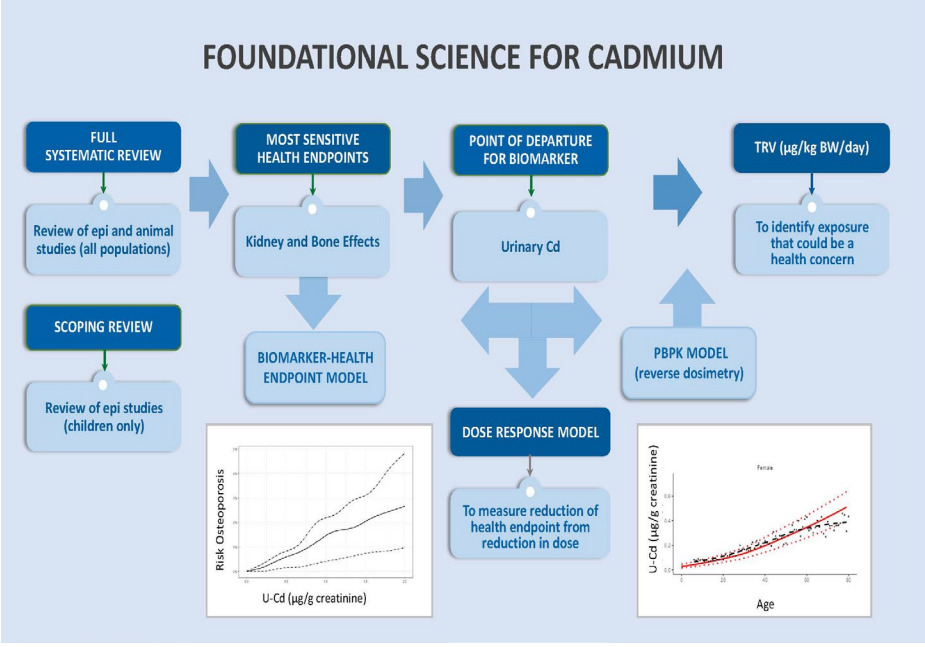
Foundational Science for Cadmium

INTRODUCTION

As a part of the Closer to Zero plan, the agency has identified actions to reduce exposures to toxic elements from foods eaten by babies and young children—to as low as possible. This includes the toxic element cadmium (Cd). Closer to Zero identifies actions the agency will take to reduce toxic element exposure from foods through an iterative approach that includes research, engagement with stakeholders, and outreach activities. To support this initiative, we have been working collaboratively to understand the adverse health effects associated with oral exposure to Cd. To date, we have conducted a systematic review (SR) of the literature and identified data that supports the bone and the kidney as critical targets of Cd toxicity. The information from the SR was used to establish points of departure (PODs) (e.g., no or lowest observed adverse effect levels) for the kidney and bone, based on urinary Cd as a biomarker of internal dose. Additionally, for children, we conducted a separate scoping review to identify available evidence for adverse health effects associated with oral Cd exposure that can be used to inform future research for this subpopulation. We reviewed, evaluated, and adapted human physiologically based pharmacokinetic models (PBPK) for use in reverse dosimetry analyses to relate internal measures of Cd exposure to external measures of exposure, specifically for the PODs for Cd biomarkers. The information from our research will be used to inform a Cd toxicological reference value (TRV) to support human health assessments and inform action levels for Cd in food. Lastly, we developed an association model that estimates low bone mass and osteoporosis risk in the U.S. population given changes in urinary Cd levels. This model calculates the impact of reducing Cd exposure on a critical adverse health effect (*i.e.,* low bone mass) identified from the SR. The research activities conducted by FDA serve as the foundational science for understanding Cd toxicity (Figure 1.)

Figure 1.



FDA CLOSER TO ZERO ACTION PLAN:

Closer to Zero: Action Plan for Baby Foods | FDA

CADMIUM FOUNDATIONAL SCIENCE PUBLICATIONS

Cd Systematic Review: A systematic review of adverse health effects associated with oral cadmium exposure
A systematic review of adverse health effects associated with oral cadmium exposure - ScienceDirect

Cd scoping Review for children:

A scoping review of infant and children health effects associated with cadmium exposure

https://www.sciencedirect.com/science/article/pii/S0273230022000423

Biomarker to Health Endpoint Quantitative Model Relating urinary cadmium level to low bone mass & osteoporosis risk

Modeling the risk of low bone mass and osteoporosis as a function of urinary cadmium in U.S adults aged 50–79 years

https://www.sciencedirect.com/science/article/pii/S0013935122006429

Cd PBPK Quantitative Model for Forward & Reverse Dosimetry

Cadmium physiologically based pharmacokinetic (PBPK) models for forward and reverse dosimetry: Review, evaluation, and adaptation to the U.S. population

https://www.sciencedirect .com/science/article/pii/S0378427422009675

OTHER CADMIUM PUBLICATIONS

Cadmium Mitigation

Cadmium: Mitigation strategies to reduce dietary exposure - PMC (nih.gov)

Children's Exposure to Lead and Cadmium

Children's exposures to lead and cadmium: FDA total diet study 2014-16 - PubMed (nih.gov)