Workshop on the Probabilistic Approaches for Marine Hazard Assessment 18-19 June 2008, Oslo

Workshop Report No. 15

EUROPEAN CENTRE FOR ECOTOXICOLOGY AND TOXICOLOGY OF CHEMICALS

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European Centre for Ecotoxicology and Toxicology of Chemicals
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Workshop on the Probabilistic Approaches for Marine Hazard Assessment

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1. SUMMARY

In order to discuss the potential use of probabilistic techniques in marine environmental hazard assessment, a workshop was organised by ECETOC and the Environmental Agency of England and Wales. Nearly 40 scientific experts from industry, academia and governmental agencies participated in the meeting hosted by the Norwegian Pollution Control Authority and held in Oslo on 18th and 19th June 2008. Seven plenary sessions were followed by four syndicate sessions, each addressing specific issues.

The overall conclusion was that the assessment factor approach described in the EU Technical Guidance Document is suitable for screening purposes to derive the initial $PNEC_{marine}$, while the probabilistic approach (using species sensitivity distribution [SSD]) provides a refined estimation of marine species sensitivity. Both of these approaches should be used in a tiered assessment manner. Both the assessment factor and SSD approaches should prioritise population relevant endpoints (e.g. survival, development, growth or reproduction) in order to directly relate to ecologically important effects. The workshop also recognised that the probabilistic approach is inherently complex, data intensive and requires advanced statistical expertise. With SSD approaches, variation in species sensitivities and some of the associated uncertainty can be taken into account. However, both the assessment factor and probabilistic hazard assessment approaches pay less attention to potential uncertainty due to selection of test species, analytical chemistry and variation between laboratories and tests. It was also highlighted that in some cases (e.g. when the identified species have protected status, specific economic value or are the key species for a specific habitat) it may be advisable to initiate a third tier assessment and perform a species-specific, biologically based assessment.

The participants agreed that there are several problems with combining species in SSDs, mainly when species are combined over large taxonomic distances. In addition, extrapolation from acute to chronic toxicity may be based on different endpoints in bioassays (e.g. LC_{50} for acute tests with marine organisms), while chronic tests are based on growth or reproduction (and expressed as NOEC [No Observed Effect Concentration]). Further research is needed on these issues.

Workshop participants also discussed whether it is scientifically justified to combine saltwater and freshwater effects data. The benefit of combining data is to render the probabilistic approach more robust (e.g. with a larger set of acute or chronic data for analysis). Nonetheless, due caution is required when choosing compounds that may interact with compounds present in seawater, (e.g. metals or organic chemicals with the potential to affect osmoregulation). For such compounds, the SSD approach should be used on marine specific data. Available data suggests that the toxicity data from organisms in one climatic zone may be extrapolated to another zone (e.g. use of data from temperate marine species in the absence of data for Arctic species). However, it is not clear whether the environmental fate and bioavailability of the substance is

different in polar versus temperate regions. While there was not a consensus on this issue, several workshop participants did recommend that further research is necessary into this matter.

The probabilistic hazard assessment approach is beginning to be applied for freshwater, marine and terrestrial risk assessment scenarios worldwide. Some key questions still remain, however, related to the comparison of acute or chronic effects data between freshwater and marine groups of organisms (it was noted that the global marine environment contains 16 animal phyla not found in freshwater ecosystems). There is also a need to strengthen the evidence base for extrapolating marine ecotoxicity data from one climatic zone to another.

A programme of research was proposed that would help resolve a number of these issues and which would lead to improvements to the current approaches being used in marine hazard assessment.

2. WORKSHOP OVERVIEW

2.1 Introduction

With the publication of the European Union's Technical Guidance Document (TGD) on risk assessment (EC, 2003), regulatory guidance is available for conducting environmental risk assessments to include marine ecosystems. In general, the described methodology to derive single-substance Predicted No Effect Concentrations (PNECs) for marine environments, based on the same approach used for freshwater ecosystems with the exception of the value of the assessment factors (referred to as the 'assessment factor' approach in this report). The greater species diversity in the marine environment, compared to freshwaters, including the presence of 16 taxa that occur only in marine environments, is used in the TGD as an argument for requiring hazard assessment data from a broader distribution of sensitivities of species. Since it was not possible to make a clear judgement on the basis of available data, the TGD considers it prudent to assume that greater diversity of taxa will produce a broader distribution of species sensitivity. Therefore, where only data for freshwater or saltwater algae, crustaceans and fish are available, an additional assessment factor of 10 in the derivation of 'marine' PNECs is prescribed by the EU TGD to reflect the greater uncertainty in the extrapolation.

The guidance on marine assessments given in the EU TGD results in challenges to comparative risk assessment models specifically developed to assess and compare the risk of different stressors. The main challenges include the imbalance in the derivation of PNECs for different chemicals with different data availabilities. For most industrial chemicals, the data often covers not more than three acute toxicity values for three freshwater species (fish, crustacean, algae). Following the EU TGD requirements, the greatest assessment factor (10,000) needs to be applied to the smallest of these toxicity values in order to derive a $PNEC_{marine}$ for these chemicals. This $PNEC_{marine}$ would be considered highly uncertain, reflecting the limited dataset available to derive it. For more common chemicals (e.g. hydrocarbons or metals) chronic ecotoxicity data for freshwater organisms are often available, resulting in a small assessment factor (up to 1000) and a potentially small and less uncertain $PNEC_{marine}$. In contrast to such common chemicals, there is often an absence of chronic data for industrial chemicals and hence using the more conservative assessment factor required by the TGD may lead to the need of more information before a conclusion can be drawn. Importantly, however, this might not arise from the fact that industrial chemicals are indeed more harmful than metals and other natural marine contaminants but just from the fact that a high safety factor that needs to be applied. A second impact of the TGD approach is that through the application of assessment factors, naturally occurring compounds (e.g. heavy metals) may have $PNEC_{marine}$ values that are in fact lower than natural background levels. This has significant implications, for example, for decision making in the offshore oil and gas industries.

It is important to make balanced evaluations of different components with different data availabilities. In extrapolation, the focus should be on variation in toxic potency, while also taking account of uncertainty due to limitations in data. Uncertainty should not be hidden in assessment factors but preferably explicitly expressed in the risk assessment endpoint (Verdonck *et al*, 2005).

Variability and uncertainty can be quantified using probabilistic techniques, which have received much attention in recent years (e.g. EUFRAM, 2006) and are included in the guidance for REACH (ECHA, 2008). In a probabilistic risk assessment, distributions are used to represent parameters which are variable and uncertain, replacing the fixed values which are used in traditional deterministic assessment.

The EU TGD and the guidance for REACH (ECHA, 2008) describes a second method for PNEC derivation which could be a way of dealing with the challenges. Instead of using assessment factors, variation in toxic potency can be addressed using a species sensitivity distribution approach (SSD) which is a type of probabilistic approach. However, currently for this approach the requirements on data availability described in the EU TGD and in the guidance for REACH (ECHA, 2008) are very comprehensive (at least 10 NOECs [preferably more than 15] for different species covering at least 8 taxonomic groups). In practice, these criteria are not met for more than a few compounds. Additional probabilistic risk assessment tools and extrapolation methods (e.g. Aldenberg and Luttik, 2002; Dyer *et al*, 2006, 2008) could be used to develop SSDs with fewer data points and species currently prescribed by the EU TGD. However, there is a need for discussion and documentation of these alternative approaches. Solid scientific arguments and proof of concept should be provided for the use of these alternative approaches instead of the EU TGD.

In order to discuss the potential use of probabilistic techniques in marine environmental risk assessment, data requirements and restrictions, the Oslo workshop was organised by ECETOC in June 2008. The main objectives of this workshop were to discuss the strengths and weaknesses of probabilistic risk assessment techniques, and to what extent they may serve as a balanced alternative for the assessment factor approach to marine hazard assessment as described by the EU TGD. This report summarises the workshop presentations and the outcome of the workshop discussions.

2.2 Workshop structure

Nearly 40 scientific experts from industry, academia and governmental agencies participated in a workshop held in Oslo on the 18th and 19th of June 2008 where seven plenary sessions were held. This was followed by syndicate sessions, where the following discussion took place:

- Marine versus freshwater species comparison;
- marine sediment issues;
- selection of marine test species and population relevant endpoints;
- statistical guidance and communication.

The discussions from the breakout groups were recapitulated in a final plenary session where several recommendations were made and conclusions drawn. A list of workshop participants is given in Appendix F, and the programme is detailed in Appendix G.

2.3 Workshop objectives

The objectives of the workshop were to discuss the applicability of probabilistic methods in marine hazard assessment as an alternative to the assessment factor methodology required by the EU TGD for calculating $PNEC_{marine}$.

The main objectives of this two-day workshop were:

1. To evaluate whether or not probabilistic hazard assessment techniques can serve as balanced alternatives for the marine environment hazard assessment as described by the EU TGD;
2. to provide an overview of required data and extrapolation techniques;
3. to publish an ECETOC report summarising the workshop presentations and discussions.

3. PRESENTATION SUMMARIES

3.1 Setting the scene: Marine environmental risk assessment in the Norwegian offshore oil and gas industry

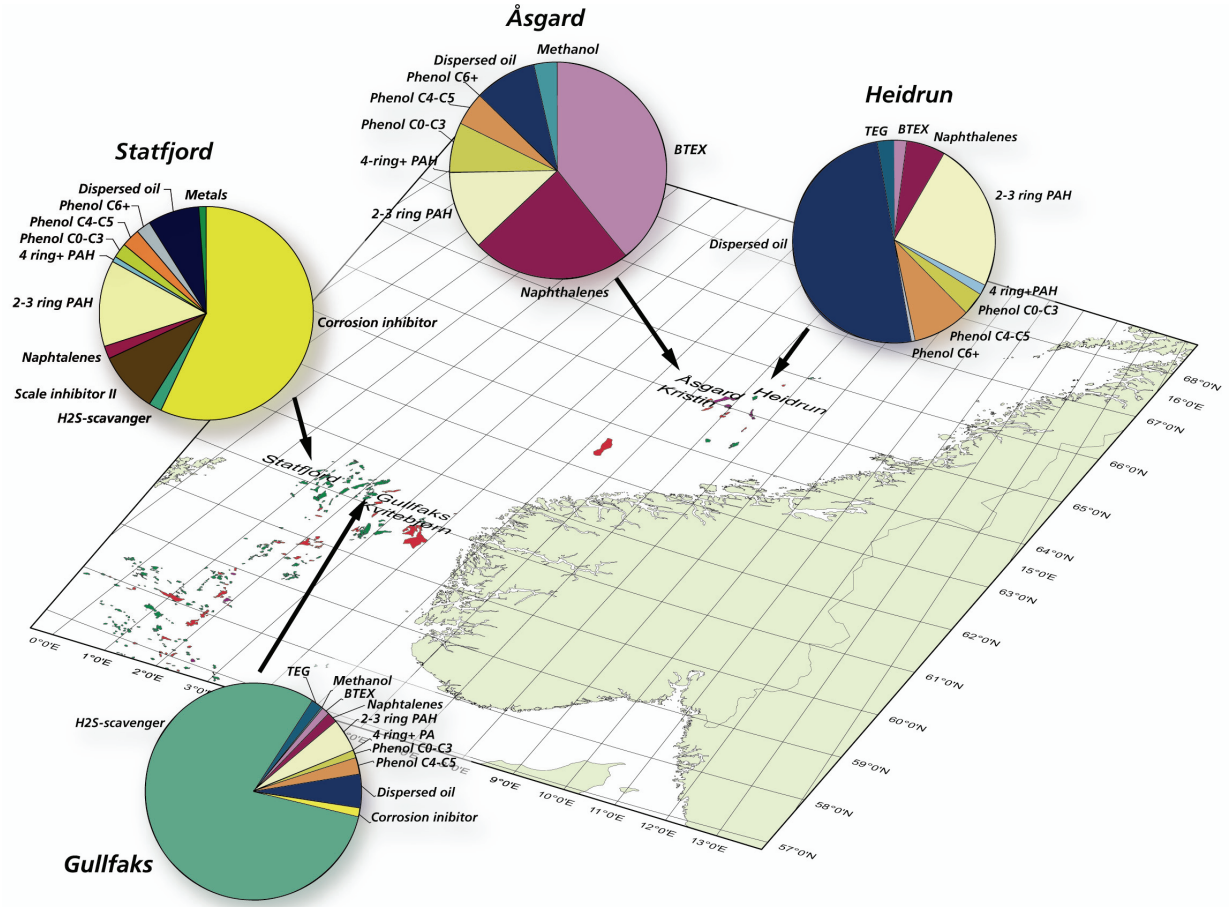
M. Smit
IRIS / StatoilHydro, Norway

The offshore oil and gas industry operates in the context of a multitude of social, economic, physical and environmental factors. As offshore oil and gas activities have local impacts, the prior assessment and verification of these impacts is important. Over the past decade a shift in regulatory approaches has taken place from a prescriptive 'command and control' approach towards a performance based approach of 'self regulation'. The growing self regulation requires in-company guidance. This has resulted in the development of Environmental Managements Systems. These systems focus on continuous improvement of the environmental performance of the industry. Additionally, in Norway the publication of the 'zero discharge report' has been an important step for the development of Environmental Managements Systems. The requirements from the 'zero discharge report', which states that environmental management of the Norwegian oil and gas industry should work towards 'no discharges, or minimisation of discharges if these discharges can lead to adverse effects in the environment', are currently referred to as the 'zero harm' requirements.

Environmental risk assessment (ERA) has been used by the oil and gas industry in Norway as a management tool towards the fulfilment of the 'zero harm' requirements. Next to the application of ERA in the selection of 'green' chemicals and in the preparation to oil and chemical spills several Environmental Impact Factor (EIF) tools have been developed. Most of these EIF tools, which focus on several discharges from the (offshore) oil and gas industry (e.g. produced water discharges, drilling discharges, air emissions, oil spills), are based on principles for ERA described by the EU TGD (EC, 2003). The EIFs include transport and fate modelling of single components and risk characterisation of these components. EIF calculations result in single-value indicators which relate to the total volume of water or total area of seafloor or land surface where a potential for environmental impacts is present. Additionally, the contribution of the risk caused by the single components to the overall risk of all components in the discharge is quantified.

This latter facilitates the selection of the most environmental beneficial and cost effective measurement to reduce overall risk per discharge stream. The EIF for produced water is fully implemented as a managements tool on all fields operating on in the Norwegian continental shelf. For example, Figure 1 shows the result of the contribution-to-risk calculation, which is a part of the EIF calculation, for four platforms on the Norwegian continental shelf.

Figure 1: Example result from four EIF and contribution-to-risk calculations for four different platforms on the Norwegian continental shelf. Different compositions of the produced water and different environmental conditions result in different contributions-to-risk from the produced water constituents



Currently the calculation of the EIFs for produced water and drilling discharges is based on a combination of a species sensitivity distributions (SSD) approach and PNECs (derived by the procedures prescribed by the EU TGD). SSDs are used in order to be able to combine risks from different stressors following the approach described by De Zwart and Posthuma (2005). PNECs are implemented in order to qualify the model for use in a regulatory context (which often implies the incorporation of EU TGD procedures). The uncertainty incorporated in the procedures for PNEC calculation however, depends strongly on the availability of data. For chemicals with a large data availability (> 15 species, > 8 taxonomic groups) the SSD approach may be used, while for chemicals that do not fulfil this requirement, assessment factors need to be applied. In the worst case this means an assessment factor of 10,000 needs to be applied to the lowest acute EC_{50} or LC_{50} value based on short-term tests with freshwater algae, crustaceans and fish. Consequently, the component with the lowest PNEC might often not be the most toxic one, but might simply be the one with the highest assessment factor. This causes problems for the

comparability of risks caused by different components in the discharges. Especially for the numerous man-made (production) chemicals which are used in the production process, often only limited ecotoxicity data are available (three acute values).

In the EIF methodology, currently PNECs based on the assessment factor approach and PNECs based on the SSD approach are treated equally, even though the PNEC calculation using assessment factors is often considered less rigorous and scientifically less robust than the SSD approach (Garay *et al*, 2000; Pennington, 2003; Tannenbaum, 2005; Jager *et al*, 2006). Nonetheless the assessment factor approach is applied in the EIF calculations in order to comply with the EU TGD. Because the EU TGD guidance hides extrapolation uncertainty in assessment factors it is not possible to assess the associated overall uncertainty (Verdonck *et al*, 2005).

It is important to improve balance in the evaluation of different components with different data availabilities in the risk calculation methodology of the EIF. In an improved methodology the focus should be on toxic potency and less on uncertainty in extrapolation. It is important to develop risk protocols for marine risk assessments where uncertainty is not hidden in assessment factors but preferably explicitly expressed in the risk assessment endpoint. The use of alternative methods for the marine assessment factors should be evaluated, and preferably, the use of advanced extrapolation techniques to construct marine SSDs should be considered.

