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REPORT OF AN OECD WORKSHOP ON METALS SPECIFICITIES IN ENVIRONMENTAL RISK ASSESSMENT

7-8 September 2011, Paris, France

Series on Testing & Assessment
No. 165

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No. 165

Report of an OECD Workshop on Metals Specificities in Environmental Risk Assessment

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FOREWORD

This is the report of an OECD workshop on metals specificities in environmental risk assessment, held on 7-8 September 2011 in Paris. The workshop was held following a proposal from the Task Force on Hazard Assessment to organise workshops on the hazard assessment of specific groups of chemicals, and identify opportunities for harmonisation of approaches across regions.

This document is published under the responsibility of the Joint Meeting of the Chemicals Committee and Working Party on Chemicals, pesticides and Biotechnology of the OECD.

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WORKSHOP ON METALS SPECIFICITIES IN ENVIRONMENTAL RISK ASSESSMENT

7-8 September 2011
OECD Conference Centre, Paris

REPORT

INTRODUCTION

1. Several properties of metals - their natural occurrence, essentiality, bioavailability, homeostatic control mechanisms and acclimatization to diverse natural environments, - require specific recognition in the context of an environmental risk assessment. New science-based concepts and methodologies taking account of these metals specificities emerged in the last years and have been used in some jurisdictions. OECD member countries and stakeholders have demonstrated great interest in broader discussions on these new concepts with the view to facilitate regulatory acceptance and harmonisation of assessment approaches.

2. In June 2010, the Task Force on Hazard Assessment endorsed a proposal to organise a *Workshop on metals specificities in environmental risk assessment*, with the aim of sharing new concepts, supported by examples of how they have been applied and ensure their regulatory acceptance. A steering group was established, based on nominations from OECD member countries and industry, to prepare the workshop documentation and illustrative examples. Preparatory material was produced prior to the workshop and is available in Annexes 3 to 6.

WORKSHOP

3. The workshop was held on 7-8 September 2011 at the OECD Conference Centre in Paris. Participants from Canada, Denmark, France, Italy, Japan, the Netherlands, Sweden, Switzerland, the United Kingdom, the United States, the European Chemicals Agency, the European Commission, and BIAC attended the workshop. The list of participants is available in Annex 1.

4. The workshop was chaired by Jack de Bruijn of the European Chemicals Agency.

5. The workshop agenda is outlined in Annex 2.

Opening

6. Bob Diderich from the OECD Secretariat, opened the workshop, and welcomed participants.

Goals of the workshop

7. The aims of the workshop were to:

- Share regional experience in dealing with metal specific environmental hazard assessment.
- Review proposed/existing guidance for metals/inorganic specific hazard assessment concepts.
- Provide examples and encourage exchange of experience in dealing with metals environmental assessment.
- Understand and apply metal and inorganic specific tools and approaches.
- Collect feedback on the proposed concepts and identify opportunities for harmonisation of approaches across countries/regions.

Format of the workshop

8. Following generic presentations on national/regional frameworks, and a short introduction to challenges and key concepts specific to metals environmental assessment, the workshop went through three specific sessions on A) bioavailability, B) effects assessment, and C) bioaccumulation. In agreement with the steering group, it was decided to focus the workshop and examples on the aquatic (freshwater/marine) and soil compartments. The sediment compartment was purposely left out of the workshop agenda given the limited time available.

9. For each specific session, illustrative examples were presented followed by a discussion around issues identified. In the last session, participants reviewed conclusions of their discussions and agreed on a number of recommendations listed below.

CONCEPTS AND ILLUSTRATIVE EXAMPLES FOR THE WORKSHOP

10. The concept papers and illustrative examples prepared prior to the workshop have been inserted in Annexes 4 (session A on bioavailability), Annex 5 (session B on effects assessment) and Annex 6 (session C on bioaccumulation and fate) of this report. Annex 3 provides a glossary and definitions of terms regularly used in the context of environmental risk assessment of metals.

11. Presentations made at the workshop are available on the OECD public website at the following address: http://www.oecd.org/document/35/0,3746,en_2649_37465_48719331_1_1_1_37465,00.html .

WORKSHOP CONCLUSIONS AND RECOMMENDATIONS

12. The following conclusions and recommendations were agreed by workshop participants.

Bioavailability

- Many OECD member countries have developed frameworks for taking into account metal-specificities in environmental risk assessment, in particular:

  - How to deal with chemicals of natural origin and in use for a long time,
  - How to deal with (very) data-rich data sets versus data-poor data sets,
  - How to deal with speciation and bioavailability.

- Bioavailability should be taken into account for hazard and risk assessment of metal compounds in order to focus on interspecies sensitivity, keeping in mind the regulatory goal;
  - A tiered approach can be used, ensuring that first tier assessments use effects data where bioavailability is maximised.
  - Knowledge of the chemistry of a compound will normally guide the need for the development of bioavailability correction models.
  - Biotic Ligand Models (BLMs) can be used to estimate bioavailability, taking into account competition from other ions and binding of metals with natural organic matter.
  - For some metals, one parameter dominates and a simplified bioavailability correction model would be sufficient.
  - In particular for soil, it is recognised that most models currently applied are empirically based.
- The mechanistic understanding of bioavailability models would increase their regulatory acceptance.
- Bioavailability models have a specific applicability domain and have to cover soil/water parameters and background relevant for the region where they are applied; in addition it may be needed to do checks with species specific for that region.
- Further research is recommended to investigate to which extent commonalities between BLMs for species from different trophic levels apply amongst different metals.
- Further discussion is needed for developing a decision scheme as to the conditions for implementing BLMs in risk assessment.

Effects Assessment

- Hazard identification of metals and metal compounds is related to the toxicity of the soluble metal ions.
- The toxicity of the metal ions and the release of these ions from the metal-containing substances are therefore used as a basis for read-across. Such read-across allows for robust environmental hazard assessments of metal-containing substances that have no toxicity data (see also OECD Guidance on Grouping of Chemicals).
- Adequate effects assessments of metals could follow the following generic strategy:
  1. Data compilation & read-across

2. Data screening for relevancy and quality
3. Database development
4. Data normalization (i.e. bioavailability correction)
5. Data aggregation
6. Species Sensitivity Distribution (SSD) construction and HC_X derivation if relevant
7. PNEC derivation (including uncertainty assessment)

- Metal-specific criteria for quality and relevancy of effects data to be used in the assessment should be developed, taking into account criteria already developed for chemicals effect data in general. First issues for consideration when evaluating existing data and recommendations for future data generation:
  - Relevancy
    - Natural background concentration in test system and culture medium;
    - Equilibrium time in test media;
    - Boundaries of physical-chemical conditions relevant to the type of assessment (e.g. local) and the region for which the assessment is performed;
    - Relevant species in relation to the type of assessment (e.g. local) and to the region of interest.
  - Quality
    - Parameters related to the relevancy criteria should be reported and made publicly available;
    - Measured dissolved concentration of metals in water test system should be reported and made publicly available.
- Results from marine species should be separated from freshwater species and separate assessments should be performed, and missing data should be generated, recognising the lack of chronic effects test methods for marine species.
- Further discussion is needed on how to use effects data of adequate quality for which sufficient information on parameters relevant for bioavailability correction is not available.
- Recommendations for adequate reporting of physical-chemical parameters and background concentrations should be included in OECD Test Guidelines and OECD Harmonised Templates.
- The OECD assessment factor scheme for the derivation of PNECs when only acute test results are available is applicable for metals but special attention should be given to metals which are also essential elements or high background elements.

- Further discussion is needed to decide whether and how BLMs for acute effects data may be applied to normalise chronic effects results.

- More guidance is needed on what statistical approaches and conditions should be used for SSD derivation.

Bioaccumulation, bioconcentration

- For some metals, background can be significant (relative to the PEC or PNEC) and should be integrated in the risk assessment in a tiered approach;

  - At the level of data selection relevancy criteria can be established corresponding to the area of assessment;

  - At the level of PEC/PNEC: the total bioavailability approach and the added risk approach could be considered;

  - Background should be measured in (relatively) unpolluted environments.

- Available data for BCFs and other Accumulation Factors for metals indicate that they are inversely related to water (and sediment, and soil) concentrations. Therefore the use of a single value for assessing risks from secondary poisoning has to be carefully considered.

- Measures of tissue concentrations along the food chain provide a useful way to assess secondary poisoning.

- Further discussion is needed as to how to improve comparisons/interpretations of BCFs and BAFs for metals to regulatory threshold values.

- For the assessment of secondary poisoning, a tiered approach should be used, taking into account:

  - High BCF values could be used as a trigger to perform more detailed assessments;

  - The water concentration used in BCF or BAF experiments should preferably be in the same range as the PEC;

  - Bioavailability of the metal in the food or incidentally ingested soil/sediment;

  - Relevant food chains should drive the selection of BAFs and oral PNEC values;

  - Dietary composition for consumer organisms.

ANNEX 1

LIST OF PARTICIPANTS

Participants list for OECD Workshop on Metals Specificities in Hazard Assessment/Liste des participants pour OECD Workshop on Metals Specificities in Hazard Assessment

7/9/2011 - 8/9/2011

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ANNEX 2

WORKSHOP AGENDA

OECD WORKSHOP METALS SPECIFICITIES IN ENVIRONMENTAL RISK ASSESSMENT

7-8 September, OECD Conference Centre, Paris

Starting at 9h30 on 7 September and ending around 13h00 on 8 September

Goals of the workshop

- Share regional experience in dealing with metal specific environmental hazard assessment
- Review proposed/existing guidance for metals/inorganic specific hazard assessment concepts
- Provide examples and encourage exchange of experience in dealing with metals environmental assessment
- Understand and apply metal and inorganic specific tools and approaches
- Collect feedback on the proposed concepts and identify opportunities for harmonisation of approaches across countries/regions

DAY 1: Environmental assessment of metals and inorganics

Welcome and introduction

Generic session (1h30+2h):

- Background: (about 1h30)
  - Needs for specific approaches for Environmental hazard and exposure assessment for metals and inorganics (Hugo Waeterschoot, BIAC) – [20 minutes]
  - Existing regional generic frameworks for metals and inorganics:
    - European Union (Marta Sobanska) [15 minutes]
    - Canada (Joël Gauthier) [15 minutes]
    - United States (Randy Wenstel) [15 minutes]

  - UK DEFRA: MERAG project (Lucy Gilliam) [15 minutes]
  - Japan (Takehiko Hayashi) [15 minutes]

- Short introduction on specific challenges & proposed concepts (2h):
  - How to correct for background and acclimatisation?
    (Frank Van Assche, IZA/BIAC) [20 minutes]
  - Bioavailability correction: general principles and techniques;
    (Patrick Van Sprang, ARCHE consulting/BIAC) [30 minutes]
  - Assessment of very large effects data sets and read-across techniques relevant for poorer data sets (Katrien Delbeke, ECI/BIAC) [30 minutes]
  - Bioaccumulation requiring specific attention for metals and inorganics.
    (Henrik Tyle, DK EPA or Bill Adams, Rio Tinto/BIAC) [20 minutes]
  - Secondary poisoning assessment to aquatic and terrestrial organisms (Bill Adams, on invitation of BIAC) [20 minutes]

Specific sessions (3 x 2 h):

It is suggested to organise 3 successive sessions of 2 hours each in the plenary room. Each section would start with a max. A 1-hour presentation of the issue and exchange on regional/national experiences and ways to deal with the issues will be illustrated by examples on the proposed way forward. This would be followed by a 1-hour debate.

Aim: solicit questions, comments and review of suggested approaches, in order to provide indicative guidance for future submissions at the Cooperative Chemicals Assessment Meeting (CoCAM, former SIAM) and feedback on regional guidance.

Session A :Bioavailability assessment (Day 1, pm) Chair: Joop De Knecht, RIVM, NL Note taker: Chris Schlekat, NiPERA on invitation of BIAC, US
Bioavailability assessment for metals, for: • the aquatic compartment • the terrestrial compartment Illustrative examples: • copper for the aquatic compartment • Antimony for the soil compartment

Session B : Effects assessment (Day 1, pm) Chair : Bill Stubblefield, Oregon University, US Note taker : Hugo Waeterschoot, BIAC

Effects assessment aspects and approaches for data rich and data poor metal files for:

- Aquatic (Freshwater and Marine)
- Terrestrial
- STP

Illustrative examples:

- Lead for the soil compartment
- Nickel for the marine compartment (see fact sheet+ addendum)
- Zinc for the freshwater compartment
- Silver for the STP assessment

Cocktail sponsored by BIAC at 18h on Wednesday, George Marshall room

DAY 2:

Session C : Fate and exposure relevant to effects assessment

Chair : Colin Janssen (Ghent University)
Note taker : Bill Adams on invitation of BIAC, US

Assessing :

- Bioconcentration

Correcting for:

- Natural background
- Variability (seasonal, …)

Illustrative examples:

- Overview on bioconcentration of metals
- Bioaccumulation of cobalt

Plenary session (1h30): Discussion and conclusion

The final plenary session would be dedicated to discuss commonalities and differences of the approaches and to discuss the needs and opportunities for cooperative work at OECD on methodologies for the assessment of metals and inorganics.

ANNEX 3

GLOSSARY AND ACRONYMS

AET	Apparent Effects Threshold
AF	Assessment factor
ambient background concentration	The sum of the natural background of an element with diffuse anthropogenic input in the past or present (i.e., influence of point sources not included)
available fraction of a metal	The fraction of the total metal that is extractable from the substrate with chemical (e.g. neutral salt, water extraction) or physical means (shaking, pore water collection), and that is generally considered to be a better estimate for the fraction that is potentially available for organisms than the total concentration
BAF	Bioaccumulation factor
baseline background concentration	The concentration of an element in the present or past corresponding to very low anthropogenic pressure (i.e., close to the natural background)
BCF	Bioconcentration factor
Bioavailability	The rate and extent to which a substance can be absorbed by an organism and is available for metabolism or interaction with biologically significant receptors. Bioavailability (biological availability) involves both release from a medium (if present) and absorption by an organism.
Bioavailable fraction of a metal	Bioavailability is a combination of factors governing metal behaviour and the biological receptor (such as route of uptake, duration and frequency of exposure). As such the bioavailable fraction is dependent on the metal forms that prevail under specific environmental conditions and the biological receptors and can be defined as the metal fraction that can be taken up and that can interact with the organism's specific metabolic machinery. Bioavailability is organism specific – what is bioavailable to a wheat plant is not necessarily bioavailable to an earthworm
BioF	Bioavailability Factor
BLM	Biotic Ligand Model. The Biotic Ligand Model (BLM) is a predictive tool that can account for variations in metal toxicity using information on the chemistry of local water sources.
Cb	Background concentration
$C_{dissolved}$	Dissolved concentration
C_{total}	Total concentration
Cs	Soluble Concentration
CEC	Cation Exchange Capacity
CLP	Regulation EC No 1272/2008 on classification, labelling and packaging of substances and mixtures
Conditions of Use	Conditions of Use include the operational conditions (OC) and risk management measures (RMM) as described in an ES
ConsExpo	Software model to calculate consumer exposure http://www.rivm.nl/en/healthanddisease/productsafety/ConsExpo.jsp

CSA	Chemical safety assessment under REACH. Process aimed at determining the risk posed by a substance and, as part of the exposure assessment, develop exposure scenarios including risk management measures to control the risks.
Dissolved concentration of a metal	Most often, the dissolved fraction in ecotoxicity tests refers to the fraction that passes through a filter of 0.45 µm. It should be noted, however, that this definition may not necessarily refer to the metals in solution. In the range of 0.01-0.45 µm colloid inert particles containing metal ions that remain suspended, may still exist
DOC	Dissolved Organic carbon content
EC50	50% effective concentration
ECB	European Chemicals Bureau (now part of JRC)
ECHA	European Chemicals Agency
Eco-region	In the context of carrying out a CSA/CSR for metals, the eco region concept is used to allow to correct for differences in abiotic parameters (present in the different ecoregions) that are potentially affecting (bio)availability. As such the ecoregions proposed in the questionnaire should be considered as representative typical examples of specific EU conditions for which the critical parameters needed to run the (bio)availability model are readily available. This allows to parameterize the (bio)availability models without the effort of collecting an extensive database on site/region specific abiotic factors. This approach would in essence still allow the REACH registrant to set region-specific PNECs for a set of default example scenarios represented by various abiotic factors.
ECx	Effective concentration at x %; a dose representing an increased incidence of x % due to a specific exposure
EC50	Effective concentration at 50%
ERVs	Ecotoxicity Reference Value
ESR	Existing Substances Regulation (EC Council Regulation (EEC) No 793/93 of 23 March 1993 on the evaluation and control of the risks of existing substances)
HC5	Hazardous concentration at 5%
HCp	Hazardous Concentration at p-protection level
ICMM	International Council on Mining and Metals http://www.icmm.com/
JRC	Joint Research Centre
Kd	Distribution coefficient
LC50 / LD50	Median lethal concentration. The concentration causing 50 % lethality /Median lethal dose. The dose causing 50 % lethality
LEC	Lowest Effective Concentration
MERAG	Metals Environmental Risk Assessment Guidance. http://www.icmm.com/page/1185/metals-environmental-risk-assessment-guidance-merag
MW	Molecular weight
NOEC	No Observed Effect Concentration
NAEC/ NAEL /NOAEL/ NOEL	No adverse effect concentration /No adverse effect level /No observed adverse effect level/ No observed effect level
Natural background concentration	the natural concentration of an element in the environment that reflects the situation before any human activity disturbed the natural equilibrium As a result of historical and current anthropogenic input from diffuse sources the direct measurement of natural background concentrations is challenging in the European environment
OC	Organic matter content

PBT	Persistent, bioaccumulative, toxic
PEC/PNEC	Predicted environmental concentration /Predicted no effect concentration
PEL	Probable Effects Level; represents the concentration above which adverse effects are frequently expected. PEL represents the lower limit of the range of the contaminant concentrations that are usually or always associated with adverse biological effects
PEC$_{\text{dissolved}}$ **/PNEC**$_{\text{dissolved}}$	Predicted environmental concentration /Predicted no effect concentration expressed as dissolved concentration
PNEC$_{\text{dissolved normalised}}$	Predicted no effect concentration expressed as dissolved concentration, normalised to standard abiotic concentations
RA /VRA	Risk Assessment /Voluntary Risk Assessment
RAF	Relative Absorption Factor
RCR	Risk Characterisation Ratio
S/A-F	Spiking-Ageing factor
SSD	Species sensitivity distribution
SS-F	Soil sensitivity factor
STP	Sewage treatment plant
TEL	Threshold Effect Level.TEL represents the concentrations of sediment-associated contaminants that are considered to cause significant hazards to aquatic organisms
TGD	Technical Guidance Document
Ticket-UWM	Tableau input coupled kinetic equilibrium transport-unit world model, developed as a screening model for assessing potential environmental risks associated with the release of metals into lakes http://blog.unitworldmodel.net/
Total concentration of a metal	For terrestrial and sediment systems, the concentration of a metal that is determined after destruction of the mineral matrix. For aqueous systems: the total amount of metal present, including the fraction sorbed to particles and to dissolved organic matter and the fraction in the mineral matrix;
toxicological bioavailable fraction	the fraction of the concentration that is adsorbed and / or absorbed by an organism, distributed by the systemic circulation and ultimately presented to the receptors or sites of toxic action
TOX$_{\text{dissolved}}$	Toxicity data expressed as dissolved ion
TOX$_{\text{metal species}}$	Toxicity data metals species under consideration
TOX$_{\text{porewater}}$	Toxicity data soluble faction in porewater
TTF	Trophic Transfer factors
UVCB	Substances of unknown or variable composition, complex reaction products or biological materials as defined in the Guidance on substance identification
UWM	Unit World Model
vPvB	very persistent, very bioaccumulative
WHAM	Windermere Humic Aqueous Model, simulating organic matter and interaction of metals
WOE	Weight of Evidence
WWTP	waste water treatment plant

ANNEX 4

SESSION A : BIOAVAILABILITY ASSESSMENT

→ Concept paper on background metal concentration and references for further reading

→ Concept paper on bioavailability and references for further reading

→ Illustrative examples:

- Copper for the aquatic compartment
- Antimony for the soil compartment

Specific challenges and proposed concepts: How to correct for background and acclimatisation in hazard assessment? Data relevance

Background paper for OECD Workshop on *Metals Specificities in Environmental Hazard Assessment*
Paris, September 7-8, 2011

***Note:** These papers were prepared by industry and reviewed by the workshop steering committee to provide some background on concepts associated with metals-specificities in environmental hazard assessment. The papers do not represent a consensus view of the OECD on how to conduct metals environmental assessment, but they should serve as a basis for workshop participants to understand the concepts proposed and already applied in some OECD countries.*

Introduction

As components of the natural environment, metals occur in natural background concentrations and organisms are conditioned/ acclimatised to these natural conditions. Moreover, some metals are essential elements and are actively regulated by organisms through homeostasis mechanisms. In terms of hazard/risk assessment, this implies that the sensitivity of organisms to metals in toxicity tests is function of the background concentration they experience, not only in the test medium, but, notably, also of the concentration in the nutrient solution in which the organisms where cultured prior to testing. This relationship has been shown both at the organism level, e.g.: for Daphnia magna (Muyssen and Janssen, 2001) and at the database level e.g. for zinc HC5 values related to different "metalloregions" (Waeterschoot et al., 2003).

