

DRAFT RSET ISSUE PAPER #17 – Tissue Bioaccumulation Triggers and Proposed Methods of Protection of Fish/ESA Species

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QUESTION/ISSUE: How should tissue bioaccumulation triggers be developed to protect fish and ESA species from exposure to contaminants that bioaccumulate?

DISCUSSION:

Background: Bioaccumulation studies are an element of Tier 3 evaluations of dredged material under existing regional and national dredging evaluation guidance. Unfortunately, there are no generally applicable tissue residue guidelines currently available that can be used to interpret the ecological implications of bioaccumulation study results with aquatic species. The Regional Sediment Evaluation Team (RSET) has identified development of tissue residue guidelines, termed tissue bioaccumulation triggers (BTs) in this paper, for protection of fish species as a high priority during its development of a regional sediment evaluation framework. The toxicity of bioaccumulated chemicals to aquatic biota can be evaluated with a tissue residue approach (TRA) toxicity assessment. The results of this assessment can be used to generate tissue bioaccumulation triggers (tissue BTs). This issue paper addresses the following questions:

- Is it feasible to develop tissue bioaccumulation triggers for protection of aquatic life?
- For what chemicals can tissue bioaccumulation triggers be developed?
- What are the appropriate toxicological endpoints to evaluate during tissue BT development?
- How can tissue bioaccumulation triggers be developed?
- Are separate tissue bioaccumulation triggers required for ESA listed species?

Summary of Issue Paper Conclusions

The conclusions of this issue paper are:

- Yes, it is feasible to develop tissue BTs. Identified technical concerns and issues that will have to be resolved before tissue BTs can be developed include limited residue-effects data availability, the computational methodology to be used to derive tissue BTs, the data quality required of information used to derive BTs, the quantity of data needed before BTs can be developed for individual chemicals, and the toxicological endpoints to be incorporated into the BTs
- Tissue BTs can be developed for most chemicals. Exceptions exist for compounds that do not appreciably bioaccumulate in tissues but are nevertheless toxic; whose mode of action do not require bioaccumulation to elicit toxicity, such as contact

herbicides; and compounds rapidly metabolized to other chemicals that are either substantially more or less toxic than the parent compound, such as many PAH compounds

- At a minimum, tissue BTs should be generally applicable to all fish species, and protective from adverse effects on survival, reproduction and growth. Other sublethal endpoints that may be considered during tissue BT development include contaminant effects on populations, behavior, immunosuppression, physiology, morphology and biochemistry. Additionally, the same BTs derived for fish will generally be applicable to all aquatic invertebrate species as well.
- Two primary methods exist for developing tissue BTs: Species sensitivity distributions and bioaccumulation modeling, with several variations and computational methodologies available for each of the two primary methods. While using measured residue-effects literature to develop tissue BTs is preferred, it must be recognized that sufficient literature to develop SSDs is available for only a limited number of chemicals. For chemicals without sufficient residue-effects literature, tissue BT development will have to be accomplished using bioaccumulation models.
- Available data to date indicate that separate tissue BTs are not required for ESA listed species, because as a group, ESA listed species appear to be neither more nor less sensitive to contaminants than non-ESA listed species. Exceptions undoubtedly exist for some species-chemical combinations

Introduction

A fundamental principle of toxicology is the dose-response relationship: the proportionality of the chemical concentration in tissue at the site of toxic action (the dose) to the toxic response. The chemical concentrations in exposure media (water, sediment, diet) commonly used as surrogates for the actual dose of toxic chemical have many limitations when used during toxicity assessments with aquatic biota, some of which are listed below.

- The bioavailable and toxicologically active fraction of the total exposure media chemical concentration may not be known
- It does not consider multiple uptake routes of chemicals
- Intermittent, pulsed or variable exposures cannot be readily assessed
- Chemical mixture toxicity cannot be easily assessed
- Exposure duration (i.e. bioaccumulation kinetics) effects on toxicity may not be well defined
- Metabolic transformations, which reduce or enhance parent compound toxicity, are not considered
- Animal behavior such as seasonal migration or toxicant avoidance is not considered
- Acclimation to toxicants can yield differential sensitivity to exposure media concentrations under different exposure regimes
- Analytical chemistry limitations (e.g. non-detectable concentrations in water) mean that the exposure concentration is often unknown

By associating the toxic response of aquatic biota with the tissue concentration of the chemical causing the effect, the above complicating factors can largely be eliminated.

