). An example of one of the earliest and most widely used plant BCF–chemical properties relationship was derived by Travis and Arms (1988):

$$\log B_s = 1.588 - 0.578 \log K_{OW}$$

where $B_s$ is the ratio of concentration in aboveground plant parts (mg of compound/kg dry plant) to the concentration in the soil (mg compound/kg dry soil). The equation of Travis and Arms (1988) was developed for 29 organic chemicals using data compiled from a review of literature sources. The chemicals used in this relationship were largely neutral pesticides ranging in log $K_{OW}$ from 1 to 9, with a majority between 3 and 7. Unfortunately, Travis and Arms (1988) did not provide specific criteria for how data were selected for their analysis (Birak et al. 2001).

**Empirical plant–air models.** In these models, air–shoot BCFs are expressed as chemical concentration ratios between the plant compartment of interest (i.e., shoot, leaves) and the air measured when the samples are collected. These air–shoot chemical concentration ratios have been used to estimate plant concentrations from measured air concentration and as inputs to mechanistic models. Based on the assumption that the lipophilic cuticle is the major plant component governing air–plant interactions, simple regression models have been developed that relate air–shoot BCFs to $n$-octanol–air partition coefficients ($K_{OA}$) (Tolls and McLachlan 1994; Thomas et al. 1998; Platts and Abraham 2000; Weiss 2000) or to a combination of Henry’s Law constants ($K_{AW}$) and $K_{OW}$s (Bacci et al. 1990). For example, one simple regression model relating the plant-air BCF (ng/L of wet leaf)/(ng/L of air) to the $K_{AW}$ and $K_{OW}$ of the target chemical developed by Bacci et al. (1990) using data for 10 neutral pesticides ranging in log $K_{OW}$ from 1 to 7:

$$\log (BCF) = -1.95 + 1.14 \log K_{OW} - \log K_{AW}$$
Because the cuticle consists of several lipid or lipid-like components including cutin, cutan, and extractable waxes that exhibit different affinities for organic contaminants, incorporation of these cuticular fractional amounts is necessary to more accurately estimate air–plant BCFs (Barber et al. 2004; Chen et al. 2008).

Mechanistic plant uptake models. Mechanistic mass balance models for estimating plant tissue concentrations from chemical exposures to air and soils include one or more compartments with rates of input, output, and accumulation expressed using equations describing partitioning, degradation, and flow or diffusion rates (Topp et al. 1986; Ryan et al. 1988; Paterson et al. 1991, 1994; Trapp and Matthes 1995; Hung and Mackay 1997; Trapp 2000, 2002, 2007; Chiu et al. 2001; Ouyang 2002; Ouyang et al. 2005; Rein et al. 2011). Parameters for mechanistically modeling the uptake of organics into plants fall into 3 general categories: 1) properties of the organic contaminants, 2) properties of the plant, and 3) properties of the environment. Chemical properties include \( K_{OW}, K_{AW}, K_{OA}, K_{OC} \) (sediment–soil organic C normalized-water partition coefficient), \( p_K \) (acid dissociation constant), aqueous solubility, vapor pressure, and chemical biotransformation half-lives or rates within the plant. Plant properties include dimensions, masses and volumes of all compartments and their growth rates, transpiration rates, and flow rates in xylem and phloem, lipid-equivalent contents, and volume fractions of water and air. Environmental properties include soil and air compositions and characteristics, temperature, and relative humidity. An evaluation of 6 plant uptake models with 5 different sets of experimental data (Collins et al. 2006; UK Environment Agency 2006) concluded that the majority of models overestimated root concentrations but estimations of shoot concentrations varied. Performance was not related to model complexity and simple empirical models were as effective as multiple compartment models. The lack of high quality data for a broad range of organic chemicals likely contributed to this conclusion.

Plant models: Limitations and gaps. The lack of experimental plant uptake data collected in a consistent, reproducible manner has greatly limited model development and validation (McKone and Maddalena 2007). Approaches to estimate uptake are based on simple bioconcentration factors (Travis and Arms 1988; Bacci et al. 1990) and measured exposure concentrations or mechanistic models (Trapp 2007) that require chemical, plant, and environmental properties as input. Until standard protocols for the measurement of plant uptake data are available and used to generate consistent, high quality data, models will be only able to provide order of magnitude estimates of root uptake and resulting tissue concentrations. However, these estimates may still be adequate for some applications. Experimental data on the fate (i.e., volatilization, biological, and abiotic transformation) of organic contaminants within plants are greatly needed (Fujisawa 2002; Fantke and Juraske 2013). Dissipation half-lives were recently compiled for pesticides in food crops and other plants (Fantke and Juraske 2013), but they do not distinguish between biological and nonbiological transformation processes.

