A Holistic Look at Consumer Exposure to Lead, Cadmium and Arsenic, including Vulnerable Populations

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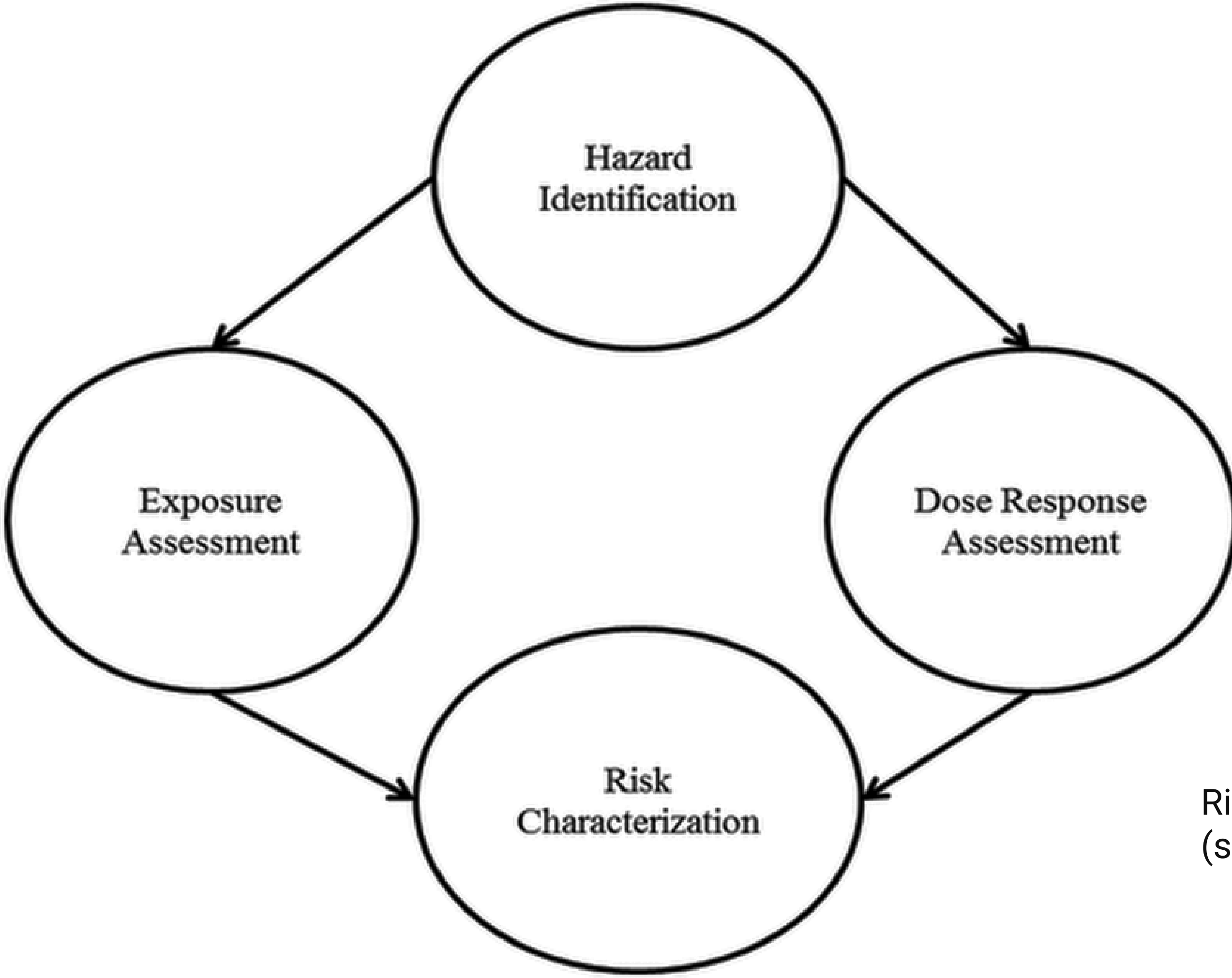
Overview

