Measuring and Estimating Dose Metrics: Linking Exposures to Effects for improved Chemical Risk Assessment

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May 11, 8:35 - 10:15, Meeting Studio 313 & 315

The objective of chemical risk assessment is to ensure that exposure to chemicals in the environment and to humans does not result in adverse effects. To determine the likelihood of an adverse effect (e.g. toxicity) to occur, three components of the process must be understood: external exposure, toxicokinetics (TK), and toxicodynamics (TD). For external exposure, a number of physical, chemical, and biological factors influence the bioavailability of a chemical in the exposure media. Similar factors also influence how a chemical is distributed within an organism or the human body (TK), where processes such as biotransformation and elimination compete with factors influencing the distribution of a chemical to a site of toxic action. A fraction of the absorbed dose reaches the target or sites of toxic action, where this target dose (also called biologically effective dose) initiates a chain of biochemical reactions influencing the TD associated with the adverse effect observed. Although the exposure dose is fundamental to accurately defining dose-response relationships associated with a specific toxicological response, the biologically effective dose at the actual site of toxic action is typically not quantified directly; only surrogate dose measurements, total internal concentration or calculated target site doses can be obtained. A key component towards improved understanding of the dose-response relationship relies on better tools that can quantify the freely dissolved concentration (Cfree) both in the external environment and internal tissues, organs, and cells of organisms or within in vitro test systems. A key objective of this session is thus to highlight advances in both modelling and measurement techniques aimed at quantifying Cfree and cellular concentrations; this would include analytical methods aimed at characterizing the partitioning and binding behaviour of chemicals to various environmental and biological matrices, developments in mechanistic TK and TD modelling tools, and application towards quantitative in vitro to in vivo extrapolation corresponding to adverse outcome pathways.