Invertebrate models

Soil invertebrates including earthworms, insects, isopods, and other soil-based organisms play an important role in the exchange of chemicals from soil to higher trophic level organisms in terrestrial food webs. Measurements of insecticide residues in earthworms and other terrestrial-based organisms from field and laboratory experiments have been made since the 1960s (Wheatley and Hardman 1968; Davis and French 1969; Davis 1971; Walters et al. 2010; Gann et al. 2015). Laboratory tests with worms are routinely performed (Belfroid et al. 1994; Belfroid, Meiling et al. 1995; Belfroid, van den Berg et al. 1995) and protocols for such tests are available (OECD-317 [OECD 2010] and ASTM E1676-12 [ASTM 2012]). Models for estimating bioaccumulation of organic chemicals by invertebrates have been developed by Connell and Markwell (1990), Belfroid, Scinen et al. (1995), Jager (1998), and Armitage and Gobas (2007) for nonionic organic chemicals. Measured log BCFs (residue in earthworms to soil interstitial water concentrations) are linearly related to the log \( K_{OW} \) of the chemicals (Connell and Markwell 1990; Jager 1998), and measured BSAFs are not related to the chemical’s \( K_{OW} \) (Belfroid, van den Berg et al. 1995). For chemicals with log \( K_{OW} \) less than 2, the Jager model approximates a BCF of 1 as the aqueous fraction of the organism’s body weight becomes the dominant phase for chemical partitioning (Jager 1998). The Jager model consistently over estimates measured concentrations by an average factor of 5.6 (Jager 1998). However, with the development of passive sampling techniques, measurements of chemical concentrations in soil may improve and better illustrate the model’s true performance.

Invertebrate models: Limitations and gaps. Invertebrate models exist for earthworms but are lacking for other soil-dwelling organisms and taxa including flying insects and isopods. The existing models (Connell and Markwell 1990; Belfroid, Scinen et al. 1995; Jager 1998) have a limited chemical domain (e.g., nonionic organic chemicals of moderate to high hydrophobicity), and data and models are needed to develop models for ionic and ionogenic organic chemicals including pharmaceuticals, pesticides, veterinary drugs, and personal care products. Most models assume negligible biotransformation of chemicals in invertebrate organisms. For substances that are biotransformed, models are needed to estimate biotransformation rates to improve estimates of bioaccumulation. In addition, the effect of “aging” and the role of organic C composition of soils on uptake and bioaccumulation in invertebrate species have been extensively studied but have been poorly represented in invertebrate bioaccumulation models. A growing area of research is the bioaccumulation of pharmaceuticals and personal care products by soil invertebrates from agricultural soils amended with biosolids and manure (Kinney et al. 2008, 2012; Pannu et al. 2012). The applicability of the Jager model (Jager 1998) to these types of chemicals needs further attention.

Avian and mammalian models

Models of the bioaccumulation behavior of chemicals in avian and mammalian species of terrestrial food webs can be divided into 2 groups: empirical and toxico kinetic models.

Empirical models. Several investigators have developed empirical BMF–\( K_{OW} \) relationships based on empirical data from
farm animal feeding studies (Kenaga 1980; Garten and Trabalka 1983). In general, BMF–$K_{OW}$ relationships from feeding studies were more variable than those for fish from water exposures (Kenaga 1980; Garten and Trabalka 1983). Factors affecting the BMF–$K_{OW}$ relationships include differences in biotransformation abilities (Ronis and Walker 1985; Wallace 1989) and respiration to air instead of water for avian and mammalian species. After these initial reports, further developments of BMF–$K_{OW}$ QSARs based on feeding studies have not been generally pursued.