Therefore conditioning/acclimatisation to natural background and essentiality make it necessary to pay special attention and apply specific approaches in selecting, handling and interpreting metal ecotoxicity data in a context of hazard/risk assessment. These aspects are shortly discussed below.

Approach: how to account for natural background and essentiality?

Natural background and essentiality of metals have to be taken into account mainly at the level of the data selection. For metals, a wide variety of ecotoxicity data may be available that are, however, not necessarily relevant for hazard (and risk) assessment. In selecting the data for the assessment, it needs to be ensured that ecotoxicity results have been obtained under conditions that are relevant for the natural environment. This relates not only to the testing conditions, but also the conditions under which the test organism was cultivated prior to testing. Nutritional requirements for essential elements like Cu, Zn and Ni need be satisfied in both media in order to correctly reflect the toxicity of the metals studied (OECD 2000). So, in addition to the check of the intrinsic quality of the data, the relevance of ecotoxicity also needs to be carefully assessed.

The conditions to be checked are mainly:

- The metal background conditions in the test and culture medium, to avoid possible conditioning/acclimatisation effects. When organisms are cultured under concentrations of the metal that are significantly higher or lower than those occurring in nature, the organisms may be acclimatised to those deviating concentrations, and their subsequent response in ecotoxicity testing may be different from organisms pertaining to the natural ecosystem. It is emphasised that this effect may occur in both directions, i.e. acclimatisation occurs towards higher and towards lower metal concentration, leading to lesser, and higher sensitivity, respectively. **To address this, the background metal concentration in both culture and test medium should be documented, and a relevant range of concentrations for the ecosystem to be assessed should be set for data selection.**
    - When considering ecotoxicity data for ERV setting, it is noted that the ECx/NOEC values will not include the natural background when nominal concentrations are used. When the real metal concentration in the test is measured, natural background is included.
- The assessment of the ecologically relevant metal concentration includes the consideration of the bioavailability of the metal in the testing/culturing media. The bioavailability of metals in the environment and in test solutions is function of the physico-chemical conditions of the water (e.g.: pH, hardness, DOC, see section on “bioavailability”). For this reason, the abiotic conditions in both testing and culturing media should reflect those of the natural environment to be assessed. **To address this, the relevant abiotic conditions of both culture and test medium should be documented, and a relevant range of conditions for the ecosystem to be assessed should be set for data selection.**
    - It is noted that in most artificial test media, the DOC concentration is (close to) zero, and metal bioavailability is maximised as such.
    - Sudden significant changes in abiotic conditions e.g. when transferring organisms to different testing media may result in secondary shock effects that are irrelevant for the response in nature.

In the definition of the relevant ranges of abiotic conditions for checking of data relevancy for hazard assessment, generally a broad range of conditions will be considered encompassing most aquatic ecosystems. For risk assessment, a more specific assessment of relevant ranges may be used at different scales.

Conclusions:

Conditioning/acclimatisation to natural background and essentiality make it necessary to pay attention and apply specific approaches in selecting, handling and interpreting metal ecotoxicity data in a context of hazard/risk assessment.

A number of aspects shall be assessed and documented, including the background metal concentrations and abiotic conditions in both culture and test medium, and relevant ranges of concentrations and conditions for the ecosystem to be assessed.

References for further reading

- OECD (2000). OECD series on testing and assessment, guidance document on aquatic toxicity testing of difficult substances and mixtures (ENV/JM/MONO(2000)6) http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=ENV/JM/MONO(2000)6&docLanguage=En
- Muyssen BTA and Janssen CR (2001). Environmental toxicology and Chemistry, 20, 2053-2060.
- Waeterschoot H, Van Assche F, Regoli L, Schoeters I, Delbeke K (2003). Journal of Environmental Monitoring 5, 95-102N

Bioavailability Correction Strategy and Tools for Metals Risk Assessment

Background paper for OECD Workshop on Metals Specificities in Environmental Hazard Assessment
Paris, September 7-8, 2011

Note: *These papers were prepared by industry and reviewed by the workshop steering committee to provide some background on concepts associated with metals-specificities in environmental hazard assessment. The papers do not represent a consensus view of the OECD on how to conduct metals environmental assessment, but they should serve as a basis for workshop participants to understand the concepts proposed and already applied in some OECD countries.*

Background

It is well established that metal bioavailability and toxicity vary as a function of the geochemistry of the environmental matrix, i.e., water, soil, and sediment. Predictive mechanistic models to correct individual chronic toxicity data and develop safe threshold values (PNEC's) for the impact of abiotic factors influencing bioavailability, have been developed/validated for the aquatic compartment and more empirical models based on correlations between toxicity and soil properties have been developed/validated for soils. These models have been used to various degrees in European metals Risk Assessments for the purpose of chemicals management (e.g. Cd, Cu, Ni, Pb, and Zn), and more are in the process of being developed/validated (e.g. Co, Al).

These bioavailability correction models however often require an abundance of data inputs, take time to run, and require expert judgement. For this reason, the available BLMs and soil empirical models have been compiled and implemented into user-friendly (electronic) tools.

The applicability of the bioavailability models has been further verified by the identification of a number of scenarios with typical abiotic conditions found in the EU.

Concept and models

Bioavailability correction models for water and soil have been developed to correct the species sensitivity distribution (SSD) and thus predict normalised safe thresholds/PNECs for metals as a function of abiotic conditions. The Biotic Ligand model (BLM) predicting the bioavailability in water includes a physico chemical speciation (WHAM[1]) and a biological component (competition of free metal ion for binding sites at the cell membrane). Soluble metal concentrations and simple abiotic parameters (e.g. pH, dissolved organic carbon, hardness) allow for the speciation predictions. Existing BLM models for metals were validated for different water types for each of the metals they were developed for. For soils more empirical derived models were developed based on correlations between relative simple soil properties (Cation Exchange Capacity (CEC), pH, ..) and toxicity have been developed and validated for soils

Strategy

A **bioavailability correction strategy** as a function of the available evidence and validation was developed under the EU-Existing Substance Framework and has more recently been included in the EU REACH guidance. It allows for a tiered approach.

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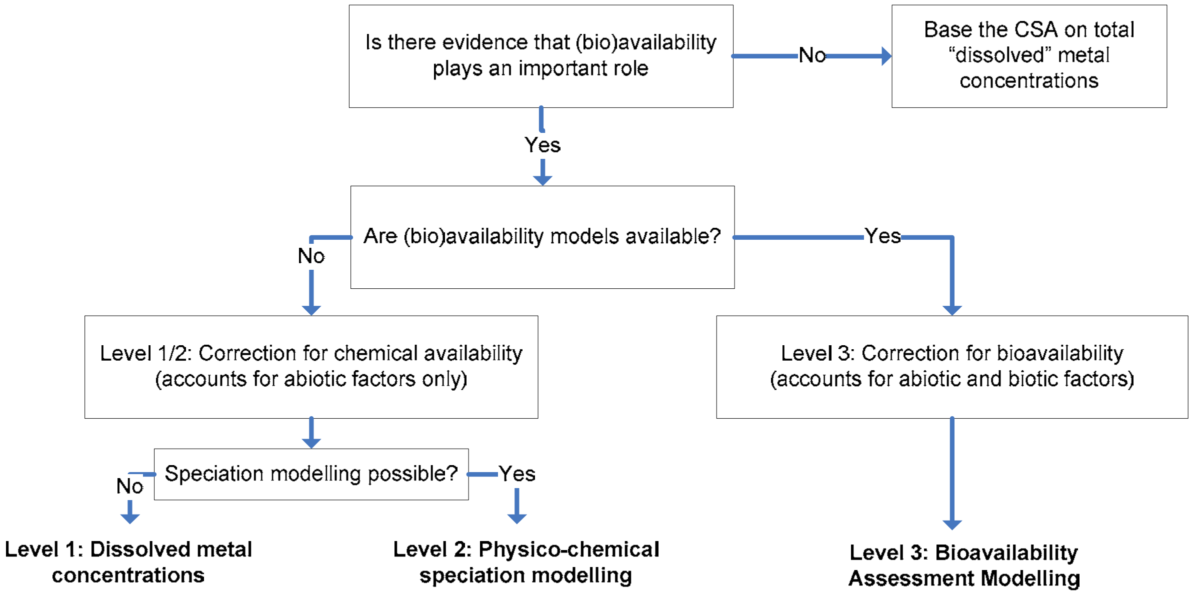
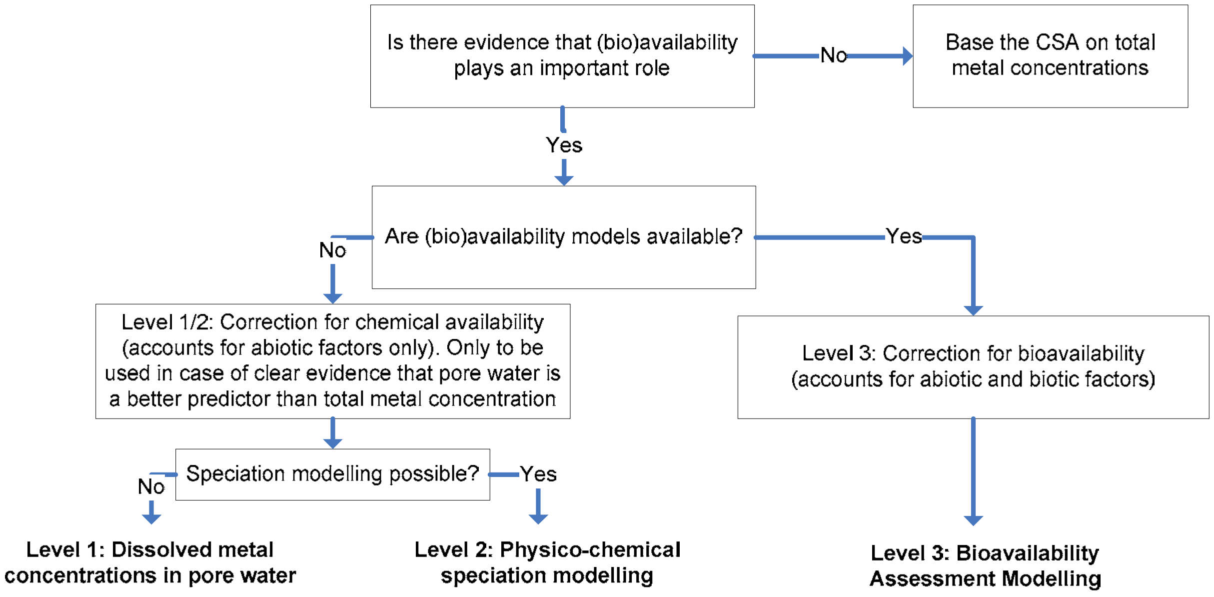
[1] Windermere Humic Aqueous Models: simulates organic matter chemistry and interaction with metals

As shown in the graphs below 3 levels or tiers of bioavailability correction for use in chemicals management schemes (incl. effect assessments) can be applied for both the aquatic and the terrestrial compartment depending on available evidence: 1) soluble metal, 2) chemical speciation model and 3) full bioavailability correction.

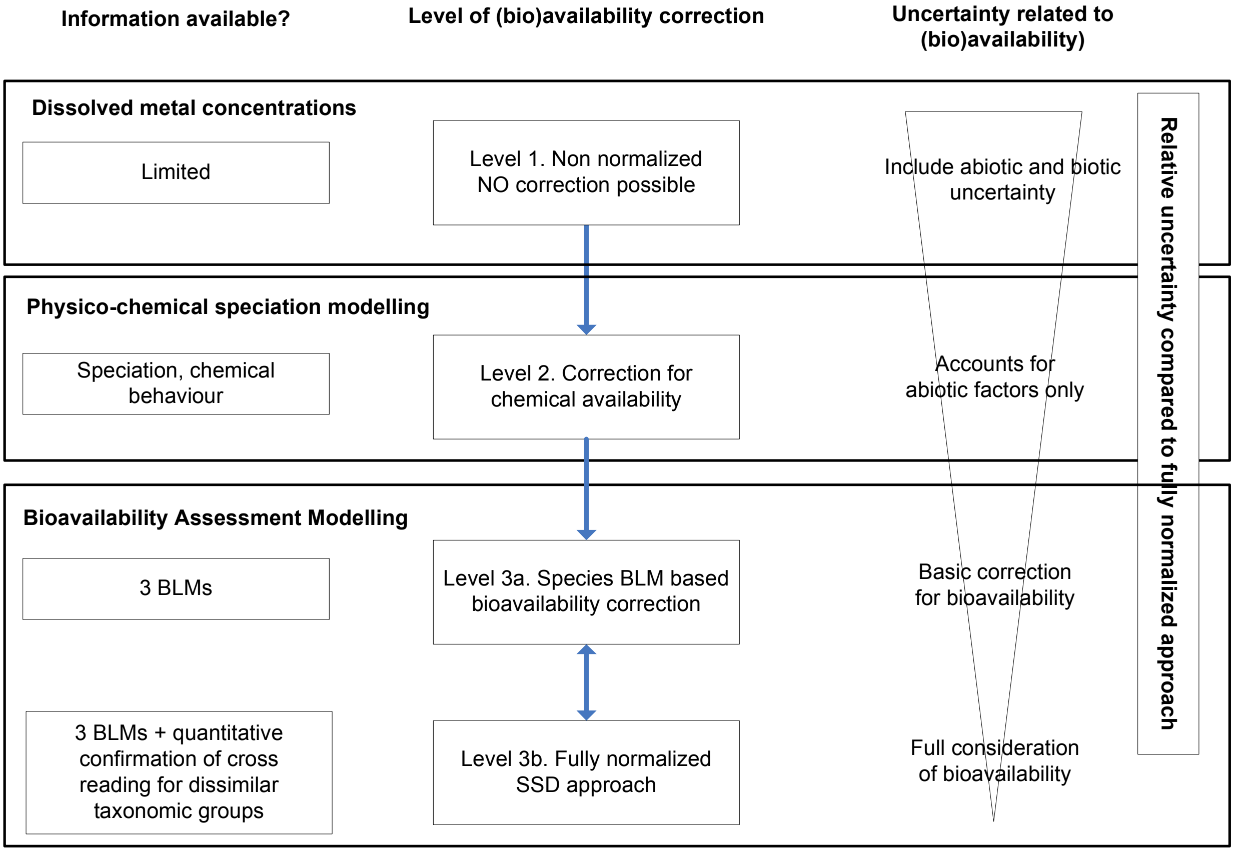
Graph 1a : Bioavailability correction levels for the aquatic ecosystem :



Graph 1b : Bioavailability correction levels for the Terrestrial ecosystem :



Graph 2: Bioavailability correction levels for the aquatic ecosystem :



Data needs for bioavailability correction

The type of correction applied for the level 3 bioavailability correction depends on the extent of evidence and validation available for the model. Such conditions include as a minimum: abiotic condition (pH, DOC, etc.) boundaries that are representative for the area under assessment (regional or local), toxicity data covering the 3 trophic levels, validation through field tests, and biological spot tests to check the relevance of the bioavailability models for other species than those for which they were developed (especially relevant for invertebrates), etc...

The empirical bioavailability regression models developed for metals for the soil compartment usually include a “spiking –ageing factor” to correct for the difference between the lab versus soil situation and a soil-sensitivity factor to correct for different soil type conditions.

Detailed schemes for bio-availability corrections for the aquatic and terrestrial environment including all described above are provided in Annex 1 enclosed.

Regional bioavailability correction

While local bioavailability corrections can use local abiotic parameters the issue of bioavailability correction at the regional scale is more complicated. A concept based on both geographical/geological and biological characteristics was developed, in the EU called as the "eco-region driven approach". This approach arises from the fact that a limited number of different ecoregions typical for the aquatic or the terrestrial environment can be identified in terms of the physico-chemical characteristics and boundaries that influence metal bioavailability.

This concept therefore recognizes that (bioavailable) background concentrations of a metal in a given ecoregion can differ from one ecosystem to the other, resulting in different sensitivities to the toxic effects of metals due to acclimation or adaptation. This approach is based on the simple principle to normalize first the PNEC or full SSD to a given abiotic condition typical for an ecoregion. This concept has been applied in the OECD Nickel effects assessment (See Ni-SIAR) and is available for several metals.

Tools available

Microsoft Excel™-based tools were developed for facilitating a more user friendly and integrated application of bioavailability correction models for water and soil. The main features of these automated tools are:

- simple calculations that can be incorporated into laboratory data management systems,
- The metal aquatic and soils effects predictions have been demonstrated being precautionary
- Many thousands of local or regional data sets can be processed to calculate the bioavailable fractions
- The bioavailability tools available at this moment were largely based on toxicity data and BLM-Soil regression models derived under the Existing Substances Regulation (793/93EC), for series of base metals and are expanded with new metal specific models when coming available

The Excell based bioavailability screening tools allow for the calculation of site-specific ecological quality standards, bioavailable fractions and eventually corresponding risk characterisation for various metals in water and soil.

The bioavailability correction screening tools can be found at:

- For water: www.bio-met.net
- For soil: http://www.arche-consulting.be/Metal-CSA-toolbox/soil-pnec-calculator).

Cases of Level 1 and 3 bioavailability assessments at local and Regional scale are available and will be presented at the workshop.

Conclusion:

Metal bioavailability corrections for the aquatic and terrestrial were developed for series of metals using a 3 level approach depending on the type, amount of toxicity and abiotic data influencing bioavailability. Models for the aquatic environment are based on the Biological Ligand Model concept while for soil more empirical models based on the difference between lab and soil conditions and the different soil types were developed. Such corrections can be applied for local environmental conditions but also for regional levels based on typical regional abiotic conditions (ecoregion approach). Existing bioavailability models for the aquatic and terrestrial compartment were compiled in excel based spreadsheets and strategies on how to derive new bioavailability models for metals are available.

References for further reading:

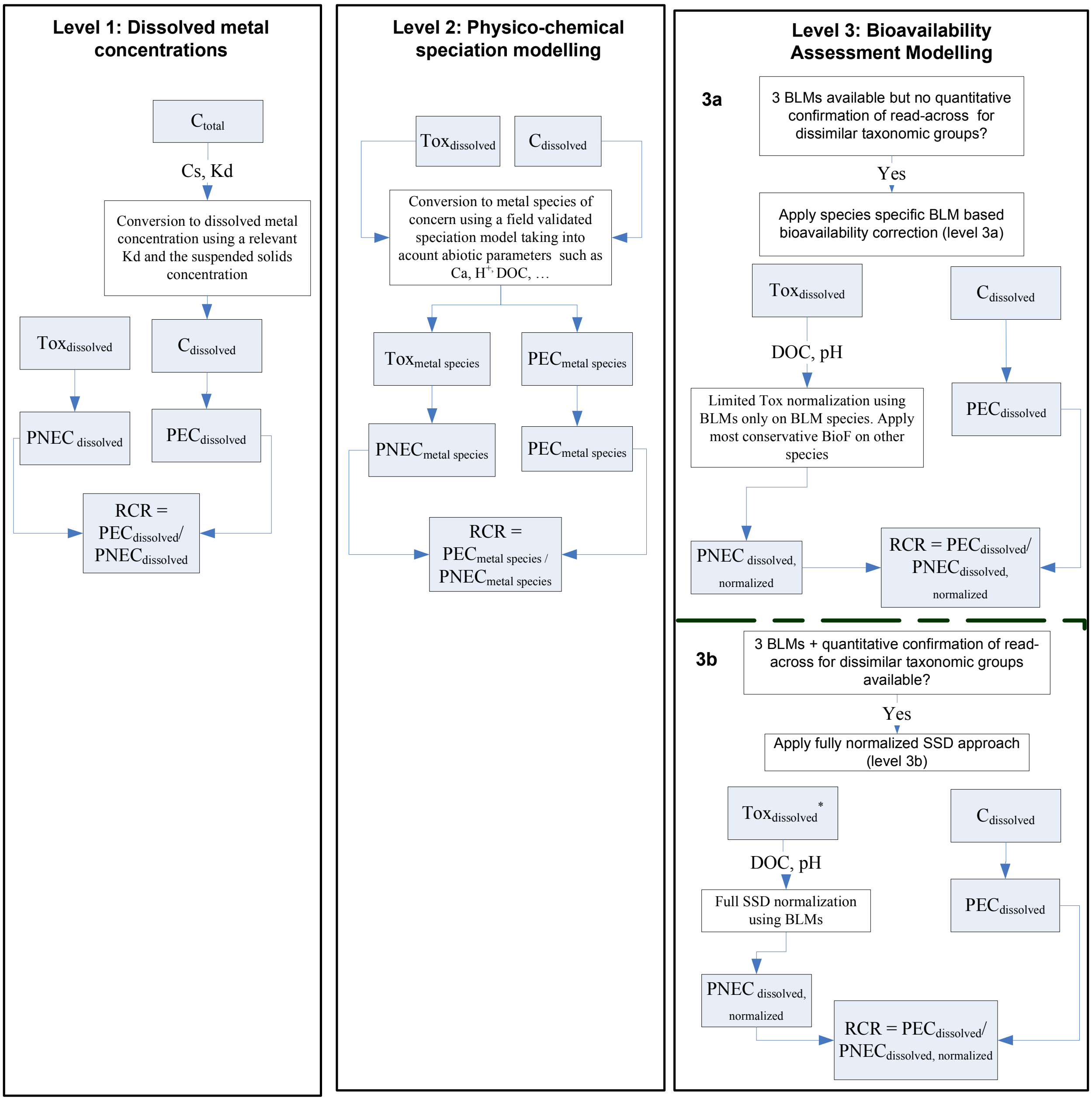
- HE Allen.2002. The Biotic Ligand Model addresses effects of water chemistry on metals toxicity. ICMM fact sheet
- ECHA guidance on CSR/Information requirements http://guidance.echa.europa.eu/docs/guidance_document/information_requirements_r7_13_2_en.pdf , from page 32 onwards
- Relevant Ni SIAR section
- EU existing substances (Voluntary) Risk Assessments for Nickel and Nickel compounds (http://www.mst.dk/English/Chemicals/Substances_and_materials/Nickel/), Copper and Copper Compounds (http://echa.europa.eu/chem_data/transit_measures/vrar_en.asp), Pb and Pb compounds (http://echa.europa.eu/chem_data/transit_measures/vrar_en.asp)
- Smolders E., K. Oorts, P. Van Sprang, I. Schoeters, CR Janssen, SP McGrath, MJ McLaughlin. Toxicity of trace metals in soil as affected by soil type and aging after contamination: using calibrated bioavailability models to set ecological soil standards. et al., Environmental Toxicology and Chemistry, Vol. 28, No. 8, pp. 1633–1642, 2009
- MERAG Fact sheets 5, 6 on bioavailability correction water/soil http://www.icmm.com/page/1185/metals-environmental-risk-assessment-guidance-merag