3.2 EUFRAM project

Andy Hart
Central Science Laboratory, York, UK

EUFRAM was a four-year EU-funded concerted action project (no. QLK5 - CT 2002 01346) on probabilistic methods for the assessment of ecological risks of pesticides, which ended in December 2006. It included 29 partner organisations (listed on the project website[1]) and extensive consultation with other interested parties, including a series of three international workshops.

Current methods for risk assessment are mostly deterministic. But in reality, toxicity, exposure and risk are variable and uncertain. Probabilistic methods use probability distributions to take account of variability and uncertainty. EU guidance documents for pesticide risk assessment (EC 2002a, b) state that probabilistic approaches are promising, but there is a lack of consensus on how to use them. The main obstacles to their uptake have been: Lack of guidance, lack of agreement on standard methods, complexity, difficulty of communicating results, risk of misleading results, the widespread view that probabilistic methods require large datasets, concerns about validity of assumptions, the need for validation, wide confidence intervals on outputs, and the lack of criteria for using probabilistic results in decision-making.

EUFRAM aimed to address these issues and helped meet the need for guidance. Its main outputs were a framework document of concepts, principles, and approaches for probabilistic risk assessment; case studies illustrating application of probabilistic methods to terrestrial and aquatic organisms; and a series of detailed reports (listed on the project website[1]) on specific aspects.

The EUFRAM framework document is written in the form of a guidance document, although it has no official status. It contains sections on basic concepts of probabilistic risk assessment; the role of probabilistic methods in tiered approaches to risk assessment; principles for planning and conducting probabilistic assessments, for interpreting and communicating results, for reporting and peer reviewing of completed assessments; and reviews of approaches for validation and decision-making.

The framework document is accompanied by two detailed case studies, providing worked examples on how the principles and approaches in the framework can be applied. It is hoped that, together, the framework document and case studies will contribute to meeting the need for guidance on conducting and communicating probabilistic assessments.

[1] www.eufram.com.

The project investigated a range of approaches for probabilistic modelling including one- and two-dimensional Monte Carlo simulation, Bayesian methods and probability bounds, but concluded that standardising on any one approach would be premature at the current state of the art. Each method has both strengths and weaknesses, and further development is needed for some aspects, e.g. how to quantify different types of uncertainty. Therefore it was recommended that practitioners should be flexible and use the methods that they consider most suited to their assessment. However, it is essential to always justify the choice of method, and to follow general principles of good practice as presented in the framework document.

The framework recognises that probabilistic assessment and indeed all higher tier risk assessments are inherently complex. Developing a probabilistic assessment from first principles requires advanced statistical expertise. This can be facilitated by provision of training and expert support. However, a more effective way of making probabilistic methods accessible and practical for the majority of potential users is to establish harmonised models for common scenarios, using peer-reviewed data and methodology, and implemented as user-friendly open-access software. This should reduce the risk of misleading results, and allow peer-review effort to be focused on assessments involving novel scenarios or approaches. Some efforts towards providing such software have been made, for example the ETx program[2] and Webfram[3]. They both include tools for SSDs, but neither has received official endorsement for use at EU level in pesticide risk assessment.

Small datasets are generally regarded as especially problematic for probabilistic approaches. A small dataset implies increased sampling uncertainty, provides less information about distribution shape, and less opportunity to detect departures from random sampling. However, these uncertainties affect any assessment using limited data, whether deterministic or probabilistic. Probabilistic methods can quantify some of these uncertainties as confidence intervals or probability bounds, which should help risk assessors and decision-makers to take uncertainty into account, provided that the unquantified uncertainties are also considered. By contrast, deterministic methods rely on conservative assumptions and assessment factors to deal with uncertainty. These are widely accepted and simple to use, but it is often unclear what level of conservatism they actually provide.

Validation is a critical step for all forms of modelling and risk assessment. However, validation in the sense of comparing predictions with real outcomes is often not feasible (e.g. if the predicted frequency of impacts is low, large field studies would be required to confirm or refute it). This type of validation should be attempted where practical but, as this will be rare, other approaches to ensure and evaluate the reliability of assessments should also be pursued. This should include validation of sub-models where this is more practical; adherence to principles

[2] http://www.rivm.nl/bibliotheek/rapporten/601501028.html

[3] www.webfram.com

of good practice for data, model design and probabilistic methods; systematic evaluation of all assumptions and uncertainties; consideration of alternative sources of evidence on the risk, where these exist (e.g. monitoring data); and peer review.

When probabilistic methods express uncertainty using confidence intervals, the width of those intervals sometimes prompts observers to suggest that they are unhelpful. This would be true if the confidence intervals exaggerate uncertainty: If there is evidence of this, then that evidence should be taken into account either qualitatively or by incorporating it into a refined model with narrower confidence intervals. If there is no such evidence, and the confidence intervals reflect uncertainty that is actually present, then it is important to communicate this so it can be taken into account in decision-making.

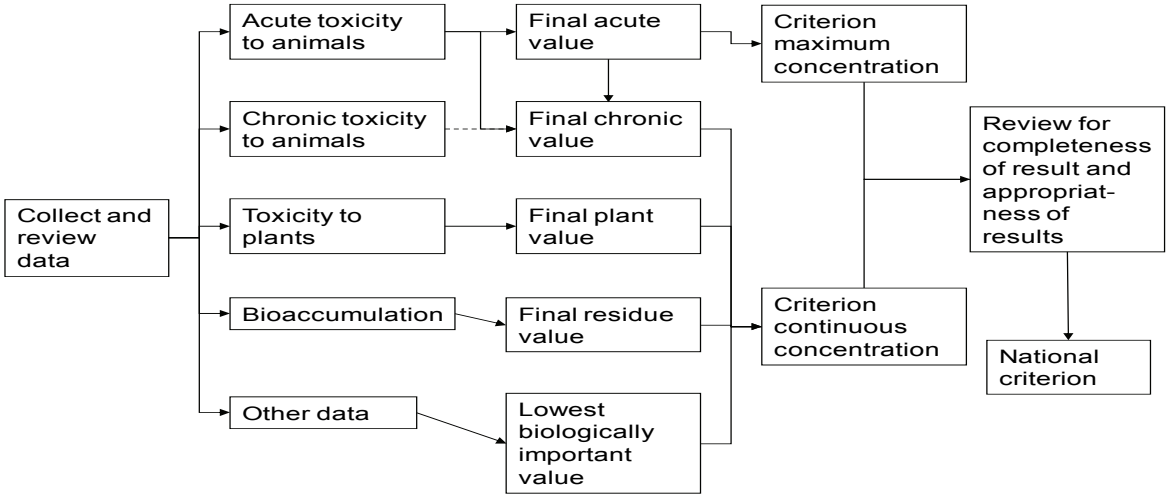
Acceptance and uptake of new methods is a slow process and at the time of writing, the EUFRAM outputs have not been formally evaluated by the authorities responsible for the regulation of pesticides. Nevertheless, many of the technical issues addressed by EUFRAM are general in nature and the findings may therefore be helpful in developing approaches for marine hazard assessment. EUFRAM also demonstrated the benefits of a collaborative approach to developing new risk assessment methods, with broad involvement of end-users through a series of workshops and web-based consultations.

3.3 North American perspective

K. Solomon
University of Guelph, Canada

The first water quality criteria (WQC) approach to use probabilistic techniques (SSDs) was the US EPA Water Quality Criteria (Stephan *et al*, 1985; Russo, 2002). In the guidelines for calculating WQCs, (called Final Acute and Final Chronic values) for protection of aquatic life, the procedure requires a distribution of toxicity values for a range of species that is prescribed. Rather than use the actual species LC or ED_{50}, a genus mean is used and the 5th centile of the distribution is used with an uncertainty factor of 2 to set the WQC. In addition, water quality parameters that reduce bioavailability may be used for metals. These effectively raise the WQC for metals in hard waters. The process is summarised in Figure 2.

Figure 2: Diagrammatic representation of the US EPA WQC process (adapted from Russo, 2002)



For developing marine WQCs, the US EPA procedure requires acute toxicity tests with at least one animal species in at least eight different families such that all the following are included: Two families in the phylum Chordata, a family in a phylum other than Arthropoda or Chordata, either the Mysidae or Penaeidae family, three other families not in Chordata, and any other family. Marine WQCs also require data from at least one acceptable test with a saltwater alga or vascular plant. At least one acceptable bioconcentration factor determined with an appropriate saltwater species, if a maximum permissible tissue concentration for protection of consumers is available.

Chronic WQCs may be estimated from acute data through the use of acute-to-chronic ratios. To do this, data from aquatic animals in at least three different families are needed provided that of the three species include at least one fish, at least one invertebrate, and at least one is an acutely sensitive saltwater species (the other two may be freshwater species). Criterion maximum concentration is calculated as half the final acute value and the criterion continuous concentration is the lowest of the final chronic value, final plant value, or final residue value for tissue concentration.

There are several problems with combinations of species in probabilistic setting of guidelines. These are exemplified in the US EPA guidelines (Stephan *et al*, 1985; Russo, 2002) where species are combined over large taxonomic distances, resulting in overly conservative values. In addition, extrapolation from acute to chronic may be based on different endpoints in bioassays. For example, acute tests are usually based on mortality (LC_{50}) while chronic tests are based on growth or reproduction and usually expressed as No-Observed-Effect-Concentration, rather than a LC_{50}. Because of this the extrapolation from acute to chronic may be incorrect.

Another issue is whether to combine saltwater and freshwater data or not. The benefit of doing this is that it makes the probabilistic approach more robust. The problem is that it cannot be done with compounds that may interact with compounds present in seawater. For example, metals have reduced bioavailability in saltwater and FW and SW data should not be combined. For simple organics, combination is possible if mode of action is unaffected by salts. For pesticides, data may be combined if mode of action does not involve neuromembrane conduction. Insect data may not be appropriate for saltwater systems as few insects are found in marine environments.

Toxicity data from organisms from a different climatic zone can be extrapolated to another (Brock *et al*, 2008), but fate of the substance may be different in colder regions.

The new Canadian WQC (CCME, 2007) process is similar to that of the US EPA and also Australia and New Zealand (ANZECC/ARMCANZ, 2000). In the Canadian guidelines, marine water is defined as water with total dissolved salt concentration greater than 5 g/L. Marine water (open ocean) generally has a dissolved salt concentration of approximately 34-35 g/L. In terms of acute and chronic guidelines, short-term exposure guidelines are designed to protect most species against lethality during intermittent and transient events (e.g. spill events to aquatic receiving environments, infrequent releases of short-lived and/or non persistent substances). Long-term exposure guidelines are meant to protect against all negative effects during indefinite exposures.

There are two types of Canadian Guidelines; type A guidelines are derived using a species sensitivity distribution (SSD) approach when there are adequate primary and secondary toxicity

data to satisfactorily fit a SSD curve. Type B guidelines are for substances that have either inadequate or insufficient toxicity data for the SSD approach (i.e. Type A guideline), but for which enough toxicity data from a minimum number of primary and/or secondary studies are available.

In the Canadian process quality criteria are used to evaluate bioassays and all appropriate data for all available species are plotted in the SSD. The lowest acceptable endpoint for appropriate, different negative effects per species is plotted. No-effect data are preferentially used and primarily plotted. In addition to the use of SSD data, there is the potential of invoking the protection clause for highly valued species such as those that are endangered.

In conclusion, probabilistic approach is being used more and more for marine (and FW) guidelines. They are used in North America, Hong Kong, Australia-New Zealand, etc. Some questions remain on related to the combination of data (FW and SW), extrapolation from one climatic zone to another, segregation of data by groups (fish vs. invertebrates) and the combination of data from tests based on different endpoints.

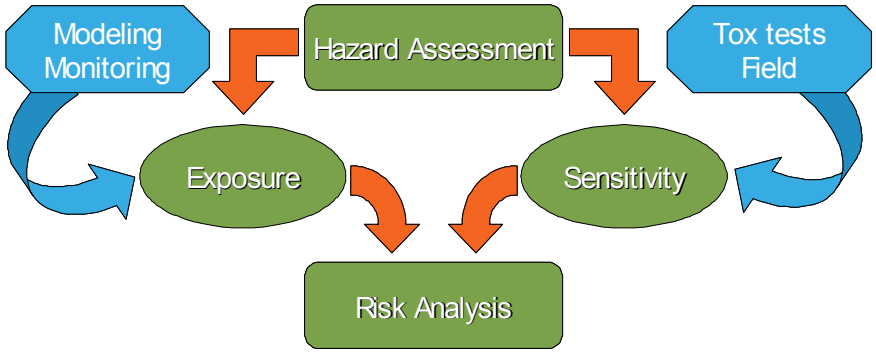
3.4 Genomic data interpretation: Assessment factors versus a probabilistic approach

C. Karman
IMARES, the Netherlands

Probabilistic risk assessment is not a recently introduced method; it has been in use in environmental sciences since the early nineties (Schobben and Scholten, 1993). Although its application has primarily been in the scientific arena, it was already in this period that, for example, in the Netherlands the Maximum Permissible Concentration of substances in fresh and marine waters was determined using an SSD approach. However, with the development of the international (European) chemical regulations, the assessment factor approach gained more attention and a higher profile in the EU TGD for chemicals assessments.

Independent of the method used; the main objective of ecological risk assessment is to determine the probability of adverse effects occurring to exposed ecosystems, due to surpassing of a (toxicity) threshold level. The generic approach to meet that objective is to perform a pre-screening of potential (intrinsic) risk to identify those environmental stressors that are likely to cause adverse effects, and to compare for those stressors the sensitivity of the receiving environment with the levels of exposure (see Figure 3). The uncertainty in the exposure levels and the sensitivity estimates need to be accounted for in the assessment.

Figure 3: Generic scheme for environmental risk assessment



Sources of uncertainty in predicted environmental concentrations (PECs) and PNEC: Uncertainty in the exposure concentration may have various sources, including:

- Variation in time, due to, e.g. process characteristics of the discharging installation;
- Variation in space, due to hydrodynamic dispersion processes;
- Sampling error, as field samples only provide an estimation of the actually occurring concentrations;
- Analytical error, caused by the sample preparation, concentration steps or the analytical equipment;
- Uncertainty in model predictions.

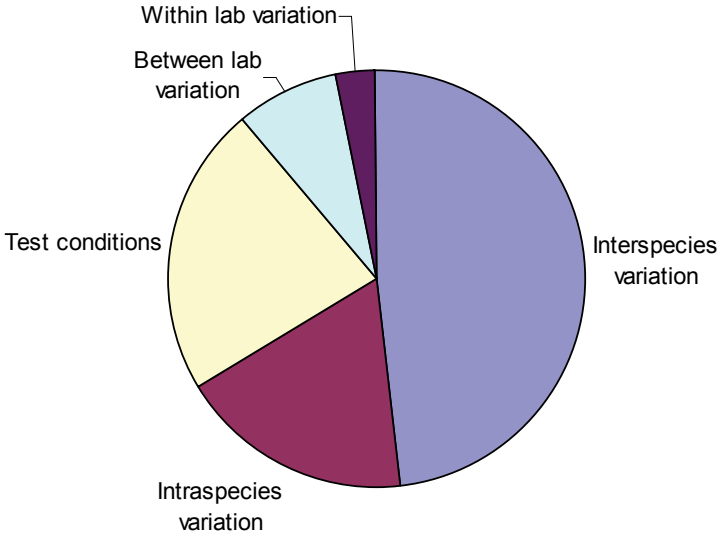
When basing a risk assessment on point estimates; this uncertainty is accounted for by using a 'worst case' (highest concentration) or 'realistic worst case' (95-percentile of concentrations). In a probabilistic risk assessment the uncertainty is included by using the frequency distribution of possible exposure levels. It must be noted that both methods usually include variation in time and space, but tend to ignore the variation caused by the sampling, analysis or modelling procedures.