- **Routes of exposure**
- **Background on occurrence and sources of heavy metals in the environment and diet**
- **Dietary exposure assessment**
  - Objectives
  - Approaches
  - Data sources
  - Analysis considerations
- **Current publicly available exposure estimates**
- **Risk management considerations**
- **Conclusions**

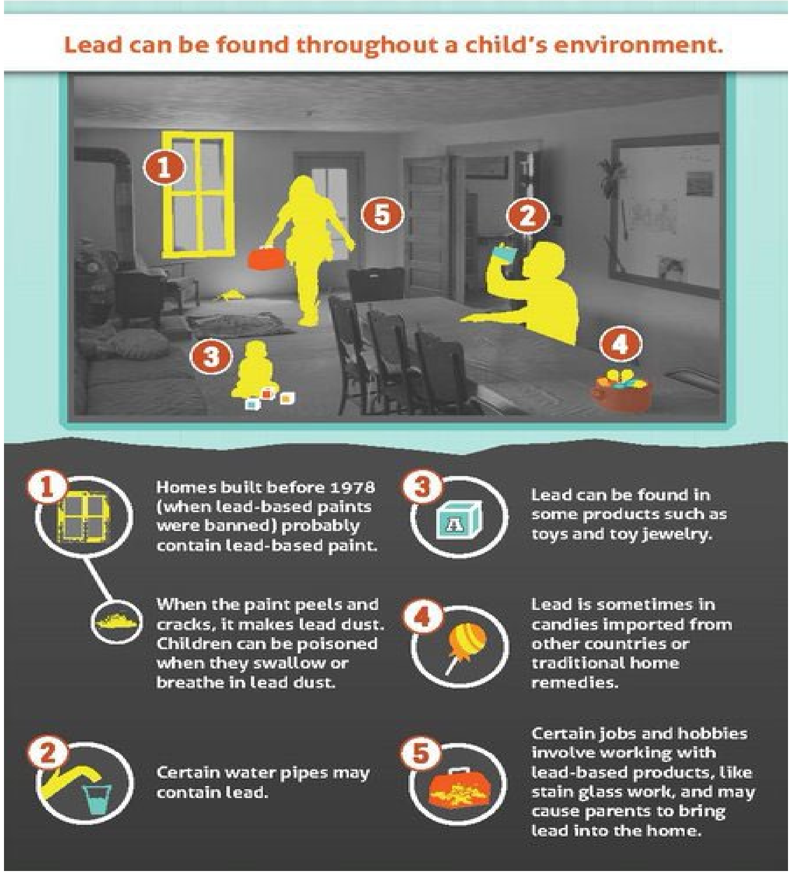
Exposure assessment as a component of risk assessment



Risk Assessment Model
(source: EPA, 1992)

Exposure assessment: Heavy metals

- Lead, arsenic, cadmium are ubiquitous in our environment
- Multiple potential routes of exposure
  - Soil
  - Dust
  - Air
  - Drinking water
  - Food



(Source: Lead in the Environment Infographic | Lead | CDC)

Contribution of exposure pathways to total lead exposure among children 0-2 years of age (Source: Zartarian et al 2017)

