



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

**SBRP Bioavailability Workshop
Elizabeth, N.J.
November 9, 2005**

**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

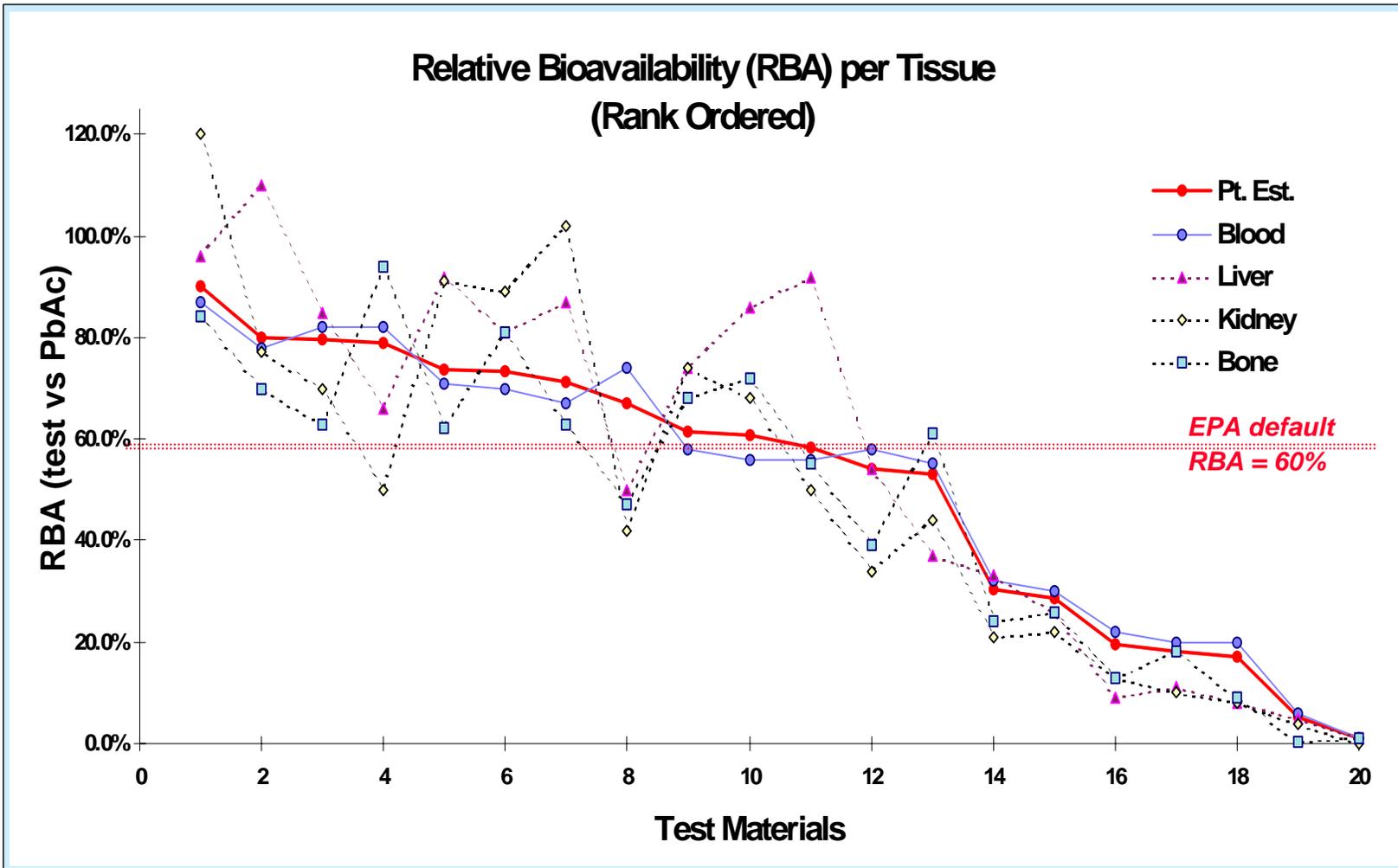
- Use the Integrated Exposure Uptake Biokinetic Model to predict blood lead levels in young children
- Absolute bioavailability of soluble lead in food/water = 50%
- Relative bioavailability (RBA) of lead in soil = 60%
 - 30% absolute bioavailability (model input)
- A sensitive parameter in predicting 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%