Others:

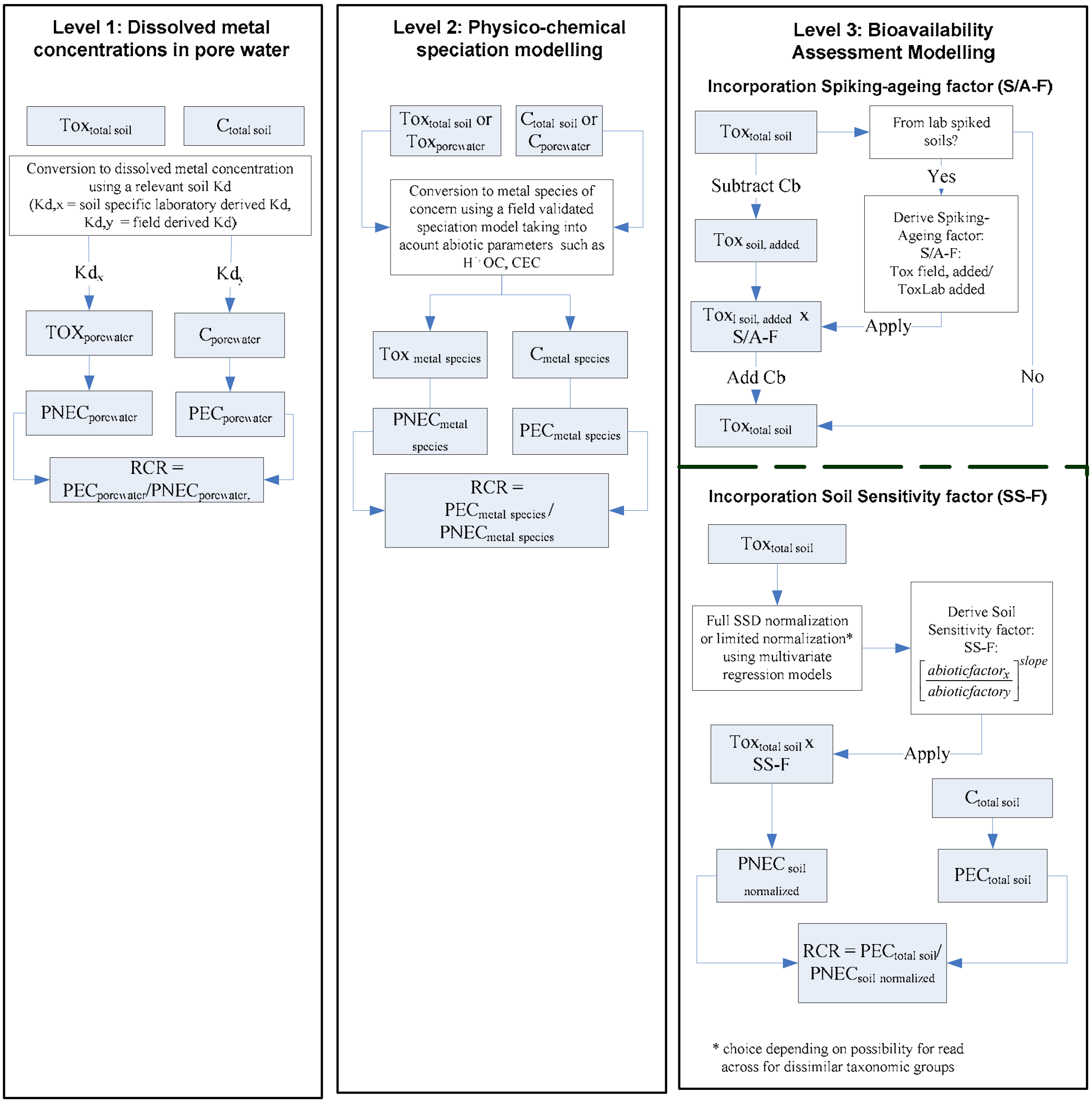
- Schlekat CE, E. Van genderen, KAC De Schamphelaere, PMC Antunes, EC Rogevich, WA Stubblefield.2010. Cross-species extrapolation of chronic nickel Biotic Ligand Models. Sci Total Envn 408: 6148-6157

Annex 1:

Scheme 1: Bioavailability assessment levels for the aquatic environment as a function of available information



Scheme 2: Bioavailability assessment levels for the soil environment as a function of available information



Session A illustrative example:
Incorporation of bio-availability in the freshwater compartment - Copper example

1. Regulatory context.

The Risk Assessment of copper and various copper compounds was completed in 2008, as an industry response to a request from the European Commission (more details in section 6). The goal of this exercise was to determine if the ongoing production and use of copper in the European Union (EU) causes risks to humans or the environment in accordance to Council Regulation (EEC) 793/93 and the detailed methodology laid down in the Technical Guidance Document on Risk Assessment for New and Existing Substances.

As required by the EU risk assessment guidance, the environmental sections of the copper risk assessment report include detailed exposure assessments, effects assessments and risk characterisations for the relevant environmental media. The copper risk assessment report was reviewed by Italy and subsequently other EU member states representatives. The copper risk assessment report and member states opinions are available from http://echa.europa.eu/chem_data/transit_measures/vrar_en.asp. A final peer review was performed by the Scientific Committee on Health and Environmental Risks (SCHER) (http://ec.europa.eu/health/scientific_committees/environmental_risks/opinions/scher_opinions_en.htm#4).

This paper summarizes the environmental sections of the copper risk assessment report, dealing with the development, validation and incorporation of bio-availability into the setting of a safe threshold value for copper in the freshwater compartment.

2. Deriving safe threshold values for the freshwater compartment

In accordance to international guidelines, safe threshold concentrations for metals in aquatic systems (e.g. Predicted No Effects Concentrations (PNEC))can be derived from both short or long term laboratory ecotoxicity tests.

Under EU regulations, long term ecotoxicity data are the basis for setting such safe threshold values. The chronic toxicity of copper to freshwater organisms was assessed, for the EU copper risk assessment, from open literature, internationally recognized databases, and industry-sponsored research programs.

The observed variability in ecotoxicity values was addressed as follows:

- ***Differences in test substances chemical speciation:*** Different metal species are used as test substances in various ecotoxicity tests (e.g. $CuSO_4$, $CuCl_2$, CuO). Considering that the Metal ion (Cu^{2+}) drives the aquatic ecotoxicity, only tests with soluble inorganic copper compounds were retained. Chronic toxicity data from the various soluble compounds (e.g. $CuSO_4$, $CuCl_2$) were combined and expressed as soluble metal ion concentrations (µg dissolved Cu/L) causing a specific effect. The selected studies were further screened, using reliability and quality criteria agreed by the TCNES, resulting in 139 high quality chronic NOEC/L(E)C_{10} values[2].

- ***Species-specific differences:*** Species-specific differences in sensitivity to copper are addressed from the availability of chronic ecotoxicity data covering a broad diversity in taxonomic groups: the 139 high quality chronic NOEC/L(E)C_{10} values represent 27 species, including fish, invertebrates, algae and higher plants[1].

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[2] More details on the data-treatment in fact sheet "Assessment of very large effects data sets and read-across techniques relevant for poorer data sets"

The uncertainty analysis demonstrated large variability in observed chronic NOEC/L(E)C_{10} within one species. The influence of abiotic parameters such as pH, hardness, and dissolved organic carbon (DOC) on the bio-availability and toxicity of copper is well-known. A sensitivity analysis demonstrated that bio-availability was a major driver for the observed intra-species variability of NOEC/L(E)C_{10} values and therefore raised the need to use a bio-availability normalization process for the PNEC derivation.

- ***Accounting for dependence on the water chemistry:*** In order to provide a mechanistic basis for understanding and predicting bio-availability through integration of chemical parameters (e.g. pH, hardness, DOC) and biological parameters (receptor sites on organism, mode of action), chronic Biotic Ligand Models (BLM) were developed. Following the principles of the acute BLMs, developed in the US, the chronic BLM models were developed from chronic toxicity studies and validated for a range of species and EU surface waters as outlined below.

3. BLM development and validation

The following steps were considered necessary for the integration of bioavailability into the PNEC setting [3].

- Demonstrated reduction in variability of ecotoxicity values when using BLMs
- Validation of the BLMs for natural waters
- Assessing read across of the BLMs to other species

a. Development of acute/chronic BLM models

BLM models are developed from the results of ecotoxicity tests carried out with test waters of varying water chemistry. BLMs are available for the 3 relevant trophic levels, respectively algae, invertebrates and fish:

- acute and chronic BLMs are available for invertebrates (*Daphnia magna*).
- acute and chronic BLM model are available for fish (chronic BLMs based on data for *Pimephales promelas and Oncorhynchus mykiss*).
- An acute and chronic model was developed for the algae (*P. subcapitata)*

The BLM constants of different Cu-BLMs are summarized in the Table below.

	Acute fish BLM	**Acute *D. magna* BLM**	**Chronic fish BLM**	**Chronic D. magna BLM**
	Di Toro et al., 2001	De Schamphelaer et al, 2002	De Schamphelaer et al., 2005	De Schamphelaer et al., 2004
Relative toxicity of Cu-complexes				
$R_{CuOH} = K_{CuOHBL} / K_{CuBL}$	0.063	0.2	0.2	1
$R_{CuCO3} = K_{CuCO3BL}$	-	0.1	0.1	0.26
Copper constants				
log K_{CuBL}	7.4	8.02	8.02	8.02
log K_{CuOHBL}	6.2	7.32	7.32	8.02
log $K_{CUCO3BL}$	-	7.01	7.01	7.44
Competition constants				
log K_{HBL}	5.4	5.4	5.4	6.67
log K_{CaBL}	3.6	3.47	3.47	-
log K_{MgBL}		3.58	3.58	-
log K_{NaBL}	3	3.19	3.19	2.91

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[3] See fact sheet “Bioavailability Correction Strategy and Tools for Metals Risk Assessment”

Table 1: BLM stability constants obtained for fish and invertebrates

The acute and chronic algae BLM only consider binding of Cu to the biotic ligand (i.e., no competition with other cations was observed). The value of the Cu- stability constant (Log K_{CuBL}), however, is pH-dependent and increases with increasing pH. The chronic algal model was formulated as: Log (E_bC10_{Cu2+}) (nM) = -1.14 pH – 0.812 ($R^2 = 0.91$) (De Schamphelaere et al., 2003).

b. Validation of the BLM models for natural waters

The acute and chronic models were validated from ecotoxicity tests carried out in a range of natural surface waters with varying physico-chemical characteristics (Figure 1).

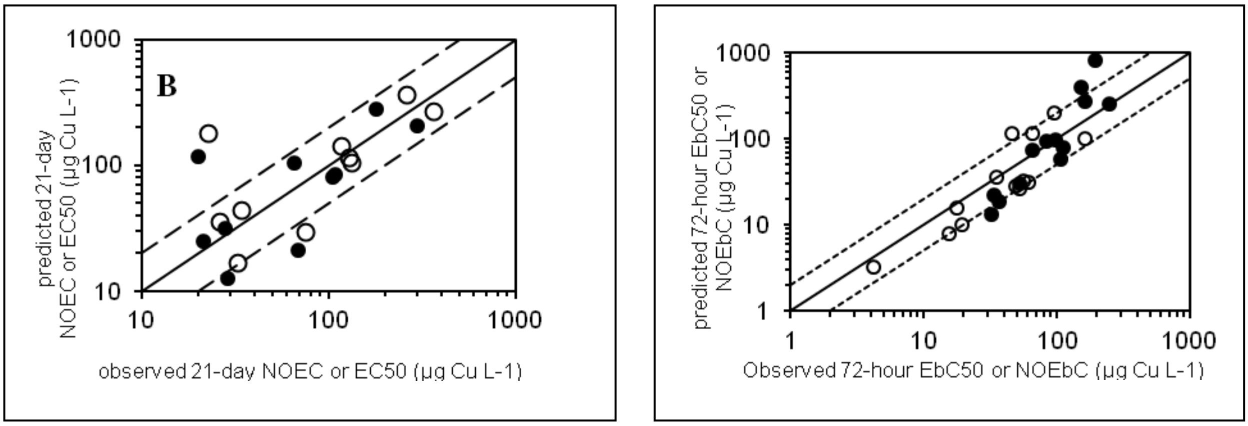


Figure 1: Relationship between observed and predicted chronic EbC_{50} dissolved (closed symbols) and NOEC dissolved (open symbols) of copper for *Daphnia magna* (figure left) and *Pseudokircherniella subcapitata* (figure right) in natural waters (De Schamphelaere, 2003). Similar figures are available for the acute model validations.

Conclusion: the variability of the chronic effects data set could be reduced from a factor 50 to, in general, a factor 2.

From the model development and model validations, the boundaries of the BLM applicability are provided in Table 2

Endpoint	Species	Range Phys-chem			Other boundaries
		pH	H	DOC	
DEVELOPED/VALIDATED					
Algae growth	*P. subcapitata*	5.5-8.7	10-500	0-20	Al< 332 mg/L and Fe < 307 mg/L
Invertebrate reproduction	*D. Magna*	5.5-8.5	10-500	0-20	Al< 332 mg/L and Fe < 307 mg/L
Fish growth	*O.mykiss / P.promelas*	6-8.6	12-360	0-18	

Table 2: Boundaries of the copper BLM. The limits to pH, Hardness (H, expressed as mg $CaCO_3$/L) and DOC (mg/L) are based on the water characteristics of the test waters used for the BLM developments. The limits to Fe and Al were added during the model validations (to address the outlier in Figure 1).

Conclusion: BLMs are applicable across a wide range of physico-chemical conditions representing most common surface waters.

c. Applicability of the BLM models to other species

The potential of the acute and chronic bio-availability models to be applicable to other species was assesses from “spot checks". The information includes:

*(1)**Invertebrates:*** the capacity of the chronic *D. Magna* BLM for predicting copper toxicity to other invertebrates was demonstrated from copper toxicity studies with *Brachionus calyciflorus*, *Hy*

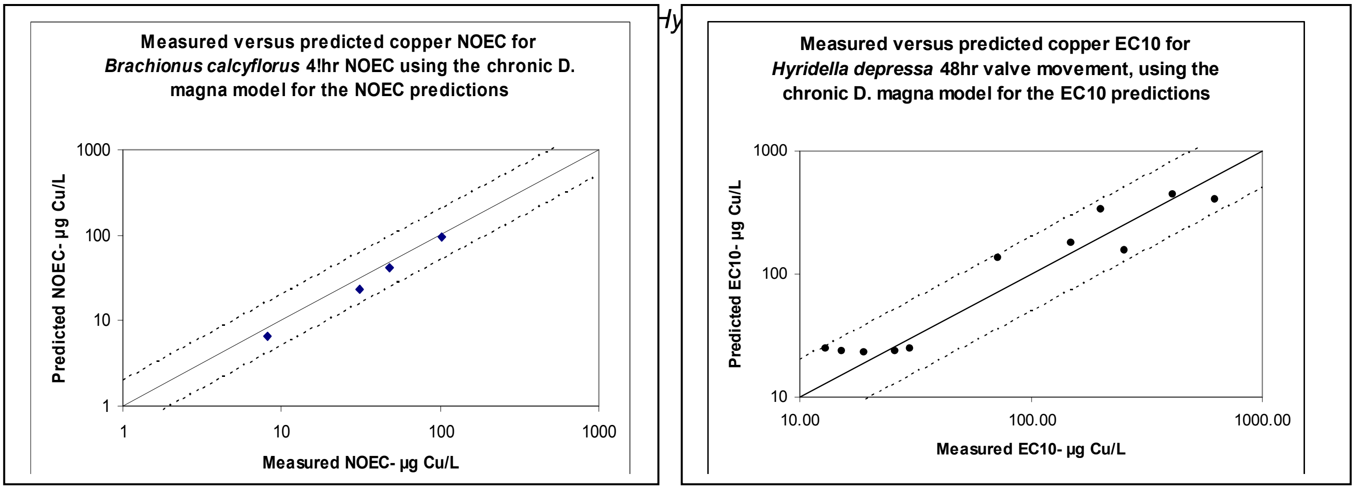


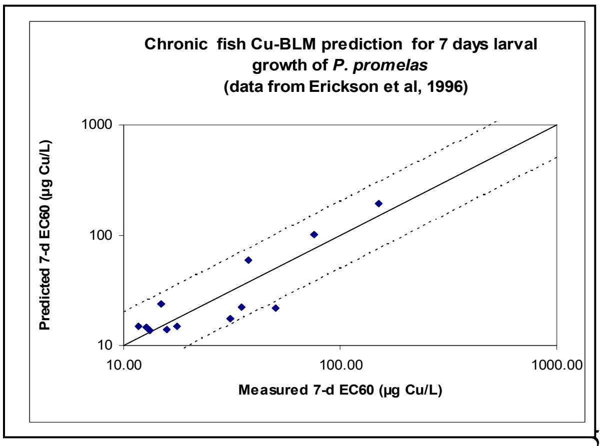
Figure 2: Examples of relationship between observed and predicted effects data for invertebrates. Life cycle data for *Brachionus calyciflorus* (data from de Schamphelaere et al., 2006) and valve movement of *Hyridella depressa* (data from Markich et al., 2003).

The water chemistry of the invertebrate spot check data-sets can be summarized as follows:

Species	Enpoint	Test Duration	pH	DOC mg/L	Ca mg/L	Mg mg/L	Na mg/L	K mg/L	Alkalinity mg CaCO3/L	Reference
Lampsilus	EC50-ELS	96 hours	8-8.7	0.5-11	11-86	3-40	3-341	1-42	40-196	Kunz et al., 2006
Hyridella	EC10	48 hrs	6.5-7.5	0.5-12	6	6	26	2	0.7-7	Marckich et al., 2003
Hyalella	LC50	1 week	6.5-8.5	0.9-1.3	4-100	0.6-15	2-125	0.2-6	0.3-126	Borgman et al., 2005
Brachionus	NOEC	48 hrs	6-7.8	5-15	32	5	37-160	3	1-15	De Schamphelaere et al., 2006

Table 3: Water chemistry of the invertebrate spot checks

*(2)**Fish***: a unified chronic BLM (Figure 3) was developed from the copper ecotoxicity data for two fish species (*Pimephales promelas* and *Oncorhynchus mykiss*).



