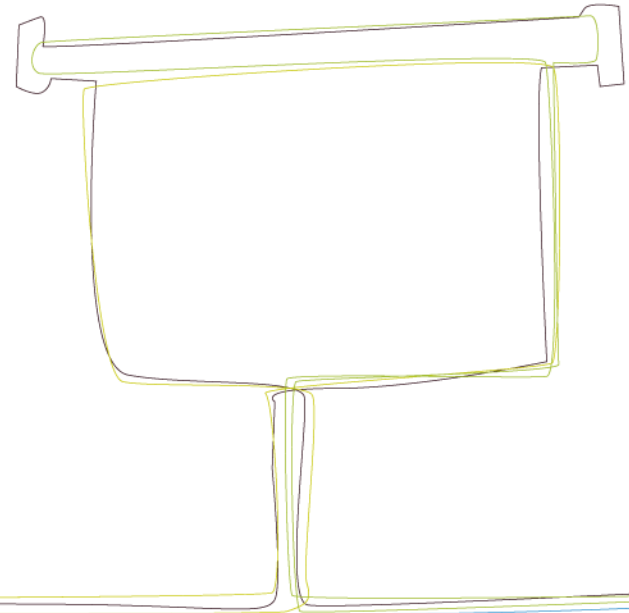




Rapporteur's Progress Report on the IDEA Workshop on

Characterization of Fragrance Allergens

August 28-29, 2013



Contact Allergy (CA) and Allergic Contact Dermatitis (ACD)



- Priming and sensitization (induction) of the immune system leads to CA, which is **symptomless**.
- Sufficiently high re-exposure (elicitation) may lead to **immune response** (ACD) – with clinical symptoms. Not all CA results in ACD.
- Both phases follow a **threshold mechanism**.
- **Preventing induction** via use of adequate RA and RM measures **prevents elicitation**.

Definition of 'contact allergen'

- A jointly agreed definition of 'contact allergen' was regarded as a pre-requisite for further discussions.
- The following general definition was agreed:

A contact allergen is a substance that is capable of inducing delayed type sensitization in humans, which may manifest as allergic contact dermatitis.

The elicitation of allergic contact dermatitis requires sufficient exposure, however, there is significant inter-individual variability.

Tools to identify skin sensitizers

- There are three types of tools to identify contact allergens:
 - Animal studies: provide reliable hazard assessment information; but raise animal welfare considerations.
 - In vitro / in silico studies: are increasingly effective at determining hazard potential; however, current methods are unable to identify potency.
 - Human studies: predictive human tests (e.g. HRIPT) should only be used to confirm no effect levels.
- Good quality human data should override animal data.

Diagnostic tools for CA

- Patch-testing is the **only available diagnostic tool** to identify contact allergens.
- The **ROAT** is used to determine the elicitation threshold of an allergen in real-life conditions.

Criteria for the categorization of allergens



- The categorization criteria used in the SCCS Opinion on fragrance allergens (SCCS/1459/11) were presented at the workshop.
- Points of refinement to the SCCS Opinion categorization criteria were identified:
 - Put the clinical data into perspective with **exposure** (clinical relevance).
 - Complement animal data with **human data** as much as possible.

Criteria for the categorization of allergens: Proposed refinements



- Use guidelines developed under EU CLP Regulation for the **interpretation of human data**.
- Have a critical evaluation of the **quality of studies** (e.g. Klimisch scoring system).
- Use relative frequencies from consecutive clinical testing (rather than absolute cases).
- Give more weight to the clinical data on proven cases of ACD.
- Blinded ROAT studies mimic real-life conditions and can provide complementary information on the issue.

Criteria for the categorization of allergens: Proposed refinements



- Taking these points of refinement into account, the categorization criteria used in the SCCS Opinion could become the basis of an effective framework for the risk assessment / management of fragrance allergens.
- **‘Levels of concern’** (based on consumer exposure per product category and relative frequencies of positive patch-testing) need to be defined.

Expand existing diagnostic methodology



- Ensure better **availability of appropriate test samples**.
- Use of **appropriate test concentrations** (to avoid false positives and false negatives).
- Test with **patients' own products** whenever possible and ensure good communication with product manufacturers to facilitate the identification of the culprit ingredient.
- Incorporate additional information on **secondary parameters** (e.g. vehicles, impurities, additives, etc.).
- Offer educational support for professional patch-test reading

Other diagnosis tools

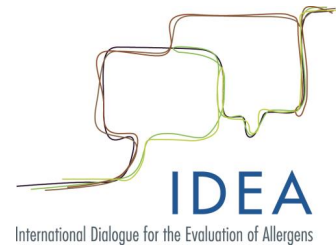
- As of today, the only established methodology to diagnose contact allergy is patch-testing. This is the gold standard.
- However, the participants agreed that there is room for the development of less invasive, time consuming and demanding supplementary diagnostic tools.
- The development of an immunological-based test (e.g. blue/red indicator test), allowing a detailed analysis of doubtful reactions would be of great value.