Toxic effects can then be directly expressed as a function of tissue residues. Elimination or minimization of the above confounding factors is the great advantage of using tissue residues to evaluate toxicity of environmental contaminants compared to evaluating toxicity using chemical concentrations in water, sediment or diet.

The main precept of the TRA is that it generates critical body residues (CBRs), such as LR_{50S}, LR_{10S}, or LOERs for a given toxicant that exhibit relatively low variability among species. The advantages of a CBR statistic used as a tissue BT to interpret bioaccumulation test results are obvious, but worth explanation. First and foremost, the reduced variability in the biological response compared to exposure media concentrations associated with toxicity (e.g. LC₅₀) is highly desirable for generating tissue BTs that are protective of all species. Additionally, CBRs are based on causal relationships between the whole body tissue concentrations and the biological response, which allows the approach to be highly technically defensible. Other advantages of a TRA approach in deriving tissue BTs are given in the bulleted list presented in the introduction to this issue paper.

In many cases the BT value developed for fish will also be applicable to aquatic invertebrates. For many contaminants, the CBRs will be the same for fish and invertebrates and data from a number of taxa will be used to generate the BTs. Not all CBRs will have broad taxonomic application and exceptions will occur (e.g., dioxins). Each compound or class of compounds will be evaluated for its ability to represent toxicity for a wide range of species.

Protocols for the Development of Tissue Bioaccumulation Triggers (BTs)

At least two methods by which tissue BTs can be developed have been identified.

1. Species sensitivity distributions (SSDs) of existing tissue residue - effects literature
2. Bioaccumulation modeling using existing water quality criteria as an input into the model

Tissue BTs can be developed for some chemicals using existing residue-effects information in the technical literature. For chemicals without sufficient residue-effects information in the literature, a bioaccumulation model would need to be used to develop tissue BTs, with a higher level of uncertainty of the usefulness of the guidelines. However, there are data quality, data availability and computational issues that need to be addressed before a decision can be made regarding how to go forward with the development of tissue BTs.

One issue of concern that applies to both the bioaccumulation modeling and SSD generation approaches is selection of the toxicological endpoints to incorporate into BT derivation. Consistency with EPA's current methodology for deriving ambient water quality criteria (Stephan et al. 1985) would dictate consideration of only contaminant effects on survival, reproduction and growth. The RSET may wish to consider other endpoints when developing tissue BTs. Possible examples of additional endpoints to consider include contaminant effects on behavior, physiology, morphology and biochemistry. Evaluation of these non-traditional endpoints in BT development may be of particular importance for fish

species such as salmonids, where contaminant impacts on swimming behavior or olfactory ability may have significant adverse effects on the ability of the fish to return to their natal streams to spawn.

The strengths and limitations of each of the two primary tissue BT development methods are described below, as are some of the available options within the two approaches.

Species Sensitivity Distribution Approach

The species sensitivity distribution approach uses existing toxicological literature in a manner that is very similar to the existing EPA methodology (Stephan et al. 1985) used to develop ambient water quality criteria. It is the approach used in Europe to derive water quality criteria, and has also been used to derive sediment quality criteria such as the Long and Morgan (1991) effects range-low (ER-L) values and Washington's sediment management standards. As used in water quality criteria development, the SSD is generated from laboratory toxicity data. The Environmental Residue Effects Database (ERED) (Bridges and Lutz 1999) and Jarvinen and Ankley (1999) are the two primary sources of residue-effects information that could be used to develop SSDs. Given its consistency with other criteria development methodologies, use of the SSD approach during tissue BT development is preferred if the toxicological data are available.

The toxicity datasets used to develop water quality criteria generally employ a statistically derived description of the concentration-response curve, such as an LC₅₀ or EC₂₀. By contrast, much of the available tissue residue literature contains no description of the magnitude of the observed effect, or of the proportion of species responding to a given tissue residue. These endpoints, termed the lowest unquantified effect dose (LUED) may be of limited utility in the derivation of tissue BTs. If it is assumed that LUED values are analogous to lowest observed effect residues (LOERs), a species sensitivity distribution could be generated with both tissue-based LUED and LOER data, providing a sizable increase in the amount of literature available for use in developing SSDs. It is unlikely that enough statistically reduced residue-effect concentrations are available in the literature to permit development of more than a few tissue BTs using only statistically reduced data to generate the SSD.