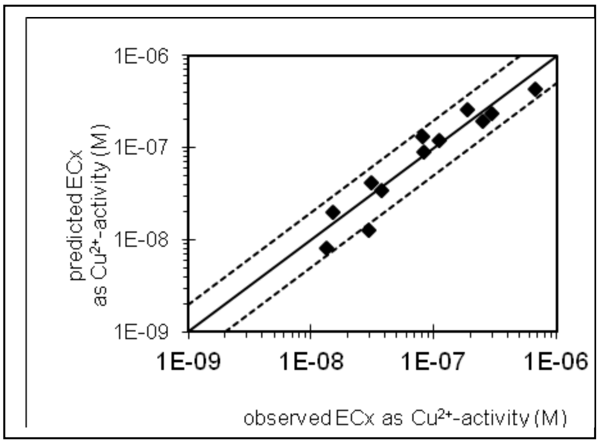


Figure 3: Relationship between observed and predicted effects data for the 2 fish species assessed from literature data (De Schamphelaere and Janssen, 2005)

(3) ***Algae***: read-across data are available for the algae *Chlamydomonas reinhardtii and Chlorella vulgaris. A* unified chronic model (Figure 4) was developed for the algae (*P. subcapitata,*

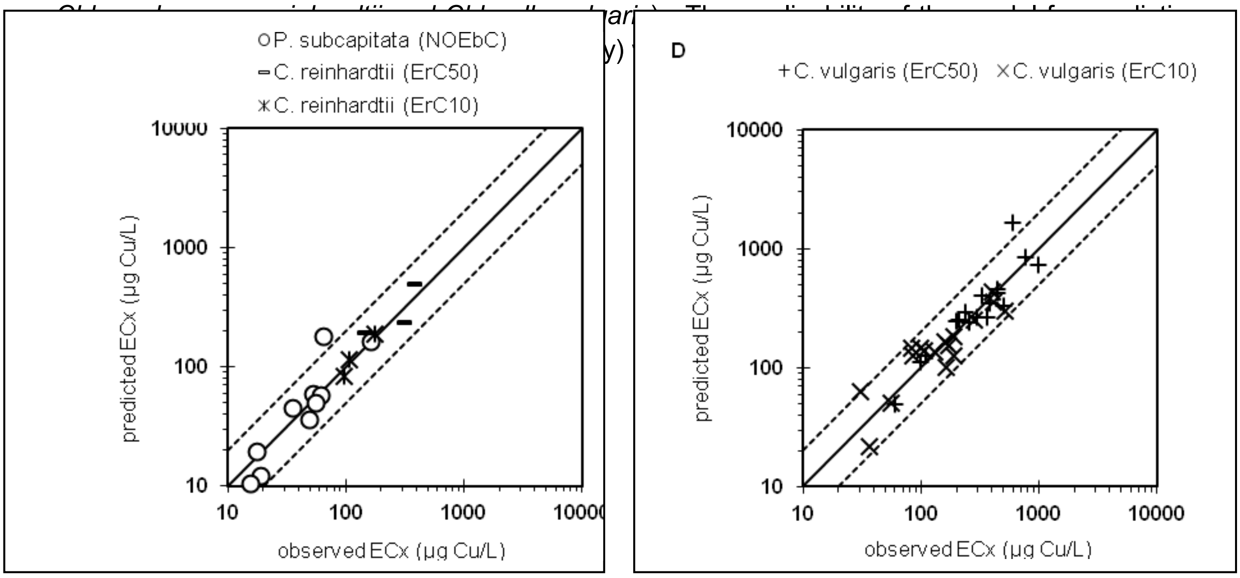


Figure 4: Relationship between observed and predicted effects data using the unified algae (From De Schamphelaere et al., 2003)

Conclusion: The applicability of the BLM model to other species than developed for could adequately be proven for the 3 considered trophic levels.

(4) Figure 5 compares the chronic NOECs dataset for copper retained under the EU copper Risk Assessment, with the chronic NOECs predicted by the BLM at the physico-chemistry of the respective tests.

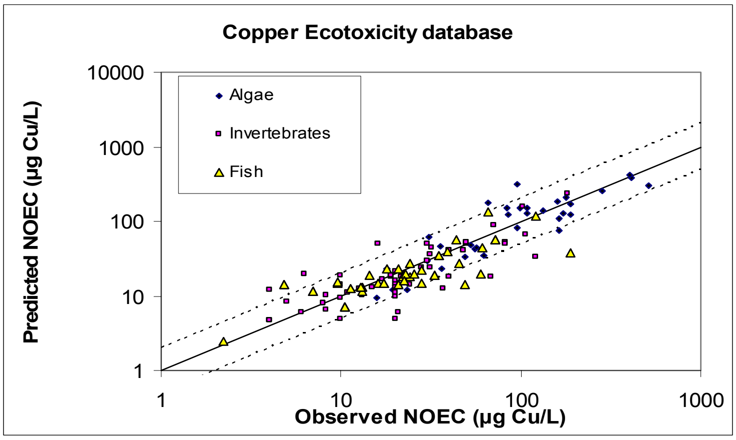


Figure 5: Observed NOECs versus BLM predicted NOECs (by endpoint) at the physico-chemistry of the ecotoxicity tests.

This graph includes all NOECs retained in the copper risk assessment freshwater database. The figure integrates the variability related to physico-chemistry of the test media (normalized by BLM) as well as intra- and inter-laboratory variability due to differences in test set-up (eg strains, exposure regimes …).

Conclusion: The individual NOECs in the database (i.e. not corrected for bio-availability) varied with a factor of 232 and could be predicted with the different chronic BLM tools within a predicted/observed ratio ranging from 0.2 to 3.3.

4. Examples of the use of BLMs to derive PNECs for regulatory applications

The copper freshwater effects database contains 139 high quality chronic NOEC/L(E)C_{10} values, representing 27 different species. Considering the large amounts of chronic NOEC/L(E)C_{10} values, statistical extrapolations can be carried out to derive the HC5-50, forming the basis for the freshwater PNEC[1].

Chronic copper BLMs are used to normalize the NOEC/L(E)C_{10}s. The chronic BLMs developed for fish (*P. promelas and O. mykiss*), invertebrates (*D. magna*) and algae (*P. subcapitata*) were used for normalizing all retained chronic NOEC/L(E)C_{10} values of respectively all fish, invertebrates and algae/plant species. Briefly, the bio-availability correction process normalizes the individual ecotoxicity data (NOEC/L(E)C_{10} values) to sets of physico-chemical conditions for important abiotic factors (i.e., pH, hardness, and dissolved organic carbon (DOC)). This approach allows for the comparison of intrinsic toxicity among organisms on an equal basis.

Example 1: ecoregions

Normalization was carried out towards seven different EU surface water scenarios, selected to include a range of typical cases of bio-availability and to encompass the 10th/90thpercentile of the DOC, pH and hardness for such EU surface waters. The normalization of the NOEC/L(E)C_{10}s with the different chronic BLMs allowed to obtain small intra-species variability and resulted in more robust and meaningful species-specific NOEC/L(E)C_{10}s values. With due considerations of bio-availability, Species Sensitivity Distributions (SSD) were constructed using the normalized species-specific NOEC/L(E)C_{10}s data. The resulting EU scenario specific HC5-50s range between 7.8 to 27.5 µg dissolved Cu/L (Table 4; Figure 6).

Water Type	Hardness (mg CaCO3/L)	DOC (mg/L)	Na (mg/L)	Alkalinity (mgCaCO3/L)	HC5-50 (µg Cu/L)
Small (ditches with flow rate of +/- 1,000 m³/d)	350.1 (Ca: 88.2; Mg: 31.6 mg/l)	12	59.8	265	27.5
Medium (rivers with flow rate of +/- 200,000 m³/d)	165 (Ca: 46.9; Mg: 11.6 mg/l)	3.2	14.2	116	7.8
Medium (rivers with flow rate of +/- 200,000 m³/d)	159 (Ca:49.9; Mg: 8.4 mg/l)	8	12.9	118	21.9
Large (rivers with flow rate of +/- 1,000, 000 m³/d)	217 (Ca:68.9; Mg: 10.9 mg/l)	2.8	36.8	119	8.2
Mediterranean river	273 (Ca: 72.9; Mg: 22.1 mg/l)	3.7	5.3	35.8	10.6
Oligotrophic systems	48.3 (Ca: 13.6; Mg: 3.5 mg/l)	2.5	2.3	50.6	10.6
Acidic system	27.8 (Ca: 8.7; Mg: 1.5 mg/l)	3.8	7.7	13.6	11.1

Table 4: Characteristics of the 7 standard EU scenario's used for BLM normalized SSDs (Figure 6) and calculations of HC5-50s

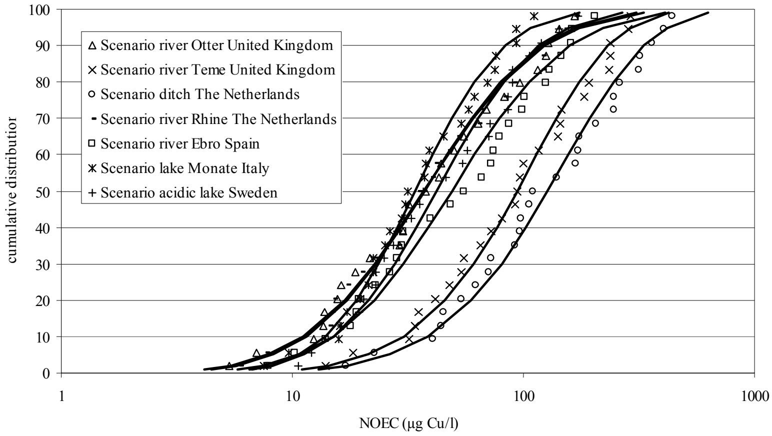


Figure 6: Overview of the SSD for the different freshwater eco-regions

Example 2: country specific assessments

The distribution of the chronic BLM-calculated HC5-50 across EU surface waters was further assessed. Therefore, site-specific information on physico-chemistry (DOC, Hardness, pH…) from Belgium, Germany, UK, Sweden, Spain, Austria, The Netherlands and France was used to calculated HC5-50 for a wide range of sites. Table 5 shows the BLM calculated copper HC5-50s (10P – 50P – 90P) per region.

	Statistical analysis of the HC5-50	
	Statistical basis	**HC5-50 µg Cu/L**
Sweden	Area-based	(13.8 - 18 - 23.3)
UK	Area-based	12-17-29
France	Area-based	7.8-13.4-19.7
Austria	Area-based	(4-7.3-17.7)
Belgium	Area-based	9.32-11.7-18.9
Germany	Point-based	11.7-20.5-29.3
Spain	Point-based	7.3-11.0-20.9
TheNetherlands	Point-based	19.5-36.8-77.4

Table 5: BLM calculated copper HC5-50s (10P – 50P – 90P) for different regions. Statistical analysis are based on classic point based assessment or "area-based kriging" techniques – where possible. Bracketed values indicate that the area-based percentiles could only be derived approximately.

When geo-referenced data are available, the variability in sensitivity (HC5-50) within a region can be further assessed, as illustrated in the Figure 7.

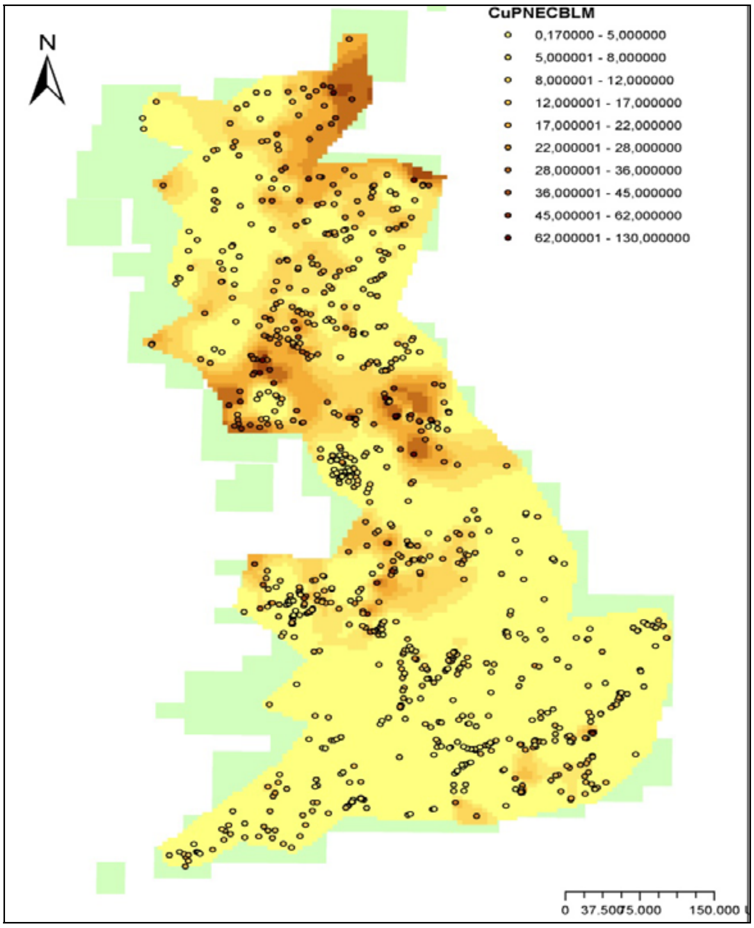


Figure 7. Overview of the copper HC5-50 values derived for UK data. (Environment agency, 2009)

Conclusion: Both examples demonstrate the added value of bioavailability normalization towards specific abiotic conditions to allow for specific regulatory uses of PNEC's for Cu.

5. Conclusions and next steps

To derive safe threshold values for copper, the incorporation of bio-availability has been crucial because it reduced the intra-species variability in NOEC/L(E)C_{10} values and increased the reliability and ecological relevancy of the PNEC values.

Following the development of acute BLMs, chronic BLMs were developed for three trophic levels (algae, invertebrates and fish). The applicability of the BLMs was demonstrated for a range of species (covering algae, invertebrates, fish and higher plants) and for a variety of natural surface water. The bio-availability normalization demonstrated significant reduction in the intra-species variability of ecotoxicity values.

The BLM development and BLM validation data have been considered as sufficient to allow their applications in EU (chronic BLMs) and US (acute BLMs) regulatory frameworks.

Model refinements are a continuous process that will allow further future improvements of model predictive capacities and software.

6. Further information on the copper EU risk assessment and BLM software

The copper risk assessment was a voluntary industry response to a request from the European Commission to "start preparing the initial assessments for substances on the EU working list as these were considered as Community priorities in the context of the industry voluntary initiatives for high production volume chemicals". The Voluntary Risk Assessment (VRA) initiative for copper and the copper compounds on the EU working list: Cu, CuO, Cu_2O, $CuSO_4$ and $Cu_2Cl(OH)_3$ was endorsed by the EU competent authorities in 2001. The Italian Istituto Superiori di Sanità acted as review country for the copper risk assessment and a scientific panel further reviewed the quality of the draft copper risk assessment report. The draft copper risk assessment report was subsequently reviewed by the European Committee for New and Existing Substances (TCNES), which was comprised of technical representatives from the EU Member States started. The TCNES opinions were formulated in 2008.

The final report on the Environmental Risk Assessment of copper and copper compounds, available from: http://echa.europa.eu/chem_data/transit_measures/vrar_en.asp.

The opinion of the Scientific committee on Health and Environmental Risks (SCHER) on the copper risk assessment report can be found on: http://ec.europa.eu/health/scientific_committees/environmental_risks/opinions/scher_opinions_en.htm#4

The BLMs have been incorporated in user-friendly tools.

- The acute BLM models were developed by Hydroqual and are available from: http://www.hydroqual.com/wr_blm.html
- The chronic BLM, used in the copper risk assessment and the assessment above has been integrated into a simplified chronic BLM by ARCHE Consulting and WCA. This user-friendly version is available from : http://bio-met.net

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Session A illustrative example: oil bioavailability assessment - the example of Antimony

Regulatory context

The terrestrial effects of antimony were originally studied in the EU Risk Assessment Report[1] (RAR) on diantimony trioxide (Sb_2O_3, ATO). The ATO RAR was carried out as a response to the publication of ATO on the 4th priority list of Existing Substances Regulation 793/93/EC in October 2000. Sweden was Rapporteur Member state. Data were discussed at EU level within the Technical Committee for New and Existing Substances (TC NES). In April 2008, the last discussion at TC NES level was held and the RAR was accepted end of May 2008. The report was reviewed and accepted at OECD-level[2] in 2008 and by the Canadian government[3] in 2010. The data of the ATO RAR have been used for the registration of antimony metal and antimony substances under the REACH regulation (EC) No 1907/2006.

This paper summarises the derivation of the terrestrial toxicity threshold for antimony using the ageing concept.

Soil effects assessment

Freshly amended soils

Terrestrial Sb toxicity has frequently been assessed using sparingly soluble ATO. As metal toxicity is exerted via metal ions in solution rather than total soil metal concentrations, the slow dissolution of ATO in the soil solution gives an increasing ‘toxic pressure’ over time (Figure 1). Incomplete ATO dissolution will, as such, result in a severely underestimated Sb toxicity. More readily soluble Sb compounds, such as antimony trichloride ($SbCl_3$, ATC), give a constant toxic pressure over time and have been used as an alternative to ATO. However, the use of readily soluble Sb compounds changes the soil chemistry due to the release of counter ions (such as chloride ions) and protons, next to increasing the Sb concentration, which might affect data interpretation. This was confirmed in a study by Oorts et al.[4]. An uncontaminated agricultural soil was artificially contaminated with ATO and ATC at 0 - 2000 mg Sb/kg. After 7 days equilibration, Sb toxicity was assessed using a microbial, invertebrate and plant assay. No Sb toxicity was observed in the ATO amended soils up the highest contamination level (2000 mg Sb/kg) whereas all endpoints were sensitively affected in the ATC amended soils (NOEC: <20 - 500 mg Sb/kg). This discrepancy between ATO and ATC was explained by the slow release of Sb ions in ATO amended soils (Sb concentrations in soil solution after ATO spiking were only 20-30% of the values at comparable ATC doses; Figure 1) and the release of the chloride ions and protons in ATC amended soils.

Aged soils

At TC NES I ’07[5], it was decided that ATO amended soils with sufficient ageing or, in other words, sufficient time to dissolve, are the preferred Sb exposure pathway for terrestrial toxicity testing. This ensures

i) a constant toxic pressure (i.e. Sb concentration in pore water) during the exposure period
ii) minimal side effects of released counter ions or protons.

The importance of ageing was previously recognized in the zinc risk assessment, and later by a lot of other elements amongst which Sb.

Therefore, the same uncontaminated soil was re-amended with ATO at 0 - 10000 mg Sb/kg, and placed outdoor in perforated plastic pots for 31 weeks. Afterwards, soil chemistry and Sb toxicity (microbial and plant assays)[6,7] were assessed in the aged ATO amended soils. In contrast with the freshly ATO amended soils, all endpoints were affected by increasing ATO concentrations in the aged soils with NOECs between 999 and 2930 mg Sb/kg.

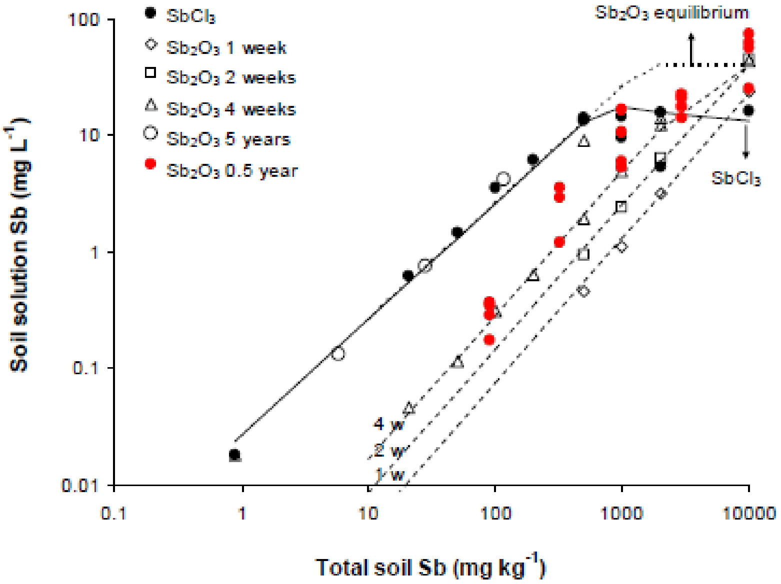

Figure 1 - Soil solution Sb concentrations in $SbCl_3$- and Sb_2O_3 amended soil samples. Red dots indicate Sb concentrations in soil solution of the 31-weeks aged ATO-amended soils. The lines represent predicted soil solution Sb concentrations for $SbCl_3$ (full line) and Sb_2O_3 (broken lines) at different times after Sb amendments as indicated next to the lines. Predictions are based on a K_d of 38 l/kg, $\log K_{sp}$ for $Ca[Sb(OH)_6]_2$ of -9.8 and a half-life for Sb_2O_3 dissolution between 50 and 250 days depending on the Sb dose (taken from Oorts et al.[8]).

PNEC derivation in aged ATO amended soils…

…based on total soil Sb concentrations

According to the standard TGD procedure, the $PNEC_{soil}$ for Sb had to be derived as the lowest NOEC of the terrestrial Sb toxicity assays in the aged soils divided by 10 giving a $PNEC_{soil}$ of 99 mg Sb/kg. However, Sb concentrations in soil solution in the aged ATO amended soils were still lower than in ATC amended soils at similar total soil Sb concentrations (Figure 1) whereas similar soil solution Sb concentrations were expected upon complete dissolution (as shown by the data of the 5-year aged soil; Figure 1). This implied that the Sb concentration in soil solution and, hence, terrestrial toxicity, would further increase over time, and that the $PNEC_{soil}$ underestimated Sb toxicity.

…based on soil solution Sb concentrations

Instead, an alternative approach was used. Metal toxicity in soil is exerted via metal ions in soil solution, and it was assumed that further dissolution of added ATO after 30 weeks of ageing was slow, giving a reasonably constant toxic pressure during the course of the bioassays (days-weeks). Knowing this, the total soil Sb concentration in fully equilibrated ATO amended soil giving the same Sb concentration in solution at the NOEC as in the 31 weeks aged soils and, hence, the same toxic pressure were calculated. Therefore, the equilibrium solid:liquid distribution coefficient K_d for Sb was calculated using dissolution data in Figure 1. This K_d value was derived from the linear part of the modelled equilibrium Sb concentration in solution based on the ATC data (which is also valid for the corresponding 5-year aged ATO amended soil), and was 38 l/kg. The Sb concentration in soil solution at the NOEC (999 mg Sb/kg) was 9.7 mg Sb/l. To be compliant with standard TGD procedures, the Sb concentration in solution at the NOEC was first divided by 10, giving a value of 0.97 mg Sb/l. Subsequently, this value was multiplied by the equilibrium K_d value to estimate the corresponding $\text{PNEC}_{\text{soil}}$, expressed as total Sb in soil, in fully equilibrated ATO amended soil. This $\text{PNEC}_{\text{soil}}$ was (9.7 mg Sb/l / 10) × 38 l/kg) 37 mg Sb/kg (on a dry soil weight basis) and suggests that the toxicity after 31 weeks ageing underestimated toxicity 2.5-fold. A $\text{PNEC}_{\text{soil}}$ of 37 mg Sb/kg was used for the ATO RAR and later for the REACH registration of other antimony substances.

