RISKeLearning

Bioavailability – Metals, Organics, and Use at Hazardous Waste Sites

June 18th, 2008 Session 3: "Use of Bioavailability Information at Hazardous Waste Sites"

Mike Beringer, U.S. EPA Region VII toxicologist
U.S. EPA Guidance for Evaluating the Oral Bioavailability of Metals

Mark Maddaloni, U.S. EPA Region II toxicologist
Point – Counterpoint
The FMC Site

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U.S. EPA Guidance for Evaluating the Oral Bioavailability of Metals

Superfund Basic Research Program
Risk-e-Learning Seminar
June 18, 2008

Mike Beringer
U.S. EPA Region VII

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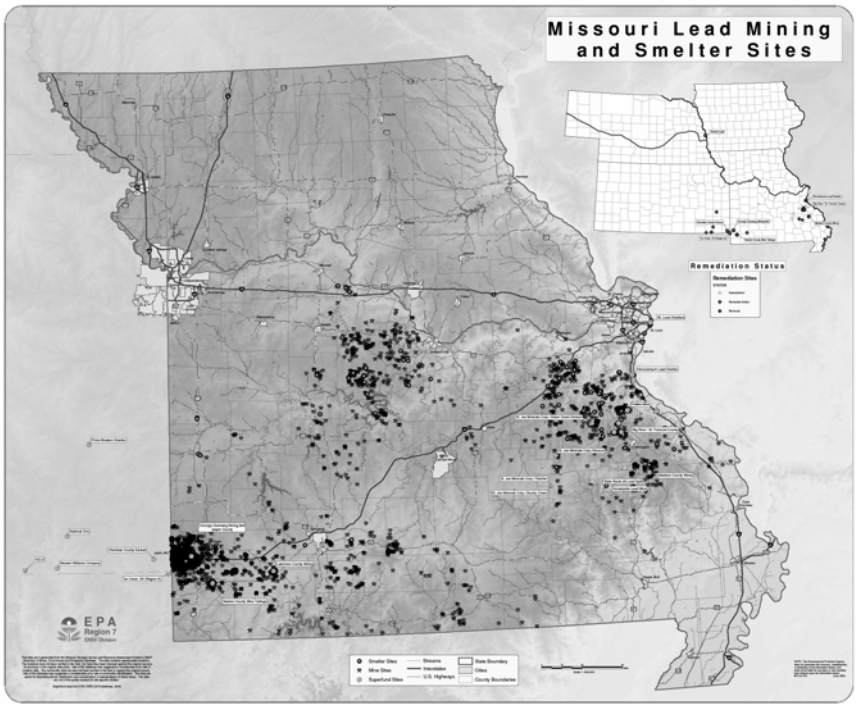
Missouri Lead Mining
and Smelter Sites
Remediation Status
EPA
Region 7

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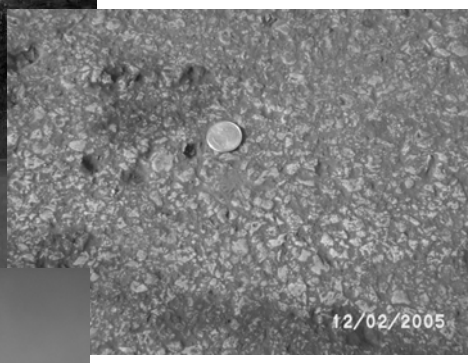

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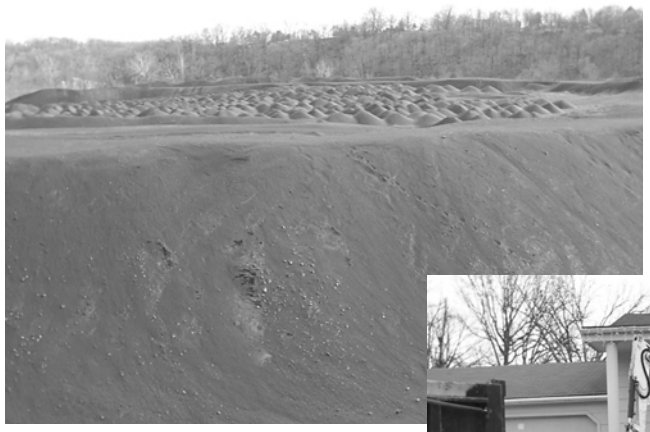

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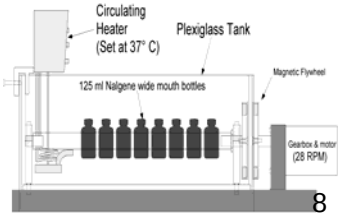
Methods for Assessing Bioavailability in Soil

- Mineralogical studies
  - Importance of speciation and particle size
  - $PbCO_3$ > Pb Oxide > PbS
  - Provides supporting bioavailability information
- *In vivo* methodologies
  - Blood concentration vs. time (AUC)
  - Quantification of amount present in urine or feces
  - Used for quantitative bioavailability adjustments
- *In vitro* methodologies
  - Physiologically-based extraction tests
  - Used for screening purposes and uncertainty analysis



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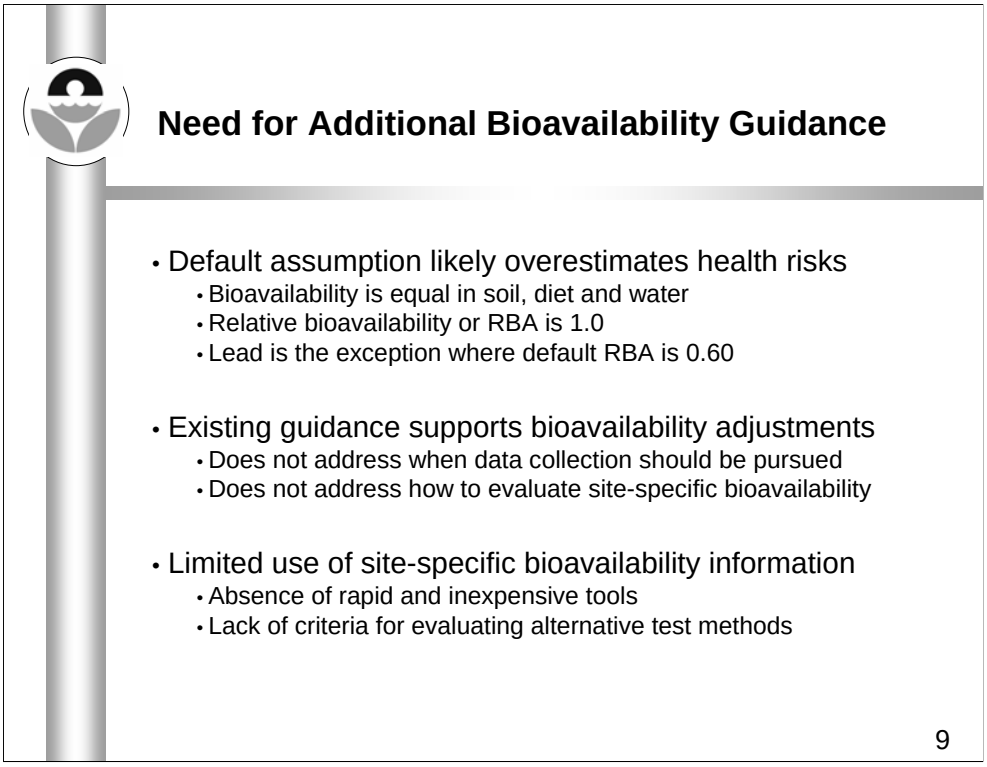

