Validation of the 21st Century Toxicology Toolbox: Challenges, Opportunities, and the Way Forward

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Abstract:
Increasing efforts are being directed at finding improved innovative methods for assessing whether chemicals may cause adverse health effects. Collectively referred to as the 21st Century Toxicology Toolbox, these methods includes a wide range of tools that increasingly incorporate understanding and detection of the molecular, genetic, structural, and cellular perturbations of pathways and mechanisms that may lead to adverse health outcomes. Applications include toxicogenomics, metabolomics, proteomics, cell based assays, biochemical activity profiles, and computational models. These tools are used to create complex biological activity profiles, with an expectation that these will eventually predict toxicity and safety without the use of animals. Much of this profile data will initially be used for prioritizing chemicals for further testing in validated test methods, decisions on product development, as mechanistic data to inform weight of evidence decisions on chemical safety, hazard, and risks, and to reduce uncertainties in risk assessment. Using such data to make regulatory risk assessment decisions will require validation to demonstrate that the proposed decision strategies can provide equivalent or improved protection of consumers and workers compared to existing test methods. Flexibility in the validation of these new tools and strategies is essential, and will vary depending on the intended purpose, applicability domain, and existing data for the proposed tools. Consideration and use of appropriate validation strategies early in the test method development process is expected to expedite acceptance of new tools and approaches that will provide improved predictions of safety and hazard and reduce and replace animal use.

Keywords: 21st Century toxicology; toolbox; toxicogenomics, metabolomics, proteomics, cell-based assays, biochemical activity profiles, computational models; validation; risk assessment; safety