**Toxicokinetic models.** Toxicokinetic and physiologically based toxicokinetic models (PBTK) provide a quantitative description of the absorption, distribution, metabolism, and excretion processes of chemicals in biota. Toxicokinetic models have been developed for several species such as cows, caribou, wolf, and herring gulls. The basic concepts, equations, parameters, and software essential for developing PBTK models for individual organisms are provided in the review by Krishnan and Peyret (2009) and further information can be found in the citations provided within their review. Considerable effort has gone into the development of physiological parameters (e.g., cardiac output, blood flows, ventilation rates, volumes of blood, liver, fat, richly perfused and poorly perfused tissues, and composition of tissues) for PBTK models for terrestrial species (rat, mouse, swine, cow, goat, etc.) (Krishnan and Peyret 2009) and compilations of these parameters are available (Mitruka and Rawlinley 1977; Arms and Travis 1988; Brown et al. 1997; Krishnan and Peyret 2009). Physiological parameters have also been developed for avian species (Nichols et al. 1995; Glaser and Connolly 2002; Drouillard and Norstrom 2003; Norstrom et al. 2007; Drouillard et al. 2012) and wolves (Gobas et al. 2003). In addition to the physiological parameters, chemical-specific partitioning relationships (e.g., fat–blood, liver–blood, and air–blood partition coefficients), tissue diffusion coefficients, absorption rates, and biotransformation rates are required for PBTK models (Krishnan and Peyret 2009). PBTK models also allow the estimations of residues in milk from lactating cows and in eggs from chickens and other avian species (e.g., gulls and swallows). The accuracy of the PBTK models depends on the accuracy of the physiological parameters and the adequacy of the parameters describing the partitioning processes among the tissues and biotransformation rates within the organism. Nichols et al. (1995) reported estimated total PCB concentrations differing by less than a factor of 3 from measured concentrations for nesting tree swallows. Norstrom et al. (2007) reported a mean ratio of estimated to measured residues in herring gull eggs of 1.0 ± 0.27 for DDE, dieldrin, mirex, and hexachlorobenzene.

Models for estimating biotransformation rates (both whole body and tissue specific) are extremely limited for terrestrial organisms. However, a fragment (i.e., molecular descriptor) based QSAR model for estimating biotransformation half-lives in humans was recently reported (Arnot et al. 2014). The approach used to develop the human half-life QSAR could be used for other organisms such as rats or mice where, potentially, enough measured half-life data exists. Development of biotransformation rate “read across” tables (Patlewicz et al. 2013) for terrestrial species should be possible for chemicals where data are available. For example, manufacturers of pharmaceuticals and pesticides are required to conduct biotransformation studies with mammals (typically rodents) before the chemical’s approval for commerce. This requirement offers an opportunity to develop better methods for read-across. The potential to “back-calculate” estimates of biotransformation rates from high quality terrestrial field data was recently demonstrated by Webster and Ellis (2012). In this approach, the biotransformation rate is the only unknown parameter in the model, and the model solution derives the estimated rate constant. The scientific literature contains numerous studies on aspects of the biotransformation of specific chemicals with birds and mammals, and the potential of these studies to provide qualitative and quantitative estimates of biotransformation rates for modeling purposes needs to be evaluated.

**Avian and mammalian models: Limitations and gaps.** For the assessment of bioaccumulation potential with PBTK models, uncertainties associated with the physiological parameters are typically small in comparison to the chemical specific parameters (i.e., partition coefficients, diffusion coefficients, absorption rates, and biotransformation rates). For the chemical specific input parameters, QSARs have been developed based on the $K_{OW}$ of the chemical except for the biotransformation rate. These QSARs are largely limited to chemicals with log $K_{OW}$ less than 5. For nonionic organic chemicals with log $K_{OW}$ greater than 5, substantial efforts are needed, and for all chemicals, the estimation of the chemical’s biotransformation rate is a major research need (Krishnan and Peyret 2009). Additionally, experimental data and QSAR submodels for estimating the dietary assimilation efficiency of chemicals in avian and mammalian species are limited. Currently, terrestrial bioaccumulation QSAR models use relationships with $K_{OW}$ (Kelly et al. 2004) or assume practically full (90%) bioavailability (Gobas et al. 2003).