Comparably, the variation in estimates of ecosystem sensitivity is usually based on interspecies variation. A dataset of sensitivity estimates does, however, include many other sources of uncertainty:

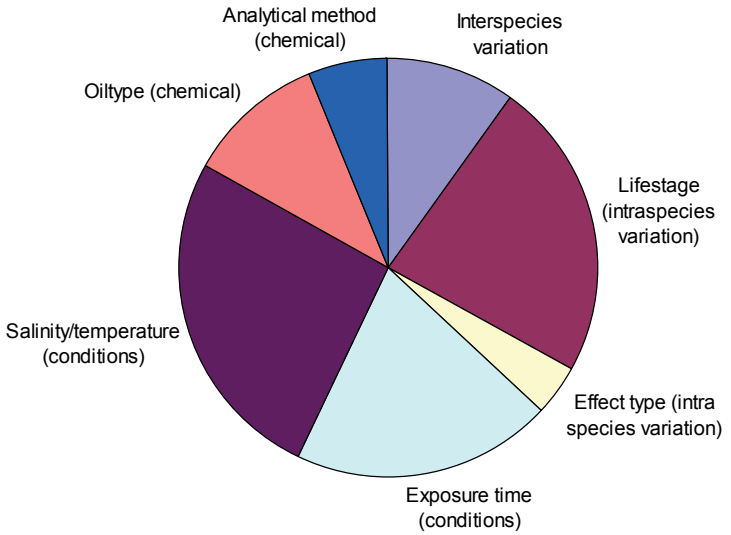
- Inter- and intra-species variation;
- inter- and intra-laboratory variation;
- acute vs. chronic exposure;
- laboratory vs. field conditions.

Studies performed in the early nineties in the IMARES laboratory (Schobben and Scholten, 1993; Scholten *et al*, 1993) indicate that intra-species variation may cover for only 50% down to 10% of the variation in an ecotoxicity dataset (see Figure 4). However, only the inter-species variation is usually included in risk assessment studies.

Figure 4: Graphical presentation of the sources of variation in (marine) datasets of cadmium and oil



Cadmium (after Schobben and Scholten, 1993)



Oil (after Scholten *et al*, 1993)

Tiered approach: As the assessment factor approach tends to disregard valuable information in the dataset it may be favourable to follow a probabilistic approach. It should be recognised, however, that generally a probabilistic approach is more data demanding and requires a higher effort. This may not always be necessary, and it is therefore recommended to follow a tiered approach to risk assessment.

In the first tier a worst case approach is followed based on point estimates for PEC and PNEC (using assessment factors). This PEC:PNEC approach provides an indication of the likelihood of adverse effects to occur. Only when the worst case assessment indicates that adverse effects are likely to occur (i.e. PEC:PNEC > 1), the second tier is initiated. This second tier should be probabilistic (preparation of an SSD), taking into account all relevant species (trophic levels or known sensitive species). From the SSD one can identify those species that are expected to be adversely affected due to exposure to the stressor (i.e. those species in the lower left tail of the distribution). In some cases (e.g. when the identified species are key species for a specific habitat have a protected status or specific economic value) it may be advisable to initiate the third tier and perform a species specific, biology based assessment (which might include DEB modelling or population or ecosystem models). Therefore, we may conclude that:

- The Assessment Factor Approach is disregarding valuable information from the dataset and demotivates the generation of additional data (as only the lowest value of the dataset is used). For reasons of simple application and low data requirement, the assessment factor approach is, however, suitable for screening purposes.
- The Probabilistic Approach uses much more information from the dataset, therewith giving a better estimation of exposure or ecosystem sensitivity, and improves by adding more data. It should be recognised that variation included is mainly based on interspecies variation, which may only cover a small fraction of the actual variation in the dataset.
- Based on the characteristics of both approaches, it is advisable to follow a tiered assessment approach; starting with an initial screening using assessment factors, if necessary, followed by more detailed (probabilistic) assessment using SSDs.

3.5 Considerations for the use of freshwater ecotoxicology data in marine risk assessments

J. Wheeler
Syngenta

The aim of this presentation was to address the use of freshwater data in marine assessments. The main points are:

- Why might there be differences between saltwater and freshwater species sensitivity?
- Is it possible to reliably extrapolate from freshwater to saltwater data?
- Outline the uncertainties associated with such extrapolations.

The presentation draws mainly on research conducted in 2001 for CEFIC under its Long Range Research Initiative programme (CEFIC LRI), addressing the question 'why might there be differences between saltwater and freshwater species sensitivity?'

Observed differences between freshwater and saltwater species sensitivities are influenced mainly by (a) biological differences; (b) chemical behaviour differences; and (c) test methodology differences. An understanding of these factors can be helpful when considering if it is appropriate to use freshwater data and the magnitude of an assessment factor applied to freshwater data.

Biological differences

Saltwater and freshwater species differ in their physiology, phylogeny and life histories traits. These differences undoubtedly lead to differences in sensitivity to toxicants. Most important is the much greater phylogenetic diversity in marine environments. Indeed there are sixteen exclusively marine phyla (e.g. Echinodermata, Cephalopoda, Ctenophora). These phyla may have marked sensitivity differences compared to those covered by the 'standard' test species (fish, crustacea and algae). Furthermore, specific differences in physiology even within the same phyla in freshwater or saltwater may influence sensitivity. For example different osmoregulation strategies will have consequences for toxicant uptake. Most marine invertebrates are osmoconformers matching their internal concentration to that of the external environment. In contrast most freshwater fish are osmoregulators actively pumping ions across the gills and secreting dilute urine. Therefore, it is clear different strategies may affect toxicant uptake and time to reach critical body burden thus resulting in sensitivity differences. There are also differences in life history traits between freshwater and saltwater organisms. Many marine organisms, particularly invertebrates, have pelagic and planktonic forms. These are early lifestages that may have marked sensitivity differences to freshwater species.

Chemical behaviour

Chemical substances will also behave differently in the two media. The net result will be differences in the bioavailability of a substance that may lead to sensitivity differences. Differences in bioavailability could be the result of speciation and/or solubility differences between the two media. The major differences between freshwater and saltwater are:

- Salinity – organic compounds can be less soluble in saltwater due to a 'salting out effect' (ionic interactions between ions and water molecules effectively squeezing compounds out of solution). This can influence partitioning, increasing absorption, uptake and the time to reach critical body burden.
- pH – influences speciation by molecular ionisation.
- Dissolved organic matter – complexation, sorption of toxicants to colloids.
- Hardness – complexation of anions and cations. Complexation usually reduces bioavailability e.g. toxic metals tend to be 'less toxic' in hard water.

Test methodology differences

It is also possible that systematic differences in the way we conduct freshwater or saltwater ecotoxicity tests may lead to observable differences in toxicity estimates. For example tests durations vary even for acute tests. The standard freshwater invertebrate test is a 48-hour *Daphnia* immobilisation test (OECD 202 and OPPTS 850.1010). Whereas the marine equivalent is a 96-hour mysid shrimp (OPPTS 850.1035) or penaeid (OPPTS 850.1045) assay. Saltwater tests are also much more likely to be conducted under flow-through rather than static or semi-static test conditions. It is plausible that the dynamics of uptake may therefore be different leading to differences in toxicity.

Is it possible to reliably extrapolate from freshwater to saltwater data?

Investigations into the extrapolation from freshwater to saltwater effects data have used data pairs or species sensitivity distributions.

Data pairs

Comparable freshwater and marine data are paired (e.g. lowest *Daphnia* EC_{50} with lowest mysid LC_{50}) and a ratio of the freshwater value over the saltwater value taken. A ratio of ≤ 1 indicates comparable or greater freshwater sensitivity. In an analysis of the enhanced ECETOC EAT database (Wheeler *et al*, 2001) 62% of acute data pairs gave a ratio of ≤ 1 and 93% of acute data

pairs fell within a factor of 10 (n = 108). For chronic data pairs all ratios were ≤ 10, although this was based on relatively few data (n = 29) and included only one algal endpoint.

Other studies have also found that freshwater and saltwater ratios typically fall within a factor of 10 (Hutchinson *et al*, 1998). However, this approach is limited in that it is based on a small number of chemicals with only single values (lowest freshwater and saltwater values only) and does not consider the comparability of endpoints. The ratio approach ignores the majority of the available data and so is sensitive to outliers. The few chronic comparisons there are cover only a limited number of taxa.

Species sensitivity distributions

An approach to overcome the issues associated with the data pair approach is to compare assemblages of freshwater and saltwater species in species sensitivity distributions. The major advantage of this approach is that it allows the use of exclusively marine taxa if they are available. The freshwater and saltwater distributions can be plotted on the same graph and visually compared (see Figure 5). The distributions are not species specific allowing the groups of species (taxonomic variety) to be assessed in one analysis. It is also possible to compare point estimates from the distributions (e.g. HC5s) and equation parameters. Therefore the magnitude of differences between saltwater and freshwater species sensitivities may be quantified. A comparison of HC5 values from 21 substances covering a range of modes of action indicated ratios typically fell within ≤ 10 (Wheeler et al, 2002).

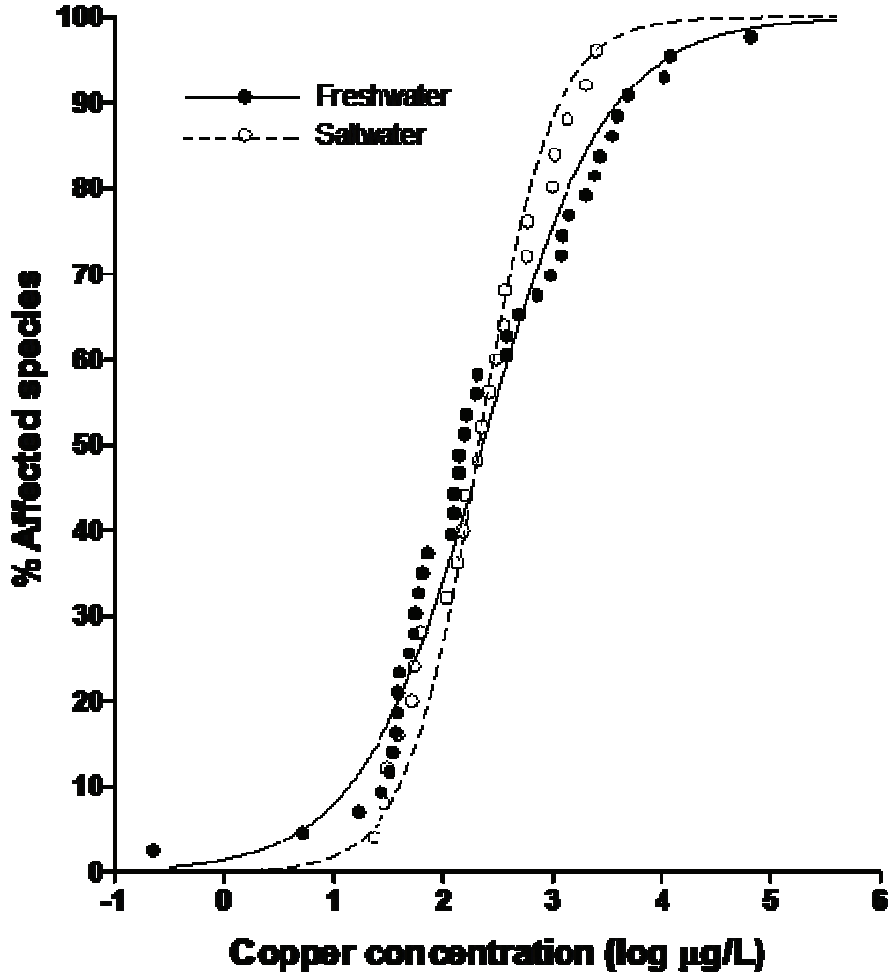
Uncertainties associated with extrapolations

There are two major uncertainties when extrapolating from freshwater to saltwater species responses:

- Are freshwater species responses predictive of saltwater responses for equivalent taxonomic groups (e.g. freshwater and saltwater fishes)?
- Are exclusively marine taxa sensitivities also covered by freshwater data?

The first point has been addressed and there is a reasonable basis for this extrapolation under certain circumstances (case-by-case justification required). However, further work is needed to address the sensitivity of exclusively marine taxa.

Figure 5: Freshwater and saltwater species sensitivity distribution for copper (taken from (Wheeler* et al*, 2002)



In summary, an understanding of the differences (biological, chemical and methodological) between freshwater and saltwater responses can be used to inform the suitability of extrapolation. Potentially, this could also be used on a case-by-case basis in the evaluation of assessment factors applied to such data. The analyses conducted to date (data pairs and species sensitivity distributions) indicate that the majority of freshwater and saltwater data are within a factor of 10 for acute effects. However, there are research needs to address chronic extrapolations and the sensitivity of exclusively marine phyla.

3.6 RISICO: Risk of Surfactants In Coastal Environments

A. Temara (*P&G, Belgium***) and G. Whale (***Shell Chemicals, UK***)**

The purpose of the RISICO project is to refine the ecological risk assessment of surfactants in coastal environments. One of the main objectives is the development of new analytical tools to predict the exposure of these xenobiotics in the marine environment. The test compounds selected were the anionic surfactant linear alkyl benzene sulphonate (LAS), and the nonionic surfactants alcohol ethoxylates (AE) - some of the most used surfactants in the formulations of detergents and other cleaning products. We have developed collaborations between Procter and Gamble, Belgium; the Institute of Marine Sciences in Andalusia, Spain; the Institute for Risk Assessment Sciences of Utrecht University, The Netherlands; the Plant Bioengineering Department of the Free University of Brussels, Belgium; and the International Atomic Energy Agency-Marine Environment Laboratory, Monaco.

The equilibrium partitioning (EqP) theory was tested experimentally to define whether water quality criteria can be used for surfactants in marine sediments to calculate sediment criteria, via the equation $PNEC_{sediment} = PNEC_{water} \times K_d$, where the sorption coefficient $K_d = C_s / C_w$. Analytical tools, including solid phase micro extractions (SPME) were developed to measure the freely dissolved concentrations of the tested materials. S. Droge and J. Hermens (IRAS, University Utrecht, NL) generated sorption isotherms for 10 AE homologues with 2 clay minerals and 6 marine sediments over a range of water concentrations > 5 orders of magnitude. A non-linear sorption model was developed combining a Langmuir and a linear term to describe the sorption processes (Droge and Hermens, 2007). For AEs with longer ethoxylates (EO) (AE > 6), the adsorption to clay dominated in the tested materials and the absorption to organic matter was negligible. It was observed that the sorption increased with the number of EO, while toxicity decreased with more EO. The sorption of the AEs was stronger (> 1 log unit) than expected by default sorption models used in many risk assessment schemes, suggesting less un-bound and therefore less bioavailable materials. In sediment toxicity tests with the amphipod *Corophium volutator*, the dissolved AE concentration determined the toxicity, supporting the pore water hypothesis. However, the quick biodegradability of AEs in sea-water decreased overlying water concentrations to non-toxic levels within a few days. Test amphipods exposed to a sediment prepared six days prior to test organism exposure were not affected by lethal concentrations measured in the pore water. While this amphipod lives in burrows in the sediment, the actual exposure concentration is strongly influenced by the overlying water. The EqP is therefore conservative for organisms living in burrows with circulating overlying water as concentrations are typically lower than in the pore water of contaminated sediments.

A similar experimental approach was used by A. Rico-Rico and J. Hermens (IRAS) to define the bioavailability of LAS to *C. volutator* in marine sediments and the EqP approach was also confirmed with experimental data (Ricco-Ricco *et al*, 2009).

In CSIC (SP), A. Mauffret and J. Blasco defined the exposure pathway of C12-LAS to the marine deposit feeder *Hydrobia ulvae*. *H. ulvae* were exposed to LAS via sea water or sediment. The sediment-pore water partitioning coefficient was assessed in the employed sediment (Kf 1175 L/kg). In the spiked sediment test, the 10d-LC_{50} value was 208 ± 3 mg/kg. The corresponding calculated LC_{50} value in the pore water was 0.15 mg/L which was 9.3 times lower than the 10d-LC_{50} value observed in the water-only test (1.39 ± 0.02 mg/L). This difference suggests that presence of sediment in the test has affected the C12-LAS exposure to *H. ulvae*. The freely dissolved fraction might have not entirely accounted for the observed toxicity in the sediment. It was concluded that the bioavailability of sediment associated LAS could be increased in the gut of these marine deposit feeders. Alternatively, the physiology of benthic organisms - including uptake and elimination rates from the pore water - could be affected in systems with no sediment.

Uptake and elimination biokinetics of C12-LAS were determined in marine organisms, including algae, mussels, and fish, using radiolabelled materials, hence working at environmentally relevant concentrations (3 µg/L). This work was undertaken at IAEA (Monaco) by F. Renaud and M. Warnau. In mussels exposed to dissolved LAS, the bioconcentration factor was ≤ 50 L kg^{-1}. During the uptake phase, rapid accumulation of ^{14}C was observed in the organs, followed by rapid elimination of most of ^{14}C within 3 days. The 20% remaining activity was eliminated after 10 days. For dietary exposure, the elimination kinetics was measured following single feeding. 80% of the LAS that had been transferred through the food were eliminated within 12 hours and only 1.9% of the initial radioactivity remained after 10d elimination, probably incorporated as organic carbon into the biomass.