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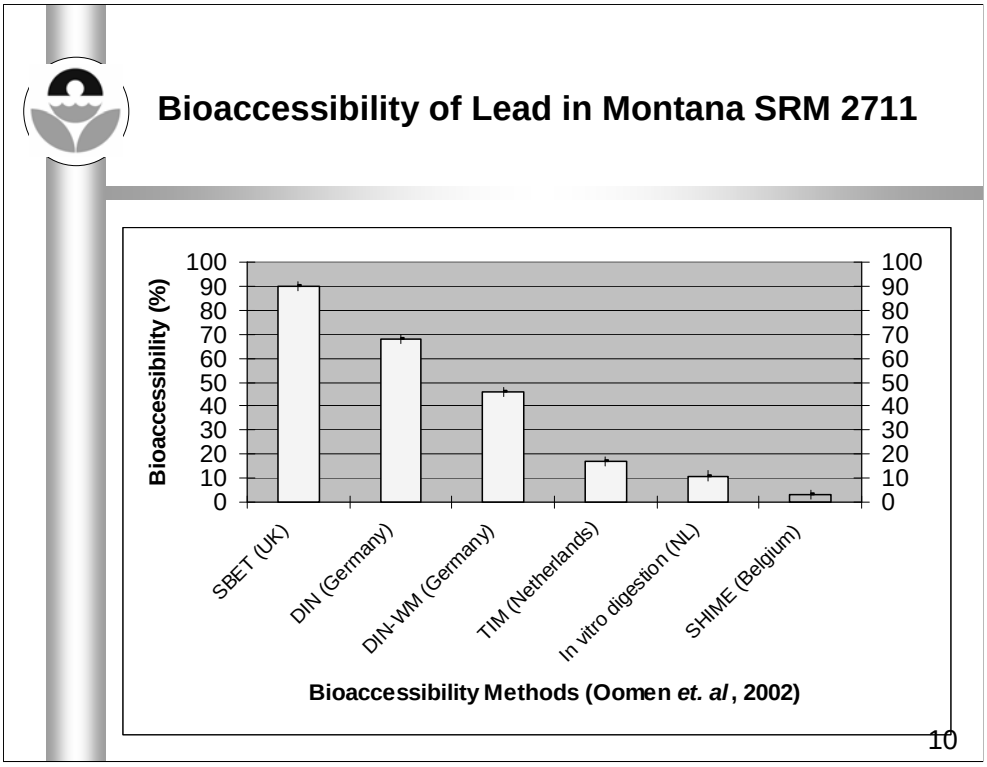

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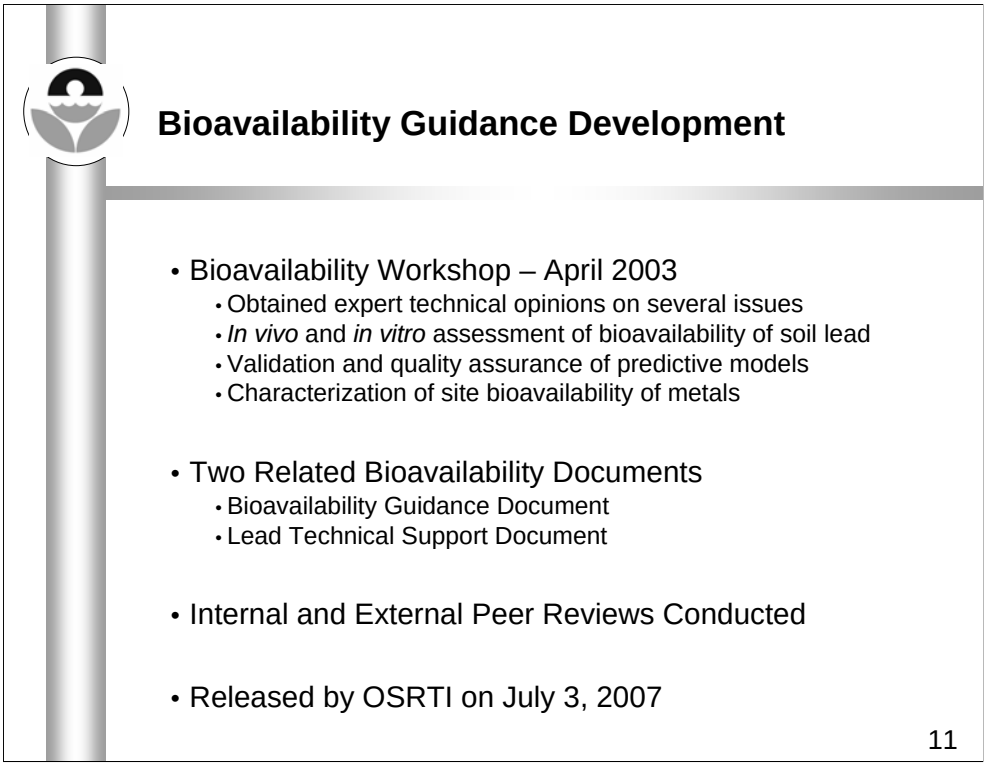

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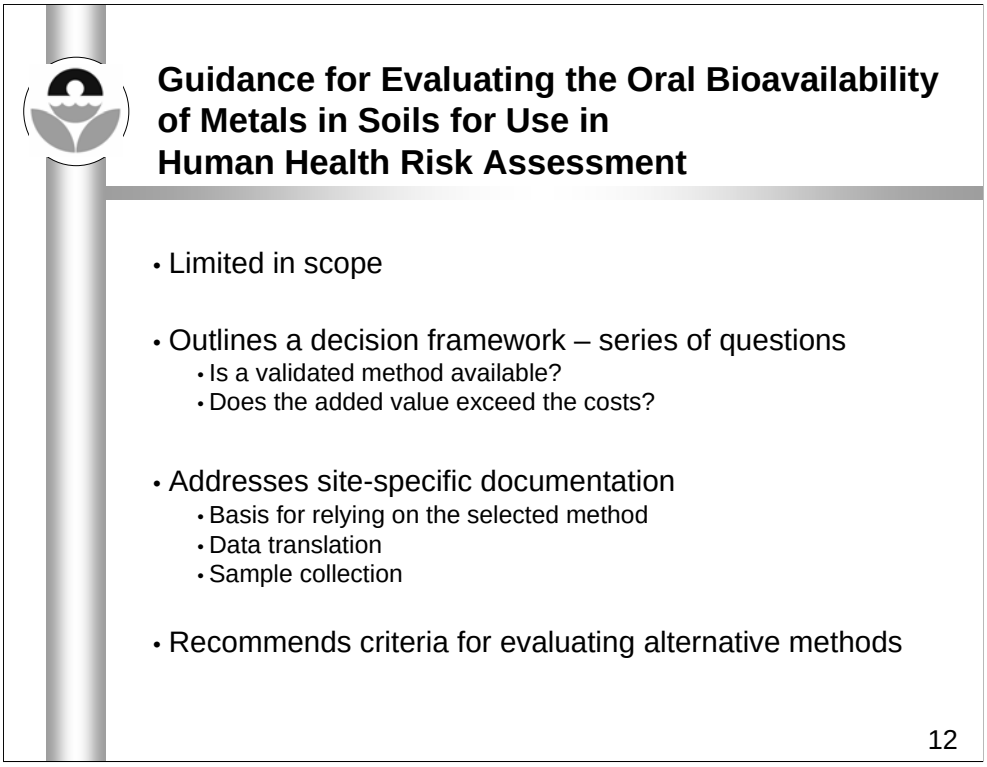

