IDEA – the International Dialogue on the Evaluation of Allergens

Update on the status of the Surveillance study

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IDEA Surveillance Study

- Context
- Rationale
- Design
- Pilot Status
- Extended study proposal
- Q&A

IDEA Surveillance Study - Context

Three IDEA Working Group meetings were held on the topic of feasibility of a study to assess the effectiveness of the quantitative Risk Assessment (QRA2) to prevent induction of sensitization.

April 6, 2016
February 15, 2017
December 7, 2017

All related documents available on IDEA website.

IDEA Surveillance Study - Context

Key conclusions/learnings from former meetings leading into the design of the study:

- A surveillance system alone may not verify whether the QRA is effective due to confounding factors.
- Complementary work would be necessary.
- Despite the confounding factors, diagnostic patch testing of dermatology clinic patients (surveillance) was seen as a critical pillar in the long term evaluation of the QRA.
- Include additional materials (beyond those already part of routine patch testing).
- Following trends for specific materials may direct additional work.
- Determine adequate patch testing concentration for new ingredients in a range-finding study and develop respective protocol.
- Arrange for data reporting and management via an existing system (EECDRG and or ESSCA) and assess most suitable approach in pilot study.

Project Rationale for EFISS (Extended Fragrance Ingredients Surveillance Study)

The project is an industry-sponsored surveillance study incorporating both additional (so far not routinely patch tested) and routinely tested materials.

It is an industry-stakeholder partnership in data generation, analysis and publication.

- It was established based on the identified needs:
  - to make the post-market monitoring more relevant and up to date,
  - to provide greater insights into potential trends in the incidence of skin contact allergy to materials used in fragrances,
  - to respond to a clear expectation of the Commission and its risk assessors that QRA2 used by the industry must be supported by a product stewardship program, which involves clinical surveillance, demonstrating industry governance.

Surveillance project – Design

- The project is set up in two phases: pilot and expanded scale.
- Despite a delay of 2 years due to Covid, 4 of originally 5 clinics contacted remain committed for the pilot: Zagreb (Croatia), Coimbra (Portugal), Malmö (Sweden), Groningen (The Netherlands).
- Data management (input on CRF/eCRF design and training) and analysis is in the hands of Wolfgang Uter at the clinic of Erlangen (Germany).
- Includes **30 existing materials** (26 allergens, 2 mixes, Peru balsam and Emulsifier) and **7 additional materials**, so far not in the scope of systematic screening by the dermatological clinics.
- The 7 additional materials were proposed by an industry working group using a set of agreed criteria and endorsed in an IDEA Workshop.
- For the patch test materials production / delivery we partnered with Chemotechnique, Malmö, Sweden.
- Project includes **new syringe dosing system** for all additional materials (expected to allow more consistent dosing) and further **quality control** elements involving site visits (managed by Marléne Isaksson).

IDEA Surveillance Study – Additional Materials

Based on criteria developed in the IDEA WG:

- Non natural ingredient
- Consideration of proposed extended EU list for consumer information
- Industry risk management driven by sensitization endpoint

in addition to fragrance markers and individual fragrance allergens more or less routinely tested, 7 fragrance materials, so far not in the scope of systematic screening, were selected.

Surveillance project – Additional materials

Name of material	CAS number of material	Volume of Use	Listed in the 2012 SCCS tables 13-1, 13-2 or 13-3, preferably on list 13-1	Listed in the 2013 Commission regulatory proposal	NESIL (µg/cm²)	Synthetic or natural	Status IFRA Standards	Used as flavour
Furaneol [4-Hydroxy-2,5-dimethyl-3(2H)-furanone]	3658-77-3	Moderate/low VoU (5000 kg/y 2015).	NO	NO	590	Synthetic material (but presence in natural extracts)	Has an IFRA Standard	YES
trans-2-Hexenal	6728-26-3	Moderate VoU (8000 kg/y 2015).	YES	NO	24	Synthetic material (presence in natural extracts limited)	Has an IFRA Standard	YES
4,8-Dimethyl-4,9-decadienal	71077-31-1	Moderate VoU (8000 kg/y 2015).	NO	NO	550	Synthetic material (presence in natural extracts limited)	Has an IFRA Standard	NO
Longifolene	475-20-7	High VoU (278000 kg/y 2015).	YES	NO	3500	Synthetic material (abundant presence in natural extracts)	Has an IFRA Standard	YES
Benzaldehyde	100-52-7	High VoU (268000 kg/y 2015).	YES	YES	590	Synthetic material (but presence in natural extracts)	Has an IFRA Standard	YES
Oak - & Treemoss (atranol & chloroatranol content at trace levels)	90028-68-5; 9000-50-4; 68917-10-2; 90028-87-4;……	High VoU (44000 kg/y 2015 & 57000).	YES	YES	700	Natural material	Has an IFRA Standard	NO