Following this major collaborative effort to generate innovative experimental data on the ecotoxicology of surfactants in marine environments, a series of draft manuscripts are being prepared for publication. However, refinement of risk assessment in marine sediments will still require fundamental collaborative research, including development of SPME for more compounds, eco-etho-physiological studies of benthic organisms in presence or absence of sediment, clarification of the assimilation process from the sorbed fraction. Overall, our data indicate that the EqP can provide a good approximate of the hazard of the tested surfactants to marine benthic organisms, but processes can be complicated by rapid degradation in the test systems. In addition, this approach applies to organisms primarily exposed through the pore water. For the many burrowers living in coastal sediments, including *C. volutator*, exposure to the overlying fraction may be relevant from a risk assessment perspective, considering that the contaminant concentrations are typically lower than in the pore water. It is eventually not surprising that actual exposure depends on the ecology of the test organisms. It is important to note that the tested surfactants were not bioaccumulative, which could be of relevance for EOSCA and OSPAR activities.

3.7 Hazard assessment with small datasets

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The EU TGD (EC, 2003) specifies a range of assessment factors to be used in deriving PNECs for marine hazard assessments. The choice of factor depends on the number and type of species tested and type of study (short/long term), and the factors include a precautionary element to allow for potentially wider variation of sensitivity when marine species are considered. The TGD also states that statistical extrapolation methods based on species sensitivity distributions (SSDs) could be used as an alternative, with a smaller assessment factor, but specifies that at least 10 NOECs (preferably more than 15) from at least 8 taxonomic groups are required. Such numbers of NOECs are not available for many chemicals, so it is useful to explore the potential of different approaches for deriving SSDs from smaller datasets.

One such approach works by augmenting small toxicity datasets with estimated toxicity values for additional species. These additional toxicity values are estimated from interspecies correlation estimation (ICE) models in toxicity, which are essentially linear regression models on log-toxicity data, derived from existing data on many chemicals, as illustrated diagrammatically in Figure 6. The ICE approach was developed by the US Environmental Protection Agency, and has been implemented as software accessible on the web[4]. Its use for building SSDs from small datasets has been described and evaluated for terrestrial vertebrates (Awkerman *et al*, 2008), and for aquatic organisms (Dyer *et al*, 2006, 2008). The latter includes an evaluation of the degree of agreement between HC5s estimated from SSDs built with ICE models and HC5s estimated directly from measured toxicity values.

A second approach for deriving SSDs for chemicals with small datasets ($n \leq 4$) works by using information from SSDs for other chemicals that have larger datasets. The original version of this approach (Luttik and Aldenberg 1997; Aldenberg and Luttik, 2002) assumes that the standard deviation for the SSD of the chemical under assessment can be estimated, without uncertainty, by the average standard deviation for other chemicals with larger datasets. The mean of the SSD is estimated directly from the toxicity values available for the chemical under assessment. The resulting mean and standard deviation describes the estimated SSD for the chemical under assessment and can be used to estimate any given percentile, such as the HC5. This process is illustrated diagrammatically in Figure 7. Recently it has been shown that the standard deviation of the SSD varies significantly between chemicals (EFSA, 2005), so it would be desirable to refine the pooled standard deviation approach to take account of this.

[4] http://www.epa.gov/ceampubl/fchain/webice/index.htm

Figure 6: Diagrammatic representation of using interspecies correlation estimation (ICE) models to construct SSDs from small datasets. Toxicity values for tested species are augmented with toxicity values for other species estimated by using ICE models

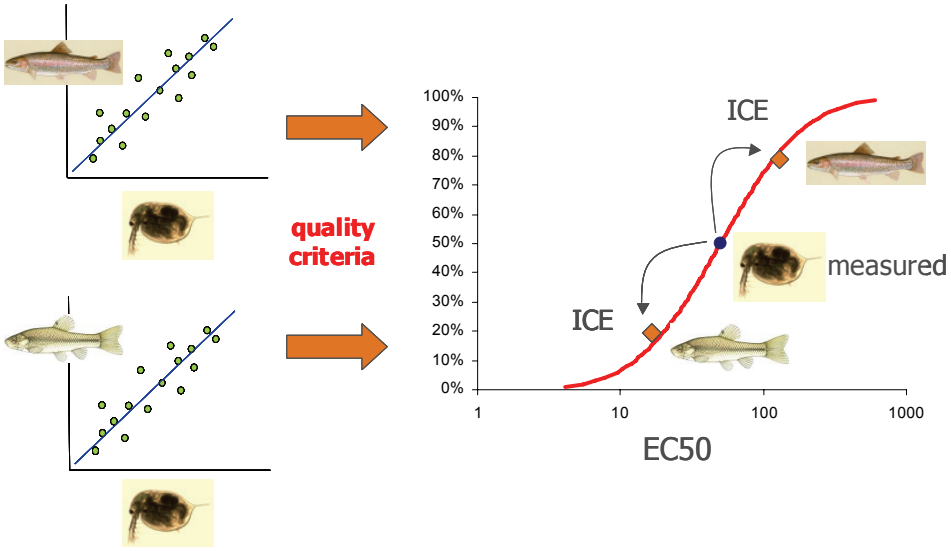
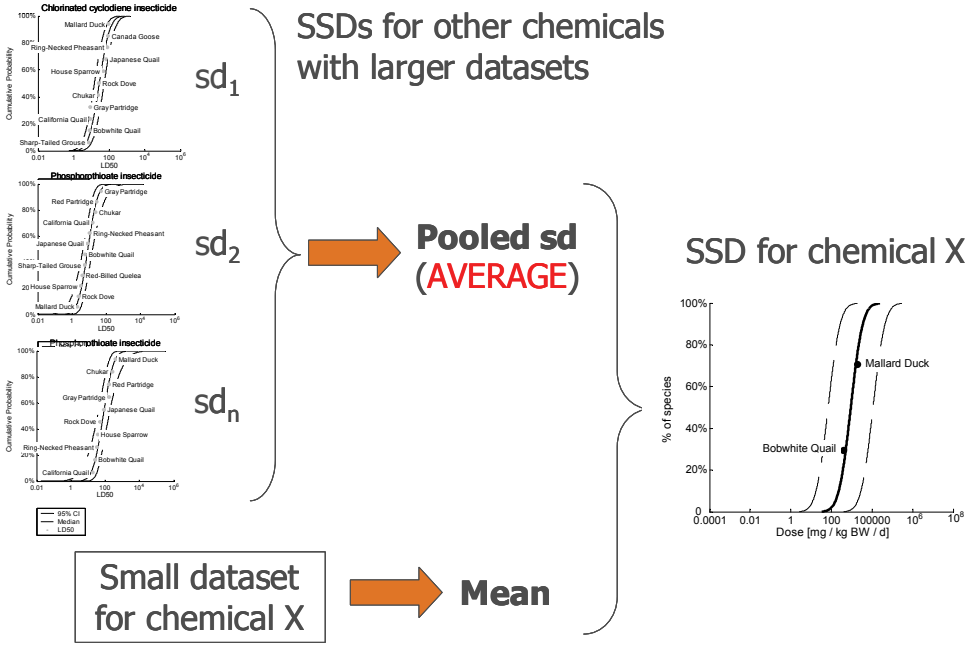


Figure 7: Diagrammatic representation of building an SSD for a chemical with a limited dataset by using a pooled standard deviation derived from other chemicals with larger datasets



Both the above approaches require a number of assumptions in addition to those already made when estimating an SSD from larger datasets of measured data. All of these assumptions should be critically examined and adjusted if necessary, e.g. a single SSD should not be constructed for two taxonomic groups (e.g. fish and invertebrates) if there are systematic differences in toxicity between them; alternative distribution shapes should be considered; and the pooled standard deviation should be modelled in a way that reflects any systematic differences between chemical classes. Further work is required on methods for calculating confidence intervals on HC5s estimated using each approach. It will be important to evaluate the performance of both the above methods, and how this changes as more species are tested, by comparing the resulting HC5s with HC5s estimated directly from measured data.

The level of protection provided by the assessment factor approaches, specified in the TGD for use with small datasets, is unknown. The performance of these approaches could also be evaluated by comparing them with SSDs estimated from large datasets, to see which percentiles of the SSD are equivalent to the PNECs produced by the different combinations of endpoints and assessment factors used in the TGD approach. A recent analysis by EFSA (2005) illustrates how the practice of applying a fixed assessment factor to the lowest available endpoint results in progressively increasing conservatism as more species are tested.

The TGD implies that the HC5 is an appropriate basis for decision-making, although it states that the choice is 'pragmatic'. We therefore suggest that instead of asking, as is often done, how many species are required for a reliable SSD, the more appropriate question is: What is the best indicator of the HC5 when you have a limited dataset? This question should be asked for the TGD assessment factors, as well as for different approaches for building SSDs. It is also useful to examine confidence intervals of the HC5, as suggested by the TGD, because they reflect part of the uncertainty that results from a limited dataset.

3.8 Existing marine hazard schemes: Assessment of chemicals used by the offshore oil and gas industry

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CEFAS

Chemicals specific to the offshore oil and gas industry are regulated in the North East Atlantic area by the Oslo Paris convention (OSPAR). The various OSPAR contracting parties (CPs) regulate offshore chemicals via OSPAR's Harmonised Mandatory Control Scheme (HMCS) for the use and reduction of discharge of offshore chemical. The HMCS is developed through OSPAR Decision 2002/2 and its supporting recommendations.

Under the HMCS, it is the chemical suppliers' responsibility to supply data on a substance level for assessment prior to product marketing. All data must meet quality standards, which include compliance with Good Laboratory Practice (GLP), and adherence to internationally recognised protocols. The data are assessed for substitution warnings against the HMCS pre-screening scheme (Figure 8). Pre-screening identifies hazardous substances within an offshore chemical product through evaluation of its persistence, bioaccumulation and toxicity properties. Substances failing the required criteria are awarded substitution warnings.

In addition, a generic deterministic risk assessment may be conducted using the CHARM (Chemical Hazard Assessment and Risk Management) model, for each product, subject to its intended use. The CHARM model calculates the ratio of predicted exposure concentration against the predicted no effect concentration (PEC:PNEC), expressed as the Hazard Quotient (HQ). The model uses biodegradation, toxicity, partitioning, use, discharge, and chemical dosage data in its calculations.

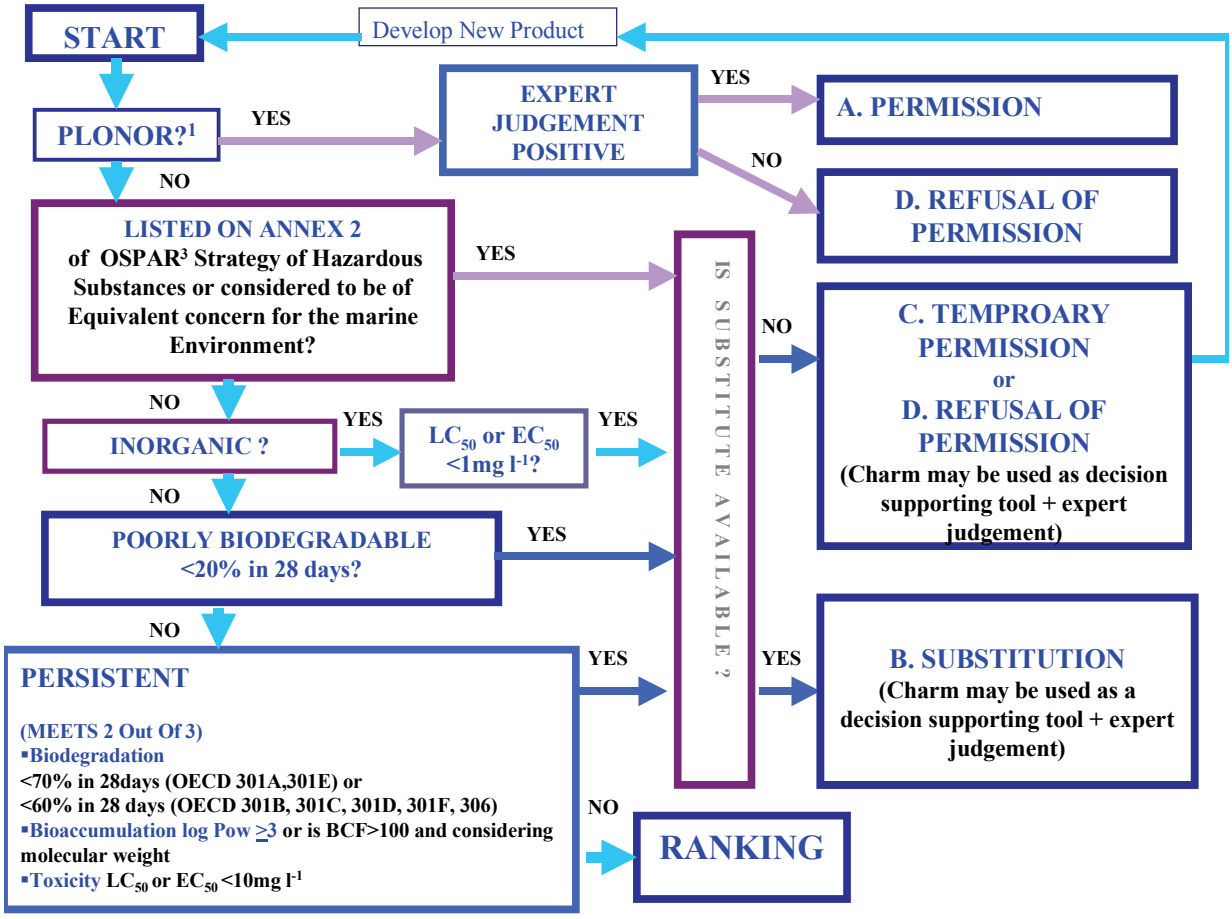
Products not applicable to CHARM (e.g. inorganic substances, and hydraulic fluids or chemicals used only in pipelines) are assessed by the various national CPs using their own methods (e.g. the United Kingdom and the Netherlands utilise a simple PBT assessment scheme that results in the award of an OCNS group).

Data collected and assessed by each CP are used for environmental management decisions and for monitoring chemical impacts on the marine environment; specifically, permitting of offshore operations based on environmental risk assessments, annual evaluation and reporting of hazardous substance discharge quantities to OSPAR; development of national strategies to phase out substitutable substances where technically feasible.

The objective of this environmental management and monitoring is to prevent pollution of the maritime area from offshore oil and gas activities by continually reducing, and eventually ceasing discharges, emissions and losses of hazardous substances to the marine environment by 2020.

Thus, this will facilitate the compliance of the offshore industry with the OSPAR Commission's hazardous substances strategy, the ultimate aim of which is to achieve chemical concentrations in the marine environment near background values for naturally occurring substances, and close to zero, for man-made synthetic substances.

Figure 8: The Harmonised Pre-Screening Scheme (shaded) as part of the whole harmonised mandatory control system for offshore substances set out in the applicable OSPAR decision



4. SYNDICATE SESSIONS

4.1 Syndicate 1: How can marine and freshwater data sets be used?

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For marine risk assessment there are usually insufficient data for saltwater organisms to predict a $PNEC_{marine}$ with confidence. Freshwater ecotoxicity data are more plentiful due to the wider availability of test methods and the early assumption that freshwater environments were at greater risk (ECETOC, 1993). The aim of this syndicate was to evaluate how available data and approaches could be used to increase a hazard assessor's accuracy when extrapolating between marine and freshwater effects assessment. The group addressed this issue by phrasing and answering a series of questions:

1. What current approaches are employed for the use of freshwater data in marine assessments?
2. What databases and prediction tools exist to collect data from?
3. How can knowledge of mode of action, animal physiology, *in vitro* methods and structure activity relationships be used when extrapolating from freshwater to marine systems?
4. What are the key knowledge gaps and research needs?

Discussions at the workshop highlighted the need for a number of case studies to address the feasibility of some of the group's recommendations. Following the workshop, case studies for benzene, phenol and chlorpyrifos were developed and can be found in Appendix A.

1. What current approaches are used for the use of freshwater data in marine assessments?

The use of freshwater data in marine hazard assessments is described in the EU TGD (EC, 2003), Canadian Water Quality Guidelines (CCME, 2007) and the USA marine water quality criteria (Russo, 2002).

In using this surrogate approach the EU TGD calls for 'a clear understanding of the comparability of effects data generated on both types of species'. In general, higher assessment factors and/or

more data are required for the use freshwater data in marine assessments compared to the derivation of freshwater PNECs. The additional assessment factor, accounting for this increased uncertainty is typically 10-fold higher to derive the $PNEC_{marine}$ (see Table 1 in Appendix B). This additional factor is intended to account for (a) the higher biodiversity found in marine environments (16 animal phyla only occur in marine ecosystems); and (b) specialised environments where particular factors lead to low species diversity (e.g. fluctuating or low salinity) requiring the protection of a low number of species in order to maintain ecological function.

