IDEA
International Dialogue for the Evaluation of Allergens

Considerations regarding a surveillance system

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IDEA WG Meeting
Leuven
February 15, 2017

Background

The surveillance system should be seen as an important element of evaluating action by industry and has been a requirement since the first SCCS opinion on the QRA.

Such a system was also discussed at various times during the IDEA process and from early on the inclusion of 'new fragrance substances' was suggested.

Background

- Surveillance system idea was further developed by a sub- group in IDEA, including Wolfgang Uter, Jeanne Duus Johansen and Ian White in 2015 into a draft protocol.
- Presented and discussed at IDEA WG meeting on April 6, 2016.
- Besides recommending testing the 26 fragrance allergens and some markers, it proposed testing new ingredients.

  Recommendation to first look at materials identified by the SCCS in its 2012 opinion:
  For other fragrance substances identified by the SCCS as (potential) allergens in humans, routine testing of groups of substances over blocks of time should provide information on the prevalence and relative importance of them as allergens (information on consumer exposure is required).

Background

Key conclusions of the April 6 WG meeting:

- The WG supports the surveillance system to assess prevalence of contact allergy in eczema patients as recommended by the dermatologists. Key additions to the proposed protocol are documented separately.
- The WG points out, that the surveillance system alone may not verify whether the QRA is effective due to confounding factors.
- Complementary work is therefore recommended and will be subject to a separate meeting.

Background

- Meetings to progress on the system development (including practical aspects of realization & budget implication):
  - Meeting in Malmö, May 23rd 2016 with Magnus Bruze and Marlene Isakson (University of Malmö), Bo Niklasson (Chemotechnique)
  - Meeting in Erlangen with Wolfgang Uter July 7, 2016 and February 1, 2017.
  - At a conference call of the IDEA sub team following the project on July 12, Ian White stated that interest in (relevant) clinics joining the system proposed by the industry is low and that failing with the surveillance system would shed a bad light on the whole IDEA project.
  - Internal industry discussions on preparing a meaningful surveillance system continued.
  - Ian White presented the context and the plan for a surveillance study under IDEA at the September 2016 ESCD meeting

FM1, FM2 and 26 Allergens

- It was suggested, with regard to routine materials in the surveillance project, to consider only including FM1 and 2 and its constituents (plus some screening materials), instead of the 26 fragrance allergens labelled in Europe.
- **FM1** (introduced as a ‚screening tool' by Larsen in 1977); mixture of 8 fragrance ingredients (each 1%) plus emulsifier Sorbitan Sesquioleate. Solvent Petrolatum.

Amyl cinnamal	Isoeugenol
Eugenol	Hydroxycitronellal
Oak moss	Cinnamyl alcohol
Geraniol	Cinnamic aldehyde

- **FM2**, introduced in 2004. Solvent Petrolatum.

Citral 1%	Citronellol 0.5%
Farnesol 2.5%	Coumarin 2.5%
Hexyl cinnamaldehyde 5%	HICC (Lyral) 2.5%

- **26 Allergens**: Amyl cinnamal, Amyl cinnamyl alcohol, Anisyl alcohol, Benzyl alcohol, Benzyl benzoate, Benzyl cinnamate, Benzyl salicylate, Cinnamyl alcohol, Cinnamic aldehyde, Citral, Citronellol, Coumarin, Eugenol, Farnesol, Geraniol, Hexyl cinamaldehyde, Hydroxycitronellal, HICC, Isoeugenol, BHMCA, d-Limonene, Linalool, Methyl heptine carbonate, alpha-iso-Methyl ionone, Oak Moss, Tree Moss

Status

- Initially, the topic of new ingredients was not broadly embraced by the fragrance industry, which could be a reason for the low interest from clinics so far in joining the surveillance system.
- In discussions with stakeholders it became clear that the inclusion of 'new ingredients' is becoming a crucial point for being able to making such a surveillance system a reality.
- Stringent criteria to select certain materials, aiming to reduce confounding factors, could potentially allow conclusions on the QRA effectiveness over a certain surveillance period.

Status

There are two types of 'new 'ingredients

- 'newly available to dermatologist' (for patch testing) in terms of screening, but already in the marketplace
- 'new to the market'.

'Newly available to the dermatologist' - includes materials identified in the SCCS opinion on fragrance allergens and recommended for consumer information.

- Including those in a surveillance study to collect additional clinical feedback could be useful in positioning them with regard to their relevance of being 'established' fragrance allergens
- In view of pending EU regulatory action on consumer information (on cosmetic products) information concerning the materials further becomes meaningful for the patient.

Status

With regard to ‘new to the market’, a subcategorization can be made.
Proprietary materials can be divided into those which are

- **newly developed and only used by the company** that developed them and
- those that are **new, but** which have **already been traded between the fragrance houses**. There should already be a broader market penetration for this second type.

The **market penetration** and thus the **likelihood of consumers getting exposed** as well as the **length** of the time **of exposure** is very relevant for the meaningfulness of patch test screening with these materials (and the interpretation of results).

Status

Criteria to be considered for new materials, to increase likeliness to draw conclusions on the effectiveness of the QRA:

- QRA2 based company policy or IFRA Standard available
- No structural similarity to materials in use
- No presence in nature
- No use as or presence in flavours
- Low likelihood of material being used outside of the fragrance industry applications (and therefore outside the control of the QRA)

Information relevant to have:

- NESIL (best not a weak sensitizer), based on LLNA, HRIPT, etc.
- Exposure info
- Volume of Use

Considerations for moving forward

Surveillance study with standard (routine) ingredients

- This is what many clinics are already doing but would be with tighter requirements with regard to performing the study (e.g. training, monitoring, combining results in centralized system, joint publication) – this may be why a number of relevant clinics have declined to participate or are very reluctant.
- While it might be possible to identify other clinics to join the exercise, the meaningfulness of such a parallel exercise is to be questioned.
- Including new materials should raise the attractiveness of the study and thereby the interest to join and at the same time increase its relevance.

Considerations for moving forward

- Including materials new or even better new to the market (likely in the category of been traded within the industry and hence resulting in broader exposure), with specific exposure characteristics could even add or increase the opportunity to collect relevant information with regard to the effectiveness of the QRA(2) – if adequate consideration is given to confounding factors.

- The proposed surveillance study will be a long-term effort. A study involving new materials might require about a decade before being able to draw meaningful conclusions on the effectiveness of the QRA.