Joint EFSA/EBTC Colloquium

Briefing notes DG1: Qualitative methods for integrating evidence within- and across evidence streams for hazard identification

1. Background

Evidence integration is the process by which diverse evidence is combined in order to answer a research question. Integration techniques are used when different pieces of evidence are relevant to a question but they are not sufficiently comparable for meta-analysis to be appropriate.

Currently, the two most fully-developed systematic approaches to integration of evidence in environmental health research are by the US NTP/OHAT (Rooney et al. 2014) and the Navigation Guide (Woodruff and Sutton 2014). These approaches first divide evidence into "streams" of broadly comparable types of research (human, animal, in vitro). They then use the "Grades of Recommendation, Assessment, Development, and Evaluation" (GRADE) methodology for assessing certainty in the body of evidence within each stream.

The GRADE approach (Guyatt et al. 2011) is one of the most well-recognized processes for qualifying certainty in the results of an evidence synthesis in systematic reviews in health care research. The GRADE approach is qualitative, setting an initial confidence rating based on study design and then either downgrading or upgrading this rating based on predefined strengths and limitations of the overall evidence base. These include imprecision, inconsistency in results and publication bias, among others.

The result of the GRADE assessment in the NTP/OHAT and Navigation Guide approaches is a statement of certainty in the evidence for each evidence stream included in the systematic review. These results are then fed into a matrix which yields an overall level of confidence in the evidence base across streams in its entirety as it relates to a conclusion for hazard identification (e.g. known, presumed, suspected, not classifiable).

This is referred to as a "GRADE-based approach" to evidence integration. Though several aspects seem to work well for hazard assessment, practitioners have identified challenges in application of GRADE (Morgan et al. 2016; NAS 2014) to evaluation of complex data from multiple streams of evidence (human observational studies, experimental animal studies and in vitro studies) vs. randomized controlled trials in humans. Integration of heterogeneous data across evidence streams is of particular challenge as it goes beyond the traditional within-streams application of GRADE.

The issue is therefore whether GRADE-based approaches, largely intended for characterising the certainty of the results of synthesising a stream of evidence, are sufficient for evaluating how different streams of evidence speak to each other in understanding if and how a chemical may present a risk to human health.

- What if animal and human evidence contradict each other, with e.g. murine models showing no effects but human observational studies suggesting adverse outcomes?

- What if the animal studies and human studies suggest that health risks occur at different doses?
- What if the animal and human studies suggest that different populations may be at particular risk?

Reconciling potentially contradictory but diverse evidence is required if systematic and evidence-based methods are to be fully implemented in the practice of risk assessment.

2. Objective

As a follow up of lecture 2, the objective of this group is to discuss the available qualitative approaches to combing evidence across streams, and to identify the structure of an evidence integration approach that provides an a priori, transparent, reproducible, and operable process for hazard identification.

The discussion will focus on:

- Is GRADE sufficient? Does it satisfactorily address how different streams influence the integration and development of conclusions? If not, how do we preserve evidence-based principles in a rich integration process?
  - How do you best combine ("integrate") evidence streams for hazard identification?
- What/which/are there other components that could or should be included in the evidence integration process?
- How are the ratings for certainty integrated within the findings to develop/systematize weight of the evidence conclusions? And how can the ratings be used to evaluate contradictory data?
- Recommendations for future developments in the field.

3. References

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DG1	Qualitative methods for integrating evidence within- and across evidence streams for hazard identification
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