Armitage et al. (2013) reported a PBTK model for bioconcentration of ionogenic organic chemicals by fish. The model was developed and evaluated using perfluoroalkyl acids and comparison to external data indicated an accuracy within a factor of 3 of estimated outcomes. However, as pointed out by Armitage et al. (2013), the estimations were highly dependent on the input parameters for the model, and they concluded that substantial laboratory work on sorption to phospholipids and biotransformation rates of the ionogenic compounds are needed to improve the model. One could argue that using perfluoroalkyl acids are not the best choice for attempting to validate a PBTK model for ionogenic compounds because the amphoteric nature of the perfluoroalkyl acids would seem to be driven more by hydrophobic and electrostatic interactions (Martin et al. 2013) rather than primarily by pH factors as is the case for the majority of other ionogenic compounds. Similar models for terrestrial species are lacking and should be developed, together with the chemical-specific parameters needed for parameterizing this model.

**Terrestrial food web bioaccumulation models**

Terrestrial food web bioaccumulation models can be divided into 2 general groups. The agricultural–foodstuffs food webs include transfer of chemical from air and soil to plants, from plants to herbivore (cow and livestock), from cow to milk and meat, followed by consumption by humans (Cullen and Connell 1994; McLachlan 1996; Douben et al. 1997; Harrad and Smith 1997). Wildlife food webs examine bioaccumulation of chemicals from air and soil up to herbivorous and carnivorous wildlife species (e.g., deer, caribou, wolves,
kingfisher) (Kelly and Gobas 2001, 2003; Armitage and Gobas 2007). These models include respiratory exchange in air breathing organisms and dietary uptake absorption. Providing estimates of numerical accuracy for model forecasts is difficult for the foodstuff based food webs because the model reports are largely focused on model development. For soil–earthworm–shrew food web (Hendriks et al. 1995; Armitage and Gobas 2007), PCB residues estimated for earthworms had mean model biases (i.e., the geometric mean of the ratio of estimated to observed concentrations for all chemicals) with 95% confidence limits (in brackets) of 1.0 (0.31–3.3) and 2.1 (0.63–6.7) for 2 sites (Armitage and Gobas 2007). For the shrews, the mean model biases were 1.1 (0.28–3.9) and 1.0 (1.12–9.1) for 2 sites (Armitage and Gobas 2007). For the Arctic food web model of lichen–caribou–wolf, estimated residues for PCBs, chlorobenzenes, hexachlorocyclohexanes, DDTs, and cyclodiene pesticides were in good agreement with the observed data, i.e., a majority of the observed data are in general agreement with the forecasted residues and most of the observed data are within the 95% confidence limits of the observed data (Kelly et al. 2007).

For humans, Czub and McLachlan (2004) developed a fugacity-based, nonsteady state, mechanistic food web model (ACC-HUMAN) to assess the bioaccumulation of PCB congeners from air, water, and soil. The model contains an agricultural food web (grass, milk cows, and beef cattle) and an aquatic food web (zooplankton, planktivorous fish, and piscivorous fish). These 2 food webs supply the food (e.g., fish, dairy products, and beef) for a lifetime exposure from birth to an adult of 80 years in age, and the model accounts for breast feeding and pregnancy exposures and losses. The estimations of the ACC-HUMAN bioaccumulation model were found to be in reasonable agreement (i.e., generally within a factor of 3) with residues measured in fish, milk, beef, and human tissues from Swedish monitoring programs.

Terrestrial food web bioaccumulation models: Limitations and gaps. Currently, the application of food web models is limited to chemicals that undergo a passive diffusion transport mechanism where lipid is a main storage compartment within the organism. Models for ionic and ionogenic chemicals including pharmaceuticals, pesticides, veterinary drugs, and personal care products that may be distributed differently in organisms as a result of nonlipid partitioning (e.g., protein binding) are lacking. Field data sets for developing and testing terrestrial food web bioaccumulation models are limited. Standardized modeling scenarios for regulatory B screening applications are unavailable and the species–taxa coverage within the existing models is limited. As noted earlier, submodels for estimating biotransformation rates and dietary assimilation efficiencies remain important areas for model improvement.

