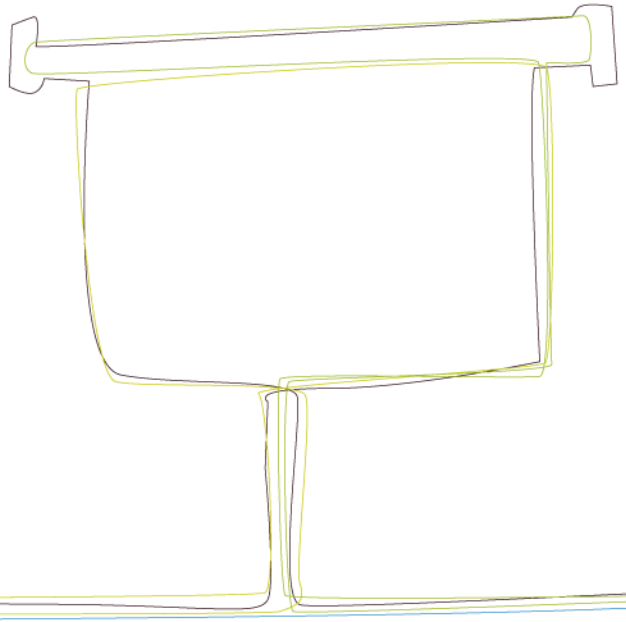
IDEA
International Dialogue for the Evaluation of Allergens

# IDEA Workshop on pre- and prohaptens

## October 20-21, 2015



## Introduction to the Workshop

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*(Moderator of the IDEA Workshops)*

# 1st IDEA Workshop on pre- and prohaptens
# May 28-29, 2013

## Key conclusions (1)

- The workshop produced a number of key conclusions on the work to date and identified a range of specific action steps:
- There is clear qualitative indication that sensitizers can be formed in some formulations under realistic conditions as a result of abiotic **hydrolysis** of fragrance ingredients. The importance of biotic **hydrolysis** in the epidermis will require further investigation.
- Contact allergy (positive patch-tests) to **oxidation** products of some fragrance ingredients is common. There is presently insufficient data on exposure to these **oxidation** products to make a correlation to disease (allergic contact dermatitis).

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## Key conclusions (2)

- On biotic and abiotic **oxidation**, the data show the complexity with great challenges for predictability and analytical testing:
  - The models do not sufficiently reflect exposure conditions or co-factors that interfere with sensitization.
  - There is a need for more rigorous protocols (including ROAT) for clinical studies.
  - Different concepts of relevance (individual, group-related and epidemiologic data) need to be refined.
- The development of new analytical methodologies such as HR MAS-NMR is a key requirement to elucidate in situ phenomena.
- The workshop produced a range of recommendations to identify and characterize pre- & pro-haptens, ranging from chemical characterization to confirmation through clinical studies.
- Future work should be conducted in transparency and with participation from stakeholders with relevant expertise.

# Key conclusions (1)

- Clinical data increasingly suggest that prehaptens, including those used as fragrance raw materials, play a significant role as cause of contact allergy.
- Prohaptens can be handled in the same way as other haptens.
- There is indication that the majority of oxidative transformations happen outside the human body (abiotic reactions). Oxidative transformations in human skin have been studied only for a few compounds.

# Key conclusions (2)

- The analytical confirmation of postulated pathways for hapten formation via pre/prohapten is facing significant challenges in that the species in question prove highly reactive and form unknown byproducts.
- The modelling of metabolic pathways via QSAR/SAR, while still in its infancy, shows potential but requires further confirmation across a wider range of chemicals.
- Promising methods for tracking prohapten metabolism include cutaneous CYPs cocktail, transporter assay systems and HRMAS NMR in reconstructed human epidermis (RHE) as demonstrated with cinnamyl-OH and eugenol/isoeugenol and their esters.

# Objectives

1) To further drive mechanistic understanding of pre- and prohapten formation and to bridge findings with clinical data.

2) Obtain an agreement on what is known respectively unknown and lay out pathways to close these knowledge gaps.

3) Work towards solid documentation of current knowledge and its implementation for risk management purposes.

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## Thank you for your attention