Additional information to monitor and to help identify potential contact allergens



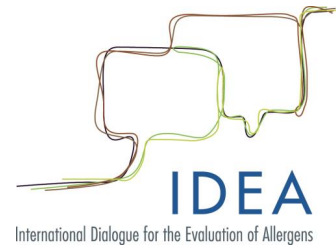
- Post-marketing surveillance (i.e. cosmetovigilance)
- Epidemiological studies
- Collection and analysis of large sets of clinical data

The optimal diagnostic approach



- Documentation of patient's history and skin effects.
- Patch-testing with commercial test series and possibly culprit (consumer) product.
- Additional breakdown testing of (consumer) products is usually necessary. The information can be accessed via:
 - Ingredient labeling on the packaging.
 - The product manufacturer. In this case, excellent communication has to be ensured between industry and the dermatology community.
- Results should be communicated to relevant networks / data centers (e.g. Revidal / Gerda).

Good communication / interface between dermatologists and Industry (upstream and downstream)

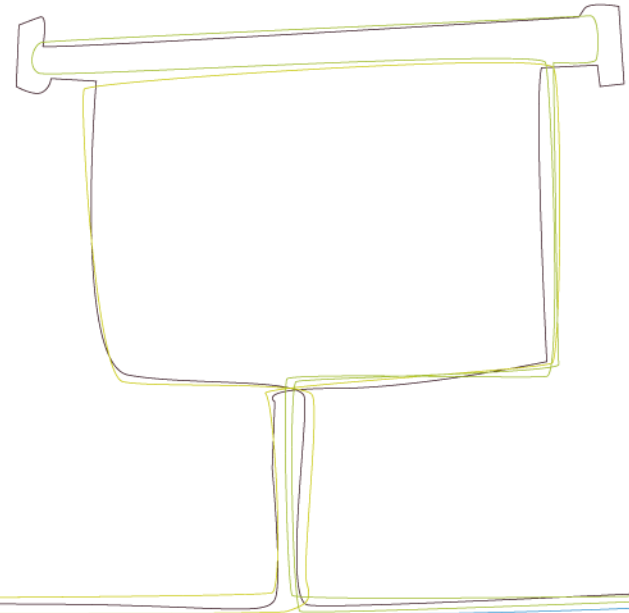


- Sources of information, including:
 - Manufacturers of finished product
 - Compounders of fragrance
 - Trade associations (e.g. IFRA, Cosmetics Europe, ...)
- Ensure standardized method to supply appropriate samples to dermatologists (standardization of vehicles, dilution of samples, normalization of labeling, etc.)
- Ensure a mechanism to communicate results between dermatologists and industry.



Progress report on actions taken

Characterization of Fragrance Allergens



Process and timeframe



- This workshop focused more on primarily strategic directions. As such a broad involvement of the workshop participants is needed to address these recommendations.
- The next workshop on characterization of fragrance allergens is scheduled for May 2014.

Proposed Actions



- Fragrance allergens characterization TF
- Expanding existing methodology TF
- Data collection TF
- Communication TF
- Other recommendations

Fragrance Allergens Categorization TF



- Call for participation sent to all workshop participants (dermatologists and toxicologists are preferred).
- Mission: improve the categorization of contact allergens for further use in risk assessment and risk management.
- The resulting categorization system should clearly define the 'levels of concerns' (based on appropriate indicators).
- Consumer exposure / product category is important and non-ambiguous product categories should be defined.
- Deliverable:
 - A draft framework of criteria for a better categorization of fragrance allergens to be presented at the next workshop.

Expanding existing methodology TF



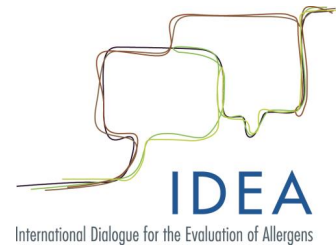
- Call for participation sent to all workshop participants (clinicians are preferred).
- Mission: expand on the existing methodologies with regard to:
 - High dose / low dose effects.
 - The link between CA and ACD.
- Deliverable:
 - A presentation at the next workshop highlighting the key conclusions of this TF.
 - Plan for further scientific studies.
 - Adapt methodologies and communication as appropriate.

Data Collection TF



- Call for participation sent to all workshop participants (dermatologists are preferred).
- Mission: improve data collection by specific centers to collect, scrutinize and publish all useful clinical data.
- Deliverable:
 - A report recommending actions to improve collection of clinical data. To be presented at the next workshop.

Communication TF



- Call for participation sent to all workshop participants (dermatologists and industry experts are preferred).
- Mission: improve the communication between dermatologists and industry.
- Deliverable:
 - A draft standard procedure for improved communication exchange of samples and results of clinical investigations between dermatologists and industry (to be presented at the next workshop).

Other recommendations

- Better understand the differences of prevalence of skin sensitization between various geographies (e.g. Europe vs. USA). Activities would include:
 - Better understanding of specific consumer habits (involving customer associations like PCPC or CosEU).
 - A geneticist or a specialist of genetic variations
 - An epidemiologist
- Explore hypothesis that many low dose exposures are more potent than single high doses.
 - A toxicologist and a dermatologist
 - Report at the next workshop.

Other recommendations



- Monitor the development of a new diagnostic tools that might help further improve diagnosis of CA. Alternatives are likely to be based on immunological concepts.
 - A toxicologist and a dermatologist



Thank you for your attention

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