MODELS SUPPORTING TERRESTRIAL BIOACCUMULATION ASSESSMENTS AND ESTIMATION

A basic bioenergetics-based model to assess the biomagnification potential of hydrophobic organic chemical among different species, including terrestrial organisms, reptiles, and amphibians has been developed and applied by deBruyn and Gobas (2006). This model can help to identify which species in terrestrial systems are most vulnerable to bioaccumulative substances. There are also numerous exposure models used to support assessments of terrestrial bioaccumulation. In general, these models provide the exposure information to the bioaccumulation models. In some cases, fate models are integrated with the bioaccumulation models into a larger exposure and risk assessment modeling framework and in other cases, outputs from the fate models are used as input for the bioaccumulation model. The supporting fate models are used in both B categorization and risk assessments of existing and new chemicals.

Multimedia models (Table 2) enable the evaluation of the impacts of emission and environmental release patterns upon the bioaccumulation of the chemicals and ultimately, the resulting ecological and human health risks of the chemicals. Depending on the model, bioaccumulation estimations are done empirically or mechanistically for terrestrial species, and in general, these models are limited to making estimations for nonionic organic chemicals (Table 2). Data needed by these models generally include physical–chemical properties of the chemical, volume, and composition of each environmental compartment, biotransformation rates in biota, abiotic half-lives, and for some models, mass transfer coefficients between compartments. For models making bioaccumulation estimations using empirical data, the empirical data needs to be available for the chemical. For the models using mechanistic bioaccumulation methods, the chemicals should ideally reside within the domain of properties for which the model is developed and tested.

In Table 3, a series of models used in pesticide registration in the United States are listed. However, similar or analogous models are available and used in other jurisdictions. The models forecast chemical residues in air, soil, and water at the field scale, which then are used for estimation of pesticide uptake from various routes of exposure including oral ingestion of contaminated food, soils, and dust; inhalation; uptake from drinking water; and uptake by plants.

In risk assessments of contaminated sites, models that incorporate organism movement across the landscape over time, habitat preferences, and life history behaviors are occasionally used to assess exposure for terrestrial organisms. The level of detail in defining spatial and temporal scales varies widely across individual sites. In most cases, increasing accuracy of exposure information increases the accuracy of model estimations of residues in terrestrial species. Table 4 describes 4 levels of increasing spatial and temporal resolution that have been used at contaminated sites. A recent workshop report by Wickwire et al. (2011) highlights and/or reviews both the value and availability of a wide range of spatial models for performing ecological risk assessments. Bioaccumulation processes in these models are most often empirical (i.e., a database of BCFs and BAFs developed through measurements). However, for site-specific applications of models, field measurements are sometimes used in the site-specific application. For further details and specifics on individual models, the reader can consult Wickwire et al. (2011).

CONCLUSIONS AND RESEARCH RECOMMENDATIONS

Develop QSARs for terrestrial bioaccumulation

Some basic QSAR models have been developed for screening neutral, nonionic organic chemicals for their biomagnification potential in air-breathing organisms such as birds and mammals (Kelly and Gobas 2001, 2003; Gobas et al. 2003;
## Table 2. Multimedia models that interface with or include terrestrial bioaccumulation

