

Future Needs and Recommendations in the Development of Species Sensitivity Distributions: Estimating Toxicity Thresholds for Aquatic Ecological Communities and Assessing Impacts of Chemical Exposures

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ABSTRACT

A species sensitivity distribution (SSD) is a probability model of the variation of species sensitivities to a stressor, in particular chemical exposure. The SSD approach has been used as a decision support tool in environmental protection and management since the 1980s, and the ecotoxicological, statistical, and regulatory basis and applications continue to evolve. This article summarizes the findings of a 2014 workshop held by the European Centre for Toxicology and Ecotoxicology of Chemicals and the UK Environment Agency in Amsterdam, The Netherlands, on the ecological relevance, statistical basis, and regulatory applications of SSDs. An array of research recommendations categorized under the topical areas of use of SSDs, ecological considerations, guideline considerations, method development and validation, toxicity data, mechanistic understanding, and uncertainty were identified and prioritized. A rationale for the most critical research needs identified in the workshop is provided. The workshop reviewed the technical basis and historical development and application of SSDs, described approaches to estimating generic and scenario-specific SSD-based thresholds, evaluated utility and application of SSDs as diagnostic tools, and presented new statistical approaches to formulate SSDs. Collectively, these address many of the research needs to expand and improve their application. The highest priority work, from a pragmatic regulatory point of view, is to develop a guidance of best practices that could act as a basis for global harmonization and discussions regarding the SSD methodology and tools. *Integr Environ Assess Manag* 2016;12:000–000. © 2016 SETAC

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INTRODUCTION

Chemicals are an integral element of human society and their production, use, and potential emissions are expected to grow in the future (United Nations Environmental Programme 2013). This implies that continued attention to the safety and evaluation of chemicals is warranted for environmental protection (e.g., environmental standards, risk assessments), management (e.g., deciding what actions are required), and remediation (e.g., deciding what level of intervention or cleanup is acceptable or needed). A critical step in the assessment and control of chemicals in the environment is to understand their hazards and to estimate tolerable thresholds

of risk. Various models and approaches are available to estimate chemical hazard levels, including species sensitivity distribution (SSD) modeling. An SSD is a probability model of the variation of species sensitivities to chemical exposure. SSDs are increasingly used in ecological risk assessment and the derivation of environmental quality standards because they can be used to develop community-level thresholds and have advantages over deterministic assessments that rely solely on application (uncertainty) factors applied to the most sensitive individual toxicity data point (Organization for Economic Cooperation and Development 1992; Wheeler et al. 2002; European Centre for Ecotoxicology and Toxicology of Chemicals [ECETOC] 2014, wherein Posthuma provides a review). Some of the advantages of SSDs over application factors (AFs) include:

- SSDs make full use of the knowledge on the toxicity of a substance.

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- SSDs are explicit in expressing uncertainty.
- The shape and form of the SSD can inform the assessor about the behavior of the substance (e.g., steep slopes are often associated with specific modes of action).
- SSDs are probabilistic and as such are aligned with the paradigm of risk assessment as a probabilistic science (vs deterministic predicted no effect concentrations [PNECs]).
- The extrapolation process is flexible in that the level of protection can be defined relative to the percent of species potentially affected.

Management of chemicals in the environment usually includes comparison of expected exposures to a critical effect limit such as a PNEC for ecosystems (European Chemicals Agency [ECHA] 2008). Concentrations less than the PNEC are considered to have a negligible potential effect on the structure or function of an exposed ecosystem. When sufficient data are available, a PNEC may be estimated as a low percentile of an SSD (Van Straalen and Denneman 1989). PNECs are most commonly deterministic and estimated by applying an AF to the data derived from the most sensitive species tested (the actual AF being a function of the type of data, acute or chronic, and the number of species tested). When PNECs are estimated using SSDs, the extrapolation of laboratory test results to protect field populations and communities usually employs lower AFs (generally 1–5), but being somewhat flexible as to the assignment of the final AF to account for the biological diversity present and the statistical qualities of the SSD being considered (ECHA 2008). In this way, pragmatic implementation of SSDs as a regulatory tool often combines the probabilistic toxicity result (usually a small percentile from the toxicity distribution) with an AF (a deterministic approach). If the toxicity data set is sufficiently robust (e.g., it is built from tests on a large number of diverse species), the regulatory use may simply be the probabilistic toxicity result. In either case, these are based on environmental policy considerations for the regulatory jurisdiction performing the assessment.