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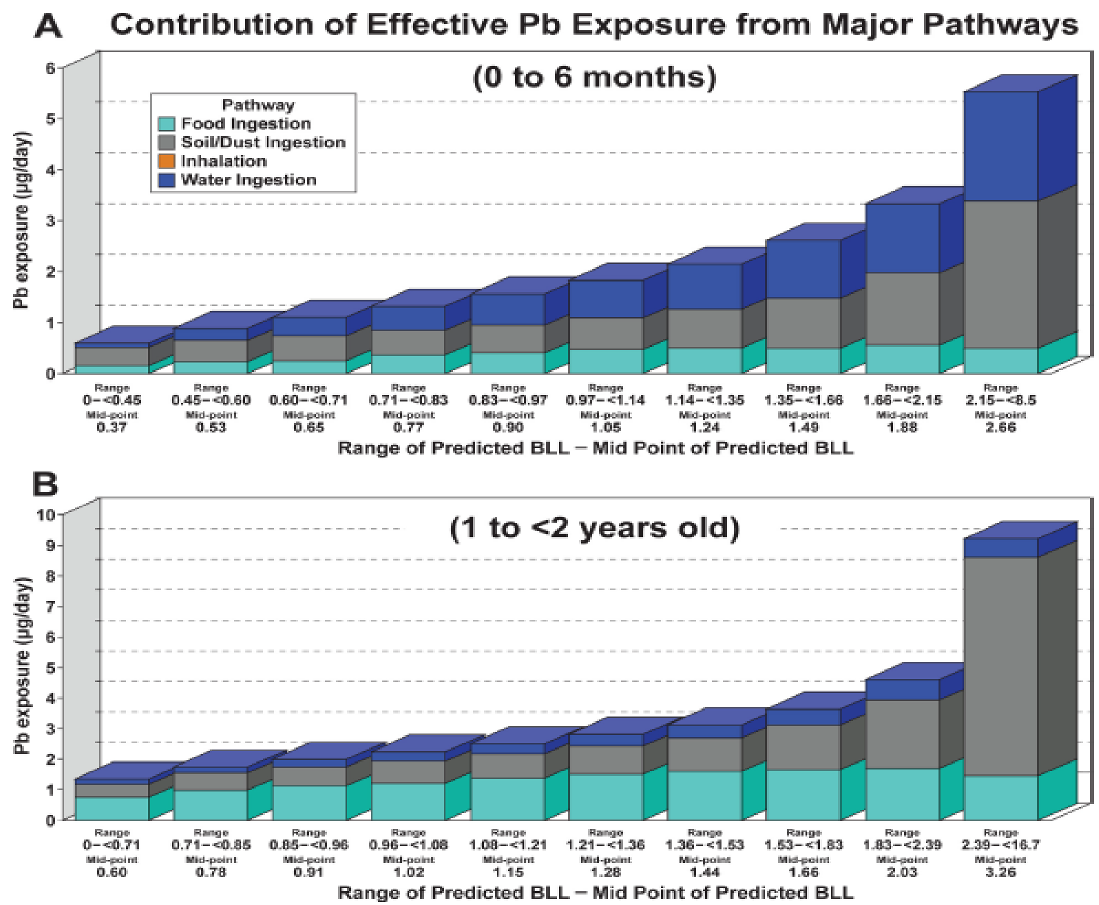

Figure 3. Estimated contribution of exposure pathways to BLL, for national scale. Bar charts provide Pb daily exposure contributions from diet, soil and dust ingestion, water, and inhalation from air for percentiles of the BLL distribution. The bars are 10% increments in the BLL distribution. The median BLL for each increment is indicated under each bar. Exposure in the figure is adjusted for bioavailability of Pb in each exposure pathway. Panel (*A*), national scale for 0- to 6-mo-olds; Panel (*B*), national scale for 1- to <2-y-olds.

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OCCURRENCE AND SOURCES OF METALS

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Arsenic

- **Arsenic (As) occurs in the environment from natural and anthropogenic sources**
  - Can be found in rocks, soil, and natural ground water.
  - Occurs in a wide variety of foods, including rice, vegetables, fruit and fruit juices.
- **Two primary forms:**
  - Organic (mostly non-toxic)
  - Inorganic (toxic) – typically present in natural ground water
- Primary exposure is food and drinking water among children (entering the food chain through water and/or soil) (EFSA 2014, ATSDR 2007).
- FDA has issued guidance on inorganic arsenic levels in apple juice and infant rice cereal

Cadmium

- Found in the earth’s crust.
- Can be emitted to the soil, water, and air through mining, manufacturing/application of fertilizers, fossil fuel combustion, and waste.
- Mobility in soil depends on factors such as pH and amount of organic matter.
- Cadmium binds to organic matter and can be taken up by plants. Tobacco leaves accumulate high levels of cadmium from the soil and the primary route of exposure to cadmium among smokers.
- Among non-smokers, primary exposure to cadmium is from the food supply including leafy vegetables, potatoes, grains, legumes and seeds.

