

## **Break-out session: case studies**

### **Case study from SEURAT-1**

#### **$\beta$ -Unsaturated alcohols: indirect acting toxicant category supported by SEURAT-1 data**

### **Application of the ECHA Read-Across Assessment Framework (RAAF) to the SEURAT-1 Read-Across Case Study on $\beta$ -Olefinic Alcohols**

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In the series of read-across case studies carried out in the EU SEURAT-1 initiative, aiming at reducing uncertainty of the read-across prediction by a strengthened weight-of-evidence provided by new alternative methods, the  $\beta$ -olefinic alcohols represent the scenario of substances that are metabolically transformed to more toxic species (Berggren et al 2015). Not the parent compounds, but the reactive metabolites resulting from biotransformation are the definitive toxicants, acting by a common mode of toxicity. The read-across category is proposed to fill data gaps for 90-day oral repeated dose toxicity of selected C3-C6 primary and secondary, straight-chain and branched  $\beta$ -olefinic alcohols. Metabolisation of the parent compounds as well as differences in strengths of effects observed, related to the potency of chemical reactivity via the Michael addition mechanism, are central issues in the similarity and read-across argument.

The ECHA Read Across-Assessment Framework (RAAF) with the scenario specific Assessment Elements (AEs) was applied to the case study in order to evaluate the information requirements allowing for hazard identification by means of the RAAF, and to facilitate a systematic assessment and identification of knowledge gaps in the weight of evidence and uncertainties in the read-across prediction. Specific consideration was given to the sub-grouping of substances forming metabolites with different reactive potency as well as to the contributions from new methods data.

The RAAF assessment indicates that the overall mechanistic justification of the category is sound, but details or quantitative evidence on some aspects of the metabolism/kinetics are required as well as more substantiate proof of the worst case approach. The new methods data supported mechanistic details and confirmed the fibrosis mode-of-action.

On the basis of this example of read-across argumentation and systematic evaluation, the break-out session will analyse the read-across case and discuss in particular the possibilities of new approach methodology data to strengthen the read-across argumentation.

Berggren E et al (2015) Chemical safety assessment using read-across: Assessing the use of novel testing methods to strengthen the evidence base for decision making. *Environ. Health Perspect.* 123: 1232-1240