If an SSD is to be used to derive tissue BTs, the RSET would have to decide at what level of effect (or the proportion of species to be protected) the tissue BT should be set. Consistency with EPA's AWQC derivation methodology would call for using the 5th percentile of the adverse effects data for survival, reproduction and growth as the selected BT. This is not the only possible level of protection or combination of toxicological endpoints available. A tissue BT could be set at any percentile agreed upon by the RSET. Examples of endpoints historically used with SSDs include the highest no effect concentration, the lowest adverse effect concentration, the 10th, 20th or 50th percentile of the adverse effects concentration, or the concentration above which adverse effects are always observed (apparent effects thresholds approach).

Another potential difficulty with using measured residue - effects data to derive tissue BTs

is data availability. There is simply less information available in the literature on tissue residues associated with toxicity than there is on water column or sediment concentrations associated with toxicity. The EPA AQUIRE database, the repository of toxicity data for chemicals in water contains over 180,000 records. In contrast, the ERED database contains approximately 4000 records. This does not preclude the use of literature data to derive tissue BTs, but the limited available information for many chemicals could in turn limit both the number and reliability of tissue BTs derived from the literature.

Bioaccumulation Modeling Approach

At its simplest, a tissue BT could be derived from the product of a water quality criterion and a bioconcentration factor (or bioaccumulation factor). As many water quality criteria and bioconcentration factors are already available, this approach could be used to quickly generate tissue BTs for a number of chemicals. The simpler bioaccumulation models are not data intensive, a potentially large advantage during the development of tissue BTs.

Through a review of the existing residue-effects literature, Shephard (2004) demonstrated that the product of existing EPA water quality criteria and a standardized set of bioconcentration factors resulted in tissue screening concentrations for aquatic life were lower than 94.5% of measured tissue residues associated with adverse effects on survival, reproduction and growth. This is excellent agreement with the intended 95% level of protection for aquatic genera that is the goal of the EPA water quality criteria (Stephan et al. 1985).

Another observation made by Shephard (2004) was that no statistically significant differences exist in tissue residues associated with toxicity in marine and freshwater biota. This leads to the possibility that generally applicable tissue BTs can be generated from bioaccumulation models, eliminating the need to derive separate sets of tissue BTs for marine and freshwater biota.

Tissue BTs derived from a bioaccumulation model have many uncertainties. These uncertainties include the accuracy of water quality criteria used as an input to the model, and the appropriateness of using a single BCF or BAF to derive generally applicable tissue BTs. Addressing these uncertainties during tissue BT development may result in BTs with large safety factors relative to the safety factors of tissue BTs derived from SSDs.

Measured contaminant residues in field collected fish tissues that exceeded tissue guidelines generated by both a bioaccumulation model and a SSD were found to be statistically significantly correlated with fish community health in a statewide survey of fish in Ohio (Dyer et al. 2000). The Dyer et al. (2000) study is one of the few available that has simultaneously evaluated the predictive utility of tissue guidelines developed from both bioaccumulation models and species sensitivity distributions.

Mixture Toxicity

One of the strong advantages of using the TRA for toxicity assessment is the ability to address mixtures of contaminants. In general, the tissue residue approach is an excellent

way to examine the toxicity of contaminants bioaccumulated by organisms in the field. Mixture toxicity studies based on tissue residues are less complicated than those with exposure concentrations because the variability observed among compounds in bioaccumulation and metabolic conversion is greatly reduced. Also, mixture toxicity from exposure concentrations can be confounded by differences in time to steady state from the various compounds in the mixture, whereas CBRs are generally time independent. The utility of mixture toxicity is supported by several studies demonstrating that multiple contaminants will produce toxicity at a small fraction of their individual effect concentration. Therefore, to generate the best available bioaccumulation trigger that will be protective of aquatic organisms, the combined effects from a complex mixture of compounds must be considered.

Chemicals for Which Tissue Quality Guidelines Can Be Derived

In theory, tissue BTs can be derived for any chemical or compound that is bioaccumulated into aquatic biota tissues. In practice, tissue residues associated with toxicity have seldom been measured for organic chemicals that are freely water soluble, or at least have a high water solubility. As shown by McCarty et al. (1991), for organic chemicals with a $\log K_{OW} < 1.5$, the chemical concentration in the water phase of the organism dominates toxicity, and total body residues associated with toxicity should be similar to the respective threshold LC_{50} in water.

