

Using NAMs to Address Variability and Susceptibility Across Populations

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Humans typically exhibit different levels of susceptibility to toxic effects from chemical exposure. These differences result in population-level variations in chemical effects that in turn affect characterization of chemical risk. Quantitative evaluations of human population variability and susceptibility could provide more robust chemical risk assessments that are protective of all populations, especially those disproportionately affected by chemical exposures. Human cell-based and computational new approach methodologies (NAMs) have the potential to model human responses better than traditional animal tests and could be used to characterize variability and susceptibility of human populations. In October 2022, NICEATM hosted a symposium aimed at initiating conversations among government, scientific experts on NAMs, and the environmental justice community about the challenges associated with population variability and susceptibility in the context of chemical risk assessment. Speakers at the symposium presented case studies in which NAMs have been applied to characterize susceptibility factors such as life stage, genetics, or lifestyle. A panel discussion considered the challenges of developing NAMs that broadly represent population variability and highlighted the need to delineate differences in susceptibility due to genetic and other intrinsic characteristics versus those due to systemic social constructs. Breakout groups discussions addressed confidence in models of population variability and susceptibility, barriers to and opportunities for applying such models, and how to best engage with local communities. This presentation summarizes the key topics and discussion points from the symposium to define the state of the science. Project was funded by NIEHS under Contract No. HHSN273201500010C.