SOT FDA Colloquia on Emerging Toxicological Science: Challenges in Food and Ingredient Safety

February 19, 2020

Route-to-Route Extrapolation in the 21st Century

Wiley Auditorium, US FDA, CFSAN, College Park, MD • Live Webcast
Chair: Harvey J. Clewell, III, Ramboll
Co-Chair: Jeffrey Fisher, NCTR

Food Safety Colloquia Series

The Society of Toxicology in conjunction with the US FDA Center for Food Safety and Applied Nutrition (CFSAN) have partnered to provide this colloquia series. The series presents scientific information that is high-quality, cutting-edge, future-oriented toxicological science to provide a well-grounded foundation to inform the work of US FDA employees. These sessions are open to the public to attend in person or via webcast. These events are not a public forum for discussion of toxicology regulatory issues.

The toxicity and pharmacokinetic profiles of substances may vary with the exposure route. If appropriately-conducted studies are available for a relevant route of exposure, generally the point of departure (POD) is calculated based on the data from the studies. However, if adequate data based on the relevant route of exposure are not available, a route-to-route extrapolation methodology may be employed to predict toxicity and estimate POD for risk assessment. This methodology evaluates data from studies based on other non-relevant routes of exposure, provided that the observed toxicity or biomarkers of toxicity are systemic and not related to portal of entry. Route-to-route extrapolation-based approaches utilize equivalent internal dose rather than external dose for predicting effects. Physiologically based pharmacokinetic (PBPK) models enable route-to-route extrapolations of pharmacokinetics and systemic toxicity by normalizing internal dosimetrics for different routes of exposure. Given that route-to-route extrapolations do not incorporate differences in modes of action between exposure routes, there could be a certain degree of uncertainty associated with the model. However, extrapolation uncertainty reduces with the incorporation of additional data or assumptions (such as 100% absorption, *in vitro*, or QSAR-based predictions), when sufficient information is available to support the changes to the model. Although route-to-route extrapolation-based approaches are being explored for predicting effects and estimating POD, there are some inconsistencies in methods used by different organizations, which may introduce variability. This session will present considerations for conducting route-to-route extrapolations and discuss the possibility of developing consistent methods for utilizing such extrapolations for risk assessment.

Schedule *(All times are Eastern US, GMT-5)*

8:00 AM–8:30 AM	**Badge Pick Up**
8:30 AM–8:40 AM	**Welcome, Overview** **Jason L. Aungst,** US FDA, College Park, MD
	Speaker Introductions **Harvey J. Clewell, III,** Ramboll, Research Triangle Park, NC
8:40 AM–9:15 AM	**Introduction to Route-to-Route Exposure** **Harvey J. Clewell, III,** Ramboll, Research Triangle Park, NC
9:15 AM–9:50 AM	**OECD Guidance on the Characterization, Validation, and Reporting of Physiologically Based Kinetic (PBK) Models** **Alicia Paini,** European Commission's Joint Research Centre, Ispra, Italy (via webcast)
9:50 AM–10:25 AM	***In Vitro* to *In Vivo* Extrapolation of Metabolism Data to Support Physiologically Based Modeling for Route-to-Route Extrapolation** **John C. Lipscomb,** CTEH, North Little Rock, AR
10:25 AM–10:40 AM	**Break**
10:40 AM–11:15 AM	**Determination of an Internal Margin of Exposure Between Rodent Oral and Human Dermal Exposures to Phenoxyethanol using Physiologically Based Modeling** **John Troutman,** Procter and Gamble, Cincinnati, OH
11:15 AM–11:50 AM	**Examples of Route-to-Route Extrapolation Conducted at the FDA Center for Food Safety and Nutrition** **Shruti V. Kabadi,** US FDA, College Park, MD
11:50 AM–12:50 PM	**Roundtable Discussion** **Moderator: Harvey J. Clewell, III,** Ramboll, Research Triangle Park, NC **All Speakers** **Jeffrey Fisher** (via webcast)

Organizing Committee

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Future Colloquia Topics

April 29, 2020	Artificial Intelligence Applications in Food and Cosmetic Safety
May 2020	Integrated Approaches to Testing and Assessment—The Future of Predictive Toxicology

Most Recent Colloquia

- **Dermal Absorption and Toxicity: Concepts for Application to Safety Assessment**
- ***In Silico* Methods for Food Ingredient, Dietary Supplement, and Cosmetic Safety**
- **Alternative Methods for Predictive Safety Testing: 3D Bioprinted Tissue Models**
- **Redesigning the Rodent Bioassay for the 21st Century**
- **Food from Genetically Engineered Plants: What Role for Metabolomics?**
- **Can Alternatives Inform the Risk Assessments of Mixtures in Food?**
- ***In Vitro* to *In Vivo* Concordance for Toxicity Prediction and Use in Safety Assessments**
- **Safety Assessment of Food Packaging and Other Food Contact Substances**
- **Considerations for the Determination of Adversity in Food Chemical Safety Evaluations**

……plus 11 additional diverse topics, and other learning opportunities, all available at www.toxicology.org

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