Tissue BTs should not be derived for chemicals that fall into three rather broad categories:

1. Chemicals that do not appreciably bioaccumulate but which nevertheless are toxic
2. External toxicants such as contact herbicides
3. Chemicals that are rapidly biotransformed into more (or less) toxic metabolites relative to toxicity of the parent compound

Some chemicals are quite toxic without appreciable bioaccumulation. Cyanide is one example of a highly toxic chemical with a low bioaccumulation potential. This should not be confused with implying that a chemical can cause toxicity without bioaccumulating at all. Most chemicals in this group have high water solubilities and may not preferentially partition from water to tissues, resulting in low tissue residues associated with toxicity. These chemicals are unlikely to be on lists of bioaccumulative chemicals, reducing the need for tissue BTs for this group.

External toxicants do not need to enter the body of an organism to elicit toxicity. In addition to contact herbicides that act by destroying the cell wall of the plant, a few other chemicals can act as external toxicants under some circumstances. Iron and aluminum are two chemicals which, under certain conditions of water quality, form flocculent materials that coat the gills of aquatic species, causing death by suffocation without entering the body of the organism.

The toxicity of some compounds is enhanced by biotransformation (biological, chemical or physical) after they have been bioaccumulated. Under these conditions, the concentration of

the parent compound in tissue may have little or no relationship to the toxicity of the transformation product. The largest group of chemicals to which this applies are PAH compounds. Some PAH compounds are metabolically transformed into more toxic PAH epoxides, the chemical form often responsible for the carcinogenic effects of some PAHs. Other PAHs are photochemically activated, which enhances the toxicity of bioaccumulated parent PAH compounds. Available tissue residue-effects literature for PAHs shows substantial variations among body residues associated with the same toxic endpoint. These variations cut across taxonomic classes (e.g. some benthic invertebrate species rapidly transform PAHs, resulting in low body burdens associated with toxicity, whereas some fish species do not rapidly transform PAHs, and are substantially more tolerant of elevated body burdens. This variability makes it difficult to develop a single PAH tissue BT that is protective of all species.

Existing data do not currently permit development of generally applicable tissue guidelines for either individual PAH compounds or mixtures of PAHs. We recommend that the RSET not attempt to develop tissue BTs for either individual PAH compounds or PAH mixtures at this time. For PAHs, it may be possible to use bioindicators of exposure, such as fluorescent aromatic compounds (FACs) in bile to assess bioaccumulation. Ongoing work at the Northwest Fisheries Science Center has found a high correlation between bile FACs and dietary intake of PAHs in salmon. PAH toxicity to aquatic species can also be evaluated by comparing their concentration in water or sediment to existing environmental guidelines, standards or criteria.

Sensitivity of Endangered Species to Chemicals

Not surprisingly, relatively few toxicity studies have been performed with endangered species, or at least with the specific ESA listed stocks, strains or subspecies of species that are more common elsewhere in their range. EPA, USFWS and USGS have combined to fund several studies of the contaminant tolerance of several ESA listed aquatic species, primarily fish, in recent years (Besser et al. 2001, Dwyer et al. 1999). The findings of these studies have provided support for the belief that most water quality criteria are protective of ESA-listed aquatic species.

On a body residue basis, additional support for this belief is available from studies with the ESA-listed bull trout (*Salvelinus confluentus*). Studies with cadmium (Hansen et al. 2002) and copper have found that while whole body residues associated with toxicity are low, they are not as low as residues associated with toxicity in other aquatic species. It is highly recommended, however, that residue-effects data for an appropriate surrogate species for an ESA listed species (e.g., rainbow trout for listed salmonids) be considered during any tissue BT development.

Summary

Tissue BTs are a promising approach for evaluating the effects of contaminants in aquatic systems. At least two methods are available for developing tissue BTs, both of which have a demonstrated relationship with adverse effects observed in field populations of aquatic

species. Use of species sensitivity distributions of toxicity data from the literature to derive tissue BTs would be computationally very similar to approaches currently used to derive ambient water quality criteria, and is the preferred method for chemicals where sufficient data are available to permit development of SSDs. The amount of data available and its quality are limiting factors for deriving tissue BTs. It should be recognized that useable tissue BTs should not be developed for some chemicals such as PAH compounds. However, with recognition of the limitations of the TRA, development of tissue BTs is a feasible approach for evaluating the toxicity of chemicals bioaccumulated in both laboratory exposed and field collected aquatic biota.

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