Evaluating Bioavailability/Bioaccessibility of Soil-Borne Contaminants: A U.S. EPA Perspective

SBRP Bioavailability Workshop
Elizabeth, N.J.
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Mark Maddaloni & Mike Beringer
U.S. EPA
Current U.S. EPA Guidance

- Risk Assessment Guidance for Superfund
  - Addresses adjustments for absorption efficiency
  - Focuses on differences between medium of exposure
  - Provides equations for adjusting relative bioavailability
  - Emphasizes the need for reliable information

- Default Assumption
  - Bioavailability is equal in soil, diet and water
  - Relative bioavailability or RBA is 1.0

- Medium- and Chemical-Specific Values
  - Lead
  - Cadmium
  - Manganese
Future U.S. EPA Bioavailability Guidance

• Limited to evaluating site-specific bioavailability of metals in soils for use in human health risk assessment

• Outlines a decision framework on how to evaluate and incorporate bioavailability information into decision-making
  • Tier 1: process for deciding whether to collect site-specific bioavailability information
  • Tier 2: process for collecting and analyzing the data

• Incorporates validation and regulatory acceptance criteria

• Will address if in vitro methods (IVBA) for lead can be used in support of site-specific bioavailability adjustments
Validation of Bioavailability Test Methods

• Relying on ICCVAM Criteria (Interagency Coordinating Committee for Validation of Alternative Methods)
  • http://iccvam.niehs.nih.gov/

• Method Validation Criteria
  • Demonstrate method is reliable and relevant for its proposed use

• Regulatory Acceptance Criteria
  • Method fulfills a specific regulatory need

• Regulatory Methodologies
  • Must satisfy both sets of criteria
  • Appropriate for making quantitative site-specific adjustments
  • Categorized based on level of confidence
Method Validation Criteria (ICCVAM, 1997)

- Scientific and Regulatory Rationale
- Relationship Between Test Method Endpoint and Biological Effect
- Detailed Protocol and Known Limitations
- Within-Test Variability and Reproducibility Among Labs
- Test Method Performance with Representative Agents
- Comparison to Existing Test Method
- Data in Accordance with Good Laboratory Practices (GLP)
- Validity Assessment Data Available for Review
- Independent Scientific Review
Regulatory Acceptance Criteria (ICCVAM, 1997)

- Independent Scientific Peer Review
- Detailed Protocol with SOPs
- Adequately Predicts Bioavailability
- Representative Chemicals Tested
- Generates Data Useful for Risk Assessment Purposes
- Documentation of Strengths and Limitations
- Robust and Transferable
- Time and Cost Effective
- Can Be Harmonized
- Suitable for International Use
- Reduction of Animal Use
Proposed Criteria for Categorizing Validation Status of Bioavailability Test Methods

• Level 1: Predicts RBA, with high confidence, in humans
  • Level 1a: Based on site-specific soil and metal characteristics
  • Level 1b: Based on a range of conditions reflective of the site

• Level 2: Predicts RBA in a suitable *in vivo* model
  • Level 2a: *In vivo* model shown to predict RBA in humans
  • Level 2b: *In vivo* model expected to predict RBA in humans

• Level 3: Not tested in an *in vivo* model, but differentiates metal species and physical properties of metal in soil, based on physical or physiological solubility or transport properties that will be predictive of *in vivo* bioavailability
Bioavailability Assumptions in Evaluating Risks to Children from Lead

- Use the Integrated Exposure Uptake Biokinetic Model to predict blood lead levels in young children

- Absolute bioavailability of soluble lead in food/water = 50%

- Relative bioavailability (RBA) of lead in soil = 60%
  - 30% absolute bioavailability (model input)

- A sensitive parameter in predicting blood lead levels and potential risks to children
  - RBA of 80% = soil cleanup goal of 265 mg/kg
  - RBA of 60% = soil cleanup goal of 400 mg/kg (default)
  - RBA of 40% = soil cleanup goal of 530 mg/kg
  - RBA of 20% = soil cleanup goal of 1075 mg/kg
Juvenile Swine Model

- Attempts to mimic childhood absorption of lead
  - Similar physiology to children
  - Dosing in a semi-fasted state
  - Similar in physiologic age and body weight to children
  - Ease of serial blood sampling

- Gold standard for measuring site-specific lead bioavailability
  - Costly and time-consuming

- Used to make site-specific bioavailability adjustments
  - Bingham Creek, Utah
    - RBA reduced from 60% to 38%
  - Murray Smelter, Utah
    - RBA increased to 70%
  - Omaha Lead, Nebraska
    - RBA increased to 88%
RBA ESTIMATES: Soil-Lead at 20 Sites

Relative Bioavailability (RBA) per Tissue (Rank Ordered)

- Pt. Est.
- Blood
- Liver
- Kidney
- Bone

EPA default
RBA = 60%
Physiologically-Based Extraction Tests

- A measure of bioaccessibility (e.g., solubility)

- Incorporates human gastrointestinal parameters
  - Stomach and small intestine pH
  - Stomach mixing
  - Stomach emptying rates

- Significant cost and time reductions
  - More completely characterize bioavailability across a site
  - Avoid or greatly reduce the number of animals used
Omaha Lead Site

- Lead smelter operated for over 100 years
- About 40,000 contaminated residential yards

- Juvenile Swine Results
  - Tested 2 soil samples
  - RBA = 75% and 102%
  - Mean RBA = 88%

- In Vitro Bioaccessibility Results
  - Tested 47 soil samples
  - RBA ranged from 50% to 97%
  - Mean RBA = 83%
  - 46 of 47 samples >70% RBA
Lead – Correlation Between *In Vivo* RBA and *In Vitro* Bioaccessibility (IVBA)
Arsenic – Correlation Between *In Vivo* RBA and *In Vitro* Bioaccessibility (IVBA)

![Graph showing correlation between In Vivo RBA and IVBA](image)

- **Equation:** $y = 0.3538x + 0.2339$
- **Coefficient of Determination:** $R^2 = 0.1732$
- **P-value:** $p = 0.06$
Status of Bioavailability Guidance

- Agency Review in Fall 2005

- Lead Technical Support Document (TSD)
  - External peer review completed February 2004
  - No significant technical issues were identified
  - Response to comments completed
  - Agency review along with Guidance Document

- Possible Future U.S. EPA Guidance
  - Guidance on sampling designs
  - Additional guidance on method validation
  - Default values for other metals
Evaluation of Other Metals

• Arsenic Bioavailability Technical Support Document
  • Evaluates *in vivo* versus *in vitro* results

• Bioavailability Scoping Reports
  • Evaluation of available bioavailability data
  • Possible use in derivation of default values
  • Identification of methodologies for estimating bioavailability
  • Cadmium, mercury, and manganese scoping reports undergoing internal EPA review
  • Nickel scoping report is in progress