Species sensitivity distributions have an established role in the assessment and management of risks posed by chemicals, and major developments around the world have provided relevant novel insights into their development and application. The formal adoption of SSDs for the derivation of environmental thresholds dates back to scientific and policy milestones of 1985 in the United States and 1989 in Europe (Stephan et al. 1985; Van Straalen and Denneman 1989). In 2001, SSDs were evaluated intensively for the derivation of European environmental quality standards (European Commission [EC] 2001). In 2002, a comprehensive overview of the principles and practices of SSD use on an international basis was made (Posthuma et al. 2002), followed by a recent updating review by Del Signore et al. (2016) on the use of SSDs with particular focus on environmental quality criteria. The latter review confirms and expands on our analyses, further underpinning the conclusions as well as the needs recommendations for future developments and use of SSDs.

In the present study we summarize the major findings of a workshop sponsored by the ECETOC and the UK Environment Agency held in February 2014 in Amsterdam, The Netherlands (ECETOC 2014). Forty experts from academia, business, and government reviewed the state of the science for estimating toxicity thresholds for aquatic ecological communities using SSD modeling and considered advances in

statistical, ecotoxicological, and ecological science applicable to SSDs that have occurred since a similar workshop was held in London in 2001 (EC 2001). New approaches or refinements to current applications of SSD modeling were evaluated against current methods in which SSDs are used in the context of environmental protection and management. The aim of the present study is to provide an overview of the findings, conclusions, and recommendations of the workshop, to derive future recommendations given the state of the science and the needs for decision support.

DERIVATION OF SPECIES SENSITIVITY DISTRIBUTIONS

Predictive risk and retrospective impact assessment of chemicals requires estimation of the toxicity thresholds of chemicals for aquatic communities as an integral aspect of defining environmental hazard. Of the available tools used in hazard and risk assessment, SSDs provide a particularly informative approach because they explicitly relate the intensity of chemical pressure (e.g., the concentration) to ecological impacts (the proportion of species at risk). Currently, hazard is most frequently predicted using concentration–effect data from single-species laboratory toxicity tests that measure effects on individuals and populations. Typically, responses of individuals include survival (applicable to acute and chronic testing), growth, and reproduction endpoints for invertebrates, fish, amphibians, and macrophytes. Population responses such as growth rate for microinvertebrates, bacteria, algal, and cyanobacteria tests are used in acute and chronic exposures. However, protection goals are generally broader than those covered by endpoints derived from laboratory toxicity testing and focus on populations, communities, and ecosystems. There is growing interest in moving from hazard levels derived from individual toxicity tests to the use of SSDs, which can better be used to estimate potential hazards to communities. Note that although SSDs include multiple species, they are the compilation of individual species responses and typically do not include interspecific interactions (predation, competition) or ecosystems processes (nutrient cycling, energy flow).

The statistical methods and underlying scientific foundation supporting the use of SSD models and the versatile use of these in environmental protection, assessment, and management were reviewed by Posthuma as discussed at the workshop and reported earlier (ECETOC 2014). In brief, the SSD method assembles single-species toxicity data to predict a hazardous concentration (HC) that affects a certain percentage (p) (HC_p) of all the species in a distribution, or to estimate the toxic pressure, expressed as the potentially affected fraction (PAF) of species, exerted on an assemblage from an observed or expected exposure concentration. SSDs can be constructed using either acute or chronic test data, depending on data availability, and they can be related to the protection goal. In comparisons among chemicals, SSDs derived from ecotoxicity data can have different positions (intercept) and shapes (slope), which has implications for the HC_p of a chemical and the toxic pressure of an environmental sample. The higher the HC_p of a chemical, the lower is its ecotoxic potential to induce impacts. Greater toxic pressure is indicated by a larger PAF for a contaminated sample. The potential for expected impacts for tested species and impacts on aquatic communities is therefore assumed to be greater when toxic pressure increases.

SSDs are constructed with the aim of predicting acute or chronic toxicity, although these are usually dealt with separately. Single-species data for acute toxicity (expressed as median lethal concentration or median effective concentration [EC50]), or estimates for chronic effects (expressed as no-observed-effect concentrations [NOECs], chronic values [defined as the geometric mean of the NOEC and lowest observed effect concentration], and effective concentrations, 10%) for several species are fitted to 1 or more cumulative distribution functions followed by evaluation and choice of the best model. The cumulative distribution function is often assumed to be log-normal or log-logistic (Awkerman et al. 2013; Posthuma et al. 2002). Other distributions have been used and can also have utility (Australian and New Zealand Environment and Conservation Council and Agriculture and Resource Management Council of Australia and New Zealand 2000; Warne et al. 2015). A typical approach uses the 5th percentile of the distribution of acute or chronic effects to derive toxicity thresholds or environmental quality criteria that should ensure that the specified level of protection is achieved. The estimation of the toxic pressure (PAF of species) given an ambient exposure allows the use of any endpoint (e.g., NOEC, effective concentration, 10%, EC50, median lethal concentration), depending on the expected level and duration of exposure. Similarly, the estimated toxic pressure can yield assessment outcomes such as a PAF_{NOEC} , or a PAF_{EC50} that specifies the fraction of species exposed greater than their NOEC or EC50, respectively. For example, an ambient exposure might predict that 50% of species are exposed at greater than their NOEC while at the same time 20% of species are exposed at greater than their EC50.

