Considerations for Scientifically Rigorous Development and Application of Critical Tissue Residues in Ecological Risk Assessment

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Steps to a Usable Critical Body Residue (CBR)

- Minimum acceptability criteria for published toxicity data
- Factors requiring consideration specifically for CBRs
  - Aggregation of values for
    » Performing statistics
    » Derivation of benchmarks
    » Making statistical comparisons
- Confronting uncertainty
Step 1: General Data Acceptability Criteria

- Relevant, peer-reviewed document
- Well-defined hypothesis with appropriate endpoints
- Clearly defined analytical design
- Effective reporting of analytical methods
- Individual chemical exposures and measured doses
- Use of controls, and appropriate control performance
- Environmentally relevant dose administration
- Statistical certainty of result is clearly provided

Source: Durda and Preziosi 2000
Step 2: Considerations for CBRs

- Exposure duration and media
- Endpoints
  - Sub-lethal
  - If lethal endpoints
    » Lower dose exposures
    » Residues in all exposed individuals (i.e., including survivors)
- Accurate classification of mechanism and mode of action
- Lipid-normalization for hydrophobic organic compounds
- Toxicity of metabolites relative to parent compound

Adapted from: Meador 2006
Exposure Duration & Media Are Important

- Fathead minnows exposed continuously for 266 days
- Exposed to spiked food, water, or food and water
  - Low and high water exposures
- Food-only exposure appears to result in stabilization of tissue DDx
- Water exposures result in unstable tissue DDx

Source: Jarvinen et al. 1977
Exposure Duration & Media Are Important

- Role of water in tissue DDx amplified at higher water concentrations
- Food plays a role in tissue burden throughout the exposure period

![Graph showing "High" water exposure](chart)

Source: Jarvinen et al. 1977
The CBR Approach Assumes...

- That whole body concentrations are a surrogate for concentrations at the site/tissue of action
  - This should be verified (e.g., USEPA 2004)
- That there is a cause-effect relationship
  - Correlation ≠ cause
- The presence of a chemical = accumulation
  - This is not true when chemicals are readily depurated or metabolized
  - Exposure and effect may be temporally distinct
Other Considerations

- Lipid-normalization may help the analysis by reducing variability, but there are still uncertainties about when and whether it is important.

- The role of metabolites
  - Are they toxic?
  - Have they mistakenly been included in concentration estimates?

- Basis for lethal residue must include both animals that are dead and those alive at the end of the test.
Application of the CBR

Photo: Les Williams
DDE in Bird Eggs

- 152 publications identified and 70 critically reviewed and ranked:
  - High quality, useable, not useable

- Data for double-crested cormorant extracted and analyzed

<table>
<thead>
<tr>
<th>DDE Egg Residue (ppm ww)</th>
<th>Eggshell Thinning (%)&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.7</td>
<td>-2.3&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Gress et al. 1973</td>
</tr>
<tr>
<td>3.9</td>
<td>4.6</td>
<td>Custer et al. 1999</td>
</tr>
<tr>
<td>6.2</td>
<td>1.5</td>
<td>Morrison et al. 1978</td>
</tr>
<tr>
<td>8.2</td>
<td>14</td>
<td>Faber and Hickey 1973</td>
</tr>
<tr>
<td>14</td>
<td>24</td>
<td>Weseloh and Teeple 1982</td>
</tr>
<tr>
<td>24</td>
<td>38</td>
<td>Gress et al. 1973</td>
</tr>
<tr>
<td>32</td>
<td>29</td>
<td>Gress et al. 1973</td>
</tr>
</tbody>
</table>

Source: Neuber et al. 2006
Significant Linear Regression

Source: Neuber et al. 2006
Regression is Consistent with BMD Result

Source: Neuber et al. 2006
Species Ranked by Sensitivity

Table 2. Relative Species Sensitivities to DDE.

