A strategy for structuring and reporting a read-across prediction of toxicity

Abstract:
Category formation, grouping and read across methods are broadly applicable in toxicological assessments and may be used to fill data gaps for chemical safety assessment and regulatory decisions. In order to facilitate a transparent and systematic approach to aid regulatory acceptance, a strategy to evaluate chemical category membership, to support the use of read-across predictions that may be used to fill data gaps for regulatory decisions is proposed. There are two major aspects of any read-across exercise, namely assessing similarity and uncertainty. While there can be an overarching rationale for grouping organic substances based on molecular structure and chemical properties, these similarities alone are generally not sufficient to justify a read-across prediction. Further scientific justification is normally required to justify the chemical grouping, typically including considerations of bioavailability, metabolism and biological/mechanistic plausibility. Sources of uncertainty include a variety of elements which are typically divided into two main issues: the uncertainty associated firstly with the similarity justification and secondly the completeness of the read-across argument. This article focuses on chronic toxicity, whilst acknowledging the approaches are applicable to all endpoints. Templates, developed from work to prepare for the application of new toxicological data to read-across assessment, are presented. These templates act as proposals to assist in assessing similarity in the context of chemistry, toxicokinetics and toxicodynamics as well as to guide the systematic characterisation of uncertainty both in the context of the similarity rationale, the read across data and overall approach and conclusion. Lastly, a workflow for reporting a read-across prediction is suggested.


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