Lead

- Found in ore deposits; widely distributed around the world
- Anthropogenic sources include
  - Leaded gasoline (banned in 1995),
  - Debris and dust from deteriorating lead paint from older housing (pre-1978).
  - Lead pipes/soldered joints
  - Mining/smelting of ore, manufacturing of lead-containing products, manufacturing and application of lead-containing pesticides, fossil fuel combustion, and waste incineration
- Primary exposure among non-smoking adults is from food and water.
- Primary exposure among children is from surface dusts and is intensified by the hand-to-mouth activity.
- FDA has issued guidance and information on lead in pottery, vitamins, wine, candy, and juices for children.

DIETARY EXPOSURE TO HEAVY METALS

Uses of dietary exposure estimates

- Provide estimates of background dietary exposure
- Monitor the impact of regulatory actions
- Identify and quantify potential health hazards
- Provide support for international food standards and risk assessments

Consumption rate of food x **Level of contaminant in food** → **Estimated daily intake**

Compare intake to safety threshold or relevant toxicological dose (e.g. RfD)

History of dietary exposure to lead, arsenic, and cadmium

- Metal contaminants in food, particularly food eaten by infants and children, have been a major focus for decades among regulatory authorities.
- Ubiquitous in the environment due to natural occurrence and/or result of environmental pollution.
- Found in air, water, and soil where they can be taken up by plants and incorporated into the foods we consume.
- Regulatory agencies have long acknowledged this dietary route of exposure and have set action levels, exposure limits safety recommendations, maximum levels, etc.

Modeling a dietary exposure assessment

- Simple model but implementation can be complex
- Does it ask the right questions
  - What will the assessment be used for?
    - Premarket approval
    - Post market issues
    - Labeling
    - Research
    - Priority setting
  - What is the toxicological concern and who is the vulnerable subpopulation?
  - Do we want to be conservative or precise?
  - What data do we have?

Data Sources

1. **Dietary Consumption Surveys**
   - CSFII 1994-96, 1998
   - NHANES 1999-2018
   - WHO Cluster diets
   - Private surveys
   - Custom surveys
2. **Contaminant Data**
   - FDA TDS/TEP
   - WHO/ Global Environment Monitoring System (GEMS)
   - Manufacturer/Industry
   - Literature

Analysis considerations

- Derive estimates for:
  - *Per capita* vs. *per user* (consumers only)
  - Vulnerable subpopulations
  - Typical consumer (average, median) or high consumer (upper 90th percentile), etc.
- Short term v usual intake:
  - Per eating occasion, 24-hr daily intake, N-day average intake, modeled usual longer-term intake
- On a g/day or g/kg bw/day basis
- Precision of the estimate

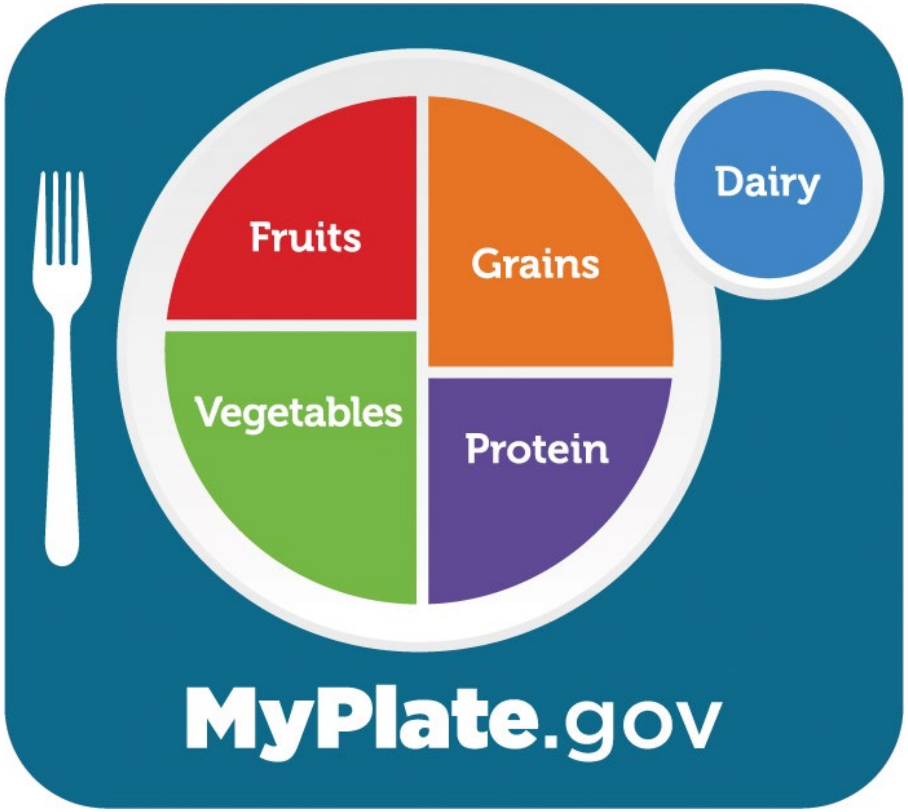
Published estimates of dietary exposure to lead, arsenic, and cadmium

