# IDEA Surveillance project

# EFISS (Extended Fragrance Ingredients Surveillance Study)

## Background and Status

## Reliable high quality clinical data are critical

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IDEA Regular Review Meeting

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# Project Rationale for EFISS

What is it?

- an industry-sponsored surveillance study with both additional and existing fragrance patch test materials
- industry-stakeholder partnership in data generation, analysis and publication

What does it offer?

- the possibility of identifying trends in the incidence of skin contact allergy

Why was it established?

- to ensure a relevant and up to date post-market system
- to provide greater insights into potential trends in skin contact allergy
- to respond to a clear expectation of the Commission that QRA2 used by the industry must be supported by a product stewardship program, which involves clinical surveillance.

# Target Outcomes

EFISS should:

- Over time, provide evidence to allow conclusions on the performance of fragrance industry's tools 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 the industry's voluntary program (IFRA Standards).

- Serve as an early alert system

- Provide learnings on exposure conditions of the patients to:
  - Gain greater insight as to whether the risk assessment and management measures in place are adequate and broad enough in scope
  - Allow corrective measures to be identified and taken if needed

# Surveillance project – Design

- The project was split in two phases: pilot and large scale study
- Data management 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
- For the patch test materials production / delivery we partnered with Chemotechnique, Malmö, Sweden.
- Pilot project included new syringe dosing system for all additional materials (aiming for more consistent dosing) and further quality control elements (training session, site visits, etc.)

# 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 | 18 | Synthetic material (presence in natural extracts limited) | Has an IFRA Standard | YES |
| 4,8-Dimethyl-4,9-decadienal | 71077-31-1 | Moderate VoU (5000 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 (269000 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; 90028-67-4;..... | Low VoU (1500 kg/y & 100 kg). | YES | YES | 700 | Natural material | Has an IFRA Standard | NO |

* Additional information: this material is not tested in the Standard series but is the quality now used in products compliant with IFRA Standards and the EU legislation.

# EFISS Pilot

## Main target:

- **Establish patch test concentrations for the additional materials**
- **Test functioning of the study processes** (incl. special auto-dosage syringes) and identify and address system bugs, e.g. linked to the data reporting system

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ORIGINAL ARTICLE

CONTACT DERMATITIS WILEY

### Results of patch testing with five fragrance materials hitherto not tested: A dose-finding study in the clinical population

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IFRA, the International Fragrance Association

**Abstract**

**Background:** Quantitative risk assessment (QRA) for skin sensitization is used to derive safe use levels of sensitising fragrance ingredients in products. Post-marketing surveillance of the prevalence of contact allergy to these ingredients provides relevant data to help evaluate the performance of these measures.

**Objectives:** To determine a suitable patch test concentration for five fragrance materials that had hitherto not been tested on a regular basis. These concentrations are then to be used in a surveillance study with patch testing consecutive patients over an extended monitoring period.

**Materials and Methods:** Furaneol, CAS.3658-77-3; trans-2-hexenal, CAS.6728-26-3; 4,8-dimethyl-4,9-decadienal, CAS.71077-31-1; longifolene, CAS.475-20-7; benzaldehyde, CAS.10052-7, were patch tested with other fragrance allergens in four clinics. Patch testing was conducted in three rounds, starting with the lowest concentrations of the five ingredients. The doses were increased in the subsequent rounds if no late-appearing positive reactions and virtually no irritant reactions were reported.

**Results:** Overall, 373 patients were tested. No positive allergic reaction was reported to the five ingredients. Patch test results of other fragrance allergens are reported.

**Conclusions:** The highest test concentrations are each considered safe for patch testing consecutive patients. Further surveillance based on these preparations will evaluate the hypothesis that QRA-driven consumer product levels of these fragrances can prevent sensitization.

KEYWORDS
4,8-dimethyl-4,9-decadienal (CAS 71077-31-1), allergic contact dermatitis, benzaldehyde (CAS 100–52-7), fragrance contact allergy, furaneol (CAS 3658-77-3), longifolene (CAS 475–20-7), quantitative risk assessment, skin sensitization, trans-2-hexenal (CAS 6728-26-3)

- **Pilot study conducted in 4 clinics in 2022**
- Around 400 patients' patch tested)
- Results published in Contact Dermatitis
- **Methodology demonstrated to work**

# Surveillance project – Extended study

**Central element of EFISS: harmonization of processes & rigid quality control**

- Patch test reading workshop organized at Malmö University hospital September 2024
- Standardization of loading patch test chambers using different techniques was trained
- Patients were invited and doctors/nurses had to do blind reading and compare; focusing on differentiating irritation from weak sensitization