Conclusions

Terrestrial metal toxicity studies are often performed in artificially metal salt amended soils. Yet, toxic thresholds in these soils are rarely comparable to those derived from field aged soils due to e.g. metal dissolution kinetics or a different soil solution chemistry. As a result, metal toxicity is under- or overestimated. For antimony, it was shown that readily soluble antimony substances severely alter soil chemistry giving an overestimation of terrestrial Sb toxicity. As the EU RAR was only focused on ATO, ATO was used to test terrestrial toxicity provided soils were sufficiently aged. The $\text{PNEC}_{\text{soil}}$ was derived based on the soil solution Sb concentration at the NOEC and the corresponding K_d to correct for incomplete ATO dissolution and, as such, to overcome Sb toxicity underestimation. Antimony speciation and bioavailability was not determined in the presented studies. Yet, it can be assumed that for cationic elements such as zinc or copper, free ions in solution can extensively be bound at soil reactive sites over time, resulting in a decreasing bioavailability (and toxic pressure). It is advised to consider the ageing-bioavailability correction concept on a metal-specific basis[9].

References

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[6]Smolders E, Mertens J and Buekers J (2007) Toxicity and Bioavailability of Sb_2O_3 after ageing in Terrestrial Environments. Final report to the International Antimony Oxide Industry Association (IAOIA).

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[9]Smolders E, Oorts K, Van Sprang P, Schoeters I, Janssen CR, McGrath SP and McLaughlin M (2009) Toxicity of trace metals in soil as affected by soil type and aging after contamination: using calibrated bioavailability models to set ecological soil standards. Environ Sci Technol 28, 1633-1642.

ANNEX 5

SESSION B: EFFECTS ASSESSMENT

→ Concept paper on Effects assessment and references for further reading

→ Illustrative examples

- Lead for the soil compartment
- Nickel for the marine compartment (see fact sheet+ addendum)
- Zinc for the freshwater compartment
- Silver for the STP assessment

Session B concept paper on assessment of very large effects data sets and read-across techniques relevant for poorer data sets

Background paper for OECD Workshop on Metals Specificities in Environmental Hazard Assessment
Paris, September 7-8, 2011

Note: *These papers were prepared by industry and reviewed by the workshop steering committee to provide some background on concepts associated with metals-specificities in environmental hazard assessment. The papers do not represent a consensus view of the OECD on how to conduct metals environmental assessment, but they should serve as a basis for workshop participants to understand the concepts proposed and already applied in some OECD countries.*

Background:

Metals are present in a variety of chemical forms (soluble compounds, sparingly soluble compounds, metals, alloys and integrated in complex inorganic minerals (e.g. concentrates)) and appear in various physical forms (powders or as massive forms)

Ecotoxicity tests are usually available for a limited number of soluble salts. To assess the toxicity of the various metal forms: different issues are to be addressed:

1. How to perform the read-across of the ecotoxicity data and hazard identification across different chemical and physical forms
2. How to derive ecotoxicity reference values for large ecotoxicity data sets.
3. How to use the ecotoxicity data in a hazard assessment and in risk characterisation context

Approach:

1. *Data selection*

   Across the various inorganic metal forms, the release of metal-ions is driving the observed ecotoxicity. Toxicity values (EC50s, NOECs) are therefore obtained from testing soluble salts and expressing the results as the metal ion concentration causing the observed toxicity in aquatic (µg soluble Me/L), sediment (µg Me/kg) and soil compartments (µg Me/kg).

   Prior to retaining any of the observed ecotoxicity values in the database, the individual records (EC50s, NOECS) need to be screened for data reliability and data relevance whereby metal-specific aspects such as bio-availability and culture conditions need to be considered.

2. *Grouping of selected data*

   To set an ecotoxicity reference value (e.g. reference NOEC (ECx) for hazard identification and safe threshold derivation (e.g. PNEC setting for risk characterisation) from the retained high quality effects database, data-aggregation and a weight of evidence (WoE) assessment is needed. Relevant aspects of such data-aggregation and WoE include: combining ecotoxicity data (NOECS expressed as µg/L) across soluble metal compounds; derivation of species-mean NOECs (ECx), assessing the extent of the data set, the species covered, appropriate statistical methods and comparisons to mesocosm and field data.

   In general, the following grouping rules can be applied on large data-sets:

- If for one species sufficient L(E)C /chronic NOEC values based on the same toxicological endpoint are available, these values are averaged by calculating the geometric mean, resulting in the "species mean" NOEC/L(E)C.
- If for one species several acute L(E)C /chronic NOEC values based on different toxicological endpoints are available, the lowest value is selected. The lowest value is again determined on the basis of the geometric mean if more than one value for the same endpoint is available.
- In some cases, L(E)C /NOEC values for different life stages of a specific organism are reported in the same study. If from these data it becomes evident that a distinct life stage is more sensitive, the result for the most sensitive life stage is selected.
- If acclimation/adaptation is important test results should be grouped on the basis of the similarity of the background in the culture medium with the background of the environment under evaluation.
- When it is apparent from the data that the observed intra- species variability in toxicity test results can be assigned to differences in bioavailability and no bioavailability model is available to normalize the data, the effect data should be grouped by similar ranges of abiotic factors that control the bioavailability of metals. The grouping should preferentially be conducted such that they reflect the range of abiotic factors encountered in the region under evaluation (e.g. soft water scenario).

3. *Assigning a reference value for hazard identification of a substance,*
   - the ecotoxicity reference values can be derived by translating the reference soluble metal ion concentration (e.g. µg Me/L) causing the appropriate standard ecotoxicity effect (lowest species-specific acute EC50 and chronic NOEC) towards the compound under investigation using the ***molecular weight ratio*** (MW substance/MW metal ion).
   - In case the solubility is limited, the release rate of metal ions from the sparingly soluble metal compounds, metals or alloys can be used as read across parameter between the toxicity of soluble metal compounds and the sparingly soluble metal compounds, metals/alloys, complex substances). Further ecotoxicity testing of insoluble forms can therefore be avoided.

4. For risk characterisation, the *safe threshold (PNEC) derivation* includes an uncertainty analysis. For small data-sets, assessment factors are used, for larger data-sets a WoE approach, assessing the extent of the data set, the species covered, the appropriate statistical methods and comparisons to mesocosm and field data is used.

Calculation of PNEC using assessment factors (data poor substances)

For some metals/metal compounds the amount of data available for predicting ecosystem effects will be limited. In these circumstances empirically derived assessment factors must be used. Typically, PNEC values are calculated from the lowest acute LC50 or EC50 or, preferably, from the lowest chronic NOEC/L(E)Cx, plus the application of an assessment factors that depend on the amount of toxicity data available. In general the size of the applied assessment factor will decrease as confidence in the data set increases. The requirements to be fulfilled for the different environmental compartments may differ.

Several sets of assessment factors have been proposed to date and lower assessment factors will be used with larger and more relevant data sets (e.g. data available for a number of trophic levels, different feeding strategies etc.).

Calculation of PNEC using statistical extrapolation methods (Data rich substances)

When a large data set for different taxonomic groups is available, the PNEC can be calculated using the statistical extrapolation method in which the susceptibility of a set of species for a given toxicant can be described by some statistical distribution (i.e. Species Sensitivity distribution or SSD). A SSD can be visualized as a cumulative distribution function (Figure 1). The cumulative distribution function curve follows the distribution of the sensitivity data obtained from ecotoxicological testing, plotting effect concentrations derived from acute or chronic toxicity tests, for example LC_{50} values and No Observed Effect Concentrations (NOECs), respectively.

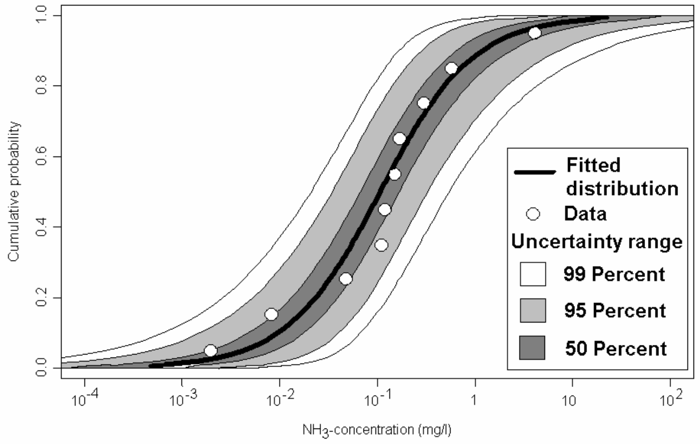

Figure 1: Example of a SSD (Species Sensitivity Distribution - loglogistic distribution) with uncertainty band and its HC5 (Hazardous Concentration at 5 %)

The most common current approach is to derive the Predicted No Effect Concentration (PNEC) from the 5_{th} percentile of SSD (EU-TGD, 1995). Historically that value is known as Hazardous Concentration at p-protection level or HC_p. The 5_{th} percentile of a chronic toxicity distribution has been chosen in the earliest methods as a concentration that is protective for most species in a community. Researchers also started to determine a confidence or uncertainty interval on the HC_5 (Figure 1). A confidence or uncertainty interval can quantify the sampling error in the HC_5 estimate.

The choice of distribution functions, dependence of SSDs on the amount and quality of available data and the choice of protection level has been particularly debated.

If relevant, bio-availability can be incorporated into the SSD (not in scope of this one pager)

Uncertainty management

Once a HC5 is chosen it is recommended to look at the remaining uncertainty. If deemed appropriate an additional assessment factors on the HC5 value could be applied. Typically in defining assessment factors the size of an assessment factor depends on the confidence with which a $PNEC_{water}$ can be derived from the available data. This confidence increases if data are available on the toxicity to organisms at a number of trophic levels, taxonomic groups and with lifestyles representing various feeding strategies. Thus lower assessment factors can be used with larger and more relevant datasets than a base-set data.” Thus, among other factors, the size of the assessment factor is mainly driven by the number of species (covering sufficient taxonomic groups). A way forward to objectively evaluate and if needed define an assessment factor to be applied on an HC5 is looking at the decrease in confidence interval surrounding the HC5 in function of the number of entries in an SSD. During this process care should be taken that the level of conservatism embedded in the recommended assessment factors is consistent with the relation to the number of species used which can done by recalibrating the factor according to the widely-accepted level of conservatism already in use (e.g.. in the EU a factor of 10 for 3 NOEC data is used in the classical AF approach).

Effects weight-of-evidence

Once a PNEC has been derived for the different compartments, either through use of assessment factors or by using a statistical extrapolation method, the weight-of-evidence from all other available data including mesocosm/field data, use of alternative sediment effect levels (such as AET, PEL/TEL values) etc should be evaluated in a final tier. This is especially important for the validation of assessment factors used on the lowest ecotoxicity value.

If the results of laboratory and field (model) ecosystem studies show that effects on ecosystems are unlikely to occur at the derived PNEC level, the assessment factor may be decreased. On the other hand, if it is clear that the PNEC is under-protective for the ecosystem the mesocosm value could be used. If specific field or mesocosm NOECs are below the PNEC derived from single species studies, it is important to understand the observed differences through detailed evaluation

Conclusions:

Hazard identification of metals, metal compounds and complex metal containing substances (alloys and concentrates) are related to the toxicity of the metal ions, the release of the metal ions and the fate of these metal ions.

The toxicity of the metal ions and the release of these ions from the metal bearing substances are therefore used as a basis for the read-across. Such read-across allows for robust hazard assessments of metal bearing substances/mixtures that have no toxicity data (e.g. read across from copper compounds to copper alloys).

Adequate effects assessments of metal includes appropriate data selection, grouping of the data and a Weight of evidence approach for the derivation of reference values for hazard identification and safe threshold values for risk characterization.

References for further reading

- UN GHS official text and corrigenda, 2007 and 2009
  http://live.unece.org/trans/danger/publi/ghs/guidance.html
- ECHA guidance section on information requirements – chapter R10 : characterization of dose (concentration)-response for environment
  http://guidance.echa.europa.eu/docs/guidance_document/information_requirements_r10_en.pdf?vers=20_08_08
- ICMM MERAG Fact sheets 3, 7 and 8: effects assessment, Uncertainty analysis and Hazard classification
  http://www.icmm.com/page/1185/metals-environmental-risk-assessment-guidance-merag

Session B illustrative example: Effects assessment in the terrestrial environment: lead

Background paper for OECD Workshop on Metals Specificities in Environmental Hazard Assessment
Paris, September 7-8, 2011

Note: *These papers were prepared by industry and reviewed by the workshop steering committee to provide some background on concepts associated with metals-specificities in environmental hazard assessment. The papers do not represent a consensus view of the OECD on how to conduct metals environmental assessment, but they should serve as a basis for workshop participants to understand the concepts proposed and already applied in some OECD countries.*

Background:

The terrestrial effects assessment for lead was originally prepared as part of the voluntary risk assessment for lead and lead compounds under the European Existing Substances Regulation (EEC) 793/93. It was further updated in 2010 for the registration of lead and lead substances under the REACH Regulation ((EC) No 1907/2006). It is currently again being updated with results from an industry sponsored research program in order to address the comments raised by the European Scientific Committee on Health and Environmental Risks (SCHER) on the voluntary risk assessment report. Because all new data are not available yet, the present document describes the terrestrial effects assessment for lead as included in the 2010 REACH registrations.

In assessing the ecotoxicity of lead, it is assumed that toxicity is not controlled by the total Pb concentration, but by the bioavailable form. For metals, this bioavailable form is generally accepted to be the free metal-ion in solution. In the absence of speciation data and as a conservative approximation, it can also be assumed that the total soluble lead pool is bioavailable. The terrestrial effects assessment for lead is therefore based on soluble Pb salts.

Approach:

5. *Data-compilation*

   The ecotoxicological data on the effect of lead on soil organisms are derived from original papers on the subject, published in international journals and from industry research projects.
   Only data from soluble lead salts ($PbCl_2$, $Pb(NO_3)_2$, lead acetate) are selected and all results are expressed as mg Pb/kg dry soil. The results of the terrestrial toxicity studies are preferentially expressed as the actual (i.e. measured) total Pb concentration (analysed after a strong acid destruction). If no measured concentrations are available, the nominal (i.e. added) concentration is used.

6. *Data screening: relevancy and quality*

   Prior to selecting any of the ecotoxicity values for the effects assessment, the individual records (EC10s, NOECS) need to be screened for data relevance and reliability.

   Relevancy

   - Only data from observations in natural or artificial soil media have been used. Tests performed in substrates that were judged as not representative for soils (e.g. nutrient solution, agar, pure quartz sand and farmyard manure) were not included in this effects assessment.

- The data used should ideally be based on organisms and exposure conditions relevant for Europe. This would, however, considerably reduce the amount of data to be used. Therefore, also data based on soils collected outside Europe have been used, excluding tests with non-EU soils that reported soil properties well outside the range of 10th-90th percentiles of European soils.
- Only studies with lead-only exposure were considered relevant. Data from mixed exposure or with indications of impurities that might affect the toxic response were rejected.
- The toxicological endpoints considered have direct effects at population level, e.g. mortality, growth and reproduction for plants and invertebrates. Soil microbial endpoints are functional variables, such as respiration, mineralization and nitrification.
- Toxicological threshold data on enzymatic processes are not included. The ecological relevance of enzyme assays is unclear. For example, these tests typically measure the enzyme activity at saturating substrate concentrations whereas these conditions rarely prevail in soils.
- Only long-term or chronic toxicity data were selected. What comprises "chronic exposure" is a function of the life cycle of the test organisms. A priori fixed exposure durations are therefore not relevant. Exposure periods of selected endpoints varied between 5 days and 6 months. Some tests provide data at different exposure times. Only data at the longest exposure time were selected, with the exception of some microbial processes where measurements were made at different moments during the exposure time. For the latter, the NOEC was taken at the most sensitive point in the microbial process.
- Standard operating protocols for toxicity tests are based on soils freshly amended with a potentially toxic substance. However, the equilibration time and treatment (e.g. leaching and pH correction) of soils between the addition of the lead substances and the start of the toxicity tests strongly affects the outcome of the toxicity tests. A large part of the toxicity in Pb^{2+} salt spiked soil is confounded by the ionic strength (the 'salt effect') and the associated pH decrease. Leaching the soils reduces toxicity as shown several studies (Waegeneers et al., 2005; Bongers et al. 2004; Stevens et al. 2003). The acidification of soils in metal salt spiked soils partly contribute to toxicity (Speir et al. 1999) and this acidification is not necessarily found in field contaminated soils (Figure 1).

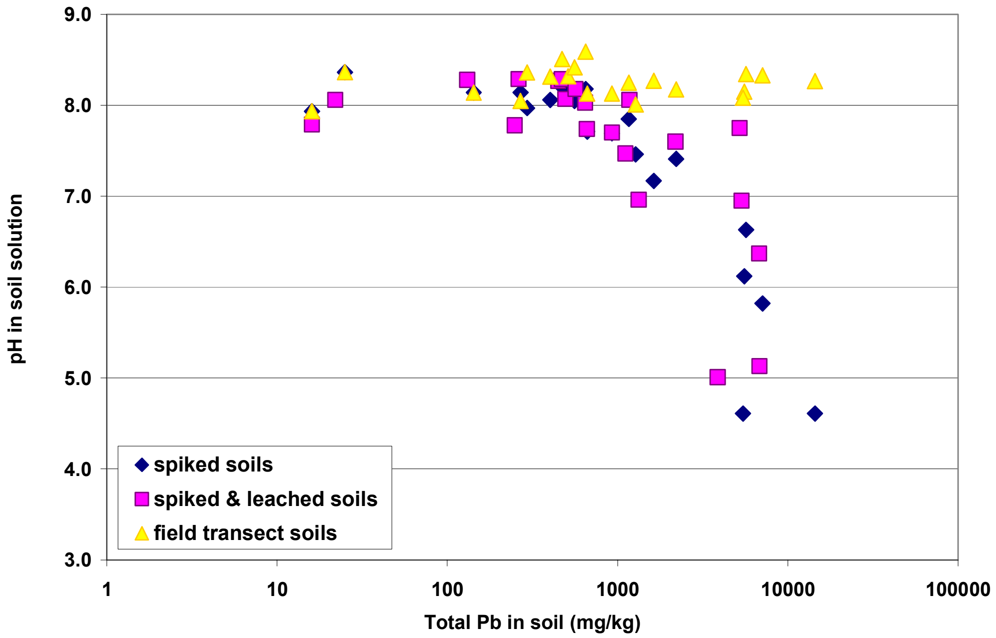

Figure 1: The pH in soil solution as a function of the total Pb concentration in soil (mg/kg) for artificially contaminated and field contaminated soils (data from Waegeneers et al. 2005).

Standard soil toxicity tests neither leached nor pH correct the spiked soils. For Pb, the confounding factors can be large since Pb immobilization in soil requires a relative large Pb dose before toxicity is reached. The discrepancy in toxicity between field soils and corresponding laboratory tests can be corrected in the effects assessment for by the application of a so-called ‘leaching-ageing factor’ (i.e. the ratio of ECx in field contaminated or leached and aged soils and ECx in corresponding freshly spiked soils. When both available, good quality data derived in leached or aged soils are preferred over results derived in corresponding freshly spiked soils.

Reliability (quality)

The relevant toxicity data that might be useful for PNEC derivation were further evaluated for the inherent quality of the methods and results reported. The following criteria were evaluated:

- Tests are preferentially performed according to approved international standard guidelines, but data from non-standardized tests were also considered. In general, toxicity data generated from standardized tests, as prescribed by organizations such as OECD and USEPA will need less scrutiny than non-standardized test data, which will require a more thorough check on their compliance with reliability criteria before being used. Both GLP and non-GLP tests were used provided that the latter fulfil the stipulated requirements.
- Test reports must provide a detailed description of the methods employed and of the results obtained.
- Data on soil pH are considered as basic information and must be reported. Missing information on soil texture, organic matter content, cation exchange capacity and background Pb concentration of the soils tested is judged not critical.
- Ecotoxicological threshold values must be derived using the proper statistical methods. EC10 values as calculated from the concentration-effect relationship were preferred for derivation of the Predicted No Effect Concentration (PNEC). When EC10 values are not reported in the original study, but data are available allowing derivation of a concentration-effect relationship (a minimum of control and 3 test concentrations), the EC10 is calculated using a logistic (sigmoidal) dose-response curve. If no reliable EC10 can be derived because e.g. no significant dose-response curve can be fitted or the EC10 is outside the concentration range tested, and a bounded NOEC value can be derived, this NOEC value will be used instead of the EC10. Unbounded NOEC values (i.e. the largest concentration in a test in which no significant effects were found up to the largest concentration tested) and unbounded LOEC values (i.e. significant inhibition >20% at first dose tested) are included as supporting information, but not selected for the effects assessment.