One of the principle advantages of probabilistic SSDs over deterministic AFs is the opportunity to express uncertainty in the point estimate (HC_p) as additional information for the risk assessor to judge the utility of the estimated threshold. Typically, the fifth percentile Hazardous Concentration (HC5) will be accompanied by a confidence limit that conveys knowledge of the shape of the statistical distribution of toxicity values and their variance. By addressing critical data that appear to strongly influence the shape of the distribution (often at the tails of tolerance and sensitivity), the risk assessor can understand the impact of particular data on the HC_p and the confidence interval around it.

ECOLOGICAL, STATISTICAL, AND REGULATORY CONSIDERATIONS

Because the sensitivity of all the species that might be exposed to a chemical cannot be known, extrapolation needs to be done from the data available. ECETOC (2014) discussed that scientifically sound extrapolation approaches based on SSDs to derive toxicity threshold concentrations should provide a more useful and transparent assessment of risks than a deterministic approach using generic factors applied to single-species aquatic toxicity test data. The SSD methodology is a valuable regulatory and management tool because it can provide greater insight into the potential effects of a particular level of exposure compared with the deterministic AF method, enabling better problem definition and decision support.

Regulatory tools such as SSD modeling are useful if they strike a balance between being overly cautious and under-protective. Being overly protective can lead to unnecessary mitigation costs and stifle innovation, whereas underprotection may result in environmental degradation (ECETOC

2014). A prospective risk assessment conducted in the context of environmental protection needs to establish that there will be acceptable risk at the criterion concentration (e.g., PNEC, environmental quality standard, or regulatory acceptable concentration). In contrast, retrospective impact assessment uses diagnostic tools to identify the cause of existing adverse effects, using SSDs to quantify expected chemical impacts compared with other stressors (De Zwart et al. 2006). When sufficiently large data sets are available, the risk for errors is reduced, while uncertainty on expected protection or impact prediction declines. In such cases, SSD modeling provides a mechanism for quantifying the relationship between chemical pressure and impact that takes account of uncertainty caused by differences in sensitivity between species. When data sets are small, uncertainty is greater and consequently the more cautious deterministic approach may be more appropriate. That is, the criterion is derived from the available data combined with an AF. Under conditions of small data sets (e.g., few species tested) or lower-quality data, a higher AF is implied and appropriate for the deterministic assessment. Similarly, the size of an assessment factor applied to an SSD will vary (minimum of 1) according to the uncertainty in the hazard estimation.

Requirements for consideration of an SSD approach vary across regulatory jurisdictions (e.g., by national regulatory authority), regulatory frameworks for specific compound classes (e.g., pesticides covered under US Federal Insecticide, Fungicide, and Rodenticide Act or European Union Plant Protection Products Directive (PPP) D [1107/2009]), or intended use in an assessment framework (e.g., water quality standards or chemical-specific risk assessments). Table 1 provides an overview of representative (not exhaustive) considerations in several frameworks. It is interesting to note the variation in species coverage, treatment of multiple data on the same species used as SSD input, and application of statistical principles that are applied. The most recent guidances on SSD use for assessing hazards of chemicals (ECHA 2008) and plant protection products (European Food Safety Authority 2013) are not surprisingly the most complete across all the facets to be considered. These guidances are consistent with discussions in Europe from 2000–2008 and form the basis of subsequent national and international guidance used in setting water quality criteria as well (e.g., Canadian Council of Environmental Ministers 2007; EC 2011).

ECETOC (2014) cautioned that continued validation of predictions made using SSDs against a reference tier, such as field and mesocosm data, is required to ensure that a threshold derived from an HC_p (sometimes coupled with an application or safety factor) or a PNEC has ecological relevance (see also Versteeg et al. 1999; Posthuma et al. 2002). A new development is the advent of the SSD approach applied to field data rather than field data being regarded as a separate line of evidence (Kwok et al. 2008). The results of any extrapolation process (including SSDs) should always be critically assessed based on all available knowledge on the substance and related substances, such as their mode of action and other lines of evidence including field and mesocosm data. Use of the SSD methodology should yield more generally conservative estimations of hazard (i.e., lower predicted effect concentrations), and thus more readily acceptable results in most regulatory contexts than those obtained from mesocosm-based methods (Versteeg et al. 1999). Differences remain across regulatory jurisdictions on this aspect; for example, Canadian and

Table 1. Examples of the use of species sensitivity distributions in several regulatory frameworks for the purposes of chemical risk assessment and formulation of water quality criteria or standards