| Model                        | Fate/exposure model                      | Bioaccumulation and biotransformation                                                                 | Species coverage                                      | Application                                          |
|------------------------------|------------------------------------------|-------------------------------------------------------------------------------------------------------|-------------------------------------------------------|------------------------------------------------------|
| GEOTOX (McKone 1989; McKone and Layton 1986) | User-defined unit world; no spatial dimension Steady-state or dynamic | Bioaccumulation: Empirical: Inputted partition coefficients for: fish BCF, milk BMF (plant to milk), beef BMF (plant to beef), plant BMF (plant to soil) Biotransformation: Empirical: Inputted parameters for biota compartment | Human exposure via ingestion, dermal, and air exposures Simple agricultural food web for species consumed by humans | Contaminated sites risk assessments Organic chemicals, radionuclides, metals |
| CalTOX (McKone 1993; McKone and Enoch 2002) | User-defined unit world; no spatial dimension Steady-state or dynamic | Bioaccumulation: Empirical: Inputted partition coefficients for 23 exposure pathways including: food BMFs, inhalation (indoor and outdoor air and particles) and dermal contact Biotransformation: Empirical: Inputted parameters for biota compartment | Human exposure via ingestion, dermal, and air exposures Simple agricultural food web for species consumed by human | Contaminated sites human health risk assessments |
| EUSES (Attias et al. 2005; Vermeire et al. 1997, 2005) | Regional distribution model (SimpleBox 3.0 model) | Bioaccumulation: Empirical: Inputted BCFs and BMFs for fish eating predators, soil invertebrate predators, and top predators Biotransformation: Empirical: Incorporated into BCFs and BMFs above | Human exposure Secondary poisoning: terrestrial species | Risk assessment of chemicals |
| ACC-HUMAN (Czub and McLachlan 2004; McLachlan et al. 2011) | User-defined unit world; no spatial dimension Steady-state or dynamic Fugacity level III | Bioaccumulation: Mechanistic: PBTK models for marine and terrestrial species, and for humans Biotransformation: Empirical: Input parameters for individual species | Human exposure via ingestion, dermal, and air exposures Agricultural and marine food webs for species consumed by humans | Risk assessment of chemicals |
| TRIM.FaTE® (USEPA 2005) | User-defined environment with spatial and temporal capabilities: Site-specific to regional scales Steady-state or dynamic | Bioaccumulation: Empirical: Computed transfer factors for all terrestrial species from ingestion rates, chemical assimilation efficiencies, and compartment properties (e.g., biomass density per unit area in spatial unit) Biotransformation: Empirical: Inputted parameters for biota compartment | Complete terrestrial food web: Plants, soil detritivores, and all exposure routes to terrestrial vertebrate wildlife | Deriving exposure and residue in biota data for ecological and human risk assessment |
| RAIDAR (Amot and Mackay 2008; Amot et al. 2006, 2010) | Defined unit world Mass balance Steady-state Fugacity level II (equilibrium in air, water, soil, and sediment) or level III (disequilibrium in air, water, soil, and sediment) | Bioaccumulation: Mechanistic: PBTK models for every vertebrate species; empirical regression and equilibrium partitioning models for plants and invertebrate species Biotransformation: User-defined vertebrate half-lives | Complete food webs: Aquatic: plankton, invertebrates, forage and piscivorous fish, seals and whales Terrestrial food web: foliage vegetation, root vegetation, invertebrates, herbivore, carnivore, avian omnivore, avian scavenger Agricultural: swine, beef and milk cows, milk, poultry, eggs, and humans. | Exposure and risk assessment of chemicals |

EUSES = European Union system for the evaluation of substances; RAIDAR = risk assessment identification and ranking; TRIM.Expo = TRIM exposure-event module; TRIM.Risk = TRIM risk characterization module.

*Models listed here require some iteration of the following input parameters:
- Physical-chemical properties of the chemical of interest, e.g., MW, $K_{OW}$, $K_{OC}$, $K_{OC,p}$, aqueous solubility, and H
- Environment and biological parameters
- Loading/source terms for the chemical of interest
- Abiotic transformation half-lives for the chemical in compartment of the environment

TRIM.FaTE outputs are designed to pass directly into TRIM.Expo that estimates human exposure from inhalation and ingestion exposures. TRIM.Expo outputs are designed to pass directly into TRIM.Risk for hazard assessment for both human and ecological endpoints.
Czub and McLachlan 2004; Armitage and Gobas 2007; Kelly et al. 2007; McLachlan et al. 2011) when the biotransformation rates of the chemicals are negligible. These QSARs are based on the $K_{OW}$ and $K_{OA}$ of the chemical. Research needed for terrestrial organisms includes the development of data and resulting QSARs for estimating the rate of biotransformation and dietary assimilation efficiencies for all levels of the terrestrial food web. Additionally, QSARs are needed for chemicals beyond nonionic organic chemicals.

**Expand species coverage**

Although several species specific submodels of the larger terrestrial bioaccumulation conceptual model (Supplemental Data; Figure S1) have received attention, others have not. For example, bioaccumulation models for mammalian species such as rats, mice, shrews, cows, caribou, wolves, and humans are available for certain classes of chemicals and can be further improved to increase their applicability to a larger domain of chemicals (e.g., ionizable and protein binding substances). Also, some bioaccumulation models exist for avian species such as swallows and herring gulls. However, chemical bioaccumulation models for terrestrial insect species are virtually absent despite the crucial role insects play in maintaining ecosystem function and transfer of contaminants in food webs. Bioaccumulation models for soil invertebrates are also lacking with models for annelids being the exception. The lack of adequate consistency and reproducibility of experimental data on chemical uptake in plants has limited the development and testing of plant bioaccumulation models. Research is also needed on the development of models for

