Challenges in Defining A Safe Level: Lead Case Study

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Understanding of the Impact of Arsenic, Cadmium, and Lead Across the Food Supply
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Blood Lead Level (BLL) Targets for Children

- **< 2012** – CDC blood lead level (BLL) – health-based level of concern (LOC) for children – 10 μg/dL CDC
- **2012** – CDC concludes "no safe level" of lead; 97.5 percentile BLL of population = 5 μg/dL, blood lead reference value (BLRV); not health-based
- **2021** – CDC BLRV 3.5 μg/dL

• Risk management decisions for lead in house dust in homes with lead in paint
• Target population(s): US children and sub-populations, e.g., based on existing dust lead levels
• Estimates BLL from dust ingestion in children at different surface lead loadings
  • Lead in dust + other contributors (e.g., food) → total BLL

• 2 exposure models to estimate BLL percentiles at different surface loadings
  • IEUBK (Integrated Exposure Uptake Biokinetic) model to relate uptake of lead loadings in surface dust, μg/ft², (converted to dust lead concentrations in mg/kg) to BLL
  • Empirical model, epidemiologically based, to correlate dust lead loadings with BLL

• Multiple comparisons of BLL percentiles to:
  • Potential association with IQ decrement
  • Comparison to various BLL metrics, e.g., CDC BLRV (at the time) of 5 μg/dL
  • Selected surface loading levels (10 μg/ft² for floors, 100 μg/ft² for window wells) based on potential association with decrement of 0.7 – 0.8 IQ points and on BLL distribution in population
US FDA Interim Reference Level (IRL) for Dietary Lead Exposure in Women of Childbearing Age (WOCBA) (Flannery et al., 2020)

- Approach for WOCBA:
  - Protection of fetus
  - Target BLL = CDC 2012 BLRV of 5.0 μg/dL
  - Dietary lead intake to achieve BLRV in WOCBA
    - $5 \mu g/dL \, BLL / (0.04 \mu g/dL \, per \mu g \, lead/d) = 125 \mu g/d$
  - Intraspecies uncertainty factor of 10, variability in uptake of lead
  - IRL = 12.5 μg lead/d, associated with BLL of 0.5 μg/dL, 10X < BLRV of 5 μg/dL
- Conceptually similar analysis conducted for children, IRL 3 μg lead/d, associated with BLL of 0.5 μg/dL
- Concluded IRLs protective of other endpoints in WOCBA and children, *e.g.*, blood pressure
US EPA Regional Screening Level (RSL) for Lead in Soil (US EPA 2021)

- Target population: children at residential sites with contaminated soil, *e.g.*, mining towns
- Estimates BLL from ingestion of lead in soil, including background sources
  - Lead in soil + other contributors (*e.g.*, food) → total BLL
  - Uses IEUBK w/site-specific parameters, esp. for soil pathway, *e.g.*
    - Soil lead concentrations
    - Bioavailability of lead in soil *versus* default bioavailability
  - Other parameters, *e.g.*, food, often national databases
• BLL results
  • Mean BLL
  • 95th percentile BLL population based on BLL GSD (measure of distribution of BLL)
• Use BLL predictions for potential risk management activities, e.g., revegetation, soil removal
  • ≤ 5 % probability for individual child or population of children exceeding 10 μg/dL (LOC) ~ 400 mg lead/kg soil
• Still recommended as screening soil lead level
• Implications of 2021 BLRV of 3.5 μg/dL for 95th percentile?
  • Not health based
  • Potential to result in unrealistically low soil lead limit
Conclusions

• Some challenges with predicting and using BLLs
  • BLL predictions
    • Differences in pharmacokinetic assumptions
    • Varying feasibility of comparison to empirical data
  • Approaches – different degrees of complexity
    • Lead in soil – simpler, incorporation of site-specific information
    • Lead in housedust – detailed characterization of uncertainty and variability
• What BLL targets to use?
  • A moving target!
  • Use of BLRV straightforward, but not health-based
Conclusions (cont.)

- Consideration of new information and approaches, e.g.,
  - ↓ in lead exposure from multiple sources over time (mostly, except for subpopulations)
  - Probabilistic approaches (stochastic human exposure and dose simulation (SHEDS) model)
  - Intermittent exposures
  - US EPA All Ages Lead Model (draft)
  - Other endpoints of interest, e.g., cardiovascular in adults (addressed explicitly in US FDA IRL)
- Note: other programs using different approaches, e.g.,
  - US EPA drinking water action level for lead & SHEDS model
  - US EPA National Ambient Air Quality Standard (NAAQS) for lead in air
  - Cal OSHA and Leggett+ model for worker exposure
  - Cal OEHHA Prop65 and maximum allowable dose level (MADL) for repro./dev. toxicity