# Challenges in Defining A Safe Level: Lead Case Study

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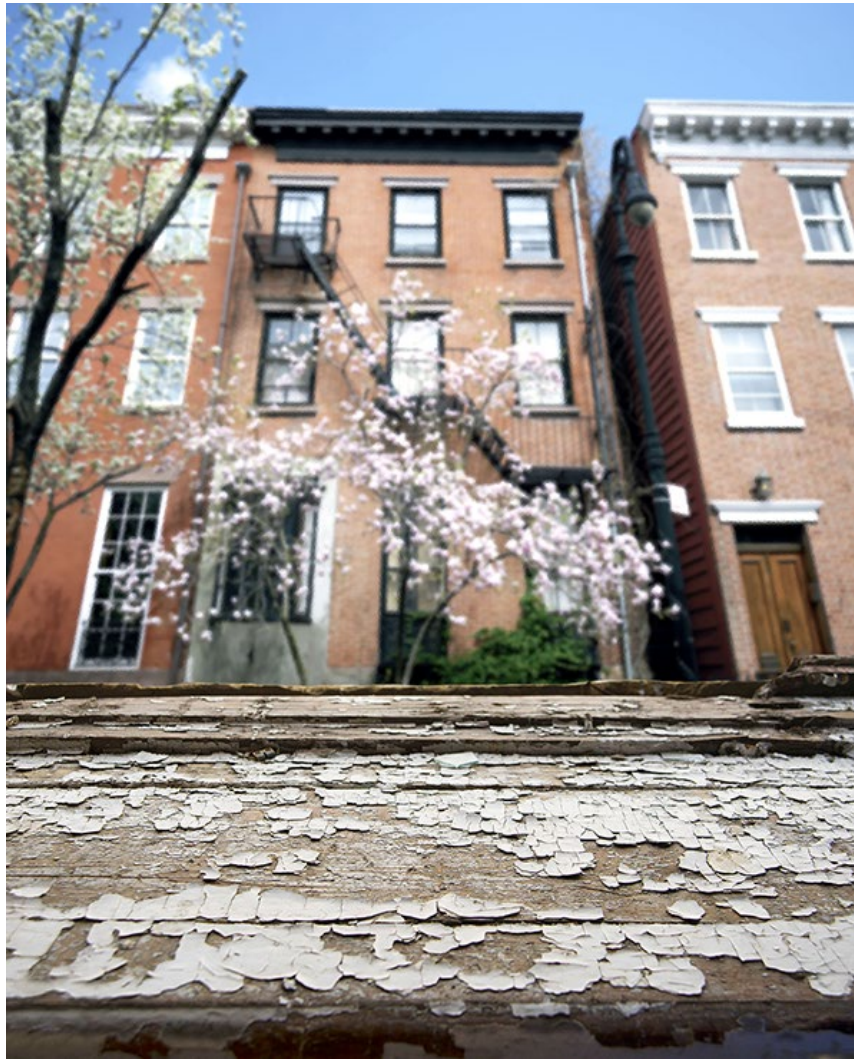
# Blood Lead Level (BLL) Targets for Children