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**Table 3. Pesticide models that interface with or include terrestrial bioaccumulation**

| Model      | Processes                                                                 | Inputs                                                                 | Outputs                                                                 | Application                                                                 |
|------------|---------------------------------------------------------------------------|------------------------------------------------------------------------|------------------------------------------------------------------------|----------------------------------------------------------------------------|
| AgDrift    | Estimates spray deposition patterns from ground and/or aerial pesticide applications | Spray method and its properties (e.g., droplet size, boon height, flight width, temperature, humidity, wind speed ...), application rate | Field scale Concentrations of pesticide in droplets                      | Inputs to plant B models                                                   |
| SCREEN3    | Estimates volatilized chemical in air on or adjacent to field site        | Field scale Concentrations in air Screening level                       | Estimate exposure via inhalation                                        |
| PERFUM     | Estimates volatilized chemical in air on or adjacent to field site        | Scenario type, meteorological data, field dimensions, application rate and number, toxicity data | Field scale Concentrations in air Refined exposure estimates            | Estimate exposure and risks via inhalation                                 |
| T-REX      | Estimates pesticide concentration from direct deposition on avian and mammalian food items | Application rate, foliar dissipation half-life, application interval, total number of applications per year, toxicity data | Field scale Exposure from consumption of contaminated grasses, plants, insects, seeds, and fruits | Risk estimation based on dietary residue concentrations (foliar spray) |
| T-HERPS    | Estimates exposure from direct deposition to terrestrial reptiles and amphibians from pesticide use | Application rate, foliar dissipation half-life, application interval, total number of applications per year, toxicity data | Field scale Exposure from consumption of contaminated small mammals and amphibians, grasses, plants, insects, seeds, and fruits | Risk estimation based on dietary residue concentrations |
| PRZM       | Surface water model that simulates chemical movement in soil within and immediately below the plant root zone | Regional climatological information, hydrology and erosion parameters, crop characteristics including emergence and harvest dates, pesticide properties and application rates, and soil characteristics, soil horizon and chemical properties | Field scale Pesticide fate and transport into crop root zone, runoff/eroded soil from fields and uptake by plants | Linked with other environmental models (e.g., EXAMS) for aquatic ecosystem fate and transport. |
| KABAM      | Estimates potential bioaccumulation of hydrophobic organic pesticides in freshwater aquatic food webs and subsequent risks to mammals and birds via consumption of contaminated aquatic prey | Ecosystem parameters, pesticide properties, and concentrations in water and sediment interstitial water | Water body scale (e.g., pond or lake) Bioaccumulation metrics, residues in tissues of aquatic organisms | Risk estimation based on dietary residue concentrations |

**EXAMS** = Exposure Analysis Modeling System; **KABAM** = $K_{OW}$ (based) Aquatic BioAccumulation Model; **PERFUM** = Probabilistic Exposure and Risk Model for Fumigants; **PRZM** = Pesticide Root Zone Model; **T-HERPS** = Terrestrial Herpetofaunal Exposure Residue Program Simulation; **T-REX** = Terrestrial Residue Exposure.
insects, other soil invertebrates, amphibians, and reptiles. Although there are studies investigating bioaccumulation of pesticides and other substances in amphibians and reptiles, there are no bioaccumulation models specific for insects, amphibians, and reptiles.

**Expand field data sets**

Model development and validation is entirely dependent on having high quality field data sets. Field data are especially needed for ionic and ionogenic chemicals such as pharmaceuticals, veterinary drugs, surfactants, and personal care products. One potential area of relatively untapped and underused field data for legacy POPs are sites having high levels of contamination, for example, Superfund sites, where all or nearly all of the data are unpublished. These data are used in making site-specific cleanup decisions. This “gray literature” contained in government files and site assessment reports is often extensive in terms of species coverage, and making this data broadly available would benefit efforts on bioaccumulation in terrestrial systems beyond the sites of interest.