		Standard for acceptance in regulatory framework		
Facet of SSD development	Factors to be considered	ECHA (2008)	USEPA Ambient Water Quality Criteria, Stephan et al. (1985)	ANZECC and ARMCANZ (2000) supplemented by Warne et al. (2015)
Type of regulatory use		Chemical hazard assessment under REACH	Development of chemical discharge criteria and impaired water assessments	Development of chemical discharge criteria
Overall quality of the database	Information or data source	Klimisch scoring, preferably in IUCLID5, documented	Data available in typed and dated form (publication, manuscript, letter, memorandum, etc.); supporting information indicates acceptability results are probably reliable	Use of acceptable laboratory practices in design and execution of tests; each study is classified as primary, secondary, or unacceptable, based on detailed inclusion criteria
	Whether data generated from true chronic studies	Required	Acute data required; chronic data are needed for ACR determination	Required for chronic SSD formulation; note that acute SSDs can be generated as well
	Chronic studies cover sensitive life stages	Required	Not required	Not defined; notation of life stages is required
	Endpoints used as input are the lowest NOECs or ECx values of the endpoints measured in relevant studies	Required	EC50 and LC50 data required; NOEC-LOEC data are needed for ACR determinations	ECx is preferred over NOECs from all studies and endpoints on each species
	Treatment of endpoint data for multiple tests on same species	Not specified	Always uses survival or immobility endpoints; thus, records are similar by definition; LC50 and EC50 estimates calculated at the genus level as geometric means	Median value for comparable records for the same endpoint when >2 data points are available; if only 2, the geometric mean is used to represent the average species effects endpoint
	Use of data on most sensitive endpoints	NOEC conclusions from the quoted studies should represent the most sensitive endpoint for the test	See above	See above
Taxonomic groups considered	Fish	At least 2 species	Salmonid is required; 2nd species of commercial or recreational importance is recommended (a 2nd fish is required)	3 species including 1 coldwater species (salmonid), 1 warmwater species, and 1 other
	Additional vertebrates	Not required	3rd chordate family required (amphibian or 3rd family of fish)	Amphibian highly desired, but not required
				No specific organism types are required; at least 4 phyla needed
				Not specified

Crustaceans	At least 1 species	Required	Required	Required	Not specified
Insect	At least 1 species	At least 1 species	Mayfly, stonefly, or caddisfly preferred but not required	Not specified	Not specified
Additional invertebrates	At least 1 additional phylum not represented by Insects or Crustaceans	At least 1 more family in a phylum other than Arthropoda or Chordata and at least 1 more family in any order of insect or any phylum not already represented	2 additional invertebrates required	Not specified	Not specified invertebrates
Algae (number unspecified)	Required but number unspecified	Not used	1 species of a plant or alga is required; 3 required if indications exist that photosynthetic organisms are sensitive	Not specified	Not specified
Higher plants (number unspecified)	Required but number unspecified	Not used	1 species of a plant or alga is required; 3 required if indications exist that photosynthetic organisms are sensitive	Not specified	Not specified
Minimal sample size	10 NOECs, preferably >15 for different species	8 different families required	At least 10, preferably 15 different species	Minimum of 5 species from at least 4 taxonomic groups, preferably >5 species	
Statistical fit to a distribution	Use of underlying distribution	Confirm model choice, flexible for data, but log-normal and log-logistic identified as most common	Log triangular required applied to the 4 most sensitive genera	Confirm model choice	Burr Type III distribution recommended (note this includes log-normal, log-logistic, and log-triangular)
Statistical GoF	Confirm by appropriate GoF test	Not considered	Confirm GoF	Confirm GoF	Confirm GoF
Conclusion	Provided overall statement as fit for purpose	Generally should discuss	Generally should discuss	Generally should discuss	Generally should discuss
Estimated parameter	HC5 and CI	HC5 with 50% CI derived and provided	HC5 is derived as input into further calculations to establish the water quality criterion	HC5 with 95% CI derived and provided	HC1, HC5, HC10, and HC20 with 50% CI derived and provided to address various protection targets
NOEC values <HC5	Discuss values that are <HC5	Required	If economically or recreationally important species are <HC5, the criterion will be lowered to protect those species; although algae and plants are not included in the SSD, algae and plant toxicity data are compared with the HC5	Discuss	HC5 should be less than the chronic effect concentration for high value or keystone species

(Continued)

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Standard for acceptance in regulatory framework

