IDEA Annual Review 2015

EUROFORUM building (EUFO)
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The project is now three years into its programme. The Annual Review provides a valuable opportunity for the stakeholders in the IDEA project to come together to exchange views, to discuss progress on the project during the year, and priorities for the coming year.
The aim of the project is to develop common protocols to try to prevent /reduce to a minimum the induction of contact allergy, in consumers, using fragranced consumer products.

The Commission continues to provide its strong support for the importance of the project and the value of the annual meetings.

QRA METHODOLOGY UPDATE and CRITICAL REVIEW OF QRA2 BY JRC

The priority for the first three years has been to focus on the improvement of exposure assessment aspects of the original QRA1 (2008).

- QRA2 in its current form represents a substantial advancement on the original QRA but remains a tool that needs to be further tested and validated by implementation and monitoring of clinical data. It has been assessed independently by JRC and an SCCS Working Group.
- JRC critically reviewed the draft QRA2 as requested by DG Grow.
- The JRC provided a report which summarized its conclusions. JRC identified a number of topics to be followed up, some of an editorial nature, some requiring further clarification. Some of those points were already raised at a meeting between SCCS – JRC – IDEA and Commission (October 30, 2015). The IDEA team responded to each of the issues mentioned and JRC did not raise any further concerns.
- The IDEA team is in the process of modifying the current QRA2 to take on board all the JRC, SCCS and other comments in order to finalize QRA2.

It is recognized that in the next phase hazard assessment must be the focus as future hazard assessments cannot involve the use of experimental animals.

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ISSUES DISCUSSED AT THE ANNUAL REVIEW

- In regard to hazard assessment, the statement was made that there are ethical concerns in Europe for using the HRIPT (not yet considered in the IDEA project), even for confirmatory purposes, as there is inevitably a potential risk of active sensitization. It was mentioned that the day before the Annual Review the SCCS issued a memorandum on the use of human data. With the concerns regarding the use of HRIPT, the loss of the animal LLNA assay and inadequate progress on alternative methods that provide reliable potency information, IDEA is faced with major challenges. It will have to identify and develop with others new approaches to overcome these.
- Polysensitised people, meaning those individuals reacting in patch test to three or more unrelated materials and therefore considered as more susceptible, represent about 6% of clinical patients or around 0.6% of the general population. As they constitute a small proportion it was questioned as to how much emphasis should be given in the IDEA project to this population since the target of risk assessment is to protect the general population. On the other hand it was pointed out that this subset presents an interesting study group that should be further investigated.
- Regarding children it was stated that in the first 6 – 9 month there is a reduced immunological response (due to a not yet fully developed immune system); after that it seems they react comparably to adults (but are not more susceptible). Studies conducted in the 60s and 80s (which might be ethically questionable if looking at them retrospectively) clearly confirm this.
- Regarding the potential relationship between skin allergy and inhalation exposure there is hardly any data available. There is no hint in the available literature of induction of skin sensitization caused by inhalation exposure and only one study where in already sensitized individuals a flare up of an existing allergy was observed at abnormally high exposure levels. Reference was made to a recently published paper by Basketter and Kimber where the authors report that no substantial evidence has been identified indicating a risk of skin allergy via the inhalation route. It was felt that there might be some for oral exposure.
- A question was raised as to how far the mouse skin (in the LLNA) adequately mirrors metabolism, in particular metabolic activation (and therefore can address pro-hapten transformation). It was answered that for all in vivo assays there has been an assumption that for them the activation is sufficiently addressed. Further there has been a retrospective analysis of 320 materials of which about 25% are pre or pro-haptens and of those 97% were correctly identified, which provides a good level of confidence.
- Regarding the issue of covering potential misuse of products, it was stated that the habits and practice data incorporated in the Creme Global Total Aggregate Exposure model actually include various intentional misuse scenarios.
- The primary objective of IDEA is consumer protection. QRA2 does not address workplace exposure, but it could be developed to integrate/address professional exposure to consumer products. In this context the specific issue of ‘aroma therapists’ and nurses frequently washing/disinfecting their hands was raised.

- It was further pointed out that sensitization to fragrance ingredients might happen in unexpected environments. The case of metal workers using self-made fragrances they add to cutting fluids was mentioned as an example. There was agreement that such types of exposures are very difficult to assess.
- It was regarded important to note (as written in the QRA2 submission) that while the QRA2 has the potential to be applied to many types of products that involve dermal contact, the QRA as currently presented has been developed for the application to fragrance sensitizers and might need adaptation before being applicable to other sensitizers (like preservatives).
- Reference was made to a statement already made at the JRC – SCCS – IDEA – Commission meeting in October with regard to ensuring that sunburned (and therefore broadly inflamed skin) is adequately addressed within the QRA.
- A member of the IDEA SG stated that the mechanism to include feedback from clinical data into the QRA process could still be improved to be able to quickly react on issues when they initially show up. It was further pointed out that it is expected that as QRA 2 is further developed and implemented, the monitoring of its impact on fragrance related contact allergy should be done in a rigorous way, e.g. in the form of a good quality prospective study. In the context of the prospective study a participant suggested to consider confining the study to certain age groups. These suggestions will be followed up in a one day IDEA Working Group meeting.
- An SCCS representative stated that the SCCS would appreciate the opportunity to stay engaged in the process via a critical review of the QRA2. To do this they would need to receive an official mandate once work on QRA2 is finalized, as they had previously for their QRA1 review.
- Another SCCS member commented on the value of the model to derive probabilistic aggregate exposure information and its general use in risk assessments. The SCCS would remain reluctant thus far to a general adoption of such a model into SCCS risk assessment considerations.

Jim Bridges, chair of the IDEA SG used the opportunity to thank JRC for their critical review and the stimulating recommendations to further improve the QRA methodology and its documentation.

RISK ASSESSMENT OF PRE- & PRO-HAPTENS

- In case of positive patch test reactions to oxidized fragrance ingredients (like Limonene or Linalool) it was recommended that in addition to analyzing the consumer products the patient has been exposed to for presence of hydroperoxides also consider testing those products suspected for having caused the clinical reaction in a ROAT. Thereby one would add an additional layer in investigating clinical relevance as the patients might be more sensitive than the analytical chemistry findings implies. With this approach there would be two avenues and the second one could serve as verification of the chemical analysis.

- The above remark was supported by another participant pointing out that the limit of quantification, that in the end might be achieved with the analytical method, might be too high to pick up all 'levels of concern' to which the consumer might be exposed.
- A member of the SCCS asked to which extent the oxidation can be prevented at the level of raw materials as well as the finished product.
- The topic was raised that some ingredients (like Geraniol) seem to have the ability to act as pre- and pro-haptens and that this requires thorough investigation as it might answer a number of questions still existing regarding observations made on materials that can be oxidized.
- An SCCS member referred to the practical example of Tea Tree oil, where the prevention of oxidation of the raw material turned out to be sufficient to address the issue of sensitization. In this context it is important to understand that the conditions to prevent oxidation might vary case by case.

THE COMMISSION'S REPORT FROM THE PUBLIC CONSULTATION ON FRAGRANCE ALLERGENS

It was recognized that the consumer information element is very challenging. Answering a question from the audience it was mentioned that regarding E-labelling the Commission will continue to discuss this approach with all Member States. It was suggested to check whether what will be proposed for fragrance allergens might be useful for application to all type of allergens.

At the end of the meeting the participants jointly worked out and agreed on a number of key conclusions. Those are available in a separate document on the IDEA website.

FOLLOW UP

The IDEA team agreed to consider all of the points raised and where possible to include them in its program for 2016.

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