**Expand model domains to include “challenging substances”**

As mentioned previously, existing bioaccumulation models are almost exclusively based on passive diffusion mechanisms of chemical uptake and loss. These models cannot address active transport processes or binding mechanisms observed with chemicals outside of the nonionic organic chemical class, for example, perfluorinated compounds and other ionic and ionogenic chemicals. Additional mechanistic information on these processes and how to accurately model them are needed. Bioaccumulation models also require input of measured or estimated chemical specific properties such as $K_{OA}$, $K_{OW}$, $K_{AW}$, $K_{OC}$, $pK_a$, and log $D$ (the n-octanol-water distribution coefficient for ionizing substances). For some chemicals lacking measured values, estimations of these properties fall outside the boundary conditions of the training set of chemicals used to develop the estimation method. As a result, extrapolations beyond the training set values potentially introducing large uncertainties in the accuracy of the estimations (i.e., garbage in is garbage out). Measurements of these physical–chemical properties for chemicals beyond the training sets would enable the development of new QSARs and improved accuracy in estimations.

**Expand model verification and performance**

Analysis of model performance is a key element of model development, and field measurements play an important role in this process (Veltman et al. 2007). Although a model performance analysis is not always possible due to a lack of appropriate data, a model verification process can be carried out to confirm that the model conforms to basic principles (Burkhard et al. 2012). For screening and lower tier models, a comparison of model outcomes and experimental laboratory measurements of these physical–chemical properties for chemicals beyond the training sets would enable the development of new QSARs and improved accuracy in estimations.

**Table 4. Levels of spatial and temporal resolution used at contaminated sites**

| Level | Space | Time |
|-------|-------|------|
| 1     | Concentration is represented by maximum of all samples. Mobile or sessile receptor is exposed at the point of maximum concentration. | Maximum concentration is static. Body burden estimated at steady-state. |
| 2     | Concentration represented by site-wide average (or upper bound on this average). Mobile or sessile receptor is exposed to a site-wide average concentration. Mobile receptors are assumed to have random, unrestricted access to entire site (i.e., they are moved “statistically” over the site). | Average concentration is static. Body burden estimated at steady-state. |
| 3     | Concentration represented by site-wide average (or upper bound on this average). Mobile or sessile receptor is exposed to a site-wide average concentration, but exposure is prorated by an “area use factor” based on size of site relative to receptor home range. Mobile receptors are assumed to have random, unrestricted access to entire site (i.e., they are moved “statistically” over the site). Sessile receptors are exposed to site-wide average concentration. | Average concentration is static. Body burden estimated at steady-state. |
| 4     | Concentration is estimated at multiple points (nodes) or as a surface (contours) across the site. Mobile receptor is assumed to move across site (and beyond) guided by movement rules (random walk), directed (searching, sensing), constrained (habitat, physical barriers), etc. Exposure of mobile and sessile receptors is a function of the colocation of a receptor and a concentration (that may itself vary through time). | Concentration can vary through time in response to chemical (e.g., decomposition), biological (e.g., microbial degradation), or physical (e.g., groundwater flow) processes external to the receptor (transport and fate modeling). Exposure of mobile receptors is also a function of the frequency and duration of its colocation with a concentration. Body burden can vary through time in response to changing exposure concentrations and dynamic uptake/biotransformation/fate kinetics internal to the receptor. May include seasonal changes in a receptor’s presence at a site (hibernation, migration) and in availability of specific prey/forage items (i.e., seasonal shifts in diet composition). |

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principles for QSAR models (OECD 2007). Models developed using the QMRF are more easily accepted by regulatory agencies and by standardizing bodies such as the Organization for Economic Cooperation and Development (OECD).

**Improve information transfer among field, laboratory, and modeling assessments**

Better coordination among field, laboratory, and modeling efforts is needed to improve bioaccumulation screening and risk assessment tools for terrestrial ecosystems. Having all 3 efforts work on common chemicals of interest and potentially the same or closely related organisms would allow data from one effort to guide or inform the other efforts. For example, laboratory-derived toxicity studies in rats are fairly common and can likely be modified with minor effort to collect information on bioaccumulation. Such data can be used in models describing uptake and elimination in rats such as those developed to model the behavior and effects of pharmaceutical drugs. Rats and other rodents play an important role in terrestrial food webs and may also be a species that can be collected at field sites. Developing collaborations among field, laboratory, and modeling efforts, through workshops, training courses, and/or research initiatives, is critical for creating the synergy needed for improving terrestrial bioaccumulation tools for current and emerging substances.

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**SUPPLEMENTAL DATA**

Table S1. Terrestrial bioaccumulation metrics

**Figure S1.** Model terrestrial food web

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