Facet of SSD development	Factors to be considered	ECHA (2008)	USEPA Ambient Water Quality Criteria, Stephan et al. (1985)	CCME (2007) (EC 2013)	ANZECC and ARMICANZ (2000) supplemented by Warne et al. (2015)
Distribution of trophic levels within the SSD	Discuss trophic level influences	Assess distribution of trophic level within the chosen distribution; use multiple curves if bimodal or multimodal	Not required	Assess distribution of trophic level within the chosen distribution; use multiple curves if bimodal or multimodal	Assess distribution of trophic level within the chosen distribution; use multiple curves if bimodal or multimodal
Knowledge of the mode of action	Discuss	Required	Indicated in documentation	Required	Indicated in documentation

This table is not exhaustive and other frameworks are used by hazard assessors globally. ACR = acute-to-chronic ratio; ANZECC = Australian and New Zealand Environment and Conservation Council; ARMICANZ = Agriculture and Resource Management Council of Australia and New Zealand 2000; Canadian Council of Environmental Ministers 2007). Mesocosms and field studies will remain valuable tools for evaluating the accuracy of SSD predictions because of the inherent interactions among populations and communities that are not inherent in single-species tests. Further, as acknowledged in many other venues, mesocosms often have the additional advantage of using more realistic field exposures (Giddings et al. 2002).

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Australian regulatory decisions would place increased emphasis on mesocosm results if conducted following sound statistical, biological, and ecological principles (Australian and New Zealand Environment and Conservation Council and Agriculture and Resource Management Council of Australia and New Zealand 2000; Canadian Council of Environmental Ministers 2007). Mesocosms and field studies will remain valuable tools for evaluating the accuracy of SSD predictions because of the inherent interactions among populations and communities that are not inherent in single-species tests. Further, as acknowledged in many other venues, mesocosms often have the additional advantage of using more realistic field exposures (Giddings et al. 2002).

A new development in the use of SSDs is an emerging interest in using field data based on population abundance and biomass as alternatives to toxicity estimates in the laboratory (Leung et al. 2005). Field-based SSDs may allow an expansion of taxonomic coverage, and thus provide insight into responses for taxa less easily tested in the laboratory but that exist temporally in the same space. In contrast, intraspecific and interspecific interactions, as well as multiple-stress responses, are certainly involved in field assessments. Therefore, the interpretation or meaning of the SSD may change compared with assessments based solely on laboratory single-species toxicity tests.

Multiple statistical approaches are available for SSD modeling, and high uncertainty can arise in cases of limited taxa diversity (ECETOC 2014). The hierarchical SSD was developed as a novel approach to address data gaps in taxa diversity and is discussed by Craig and colleagues (Craig et al. 2012; Craig 2013; ECETOC 2014). This can be used to predict thresholds for defined species assemblages using knowledge of the general trends in how species sensitivity is related to their taxonomic distance. Other methods for addressing data gaps in taxa diversity include the US Environmental Protection Agency (USEPA) Web-based Interspecies Correlation Estimation (Web-ICE) tool (<https://www3.epa.gov/ceampubl/fchain/webice/>; Raimondo et al. 2016), which uses interspecies correlation estimation models to estimate toxicity for taxa with limited data (Awkerman et al. 2013). The USEPA Web-ICE tool also explored interspecies toxicity estimation as a function of taxonomic distance and showed the phenomenon is generally important. Although the investigations do not aim to assess the influence of chemical class on the relationship, the fact that many modes of action are present in the database suggest it is a generalized phenomenon. Traditional statistical approaches, Web-ICE, and the hierarchical SSD prototype were compared and contrasted by ECETOC (2014) using case studies involving the surfactant linear alkylbenzene sulfonate and the insecticide chlorpyrifos. Three distinct regulatory applications associated with the use of SSDs are evident. First is the derivation of generic protective threshold concentrations applied to many different locations, perhaps over very large geographical regions. These are assumed to offer sufficient protection everywhere, even in the most sensitive systems. The 2nd application is the derivation of scenario-specific protective thresholds that more closely reflect local conditions (e.g., constrained to resident species or for a certain water quality condition), but which may not be transferable from one place to another. The 3rd application is identifying the causes of biological impact (“diagnosis”) or expected impact magnitudes of existing or expected (mixture) contamination, to inform the need and

focus for any remedial or management action. The first 2 applications are protective, and thus will tend to include a certain amount of precaution, whereas the 3rd application needs to be predictive. The diagnostic use of SSDs has recently been summarized by Posthuma et al. (2016).