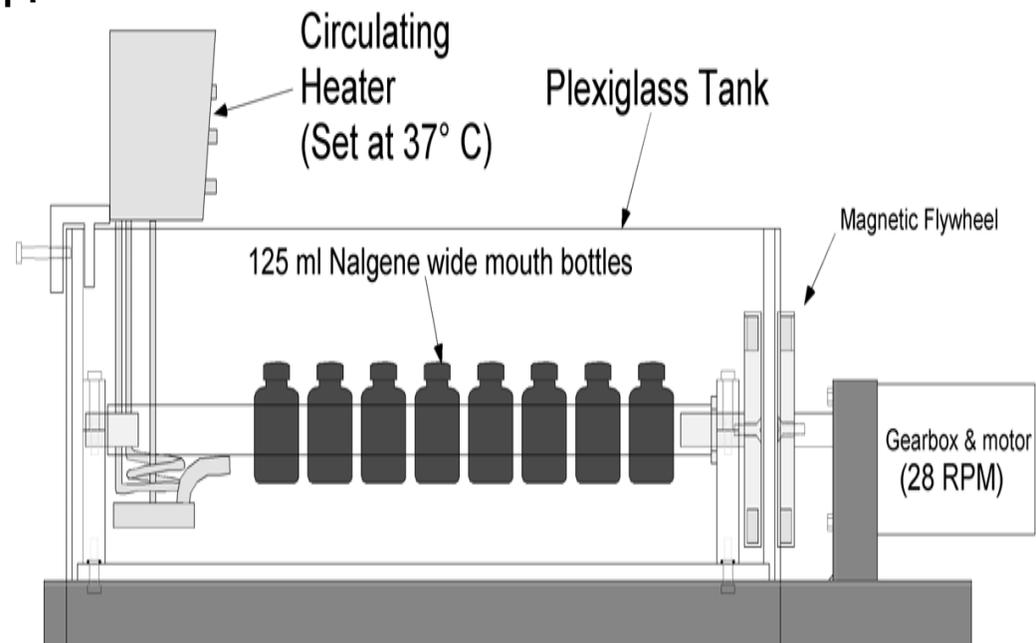
RBA ESTIMATES: Soil-Lead at 20 Sites





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

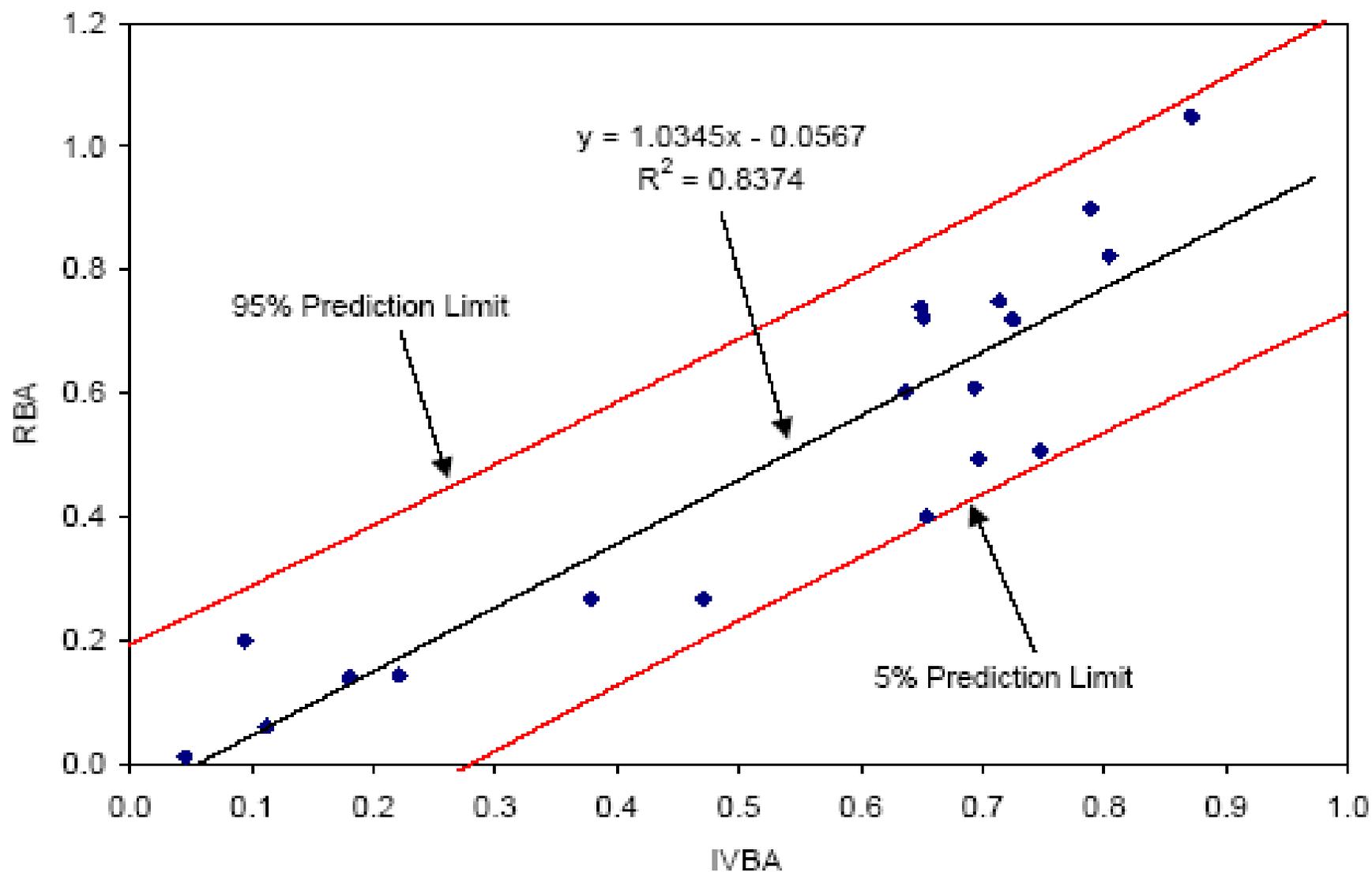


Omaha Lead Site

- 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