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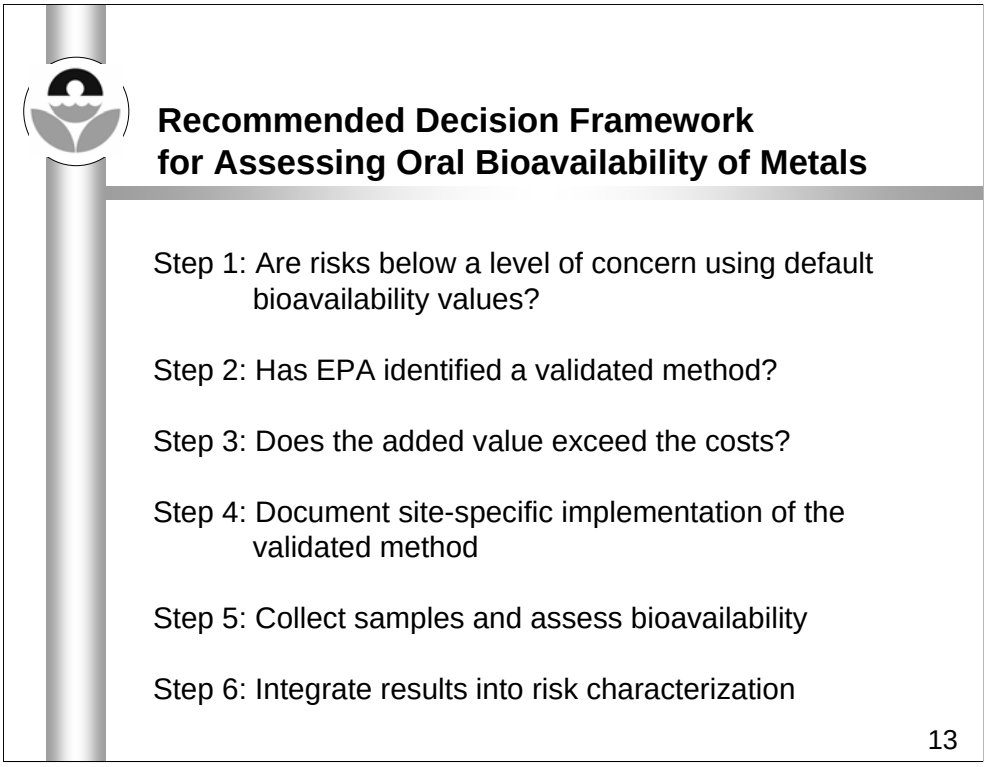

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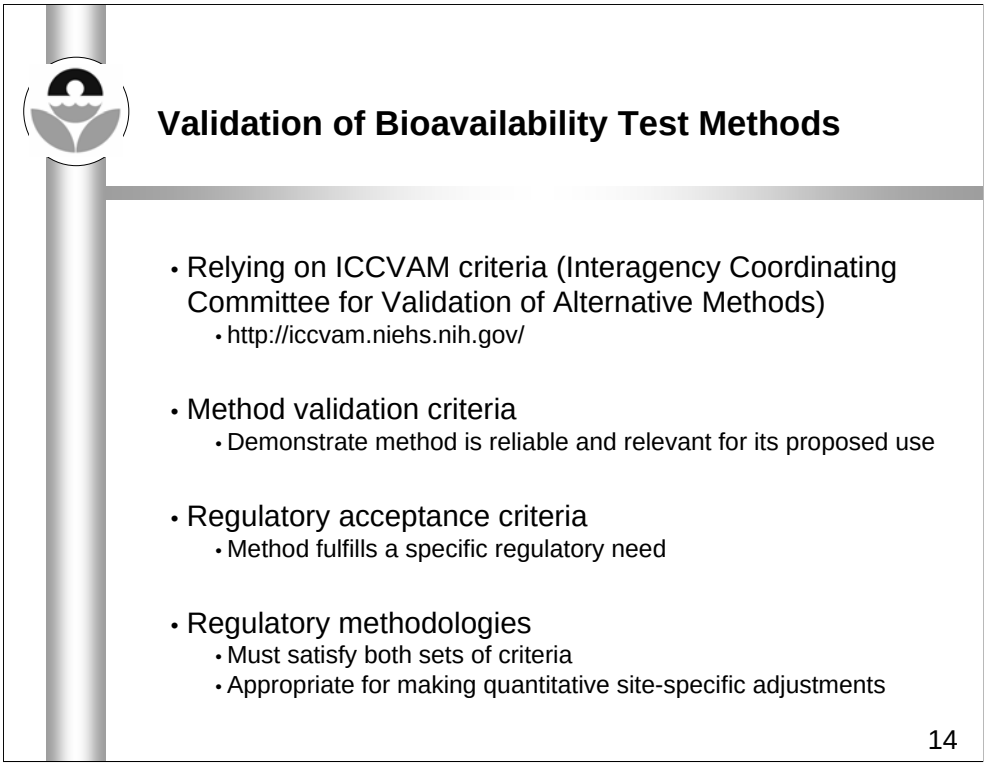