Metal	Population	Mean/Median	Upper percentile	Reference
Lead (ug/day)	1-6 y	1.2-3.2	2.0-4.6[a]	Spungen 2019
	1-3 y	1.0-3.0	1.8-4.4	Spungen 2019
	4-6 y	1.3-3.4	2.1-4.8	Spungen 2019
Inorganic arsenic (µg/kg bw/day)				
	<1 y	0.23 (food) 0.014 (water)	0.53 (food) [c] 0.05 (water)	Xue et al 2010; JECFA 2011b
	1-2 y	0.10 (food) 0.03 (water)	0.29 (food) 0.15 (water)	Xue et al 2010; JECFA 2011b
	3-5 y	0.08 (food) 0.04 (water)	0.21 (food) 0.15 (water)	Xue et al 2010; JECFA 2011b
Cadmium (µg/kg bw/day)	1-6 y	0.41	0.66	Spungen 2019
	1-3 y	0.43	0.70	Spungen 2019
	4-6 y	0.38	0.59	Spungen 2019

[a] 90th percentile
[b] JECFA estimates were provided on mean weekly body weight basis; ug/day estimates were calculated from µg/kg bw/week by multiplying by the default bodyweight (bw) provided in the JECFA assessment (JECFA 2011a) and dividing by 7 days/week.
[c] 95th percentile

Contribution of food sources to dietary exposure to heavy metals among children

- Need to consider both amount of food consumed **and** levels of metals in the food
- The highest contributor to exposure is not necessarily from the foods with the highest metal content
  - For example, the highest contributor to lead exposure among children >1 year of age are among fruits, vegetables, dairy, and mixtures.
  - Many of the foods within those categories have non-detectable levels of lead (<5 ppb)



Data source: Spungen 2019; FDA Closer to Zero, November 2021 public meeting.

RISK MANAGEMENT

Risk management

- Heavy metals are ubiquitous in our environment and our food supply
- Generally, can not point to any single food or food group as the primary source of dietary exposure
- Level of metals in any single food or food group is low
- Goal is to *minimize* risk
  - Recent FDA draft action level for lead in juices focused on potential reduction in dietary exposure to lead among children
- Many nutritious foods contain these metals – can not consider in isolation

