IDEA Annual Review 2014

EUROFORUM building (EUFO)
10, rue Robert Stumper
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During the Annual Review, following the presentations made, several issues were highlighted or statements were made by the attendees such as:

General Remarks

- The IDEA project developed into a very useful tool in enabling a solution oriented, forward looking dialogue of the various stakeholders engaged in the topic of (fragrance) allergy. In this context it is very important to respect the different roles of all stakeholders.
- A lot of the learnings and outcome of IDEA could be valuable beyond the fragrance industry and be meaningful for the whole range of allergens and thereby become useful for other areas.
- Understanding exposure (volume, use levels, product types in which typically used) is a critical element in understanding clinical observations and deserves a separate activity.
- Product ingredient labelling is still an important tool for the clinician.

QRA Refinement

- It was clarified that the HRIPT is not used as a predictive tool by the industry but only as a confirmative tool. This should address ethical concerns.
- Concern was expressed regarding the future use of the HRIPT and the opportunity was raised to move away from the confirmatory HRIPT once integrating new methodologies (alternatives to animal testing) for hazard assessment.
- The aggregate exposure model, which is valued very much, should be presented in more detail and it should be aimed to make it more user friendly in its application for those not too familiar with it. It was stated that the model is based on the Monte Carlo principles and that two publications are under way to describe the model in more detail. Once available they will be shared with the IDEA WS participants.
- The degree of uncertainty around the EC3 value was raised and discussed. It was mentioned that there is publications out there linking the EC3 value with human data. The mouse being a good, but not perfect predictor for human effects is a reason why the fragrance industry does run the HRIPT as a confirmatory test.

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- The potential impact of vehicles as potential skin penetration enhancers and the potential resulting effect on the outcome of the LLNA was raised and it was stated that there is a reasonable amount of published data demonstrating that most vehicles have a moderate impact on the observed sensitization compared to effects from biological variation or the chemical properties.
- With regard to 'validation', the best would be to work with a new ingredient (not necessarily a fragrance ingredient) as for existing materials usage trends can have a big impact on the clinical observations.
- 'QRA2' has to be understood as a snapshot in time and QRA be looked at as an evolving tool.

Pre- and pro-haptens

- When investigating into the oxidation issue, give sufficient consideration to changes potentially resulting during shelf- life by including experiments that would mimic the shelf- life.
- When investigating pro-haptens potentially go beyond fragrance ingredients and look into the area of carcinogens, where the metabolic pathways are often better characterized. In this context it was stated that while this is true, there is the issue of metabolites sometimes being very cytotoxic and therefore not suitable to be investigated in in-vitro systems.
- Regarding hydroperoxides the bigger issue seems to be with the abiotic formation but when it comes to secondary oxidation products, those might also be formed biotically.
- When investigating for biotic oxidation pathways ensure that the testing material well characterized and not already transformed to a certain extent.
- When investigating for effect levels of hydroperoxides, consider clinical studies (patch test and ROAT) with product under suspicion (based on analytical results) involving sensitized patients for which relevance has been demonstrated.
- Investigate for the hydroperoxide levels in patch tests to confirm standardization.

Characterization and Categorization of Allergens

- A confirmed positive patch test is a reconfirmation that an ingredient is an allergen.
- Regarding genetic factors, when doing clinical studies, more focus on sensitive subpopulations could be considered.
- Do not focus too much on classification of allergens based on hazard as the categories can become somewhat artificial – the most potent allergen can be safely used if the exposure is adequately managed (and vice versa) – it is important to look into the whole picture (potency and exposure).
- Identifying the cause for the induction of contact allergy is tricky, especially for reactions on body seats where a multitude of exposures (workplace and consumer product related) can happen (e.g. axilla versus hands).
- Consider the presence of potential impurities when investigating an issue with a material and assessing exposure.