RESEARCH NEEDS

The overview of SSD practices as discussed during the workshop has shown that SSDs currently have a significant influence on national and international decision making regarding assessments of chemical exposure to ecosystems. It is evident from review of current applications of SSDs in regulatory decision making that better understanding of the state of the science and answers to frequently asked questions would encourage best practices in the use of SSDs by regulators, risk assessors, and risk managers. Although expert judgment has a role in the interpretation of SSD models, a compilation of current best practices would provide a valuable compendium of regulatory experiences beneficial to countries seeking to derive their own environmental quality standards or to scientists seeking to understand the significance of emerging chemicals or new applications of existing chemicals on ecosystems. An array of modeling tools has extended the statistical evaluation of SSD “quality” that builds on progressively better and more available input data as a result of global chemical management programs (e.g., Organization for Economic Cooperation and Development HPV [High Production Volume] Challenge program, European REACH (Registration, Evaluation, Authorization and Restriction of Chemicals), Canadian Categorization of the Domestic Substances List, and others). According to ECETOC (2014), the use of SSDs in ecological diagnostics links policy targets on ecological integrity, monitoring data, SSD modeling, and landscape-level mixture impact diagnosis. Therefore, research that builds a stronger scientific foundation is preferable to work focused narrowly on a single species or taxa.

Specific research needs were identified in the workshop that would augment the application of SSDs in most circumstances: The research needs were divided into the following themes: use of the SSD, ecological considerations, guideline considerations, model development and validation, toxicity data, mechanistic approaches, and uncertainty (Table 2). The most important of these needs are highlighted.

1. Tools for regulatory decision making should be given high priority with particular focus on: 1) SSDs for chronic toxicity; 2) validating HC5s with mesocosms and real ecosystems; and 3) maximizing the use of available data, for example, by applying weighting criteria.

Rationale: The most potentially influential use of SSDs is establishing safe concentrations for ecosystems associated with long-term, low-level exposure to chemicals; therefore, assessments based on chronic exposures are essential. However, the use of SSDs in general should be somewhat more conservative (i.e., predict lower hazardous concentrations) for routine use than higher-tier studies (e.g., mesocosms). Higher-tier studies should still behave consistently with predictions provided by SSDs (Versteeg et al. 1999). Roles for acute SSDs can also be relevant, and in some situations critical, such as short-term pesticide exposures.

2. Mechanisms to maximize the use of available data should be further developed, for example, by applying weighting

criteria to broaden taxonomic coverage and use of nongood laboratory practice studies.

Rationale: The majority of standardized toxicity tests focus on relatively few species. Taxonomic coverage is a key facet of developing SSDs, and nonstandard tests are increasingly used as input. These are also most often not performed under a good laboratory practice framework. Weighting or valuing different types of studies should be explored to maximize the use of all available high-quality data. The inclusion or exclusion of studies has been shown to be one of the single largest contributors to variance in PNEC and SSD derivation (Hahn et al. 2014). A recent Pellston Workshop entitled “Use of Ecotoxicology in Regulatory Decision-Making” in Shepherdstown, West Virginia, USA (30 August to 4 September 2015) was held to frame this issue and propose solutions (Hanson et al. 2016).

3. Further development of tools for assessing mixtures of chemicals is needed.

Rationale: Aquatic and sediment environmental exposures are rarely to single-chemical or single-stressor insults and are more commonly to mixtures. Methods to perform aggregate and cumulative assessments are needed for the future as mixture assessments are increasingly demanded by the stakeholders. Effluent toxicity assessments address this to a degree, but SSD-based mixture assessments are possible if mode of action and theories of concentration addition and independent action can be accounted for (Kapo et al. 2014).

4. Trait-based SSDs appear to offer advantages over conventional taxonomic-based approaches, but there is currently no practical application.

Rationale: This continues to be a developing science in ecotoxicology. It is likely that responses to chemicals are in part based on ecological traits (much like their classifications in feeding or trophic ecology), with some trait types more sensitive to certain types of exposures than others (Pilière et al. 2014). In this context, traits are morphological, physiological, or phenotypic heritable features that are measurable at the level of the individual. Trait-based ecotoxicology proposes to link stress–response patterns of species to effects at the level of ecosystem properties. Trait-based SSDs then would focus on groupings, other than species, as inputs to the SSD, thereby acknowledging the importance of preserving organism functional roles in addition to classical biodiversity.

5. SSDs for more taxa including plants and, possibly, microorganisms are needed.

Rationale: It is well established that photosynthetic microalgae are frequently more sensitive than fish or invertebrates (Jeram et al. 2005) but are sometimes not considered in SSD formulation. Photosynthetic and nonphotosynthetic microbes, aquatic macrophytes, and plants play crucial roles in ecosystem structure and function; therefore, including these species in SSDs more frequently may improve robustness of predictions.

