Critical aspects in the assessment of read-across adaptations: the role of supporting evidence

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Grouping of substances and read-across is one of the most commonly-used alternative approaches for filling data gaps in registrations submitted under REACH. This approach uses relevant information from analogous ('source') substances to predict the properties of 'target' substances. In dossier evaluation, ECHA has to evaluate whether the provisions in the REACH Regulation are met for this adaptation of standard tests.

In response to this challenge, in May 2015 ECHA developed and published the Read-Across Assessment Framework (RAAF). The abstract and poster by Anderson et al. (2016) describes the main characteristics of the RAAF: adaptations based on read-across approaches are assessed through the use of different scenarios and their respective assessment elements and assessment options.

The assessment elements investigate in a structured way the scientific aspects of the read-across hypothesis. Supporting evidence is required to substantiate the scientific hypothesis which establishes the basis for predicting properties and is therefore crucial in the read-across arguments. All types of supporting evidence provided are considered when conducting an assessment according to the RAAF.

This also applies to results obtained by new approach methodologies (NAM). A considerable effort in developing new approaches and methodologies for investigating properties of substances has been made over the past years. Significant results have been obtained in the development of *in vitro* test batteries as our understanding of adverse outcome pathways expanded. High throughput screening (HTS) methods and omics techniques have gathered a vast amount of information on the interaction between substances and biological systems.

In registration dossiers, ECHA has identified supporting evidence for read-across ranging from theoretical considerations or expert systems, to results from *in vivo* or *in vitro* studies. (Q)SARs, alert-based mechanistic profiles, or *in vitro* assays (e.g. metabolism investigations in cells or cell homogenates) are used.

Toxikokinetic information supporting quantitative conclusions is unfortunately not so frequently available. Results obtained with more recent methods such as "omics" techniques or HTS are apparently not yet used in registration dossiers.

Therefore, it is timely that the workshop will explore such techniques in their potential and limitations to investigate their future use in read-across approaches. In the workshop, three case studies will be presented and discussed which use NAM data as supporting evidence. The RAAF was used as a tool to identify the areas where this additional information may improve the confidence in the attempted predictions.