Recommendations that infants and toddlers consume a variety of foods

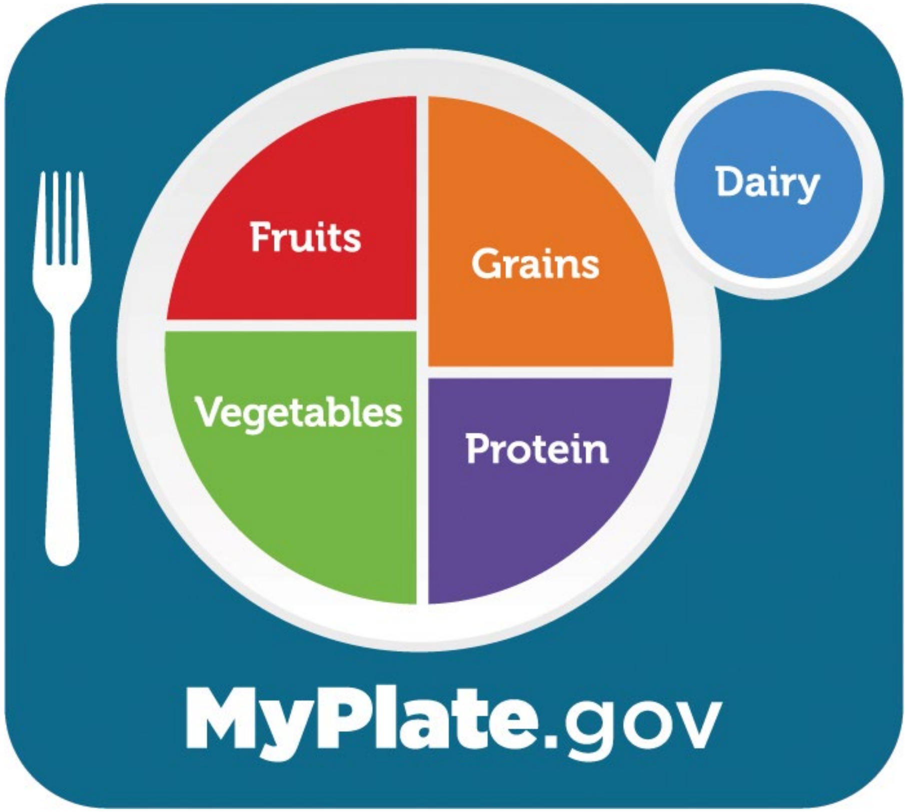
Healthy U.S. Style Dietary Pattern: Toddlers Ages 12 Through 23 Months Who Are No Longer Receiving Human Milk or Infant Formula

CALORIE LEVEL OF PATTERN[a]	700	800	900	1,000
FOOD GROUP OR SUBGROUP[b,c]	Daily Amount of Food From Each Group[d] (Vegetable and protein foods subgroup amounts are per week.)			
Vegetables (cup eq/day)	⅔	¾	1	1
	Vegetable Subgroups in Weekly Amounts			
Dark-Green Vegetables (cup eq/wk)	1	⅓	½	½
Red and Orange Vegetables (cup eq/wk)	1	1 ¾	2 ½	2 ½
Beans, Peas, Lentils (cup eq/wk)	¾	⅓	½	½
Starchy Vegetables (cup eq/wk)	1	1 ½	2	2
Other Vegetables (cup eq/wk)	¾	1 ¼	1 ½	1 ½
Fruits (cup eq/day)	½	¾	1	1
Grains (ounce eq/day)	1 ¾	2 ¼	2 ½	3
Whole Grains (ounce eq/day)	1 ½	2	2	2
Refined Grains (ounce eq/day)	¼	¼	½	1
Dairy (cup eq/day)	1 ⅔	1 ¾	2	2
Protein Foods (ounce eq/day)	2	2	2	2
	Protein Foods Subgroups in Weekly Amounts			
Meats, Poultry (ounce eq/wk)	8 ¾	7	7	7 ¾
Eggs (ounce eq/wk)	2	2 ¾	2 ¼	2 ¼
Seafood (ounce eq/wk)[e]	2-3	2-3	2-3	2-3
Nuts, Seeds, Soy Products (ounce eq/wk)	1	1	1 ¼	1 ¼
Oils (grams/day)	9	9	8	13

DGA Dietary Guidelines for Americans

Public health impact

- Many of the foods that contribute to exposure also provide essential nutrients such as iron and zinc
- Arsenic in rice example:
  - Consumption of brown rice (and intake of nutrients found within, including folate, iron, and fiber) is associated with reduced risk of several chronic disease outcomes
  - Infants and toddlers with dietary patterns that contain rice and non-rice cereal have significantly higher intakes of essential nutrients and lower intake of processed foods[1]



1. Nicklas, T. A., O'Neil, C. E., & Fulgoni, V. L., 3rd (2020). Nutrient intake, introduction of baby cereals and other complementary foods in the diets of infants and toddlers from birth to 23 months of age. AIMS public health, 7(1), 123–147. https://doi.org/10.3934/publichealth.2020012.

