THE IEUBK MODEL FOR LEAD IN CHILDREN

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IEUBK Model Development

• Developed from a conceptual design based on published biokinetic data
• Computer code written in C++
• Calibrated with actual blood lead studies
• Validated according to existing standards
IEUBK Model Development

- Model was developed 1990-1993 by a team of EPA scientists
- The team later organized the Technical Review Workgroup (TRW) for Lead to support the public use of the model
  - TRW website: www.epa.gov/superfund/programs/lead/
IEUBK Model Design

- Two earlier lead models formed the conceptual basis for the IEUBK model
  - ECAO (now NCEA) multi source exposure model
  - OAQPS biokinetic model based on Harley and Kneip data
- Absorption interface developed to link the two models
USER OPTIONS

- Most exposure and absorption coefficients are user selectable.
- All biokinetic parameters are inaccessible to the user.
IEUBK Model Structure

- The compartmental approach follows the design of Harley and Kneip

- Compartments represent fluid volumes and organ weights
• For each time step, an incremental mass of lead is added to and transferred from each compartment

• Lead is tracked as a function of red blood cell concentration to maintain physiologically significant limits
• Each compartment increases in mass at each time step, simulating the specific growth of the organ or tissue.
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Transfer Limited - 
“Compartimental”

\[ \frac{dM_1}{dt} \cong k_{12} \cong M_1 \% k_{21} \cong M_2 \cong 0 \]

\[ \cong k_{12} \cong V_1 \cong C_1 \% k_{21} \cong V_2 \cong C_2 \cong 0 \]

let \( k_t \cong k_{12} \cong V_1 \cong k_{21} \cong V_2 \)

\[ \frac{dM_1}{dt} \cong k_t (C_1 \& C_2) \]

Units: \( \frac{\text{mass}}{\text{time}} \cong \frac{\text{volume}}{\text{time}} \times \frac{\text{mass}}{\text{volume}} \)
• The compartments represent anatomically and physiologically correct components of the body critical to lead uptake, storage, and elimination

• The compartments simulate physiological properties, not just kinetic properties
• Transfer between compartments is not directly related to blood flow, as is the case for many physiologically based pharmacokinetic models
Flow Limited - “PBPK”

\[
\frac{dM_{\text{blood}}}{dt} \rightarrow V_{\text{blood}} \approx \frac{dC_{\text{blood}}}{dt}
\]
\[
\rightarrow Q_{\text{blood}}(C_{\text{blood}} & [C_2])
\]

\[
\frac{dM_b}{dt} \rightarrow Q_b(C_b & [C_2])
\]

*Assume Steady State

Units: \(\frac{\text{mass}}{\text{time}} \rightarrow \frac{\text{volume}}{\text{time}} \times \frac{\text{mass}}{\text{volume}}\)
• The mass of lead in each compartment is recalculated for each time step

• The blood lead is reported as the Pb in the red blood cell compartment and in the plasma portion of the central plasma/ECF compartment
• the compartments grow synchronously and maintain physiologically significant concentrations of lead

• blood plasma and extracellular fluids are the mechanisms of transfer between compartments
• cortical and trabecular bone compartments typically accumulate the largest amount of lead, as much as 90% of the body burden in adults

• kidney and liver are important targets of toxicity
• There are three routes of elimination
  – urine
  – bile/feces
  – soft tissue: skin, hair and nails
• These outputs maintain the dynamic equilibrium with absorption inputs