IDEA Surveillance Study – Additional Materials

Based on available data on irritation and sensitization concentration the following concentrations were derived for the pilot:

	Additional materials	Concentrations %		
		Round 1	Round 2	Round 3
1	Furaneol[4Hydroxy-2,5-dimethyl-3(2H)-furanone]: CAS 3658-77-3	0.6	0.9	1.4
2	trans-2-Hexenal: CAS 6728-26-3	0.02	0.03	0.05
3	4,8-Dimethyl-4,9-decadienal: CAS 71077-31-1	0.5	0.8	1.3
4	Longifolene: CAS 475-20-7	3.5	5.3	8.0
5	Benzaldehyde: CAS 100-52-7	0.6	0.9	1.4
6	Tree Moss (CAS 90028-67-4, 68648-41-9, 68917-40-8) new quality	2.0	2.0	2.0
7	Oak Moss (CAS 90028-68-5; 9000-50-4; 68917-10-2)	2.0	2.0	2.0

Surveillance project – Pilot Status 1

- Pilot launched in May 2022, including 3 rounds of testing.
- Each round lasted between 9 and 10 weeks.
- In addition to the readings, based on consultation with various stakeholders, a 3 week waiting period after last patient patch tested in each round was included to allow for identification of potential active sensitization.
- Data entered on total of 379 patients.
- 6 patients were tested but readings were not carried out.
  - Patches fell off 4 patients due to extremely hot weather.
  - 2 patients got ill (unrelated) before readings could be completed.
- Clinical work completed mid of November 2022.

Surveillance project – Pilot Status 2

- Pilot study did
  - serve as dose range-finding study for adequate patch test concentration of the 7 additional materials
  - test the functioning of the study processes and allow to identify and address system bugs, e.g. linked to the data reporting system
  - test functioning of calibrated syringe system with mixed reports from sites
  - after completion and analysis of the outcomes, serve as basis for the envisaged European multicenter study “Extended Fragrance Ingredient Surveillance Study (EFISS)”.
- No unexpected reactions have been observed by the clinics to any of the 7 additional materials at any of the concentrations utilized in the range-finding.
- Additionally, the pilot was very successful, proving the study systems worked and building trust and reputation for the fragrance industry as a reliable partner to the dermatological community.

Surveillance project – Main study

- Will be a long-term commitment over approximately 5 years (3 cycles), each lasting about 15 - 18 months)

- Proposal to move from the current 4 sites to 8 or 9 clinics, distributed across Europe.

- Next steps:
  - Pilot study results will be summarized and discussed in the Steering Committee and in an investigators meeting and are being considered for publication.
  - Also, planned presentation at conference being organized by one of participating sites.
  - A revised protocol for the main study will be developed based on the protocol for the pilot in Q1 2023.
  - Recruitment of additional clinics during Q1 – Q3 2023.
  - Prepare for study start end of Q3, beginning of Q4 2023.

Surveillance project – Main study

❖ Key deliverables of the main study are:

- Provide new insights on fragrance materials so far not routinely patch tested.
- Create a dialogue with key researchers such that potential issues can be identified (early alert system) and are addressed via engagement.
- Allow corrective measures to be identified and taken when needed.
- Contribute to better understanding of clinical relevance and provide insight on potential sources of induction to fragrance ingredients from non-fragrance uses.
- Over time, contribute to the long-term acceptance of the QRA2 as the key tool to prevent induction of skin sensitization for the majority of the population, during the typical and foreseeable use of the products within the scope of our voluntary program (IFRA Standards).
- Will provide high quality and reliable clinical data, which are relevant as a complement to a meaningful product stewardship program by providing insight as to whether the risk assessment and management measures in place are adequate and broad enough in scope.

Muchas Gracias

THANK YOU

DANKE SCHÖN

Surveillance project – Perspective of IDEA Annual Review Participants

MERCI BEAUCOUP

GRAZIE

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