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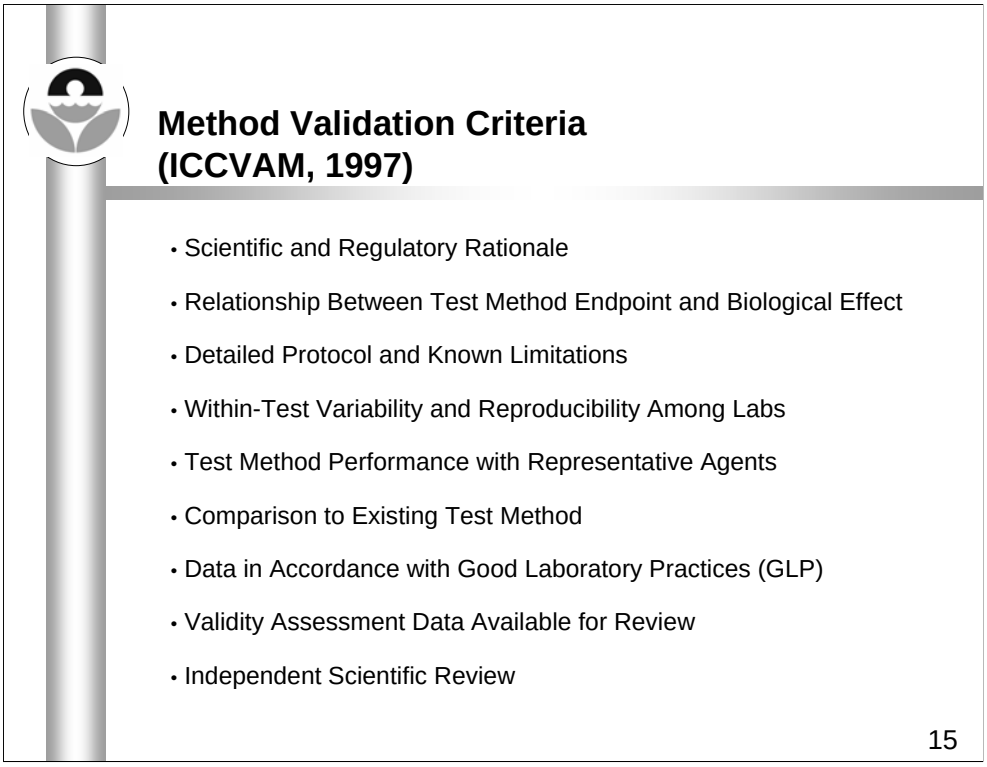

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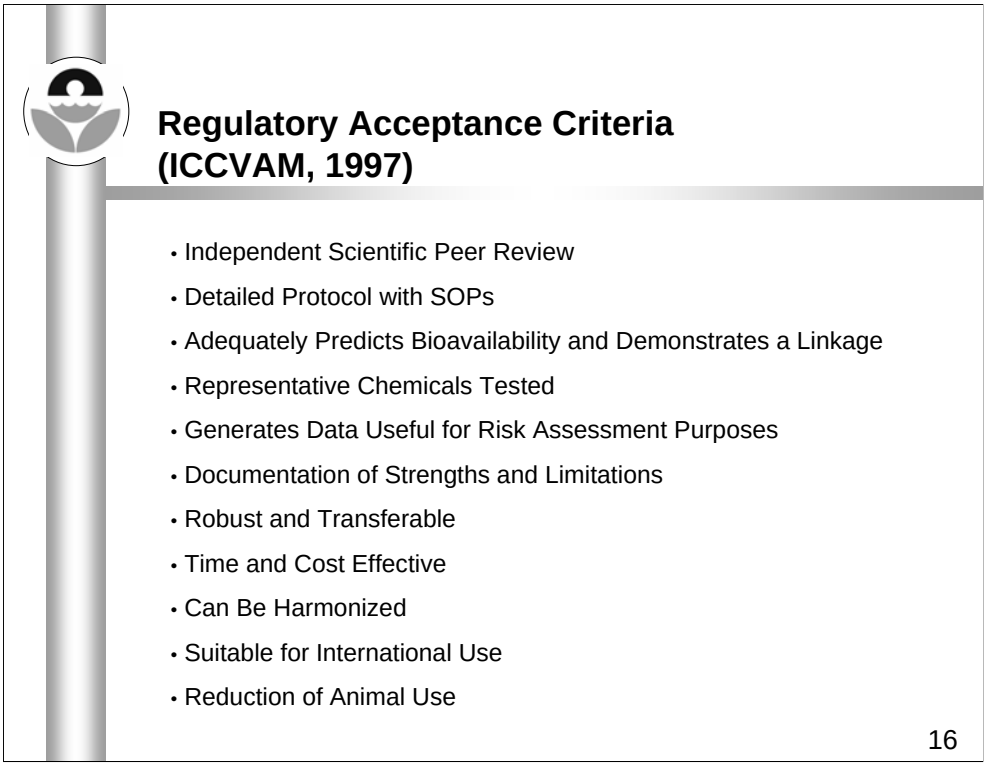

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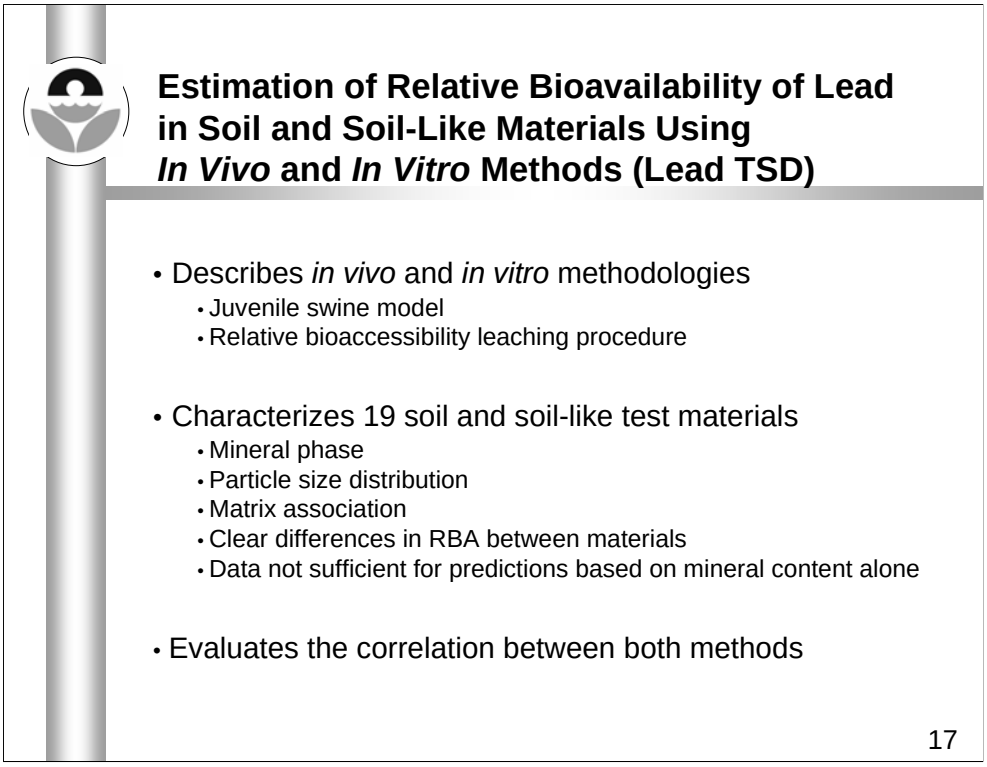

