

Sapphire News

Acrylamide: Consideration of Species Differences and Nonlinear Processes in Estimating Risk and Safety for Human Ingestion.

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Acrylamide in cooked foods results in wide-spread, low-level human exposure. Potential risks from dietary intake remain unclear due to apparent conflicting results from cancer bioassays conducted in rats that reported tumors and epidemiology studies that are suggestive but provide little or no evidence of increased cancer. Risk estimation often includes two common assumptions: (1) tumor response rates in test species can be extrapolated systematically to estimate human response rates; (2) tumor rates observed following highdose exposures can be linearly extrapolated to predict response rates following lowdose exposures. The validity of these assumptions was evaluated for acrylamide based upon examination of relevant toxicokinetic and toxicodynamic differences between humans and rats, including sources of nonlinearity that modify high-to-low dose extrapolation of cancer incidence. Important species differences and sources of nonlinearity are identified, and recommendations for addressing them within the quantitative framework of a PBTK/TD model are discussed. These differences are likely to estimate risk levels up to several orders of magnitude lower in humans than in rats. Quantitative inclusion of these TK/TD factors will more closely estimate actual human cancer risk derived from high-dose rodent studies, since detoxification processes for acrylamide and glycidamide appear adequately protective against toxicity from human dietary doses.