- **< 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

# US EPA (2019) Residential Dust Lead Hazard Standards

- 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



# US EPA (2019) Residential Dust Lead Hazard Standards (cont.)

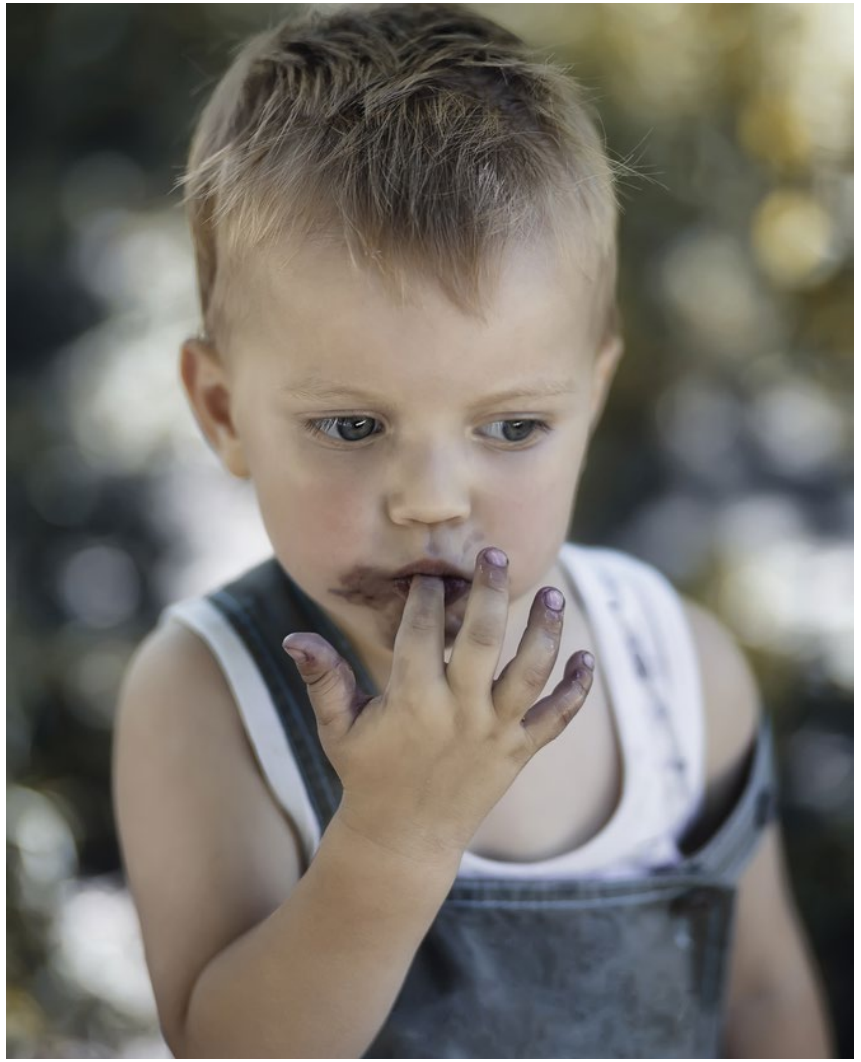
- 2 exposure models to estimate BLL percentiles at different surface loadings
  - IEUBK (Integrated Exposure Uptake Biokinetic) model to relate uptake of lead loadings in surface dust, µg/ft$^2$, (converted to dust lead concentrations in mg/kg) to BLL
  - Empirical model, epidemiologically based, to 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/ft$^2$ for floors, 100 µg/ft$^2$ 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 µg/dL BLL/ (0.04 µg/dL per µg lead/d) = 125 µg/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

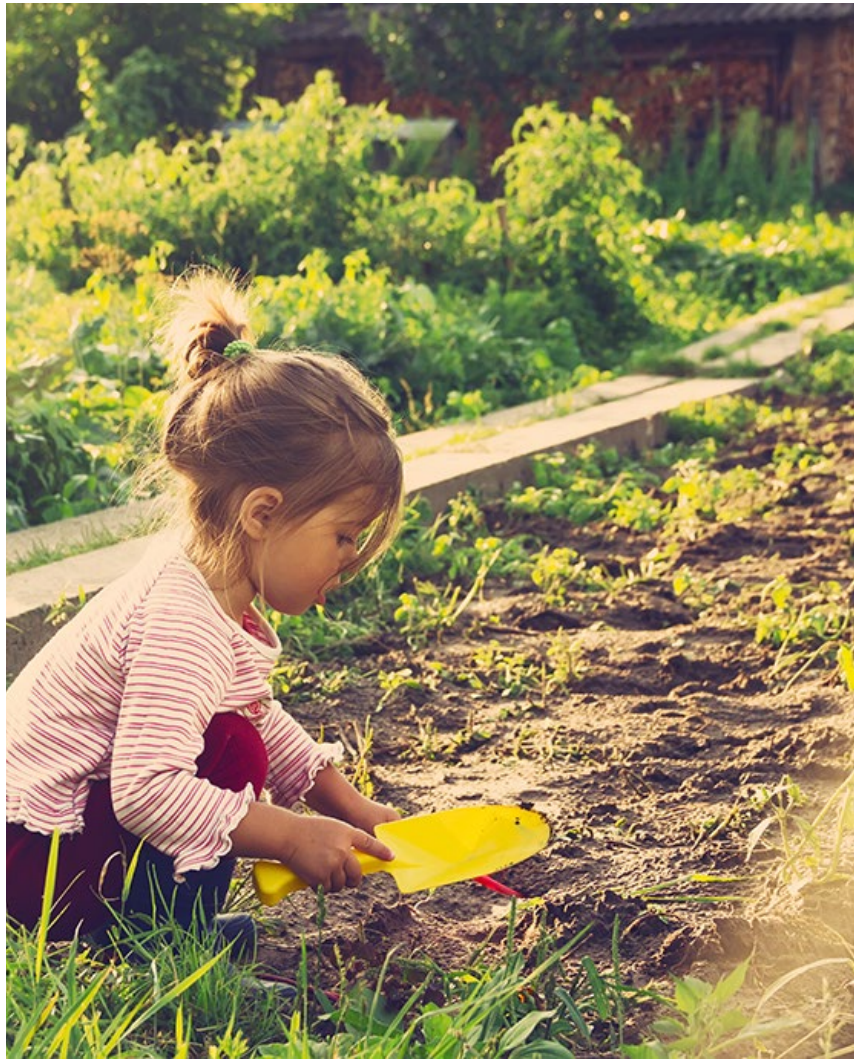
# US EPA Regional Screening Level (RSL) for Lead in Soil (US EPA 2021)