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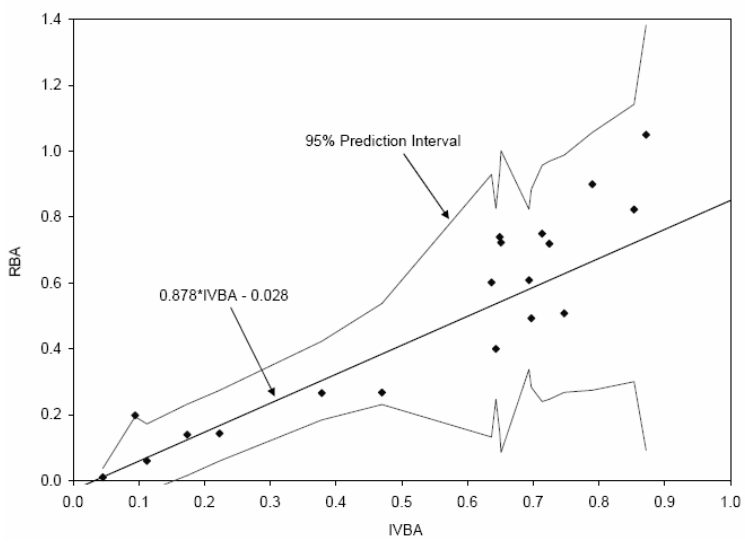
Lead – Correlation Between *In Vivo* RBA and *In Vitro* Bioaccessibility (IVBA)



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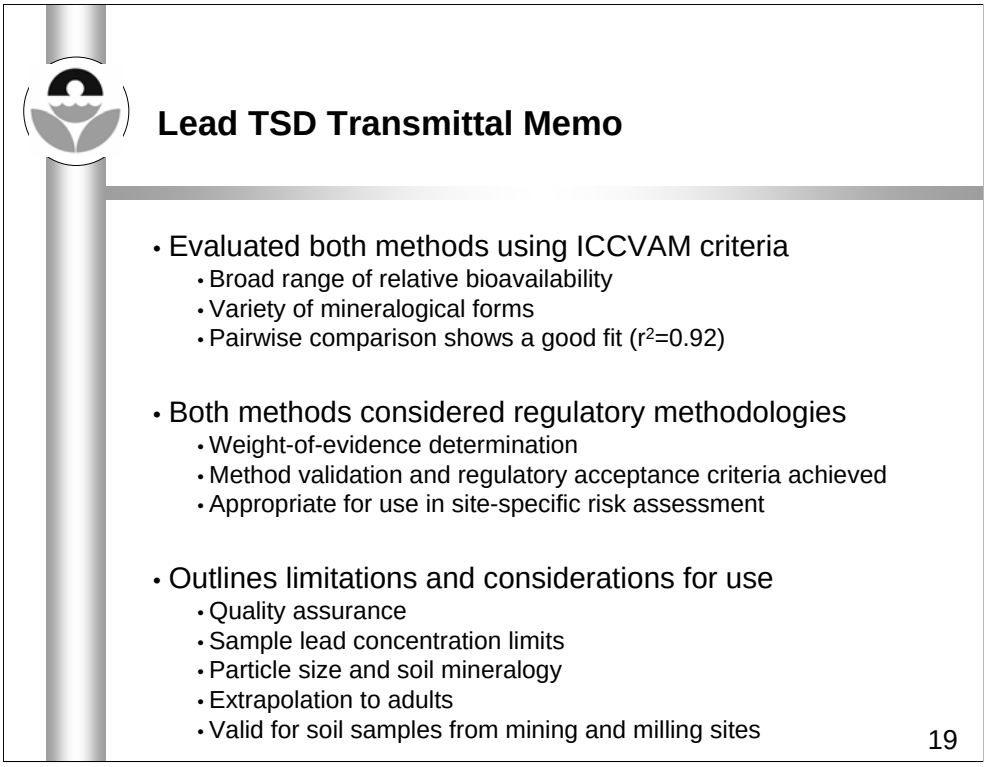

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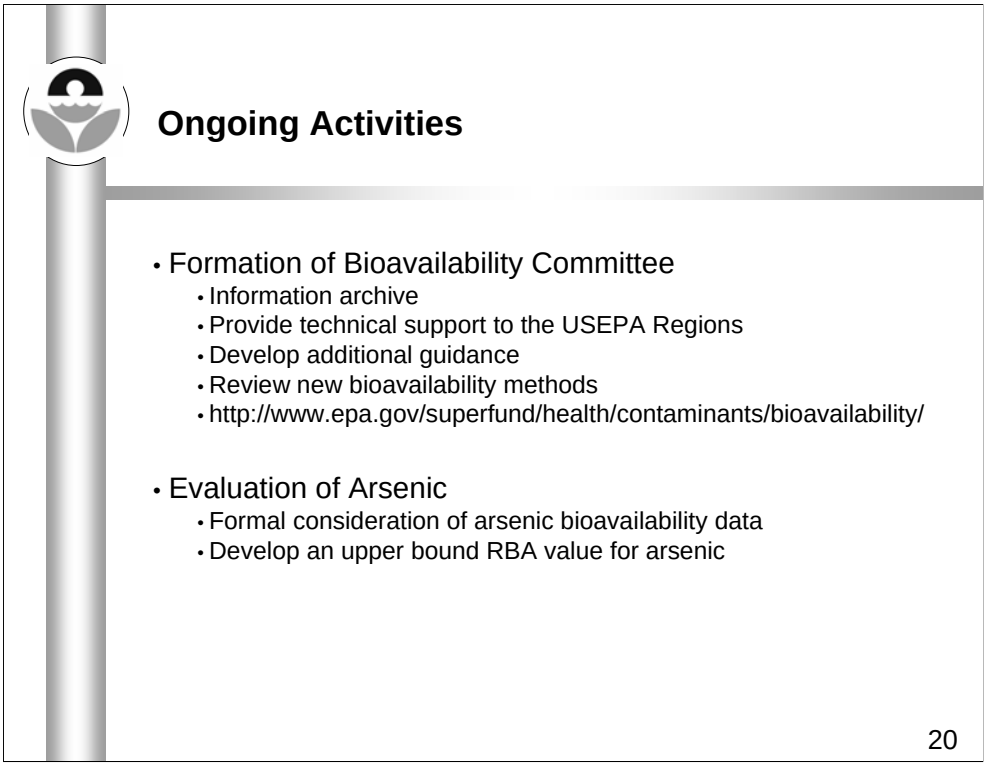

