White Paper: Fit-For-Purpose Assays

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As regulatory agencies around the world have become increasingly restrictive on the use of animal-based assays for chemical risk assessment, the lack of suitable in vitro testing alternatives for many human organs and tissues has left a vacuum in which the bioactivity of new chemicals cannot be reliably assessed. To bridge this gap, it is imperative to develop novel in vitro cell-based assays that are biologically relevant and reliable that can recapitulate the human response to chemical exposure. Over the last several years, ScitoVation scientists have been leading the way in the development of cell based assays fit for the purpose of evaluating dose-response and identifying regions of safety for chemical exposure. We began with the underlying premise that the development of in vitro based points of departure (PoDs) sufficient for safety assessments would require the use of intact human cells. The resulting assays would be (1) consistent with biology in the species of interest, (2) designed based on normal biological signaling networks, and (3) capable of returning robust information on the concentration-response for chemical perturbation. The goal of this white paper is to review the current state of the science, describe the lessons learned from our long-standing efforts to develop strategies and tools for in vitro based chemical safety decisions, and recommend a path forward for the implementation of in vitro methods in risk based safety decisions.

Implications: Although high throughput screening approaches can generate a tremendous amount of data on bioactivity of chemicals, these assays often sacrifice biological rigor for speed and quantity. As the field moves toward 21st century risk assessment, regulatory agencies and industry are beginning to implement tiered approaches that leverage the high throughput screening capabilities for prioritization and evaluation. Prioritized chemicals can then be analyzed in more biologically and human relevant fit-for-purpose in vitro assays that can be used to determine regions of safety. The work to develop this topical white paper will collect the most current information on the state of in vitro alternative method development and ultimately provide recommendations for the path forward in ensuring the most appropriate and impactful uses of these technologies.

Collaborations: Various regulatory, industry and academic subject matter experts

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