- 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



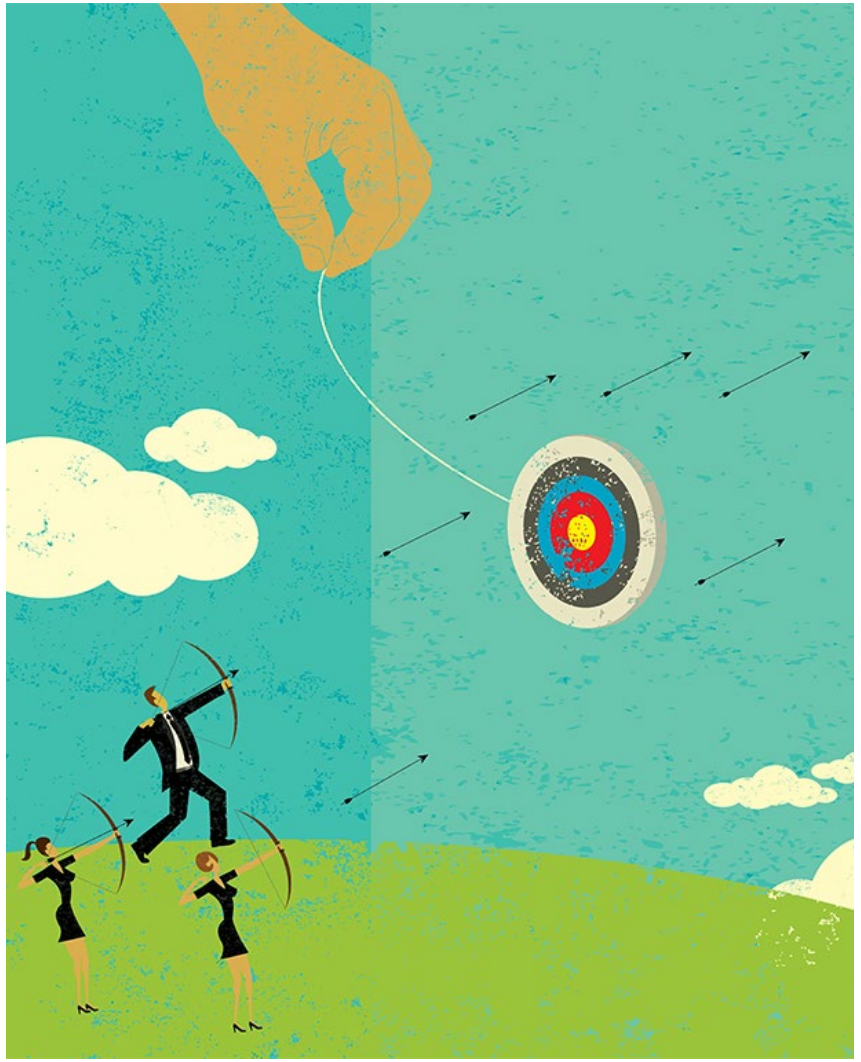
# US EPA Regional Screening Level (RSL) for Lead in Soil (US EPA 2021) (cont.)

- BLL results
  - Mean BLL
  - 95$^{th}$ 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 95$^{th}$ 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