However, the TGD allows for the size of the assessment factor to be varied on a case-by-case basis. The factor may be lowered (at least on base-set data) by knowledge of structurally similar substances, known non-specific mode of action or availability of additional data for the most sensitive group.

The Canadian Water Quality Guidelines for the protection of aquatic life also allow for the use of freshwater ecotoxicity data in marine risk assessments (CCME, 2007). The current protocol states: "... for substances for which no significant influence on chemical behaviour can be shown or reasonably anticipated, and where no differences in toxicity toward freshwater and marine organisms (by comparison of similar taxonomic groups) can be seen, toxicity data from freshwater organisms may be used on a case-by-case basis in order to broaden the marine database."

Unlike the EU TGD approach, the minimum data requirements for freshwater and marine environments (both long and short term) are virtually identical[5]. Although the guideline acknowledges the greater taxonomic diversity of marine ecosystems "the reality of data availability and societal and policy considerations" also come into play.

The United States Marine Quality Criteria also allow for freshwater data to be mixed with saltwater values particularly at the chronic level (Russo, 2002). However, there is no process for the surrogate approach (freshwater in place of saltwater data) at either the acute or chronic levels.

The EU TGD and the Canadian water quality guidelines allow for the use of freshwater endpoints in deriving $PNEC_{marine}$ values. Both regulations require argumentation on a case-by-case basis for the inclusion of freshwater data. Guidance is needed to aid an assessor to decide when such extrapolations are appropriate and to what extent it may be necessary to increase or reduce a safety factor concomitant to the level of uncertainty.

[5] The only difference is the requirement for a marine temperate vascular plant or algal species for the Type A and B1 short term guideline (CCME, 2007).

2. What databases and prediction tools exist to collect data from?

There are a number of databases that contain relevant freshwater and marine ecotoxicity data. These can be considered data repositories that may be useful for the extraction of relevant data to refine a marine effects assessment (e.g. data for structurally similar substances). There are also a number of *in silico* tools that could be used to predict marine ecotoxicological responses. Both types of resources were discussed by the syndicate and are described in Table 2 of Appendix B.

Data repositories

A number of regulatory and industry databases have been developed and are widely available (see Table 2 in Appendix B). The databases vary in size and their utility to address the issue of extrapolation from freshwater to marine species response. The ECETOC EAT and EAT 3 databases (ECETOC 1993, 2003) contain a considerable amount of relevant published data that have been rigorously quality assessed. The US EPA ECOTOX database is much larger (and is updated quarterly); it incorporates published literature, US and several EU country regulatory data sources. The ECOTOX database contains a great deal of valuable marine ecotoxicity data most likely due to historical test method development with marine species in the US (particularly with sheepshead minnow and mysid shrimp). However, the ECOTOX database has more limited quality criteria (e.g. measured concentration descriptions) and would require much greater reference to the original data sources for confident use in a regulatory context. Other data sources exist which are either more difficult to access (industry data) or of a more specialist use (REDs for agricultural or biocidal active ingredients).

Many of the databases described above have been used to assess the appropriateness of extrapolating from freshwater to marine ecotoxicity datasets. For example the ECETOC databases have been used to make generalisations about freshwater to saltwater extrapolations (Hutchinson *et al*, 1998; Peters *et al*, 2005; Floeter *et al*, under revision; Wheeler *et al*, 2001), whilst the EPA ECOTOX database has been used to compare freshwater and saltwater species assemblages using species sensitivity distributions (Wheeler *et al*, 2002). For regulatory purposes the databases may be interrogated to improve the accuracy of a predicted saltwater response from freshwater data. This may be in the surrogate sense or as a means to justify a reduction in an assessment factor applied to derive the $PNEC_{marine}$. The following approaches were considered by the syndicate:

- Extraction and quality assessment of any relevant freshwater data.
- Extraction and quality assessment of any marine data.
- Extraction of any freshwater or marine data for substances similar to that of interest:
  - Structurally similar substances;
  - substances sharing a mode of action.

These data may be used to make inferences based on mode of action and/or structural similarity. If there is a sound basis for the congruence of freshwater and marine data a reasoned argument for the use of freshwater data should be possible. Alternatively, the analysis may be used to inform the magnitude of the assessment factor to be applied. Such an approach is currently possible under the EU TGD (EC, 2003).

Prediction tools

It is also possible to predict marine species responses *in silico*. QSARs can be used to predict marine species responses from the physico-chemical and structural properties of the substance. Alternatively, if freshwater data are available, correlations between species responses may be used to estimate the marine toxicity of a substance.

ECOSAR and Web-ICE are useful tools to aid further investigations. ECOSAR is an established method with regulatory applications (e.g. Pre-Manufacture Notices under the US Toxic Substances Control Act). The Web-ICE tool has great potential to be applied to the extrapolation of marine species responses. It is freely available, simple to use and has transparent quality criteria. However, both ECOSAR and Web-ICE are limited in that it is currently not possible to predict marine algal ecotoxicity endpoints (see case studies in Appendix A). Web-ICE is described in Appendix D and ECOSAR in Appendix E.

3. How can knowledge of mode of action, animal physiology and structure activity relationships be used when extrapolating from freshwater to marine systems?

Knowledge of mode of action, physiology of the receptor organism and structure activity relationships (both biological and physico-chemical) can be used to increase accuracy and confidence when making freshwater to marine extrapolations.

Mode of action

The syndicate recognised the value of applying the Verhaar scheme (Verhaar *et al*, 1992) to classify substances based on acute mode of toxic action. The Verhaar scheme has been used recently by an ECETOC task force addressing Intelligent Testing Strategies (ECETOC, 2007). The scheme has four categories as described in Table 3 of Appendix B.

The extrapolation from freshwater to marine base set data (*Daphnia*, fish and algae) was discussed. The following was concluded:

- Modes of action 1 and 2 (narcotic and polar narcotic) substances direct read across from freshwater to marine data should be possible.
  - For crustaceans and fish, there is a large body of evidence supporting this approach (Hutchinson *et al*, 1998; Leung *et al*, 2001; Peters *et al*, 2005; Floeter *et al*, under revision; Wheeler *et al*, 2001, 2002).
  - For algae, further work may be required to support read across as sensitivity differences between freshwater and marine species for mode of action 1 substances have been observed (Peters *et al*, 2005; Floeter *et al*, under revision).
- Mode of action 3 (reactive) currently has insufficient information to allow for direct read across.
- Mode of action 4 (specifically acting) may typically require specific marine species testing.

Therefore, in terms of base set studies, the syndicate believed there are opportunities for direct read across. However, the discussions highlighted the need for further work in certain areas. One of these areas was the sensitivity differences between freshwater and marine algae for mode of action 1 substances. Potentially this sensitivity differential could be the result of the large surface area to volume ratio of algal cells (Peters *et al*, 2005; Floeter *et al*, under revision), thus resulting in greater sensitivity to differences in octanol-water partition coefficients between fresh and saltwater. This could be explained by a 'salting out effect' (Gordon and Thorne, 1967) effectively increasing the log K_{ow} in saltwater over that in freshwater. If this explanation holds it is likely that the observed differences in toxicity will be relatively small and constant across substances within the narcotic (MOA1) and polar narcotic (MOA2) modes of action. Consequently it is feasible that further investigation will be able to identify a suitable 'extrapolation factor' that could be confidently applied to freshwater data in order to be protective of marine algae. Further work into identifying patterns in the reactive mode of action datasets was also recommended. The lack of clear correlations observed to date may result from the range of bio-molecule targets that are encompassed by this category (see Appendix B, Table 3). Further division of this category by structure or physico-chemical properties may be required to provide a robust basis for freshwater to marine extrapolations. For specific acting substances covering a wide range of toxic mechanisms it is currently not possible to make direct extrapolations. Therefore, specific saltwater species testing may be required for marine assessments.

Chronic effects assessments were also discussed. The syndicates believed at this point there is insufficient evidence to support chronic freshwater to marine extrapolation for any of the Verhaar modes of action. Extrapolation for chronic effects is likely to be more challenging than for acute effects:

- Not just predicting a single toxic outcome (mortality) but a large number of endpoints that will vary in sensitivity (growth, development and reproduction).
- Chronic, longer study durations mean the test substance is more likely to reach equilibrium magnifying any observed sensitivity differences.

- Differences in species life history traits between standard freshwater and marine test species may complicate extrapolations.

Consequently the syndicate believes further research into the extrapolation of chronic effects is warranted. This could take the form of developing training set examples with data extracted from the relevant databases. It would also be informative to validate Acute to Chronic Ratios (ACRs) for both freshwater and marine species responses.

In conclusion, it is clear there are opportunities for direct extrapolations for certain modes of action (narcotic and polar narcotic). However, for reactive and specific acting substances covering a broader range of toxicological mechanisms of action further research is required. Further work is also required to establish the feasibility of extrapolations for chronic effects.

Animal physiology and in vitro *methods*

Knowledge of mechanisms of action and animal physiology may be especially useful for the specific acting substances. Development in this area offers great potential to employing Intelligent Testing Strategies (ECETOC, 2007). For example, mammalian *in vivo* and *in vitro* data may help to identify relevant or sensitive taxa by providing further elucidation of the mode of action. In the context of freshwater to marine extrapolation the ITS approach may be used to justify the testing of specific marine taxa only (based on the relevance of the receptor to the mode of action). This approach may be informative in order to limit the amount of vertebrate testing where there is an *a priori* expectation that other taxa will be more sensitive.

QSARs

The use of QSARs to predict biological responses is covered by prediction tools (above). ECOSAR has been used as a key example as it currently is in regulatory use (US EPA). Many QSAR models are available and, pending thorough evaluation, could be considered particularly if they incorporate specific models to predict marine responses (ECOSAR was limited in this respect; see Appendix A: Case Studies). These biological QSARs will not be discussed further here. However, (Q)SAR models to predict physico-chemical properties of substances under certain conditions (in this context read fresh and saltwater media) may be informative. For example predicting large differences in solubility between freshwater and saltwater could have a toxicological impact. Bioavailability may be greater in saltwater since substance partitioning may increase absorption and biological uptake. Therefore, in a weight of evidence assessment *in silico* predictions of a substance's physico-chemical properties in freshwater and saltwater could be used to help justify the use of freshwater ecotoxicity data.

4. What are the key knowledge gaps and research needs?

The syndicate discussions highlighted several areas that require further research:

- Case studies to assess the feasibility of the approaches outlined. More case studies with a broad range of substances are required to demonstrate the tools and further develop the interpretation of results. Such examples should consider what impact surrogate and extrapolation approaches have on defining $PNEC_{marine}$ values.
- Research to address the sensitivity of exclusively marine taxa is required. There is a need to establish to what extent marine and freshwater standard test species cover the responses of exclusively marine taxa (16 groups including echinoderms, ctenophores etc). However, to achieve this it was recognised that there will need to be flexibility on specific species to be tested. Furthermore the use of field collected test organisms may be necessary since culture conditions are not established for many of the groups. However, rigorous quality control procedures or reference toxicant testing may be required to support the validity of results from collected material.
- Further analysis and collection of algae datasets for MOA1 and MOA2 is required in order to establish the magnitude of the observed sensitivity difference (Peters *et al*, 2005; Floeter *et al*, under revision) and, if possible, to define an appropriate 'extrapolation factor'.

Conclusions

There are opportunities to use freshwater ecotoxicity data for $PNEC_{marine}$ derivation, although it is clear that a case by case justification for the use of freshwater data or varying assessment factors is required. This syndicate discussed some of the resources and tools that could be used to scientifically make these cases. The advantages and limitations of selected databases and prediction tools are described. Furthermore, knowledge of mode of action may allow for read across from freshwater to marine data in some circumstances. An understanding of physiology and data from *in vitro* methodologies could also be applied to identify particular receptors where specific marine testing is required. Potentially this offers an Intelligent Testing Strategy process in which to limit the amount of vertebrate testing.

These resources offer the prospect of increasing the accuracy of an assessment when extrapolating between marine and freshwater effects. Further research areas are recommended to take this forward.

4.2 Syndicate 2: Key issues in marine sediment assessment

Moderator: G. Whale
Rapporteur: L. Weltje
M. Breitholtz
N. Carmichael
F. Lewis
S. Lingdon
T. Millais
J. Straub
J. Tolls

The assessment of the hazards of chemicals likely to be partition to sediments poses unique challenges over and above those for assessing aquatic effects. This is because chemicals 'bound' to sediments can cause direct toxic effects to benthic organisms as they are released from sediments through partitioning to pore water and/or overlying water and/or uptake via ingestion of sediment particles. Furthermore, there are a number of factors that potentially determine the fate of chemicals in sediments and consequently whether adverse effects will occur. These include the physical and chemical nature of the sediment, method of chemical dosing and biology of the test species. Without understanding these issues quantification of dose levels in sediments alone is not sufficient to assess potential hazards to aquatic organisms. This raises fundamental questions about the design of any sediment toxicity tests.

Once sediment toxicity testing is triggered by a chemical's characteristics (mostly related to its environmental fate or physico-chemical properties) the testing results can be used for a hazard assessment for marine sediments. In case similar endpoints (e.g. LC_{50}, NOEC) for a number of different organisms are available, probabilistic hazard assessment in the form of a species sensitivity distribution (SSD) offers an interesting higher-tier option for the derivation of a refined PNEC value (usually a hazardous concentration for 5% of the species [HC5] divided by an assessment factor of 1 - 5).

1. Should all sediment toxicity assessments be undertaken using a 'standard' marine sediment system and seawater and which factors should determine the dosing of a chemical into marine sediments?
2. What is the most 'appropriate' test species for assessing sediment toxicity?
3. How can probabilistic approaches (SSDs) be introduced into marine hazard assessment?
4. The final 'catch 22' is: "Are sediment toxicity tests necessary because the bioavailability of the chemical is the key to determine their hazard although ultimately a sediment toxicity test measures bioavailability?"

The breakout group on sediment testing discussed specific aspects of marine sediment testing and drew from experiences made with freshwater sediment toxicity testing.

1. *Should all sediment toxicity assessments be undertaken using a 'standard' marine sediment system and seawater and which factors should determine the dosing of a chemical into marine sediments?*
   There was consensus that a standard marine sediment would be desirable to be able to compare different results/chemicals/organisms. Existing methods and testing/assessment schemes (such as those developed for pesticides and freshwater assessments) should be used in order to warrant consistency. Analytical measurements should be made to be able to express endpoints in bulk sediment, pore water concentrations (which could be measured with the aid of SPME fibres) or overlying water concentrations. Endpoints should be expressed in the same unit as the predicted no effect concentration (PNEC) in sediment for compatibility reasons in the environmental risk assessment (ERA). Dosing of chemical to the sediment may be via water or sediment. The decision on the dosing method should be made considering the characteristics of the chemical or its predominant entry route.

2. *What is the most 'appropriate' test species for assessing sediment toxicity?*
   Sediment testing focuses on invertebrates and more specifically on arthropods. In marine ecosystems this is further narrowed down by a focus on crustaceans. Suggested marine species are: The amphipod *Corophium volutator* (for which an ISO guideline was issued in 2005), copepods (several species possible. ASTM guideline is available, while presently a guideline for a life-cycle test with *Amphiascus* is under development at OECD) or *Leptocheirus plumulosus* (US guideline available).

3. *How can probabilistic approaches (SSDs) be introduced into marine hazard assessment?*
   At present, the use of SSDs for (marine) sediment is hampered by a lack of sediment toxicity data to populate the SSDs. So, the questions is whether toxicity data generated for freshwater sediment-dwelling organisms (e.g. non-biting midges *Chironomus riparius* or *C. dilutus*, amphipod *Hyalella azteca*, oligochaete *Lumbriculus variegatus*; for which ASTM, ISO or OECD testing guidelines are available) can be employed as surrogate for marine sediment data. While the test used in data generation may be different (for instance in case of chironomids it concerns a systematic group, insects, not occurring in marine environments) the data may be useful in constructing SSD which are protective. A second approach to broadening the data base for constructing species sensitivity distributions is to employ the equilibrium partitioning theory to generate toxicity endpoints for sediment from water only tests. Vice versa, sediment tests may be employed and the relevant bioavailable concentrations may be incorporated into an overall SSD covering sediment dwelling and aquatic species simultaneously. Such an approach may not be applicable to all, e.g. ionising, chemicals.

4. *The final 'catch 22' is: "Are sediment toxicity test necessary because the bioavailability of the chemical is the key to determine their hazard although ultimately a sediment toxicity test measures bioavailability?"*
   There is a need to understand the mechanisms of reduction of bioavailability in marine and freshwater sediments. If those are sufficiently well understood, the reduction in bioavailability through sediments may be approximated with confidence through empirical relationships. Ultimately, this might allow for expressing a sediment test endpoint in water concentrations and to feed such an endpoint into an aquatic SSD. In a first step into that direction, the available information should be mined for data pairs on marine and freshwater species and endpoints. The OECD DRP on aquatic arthropods might serve as a starting point. In a second step, generation of data pairs may be considered, possibly as a CEFIC-LRI project.

