In a nutshell:

**Defining the role of chemical activity in environmental risk assessment within the context of mode of action**

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At its most basic level, chemical risk assessment involves an assessment regarding both the toxicity and exposure mechanisms associated with a specific chemical. It is well understood that the toxic effects of a given chemical depend on the dose (how much), frequency of exposure (how often), and the route by which the chemical enters the body. Mechanisms that influence toxicity and exposure of chemicals are governed by thermodynamics. As such, understanding these mechanisms can be useful in identifying chemicals that represent unacceptable risks to humans and the environment.

Recently there have been a number of studies that have aimed at demonstrating that chemicals that interact with biological systems through relatively weak and reversible hydrophobic interactions to cause non-specific baseline toxicity, or ‘narcosis’, are associated with a narrow range of internal body concentrations (2-8 mmol/kg). Alternatively, the same information can also be expressed based on the concept of a dimensionless thermodynamic chemical activity, of between 0.1 to 0.001. The chemical activity concept is attractive in that it is possible to compare the chemical activity of a chemical, or mixture of chemicals, not only between different biological organisms, but also between various environmental media, such as air, water, soil, and sediment. Consequently, the concept of chemical activity provides a relatively simple and coherent framework for shaping the study of toxicity pathways and assessing risks for both terrestrial and aquatic ecosystems.

To date the use of the chemical activity concept, however, has largely been targeted at interpreting acute toxicity data for chemicals with non-specific, or baseline toxicity. Concerns related to long-term exposures of low concentrations of individual chemicals, and chemical mixtures, however, are increasing. There is thus a need for an improved basis for assessing the risks associated with chronic exposures. Given the appeal of chemical activity as an integrating concept for baseline toxicants, it would be of interest to assess the utility of the concept to chronic toxicity of baseline toxicants as well as to the acute toxicity of chemicals with more specific modes of action.

ECETOC in collaboration with RIFM organised a two-day workshop to assess the feasibility and applicability domain of the chemical activity concept within chemical risk assessment. The workshop reviewed the use of chemical activity as an applied tool for assessing the environmental risks of neutral hydrophobic chemicals known to act as baseline toxicants, and worked towards identifying data gaps. The accompanying workshop report summarises a research strategy defined to address existing data gaps needed to expand the applicability domain to miscible and ionisable organic chemicals with specific modes of action, and application of the concept to chronic toxicological endpoints.


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