Integrated Exposure Uptake Biokinetic (IEUBK) Model for Lead in Children

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U.S. EPA Technical Review Workgroup Lead Committee **www.epa.gov/superfund/lead**

Overview of IEUBK Model

- Introduction
  - Why do we need models?
- The IEUBK Model — Structure and Components
- Discuss IEUBK Model Inputs
  - Review data entry windows and input variables, and why some are controversial
- Risk Assessment Issues and Guidance
- Calculation of Blood Lead Concentration, Risk Calculation & Hazardous Waste Site Cleanup Goals (PRGs)

What is a Biokinetic Model?

- Biokinetic models assess the routes of environmental exposure to a substance and determine the distribution of this substance among the various body tissues in humans.

- Biokinetic models work best when there is a known effect that is associated with a specific tissue concentration in humans.
  - *e.g.,* reduced IQ in children at 10 µg Pb/dL blood

- Biokinetic models also enable the risk assessor to predict the relative effect of an increase in body tissue that might result from a specific increase in environmental exposure.
  - *e.g.,* the expected blood lead concentration that would result from an increase in soil lead concentration to 750 mg/kg

Lead Risk Assessment is Different

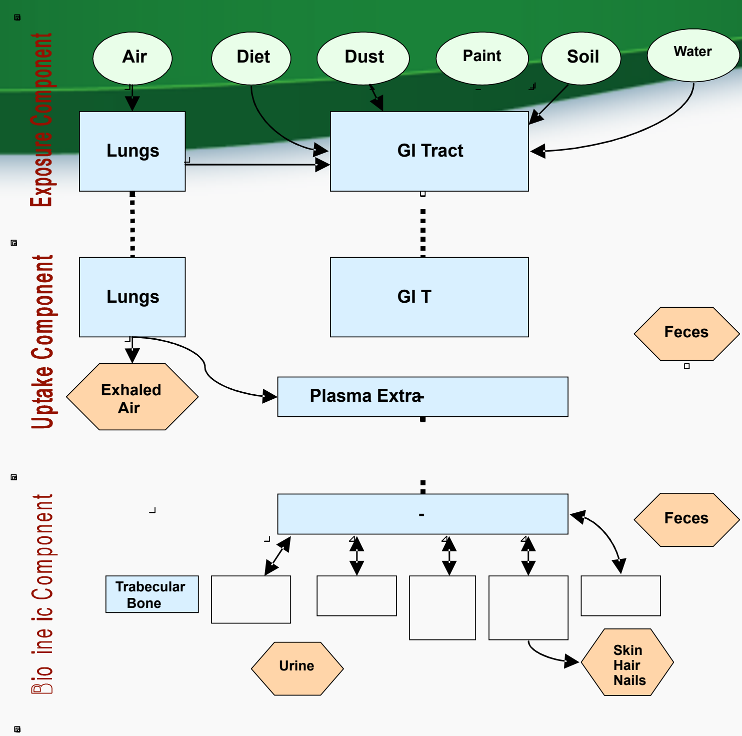
- In comparison to most other environmental contaminants, the degree of uncertainty about the health effects of lead is quite low.
- Some of these effects, such as aspects of children's neurobehavioral development (IQ), may occur at blood lead levels so low as to be essentially without a threshold.
- U.S. EPA regulates lead exposure by using a biomarker (blood lead concentration).
- Environmental exposures to lead are <u>modeled</u> to predict blood lead levels associated with those exposures.
- The blood lead level was established as 10 µg/dL as the U.S. Federal level of concern in 1991 by U.S. CDC and adopted as U.S. EPA policy for Superfund in 1994.
  - Recent epidemiological evidence has demonstrated measurable IQ losses in children at 10 µg/dL, down to 5 µg/dL and possibly lower (CASAC, 2007; OPPT SAB Dust Lead Hazard Standard, 2011)

OSWER Lead Risk Assessment Policy

- The IEUBK Model as the primary tool to generate residential risk-based soil cleanup levels in the United States.
- U.S. EPA's Superfund risk reduction policy is for no child to have greater than a 5% probability of having a blood lead level >10 μg/dL.
- Modeling is used to associate environmental exposures with risk and inform cleanup decisions (relative to U.S. EPA's risk reduction goal).
- In general, blood lead monitoring survey data should not be used as the only basis for cleanup decisions.

Purpose of the IEUBK Model

- Predicts the blood lead concentration in children (<7 years old) who are exposed to environmental lead from many sources.
- Predicts the risk (probability) that a typical or hypothetical child exposed to specified media lead concentrations will have a blood lead level ≥10 µg/dL (the blood lead level of concern).
- Predicts cleanup levels for various media for residential land use.
  - Assesses risk and determines cleanup levels for trespasser or recreational scenarios.