Probabilistic approaches (SSDs) for hazard assessment

- SSDs for (marine) sediment are hampered by a lack of sediment toxicity data to populate the SSDs.
- So, can toxicity data generated for freshwater sediment-dwelling organisms (e.g. non-biting midges *Chironomus riparius* or *C. dilutus*, amphipod *Hyalella azteca*, oligochaete *Lumbriculus variegates*) for which ASTM, ISO or OECD testing guidelines are available be used?
- Such a freshwater sediment test may be different (for instance in case of chironomids it concerns a systematic group, insects, not occurring in marine environments) but the main aim is to be conservative/protective.
- Or, can the equilibrium partitioning theory to generate toxicity endpoints for sediment from water only tests (may not be applicable to all, e.g. ionising, chemicals) be used?

Action points

- Data mining to compare (marine and freshwater) species and endpoints (starting point could be the OECD DRP on aquatic arthropods).
- To aid and facilitate comparisons it may be desirable to generate data pairs (within a CEFIC project?).

4.3 Syndicate 3: Criteria for selecting marine test species and endpoints

Moderator: J. Hendriks
Rapporteur: L. Camus
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M. Galay Burgos
E. Lystad
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D. Saward
K. Solomon
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Traditionally, aquatic hazard assessments often include data on microbes, plants, invertebrates and fish. Depending on the physico-chemical characteristics of the test substance(s), emphasis of these hazard assessments may focus on water column or sediment dwelling organisms. However, for practical and ethical reasons, this may not always be necessary or feasible for many marine organisms, which raises the following questions:

1. How can appropriate guidance be given for the selection of marine test species and development of test protocols to account for substance properties, lifecycle stages, etc?
2. How can information obtained in non-standard assays (e.g. cellular or molecular biomarker information, non-standard marine species) be employed in species extrapolation?
3. Can the concept of critical body burden concept be used for selecting test species?

1. *How can appropriate guidance be given for the selection of marine test species and development of test protocols to account for substance properties, lifecycle stages, etc?*

In general, it is recommended that standardised species and protocols be used as a generic approach to data acquisition for developing species sensitivity distributions (SSDs). This will increase transparency, data availability, and application to a broader group of end users.

However, when comparing temperate and polar ecosystems, the standardised species should belong to similar taxonomic groups from both temperate and polar regions. Standardised protocols are recommended, although not the same protocols for all conditions. These should be adapted accordingly (e.g. to study effects, time should be taken into account; to study exposure and fate of contaminants, the two ecosystems differ due to differences in water temperature, etc).

The syndicate discussion addressing whether Arctic species respond differently to contaminants compared to temperate organisms revealed conflicting opinions between the syndicate members. One scientific viewpoint was that there are no indications that Arctic species deviate toxicologically or ecologically in their sensitivity to anthropogenic stressors compared with temperate or tropical species. Participants involved in polar ecotoxicological studies strongly disagreed. In support of their argument they have added their published evidence to this report (see Appendix C).

Although there is data to suggest that it is appropriate to extrapolate from temperate to Arctic species in terms of sensitivity, testing key type substances to characterise sensitivity in Arctic versus temperate species and different life stages is recommended to further provide data for extrapolation. It should be noted that the behaviour of many substances may be quite different in polar regions than in temperate or tropical regions and that this must be considered when characterising exposures.

2. *How can information obtained in non-standard assays (e.g. cellular or molecular biomarker information, non-standard marine species) be employed in species extrapolation?*

The panel also had differing opinions on whether biomarkers can give any information on the effect of chemicals at the ecosystem level.

In general there was agreement that biomarkers, such as changes in physiological or biochemical processes, cannot be used for extrapolating effects at the population level and in the community. Biomarkers may, however, be useful indicators of exposure and in some cases, like e.g. oil, responses on biomarker and population level have been compared, providing tentative indications of risk.

Biomarkers can be specific to key types of substances and to substances with different mode of actions, and for different life stages. It was proposed to compare life stage rather than time, i.e. 24-h or 96-h acute toxicity endpoint may not elicit comparable response in polar and temperate organisms due to different rates of uptake and metabolism.

Biomarkers at present are useful for predicting ‘no effect’ at population level, i.e. in case of undetectable biomarker response, no effect should occur at the population level. This implies to be able to catch signal response, early warning (i.e. appropriate time frame so that recovery has not yet taken place, in case of non constant exposure). In this respect, biomarker responses can be used as ‘safe threshold levels’.

Therefore biomarkers are useful to study causal relationships of effects observed at population and community levels in the field and also to improve mechanistic understanding of effects.

3. *Can critical body burden concept help for selecting test species?*

Although there was no consensus on the use of critical body burden (CBB), this concept is currently being assessed for the identification and characterisation of persistent organic pollutants (POPs) and substances that are persistent, bioaccumulative, and toxic (PBTs). As the understanding in the area increases, the CBB concept can allow for a comparison of different routes and periods of exposure of species with different kinetics to chemicals with various modes of action.

Owing to the highly seasonal body lipid content in arctic organisms (Jørgensen *et al*, 1999), the same body burden of a contaminant can be related to different biological effects depending on the season. Therefore, to compare body burden and toxic effects elicited in standardised species, elicit species from both temperate and polar waters.

Conclusions

- When developing SSDs, caution must be taken when comparing polar and temperate species.
- There is a need to test the sensitivity of some arctic species to environmental stressors.
- There is a clear need to test the ecological relevance of biomarkers, but they can be useful in field studies.
- Use of the CBB concept when comparing polar and temperate species is not straightforward.

4.4 Syndicate 4: Statistical guidance and communication needs

Moderator: S. Johnsen
Rapporteur: P. Chapman
A. Hart
G. Hickey
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V. Koch
M. Liess
T. Ratte
S. Robertson
M. Smit

In order to use the SSD approach to derive quality criteria, the EU TGD prescribes a minimum dataset of 15 NOECs for 8 taxonomic groups. For many chemicals, especially production chemicals, ecotoxicity data are limited to 3 acute EC_{50}s for freshwater algae, zooplankton and fish. Extrapolation techniques like comparison of SSDs for toxic modes of action or interspecies correlation models can be applied to construct SSDs for chemicals with low data availability. Different extrapolation techniques are inherent to different levels of uncertainty. The success of risk communication depends largely on the endpoints used and the way uncertainty is dealt with in these endpoints. There is a need to formulate recommendations on the way the outputs of probabilistic risk assessment should be communicated.

1. Should a minimum data level for marine species be defined? And if so, what would the basis for such a level be?
2. Are current extrapolation techniques applicable for marine assessments?
3. How should uncertainty in marine assessments be assessed and expressed?
4. Which endpoints should be considered for risk communication?

Background

Deterministic ecological risk assessments rely on worst-case aquatic toxicity endpoints that are derived from laboratory studies. Typically, long-term (chronic) and/or short-term (acute) studies are conducted to derive NOEC and LC/EC_{50} values for three taxonomic groups (fish, aquatic invertebrates and algae). Typically the lowest NOEC is used in the risk assessment and an assessment factor (AF) applied to derive a Predicted No Effect Concentration (PNEC). The lowest AF that can be used in a deterministic ecological risk assessment is 10, which is only applicable for datasets containing NOECs for fish, aquatic invertebrates and algae. Where additional uncertainty/variability has been addressed through the collection of additional toxicity endpoints it may be possible to use a lower AF (1-5).

Ecological probabilistic risk assessment (PRA) approaches also allow additional data to be analysed and interpreted. The effects component of an ecological PRA involves fitting a frequency distribution (typically a log normal or a log logistic) to a set of NOECs. This is called a species sensitivity distribution (SSD) from which the lower 5th percentile (HC5) or the lower confidence limit[6] of the HC5 (HC5 [lower]) can be calculated and can be used (possibly after applying an AF) to derive a PNEC. The EU TGD states that at least 10 species from 8 taxa should be used to derive an SSD.

The availability of additional endpoints that satisfy the strict requirements of the TGD are rare, the cost of generating additional data is expensive and resource intensive. So, it would be beneficial to explore alternative approaches for deriving scientifically robust PNECs using a variety of techniques without the need to generate additional laboratory endpoints. Some alternative approaches (described below) have potential to deliver such benefits but need to be validated.

- A method which uses a pooled estimate of variance from historic database as an estimate of variance for SSDs for new or untested chemicals has been proposed (Luttik and Aldenberg, 1997; Aldenberg and Luttik, 2002).
- The interspecies correlation estimation (ICE) was developed by the US EPA and exploits correlations between different species. Ecotoxicological endpoints (e.g. a NOEC or LC_{50}) for a reasonable number of chemicals for each of two species can be used to demonstrate correlations, and straight-line regression models fitted to such data can be used to predict endpoints for the second species when they have only been measured on the first. So, for example, a small set of NOECs could in theory be considerably expanded by use of ICE regressions. See the WEBICE home page[7]. For a case study, see Awkerman *et al*, (2008).

1. Should a minimum data level for marine species be defined? And if so, what would the basis for such a level be?

A small dataset increases uncertainty about the shape and parameters of the distribution for the population which it is assumed to represent, in this case an SSD for marine species. The purpose of setting a minimum number of data is to limit this uncertainty. Therefore, the minimum dataset should be determined by the level of certainty that is required for marine risk assessment. However, in theory the level of certainty required depends on how close the estimated HC5 is to the PNEC. If the same size dataset was stipulated for all cases, this would provide unnecessarily high certainty for some cases and insufficient certainty for others. A more efficient approach

[6] Commonly 95% confidence intervals are used, but section 3.3.1.2 of the EU TGD states that a 50% confidence interval should be provided with the HC5.

[7] http://www.epa.gov/ceampubl/fchain/webice/index.htm

would be to allow datasets of varying size to be used, but to require that the estimated HC5 should be accompanied by a measure of its uncertainty, e.g. a 50% confidence interval (as required by the TGD). Uncertainty regarding distribution shape and the representativeness of tested species should also be taken into consideration, whichever approach is adopted (standard minimum data level or characterisation of uncertainty). In summary, it would be more efficient (in terms of minimising testing requirements) to characterise the uncertainty of the estimated HC5, rather than to specify the same minimum dataset for all cases. However, implementation of either approach will require further research on the uncertainties affecting estimation of the HC5 for marine species.

2. Are current extrapolation techniques applicable for marine assessments?

Currently available extrapolation techniques comprise:

1. The use of uncertainty factors applied to the most sensitive tested species (EU TGD).
2. Estimation of the HC5 together with 50% confidence intervals based on the specified minimum level of data (EU TGD).
3. Estimation of the HC5 together with 50% confidence intervals based on a smaller dataset, using the small-sample methods (e.g. Aldenberg and Luttik, 2002).
4. Estimation of the HC5 together with 50% confidence intervals based on a smaller dataset, using the ICE method (e.g. Awkerman *et al*, 2008).

These techniques are all theoretically applicable to marine assessments. The level of protection provided has not been quantified for any of them, although as methods 1) and 2) are specified in the EU TGD it is implied that the level of protection they provide is appropriate. In order to support acceptance of methods 3) and 4) it would be necessary to demonstrate that they provide an equivalent level of protection to methods 1) and 2). This would require further research to evaluate and compare all four methods.

3. How should uncertainty in marine assessments be assessed and expressed?

The primary approach in the EU TGD for dealing with uncertainty is the use of uncertainty factors. When an HC5 is estimated, the TGD specifies that it should be accompanied by a 50% confidence interval. This represents only sampling uncertainty and not other uncertainties such as those concerning distribution shape and the representativeness of tested species, which are much more difficult to quantify. Qualitative approaches for assessing and expressing unquantified uncertainties are described in chapter 19 of the REACH guidance (ECHA, 2008), but were not discussed by the syndicate.

4. Which endpoints should be considered for risk communication?

This was not discussed by the syndicate group due to lack of time. The EU TGD states the preferred measure of risk is the PEC/PNEC ratio, although qualitative characterisation of risk may be used in cases where a quantitative assessment cannot be carried out (TGD section 5.6).

Recommendations

A programme of work should be carried out with the objective of evaluating and validating a number of extrapolation methods focusing on key chemicals. In particular, the following methods should be evaluated and compared:

- The current deterministic method but using different numbers of species and various values for assessment factor.
- A 10-species SSD.
- Small sample methods using a pooled estimate of variance from a historic database (e.g. Luttik and Aldenberg, 1997).
- The interspecies correlation estimation (ICE) was developed by the US EPA which exploits correlations between different species (e.g. Awkerman *et al*, 2008).

It would be useful to compare the above methods with data on impacts in the field, but it is not clear to what extent this will be possible.

In order to include assessment factors for acute data in comparisons it will be necessary to investigate acute to chronic ratios (for an example case study, see Raimondo *et al*, 2007).

In the course of doing this work it would be useful to evaluate the extent to which the assumption of randomness is met. The potential impact of lack of randomness is a major criticism of the SSD approach which has never been satisfactorily addressed (see Forbes and Calow, 2002).

CONCLUSIONS AND RECOMMENDATIONS

The workshop promoted discussion on how approaches to marine hazard assessments could be improved. Whilst the deterministic (assessment factor) approach can be considered appropriate for some chemicals there is a need to offer refinements options for the assessment of other substances. Such substances may fail assessments based on the use of conservative assessment factors though safe use may be demonstrated by applying the techniques outlined in this report. As a consequence, the probabilistic assessment approaches are being applied for freshwater, marine and terrestrial risk assessment scenarios worldwide.

However, probabilistic approaches tend to require more data which are often not available for marine species. Therefore the question of extrapolation was discussed. For certain modes of action (MOA1, narcotic and MOA2, polar narcotic), it is clear there are opportunities for direct extrapolations between freshwater and marine taxa for acute effects. Justification for this will need to be done on a case by case basis. Further work is however required for substances covering a broader range of toxicological mechanisms of action (i.e. MOA3 reactive and MOA4 specific acting substances). Work is also required to establish the feasibility of extrapolations for chronic effects in marine species. In order to establish the magnitude of the observed sensitivity difference and, if possible, to define an appropriate 'extrapolation factor' further analysis and data collection of algae data sets for mode of action 1 and 2 chemicals are required.

In addition, some key research is still required to address the sensitivity of exclusively marine taxa (echinoderms, ctenophores, etc) for a range of case study chemicals and the extent to which these are covered by the data on marine (e.g. echinoderms, ctenophores, etc) and freshwater standard test species (e.g. algae, crustaceans and fish).

For marine sediment assessments, in order to make probabilistic approaches practical without extensive testing, an extrapolation framework is required. A priority activity should be devoted to develop an overall framework to include all existing knowledge to construct an SSD on an un-assessed substance. This knowledge may pertain to the known variance of already established species sensitivity distributions and the relative sensitivities of species. Constructing such a framework requires knowledge on the differences between freshwater and marine situation both, with regard to partitioning behaviour and to sediment toxicity data. It was suggested to use data mining to compare (marine and freshwater) species and endpoints (starting point could be the OECD DRP on aquatic arthropods). However, to aid and facilitate comparisons it may be desirable to generate data pairs.

Studies to compare the relative sensitivities of polar and temperate species were also recommended.

The workshop further concluded that a work programme should be carried out with the objective of evaluating and validating a number of extrapolation methods. The programme would evaluate a variety of methods and available data sets to determine and compare the changes in output resulting from different levels of data availability and method of derivation. The methods applied as mentioned before would include the following:

- The current deterministic method but using different numbers of species and various values for assessment factor.
- A 10-species SSD using both acute and chronic data.
- Small sample methods using a pooled estimate of variance from a historic database (e.g. Luttik and Aldenberg, 1997).
- The interspecies correlation estimation (ICE) developed by the US EPA which exploits correlations between different species (e.g. Awkerman *et al*, 2008).

This programme will enable the industry to adopt a single methodology for creating SSDs and estimating PNEC values for a wide range of chemicals that do not strictly meet the TGD testing requirements. In addition, it will potentially reduce the uncertainty associated with the current risk assessments for chemicals without the need to generate additional laboratory endpoints. In the course of doing this work a potential ECETOC task force could also evaluate the extent to which the assumption of randomness is met. The possible impact of lack of randomness is a major criticism of the SSD approach which has never been satisfactorily addressed (see Forbes and Calow, 2002).

