Questions and Comments Received From Webinar Attendees Directed to Specific Speakers: Jeff Dawson

Q: You show that exposure for most reviewed materials in the regulatory context is usually much lower than the potential exposure. This is great. The key being potential, with some casting doubt on the models on exposure calculations. How critical do you think it is to characterize hazard for these chemicals if exposure is underestimated? This is because one concern is exactly the underestimation of exposure. Is it then crucial to understand the exposure models and their uncertainty?

A: I absolutely agree that it is important. For today's purposes it was too difficult to go into that topic in an extensive manner. The goal of exposure assessment in regulatory settings is typically to provide protective estimates of exposure and not underestimate, if at all possible. A key aspect of this process is risk characterization, which should address these issues. More can be provided regarding how uncertainty and variability are addressed in exposure assessment. I hinted at this in Slide 8, which mentioned statistical sampling design and protective adjustments to data. Perhaps the limit doses used in guideline studies could be updated to allow for a dose that is beyond the highest anticipated exposure level by some reasonable factor, unless it is shown by toxicokinetic studies that the kinetic maximum dose (KMD) is achieved at a dose lower than the highest anticipated exposure. This would avoid generating adverse data at doses that would not be anticipated to occur in the real consumer/occupational exposure context.

Q: Shouldn't there always be a gap between exposure results and the dose tested? The goal is to ensure that there is such a gap, for safety, between the levels where humans are exposed and the dose levels.

A: Speaking personally, I would flip this around and say that the goal of regulation is to ensure that a gap exists. As use and understanding of toxic mechanisms change it is always possible that margins will change, perhaps adversely. But regulatory agencies would then be able to act to correct this.

Q: The whole point of KMD is to assess toxicity at biologically relevant doses that still represent enough of an increase above no-effect/lowest-effect levels to address risk assessment needs.

A: Fair point.