WEIGHT-OF-EVIDENCE APPROACHES

INVITED EXPERT MEETING ON REVISING USEPA’S GUIDELINES FOR DERIVING AQUATIC LIFE CRITERIA
PRESENTATION OVERVIEW

Background

Applicability to derivation of aquatic life criteria

Case example

- Weight-of-evidence analysis (WOE)
- Multicriteria Decision Analysis (MCDA)
WOE CONCEPT

Wise to consider multiple lines of evidence

• But often outcomes conflict
• And professional opinions differ

Weighing each line of evidence systematically allows

• Transparent characterization of uncertainty
• Explicit documentation of professional judgment
• Balanced conclusion
WOE PRECEDENTS

- USEPA Integrated Risk Information System
- CADDIS
- MADEP WOE Work Group

_DRAFT REPORT
A WEIGHT-OF-EVIDENCE APPROACH FOR EVALUATING ECOLOGICAL RISKS

Prepared by
Massachusetts
Weight-of-Evidence Workgroup

November 2, 1995

_C.11. Carcinogenicity Assessment for Lifetime Exposure_
Substance Name — alpha-Hexachlorocyclohexane (alpha-HCH)
CASRN — 310-64-6
Last Revised — 07/01/1993

Section 11 provides information on three aspects of the carcinogenic assessment for the substance in question: the weight-of-evidence risk estimate, the quantitative risk estimates, and the health effects. The second part of Section 11 describes the health effects, which are divided into three categories: (1) cancer risk per ug/L drinking water or risk per ug/m3 air breathed. The third form in which risk is presented is a drinking water or air concentration of the substance that is associated with the lowest risk of health effects. The section also includes a discussion of the health effects of the substance, which are described in the Risk Assessment Guidelines (EPA/630/8-87/045) and in the IRIS Assessment report. Users are referred to the guidelines for more information.

_C.11.A. Evidence for Human Carcinogenicity_


Classification — B2; probable human carcinogen

Basis — Dietary alpha-HCH has been shown to cause increased incidence of liver tumors in five mouse strains and in litters.

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MCDA BACKGROUND

• Sub-discipline of operations research since 1970s, drawing on mathematics, behavioral decision theory, economics, software engineering, and information systems

• 2011 publication of Linkov & Moberg mainstreamed MCDA’s application to environmental decision making

• Many MCDA methods exist:
  • Aggregated Indices Randomization Method
  • Analytic hierarchy process
  • Analytic network process
  • Best worst method
  • Characteristic Objects Method
  • Choosing By Advantages
  • Data envelopment analysis
  • Disaggregation – Aggregation Approaches
  • Dominance-based rough set approach
  • Outranking
  • Evidential reasoning approach
  • Goal programming
  • Inner product of vectors
  • Multi-Attribute Global Inference of Quality
  • Multi-attribute utility theory
  • New Approach to Appraisal
  • Potentially all pairwise rankings of all possible alternatives
  • Superiority and inferiority ranking method
  • Technique for the Order of Prioritisation by Similarity to Ideal Solution
  • Value analysis
  • Value engineering
  • VIKOR method
  • Fuzzy VIKOR method
  • Weighted product model
  • Weighted sum model
  • Rembrandt method
PROPOSED APPLICATION IN ALC DERIVATION

From Suter’s WOE presentation

Illustrated here with a constructed dataset for a hypothetical substance lacking an ALC or with an outdated ALC

Weighing Evidence in SSDs—Meta-analysis

- Equal weight for tests and species using geometric means
  \[ \text{SMAV} = \exp \left( \frac{\sum \log \text{LC50}}{n} \right) \]
  \[ \text{GMAV} = \exp \left( \frac{\sum \log \text{SMAV}}{n} \right) \]
- Could weight tests based on quality, # of partial responses, etc.
  \[ \text{SMAV} = \exp \left( \frac{\sum w \times \log \text{LC50}}{\sum w} \right) \]
- Could weight species based on number of tests
  \[ \text{GMAV} = \exp \left( \frac{\sum w \times \log \text{SMAV}}{\sum w} \right) \]
EXAMPLE ATTRIBUTES FOR WEIGHING STUDY QUALITY, DEFINED A PRIORI

