

### **Toxicology of “The Big Four” (Pb, Hg, As, and Cd)**

What is considered safe? For a mother the only safe level of a toxic substance in anything ingested would be “zero.” However, we all know, “absolute” zero is a problem for quantitative science. Toxicity is influenced by many factors including age, weight, exposure route, organic compounds and forms of heavy metals (such as As) as well as metabolic differences.

### **Current Inputs for Assessing Acceptable Exposure for Metals:**

- 1.) Human and animal toxicity data associated with exposure to the metal (human data is of course, preferred).
- 2.) Likelihood of the presence of the metal in the article to be tested.
- 3.) Level and pattern of use or consumption of the article or product.
- 4.) Level of exposure to the metal
- 5.) Other sources of exposure to the metal
- 6.) Other factors that may affect toxicity (e.g., co-exposure to other metals)
- 7.) Data quality and individual variability
- 8.) Special populations at increased risk for toxicity.

### **Quantifying Toxicity:**

- 1.) Impact the development or functioning of the whole body or specific organs.
- 2.) “Toxicity threshold” – The dose below which adverse health effects are not expected to occur.
- 3.) Potential for adverse effects increasing as dose increases above toxicity threshold (dose response).

### **Dose Levels and Toxicity:**

- 1.) NOEL: No-Observed Effect Level.
- 2.) NOAEL: No-Observed-Adverse Effect Level.
- 3.) LOAEL: Lowest-Observed-Adverse Effect level.
- 4.) MTD: Maximum Tolerated Dose.
- 5.) LD(50): Lethal Dose to 50% of the population.

### **Reference Dose (RfD):**

- 1.) An estimate of the daily dose of a chemical that will avoid toxic effects other than cancer.
- 2.) NOAEL or LOAEL is adjusted by uncertainty factors (UF) to allow for differences in sensitivity to chemicals:
  - a. Human data UF = 10
  - b. Animal data UF =
    - i. 100 (NOAEL)
    - ii. 1000 (LOAEL)
    - iii. 1000 (NOAEL, less data)

3.) The Reference Dose (RfD) is used to calculate the Permissible Daily Exposure (PDE):  $RfD \times \text{weight} = PDE$ .

**Some Sources of toxicity Information:**

- 1.) IRIS – Integrated Risk Information Service.
- 2.) EPA Criteria Documents.
- 3.) HEAST – Health Effects Assessment Summary Tables.
- 4.) ATSDR – Agency for Toxic Substances and Disease Registry.
- 5.) Food and Drug Administration.
- 6.) Peer-Review literature.