IN VITRO DISCUSSIONS AND IDEA:

SUMMARY OF THE MAY 2018 WORKSHOP AND BACKGROUND TO TODAYS WORKSHOP

IDEA: MAY IN VITRO WORKSHOP AIMS

- Identify the tests that can be used for hazard assessment
- Consider the basis for the choice of dose selection and benchmarks
- Assess the reliability of potency measurements
- Characterise uncertainties in the use of the in vitro tests discussed for determining induction potential

OUTCOMES OF THE IDEA WORKSHOP ON IN VITRO METHODS : MAY 2018

- SAR. Alerts for certain chemical substituent features were identified
- Benchmarks. Substances studied each had been previously tested in LLNA test (Gold standard for any in vitro test?)
- Tests selected. Different research groups are using different combinations of tests, nearly all include a KE1 hazard identification test. Various approaches used for dose selection.

NB. No information provided on xenobiotic metabolising ability of any test (a probiotic evaluation issue?)

OUTCOMES OF THE IDEA WORKSHOP ON IN VITRO METHODS: MAY 2018

- Weight of evidence. In order to utilise findings from a number of different tests along with various other sources of relevant information requires a well considered weight of evidence procedure. Bayesian networks and artificial or networks were favoured for this purpose. It was not possible at the Workshop to examine details of these methods purpose.
- Conclusion. A non-animals hazard assessment, based on tests designed on the sequence of initial stages of induction (KE1, KE2 and KE3), is feasible but potency determination requires more work.

MAY WORKSHOP AND QUESTIONS LEADING TO TODAY'S WORKSHOP

- Is the AOP to the LLNA endpoint the only pathway needed in the design and development of in vitro tests for induction and elicitation?
- To be allergen does a fragrance need to be an electrophile and to become covalently bonded to lysine/cysteine on a target protein(s)?
- What is the rate limiting step in the AOP and why if it is a linear process do we need tests for each step?
- What are the mechanistic explanations for human variability in sensitivity?
- What are the priorities for the way forward?