7. *Bioavailability correction and data aggregation*

Tests that comply with all the above-mentioned criteria are selected for the effects assessment. This results in a total of 62 individual high quality toxicity thresholds, ranging from 57 mg Pb/kg (shoot yield for *Hordeum vulgare*) to 5225 mg Pb/kg (shoot yield for *Triticum aestivum*), and covering 12 plant species, 4 invertebrate species and 5 microbial functional parameters.

All EC10 and NOEC values selected were corrected towards field conditions:

- Thresholds derived from freshly spiked soils without leaching and long-term equilibration (i.e. >180 days) treatment were corrected towards field conditions through the application of a so-called leaching-ageing factor. This leaching-ageing factor is a measure for the relative decrease in toxicity in field contaminated or leached and aged soils compared to corresponding freshly spiked soils. A leaching-ageing factor of 4.2 was selected based on comparison of Pb toxicity in field soils with corresponding control soils freshly spiked with $Pb(NO_3)_2$.

- The few data available from soils spiked with soluble Pb salts, leached and equilibrated for a long-term (> 180 days) were not further corrected, as they already represent realistic field conditions

There were no models available that relate Pb toxicity in soils to abiotic soil properties (pH, organic carbon content, clay content or cation exchange capacity) and therefore the "aged" EC10 and NOEC values were not further corrected or normalized towards specific soil properties. The results of the current research program also indicate that not all endpoints show a significant effect of soil properties on the bioavailability and toxicity of Pb. This is e.g. the case for plants (tomato and barley) and might be explained by phosphorus deficiency induced by precipitation of lead-phosphates after amendment of soluble Pb salts to a soil. For other endpoints (nitrification and *Eisenia fetida* reproduction), highly significant normalization models for the effect of soil properties on Pb toxicity were observed.

Because of the absence of normalization models, variation in toxicity data for the same endpoint across soils is not only caused by intra-species and inter-laboratory variation, but also by potential differences in bioavailability of lead among soils. Therefore, toxicity results for the same endpoint, but derived in different soils were not aggregated. Only if similar toxicity tests (i.e. using the same organism, endpoint, soil and test conditions) are reported in different source documents, a geometric mean value is calculated.

For many studies the Pb concentration of the control test soil (Cb) was not reported in the original studies. The effect assessment is however performed on total Pb concentrations in the soil, i.e. including the Pb concentration of the control test soil (total risk approach). A potential, conservative approach is to assume that the control soil does not contain Pb. This assumption may have little effect on this assessment for NOEC values well above typical ambient concentrations. However, for low NOEC values (expressed as added Pb) this assumption is critical (over-conservative). On the other hand, rejecting such nominal data without information on background soil Pb concentration would create a bias in the database towards larger NOEC values. Since a few selected NOEC values (added Pb) are below 100 mg Pb/kg (2-6 fold above typical ambient concentration), an estimate for ambient Pb concentrations in the test soil is required. First of all, it was assessed if the Pb concentration in the control test soil could be estimated from soil texture for all data where this concentration is missing. This approach was not successful and therefore no such estimates were used in the total risk approach. The second option, and which was finally adopted, was the following: the Cb is assumed zero, unless the nominal NOEC is near ambient concentrations (NOEC < 100 mg kg^{-1}) in which case a hypothetical small ambient concentration is added to estimate the total Pb concentration. The hypothetical small value is the 10th percentile of ambient Pb concentrations in soils away from point sources, i.e. 15 mg Pb/kg.

8. Construction of species sensitivity distribution

The available ecotoxicity database for effects of Pb to soil organisms is large, and therefore the use of the statistical extrapolation method via the construction of a species sensitivity distribution (SSD) is preferred for the terrestrial effects assessment. In total, high quality data are available for 22 species or microbial functional parameters. In contrast to the aquatic compartment, there is no strict guidance on the minimum taxonomic groups of soil organisms to be covered. The Pb database complies with the taxonomic group requirement developed in the MERAG document (ICMM, 2007):

- Higher plants (monocotyle)
- Higher plants (dicotyle)
- Arthropoda (e.g. Collembola)
- Oligochaeta (e.g. Eisenia)

- Another family in any order of oligochaete or any phylum not already represented
- Microbe-mediated processes (e.g. respiration, nitrification)

The distribution in toxicity thresholds for the effect of Pb on soil organisms is properly described by a log-normal distribution (Figure 2). From this SSD, the median 5th percentile, (HC5 or the hazardous concentrations at 95% protection level), is calculated using the ETX software program (Van Vlaardingen et al., 2004).

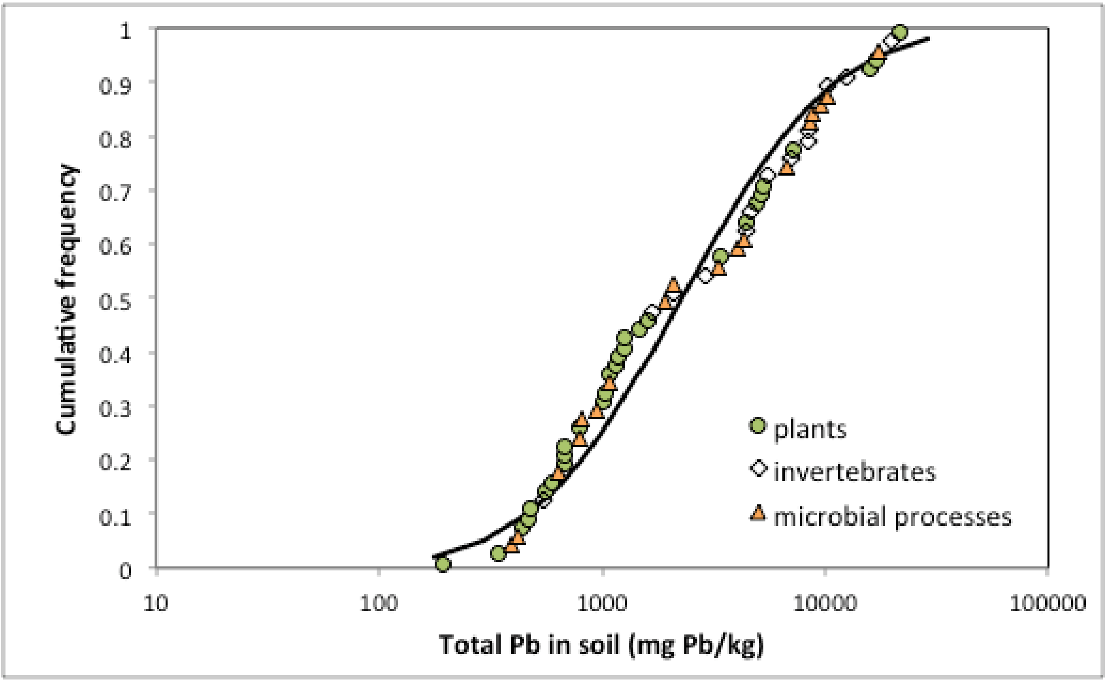

Figure 2: The cumulative frequency distribution of selected NOEC values accounting for differences in toxicity between Pb in spiked soils and field contaminated soils. Observed data and log-normal distribution curve for the dataset fitted on the data.

The variation in toxicity thresholds for a species or microbial process is generally larger than variation across the various species or processes covered. Therefore, it is concluded that including all individual NOEC and EC10 values selected in the SSD does not create a bias towards species or microbial endpoints with multiple data. The NOEC and EC10 values of the 3 trophic groups (higher plants, invertebrates and microbial processes) overlap in the frequency distribution, suggesting that the sensitivity range of these organisms is overlapping.

9. *PNEC derivation and uncertainty analysis*

The PNEC value is calculated based on the median HC5 value and an additional assessment factor (thus PNEC = HC5/AF), with an AF between 1 and 5, to be judged on a case-by-case basis. The following points were considered when determining the size of the assessment factor for the PNECsoil for Pb:

- The overall quality of the database and the end-points and soil types covered.
- The diversity and representativeness of the taxonomic groups covered by the database
- Statistical uncertainties around the 5th percentile estimate, e.g., reflected in the goodness-of-fit or the size of confidence interval around the 5th percentile

- Comparisons between field or mesocosm studies and the 5th percentile to evaluate the laboratory to field extrapolation

The overall quality of the database was considered optimal because chronic data are available for multiple endpoints for plant species, invertebrate species and microbial processes, and for a representative range of soil types. In total, 12 plant species, 4 invertebrates and 5 microbial processes are covered and all major taxonomic groups are included. The fit of the log-normal distribution to the Pb dataset used for the calculations of the 5th percentile values was accepted according to the Anderson-Darling goodness-of-fit test. This goodness-of-fit test highlights differences between the tail of the distribution (lower tail is region of interest) and the input data. The lowest individual aged NOEC or EC10 values are within a factor 2 of the HC5. The dataset contains many unbounded NOEC's, i.e. concentrations of Pb in the soil that were the highest tested and for which no toxic effect was observed. These unbounded NOEC's range from ≥ 560 to ≥7500 mg Pb/kg and are all well above the HC5 value. Also the available field data were unable to demonstrate toxicity below the HC5.
An assessment factor of 2 was selected as a conservative approach, resulting in a generic soil PNEC = median HC5 / 2 = 294 / 2 = 147 mg Pb/kg dry soil.

References

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Session B illustrative example: Addendum to Fact Sheet entitled “Data Compilation, Selection, and Derivation of PNEC Values for Nickel for the Marine Aquatic Compartment”

The Ni Marine fact sheet describes the fundamental steps that were taken during the Existing Substances Risk Assessment of Nickel in the determination of the PNECmarine value for Ni. Several detailed steps are not covered by the Fact Sheet, although they may be of relevance to the OECD Bioavailability of Metals workshop. The purpose of this addendum is to present these steps and to discuss their relevance in the PNECmarine determination process.

1. Assessment Factor approach for determining PNECmarine

Two ecotoxicological extrapolation methods are described in the TGD for deriving PNECmarine values: a) the assessment factor approach and b) the SSD approach. In the assessment factor approach the PNEC is calculated from the lowest acute LC50 or EC50 or, preferably, from the lowest chronic EC10 or NOEC, value using assessment factors that depend on the available toxicity data (TGD - Chapter 3). Given that chronic NOECs are available for >3 species the TGD requires that an assessment factor of 10 be applied to the lowest EC10 or NOEC value. In the case of the Ni marine database, the lowest EC10 value (22.5 µg/L) was reported for the polychaete, Neanthes arenaceodentata; therefore, the calculated PNECmarine using the assessment factor approach would be 2.3 µg/L.

During discussions at the Technical Committee for New and Existing Substances (TC NES), very little support was given to the use of the Assessment Factor approach. First, it was felt that sufficient data were available to apply the SSD. Specifically, chronic ecotoxicity data were available for 15 species. This is more than the minimum number of species suggested by the TGD for using the SSD, which is between 8 and 10 species. Also, the value of 2.3 µg Ni/L is low relative to ambient Ni concentrations in European coastal marine waters. Specifically, a PECregional value of 3.34 µg Ni/L (range: 0.26 – 3.75 µg/L) was determined in the EU RAR of Ni. Thus, using the Assessment Factor approach would result in conclusions of risk for the regional scale, and for 100% of operations that emit Ni to the coastal marine environment.

2. Pooling freshwater and marine ecotoxicity data for determining PNECmarine

The TGD also indicates that freshwater and marine ecotoxicity data can be pooled in the determination of the PNECmarine under certain circumstances.

The issue of pooling freshwater and marine ecotoxicity data for Ni was thoroughly discussed at the TC NES level, and it was agreed that the scientific evidence did not support the pooling of data. The major constraints to reject the use of freshwater data were:

- Pooling of freshwater and marine data will introduce a certain degree of uncertainty. One relevant element of uncertainty is the apparent difference in the mechanisms of Ni toxicity between freshwater and marine organisms. For example, marine teleost fish have completely different osmoregulatory strategies than freshwater teleosts. This means that the ionoregulatory mechanism of toxicity observed for freshwater fish does not occur in marine fish. This is validated by the observation that marine teleost fish are more than 10-times less sensitive to chronic Ni exposures than freshwater fish.
- Pooling would only be justified if it can be demonstrated that the species distributions for freshwater and marine chronic toxicity were statistically the same when compared on a free nickel ion basis.
- Abiotic factors of marine waters are outside the boundaries of the freshwater Ni BLMs, and therefore the BLMs could not be used to normalize the freshwater data to marine conditions. For example, concentrations of Ca^{2+} and Mg^{2+}, both of which have been shown to control Ni toxicity to freshwater organisms, are 50- and 173-times greater, respectively, in marine waters than in freshwaters.

The TC NES ultimately decided that the PNECmarine for Ni should be determined from the marine chronic Ni ecotoxicity database. The steps for populating the marine SSD and its subsequent analysis are discussed in the Ni Marine Fact Sheet.

Session B illustrative example: Data compilation, selection and derivation of PNEC values for the aquatic compartment: Zinc example

1. Regulatory context

Zinc metal (Zn) and five zinc compounds, i.e. zinc oxide (ZnO), zinc chloride ($ZnCl_2$), zinc sulphate ($ZnSO_4$), zinc phosphate ($Zn_3(PO4)_2$ and zinc distearate ($(C_{18}H_{35}O_2)_2Zn$) were prioritized under EU Regulation EEC/793/93 in September 1995. This implied that a full risk assessment (RA) for Zn needed to be carried out, following the guidelines detailed in the Technical Guidance Document (TGD) on Risk Assessment for New and Existing Substances (EU, 2003). The Netherlands acted as the Rapporteur country in this process, in close collaboration with the international zinc industry. The draft final European Union Risk Assessment Report (EU RAR) on zinc (environmental part) has become available in 2006 (EU, 2006) after thorough review by the Technical Committee on New and Existing Substances, which was comprised of technical representatives from the EU Member States. A final peer review was provided by the Scientific Committee on Health and Environmental Risks (SCHER) in November 2007 (Http://ec.europa.eu/health/ph_risk/committees/04_scher/docs/scher_o_069.pdf1.3). The RA was published in 2008 (ECB, 2008). It is noted that both the effects data set and the bioavailability correction were updated under the REACH registration process. This new evidence is not included in this assessment.

2. General process

Environmental risks are typically characterized in the risk assessment framework by considering the ratio between exposure concentrations and critical effect concentrations. In OECD countries, critical effect concentrations are based on Predicted No Effect Concentrations (PNEC), which are typically derived from long-term laboratory-based ecotoxicity tests using well-defined protocols on a limited number of species. Such information is usually retrieved from relevant literature and/or internationally recognized databases. Because the quality of the extracted data may vary considerably among individual source documents, it is important to evaluate all ecotoxicity data with regard to their adequacy for PNEC derivation and risk assessment. This document provides an example on how such evaluation for the freshwater aquatic compartment including criteria for acceptance (or rejection) of a study, was conducted for Zinc in the EU RA made by The Netherlands.

The following steps need to be accomplished in order to derive the critical effect concentrations (PNEC) of Zn for the freshwater compartment (Figure 1):

Figure 1: Stepwise approach used for the derivation of the freshwater PNEC value.

3. Example: Zinc Risk Assessment (ECB 2008)

3.1 Data compilation

The data on the toxicity of Zn to freshwater organisms were compiled from 3 main sources: open literature, internationally recognized databases, and industry sponsored research programs. A large dataset on the chronic ecotoxicity of Zn to freshwater organisms was compiled. All gathered data were further screened using the criteria as outlined in Section 3.2.

3.2 Data quality screening

Each individual ecotoxicity data point was screened for quality before incorporation in the zinc ecotoxicity database based on the following criteria:

- data were retained for the following groups of organisms: *algae, invertebrates and fish*;
- data covered the following relevant endpoints: *survival, growth, hatching and/or reproduction*;
- the *pH, hardness and dissolved organic carbon (DOC) of the exposure media should be reported.* In cases where one or more of these variables were not reported in the original publication, the values of the missing variables were estimated based on, e.g. (i) monitoring data (e.g., in cases where test media were natural waters), (ii) published test guidelines (e.g., in cases where only a reference to a standard medium published in a standard testing guideline was given), (iii) charge balance and ionic strength considerations, etc.
- the data were from studies conducted according to approved *international standard test guidelines*. However data from *non-standardized tests* were also assessed;
- only *long-term or chronic toxicity data*, involving endpoints that are realized over periods of several days to years depending on the organism, were used;
- the tests were performed according to standard operational procedures, with a *detailed description of the methods* employed during toxicity testing;

- both nominal and *measured zinc concentrations* in the test concentrations are retained[4];
- a *clear concentration-response* was observed;
- the toxicity tests were performed with *soluble zinc salts (e.g., $ZnCl_2$, $ZnSO_4$). Data derived from the direct testing of the poorly soluble compounds or the metals were rejected*;
- the toxicity test results reflected *dissolved zinc concentrations* and were expressed as *µg Zn/L*;
- ecotoxicity threshold values, *$L(E)C_{10}$* or *NOEC values*, were derived using *proper statistical methods*.

3.3. Data relevancy screening

Ecotoxicity data, especially those reported in the open literature, can be obtained under widely varying test conditions. Testing medium factors that were identified to significantly influence ecotoxicity data for zinc were a) background concentration in test medium and culture medium prior to testing: related to possible conditioning of organisms, see item "adaptation to natural background") and b) physico-chemical conditions influencing bioavailability (see corresponding item). To ensure that reported ecotoxicity data were relevant for the European environment, a number of data relevancy criteria were applied to the zinc dataset, in addition to the criteria for quality screening (3.2.):

- the range of the *physico-chemistry of the test media* (pH, hardness) were within the range of observed values in the EU, i.e. pH should be between 6 and 9, hardness between 24 and 250 mg/L $CaCO_3$;
- adaptation of the organisms to very low or very high zinc concentrations may influence the sensitivity to zinc. In that respect, if the dissolved *zinc concentration in the culture media* of the test organism was *below 1 µg/L*, the study was not retained. However, some studies conducted in natural waters at levels below 1 µg/l were maintained;

Only identified ecotoxicity data fulfilling the criteria mentioned under 3.2. and 3.3. were used for the freshwater PNEC derivation.

3.4. Database development

Applying the above mentioned quality and relevancy screening criteria to the identified ecotoxicity data resulted in the selection of an extensive high quality database on the chronic ecotoxicity of zinc to freshwater organisms. Indeed, the database comprised 19 different 'species means' from 131 individual high quality $L(E)C_{10}$/NOEC values (35 individual $L(E)C_{10}$/NOEC values for algae; 55 for invertebrates; 41 for fish), covering good distribution of trophic levels and species families.

3.5. Incorporation of Bioavailability (Data normalization)

There is extensive evidence demonstrating the importance of bioavailability altering water quality factors on the toxicity of zinc towards aquatic organisms. Indeed, site-specific geochemical conditions (e.g. pH, Hardness, Dissolved Organic Carbon) influence the degree to which organisms take up zinc, and exhibit effects from such uptake. From a risk assessment perspective, it is therefore critical to consider bioavailability, as geographically distinct eco-regions, watersheds and sites will often show distinctive geochemical characteristics therefore leading to different critical effects concentrations (PNECs).

In the EU zinc RA, bioavailability was taken into account at the exposure side of the risk equation[5]. The effects database was not normalised, but a generic PNEC was derived (which was proven to correspond to realistic worst case water physico-chemistry).

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[4] Nominal concentrations were checked to be corresponding to real test levels.

For reasons of completeness and illustration, the zinc effects data are normalized in this example towards the following physico-chemical conditions using a state-of-the-art bioavailability model (BLM; BIOMET 2011): pH: 7.9, Ca: 40.1 mg/L, DOC: 2.1 mg/L.

3.6. Data aggregation

Normalized high quality ecotoxicity data are grouped/aggregated in order to avoid over representation of ecotoxicological data from one particular species. The following major rules were used to aggregate data:

- If several chronic NOEC/L(E)C_{10} values based on the same toxicological endpoint, were available for a given species, the values were averaged by calculating the geometric mean, resulting in the "species mean" NOEC/L(E)C_{10}.
- If several (geometric mean) chronic NOEC/L(E)C_{10} values based on different toxicological endpoints were available for a given species, the lowest (geometric value) value was selected.

After the data aggregation step, only one ecotoxicity value (i.e. the geometric mean for the most sensitive endpoint) was assigned to a particular species.

An overview of the normalized species mean NOEC/L(E)C_{10} value for the most sensitive endpoint is provided in Table 1.

Table 1: Selected freshwater normalized species mean ecotoxicity data to Zn for the most sensitive endpoint

Taxonomic group	Species	Most sensitive endpoint	Species mean NOEC/L(E)C_{10} value (µg/L)
Algae	*Pseudokirchneriella subcapitata*	Growth rate	12.6
	Chlorella sp.	Growth rate	28.3
Rotifer	*Anuraeopsis fissa*	Population growth	116.2
	Brachionus rubens	Population growth	116.2
Molluscs	*Dreissena polymorpha*	Mortality	179.2
	Potamopyrgus jenkinsi	Growth	39.1
Cladocerans	*Ceriodaphnia dubia*	Reproduction	34.4
	Daphnia magna	Reproduction	151.7
	Daphnia longispina	Reproduction	205.4
Insects	*Ephoron virgo*	Mortality	438.2
Amphipods	*Hyalella azteca*	Mortality, reproduction	43.3
Fish	*Jordanella floridae*	Growth	74.9
	Phoxinus phoxinus	Mortality, growth	110.8
	Pimephales promelas	Reproduction	214.2
	Oncorhynchus mykiss	Mortality	291.9
	Salvelinus fontinalis	Hatching	1476.5
	Danio rerio	Hatching	1218.3
	Salmo trutta	Hatching	182.4
	Cottus bairdi	Mortality	137.2

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[5] Different as for other EU metal risk assessments (Cu, Ni, …) where ecotoxicity data sets and PNECs were normalized for bioavailability.