6. A more scientifically critical role for cheminformatics approaches needs to be developed.

Rationale: Future environmental toxicology approaches should be able to take advantage of the large efforts ongoing in programs such as the US National Research Council “Toxicity Testing in the 21st Century” (National Research Council 2007). Cheminformatics is the strategic

Table 2. Major categories of work that could improve the long-term application, usability, and interpretation by risk assessment practitioners

Research area	Description
Uses of SSD	Collate and review the uses of SSDs for purposes other than estimating the HC5 (e.g., using the entire SSD for probabilistic risk assessment and deriving other values [e.g., HC50] for trigger management action).
Ecology	Investigate whether an approach that allows better extrapolate to all ecosystems is viable.
	Compare trait-based SSDs with traditional strictly taxonomic-based SSDs and define what traits are most relevant to SSD generation. Alternative approaches should be explored, including focusing on sensitive taxa rather than broadly populating an SSD. However, there is uncertainty regarding what the sensitive taxa will be for many substances. A sensitive species approach may require novel methods development, including integrating chemical structure, genomic traits, and MOA information.
	Compare SSD-based approaches with the use of generic AF values under different scenarios of data richness, and the need to explore uncertainty in relaxed (10 species/8 taxa group) requirements versus AF uncertainty and conservatism. Determination of the ecology and composition of representative ecosystems should inform requirements for taxa composition in SSDs. SSD-based estimates determined from various approaches and data richness scenarios should be compared with field data, and field monitoring should be performed to verify SSD-based predictions of community-level effects.
	(Further) Develop a model that takes account of the number and type of species in a community and that shows the consequences and reliability of the results. Establish what validity criteria are needed.
	Determine what additional ecological knowledge needs to be included to add value for the risk assessors.
Guidelines	Develop a formal and transparent decision tree approach that is inclusive of the available data and that considers the generic or specific use of SSDs in environmental protection and management.
	Develop guidelines on how to deal with data quality (of the input data on species sensitivities, or sometimes functions sensitivities).
	Develop guidance on the use of nonstandard test species.
	Develop guidance on which methods and tools can be used to generate SSDs; this requires sensitivity analysis, identification of causes of differences, etc.
Model development and validation	Investigate the limitations of the models and whether they are fit for the purpose for which they are used.
	Evaluate the viable methods for incorporating all relevant data in SSDs.
	Further validation of SSDs derived from laboratory data against field and mesocosm studies is required, as is guidance on the different approaches (including their limitations) that can be taken.
	Further validation for extrapolations that are in relevant models (i.e., hierarchical SSD and Web-ICE) and of consequences for HC5 uncertainty.
	Validation of hierarchical SSD scenario-specific HC5s relative to the field and/or mesocosm studies.
	Critically review whether any of the growing amount of information types about chemicals and their impacts that are now available should be used to inform SSD development, application, and interpretation, including, for example, knowledge of omics, mechanisms, chemical properties, and exposure scenarios.
Toxicity data	Research is needed to determine how best to use available data (e.g., strict standardization criteria with resulting loss of species diversity or use weighting based on data quality). The focus of SSD development has been on acute toxicity data, and chronic toxicity estimation approaches will need the same level of evaluation (e.g., minimum data sets, acute-to-chronic ratio estimation, lowest toxicity value approaches). Develop better application of toxicological data in SSDs, for example, using more chronic data and mechanistic understanding. Develop methods to expand on data availability by adding less strictly selected input data and putting less weight on their inclusion, based on reliability of data.
	Develop methodology to improve the use of predictive modeling to overcome limited data sets. The applicability of toxicity extrapolation method should be further validated for acute effects and should also be evaluated for chronic effects. Develop and extend software tools to add the capacity to predict chronic toxicity and approaches applicable to other environmental compartments (such as sediment, soil, and air); both remain significant research needs.

(Continued)

Table 2. (Continued)

Research area	Description
	Investigate the value of including microorganisms in SSDs to protect ecosystem functions, for example, when assessing the ecological risk of fungicides; investigate the effects of including various fungal species in the test battery and incorporating their data into the SSD. Microorganisms should be considered in the HCx derivation, but development is currently hindered by the lack of available approved testing procedures for different groups of microorganisms.
Mechanistic understanding	Investigate whether critical body residue–based SSDs could be developed.
	MOA is an important determinant of species sensitivity. Research is needed to determine linkages between MOA and SSD composition requirements. Investigate whether it is possible to treat MOA in the statistical models in the same way taxonomic distance is being used. (In particular, is this feasible for Web-ICE and hierarchical SSD?)
Uncertainty	Develop an understanding of uncertainties within the assessment that are currently unquantifiable. Studies should be conducted to identify the magnitude of the uncertainty of various components of the SSD methodology. Uncertainty may be related to lack of data, (non)representativity of data, MOA considerations, and many other aspects of real exposure situations. An understanding of the mathematical magnitude of uncertainty alone may not be enough because it is possible that large sources of error may have little ecological importance, and vice versa. Research should then be focused on reducing the uncertainty of the most important sources of uncertainty in the SSD methodology. The group believed that uncertainty-driven research would be an important means to improve SSDs and maximize their usefulness in a cost-efficient manner. An uncertainty-driven research agenda is also likely to increase uptake of the other methods that can be used in combination with SSDs, for example, QSARs or Web-ICE.
	A simple example of uncertainty-driven research would be the selection of chemicals (or species) to be used in ecotoxicity tests. If the toxicity of a chemical to a large number of species belonging to different taxonomic groups has been determined, then the need for further research for that chemical may be low compared with a chemical that has been the subject of no or minimal toxicity testing. Another example is that very few SSDs have been conducted for nonchemical stressors (e.g., temperature, salinity) or the combined action of chemical and nonchemical stressors. Conducting such research could dramatically reduce uncertainty in the ecological relevance of single-chemical SSDs and place the risks posed by chemicals into a more meaningful context that addresses all possible pressures.

