

Developing Data Based Defaults for Risk Assessments

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Many toxicity tests are conducted by unrealistic dose routes (e.g., dosing chemicals orally in large single doses via a feeding tube). One class of chemicals studied in this fashion is the commercially important phthalate ester plasticizers. CIIT scientists have developed mathematical models that describe the uptake, metabolism, and distribution of these esters and their metabolites. These models serve to improve human health risk assessments by basing decisions on dosage of active metabolites to tissue targets in the body. This research builds upon previous results by comparing tissue dose for single oral doses by feeding tubes with tissue doses in feeding studies. The refined pharmacokinetic model derived from this work will produce a tissue-dose-based risk assessment that considers the differences between these two dose routes.

Implications: Most risk assessment approaches are based on default, policy decisions rather than the data from specific studies on test chemicals. This research effort demonstrates the use of specific pharmacokinetic data for refining current defaults in risk assessment. Laboratory studies use single, bolus doses whereas generally, environmental exposures are low concentrations ingested over the course of the day. The results of a comparison between bolus phthalate dosing and feed administration will be essential for future risk assessment calculations for phthalates and many other groups of compounds tested by single dose intubation.

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