Use of Toxicokinetic Data to Replace Default Uncertainty Factors for the Derivation of a Reference Dose for Boron

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Key Words: risk assessment, drinking water, internal exposures, toxicokinetics, human models

Boron is on the Office of Water's Candidate Contaminant List, indicating the potential for regulatory consideration. The Office of Research and Development's (ORD) National Center for Environmental Assessment (NCEA) is charged with assessing risks from exposure to environmental contaminants and developing and applying advanced risk-assessment methods. The reassessment of boron's health risks presented a unique opportunity to develop and apply chemical-specific information in quantitative human health risk assessment. Chemicals are absorbed, distributed, and eliminated from animals through toxicokinetic (TK) processes, while toxicodynamic processes (TD) deal with the response of the target tissue to a given dose. For risk assessment, differences between animals and humans and differences within humans are each addressed with a default uncertainty factor of 10 and can be divided into TK and TD components. The default value for each component can be replaced with data-derived values. Prior to initiating the boron risk assessment, no such data existed to evaluate TK differences between animals and humans or TK differences among humans. Through a partnership with industry (US Borax), NCEA guided the planning, development, conduct, interpretation, and presentation of studies to determine boron TK in pregnant rats and pregnant humans. Human studies were funded by US Borax and conducted by the University of California at Irvine; results were published in the peer-reviewed literature. NCEA scientists used these data to develop a value to replace the default value for the TK component of animal to human extrapolation. NCEA scientists critically evaluated a diverse set of data on kidney function to determine how boron is removed from mammals, and they used variability in renal function among humans to develop a value to replace the default value for the TK component of the interindividual uncertainty factor. This precedent-setting assessment demonstrates NCEA's adherence to reducing uncertainties in human health risk assessment and our intent to include quantitative information, when possible, in Agency risk assessments. This interaction and its outcome highlight ORD's ability to partner with industry to fill data gaps and are important for enabling an improved scientific basis for risk assessment. This assessment, with its inclusion of data-derived uncertainty factors, will stimulate similar advances in the use of TK data when they are available for other chemicals. The Risk Assessment Forum is considering whether to guide the replacement of default uncertainty factors with data-derived uncertainty factors; this assessment will be useful as a case study in that decision.