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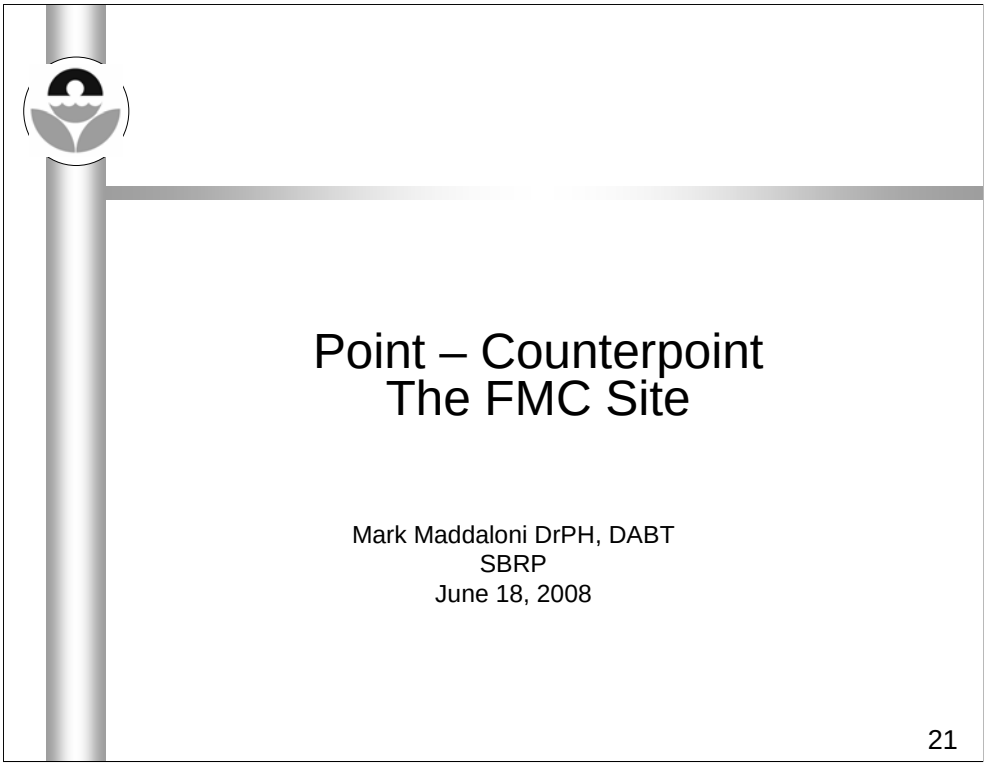

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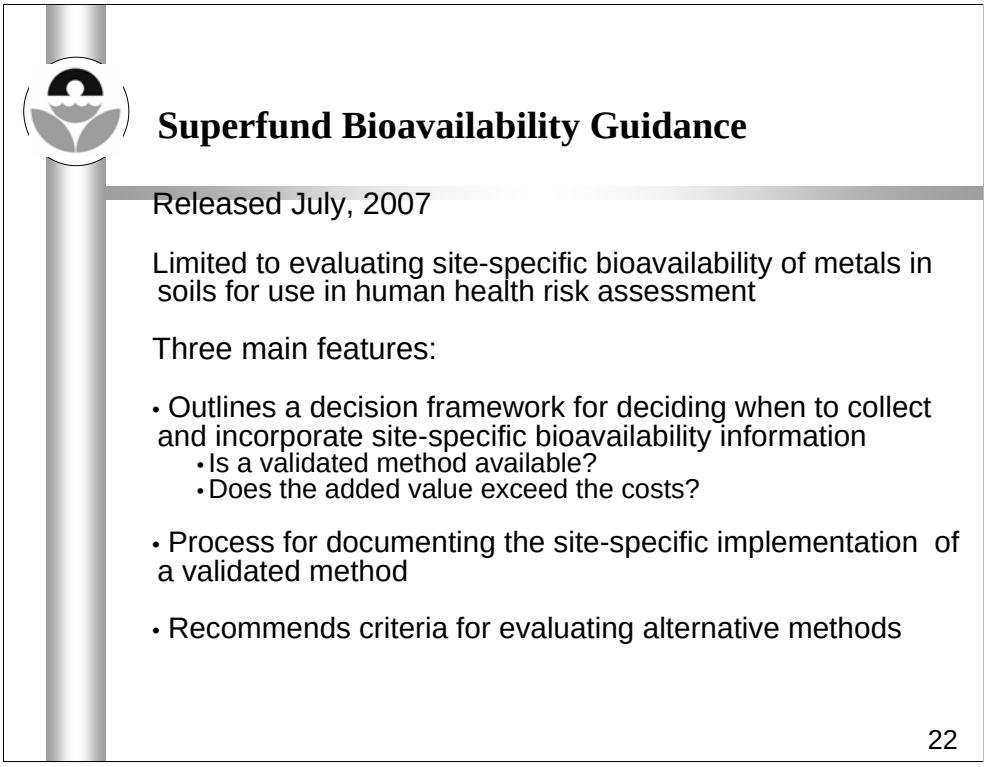

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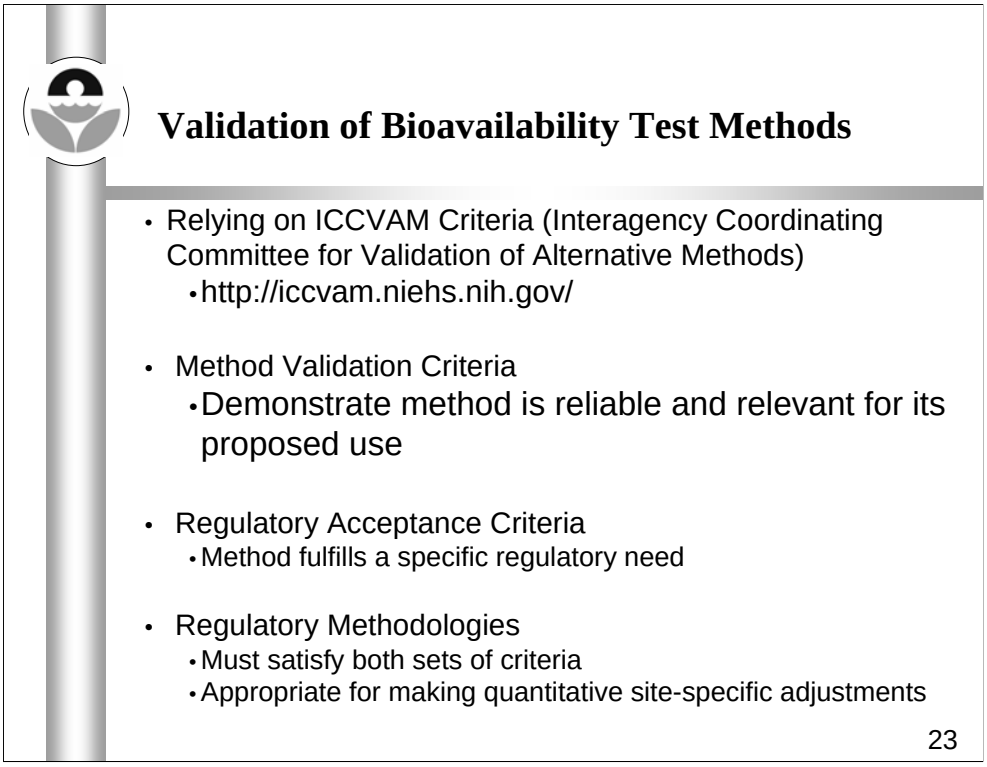

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Middleport Former Arsenic Pesticide Plant

- Production stopped in the 1970s
- Offsite arsenic due to air deposition and runoff
- High proportion of land area former orchardland
- Biomonitoring did not detect exposures
- Oral and dermal bioavailability examined

What bioavailability studies have been done with Middleport soils?

