Breakout Group Questions

In Vitro to In Vivo Extrapolation for High Throughput Prioritization and Decision Making

- During the discussion, keep in mind the following global questions:
  - What are the effects/implications when considering human vs. rat values, or non-animal vs. in silico values?
  - How are we defining the "purpose" in fit-for-purpose, and what are the implications for using the approach or assumption in each application (prioritization/screening/risk assessment)?

	Group A: **TK Model Considerations**	**Group B:** **In Silico and Non-Animal Methods for Obtaining TK Parameters**	**Group C:** **Application to Prioritization/ Screening/Risk Assessment**
Session 1 **8:30-10:00 a.m.**	• What needs to be done to determine the state of the science (including current toolbox)? How well are these tools working for understood chemicals / kinetic processes? • What are the pros and cons of a simple (one-compartment) model? How do we assess when models are good enough?	• What experiments/methods are needed for determining oral bioavailability? What about methods for other routes of exposure? • What is best practice for rapidly parameterizing a model? How should confidence in these parameters be evaluated and reported?	• Who are the stakeholders? What are their needs? How do their needs vary? • How do we increase buy-in and what are the training needs? On regulatory and industry side? How do we build capacity and what resources are needed?
Session 2 **10:15-11:45 a.m.**	• How can the in vitro output be related to the in vivo toxicity/adverse outcome? • How do we validate methods and approaches (context, limitations, scope)?	• How do we define the domain of applicability for the in silico models? How should this be evaluated and reported? • How do we store/share models and information/data? What reporting requirements are needed? Do existing reporting formats currently exist, or can existing formats be changed to meet our needs?	• Can IVIVE refine how default uncertainty factors are applied? Can it be used to develop data-driven uncertainty factors (interspecies and inter-individual)? • What are the requirements or implications for use in prioritization/regulation? What areas are ready to incorporate IVIVE in the short term? In the long term?