Topical Scientific Workshop on New Approach Methodologies in Regulatory Science
19-20 April 2016

Questions for break-out groups

In all break-out groups, the same questions should be posed, so as to make the results and conclusions comparable and derive coherent claims and research needs.

Question block 1: Case description		
Question	Prerequisites and clarification needs to answer the question	Comment
1. Are the chemical structures from the source substances and target substances sufficiently described to determine the structural (dis)similarities?	List of structural features and parameters to characterise the substances, additives and impurities; to assess if the group members are properly defined.	This needs to be properly addressed in registration dossiers.
2. What is the regulatory purpose for which the case is prepared?	What will be in the focus in particular, considering the regulatory purpose specified?	We assume data gap filling under REACH.
3. What is the property for which a prediction is attempted?	In case of data gap filling, which experimental test result is to be predicted?	We assume it is a REACH-relevant endpoint.
4. What is the hypothesis under which the prediction is attempted?	Characteristics of the case; analogue vs category, mechanistic explanation, quantitative prediction model	Where necessary, hypothesis may be set in steps.
5. What information obtained in animal studies is provided to support the prediction?	Are the source studies adequate and relevant (coverage of key parameters, length of exposure, identification of NOAEL, dose/effect relationship, quality assurance, etc.)? What are the "anchor" studies for the target substance? Consistency in data matrix?	Include what kind of supporting evidence is used (without considering NAM data).
6. What are the weak points of the justification, which are identified by the assessment according to the RAAF?	Discuss any weakness in the justification, including an assessment of how the prediction was derived.	Suggest ranking of weak points, if necessary.

7. What supporting evidence is still missing or could be added to increase the confidence in the prediction?	List the types of evidence needed and the methods to generate the pertinent information. State whenever there are different alternatives to generate the evidence.	This could be any *in vitro*, *in silico*, toxicokinetic or *in vivo* effects data.
Question block 2: Contribution of NAM information		
8. What types of NAM information have been used in the case to increase the confidence in the prediction?	Analysis of NAM information used in case studies, as provided in the background papers.	Highlight added value of the used NAM evidence.
9. Were the weak points in the prediction addressed or at least partly addressed by NAM, and has the confidence in the prediction increased?	Which weak points have been successfully addressed, and which weak points remain (if)?	Focus on NAM data.
Question block 3: Detailed characteristics of the NAM information provided		
10. Are the NAM methods used in the case study generally available?	Is there a need for NAM data which is specific to the case only? Are there universal NAM methods used?	Do you see future research needs/improvement potential for the NAM information provided for this case study?
11. What scientific limitations are evident for the NAM information in the case study?	Identify what are the limitations of the applied NAM; is there a difference between supporting a prediction of effects or a prediction of absence of effects?	By design specific methods have specific limitations.
12. What could be the barriers in using or generating the necessary NAM data?	State for each type of NAM data that has been found necessary - Accessibility - Validity - Transferability - Standardisation - Quality assurance (including positive and negative controls) - Qualitative vs. quantitative evaluation (e.g. what is a positive response against historical control data?)	These could be just briefly touched.