- 1995 study showed arsenic bioavailability was only 20 percent compared to arsenic dissolved in water.
- Recent studies directed by Yvette Lowney and Mike Ruby of Exponent (part of SERDP grant).
- Electron microprobe studies have found less soluble mineral forms of arsenic in Middleport soil (Univ. of CO).
- An oral bioavailability study in monkeys has shown reduced arsenic absorption from soil (19-28% relative bioavailability) (Univ. of FL).
- A monkey study of dermal absorption has shown that soil arsenic absorption across skin is negligible (Univ. of CA).

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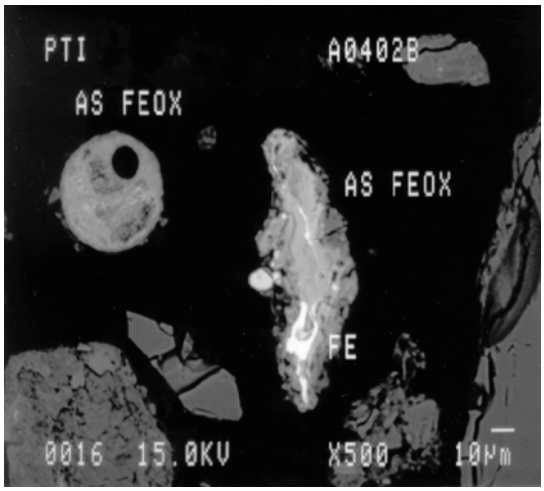
Soil Arsenic Mineralogy Supports Bioavailability Study Results

Most arsenic is associated with iron oxides or arsenic-iron oxides.



Photomicrograph of Arsenic-Iron Oxide Grain

Relative Oral Bioavailability Studies of Arsenic in Cynomolgus Monkeys

- Conducted by Dr. Stephen Roberts at the University of Florida in collaboration with Yvette Lowney
- Results for 14 soils from 12 sites
- Positive and negative reference materials also tested
- Results published in 2007 in *Toxicological Sciences*

Selection of Research Model

- Arsenic
  - Simple pharmacokinetics
  - Rapid elimination
- Use of cynomolgus monkey vs. swine
- Primates phylogenetically closer to humans
- GI physiology — similarities to human
- Evaluated for bioavailability research in the study of pharmaceuticals
  - "Good model for oral bioavailability in humans" (Ikegami, 2003)

Study Design

- Low arsenic diet prior to dosing
  - Dosed with slurry of soil in water Soil dose </= 1 g/kg bw
  - Arsenic dose </= 1 mg/kg bw
- Collection of urine and feces
- Five animals received each treatment

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Study Design – Reference Doses

- Intravenous administration of sodium arsenate (1 mg As/kg bw)
- Oral dosing of sodium arsenate by gavage (3 dose levels)
- Oral dosing of sodium arsenate mixed with soil
- Oral dosing of arsenopyrite (FeAsS) mixed with soil

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Relative Bioavailability (RBA) Calculations

- RBA = (% of soil As dose in urine) – (background)
- (% of soluble As dose in urine) – (background)

- *Corrections made on animal-specific basis

Soil Arsenic Relative Bioavailability

Soil Sample	Relative Bioavailability[a]
WAOS	**0.24** ± 0.09
NYOS	**0.15** ± 0.08
NYF-5B	0.19 ± 0.05
NYF-8B	0.28 ± 0.10
NYF-13B	0.20 ± 0.10
AsPyrite spike	**0.002** ± 0.003
Arsenate spike	**0.94** ± 0.05

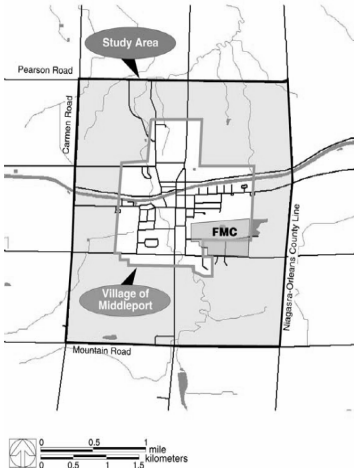
[a] Relative Bioavailability = % Dose in urine (soil) / % Dose in urine (arsenate)
Results expressed as mean ± SD (N=5)

Middleport Environmental Exposure Study - 2003

- Conducted by Exponent independent of FMC
- Review of study design and results overseen by an independent panel of experts*
- Participation was voluntary
- Results have been published in *Env. Health Perspectives*

*Members of the scientific advisory panel:
D. Barr, R. Bornschein, F. Frost Jr., D. Gute, P. Kostecki, H. Pastides, and P. Succop

Middleport Study Area



Middleport Environmental Exposure Study Design

- Participants – 439 of 1,930 residents in study area, including 77 of 164 children < 7 years old.
- Collected first morning urine sample on 2 days, analyzed for total and speciated As and for creatinine, plus toenail samples (84).
- Collected soil from yards (84), gardens (23), and play areas (28), plus indoor dust (111) and vegetables (42 gardens).
- Administered questionnaire on demographic, socioeconomic, and behavioral information and housing characteristics.

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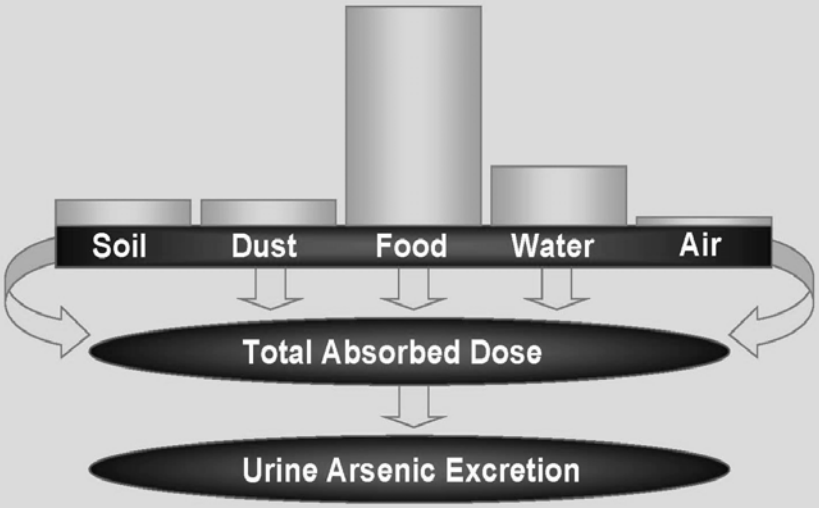
Contributions to Background Arsenic Exposures