AF=application factor; HC5=5th percentile hazardous concentration; HCx =the xth percentile hazardous concentration; MOA=mode of action; QSAR=Quantitative Structure Activity Relationship; SSD=species sensitivity distribution; Web-ICE=Web-based Interspecies Correlation Estimation.

use of computer and informational techniques applied to a range of problems in the field of chemistry including those of drug discovery, development of *in silico* models, and relating key chemical attributes to the potential for hazard. Environmental scientists generally have a strong appreciation for physical-chemical attributes in testing and assessment that will bridge well to cheminformatics. How SSD approaches can take advantage of cheminformatics developments should be explored.

- There needs to be a focus on sensitive groups.
Rationale: A better understanding of the frequency of bimodality in SSDs (i.e., when one taxonomic group is more sensitive compared with others) and how to further incorporate this into assessment methodologies is needed. Certain groups of chemicals may even benefit from a greater focus on sensitive subgroups, for example, microalgae to antimicrobials, as a stronger basis for extrapolation for environmental protection.
- The usefulness and applicability of SSDs for defined communities need to be determined.
Rationale: Approaches of the hierarchical SSD form provide some unique advantages to probe relationships between available studies used as SSD inputs and actual distributions of species based on taxonomy observed in the field (Craig et al. 2012; Craig 2013).
- Internal dose (critical body burden [CBB])-based approaches have the potential to incorporate mechanistic

toxicokinetic-toxicodynamic modeling evidence that could help explain sensitivity differences between taxa and/or traits.

- Rationale: Critical body burden concepts allow a technically defensible determination of exposure to chemicals at the target organ of interest resulting in acutely or chronically toxic effects (McCarty et al. 1992; McElroy et al. 2011). CBB approaches have generally been investigated for organic compounds and are not only more mechanistically based, a laudable goal in any toxicological investigation, but also have the attractive feature of providing insight into mixture assessments. Greater emphasis on developing CBB for algae and invertebrates would need to be undertaken because fish have been the primary group of interest until now. Development of CBB data for a broader array of taxa would need to be addressed for body burdens to be used in SSD development. SSDs based on CBB could conceivably provide deeper insight into true hazardous concentrations versus those based on external concentrations only. A new framework for regulatory use (e.g., SSDs per taxonomic group) may be needed because modes of action for single chemicals may not translate well across taxa.
- Uncertainty as an alternative to standard AFs needs to be quantified.
Rationale: It is acknowledged that this will be a challenge for any regulatory framework; however, it is consistent

with the goals of risk assessment, which is fundamentally probabilistic in nature. Research is needed to ascertain the relationship of statistical uncertainty with deterministic AFs typically applied to small data sets. Improvements to the role of AFs, even as they are applied to SSD results, because of variation in SSD quality, are also warranted.

11. The level of confidence provided by the various but current SSD criteria needs to be determined.

Rationale: Through the development of more unified global best practices, the means to value the varying levels of quality resulting from SSD methods may become clear. Treatment of data (multiple studies on the same species, different endpoints used even for the same species), taxonomic coverage (breadth of species, species choices), statistical models used, and how these affect HC5 predictions and their uncertainties are essential for long-term support of the tool.

Acknowledgment—The present study summarizes the primary outcomes from a workshop entitled “Estimating Toxicity Thresholds for Aquatic Ecological Communities from Sensitivity Distributions” (held 11–13 February 2014 in Amsterdam, The Netherlands). The objectives of the workshop were: 1) to study and where possible improve the ecological relevance of SSDs; 2) to collate, compare, and where possible improve statistical approaches for SSD modeling; and 3) to describe and evaluate regulatory applications of SSDs. The workshop was supported by the ECETOC and the Environment Agency for England and Wales. L Posthuma was supported by the CEO of National Institute for Public Health and the Environment under project S/015031.

Disclaimer—The present study has been reviewed according to USEPA guidelines, and the opinions expressed in this work are those of the authors and do not represent the policies or opinions of the USEPA.

Data availability—No actual data are presented in the present study.

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