3.7 Calculation of HC5 using statistical extrapolation methods

3.7.1 Estimation of the HC_5 from the species sensitivity distribution (SSD)

When a large data set for different taxonomic groups is available, the PNEC can be calculated using a HC5 value following from a statistical extrapolation method.

Usually, the log-normal distribution (e.g. the methods of Wagner & Løkke (1991) and Aldenberg & Jaworska (2000)) and the log-logistic distribution (Aldenberg & Slob, 1993) are pragmatic choices because of their mathematical properties (methods exist that allow for most in-depth analysis of various uncertainties). However, several other SSD curve fitting functions could also used in order to derive SSDs. The probability distribution fitted to the datasets used for the calculations of the 5th percentile values have been checked with the Anderson-Darling (A/D) goodness-of-fit test for normality and with the Kolmogorov-Smirnov (K/S) test[6]. In the zinc RA, the log-normal distribution was used, since it was proven statistically significant.

Fitting the distributions to the normalized toxicity data as mentioned in Table 1 revealed that the logistic distribution on the log-transformed toxicity data was the best fitting distribution. It must be emphasized that both distributions, i.e. the logistic and the normal distributions, were accepted at the significance level of 0.05 according to both the A/D and K/S goodness-of-fit statistics. An overview of the best fitting (i.e. logistic SSD on the log-transformed toxicity data) and normal SSD on the log-transformed toxicity data is presented in Figure 2 and 3.

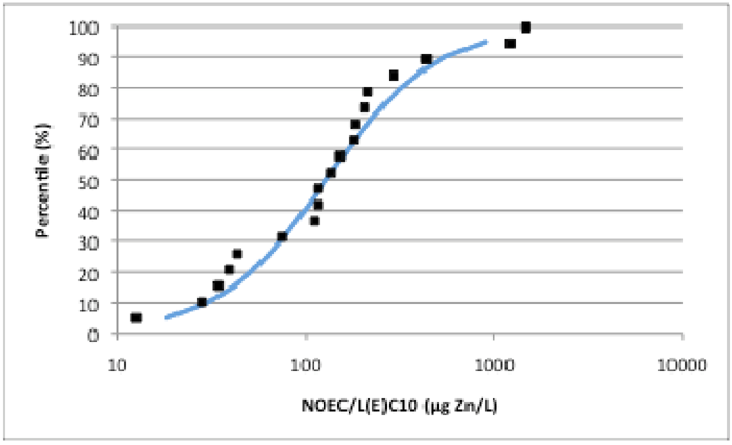

Figure 2: The cumulative frequency distributions of the normalized species mean NOEC/L(E)C_{10} values from the chronic Zn toxicity tests in the dataset of freshwater organisms. Geochemical parameters for this scenario were: pH = 7.9, Ca = 40.1 mg/L, DOC = 2.1 mg/L. Observed data and logistic distribution curve (best fitting curve) on the log-transformed toxicity data.

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[6] The Anderson-Darling goodness-of-fit test highlights differences between the tail of the distribution and the input data, while the Kolmogorov-Smirnov test focuses on differences in the middle of the distribution and is not very sensitive to discrepancies of fit in the tail of the distribution.

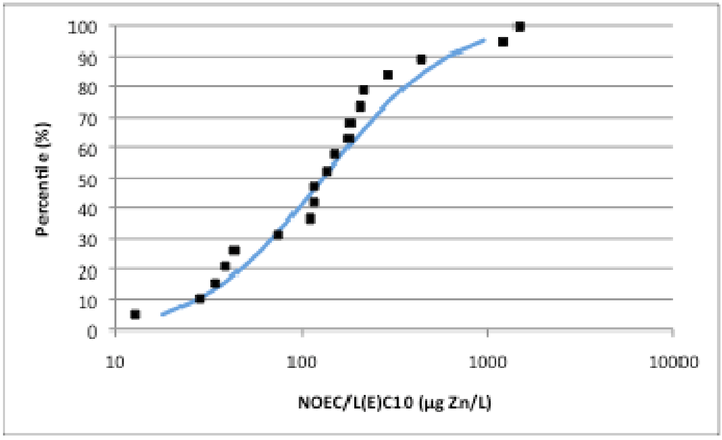

Figure 3: The cumulative frequency distributions of the normalized species mean NOEC/L(E)C_{10} values from the chronic Zn toxicity tests in the dataset of freshwater organisms. Geochemical parameters for this scenario were: pH = 7.9, Ca = 40.1 mg/L, DOC = 2.1 mg/L. Observed data and normal distribution curve on the log-transformed toxicity data.

From the SSD, a 5^{th} percentile value (at the median confidence interval) is further calculated (i.e. median HC_5) using the software program ETx for the normal distribution (Van Vlaardingen et al., 2004) and using the Aldenberg and Slob (1993) equation for the logistic SSD. The calculated median 5^{th} percentile values (i.e. HC_{5-50} value) for both distributions (with lower confidence limit) are shown in Table 2.

Table 2: Overview of the HC_{5-50} value (µg/L) with confidence interval

Distribution function	**HC_{5-50} value (µg/L)**	**Lower 95^{th} % confidence limit (µg/L)**
Logistic (best fitting)	17.1	6.2
Normal	17.3	7.0

3.7. Selection of an appropriate assessment factor (AF) and derivation of the PNEC

To account for uncertainty, an assessment factor (AF) may be applied to the median HC_5. In general, such AFs vary between 1 and 5, and are determined on a case-by-case basis. The freshwater PNEC would therefore be calculated as follows:

Freshwater PNEC = median HC_5/ AF

Based on the available chronic NOEC/L(E)C_{10} data, the following points are considered when determining the AF:

- The overall quality of the database and the end-points covered (e.g. are all the compiled data representative of "true" chronic exposure ?),
- The diversity of the taxonomic groups covered by the database (e.g., do the databases contain at a minimum organisms belonging to the following 8 taxonomic groups ?, as defined by the London workshop (2001); Table 3),

Table 3: Taxonomic group requirements according to the criteria developed at the London workshop (2001)

	Taxonomic groups
1	Fish (usually tested species like salmons, bluegill, channel catfish, etc.)
2	A second family in the phylum Chordata (fish, amphibian, etc.)
3	A crustacean (e.g. cladoceran, copepod, ostracod, isopod, amphipod, crayfish etc.)
4	An insect (e.g. mayfly, dragonfly, damselfly, stonefly, caddisfly, mosquito, midge, etc.)
5	A family in a phylum other than Arthropoda or Chordata (e.g. Rotifera, Annelida, Mollusca, etc.)
6	A family in any order of insect or any phylum not already represented
7	Algae
8	Higher plants

- The number of species (e.g., does the SSD cover at least 10 different L(E)C_{10}/NOECs, and preferably more than 15 ?),
- Use of bioavailability models and approach for bioavailability correction (e.g., do the bioavailability models allow the toxicity data for all species to be normalized?),
- Statistical extrapolation (e.g., how well does the SSD fit the toxicity data?)
- Comparisons between field and mesocosm studies and the PNEC (e.g., is the PNEC value protective for the effects observed in mesocosm/field studies?).It is clear that the definition of the AF is function of the information available.

4. REFERENCES

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Session B illustrative example: Sewage Treatment Plant assessments

Case study: Levels of Ag in Wastewater Effluents in England and Wales.

1. Regulatory context

Waste Water Treatment Plant (WWTP) are a main source of emissions for metals and therefore a key endpoint in many Risk Assessment systems including the EU-REACH system. WWTP environmental Risk Assessments are most often conducted on a modelled basis using effects info on and calculated/modelled emission scenarios. Effects data assessment for metals is handled by another fact sheet and examples. Modelled assumptions for WWTP's in risk assessment schemes (EUSES and others) are often of low relevance for metals and inorganics, given they are designed for (based on) organic treatment and reactions. Metals WWTP assessments are therefore often default assessments (e.g. WWTP size, and removal efficiency rate) requiring monitoring data sets for refinement to assess there impact on the local environment in a more precise way.

2. Data availability

In order to assess potential aquatic risks of silver there is a requirement for both effects and exposure data both aspects are shortly discussed below.

Effects data

A Predicted No Effect Concentration (PNEC) for dissolved silver of 40 ng l^{-1} has been derived by the Environment Agency of England and Wales[7]. This is based on chronic toxicity data for 16 aquatic species, including 3 fish, 7 invertebrates, 3 algae, and 3 plants. A species sensitivity distribution (Figure 1) was used to derive the PNEC from these data.

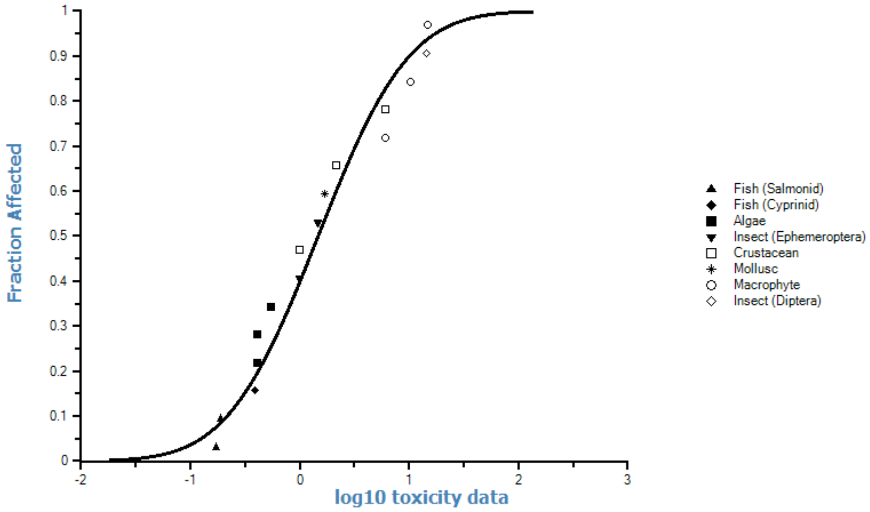

Figure 1 Species Sensitivity Distribution used for silver PNEC derivation.

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[7] Environment Agency. 2010. Proposed EQS for Water Framework Directive Annex VIII Substances: Silver. SC080021/R8la.Environment Agency, Bristol, UK.Internal report.

The PNEC was derived using an assessment factor of 3 on the hazardous concentration for 5% of species (HC5) resulting in a PNEC of 40 ng l^{-1} as dissolved silver.

Exposure data

There is a paucity of monitoring data for silver in freshwater environments in Europe and even more for STP emissions. There are several reasons for this, principally the very low levels of silver typically present in the aquatic environment and the requirement for commensurately low levels of detection (<100 ng l^{-1}), which are generally not routinely achieved in analytical laboratories.

Analysis of the levels of silver in both effluents and in the receiving environment provide valuable information for refinement of modelled emission scenarios for silver, and provides a valuable indication of how such modelled estimates compare to the actual situation.

Exposure monitoring in freshwaters indicates that exposures are generally very low[8].

The objective of this paper is to describe monitoring of the silver emissions from effluent discharges that provides context to this PNEC and to interpret these monitoring data in relation to European regulatory drivers such as REACH and the Water Framework Directive (WFD).

3. Methods

The monitoring programme was based on 86 sampling stations selected from the Environment Agency's network of river monitoring sites, and 17 effluent sampling stations. Sampling of wastewater treatment effluents was also based on an existing Environment Agency's monitoring programme. The effluent sampling programme comprised17 sites across England and Wales including 13 sewage treatment works final effluents, three landfill leachates and a minewater discharge. Dissolved silver (< 0.45 µm) and dissolved organic carbon (DOC) analyses were undertaken on each of the samples. DOC was included because of its importance in silver speciation and bioavailability. The effluent from each site was sampled on five occasions at monthly intervals from February 2010 to June 2010.

The concentration of dissolved silver was determined by Inductively Coupled Plasma Mass Spectrometry (ICP MS). An updated method for low level dissolved silver was developed specifically for this monitoring programme. The achieved limit of detection (LOD) was 2.2 ng l^{-1}, equivalent to a limit of quantification (LOQ) of 6.6 ng l^{-1} (calculated as three times the LOD). This method is compliant with the technical specification for chemical analysis set out by the European Commission for water quality monitoring (EC 2009), which requires a method to have an LOQ of equal to or below a value of 30% of the relevant environmental quality standard (i.e. 30% of 40 ng l^{-1} dissolved silver).

Where the concentration of dissolved silver in a sample was reported as below the limit of quantification (LOQ = 6.6 ng l^{-1}) a value of half the LOQ was substituted for the purposes of calculating arithmetic mean concentrations for each monitoring site. Where all silver results for a site were reported as below the limit of quantification, the mean value for the site was reported as "below the limit of quantification" (<LOQ), and a value of 3.3 ng l^{-1} (0.5 times the LOQ) has been used for figures and calculations.

4. Results

Mean dissolved silver concentrations at individual sites are shown in Figure 2, along with the standard deviation from repeated measurements. Figure 3 shows the cumulative frequency distribution of silver concentrations relative to the proposed PNEC value.

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[8] Peters, Simpson, Merrington, Rothenbacher, Sturdy 2011.Bull Environ Contam Toxicol. 86:637.

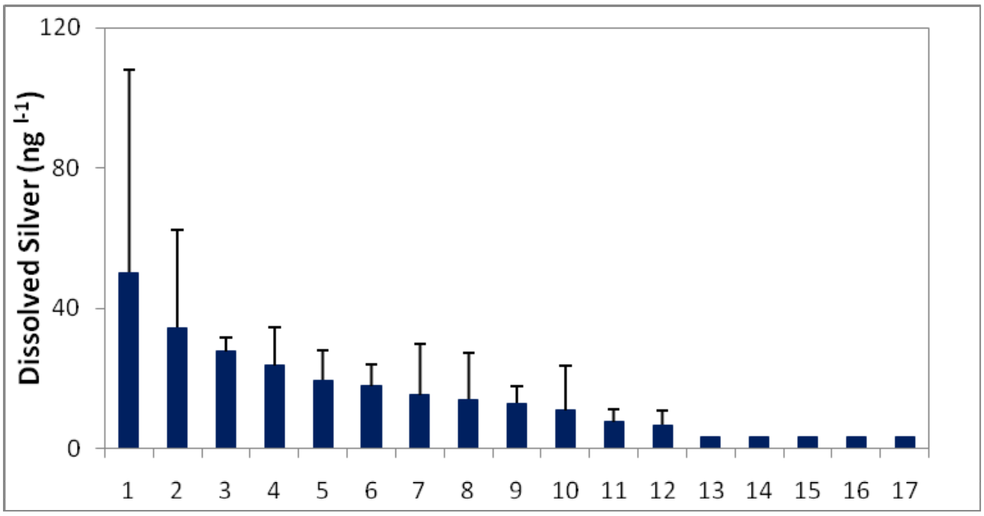

Figure 2 Mean dissolved silver concentrations (blue bars), and standard deviations (black lines), in 17 wastewater effluents

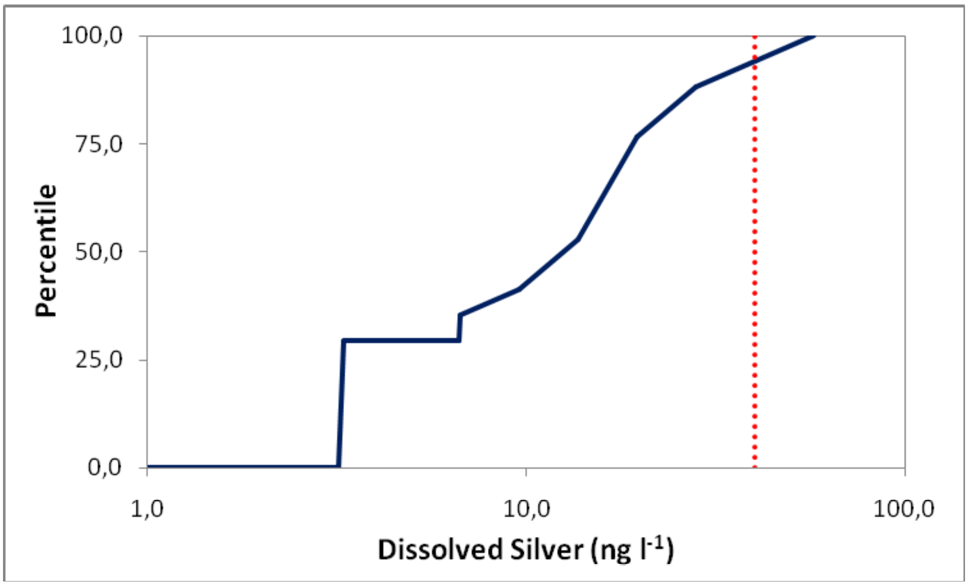

Figure 3 Cumulative frequency distribution of dissolved silver concentrations in 17 wastewater effluents. The vertical dotted line indicates the proposed PNEC for silver in the receiving waters

No natural background correction was conducted for dissolved Ag given natural background was assumed to be below the LOQ in all cases.

Silver concentrations in wastewater effluents can be highly variable, although in the vast majority of cases the silver levels in the effluents at the point of discharge are below the proposed PNEC for the receiving waters. Dilution of the effluents into the receiving waters will cause a further reduction in the silver levels.The variability ofeffluent concentrations may be due to variability in the influent concentrations of silver, and variation in the degree of retention of silver in sludge.

Dissolved organic carbon (DOC) concentrations were also monitored in the wastewater effluents, and showed no correlation with dissolved silver concentrations (Figure 4).

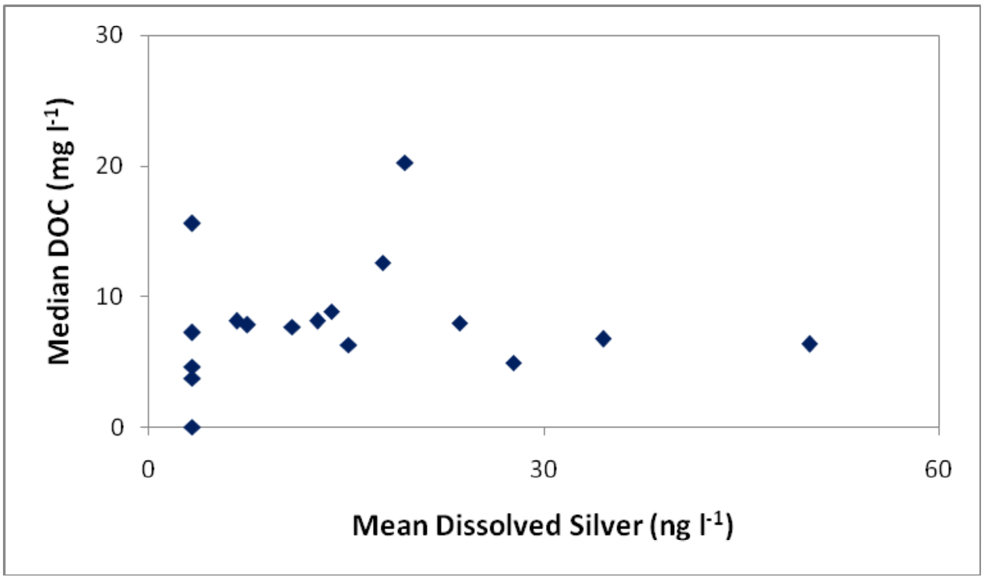

Figure 4 Dissolved silver and DOC concentrations in wastewater effluents

The maximum mean concentration of dissolved silver measured in sewage treatment effluents was 50.2 ng l-1 (Standard Deviation = 57.9 ng l^{-1}, number of samples = 5. The 90th percentile of mean dissolved silver concentration in treated sewage effluents was 33.2 ng l^{-1}. It should be noted that these measurements are from the effluents and do not take into account of the mixing zone and any dilution in the receiving environment. Dissolved silver was reported as below the limit of quantification in all of the landfill leachates sampled and in the single mine water discharge.

5. Discussion

Based on default assumptions in models like EUSES, a potential risk would be expected for most sewage treatment works, especially those receiving consented discharges from silver producers or downstream users, particularly as the discharges from some treatment works in England and Wales have low dilution rates into the receiving waters. However, the data generated in this exercise demonstrate that this is not the case. Also, an accompanying surface water survey[1]indicative for a regional risk assessment level, showed that receiving waters across England and Wales showed high levels of compliance with the Environment Agency's proposed PNEC for silver of 40 ng l^{-1}.

Nevertheless, the coverage of effluent sites in this monitoring programme was relatively limited and more data is needed, as well as data on silver retention rates and partitioning within different types of wastewater treatment plants. This information would give an indication of potential effluent maxima for silver and enable verification of modelled estimates of potential silver release and subsequent aquatic exposure.

The fate and behaviour of silver in the aquatic environment continues to receive a great deal of academic and regulatory interest. This study has clearly shown that in order to provide data to support evidence-based regulatory decisions it is necessary collect and analyse appropriate data using suitable methods with adequate sensitivity to overrule modelled risk estimates for this metal. The data presented in this programme currently represent a relatively comprehensive data set for silver in European wastewaters.

Chromium reducible sulphide (CRS), a very strong Ag-complexing agent, might commonly be present in excess of the relatively low Ag levels reported above. If so, it could be expected to complex silver and, possibly, mitigate any potential for causing adverse effects. Further work is under way to investigate this possibility.

