ID 11.1

Modern in vitro screening tools to enhance quantitative chemical risk assessment

M. A. Beal*

Health Canada, Ottawa, Canada
** marc.beal@hc-sc.gc.ca*

Chemical risk assessments are undergoing a renaissance as the international regulatory community moves away from animal toxicity tests in favour of robust non-animal alternative tests. These alternatives to animals are often referred to as new approach methodologies (NAMs), which are broadly defined as any novel method and/or approach that can support chemical risk assessment without using animals (i.e., in vitro or in silico methods). Advancements in NAMs are enabling higher-throughput and/or higher-content genotoxicity assessment. Furthermore, toxicokinetic models can be employed to model chemical disposition and support interpretation of NAM data in an in vivo context. Recent work has established that application of in vitro to in vivo extrapolation (IVIVE) models to NAM data tends to provide surrogate points-of-departure (PoDs) that are protective of human health relative to in vivo animal PoDs. Additional efforts are exploring the utility of computational models that estimate freely dissolved concentrations of test chemicals by accounting for in vitro assay conditions and physicochemical properties. These models are capable of providing a better estimate of the cellular exposure conditions compared to the nominal concentration in aqueous solution. Finally, the emergence of three-dimensional cell cultures and complex organ-on-a-chip technologies, that recapitulate aspects of human physiology, are further bridging the gap between NAMs and in vivo toxicity assessment. For instance, liver-on-a-chip technologies can use human-derived cell lines to provide a more robust assessment of genotoxicants that require metabolic activation and can be coupled with other organotypic tissues (i.e., gut-on-a-chip) to mimic complex physiological processes. The presentation will highlight NAM developments and provide examples where NAM testing strategies are being employed to screen chemicals with a potential for concern.

Keywords:
new approach methodologies; in vitro to in vivo extrapolation; organ-on-a-chip; risk assessment.