Development of Tissue Residue Threshold Values

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Background

A chemical residue-based approach for evaluating dose, also called critical body residue (CBR) or lethal body burden (LBB), has been advocated as an improvement for prediction of toxicity to organisms in the environment (Friant and Henry, 1985; McCarty, 1986; Cook et al., 1987; Van Hoogen and Opperhuizen, 1988; Cook et al., 1991; McCarty, 1991; McCarty et al., 1991; Tas et al., 1991; Landrum et al., 1992; and McCarty and MacKay, 1993). The correlation of body residues to toxic effects (residue-based dose) has a number of advantages over using an exposure-based approach (i.e., water or food concentrations that cause toxic effects). As outlined by McCarty and MacKay (1993), these advantages include the following: (1) bioavailability is explicitly considered; (2) accumulation kinetics are considered, which reduces the confounding effect of exposure duration when interpreting results; (3) uptake from food (as distinct from water) is explicitly considered; (4) toxic potencies are expressed in a less ambiguous manner, facilitating identification and investigation of different modes of toxic action; (5) effects of metabolism on accumulation are considered; (6) mixture toxicity can be more readily assessed; and (7) experimental verification can be more readily determined between laboratory and field.

Bioaccumulation testing is being used increasingly in various environmental monitoring and regulatory programs involving sediments. In these tests, sediment organisms are exposed to sediment samples for a prescribed time period (e.g., 28 days). Following this uptake period, exposed organisms are analyzed for chemicals of interest. While these tests are one mechanism for assessing the bioavailability and accumulation of sediment contaminants, they do not intrinsically predict the toxicological effects of bioaccumulative toxicants. For this prediction, some association between tissue residues and toxicological effects must be developed. Thus, bioaccumulation tests are a natural application for residue-based effects assessment.

To help evaluate the basis for, and applicability of, residue-based effects assessment, we have undertaken the development of a comprehensive database containing literature data on tissue concentrations of toxicants and associated biological effects for aquatic animals. The purpose of this presentation is to describe the database and provide some examples of analyses that can be conducted from these data.

Database Content and Development

Pertinent literature was identified through several search mechanisms, including electronic databases (e.g., POLTOX P®; Cambridge Scientific Abstracts), in-house literature files, Current Contents®, and other assorted sources. For all literature, hard copies of the primary literature were obtained and are maintained in the project files.

From this literature, residue/effect information was manually extracted. General inclusion criteria were:

- Organism was a marine or freshwater fish, invertebrate, or aquatic lifestage of amphibian (terrestrial animals, birds, and plants were not included);
- There was a measured chemical concentration in the whole body or a specific tissue; and
- There was some observation of biological effect in the form of survival, growth, or reproduction (physiological and biochemical endpoints were not considered).

In general, only data from exposures using a single chemical were used; information from mixture studies was not used unless the mixture contained only related chemicals (same mode of action). Control treatments were required as a basis for comparison of biological effect, except in studies where survival was ≥90 percent (thus survival was not reduced). All chemical types (e.g., organic and inorganic, ionic and nonionic) were included.

For references meeting these criteria, specific information was extracted for inclusion in the database. Database fields are as follows:

- **Study Type**: acute or chronic
- **Chemical Name**: exact chemical form (e.g., metal salt) is included parenthetically
- **CAS Number**
these chemicals were for whole-body analyses, the exposure regimes varied widely with regard to species, lab versus field, and route of exposure, among other variables. Regardless of these differences, these values do suggest a range of chemical residues associated with biological effects, with the threshold for reported effects in the vicinity of 1 µg/g wwt for both chemicals.

Once data entry, accuracy checking, and initial analysis are complete, it is our intention to make this database available to the scientific community for further analysis.

References


Example Data Sets

Compilation and analysis of the data are ongoing at this time. However, as an example of data analyses than can be performed using the database, we extracted data for chlorpyrifos (Jarvinen et al., 1983; Macek et al., 1972; Serrano et al., 1995; Hansen et al., 1986; Montanes et al., 1995) and kepone (Buckler et al., 1981; Hansen et al., 1977a, 1977b; Fisher and Clark, 1990; Sanders et al., 1981; Stehlik and Merriner, 1983; Fisher et al., 1983; Fisher et al., 1986; Goodman et al., 1982).