1 Test organisms
   sensitivity, similarity to target species with respect to taxonomy and feeding guild

2 Endpoints
   effects measured are most sensitive, diagnostic, and relevant to population sustainability

3 Study design
   sample size, acclimation, dosing methods, exposure duration

4 Data quality
   QA/QC, statistical analysis, confounding factors

5 Study execution
   methodological contributions to uncertainty
<table>
<thead>
<tr>
<th>Score</th>
<th>Test organisms</th>
<th>Endpoints</th>
<th>Study design</th>
<th>Data quality</th>
<th>Study execution</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Insensitive species, not native or closely related</td>
<td>Insensitive, nondiagnostic endpoint</td>
<td>Meets &lt;1 of 5 key aspects of study design (as described under Score 5)</td>
<td>Inappropriate statistical analyses and/or errors and/or unaddressed confounding factors</td>
<td>Flaws in study execution preclude reliance on all conclusions</td>
</tr>
<tr>
<td>2</td>
<td>Insensitive, native species</td>
<td>Somewhat diagnostic and sensitive endpoint</td>
<td>Meets 2 of 5 key aspects of study design (as described under Score 5)</td>
<td>Analyses and/or QA/QC are questionable but errors not definitively identified</td>
<td>Flaws in study execution preclude reliance on some conclusions</td>
</tr>
<tr>
<td>3</td>
<td>Sensitive species, not native or closely related</td>
<td>Moderately diagnostic and sensitive endpoint, not closely tied to population sustainability</td>
<td>Meets 3 of 5 key aspects of study design (as described under Score 5)</td>
<td>Statistical analyses appropriate though potential confounding factors not fully addressed and discussion of QA/QC limited</td>
<td>Minor flaws in study execution, but not adequately explained</td>
</tr>
<tr>
<td>4</td>
<td>Sensitive species closely related to native species</td>
<td>Diagnostic and sensitive endpoint, linked to population sustainability</td>
<td>Meets 4 of 5 key aspects of study design (as described under Score 5)</td>
<td>Robust statistical analyses and confounding factors addressed, but limited discussion of QA/QC</td>
<td>Minor flaws in study execution are adequately explained</td>
</tr>
<tr>
<td>5</td>
<td>Sensitive, native species</td>
<td>Highly diagnostic and sensitive endpoint that drives population sustainability</td>
<td>Strong sample size, acclimation, dosing methods, number of dose groups, and exposure duration</td>
<td>Robust statistical analyses and QA/QC; any potential confounding factors addressed</td>
<td>No flaws in study execution identified</td>
</tr>
</tbody>
</table>
## EXAMPLE WEIGHING OF STUDIES

<table>
<thead>
<tr>
<th>Attribute</th>
<th>Study1</th>
<th>Study2</th>
<th>Study3</th>
<th>Study4</th>
<th>Study5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test organisms</td>
<td>1</td>
<td>3</td>
<td>4</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Endpoints</td>
<td>2</td>
<td>4</td>
<td>5</td>
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<td>5</td>
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<tr>
<td>Study design</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Data quality</td>
<td>2</td>
<td>5</td>
<td>2</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Study execution</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td><strong>Average score (weights)</strong></td>
<td><strong>1.4</strong></td>
<td><strong>3.2</strong></td>
<td><strong>3.4</strong></td>
<td><strong>3.2</strong></td>
<td><strong>4.4</strong></td>
</tr>
</tbody>
</table>
RESULTANT WEIGHTS THEN APPLIED TO SMAV CALCULATION

• Scores derived above serve as $w_t$

<table>
<thead>
<tr>
<th>Study</th>
<th>Weight</th>
<th>LC50</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.4</td>
<td>5</td>
</tr>
<tr>
<td>2</td>
<td>3.2</td>
<td>15</td>
</tr>
<tr>
<td>3</td>
<td>3.4</td>
<td>2</td>
</tr>
<tr>
<td>4</td>
<td>3.2</td>
<td>25</td>
</tr>
<tr>
<td>5</td>
<td>4.4</td>
<td>10</td>
</tr>
</tbody>
</table>

• Unweighted SMAV = 8.2
• Weighted SMAV = 8.7
OVERCOMING TECHNICAL
CHALLENGES IN DERIVING
AQUATIC LIFE CRITERIA FOR
CONTAMINANTS OF EMERGING CONCERN (CECs)

OTHER POTENTIAL WOE APPLICATIONS IN
ALC DERIVATION

Cases where QSAR indicates toxicity of Chem1<Chem2, but tier II paradigm prevents consideration of that information

Overcoming technical challenges in deriving aquatic life criteria for contaminants of emerging concern (CECs)
## CONCLUSIONS

<table>
<thead>
<tr>
<th>Tool for reconciling conflicting lines of evidence and appropriately considering each line of evidence</th>
<th>Acknowledges that quality in studies varies and professional judgment is used when deriving ALC</th>
</tr>
</thead>
<tbody>
<tr>
<td>❖ We currently use professional judgment when we assume all studies are of equal quality (i.e., in not weighing evidence)</td>
<td></td>
</tr>
</tbody>
</table>

| MCDA/WOE widely applied and accepted | Not difficult to understand or implement |
THANK YOU

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