Action levels/maximum limits for metals in dietary sources in the US

Metal	Source	Limit	Regulatory agency
Food/bottled water			
Lead	Bottled water	5 ppb	FDA
Lead	Apple juice/other juices	20 ppb/10 ppb	FDA (DRAFT Action Levels)
Lead	Candy	100 ppb	FDA
Inorganic arsenic	Infant rice cereal	100 ppb	FDA
Inorganic arsenic	Bottled water	10 ppb	FDA
Inorganic arsenic	Apple juice	15 ppb	FDA
Cadmium	Bottled water	5 ppb	FDA
Drinking water			
Lead	Drinking water	15 ppb	EPA
Arsenic	Drinking water	10 ppb	EPA
Cadmium	Drinking water	5 ppb	EPA

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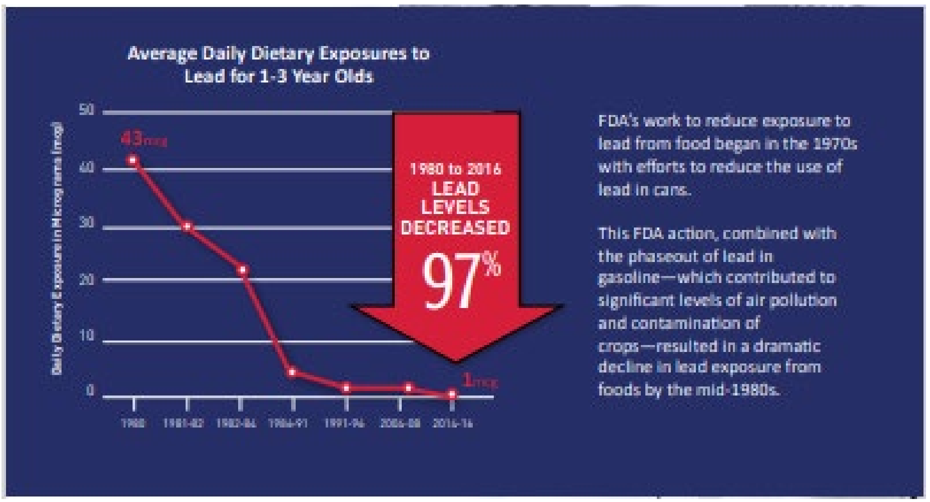
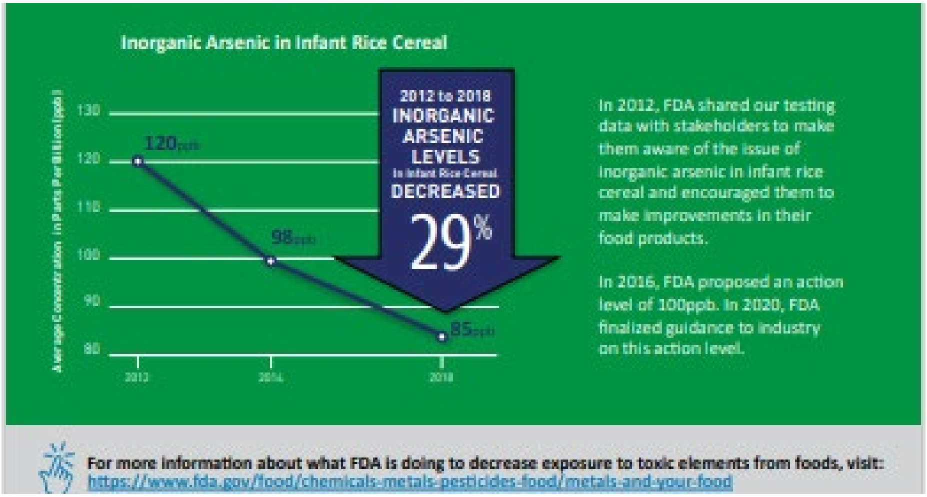
Examples of results from program efforts to reduce exposure to metals among US children





[Source: Closer to Zero: Action Plan for Baby Foods | FDA]

Conclusions

- Exposure to heavy metals among children results from numerous routes
- Dietary exposure assessment allows for:
  - Combination of data on amount of foods consumed with levels of metals in the foods
  - Identification of research and regulatory priorities
  - Estimation of the potential reduction in risk that can occur with action levels
- Need to consider the public health impact of regulating or warning on foods that also contribute to the nutritional needs of young children

Thank you!

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