Figures 1 and 2 display the residue/effect pairs for chlorpyrifos and kepone, segregated by biological endpoint (survival, growth, or reproduction). Although all residues reported for

![Chlorpyrifos Residues Versus Biological Responses](image-url)


**Figure 2. No effect (squares) and effect (diamonds) concentrations for kepone in tissues.**
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Impetus for Research

● Need for interpretive guidance for bioaccumulation testing
● Desire for decision criteria that are based on biological effects
Impetus for Research

- Proposal that risk assessment be based on tissue residues rather than concentrations in environmental matrices
- Assemble data necessary to evaluate a tissue residue approach
- Evaluate tissue residue approach relative to mode of action or other characteristics

Tissue Residue/Toxicity Database

- Exhaustive search of literature for residue data linked to biological effect observations
- Selection criteria designed to maximize quality, comparability, and interpretability of resulting data
## Scope of Data Collection

- marine and freshwater, fish and invertebrates
  - does not include amphibians, terrestrial vertebrates or birds
- endpoints focused on survival, growth, and reproduction
  - histological/biochemical/physiological endpoints not included
- virtually all chemicals included, regardless of mode of action

## Database Fields

- Acute/chronic
- Chemical name
- CAS number
- Log Kow
- Molecular weight
- Species
- Life stage
- Lab/field
- Test conditions
- Exposure route
- Exposure concentration
- Test duration
- Tissue analyzed
- Residue
- Effect
- Reference
- Comments
Criteria for Data Inclusion

- Measured tissue residue (whole body or specific tissue)
- Effect data or statement concerning the health of the test organisms
- Mixture papers used only if no effect was observed
- Control not necessary if no mortality was observed

Database Content

- Currently, the database contains approximately:
  - 485 references
  - 200 chemicals
  - 2,552 residue/effect pairs
Largest Datasets

- More than 400
  - cadmium
- 100-250
  - DDT
  - TCDD
  - hexachlorobenzene
  - mercury
  - PCB(s)
  - selenium
- 40 to 100
  - aminocarb
  - arsenic
  - copper
  - 2,4 dinitrophenol
  - endosulfan
  - endrin
  - fenvalerate
  - kepone
  - lead
  - lindane
- 100-250
  - nickel
  - 4-nitrophenol
  - pentachlorophenol
  - terbofos
  - toxaphene
  - tributyltin
  - zinc

Kepone Data

- 32 residue/effect pairs
  - 8 references
  - 6 species (3 fish, 3 invertebrate)
  - lab exposures only
  - water, diet, parental exposures
  - exposures 4 to 141 days
# Chlorpyrifos Data

<table>
<thead>
<tr>
<th>Species (n)</th>
<th>Age</th>
<th>Days</th>
<th>S/G/R</th>
<th>Source</th>
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<tbody>
<tr>
<td>Fathead minnow (6)</td>
<td>Larva</td>
<td>Lab 200</td>
<td>S,G,R</td>
<td>Jarvinen et al. 1983</td>
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<tr>
<td>Bluegill (2)</td>
<td>Juvenile</td>
<td>Field 63</td>
<td>S</td>
<td>Macek et al. 1972</td>
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<td>S</td>
<td>Macek et al. 1972</td>
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<tr>
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<td>Lab 4</td>
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<td>Serrano et al. 1995</td>
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<td>Lab 4</td>
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<td>Serrano et al. 1995</td>
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<td>Hansen et al. 1986</td>
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<tr>
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<td>Field 23</td>
<td>S,G</td>
<td>Montanes &amp; Hattum 1995</td>
</tr>
</tbody>
</table>

## Chlorpyrifos Residues Versus Biological Responses

![Graph showing Chlorpyrifos residues versus biological responses](image)
Kepone Residues Versus Biological Responses

BAF versus Exposure Duration
Kepone (water exposures)
Paired Effect/No Effect Data
Chlorpyrifos

<table>
<thead>
<tr>
<th>Survival</th>
<th>Effect</th>
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<tr>
<td>Gulf toadfish</td>
<td>770</td>
<td>175</td>
<td>367</td>
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<td>Mussel (Mytilus)</td>
<td>53</td>
<td>4</td>
<td>14.6</td>
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<tr>
<td>Fathead minnow</td>
<td>5.11</td>
<td>3.03</td>
<td>3.93</td>
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<td>Isopod (Asellus)</td>
<td>1.79</td>
<td>0.97</td>
<td>1.32</td>
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<tr>
<td>Bluegill</td>
<td>3.82</td>
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<td>Largemouth Bass</td>
<td>2.55</td>
<td>0.47</td>
<td>1.09</td>
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<table>
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<td>Fathead minnow</td>
<td>3.03</td>
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<td>Gulf toadfish</td>
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<td>0.14</td>
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<table>
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<td>Fathead minnow</td>
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<td>0.47</td>
<td>0.67</td>
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</table>
**Interpretation Issues**

- Quantity and type of data varies greatly between chemicals
- Target tissue data not available consistently
- Relatively few data for individual PAH
- PCB mixtures vs. single congeners