To calculate the probability of exceeding the 10 µg/dL level (P_{10}):

$$Z = [\ln(10) - \ln(GMPbB)] \,/\, \ln(1.6)$$

$$P_{10} = 1 - P < Z \text{ (expressed as a percent)}$$

Environmental Media

Body compartment or elimination pool required in more than one component

Elimination Pools of the Body

Body Compartments

Intake – Uptake – Biokinetic Relationship

- Daily **Intake** of lead is calculated as follows:

  Intake = Media Concentration x Media Intake Rate

$$\mu g\ lead/day = (\mu g\ lead_{media} / grams_{media}) \times (grams_{media} / day)$$

- **Uptake** is calculated based on media-specific absorption values (defaults are available):

$$Uptake_{media} = Intake_{media} \times Absorption\ Factor_{media}$$

- **Biokinetic** module estimates transfer rates for Pb moving between compartments and through elimination pathways to derive a predicted long-term steady-state geometric mean PbB concentration.

- In the final step, the **Probability** module estimates a plausible distribution of PbB concentrations for the population (based on the geometric standard deviation). The distribution is centered on the geometric mean PbB concentration calculated by the Biokinetic Module.

History of the IEUBK Model Development

Product of many years of development

- 1985–1989: Initially Office of Air Quality Planning Standards
- 1989: Development by Superfund following SAB review
- 1989–2001: DOS version (0.99d) development
- 1994–2001: Release of 0.99d version by Superfund with input from EPA, ATSDR, CDC, and SAB
- 1998: Independent Validation and Verification (IV&V)
- 1997–2001: IEUBK (0.99d) was converted to Windows
- 2001–present: IEUBKwin 1.0 and IEUBKwin 1.1
- 2005: NAS review

Independent Reviews of the IEUBK Model

The reviewers have generally found that the model was scientifically sound and useful for lead risk assessment.

- 1990: SAB review for NAAQS
- 1992: SAB review and External Peer Review of model
- 1998: Independent Validation and Verification
- 1998: SAB review for TSCA Section 403 Regulation
- 2005: National Academies of Science (NAS) review for Coeur d'Alene site report

Evaluation of the IEUBK Model

Validation evaluated the following:

- Scientific underpinnings of the model structure
- Adequacy of parameter estimates
- Mathematical relationships (as computer code)
- Empirical comparisons (predicted vs. observed)

The process and results of the IEUBK Model validation are available online (TRW web site)

- 1994 Validation Strategy for the IEUBK
- 1998 Empirical Comparisons Manuscript (Hogan et al., 1998)

IEUBK Model Predictions vs. Observed PbB

Comparison of Observed and Predicted Geometric Mean Blood Lead and Risk of Exceeding 10 µg/dL

Dataset	N	Observed Blood Lead (µg/dL) GM (95% CI)	Observed Blood Lead (µg/dL) Percent >10 (95% CI)	Model Predictions (µg/dL) GM (95% CI)	Model Predictions (µg/dL) Percent >10 (95% CI)
Galena, KA Jasper Co, MI[a]	111	5.2 (4.5–5.9)	20 (13–27)	4.6 (4.0–5.3)	18 (11–25)
Madison Co, IL[a]	333	5.9 (5.5–6.4)	19 (15–23)	5.9 (5.4–6.3)	23 (19–28)
Palmerton, PA[b]	34	6.8 (5.6–8.2)	29 (14–44)	7.5 (6.6–8.6)	31 (16–47)

Excerpts from Air Criteria Document for Lead (October 2006). Original data from Hogan et al. (1998)

[a]Children away from home ≤10 hours/week
[b]Children away from home ≤20 hours/week

CI = confidence interval; GM = geometric means

Sensitivity Analysis

- Predicted PbB and total lead uptake were most sensitive to the amount of soil/dust ingested per day.
- Predicted PbB and total lead uptake were moderately sensitive to the following (listed in decreasing relative sensitivity):
  - Absorption fraction for soil/dust and diet
  - Soil lead concentration
  - Indoor dust lead concentration
  - Dietary lead concentration
  - Contribution of soil lead to indoor dust lead
  - Half-saturation absorbable intake (based on output-input ratio)
- The predicted probability of exceeding a specified level of concerns is very sensitive to changes in the GSD.

IEUBK Strengths and Limitations

Strengths

- Integrates multimedia exposure and relates it to a well-characterized biomarker of effect
- Risk predictions and PRG over a range of exposure scenarios
- Inputs tailored to support Superfund site risk assessment
- Risk information complementary to a public health (PbB) study or when no public health (PbB) study is available

Limitations

- Cannot assess short-term, periodic or acute exposures (exposures must be for ≥1 day/week for 90 consecutive days)
- Cannot assess pica exposures
- Cannot assess dust exposures using loading data
- Cannot assess age groups >7 years

Effectiveness of Remedial Response

Superfund Site	Pre Remedial Average PbB (year)	Post Remedial Average PbB (year)
Bunker Hill, ID	~65 µg/dL (1974)	2.7 µg/dL (2001)
Jasper, UT	6.2 µg/dL (1991)	3.8 µg/dL (2000)
Midvale, UT	5.6 µg/dL (1989)	3.0 µg/dL (1998)
Tar Creek, OK	~24 µg/dL (1997)	~4 µg/dL (2000)