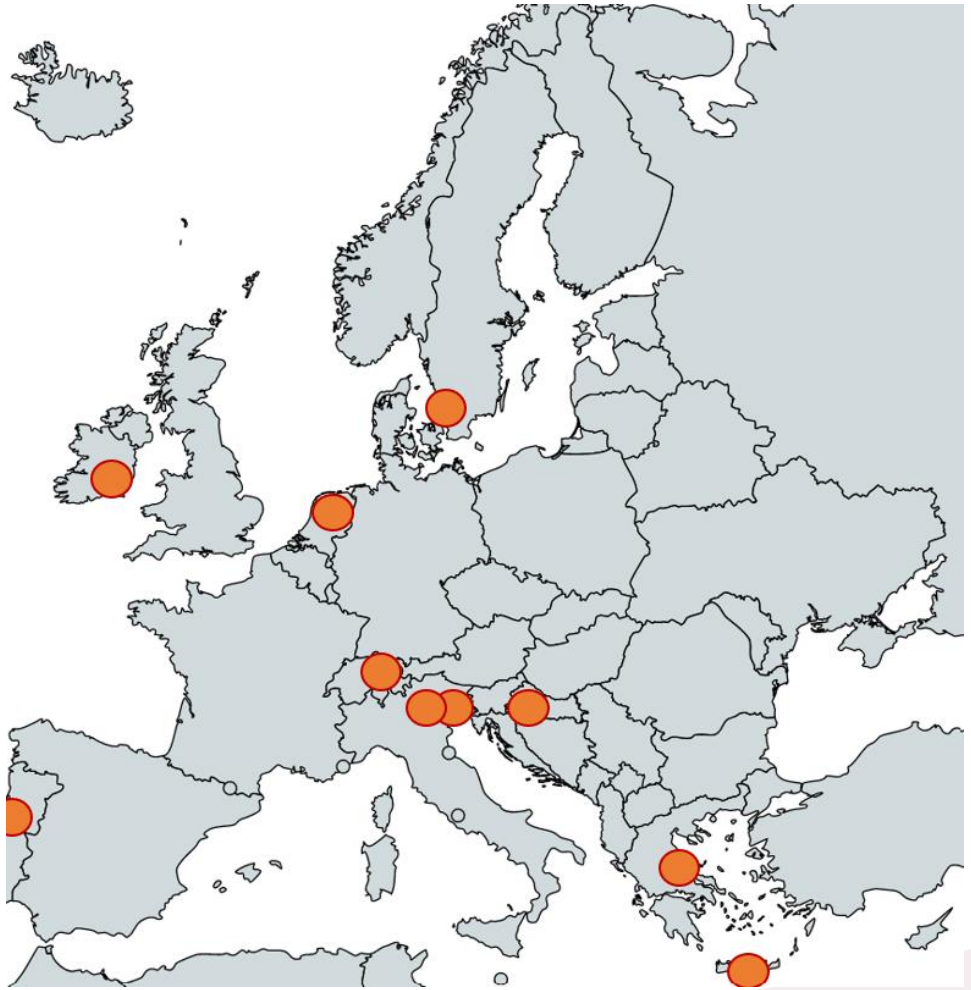
# Surveillance project – Extended study

Recruitment of additional clinics completed 9 (10) clinics in 8 European countries.

Contracts and ethical approval process nearly completed.

Table 2 Participating departments

| Institution | Investigators |
|---|---|
| Dermatologische Klinik, Universitätsspital Zürich, Switzerland | Claudia Lang |
| University of Athens, Andreas Sygros Hospital, Greece | Stamatis Gregoriou |
| University Hospital of Heraklion, Crete, Greece | Dimitra Koumaki |
| Department of Dermatology and Venereology, University Hospital Center Zagreb, University of Zagreb School of Medicine, Croatia | Suzana Ljubojević Hadžavdić |
| South Infirmary Victoria University Hospital Cork, Ireland | John Bourke |
| Department of Medicine DIMED, University of Padova, Padova, Italy | Anna Belloni Fortina, Anna Zambello |
| Department of Dermatology, AULSS8 Berica, Ospedale San Bortolo, Vicenza, Italy | Elena Pezzolo |
| University Medical Center Groningen, Department of Dermatology, Groningen, The Netherlands | Marie-Louise A. Schuttelaar |
| Serviço de Dermatologia Centro Hospitalar e Universitário de Coimbra, Portugal | Margarida Gonçalo, Ana Carolina Figueiredo |
| Skane University Hospital and Department of Occupational and Environmental Dermatology, Lund University Malmö, Sweden | Cecilia Svedman, Magnus Bruze |



# Surveillance project – Extended study

Study protocol published in June 2025.

3 cycles of testing of about 15 months each targeting 2700 patients per cycle to reach a total of more than 8000 patients

First cycle ongoing, aiming completion in Q1 2026.

Archives of Dermatological Research (2025) 317:778
https://doi.org/10.1007/s00403-025-04286-9

STUDY PROTOCOL

**Extended fragrance ingredients surveillance study (EFISS)—protocol for a clinical surveillance study on contact allergy to 7 fragrance materials in widespread use but hitherto not systematically patch tested**

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Current state of testing - numbers already entered in system (numbers reported as tested):

| | | | | | |
|---|---|---|---|---|---|
| CH | Zürich | 111 (111) | NL | Groningen | 187 (288) |
| GR | Athens | 68 (68) | PT | Coimbra | 9 (191) |
| GR | Heraklion | 6 (100) | SE | Malmö | 287 (440) |
| HR | Zagreb | 343 (400) | IT | Padova | 0 (0) |
| IE | Cork | 230 (230) | ~~IT~~ | ~~Vicenza~~ | - |

Total: **1241 (1828) – Projection 2240 - 2250 (about 85% by end of Q1)**

*Thank you for your attention*