6. Conclusions

Silver environmental impact assessments based on modelled assumptions using existing regulatory tools (e.g. EUSES) provide overestimates of the potential risk. This is principally due to the fact that the model assumptions are based on approaches for organic chemicals. Silver monitoring in the effluents of WWTPs was therefore required and conducted for 17 wastewater discharges. Most emissions were below the PNEC established for the receiving waters at the point of discharge. Silver was not detectable in 30% of the wastewater effluents. Risks due to the presence of silver in receiving waters are extremely unlikely due to the low levels of silver present in the wastewater effluents. This data provides a valuable comparison against the estimates of silver emissions that have previously been used to assess the potential exposure levels of silver in effluents. A key challenge included the application of appropriate detection levels for silver in these matrices.

ANNEX 6

SESSION C: BIOACCUMULATION AND BIOCONCENTRATION

→ Concept paper on bioaccumulation potential in aquatic biota and references for further reading
→ Concept paper on secondary poisoning assessment for metals and references for further reading
→ Illustrative example:
    - Bioaccumulation of cobalt

Bioaccumulation Assessment for metals

Background paper for OECD Workshop on *Metals Specificities in Environmental Hazard Assessment*
Paris, September 7-8, 2011

Note: *These papers were prepared by industry and reviewed by the workshop steering committee to provide some background on concepts associated with metals-specificities in environmental hazard assessment. The papers do not represent a consensus view of the OECD on how to conduct metals environmental assessment, but they should serve as a basis for workshop participants to understand the concepts proposed and already applied in some OECD countries*

Introduction

Bioaccumulation potential in aquatic biota is typically expressed using ratios of chemical concentrations in organism tissue (typically whole body) relative to chemical exposure concentrations (water or water and food), and result in bioconcentration factors (BCFs) and/or bioaccumulation factors (BAFs), respectively.

BCFs and BAFs[9] have been widely used as the criterion for assessing the extent of bioaccumulation in tissue in the context of identifying substances that have specific hazard properties to the aquatic environment, as well as a predictor for secondary poisoning for organic substances.

BCF/BAF criteria were originally developed for non-polar organic compounds as surrogates for long term / chronic toxicity in hazard assessment schemes and for potential to transfer through the food chain; this has been shown repeatedly to be inappropriate for metals and inorganic substances. In a broader context, bioaccumulation data are widely used in effects/risk assessments of various types. BCFs and BAFs for metals, unlike organic substances, find their greatest utility in site-specific risk assessments.

Literature Reviews and Resulting Conclusions

Past reviews of metal BCFs for aquatic biota (water-only exposures) have shown that BCFs are often highly variable between organisms and most often inversely related to exposure concentration. Natural aquatic food webs are rarely sufficiently understood to properly evaluate exact predator-prey relationships, however, results indicate that field BAFs, like laboratory BCFs, tend to be significantly ($p \leq 0.05$) inversely related to exposure concentration. Bioaccumulation factors are frequently 100 – 1,000 times larger than BCFs for the same metal and species. This difference is attributed to both lower exposure levels in the field and inclusion of the dietary exposure route and appears to be universal even including metalloids such as mercury and selenium. BCFs/BAFs from field collections are often in the range of 1000 to >100,000 for most metals including essential metals.

Trophic transfer factors for the metals reviewed, including selenium and methyl mercury, were also observed to be inversely related to exposure concentration. These inverse relationships have important implications for environmental assessments (e.g., hazard identification and tissue residue-based assessments like water quality criteria) and for the use of metal bioaccumulation data in site-specific environmental evaluations, such as ecological and human health risk assessments. Data reviews indicate that for metals and metal substances, unlike organic substances, no one BCF or BAF can be used to express bioaccumulation hazard.

Recent literature reviews [1,2,3,4,5,6,7] conclude that BCF/BAF criteria (i.e., values greater than 1000 or 5000) are inappropriate for the hazard assessment of metals. Furthermore, using BCF and BAF data leads to conclusions that are inconsistent with the toxicological data as values are highest (indicating hazard) at low exposure concentrations and are lowest (indicating no hazard) at high exposure concentrations where impacts are likely. This is the exact opposite of the intended use of the “factor” concept.

BCFs/BAFs do not distinguish between essential mineral nutrient, normal background metal bioaccumulation, the adaptive capabilities of animals to vary uptake and elimination within the spectrum of exposure regimes, nor the specific ability to sequester, detoxify and store internalized metal from metal uptake that results in adverse effect. A recent SETAC workshop [4] concluded: “*In the meantime, and for the foreseeable future, whenever possible, assessments of chronic toxicity should use chronic toxicity data (which are available for many metals) with an emphasis on studies that account for dietary exposures rather than a surrogate such as bioaccumulation*.”

The question has been raised repeatedly over the past decade, “*how do we use BCFs/BAFs for metals to assess hazard?*” The simple answer is - that it is with the present knowledge not possible. This approach, designed for organic substances, will not work as such for metals and inorganic substances. There is “no one value” that by itself that denotes a hazard. Large values indicate extremely clean environments and

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[9] Bioconcentration factors (BCF’s) reflect whole body measurement of a chemical in relation to the water exposure concentration in an experimental setting where diet was not considered. BAFs are a measure of whole-body concentration of chemical in relation to the water exposure level where dietary and water exposure occurred simultaneously, i.e., usually in a natural environment

for essential elements could indicate deficient status. Data are emerging, that in time, may allow for the use of target-organ tissue concentrations (not BCFS/BAFs) that constitute a hazard.

The SETAC Pellston Workshop [4] also concluded that the best approach for assessing the hazard of metal substances in aquatic environments is to use an integrated approach that allows for consideration of fate parameters that are specific to metals, as well as toxicity data. A unit world model (UWM) approach was proposed for both hazard and risk assessments. This model approach embodies the development of a methodology for evaluating metals in a unified framework in which hazard/risk decisions are based on meaningful simulation of environmental fate, bioaccumulation and toxicity processes. TICKET-UWM has been developed as a screening-level model for metals in lakes and is based on appropriate model descriptions for chemical speciation and other governing processes affecting metal transport and bioavailability [8]. The model is intended to be used for conducting hazard assessments, preliminary site risk assessments and in developing integrated rankings of metals based on, chemical behavior, bioaccumulation at the toxic site of action and toxicity.

Alternative initial guidance was also developed under the EU Water Framework Directive – guidance for deriving environmental quality standards. It was concluded/confirmed that BCF for metals cannot be used as a surrogate for secondary poisoning potential. Instead, a case-by-case weight of evidence evaluation of the possibility of significant dietary toxicity as a trigger for secondary poisoning is proposed based on information on: metal mode of action and homeostatic (internal regulation) controls, essentiality, potential for biomagnification (BMF), and major toxicities i.e. whether main risks are through direct toxicity to pelagic organisms or secondary poisoning. With regards to the potential for secondary poisoning the assessment of the mode of toxic action in both prey and predator is a key consideration. If there is no evidence of biomagnification (i.e. BMF<1) and no specific toxicity in birds and mammals compared to fish (on a dose-based approach), the water quality standard should be protective for birds and mammals as well as pelagic organisms.

References for further reading:

- Executive summaries of reference 3, 4, 6 and 9 below

TIER 3: Further interesting background information on the fact sheet:

1. Adams, W.J., Conard, B., Ethier, G., Brix, K.V., Paquin, P.R., Di Toro, D.M., 2000. The challenges of hazard identification and classification of insoluble metals and metal substances for the aquatic environment. Human Ecol Risk Assess 6(6), 1019-1038.
2. Chapman, P.M., F. Wang. 2000. Issues in ecological risk assessment of inorganic metal substances for the aquatic environment. Human Ecol Risk Assess 6:1019-1038.
3. McGeer, J.C., Brix, K.V., Skeaff, J.M., DeForest, D.K., Brigham, S.I., Adams, W.J., Green, A., 2003. Inverse relationship between bioconcentration factor and exposure concentration for metals: Implications for hazard assessment of metals in the aquatic environment. Environ Toxicol Chem 22(5): 1017-1037.
4. Adams W.J., P.M. Chapman. 2005. Assessing the hazard of metals and inorganic metal substances in aquatic and terrestrial systems: Summary of a SETAC Pellston Workshop. Pensacola (FL): Society of Environ Toxicol and Chem (SETAC).
5. Adams, W.J., Chapman, P.M., 2006. Assessing the hazards of metals and inorganic metal substances in aquatic and terrestrial systems, SETAC Press, Pensacola, FL 32501.
6. DeForest, D. K., K.V. Brix, W.J. Adams, 2007. Assessing metal bioaccumulation in aquatic environments: The inverse relationship between bioaccumulation factors, trophic transfer factors and exposure concentration, Aquatic Toxicology 84 (2007) 236–246.

7. United States Environmental Protection Agency (USEPA). 2007. Framework for metal risk assessment. EPA 120/R-07/001, Washington, D.C. [http://www.epa.gov/osa/metalsframework/].

8. Farley, K.J., R.F. Carbonaro, C.J. Fanelli, R. Costanzo, K. Rader, D.M. Di Toro. TICKET-UWM: A coupled kinetic equilibrium and transport screening model for metals in lakes. Environ Toxicol Chem 30, 2011.

9. Common Implementation Strategy for the Water Framework Directive (2000/60/EC) - WG E(9) –10-03e – TGD-EQS (final draft). Technical guidance for deriving Environmental Quality Standards. Available from: http://www.oekotoxzentrum.ch/expertenservice/qualitaetskriterien/doc/TGD-EQS_finaldraft.pdf. SCHER opinion on the guidance available from: http://ec.europa.eu/health/scientific_committees/environmental_risks/docs/scher_o_127.pdf

Secondary poisoning assessment for metals

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Background

The need for a separate secondary poisoning assessment focusing on higher members of the food chain hypothesize either that higher trophic level organisms are more sensitive than lower trophic level organisms or that the tissue concentrations of the accumulated substance may increase at higher trophic levels (i.e., the substance biomagnifies). There are insufficient toxicity data to support or refute whether higher trophic level organisms are intrinsically more sensitive to metals than lower trophic organisms. Contrary as for organometal forms, most inorganic metal substances lack evidence of biomagnification. To the contrary, some studies suggest that metals like e.g. Ni exhibit biodilution, i.e., decreases in concentration with increasing levels of the food chain (Campbell et al. 2005). Regardless, dietary metal exposure can be an important pathway for wildlife, irrespective of their trophic position (Fairbrother et al., 2007; McLaughlin et al.,2010).

Approach

Guidance for performing secondary poisoning assessments is e.g. offered in REACH, and Guidance Documents. The direct application of this guidance originally designed for organics, to metals therefore requires refinement. The generic approaches described in the guidance, include a default assumption for the evaluation of secondary poisoning to a generic consumer organism of 100% bioavailability of substances following dietborne exposure. This leads to unrealistic conclusions for metals (e.g., ambient background metal concentrations posing potential risk when modeled in a food chain). Accordingly, a tiered approach was developed based on increasing levels of refinement to improve the environmental relevance of the Predicted Environmental Concentrations (PECs) and Predicted No Effects Concentrations (PNECs) (Figure 1 below).

The four tiers of the Tiered Approach are as follows:

Tier 1: Default Assessment

- PNEC-oral values are derived from reference NOAELs (from long-term studies) without species-specific modifications;
- bioavailability of dietborne metal is assumed to be 100%;
- diets are composed of one food source with a single metal concentration.

Tier 2: Derivation of Species-specific PNECoral values based on allometric parameters

- PNEC-oral values based on the ingestion rate-to-body weight ratios of relevant consumer organisms are developed.

- Adjustment of the assessment Factor (AF) in deriving the PNEC by accounting for quantifiable inter-species differences in toxicologically relevant characteristics (e.g., food ingestion rate-to-body weights ratios) between the test organism and the relevant consumer organism.

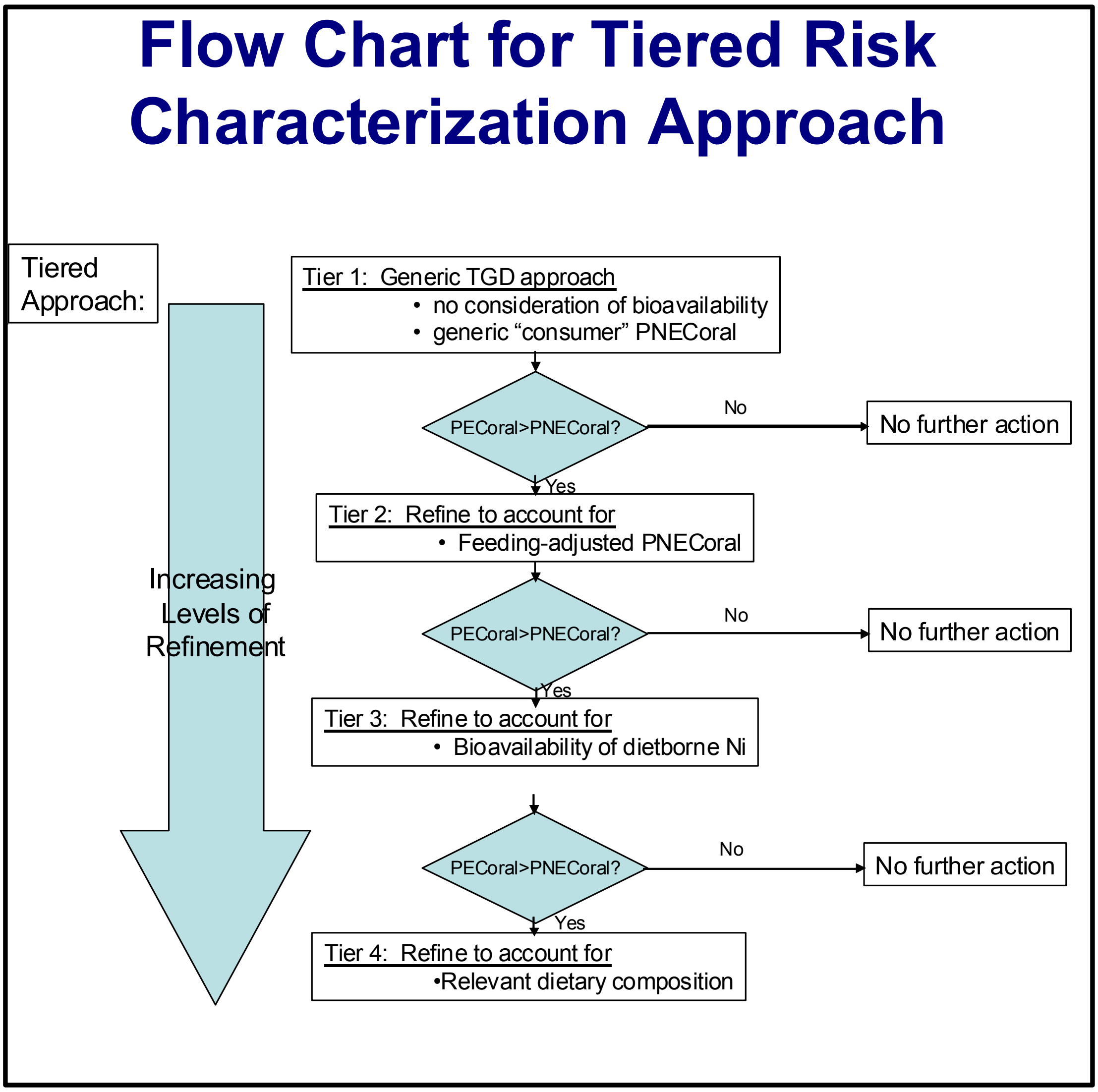

Figure 1: Flowchart for tiered risk characterization approach

Tier 3: Correction for bioavailability of the dietborne fraction

Bioavailability of dietborne metal is incorporated into the assessment. Relative absorption factors (RAFs) are derived from the literature for different relevant dietary components in the mammalian food chain, including a soil RAF and a comprehensive RAF used for other dietary components.

Tier 4: Correction for diet composition

A more realistic dietary composition is used instead of assuming that the predator consumes only one food source containing the metal in question. For example, a default assumption that a diet of a mammal or a bird is comprised entirely of earthworms will maximize the estimated metal dose because soil in the earthworm gut contributes more to the metal dose than will metal in earthworm tissue. Basing the exposure on distributions of diets observed for the identified consumer organism is the next level refinement step that can be applied.

Conclusion:

Generic approaches for assessments of risk of secondary poisoning for metals are often not suitable, as the default assumptions in these approaches often result in conclusions of risk at natural background concentrations of metals in relevant media, e.g., water and soil. To this end, a tiered approach is recommended, in which sequential refinements are made to the generic approach. The most important variables where refinement should be considered include the AF of 30 applied to NOECs when deriving the PNECs; the assumption of equivalent metal bioavailability in natural dietary doses versus the doses used to derive the NOECs; and the assumption that the diet consists of 100 percent of the prey organism with the highest metal concentration. When used in a tiered assessment, these refinements focus attention to those conditions where the risk of secondary poisoning from metals is of genuine concern.

References for further reading:

- Ni EU RAR section on secondary poisoning, http://www.mst.dk/NR/rdonlyres/AEE6FA90-B26C-4D39-BA59-B88C35D2E2F6/0/081107NiENVRiskAssessment_Section32_Effects.pdf, from page255 onwards
- *DeForest DK, CE Schlekat, KV Brix, A Fairbrother. 2011. Secondary Poisoning Risk Assessment of Terrestrial Birds and Mammals Exposed to Nickel. Integrated Environmental Assessment and Management.* Accepted
- Campbell LM, RJ Norstrom, KA Hobson, DCG Muir, S Backus, AT Fisk. 2005. Mercury and other trace elements in a pelagic Arctic marine food web (Northwater Polynya, Baffin Bay), Science of the Total Environment 351–352 : 247–263
- Fairbrother A, R. Wenstel, S. Sappington, W. Wood. 2007. Framework for Metals Risk Assessment. Ecotox. Environ. Safe, 68: 145-227
- McLaughlin MJ, S.Lofts, M.Warne, MJB Amorim, A.Fairbrother, R.Lanno, W.Hendershot, CE Schlekat, Y. Ma, GJ Paton, G.J. 2010.Derivation of ecologically based soil standards for trace elements.Soil Quality Standards, Eds. G. Merrington and I. Schoeters, SETAC Press, Pensacola, Florida *(in press).*

Session C Illustrative example: Cobalt assessment:

See: [http://www.ec.gc.ca/ese-ees/default.asp?lang=En&n=8E18277B-1]

Annex 1: Application of tiered approach to the freshwater mammalian food chain secondary poisoning assessment of Ni

Table 1 presents the results of risk characterizations for the first three tiers of the approach shown in Fig. 1. In Tier 1, which is considered the most cautious scenario, PEC-regional values calculated for 6 different European Freshwater types covering > 90 % of the variability of European water systems were compared to the generic PNEC-oral of 0.73 mg kg^{-1} assuming an RAF of 1 (that is, assuming that 100% of Ni associated with the diet of the consumer organism is absorbed). . The PEC-regional ratios range from 1.4 to 2.9 in three of the scenarios and are less than 1.0 in the remaining three scenarios. In Tier 2, which uses a PNEC-oral value adjusted for ingestion rate-to-body weight ratio of the European otter, all ratios are less than 1.0. Tier 3 shows the additional impact of applying bioavailability normalization, where the application of a Ni-specific RAF is used. All ratios are less than ≤0.02 if the RAF is also incorporated.

Tier	**PNECoral** [1]	**RAF** [2]	**Type**	**PECoral** [3]	**PECoral/ PNECoral Ratio**
1	Generic = 0.73 mg kg^{-1}	1	1. Small Stream	PECregional = 2.1 mg kg^{-1}	**2.92**
			2. Medium River – High bioavailability	PECregional = 1.0 mg kg^{-1}	**1.41**
			3. Medium River – Moderate bioavailability	PECregional = 1.4 mg kg^{-1}	**1.89**
			4. Large River	PECregional = 0.5 mg kg^{-1}	0.67
			5. Mediterranean River	PECregional = 0.7 mg kg^{-1}	0.92
			6. Neutral acid lake	PECregional = 0.2 mg kg^{-1}	0.26
2	Otter = 2.3 mg kg^{-1}	1	1. Small Stream	PECregional = 2.1 mg kg^{-1}	0.93
			2. Medium River – High bioavailability	PECregional = 1.0 mg kg^{-1}	0.45
			3. Medium River – Moderate bioavailability	PECregional = 1.4 mg kg^{-1}	0.6
			4. Large River	PECregional = 0.5 mg kg^{-1}	0.21
			5. Mediterranean River	PECregional = 0.7 mg kg^{-1}	0.29
			6. Neutral acid lake	PECregional = 0.2 mg kg^{-1}	0.08
3	Otter = 2.3 mg kg^{-1}	0.025	1. Small Stream	PECregional = 2.1 mg kg^{-1}	0.02
			2. Medium River – High bioavailability	PECregional = 1.0 mg kg^{-1}	0.01
			3. Medium River – Moderate bioavailability	PECregional = 1.4 mg kg^{-1}	0.01
			4. Large River	PECregional = 0.5 mg kg^{-1}	0.01
			5. Mediterranean River	PECregional = 0.7 mg kg^{-1}	0.01
			6. Neutral acid lake	PECregional = 0.2 mg kg^{-1}	0.00