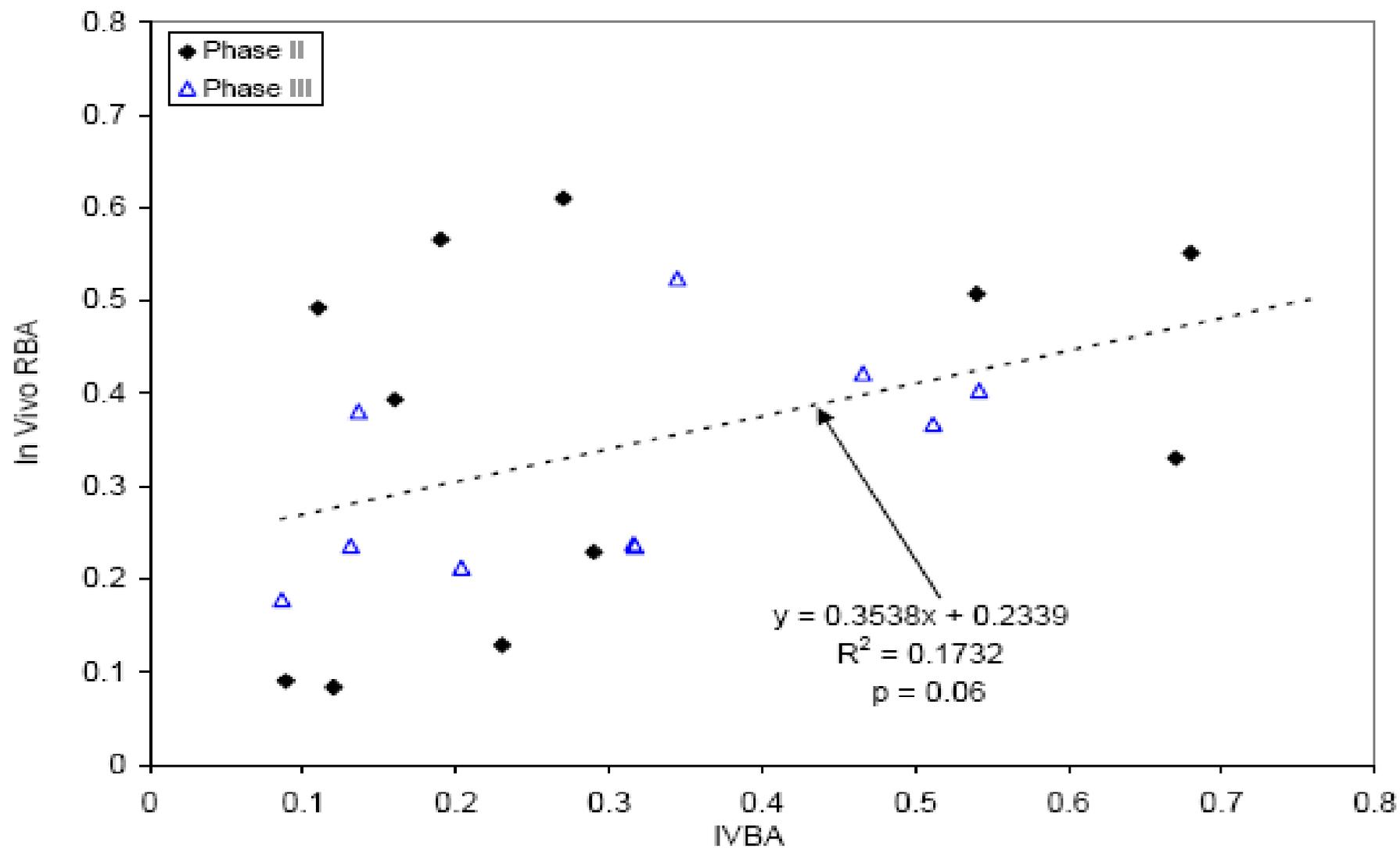


Lead – Correlation Between *In Vivo* RBA and *In Vitro* Bioaccessibility (IVBA)





Arsenic – Correlation Between *In Vivo* RBA and *In Vitro* Bioaccessibility (IVBA)





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