Predictive Models for Acute Oral Systemic Toxicity Workshop

Breakout Group Session Topics

Thank you for agreeing to participate in the Breakout Group Sessions at the Predictive Models for Acute Oral Systemic Toxicity Workshop on April 11-12, 2018, at the William H. Natcher Conference Center, NIH Main Campus, Bethesda, MD. Listed below are the discussion points for the Breakout Groups that have been identified by the Organizing Committee.

Breakout Group A: Practical Applications

- What are the challenges that need to be addressed to facilitate use of these models? In what contexts?
- Identify specific opportunities (now and in the future) to use these models in:
    - Regulatory decision-making
    - Prioritization/Lead Screening/Industry applications
    - Others
- At what point is a computational approach suitable (or sufficient) for an actual risk assessment?
- For what regulatory decisions can (or should) these models be used now? Under what conditions?
- What would render models unacceptable for regulatory use, and are there conditions that could be met to increase acceptability? For example, increase the transparency of the algorithm, validate it for certain groups of substances, use it in combination with other non-animal methods?
- Do regulatory agencies need to use open source and freely available software (as in no cost) when making a screening, regulatory or policy decision? Is a proprietary algorithm/code a show stopper for regulatory decisions for these endpoints?
- How would we go about building software tools for a combined approach (e.g. QSAR + read-across + structural alerts)?

Breakout Group B: Interpretation, Characterization, and Extension

- What types of approaches should be used to account for variability in the data or the uncertainties in the predictions?
- How should we communicate the variability in the reference data to establish a basis for performance of new approaches and set appropriate expectations?
- What type of requirements need to be fulfilled regarding uncertainty characterization if we are to start applying these models in practice?
- How can we better characterize the landscape of the inventories for which we need to make predictions, and how can we integrate that to the capacity of the existing models that have been created to date using this modeling set?
- For regions of the chemical landscape where we are not anchored to legacy animal data, what other tools and approaches could be applied to characterize the acute toxicity profile (ie. may not be structure-based)?
- When is mechanistic information essential in order to accept predictions, and when is having a good performing model is enough?
- What level of model performance is needed to provide sufficient confidence in the prediction?
- How do we build confidence and trust in machine learning models for regulatory toxicology?
- What is the perspective on regulatory acceptance of "black box" or semi-black box prediction models (i.e. ANN, deep learning, etc)?
- How to address mechanistic relevance of models like neural networks, or deep learning?
- Should simple models like similarity search, hierarchical clustering, or k-NN be prioritised with respect to others?
- How can we improve the coverage and interpretation of the ensemble model?