ABBREVIATIONS

ACR	Acute to chronic ratio
AE	Alcohol ethoxylates
AF	Assessment factor
ASTM	American Society for Testing Materials
CBB	Critical body burden
CHARM	Chemical hazard assessment and risk management
CPs	Contracting parties
DEB	Dynamic energy budget
EAT	ECETOC aquatic toxicity
ED_{50}	Ecological dose value
EFSA	European Food Standards Agency
EIF	Environmental impact factor
EO	Ethoxylates
EOSCA	European Oilfield Speciality Chemicals Association
EqP	Equilibrium partitioning
ERA	Environmental risk assessment
GLP	Good laboratory practice
HC	Hazardous concentration
HMCS	Harmonised mandatory control
HQ	Hazard quotient
ICE	Interspecies correlation estimation
ISO	International Organisation for Standardisation
LAS	Linear alkylbenzene sulphonate
LC_{50}	Median lethal concentration
NEC	No effect concentration
NOEC	No-observed effect concentration
OCNS	Offshore chemical notification scheme
OECD	Organisation for Economic Co-operation and Development
OECD DRP	OECD detailed review paper
OPPTS	Office for Pollution, Pesticides and Toxic Substances
OSPAR	Oslo Paris convention

PBT	Persistent, bioaccumulative, toxic
PEC	Predicted environmental concentration
PNEC	Predicted no effect concentration
POP	Persistent organic pollutants
PRA	Probabilistic risk assessment
QSAR	Quantitative structure activity relationship
RCR	Risk characterisation ratio
RED	Reregistration eligibility decisions
SPME	Solid phase micro extraction
SSD	Species sensitivity distribution
TGD	Technical Guidance Document
US EPA	United States Environmental Protection Agency
WQC	Water quality criteria

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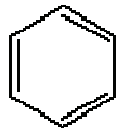
APPENDIX A: CASE STUDIES

A series of case studies have been generated using the following approach: (1) Gather background information (including standard physico-chemical and structural data); (2) Aquatic ecotoxicity data extraction for freshwater and marine invertebrates, fishes and algae[8] (base set data only) from the US EPA ECOTOX database; (3) ECOSAR toxicity estimates; and (4) Web-ICE predictions for marine species within the same taxonomic group.

1) Mode of Action 1 (narcotic)

Benzene

Structure and physico-chemical properties



SMILES: C1=CC=CC=C1
CAS number: 71-43-2
Molecular weight: 78.1134
Water solubility: 1800 mg/L
Log K_{ow}: 2.13

Ecotoxicity data

Table 1: Freshwater data

Group	Species	Endpoint		Value (mg/L)	Geometric mean of *n* studies
Invert	*Daphnia magna*	48-h	EC_{50}	221.3	14
Fish	*Lepomis macrochirus*	96-h	LC_{50}	191.3	10
	Oncorhynchus mykiss	96-h	LC_{50}	6.6	3
	Pimephales promelas	96-h	LC_{50}	22.1	8
Algae	*Pseudokirchneriella subcapitata*	72-h	EC_{50}	29.0	

[8] Multiple studies were summarised using the geometric mean. The following freshwater endpoints were extracted: *Daphnia magna* (only) 48-h EC_{50}, any standard OECD freshwater fish species 96-h LC_{50} and any freshwater algae 72 or 96-h EC_{50}. The following saltwater endpoints were extracted: Any marine aquatic invertebrate 96-h $E(L)C_{50}$, and any marine fish species 96-h LC_{50} and any marine algae 72 or 96-h EC_{50}.

Table 2: Marine data

Group	Species	Endpoint		Value (mg/L)	Geometric mean of *n* studies
Invert	*Palaemonetes pugio*	96-h	EC_{50}	27.00	
Fish	*Morone saxatilis*	96-h	LC_{50}	7.95	2
	*Oncorhynchus gorbuscha**	96-h	LC_{50}	8.47	
	*Oncorhynchus nerka**	96-h	LC_{50}	5.55	
	Salvelinus malma	96-h	LC_{50}	6.30	
Algae	*Skeletonema costatum*	-	EC_{50}	10.00	

*Saltwater form

Are freshwater values a suitable surrogate for marine species responses?

- Freshwater invertebrates are less sensitive than the marine inverts. The difference is ca. eight-fold.
- Two out of three freshwater fish are less sensitive than their marine counterparts. Fathead minnow was ca. four-fold less sensitive than the most sensitive marine species (*Oncorhynchus nerka*), whilst bluegill sunfish was ca. 35-fold less sensitive than *O. nerka*.
- The freshwater alga was ca. three-fold less sensitive than its marine counterpart.

ECOSAR predictions

Table 3: Freshwater estimates

Group	Species	Endpoint		Value (mg/L)
Invert	Daphnid	48-h	EC_{50}	47.3
Fish	Fish	96-h	LC_{50}	43.7
Algae	Green algae	96-h	EC_{50}	29.8

Table 4: Marine estimates

Group	Species	Endpoint		Value (mg/L)
Invert	Mysid shrimp	48-h	EC_{50}	11.49
Fish	Fish (SW)	96-h	LC_{50}	10.66
Algae	-	-	-	-

Can ECOSAR provide useful estimates of marine ecotoxicity endpoints?

- Freshwater predictions were all within a factor of ca. 7 of the experimental values.
- Predicted marine invert value was a factor ca. 2.4 lower than the experimental value.
- Predicted marine fish values were in good agreement with experimental data (within a factor of ca. 1.3 to 1.9).

Web-ICE predictions

Table 5: Predicted acute toxicity values

Group	Freshwater surrogate	Predicted marine species	Acute toxicity (mg/L)
Invert	*Daphnia magna*	*Americamysis bahia*	17.90
Fish	*Lepomis macrochirus*	*Cyprinodon variegatus*	*
	Oncorhynchus mykiss	*Cyprinodon variegatus*	7.30
		Menidia menidia	4.40
		Menidia peninsulae	10.30
		Micropterus dolomieu	6.46
		Micropterus salmoides	7.74
	Pimephales promelas	*Cyprinodon variegatus*	10.90
		Micropterus dolomieu	*
		Micropterus salmoides	6.10
Algae	-	-	-

*Surrogate toxicity outside model range.

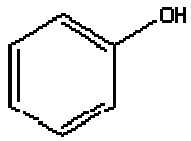
Can Web-ICE provide useful estimates of marine ecotoxicity endpoints?

- The marine invertebrate prediction is ca. 1.5-fold less than the experimental value.
- The saltwater fish predictions are in good agreement with the experimental values.
- No algae predictions were possible.

2) Mode of Action 2 (polar narcotic)

Phenol

Structure and physico-chemical properties



SMILES: OC1=CC=CC=C1
CAS number: 108-95-2
Molecular weight: 94.1128
Water solubility: 82800 mg/L
Log K_{ow}: 1.46

Ecotoxicity data

Table 6: Freshwater data

Group	Species	Endpoint		Value (mg/L)	Geometric mean of *n* studies
Invert	*Daphnia magna*	48-h	EC_{50}	22.6	25
Fish	*Danio rerio*	96-h	LC_{50}	26.9	2
	Lepomis macrochirus	96-h	LC_{50}	18.5	10
	Oncorhynchus mykiss	96-h	LC_{50}	8.6	12
	Oryzias latipes	96-h	LC_{50}	33.5	2
	Pimephales promelas	96-h	LC_{50}	32.6	26
Algae	*Chlorella vulgaris*	96-h	EC_{50}	370.0	
	Navicula seminulum	96-h	EC_{50}	257.5	12
	Pseudokirchneriella subcapitata	96-h	EC_{50}	150.0	

Table 7: Marine data

Group	Species	Endpoint		Value (mg/L)	Geometric mean of *n* studies
Invert	*Americamysis bahia*	96-h	EC50	12.50	
	Palaemonetes pugio	96-h	EC_{50}	5.80	
Fish	*Kuhlia sandvicensis*	96-h	LC_{50}	11.00	
	Phoxinus phoxinus	96-h	LC_{50}	9.50	
	Platichthys flesus	96-h	LC_{50}	20.45	2
	Solea solea	96-h	LC_{50}	14.23	
	Terapon jarbua	96-h	LC_{50}	40.00	
Algae	*Gracilaria tenuistipitata*	96-h	EC_{50}	146.90	2
	Nitzschia closterium	72-h	EC_{50}	53.64	

Are freshwater values a suitable surrogate for marine species responses?

- *Daphnia* was less sensitive than the marine invertebrates, but only by a factor of 1.9 - 3.4.
- There was reasonable agreement amongst freshwater and marine fish species. However, as a worst case marine fish ranged from a factor of 0.8 - 3.4 from the least sensitive freshwater fish (*Oryzias latipes*).
- Marine algae were more sensitive than the freshwater counterparts (2.5 - 6.9 from the least sensitive freshwater species [*Chlorella vulgaris*]).

ECOSAR predictions

Table 8: Freshwater estimates

Group	Species	Endpoint		Value (mg/L)
Invert	Daphnid	48-h	EC_{50}	8.4
Fish	Fish	96-h	LC_{50}	29.7
Algae	Green algae	96-h	EC_{50}	140.4

Table 9: Marine estimates

Group	Species	Endpoint		Value (mg/L)
Invert	Mysid shrimp	48-h	EC_{50}	-
Fish	Fish (SW)	96-h	LC_{50}	-
Algae	-	-	-	-

Can ECOSAR provide useful estimates of marine ecotoxicity endpoints?

- Freshwater predictions were all within a factor of 0.28 - 2.7 of the experimental values.
- ECOSAR did not provide any estimates for marine species.

Web-ICE predictions

Table 10: Predicted acute toxicity values

Group	Freshwater surrogate	Predicted marine species	Acute toxicity (mg/L)
Invert	*Daphnia magna*	*Americamysis bahia*	2.82
Fish	*Danio rerio*	-	-
	Lepomis macrochirus	*Cyprinodon variegatus*	15.78
		Menidia menidia	9.90
		Menidia peninsulae	*
		Micropterus dolomieu	12.72
		Micropterus salmoides	18.12
	Oncorhynchus mykiss	*Cyprinodon variegatus*	8.89
		Menidia menidia	5.93
		Menidia peninsulae	13.90
		Micropterus dolomieu	8.93
		Micropterus salmoides	10.27
	Oryzias latipes	-	-
	Pimephales promelas	*Cyprinodon variegatus*	14.52
		Micropterus dolomieu	*
		Micropterus salmoides	8.76
Algae	-	-	-

*Surrogate toxicity outside model range.

Can Web-ICE provide useful estimates of marine ecotoxicity endpoints?

- Marine invertebrate predictions were lower than the experimental data by a factor of 0.2 - 0.5.
- Marine fish predictions were in good agreement with the experimental data. Predictions were within a factor of 0.6 - 1.6 of the most sensitive marine fish species tested (*Phoxinus phoxinus*).
- No algae predictions were possible.

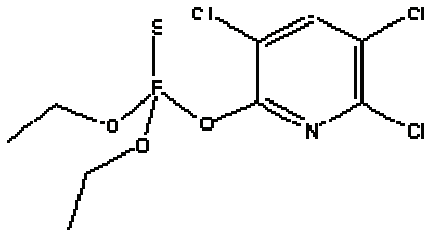
3) Mode of Action 3 (reactive)

There was insufficient marine data for a mode of action 3 (reactive substance) to permit meaningful comparisons.

4) Mode of Action 4 (specifically acting)

Chlorpyrifos

Structure and physico-chemical properties



SMILES:	CCOP(=S)(OCC)Oc1nc(Cl)c(Cl)cc1Cl
CAS number:	2921-88-2
Molecular weight:	350.58356
Water solubility:	1.398 mg/L
Log K_{ow}:	4.7

Intended biological activity

Chlorpyrifos is a broad spectrum non-systemic organophosphate insecticide that has widespread agricultural uses. It is also found in a number of insecticide products that are used in or around homes and gardens, including use as a termiticide.

Chlorpyrifos is an acetylcholinesterase inhibitor which affecting the insect's nervous system. This interference causes an increase in levels of the nerve transmitter chemical, acetylcholine, leading to over-stimulation of the nervous system and paralysis of muscles.

Ecotoxicity data

Table 11: Freshwater data

Group	Species	Endpoint		Value (µg/L)	Geometric mean of *n* studies
Invert	*Daphnia magna*	48-h	EC_{50}	0.51	5*
Fish	*Lepomis macrochirus*	96-h	LC_{50}	5.72	14
	Oncorhynchus mykiss	96-h	LC_{50}	13.00	12*
	Pimephales promelas	96-h	LC_{50}	186.10	12
Algae	*Scenedesmus bijugatus*	96-h	EC_{50}	1000.00	
	Pseudokirchneriella subcapitata	72-h	EC_{50}	1000.00	

*One value excluded as orders of magnitude outside of the range of other values.

Table 12: Marine data

Group	Species	Endpoint		Value (µg/L)	Geometric mean of *n* studies
Invert	*Americamysis bahia*	96-h	EC_{50}	0.046	5
	Ampelisca abdita	96-h	EC_{50}	0.302	4
	Amphiascus tenuiremis	96-h	EC_{50}	2.844	4
	Neomysis integer	96-h	EC_{50}	0.155	3
	Palaemonetes pugio	96-h	EC_{50}	1.083	5
Fish	*Cyprinodon variegatus*	96-h	LC_{50}	140.800	3
	Menidia menidia	96-h	LC_{50}	1.977	25*
	Menidia peninsulae	96-h	LC_{50}	1.346	27
	Morone saxatilis	96-h	LC_{50}	0.580	
Algae	*Dunaliella tertiolecta*	96-h	EC_{50}	769.000	
	Isochrysis galbana	96-h	EC_{50}	138.000	
	Skeletonema costatum	96-h	EC_{50}	297.800	5

*One value excluded as orders of magnitude outside of the range of other values

Are freshwater values a suitable surrogate for marine species responses?

- *Daphnia* was less sensitive than three out of the five marine invertebrates tested (by a factor 1.7 - 11.1) and more sensitive than the other marine species tested (factor 0.18 - 0.5).
- There was a large range amongst freshwater and marine fish species. As a worst case marine fish was more sensitive by a factor of 1.3 - 321 from the least sensitive freshwater fish (*Pimephales promelas*).
- Marine algae were more sensitive than the freshwater counterparts by a factor of 1.3 - 7.2.

ECOSAR predictions

Table 13: Freshwater estimates

Group	Species	Endpoint		Value (mg/L)
Invert	Daphnid	48-h	EC_{50}	0.97
Fish	Fish	96-h	LC_{50}	1.91
Algae	Green algae	96-h	EC_{50}	0.17

Table 14: Marine estimates

Group	Species	Endpoint		Value (mg/L)
Invert	Mysid shrimp	48-h	EC_{50}	-
Fish	Fish (SW)	96-h	LC_{50}	-
Algae	-	-	-	-

Can ECOSAR provide useful estimates of marine ecotoxicity endpoints?

- Freshwater predictions were not in good agreement with the experimental data (range from 0.17 - 1.906).
- ECOSAR did not provide any estimates for marine species.

Web-ICE predictions

Table 15: Predicted acute toxicity values

Group	Freshwater surrogate	Predicted marine species	Acute toxicity (µg/L)
Invert	*Daphnia magna*	*Americamysis bahia*	0.478
Fish	*Lepomis macrochirus*	*Cyprinodon variegatus*	15.470
		Menidia menidia	4.090
		Menidia peninsulae	3.420
		Micropterus dolomieu	*
		Micropterus salmoides	6.040
	Oncorhynchus mykiss	*Cyprinodon variegatus*	73.440
		Menidia menidia	3.610
		Menidia peninsulae	7.740
		Micropterus dolomieu	2.810
		Micropterus salmoides	8.680
	Pimephales promelas	*Cyprinodon variegatus*	326.900
		Micropterus dolomieu	66.300
		Micropterus salmoides	68.800
Algae	-	-	-

*Surrogate toxicity outside model range.

Can Web-ICE provide useful estimates of marine ecotoxicity endpoints?

- Marine invertebrate predictions varied by a factor of 0.17 - 10.4 from the experimental marine data.
- There was a wide range in the predictions for marine fish species. Predictions ranged from a factor of 4.8 - 564 from the most sensitive marine fish species tested (*Morone saxatilis*).
- No algae predictions were possible.

5) Case studies summary

The case study examples provide useful insight into the applicability of using the tools described in this document. It is clear that further investigation and case studies with a wider range of substances will be required. However, such an approach should enable a better understanding of the range of values generated and what impact these methodologies would have on deriving a marine PNEC.

On the base of the case studies, considering one substance for each MoA, we can tentatively conclude:

Modes of Action 1 and 2

- Marine base set data are typically with a factor of 10 from their freshwater counterparts.
- ECOSAR provided good estimates of freshwater ecotoxicological responses. For benzene it also provided reasonable predictions for marine invertebrates and fish. ECOSAR was unable to provide any marine algae estimates.
- Web-ICE provided reasonable predictions of marine data. These predictions were conservative compared to measured experimental saltwater data. Web-ICE was unable to provide any marine algae predictions.

