THE EDEN GLOBAL STUDY ON THE PREVALENCE OF CONTACT ALLERGY TO FRAGRANCES (Sponsored by RIFM)

One of the basic questions that our industry cannot address is:
“How common is fragrance allergy in the general population?”

- Claims of high rates of fragrance allergy based on selected patient populations from diagnoses on patch tests without documenting allergen-specific skin disease
- Allergy is a health effect, not a test result
- Definitive data are needed to address unfounded extrapolations to the general population from often cited but limited studies on diseased skin in clinic patients. Incidence in patients has no relevance to the general population.
- The use of selected populations to detect sensitization without proving relevance is inappropriate
- Population based studies are the only method for obtaining accurate prevalence data

THE STUDY
The European Dermato-Epidemiology Network (EDEN) Global Study on the Prevalence of Contact Allergy to Fragrances will provide data on the prevalence of contact allergy to fragrances in the general population in different countries, establish a standardized methodology and facilitate international collaboration. It will assess:
- the prevalence and severity of contact dermatitis in the general population through a questionnaire.
- the rate of sensitization to fragrances as documented by standard patch test procedures in the same population, relating sensitization to documented clinical manifestations.

THE RATIONALE
A prevalence study on contact allergy to fragrances in the general population is needed because the other two studies that exist are too small. The Meding, 1990 study (Acta Derm Venerol suppl153:1-43) was limited to Gothenburg, Sweden and involved testing only some of the participants. The Nielson and Meuring, 1993 study (Ann Dermatol Venereol:120:33-36) was limited to Denmark, involved only 800 subjects and lacked a precise prevalence.

Most of the claims of high rates of fragrance allergy are based on selected, tertiary-care patient populations with diagnoses based on patch tests without documenting concomitant allergen-specific skin disease (allergy is a health effect, not a test result). Definitive data are needed to address often cited, yet unfounded, extrapolations to the general population from limited studies on diseased skin in clinic patients. The use of selected populations to detect sensitization without proving relevance is inappropriate. Population based studies are the only method for obtaining accurate prevalence data.

THE INVESTIGATORS:
EDEN is a European initiative aimed at: 1) improving the role of epidemiology in dermatology, 2) sharing expertise, 3) producing high quality work and 4) contacting isolated groups and encouraging them to join in. EDEN consists of having one specific contact person in each country in Europe and a Steering Group. A fragrance subcommittee was formed to conduct a one-year prevalence study of contact allergy to fragrances in the general population. The fragrance subcommittee consists of the following scientists: Luigi Naldi (Clinica Dermatologica Ospedali Riuniti Largo Barozzi, Bergamo, Italy) - Study Coordinator, Thomas Diepgen (Dept. of Clinical Social Medicine of University of Heidelberg, Heidelberg, Germany) - Study Statistics and Data Collection, Pieter-Jan Coenraads (Occupational & Environmental Dermatology Unit, Groningen University Hospital, Groningen, The Netherlands), Peter Eilsner (Department of Dermatology, University of Jena, Jena, Germany), Margarida Gonçal (Department of Dermatology, University of Coimbra), Ake Svensson (Department of Dermatology, University of Lund, Malmo, Sweden).

THE DESIGN (a detailed technical outline is available)
The aim of the questionnaire is to identify those people who have had a reaction that is likely to be “contact dermatitis” over one month, one year (period prevalence) based on the reported symptoms and diagnoses. The severity of the disease will be also assessed by the instrument.

The goal of the study is to have 1,500 individuals per region respond to the questionnaire and to patch test 500 of those individuals. The questionnaire will be conducted in a structured interview by a trained technician in person. After the questionnaire is completed, a patch test will be conducted to assess the rate of sensitization to fragrances in the same population, relating sensitization to documented clinical manifestations. During the patch test phase there will be an equal number of individuals in the control group.
Benefits of the Study

- Sets a gold standard for patch testing; calibration never done before (e.g. training, controlled commercial grade samples, blind comparison patch test & history).
- Baseline data for QRA.
- An international study of the prevalence of contact allergy to fragrances, not extrapolated data from clinical reports or from limited existing data.
- Conducted by an independent expert group (EDEN), endorsed by the Expert Panel that reviews RIFM’s research.
- Conducted in cooperation with the European Society of Contact Dermatitis.
- RIFM becomes a focus point or resource for epidemiology data on fragrance allergy.
- Unprecedented fragrance study design.
- Influences regulatory actions.
- Expands scientific interactions with dermatology community including patch testers, clinicians and epidemiologists.
- Expands associations with academic biomedical investigators.

**European Study**

*(Italy, Germany, The Netherlands, Portugal and Sweden)*

**2005/2006 Phase I Validation**
- Questionnaire
- Code Book & Data Entry
- Data Collection: Italy, The Netherlands, Sweden
- Questionnaire Reproducibility
- Patch Test Procedures

**2008-2010 Phase III Full Study**
- Data Collection: 15,000 Subjects (2,500 per center)
- Statistical Analyses: Pooled Data Heidelberg Center in collaboration with Italy group

**2007/2008 Phase II Pilot Study**
- Definition of Sampling Procedures & Subject Recruitment
- Recruitment 600 subjects: (100 per center) General Population
- Statistical Analyses
- Study Modalities Evaluation

**2011/2012 North America**

**2013/2014 Asia**

**Progress**

Detailed presentations were given to the Expert Panel in September 2009. The full study began in October 2009. The full study includes a total of 1,500 subjects interviewed per site (for a total of 9,000 subjects) and 500 individuals interviewed and patch tested per center (for a total of 3,000 subjects). We anticipate that the study will end in April 2011 and results will be available by the end of 2011. The first paper from this study, published in the peer reviewed scientific literature by Rossi, *et al* (2010) in *Dermatology*, describes the methodology and feasibility of the study.

Conducting this seminal prevalence study has provided an opportunity to learn more about fragrances and patch testing. Epidemiology is not developed in this area and the EDEN Global Study on the Prevalence of Contact Allergy to Fragrances has established a uniform global method. This study also helped to set a standard for patch testing which has never been done before. The training implemented for a multi-center study ensures calibration of the sample amount and dosing in all centers. Each reaction will be read in the same way in all centers and the full study will allow a baseline for the dermal sensitization QRA methodology.