Fit for purpose evaluation of in vitro assays for IVIVE

Xiaoqing Chang[1], Shannon Bell[1], Jaleh Abedini[1], Dave Allen[1], Nicole Kleinstreuer[2]

[1]Inotiv, Research Triangle Park, NC, United States; [2]NIH/NIEHS/DNTP/NICEATM, Research Triangle Park, NC, United States

In vitro assays are a quick and often cost-effective way to generate information on how a chemical might interact with biological systems. Compared to in vivo studies, which integrate several underlying processes and observe apical endpoints, in vitro assays are typically mechanistic and inform a specific biological process. When combined with in vitro to in vivo extrapolation (IVIVE), which allows estimation of in vivo external exposures yielding internal concentrations equivalent to in vitro bioactive concentrations, in vitro assays can also provide insight on safe exposure levels. User-friendly tools now exist that facilitate access to data based on alternative methods and make IVIVE analysis more widely accessible. One of these tools is the Integrated Chemical Environment (ICE: https://ice.ntp.niehs.nih.gov/). Whatever tool is used, understanding the modeling assumptions, application scenarios, and limitations of this approach is important for obtaining the desired outcome. This presentation will present the criteria and considerations for conducting IVIVE analysis with a focus on in vitro assay selection and IVIVE results interpretation. Case studies using ICE will be provided to highlight the impacts of decisions on input factors such as bioactivity concentration metrics and in vitro assay type on IVIVE outputs. The presentation will also discuss strategies for in vitro assay selection under different fit-for-purpose scenarios, as well as possible challenges when relating IVIVE outputs to in vivo toxicity data. This project was funded by the National Institute of Environmental Health Sciences, National Institutes of Health, under Contract No. HHSN273201500010C.