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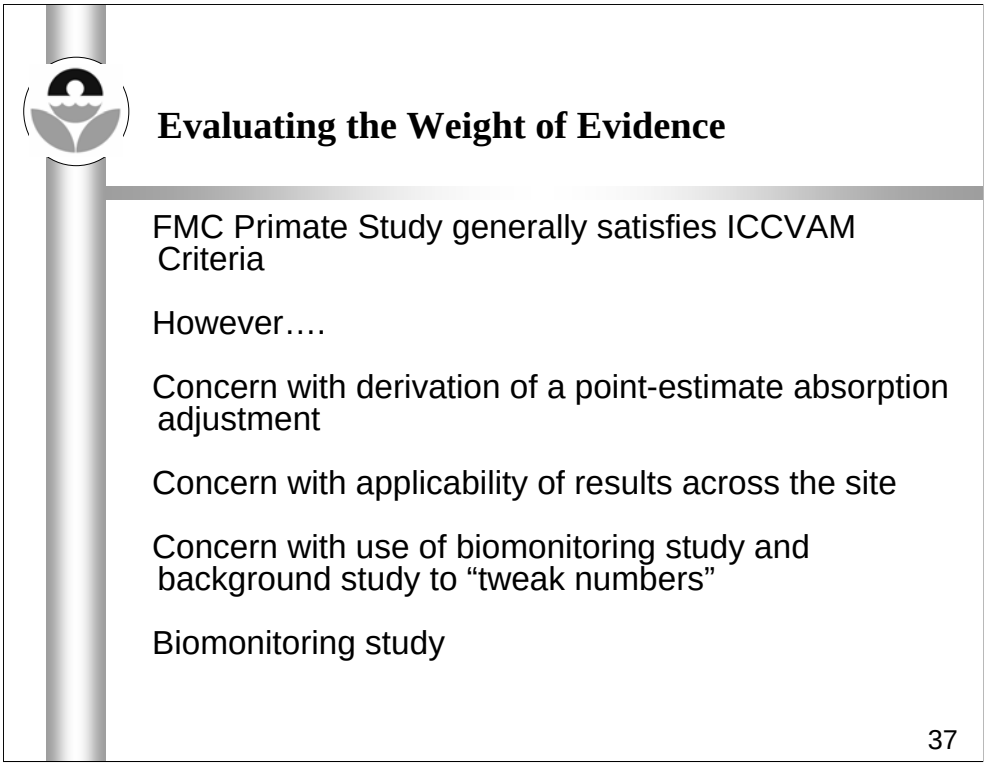
General Conclusions

- Low level As presence in soils (i.e., <50ppm) is widespread in the U.S.
- In most cases, the amount of As that could be absorbed from soils is small compared to natural sources (i.e., diet)
- There is no measurable difference in exposure and health risk from soil containing 20 or 50 ppm of arsenic



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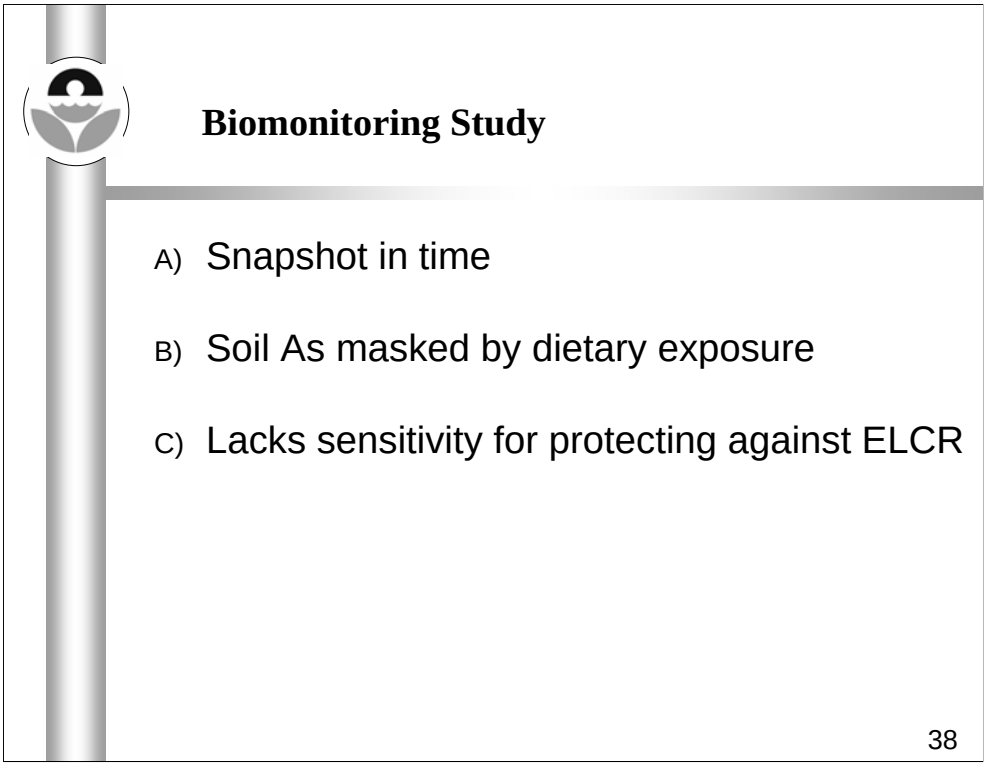

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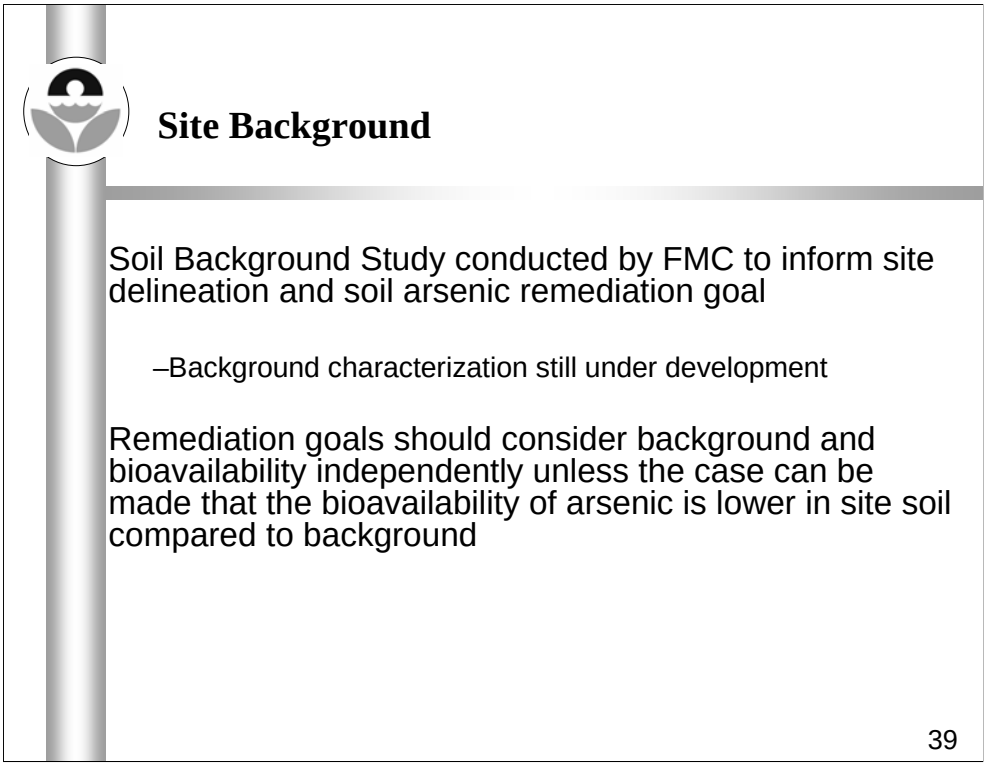

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