<table>
<thead>
<tr>
<th>Bird Species</th>
<th>Linear Relationship between DDE in Egg Residue and Eggshell Thinning</th>
<th>Statistical Significance and Correlation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Most Sensitive</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brown Pelican</td>
<td>$y = 6.0x + 3.4</td>
<td>$p = 0.0002$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>$r^2 = 0.51$</td>
</tr>
<tr>
<td>White Faced Ibis</td>
<td>$y = 4.1x + 3.9</td>
<td>$p = 0.01$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>$r^2 = 0.83$</td>
</tr>
<tr>
<td>Osprey</td>
<td>$y = 6.4x - 4.6</td>
<td>$p = 0.0007$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>$r^2 = 0.95$</td>
</tr>
<tr>
<td>Black Crowned Night Heron</td>
<td>$y = 1.4x + 3.6</td>
<td>$p = 0.002$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>$r^2 = 0.51$</td>
</tr>
<tr>
<td>Great Blue Heron</td>
<td>$y = 1.7x + 0.89</td>
<td>$p = 0.02$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>$r^2 = 0.78$</td>
</tr>
<tr>
<td>Green Backed Heron</td>
<td>Limited Data; Available data points considered (3.9 ppm ww, 8% thinning; 7.4 ppm ww, 11% thinning)</td>
<td>NA</td>
</tr>
<tr>
<td>Least Sensitive</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cormorant</td>
<td>$y = 1.2x + 0.033</td>
<td>$p = 0.007$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>$r^2 = 0.79$</td>
</tr>
</tbody>
</table>

Source: Neuber et al. 2006
Step 3: Confronting Uncertainty

Photo: Igor Tupitsyn
“Risk” Should Address Probability

- Joint probability: An X% probability of exposure exceeding threshold
- Binomial method: An X% probability of effect in 10 animals out of 100
- Risk curve method: An X% probability of a 50% response

Source: Hope et al. 2007
Example Species Sensitivity Distribution: 2,3,7,8-TCDD in Fish

<table>
<thead>
<tr>
<th>Species protection level</th>
<th>Benchmark value (ng TCDD/g lipid)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>LCL</td>
</tr>
<tr>
<td>Species protection level</td>
<td>LCL</td>
</tr>
<tr>
<td>Geometric mean of NOER and LOER</td>
<td></td>
</tr>
<tr>
<td>99%</td>
<td>0.015</td>
</tr>
<tr>
<td>97.5%</td>
<td>0.040</td>
</tr>
<tr>
<td>95%</td>
<td>0.088</td>
</tr>
<tr>
<td>90%</td>
<td>0.199</td>
</tr>
</tbody>
</table>

Source: Steevens et al. 2005
Applying the CBR Approach: Case Study

- Revised AWQC for selenium uses a concentration in whole fish as the FCV. Why?
  - Selenium geochemistry is complex - CBR integrates complex exposures
  - Primary exposure route for fish is ingestion
  - Criterion as \([\text{Se}]_{\text{prey}}\) impractical
  - Reasonable data were available (though not perfect)
  - Weight of evidence suggested a legitimate CBR-effect relationship
Applying the CBR Approach: Case Study

- Revised AWQC for selenium as a concentration in whole fish has problems, e.g.,
  - FCV is deemed protective of all aquatic species, even though almost all data are for fish
  - Some of the studies used violated key acceptability criteria, e.g., tightly controlling exposures of test animals

- EPA (2004) seems to recognize that the FCV isn’t perfect:
  “...results from appropriate site-specific studies could be used to modify the criterion.”
Acceptable CBR(s) Are Scarce to Absent

- Pursue other lines of evidence, e.g.,
  - Site-specific toxicity tests
  - Site-specific biological surveys
- Perform a weight-of-evidence analysis
- Acknowledge uncertainty
- Do not apply meaningless values!
Summary and Conclusions

• Toxicity data used in ecological risk assessment must be carefully evaluated and its shortcomings addressed
• Be aware of potentially misleading information
• When adequate data are available, risk conclusions should be stated as probabilities
• Consider alternative lines of evidence
• Developing effective CBRs is an emerging science...watch for new developments
References


Hope, B.K., P. Allard, A. Fairbrother, R. Hull, M. Johnson, L. Kapustka, G. Mann, B. McDonald, and Bradley Sample. 2007. Representation and consequences of uncertainty in the toxicity reference value. This poster is one of a series originating from a meeting held May 1 - 2, 2007 in Burnaby, BC. Logistical support for the meeting was funded by the British Columbia Ministry of Environment with time donated by participants and coordinated with the assistance of the Pacific Northwest SETAC chapter.

