

Panel Discussion Questions for Translational Alternative Models and Biomarkers Predictive of Drug or Chemical Cardiovascular Risk

Opening Session

1. How could the current ability of the regulatory sector/public health community to adequately assess potential cardiovascular risks to human health from drugs or chemicals in the environment be improved? What human cardiovascular safety endpoints are most critical for chemicals? For drugs?
2. What elements of the current regulatory cardiovascular safety testing paradigms for drugs could help inform environmental chemical safety testing, and vice versa? For what situations?
3. What might be the challenges as well as benefits associated with integrating more extensive cardiovascular testing into current environmental chemical evaluation paradigms?
4. What are the opportunities to more effectively integrate public health level observations and evaluations (behavioral data, disease prevalence, nutritional status, co-exposures in the environment, etc.) to create a more realistic scenario of the cumulative effects of drugs and chemicals? What are the specific challenges and research gaps?

Session 1: *In Vitro* Approaches to Assessing Risk of Cardiovascular Toxicity

1. At a minimum, what *in vitro* models and endpoints should be used to screen for cardiovascular toxicity?
2. Can *in vitro* screening procedures be tailored to certain types of compounds to be tested? How?
3. What kinds or types of information generated by *in vitro* models would be most useful in addressing contemporary risk assessment and/or risk management issues?
4. What *in vitro* models and/or endpoints are critically needed to evaluate environmental chemical safety and public health risk? How can we best develop new models?
5. How can *in vitro* models be used to guide targeted testing in animals, thereby reducing the use of animals in cardiovascular toxicity testing?

Session 2: *In Silico* Approaches to Cardiovascular Toxicity Risk

1. How can *in silico* models be used to assess the risk of cardiovascular toxicity?
2. What are the current information gaps that can be filled by *in silico* assessments to improve risk assessments for cardiovascular toxicity? What types of *in silico* models are needed?
3. How can *in silico* models be used to guide follow-up *in vitro* and animal testing?
4. What critical data would enable the use of *in silico* models to evaluate environmental chemical safety and public health risk?

Session 3: Modeling Sensitive or Susceptible Individuals and Populations

1. What are the current information gaps that should be filled to improve risk assessments for sensitive subpopulations?
2. To what extent do European regulatory efforts incorporate susceptible or sensitive populations into their drug safety or environmental chemical health risk assessments?
3. What *in silico*, *in vitro*, and/or *in vivo* models can fill the current information gaps?
4. What health conditions are critically needed to evaluate environmental chemical safety and public health risk?

Closing Session

1. What are the most critical gaps in the ability of the regulatory sector/public health community to adequately assess potential cardiovascular risks for drugs and/or chemicals?
2. What specific tools and approaches should be further developed to address these gaps?
3. How can data from various *in silico*, *in vitro*, and *in vivo* tests be integrated to reduce the uncertainties in risk assessment and safety assessment of chemicals and pharmaceuticals?
4. What research initiatives would address the current information gaps and improve risk/safety assessments for drug and/or chemical cardiovascular toxicity?