Mode of Action 3

- It was not possible to extract sufficient data for a substance for meaningful comparisons.

Mode of Action 4

- There was a much greater variation in the sensitivity of freshwater and marine data.
- ECOSAR provided poor estimates of freshwater species responses. ECOSAR was unable to provide any marine estimates.

Web-ICE provided reasonable predictions of marine invertebrate data but less for fish). Web-ICE was unable to provide any marine algae predictions.

APPENDIX B: SYNDICATE 1 - HOW CAN MARINE AND FRESHWATER DATA SETS BE USED?

Table 1: Summary of Technical Guidance Document assessment factors to derive freshwater and marine PNECs. Marine PNEC requirements are for data on more species/taxonomic groups and/or a 10-fold higher assessment factor

Available data set		Assessment factor	
$PNEC_{freshwater}$	$PNEC_{marine}$	Freshwater	Marine
At least one short-term $L(E)C_{50}$ from each of three trophic levels of the base set (fish, *Daphnia* and algae)	Lowest short-term $L(E)C_{50}$ from freshwater or saltwater representatives of three taxonomic groups (algae, crustaceans and fish) of three trophic levels	1,000	10,000
	Lowest short-term $L(E)C_{50}$ from freshwater or saltwater representatives of three taxonomic groups (algae, crustaceans and fish) of three trophic levels, plus two additional marine taxonomic groups (e.g. echinoderms, molluscs)		1,000
One long-term NOEC (either fish or *Daphnia*)	One long-term NOEC (from freshwater or saltwater crustacean reproduction or fish growth studies)	100	1,000
Two long-term NOECs from species representing two trophic levels (fish and/or *Daphnia* and/or algae)	Two long-term NOECs from freshwater or saltwater species representing two trophic levels (algae and/or crustaceans and/or fish)	50	500
Long-term NOECs from at least three species (normally fish, *Daphnia* and algae) representing three trophic levels	Lowest long-term NOECs from three freshwater or saltwater species (normally algae and/or crustaceans and/or fish) representing three trophic levels	10	100
	Two long-term NOECs from freshwater or saltwater species representing two trophic levels (algae and/or crustaceans and/or fish) plus one long-term NOEC from an additional marine taxonomic group (e.g. echinoderms, molluscs)		50
	Lowest long-term NOECs from three freshwater or saltwater species (normally algae and/or crustaceans and/or fish) representing three trophic levels plus two long-term NOECs from additional marine taxonomic groups (e.g. echinoderms, molluscs)		10
Species sensitivity distribution (SSD) method		5-1	

Table 2: Description of databases and prediction tools that may be useful for the extrapolation from freshwater to marine effects data

Name	Description	Quality criteria	Source
ECETOC Aquatic Toxicity (EAT) database	Published literature compilation. Data for approximately 360 substances.	Yes, fully described in ECETOC (1993).	Available from ECETOC on request.
EAT 3 database	Enlarged version of the EAT database. Data for approximately 735 substances. Revised again in 2004 (MARSENS)	Yes, fully described in Wheeler *et al* (2001) and ECETOC (2003). Peters *et al*, 2005; Floeter *et al*, under revision.	Available from ECETOC on request. http://www.cefic-lri.org
ECOTOX US EPA database	Published literature and regulatory datasets. Aquatic component formerly the AQUIRE database. Large data source.	Not specified. Recommendation to check original references.	http://cfpub.epa.gov/ecotox/
Industry data	In house proprietary data.	Not specified.	
IUCLID (International Uniform ChemicaL Information Database)	Software to store chemicals information, prepare and submit dossiers in OECD format. Maintained by the European Chemicals Bureau. Contains few marine ecotoxicity data.	Not specified.	http://ecbwbiu5.jrc.it/
REDs (Reregistration Eligibility Decisions)	US EPA registration documents containing aquatic ecotoxicity data for pesticides and related substances. Typically guideline studies conducted to GLP.	Yes evaluated by the US EPA.	http://www.epa.gov/pesticides/reregistration/status.htm
ECOSAR (Ecological Structure Activity Relationship)	US EPA tool that implements over 100 Structure Activity Relationships covering 42 chemical classes.	Not specified.	http://epa.gov/oppt/newchems/tools/21ecosar.htm
Web-ICE (Interspecies Correlation Estimation)	US EPA online tool that estimates acute toxicity to aquatic and terrestrial organisms. Web-ICE includes a total of 2081 models for aquatic taxa.	Not specified for the input data. Guidance for selecting only models with low uncertainty is available.	http://www.epa.gov/ceampubl/fchain/webice/index.htm

Table 3: Verhaar chemical classification scheme based on acute modes of toxic action (Verhaar* et al*, 1992)

Class		Description	Examples
1	Narcotic or inert	Inert compounds which have a totally non-specific mode of toxic action or baseline toxicity. Potency entirely dependent on hydrophobicity. Usually of low polarity.	Alcohols, glycols etc
2	Polar narcotic or less inert	Inert compounds, un-reactive, but usually with hydrogen bond donor acidity.	Aromatic amines, phenols, nitroaromatics etc
3	Reactive	Covers different modes of action, grouped on the basis of enhanced toxicity over baseline. React unselectively with structures found in bio-molecules. Or chemicals that are metabolised into more toxic species (bioactivation).	Epoxides, aldehydes etc
4	Specifically acting	Diverse set of substances that interact with specific receptor molecules leading to toxicity.	DDT and analogues, (dithio) carbamates, organotin compounds, pyrethroids, organophosphorothionate esters etc

APPENDIX C: SYNDICATE 3 - CRITERIA FOR SELECTING MARINE TEST SPECIES AND ENDPOINT

Temperate species v arctic species

Ecotoxicological

Polar ecotoxicology data are relatively scarce as highlighted by Chapman and Riddle (2003, 2005). In a more extensive review, Camus *et al* (2008) looked at ~38 peer-reviewed publications and ~21 un-published reports and found that 92% of these toxicity studies were performed to measure the biological effects of oil compounds. They concluded that Arctic organisms and communities, because of their specific physiological adaptations to the polar ecosystem, respond differently to contaminants.

Adaptation to sub zero temperature

Polar cod produces antifreeze proteins in order to colonise and thrive successfully in waters at sub zero temperature. As a result of this, the fish is characterised by important biliary excretion owing to agglomerular kidneys designed to prevent the loss of these antifreeze molecules (Christiansen *et al*, 1996; Ingebrigtsen *et al*, 2000). The direct consequence of enhanced biliary excretion versus urine is an enhanced recirculation of contaminants and therefore a longer exposure time and lasting biomarker responses (Christiansen *et al*, 1996; Ingebrigtsen *et al*, 2000). Another consequence is the high fluorescence signal generated by natural compound excreted in the bile which reduces the good detection and semi quantification of polyaromatic hydrocarbon metabolites (Nahrgang *et al*, 2009, in preparation).

Seasonal variation in lipid

Owing to the highly seasonal solar radiation, the polar aquatic ecosystems are characterised by a very short, but intense, phytoplankton bloom from May to July. Therefore, aquatic organisms build up lipid to store energy that can be used during foot shortage from August until May. This bioenergetic strategy has consequences in relation to the effect of liposoluble contaminants. Jørgensen *et al* (1999) investigated different biomarkers (cytochrome P450 [CYP1A], pre- and post-stress plasma cortisol concentrations and fin erosion) responses in groups of PCB-exposed and unexposed Arctic charr. Following treatment (PCB administration), fish were held for 141 days under either a restricted feeding regime or without food. PCB exposure did not effect either growth or organ lipid concentrations. Food deprivation resulted in a marked reduction in lipid concentration in muscle and kidney, and a 3- and 11-fold increase in the PCB concentrations in the kidney and liver of the PCB-exposed fish respectively. Food deprivation did not appear to influence hepatic EROD activities and CYP1A content, but the elevated PCB concentration in the liver of the fasted, PCB-exposed fish seemed to result in a dose-related increase in EROD activity and CYP1A content. Plasma cortisol concentrations of unstressed fish were below the detection limit. Post-stress plasma cortisol concentrations were low in the food deprived fish, irrespective

of PCB exposure. The highest post-stress plasma cortisol concentrations were recorded in PCB-exposed, fed fish. The fish that were held without food had the lowest incidence of fin erosion, whereas the combination of food deprivation and PCB exposure resulted in the highest prevalence of fin erosion. Thus, nutritional status (i.e. long-term food deprivation) influenced both tissue concentrations of PCB, and biomarker responses. This must be borne in mind if biomarkers are to be used in environmental monitoring programmes.

Benthic communities

The clear differences in the response of Arctic benthic communities to petroleum compounds compared to temperate benthic communities is likely related to differences in community structure, sensitivity of individual taxa to petroleum-related compounds and different contamination history of the two study areas (Olsen *et al*, 2007). This study highlighted the need for a better understanding of interactions among petroleum related compounds, fauna, sediment characteristics, temperature and bacterial responses in Arctic and temperate sediments.

Acute effect/LC_{50}

Chapman and Riddle (2005) put forward that, on the basis of some very limited comparisons between the sensitivities of polar and temperate species to specific toxicants using LC_{50}, polar species may be similarly sensitive or more sensitive to copper, variably sensitive to cadmium and zinc, and less sensitive to lead. Despite the limited amount of data, what is clear at this point is that polar marine organisms have consistently longer acute response times. For this reason, comparisons between the acute response of polar and temperate marine biota should be based on similar portions of the toxicity curve, which can mean comparing 14-day LC_{50} results for polar organisms with 4-day LC_{50} results for temperate organisms. This observation was corroborated by Honkanen *et al* (2008) on polar cod LC_{50} with different chemicals. Longer response times for polar marine biota are probably due to the low ambient temperature, which results in both a low metabolic rate and slow uptake kinetics.

APPENDIX D: WEB-ICE

Web-ICE[9] is an online tool that employs least square regressions between a surrogate species (available experimental data) and the predicted taxa to estimate the toxicity to another species. Therefore, where correlations exist, it is possible to predict saltwater species responses from freshwater experimental data. The underlying aquatic database is in development and is currently composed of 4706 LC_{50}/EC_{50} values for 217 species and 695 chemicals (Raimondo *et al*, 2007). The models are based on data derived from the US EPA ECOTOX database (see above). The database and hence predictions are limited to acute fishes and invertebrates (daphnids, mysids and molluscs). Therefore, similar to the ECOSAR tool, it is currently not possible to derive values for saltwater algal species. It is also not possible to use some of the predictions for anadromous or catadromous species since it is not clear whether the freshwater or saltwater form has been tested or predicted. Web-ICE is useful as it estimates a marine response based on an actual ecotoxicological response (here a freshwater endpoint) and the underlying correlation between species responses. The Web-ICE program also delivers outputs that can be used to assess the degree of model uncertainty (Raimondo *et al*, 2007). Therefore, it is possible to make an easy assessment of the likely robustness of a predicted response. The tool has been used in the construction of 'theoretical' SSDs (Dyer *et al*, 2006). A validation exercise looking at HC5s determined from the acute toxicity of 55 chemicals from the United States Environmental Protection Agency Ambient Water Quality Criteria (AWQC). This analysis demonstrated that a combination of fish and invertebrate surrogate species could typically predict HC5 values within an order of magnitude of measured-based toxicity HC5s (Dyer *et al*, 2008).

Enhancements to Web-ICE

EPA is continuing the development of Web-ICE, including expansion of toxicity databases, new estimation modules, and improving functionality:

Database expansion: Over 100,000 records have been obtained for aquatic invertebrates and fish through partnerships with EPA Program Offices, the ECOTOX knowledge system, and scientific literature. The database is currently undergoing rigorous quality assurance/quality control (QA/QC) and standardisation procedures.

Model expansion and uncertainty analyses: Models will be developed and validated using the expanded aquatics database. Sources of model uncertainty, including chemical mode of action and chemical class, taxonomic distance, test conditions, and organism life stage will be evaluated and reported.

[9] http://www.epa.gov/ceampubl/fchain/index.htm

Additional research: EPA and Procter and Gamble are collaborating in three areas of research: a) developing algae-algae toxicity estimation models and SSDs; b) using quantitative structure activity relationships (QSAR) and ICE to generate SSDs in aquatic species; and c) exploring chronic toxicity estimation models and SSDs.

Module enhancements: a) The SSD modules will be updated to expand capabilities; b) an endangered species module will be developed for endangered species risk assessments; c) the wildlife database will be expanded to include laboratory rodent data and provide a linkage between human and wildlife toxicity studies; and d) an algal module will incorporate ICE models developed in collaboration with Procter and Gamble.

APPENDIX E: ECOSAR

The ECOSAR computer program allows access to over 100 Structure Activity Relationships for 42 different chemical classes. The program requires the octanol-water partition coefficient ($\log K_{ow}$) and the Simplified Molecular Input Line Entry System (SMILES) notation for a structural description of the substance. With this information, ECOSAR can perform an analysis and automatically estimate standard aquatic toxicity values for the substance. In the context of saltwater data predictions, for certain chemical classes ECOSAR can output estimates of marine ecotoxicity data. However, during the development of the case studies (see Appendix A) saltwater data were only generated for benzene (narcotic mode of action). Values for mysid shrimp and a generic saltwater fish were predicted. It was not possible to generate a value for saltwater algae. No saltwater estimates were generated for the other case study substances. In principle, using ECOSAR or other appropriately validated SAR methods to predict saltwater responses from chemical descriptors offers an opportunity generate useful marine data *in silico*. The validity of such predictions can be benchmarked against any available freshwater data (including the model prediction for freshwater species).

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APPENDIX G: WORKSHOP PROGRAMME

Wednesday 18th June 2008

Chairmen: J. Tolls and T. Hutchinson

12.00 - 13.20	Registration and lunch	
13.20 - 13.30	**Opening the meeting**	N. Carmichael ECETOC
13.30 - 13.40	**Welcome**	T. Hutchinson PML
13.40 - 14.10	**Setting the scene: Marine environmental risk assessment in the Norwegian offshore oil and gas industry**	M. Smit IRIS / StatoilHydro
14.10 - 14.40	**EUFRAM project**	A. Hart CSL
14.40 - 15.10	**North American perspective**	K. Solomon University of Guelph
15.10 - 15.40	**Assessment factors versus a probabilistic approach**	C. Karman IMARES
15.40 - 16.00	Break - tea/coffee	
16.00 - 17.00	**Four breakout groups A-D to refine key questions for day 2**	
17.00 - 17.30	**Plenary feedback from groups A-D**	
19.30	Workshop dinner hosted by StatoilHydro	

Thursday 19th June 2008

09.00 - 09.10	**Welcome**	J. Tolls Henkel
09.10 - 09.25	**Considerations for the use of freshwater ecotoxicology data in marine risk assessments**	J. Wheeler Syngenta
09.25 - 09.40	**Marine sediment risk assessment: ERASM contributions**	G. Whale Shell
09.40 - 09.55	**Hazard assessment with small datasets**	A. Hart CSL
09.55 - 10.10	**Existing marine hazard schemes: Assessment of chemicals used by the offshore oil and gas industry**	A. Millais CEFAS
10.10 - 10.25	Break - tea/coffee	
10.25 - 11.40	**Four breakout groups A-D**	

Group A: **"How can marine and freshwater data sets be used?"**
Moderator: **T. Frost, StatoilHydro**
Rapporteur: **J. Wheeler, Syngenta**

Group B**: "Key issues in marine sediment assessment."**
Moderator: **A. Temara, P&G**
Rapporteur: **L. Weltje,BASF**

Group C: **"Criteria for selecting marine test species and endpoints."**
Moderator: **J. Hendriks, Radbound University**
Rapporteur: **L. Camus, Akvaplan-NIVA**

Group D: **"Statistical guidance and communication needs."**
Moderator: **S. Johnsen, StatoilHydro**
Rapporteur: **P. Chapman, Unilever**

11.40 - 12.40	**Plenary feedback**	Moderator: G. Whale Shell
12.40 - 13.00	**Conclusions, research needs and workshop deliverables**	T. Hutchinson, PML J. Tolls, Henkel
13.00	Lunch and Close of Workshop	

APPENDIX H: ORGANISING COMMITTEE

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Established in 1978, ECETOC (European Centre for Ecotoxicology and Toxicology of Chemicals) is Europe's leading industry association for developing and promoting top quality science in human and environmental risk assessment of chemicals. Members include the main companies with interests in the manufacture and use of chemicals, biomaterials and pharmaceuticals, and organisations active in these fields. ECETOC is the scientific forum where member company experts meet and co-operate with government and academic scientists, to evaluate and assess the available data, identify gaps in knowledge and recommend research, and publish critical reviews on the ecotoxicology and toxicology of chemicals, biomaterials and pharmaceuticals.