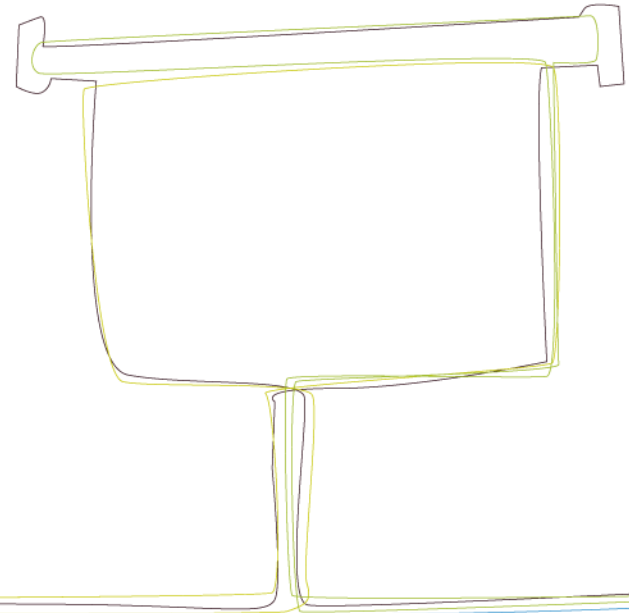


What is needed to integrate pre- and prohaptens in the QRA?

Summary of the Breakout group 1



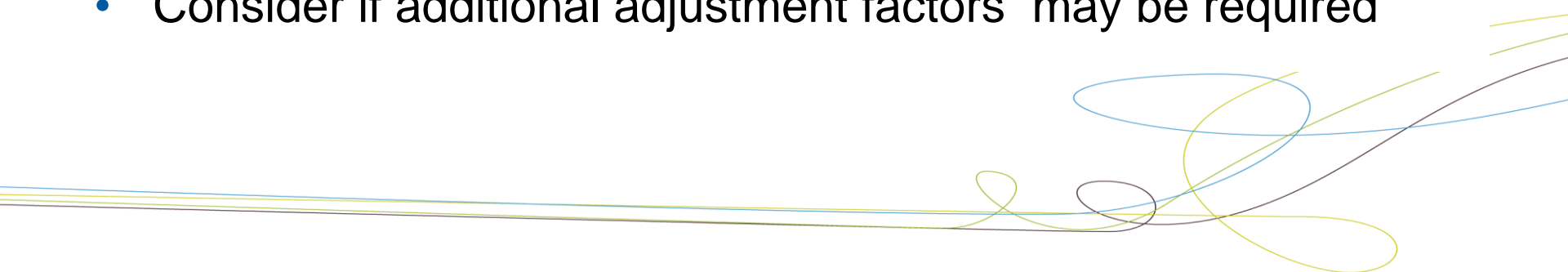
Participants



- Anne Marie Api
- Peter Cadby
- Graham Ellis
- An Goossens
- Carsten Goebel
- Etje Hulzebos
- Chanita Kuseva
- David Lovell
- Hans Merk
- Boris Müller
- Chris Powell
- Scott Schneider

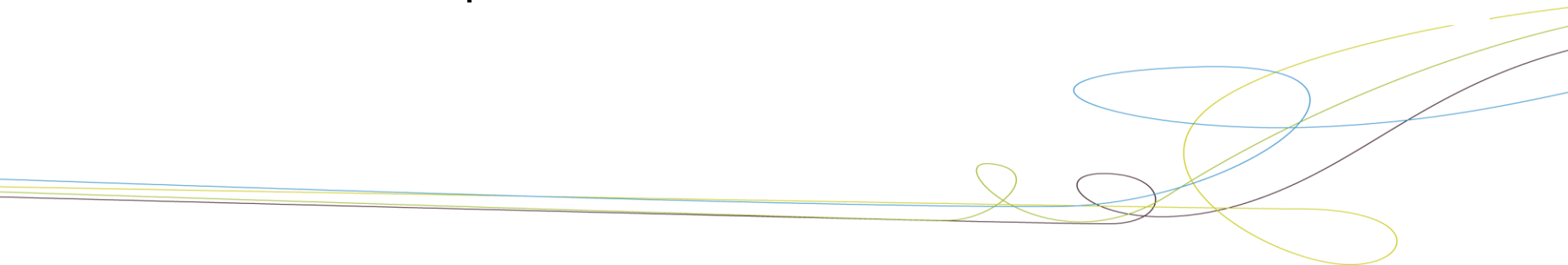
Pre-haptens (hydroperoxides formed by autoxidation outside the skin)

- Sensitization potential is known
- As a first step, when the EC3 of the hydroperoxide is known, apply the QRA
- Consider this as limiting level in the raw materials, which leads to a certain maximum presence of those
- Confirm in the finished product (at various stages of its lifecycle, provided analytical method developed)
- Understand if activation in the skin may contribute to hydroperoxide formation
- Consider if additional adjustment factors may be required



Pre-haptens (hydroperoxides formed by autoxidation outside the skin)

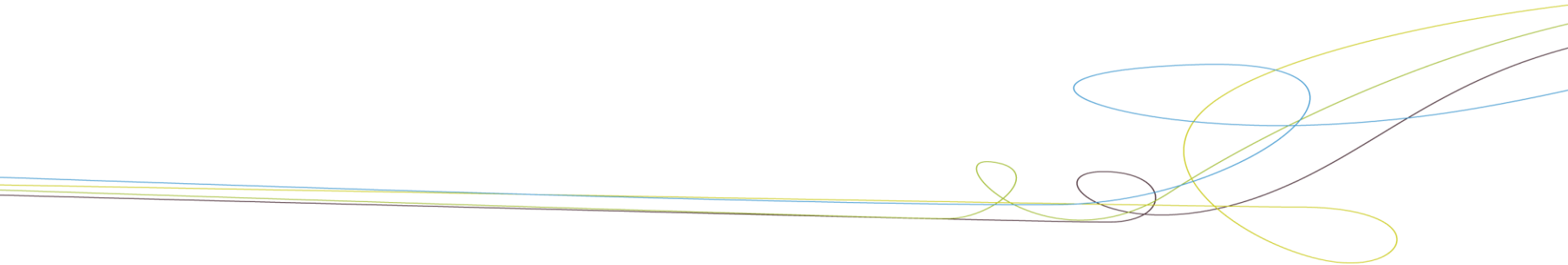
- Sensitization and hydroperoxide formation potential is unknown
- Modeling tools (like TIMES) can be used to screen for materials that can oxidize
- Confirm in laboratory experiments
- As the EC3 values are unknown, use a non animal approach (read across, in silico and in vitro tools)
- An analysis of all of the sensitization data of hydroperoxides should be completed and the lowest should be used



Pre-haptens (hydrolysis in the product)



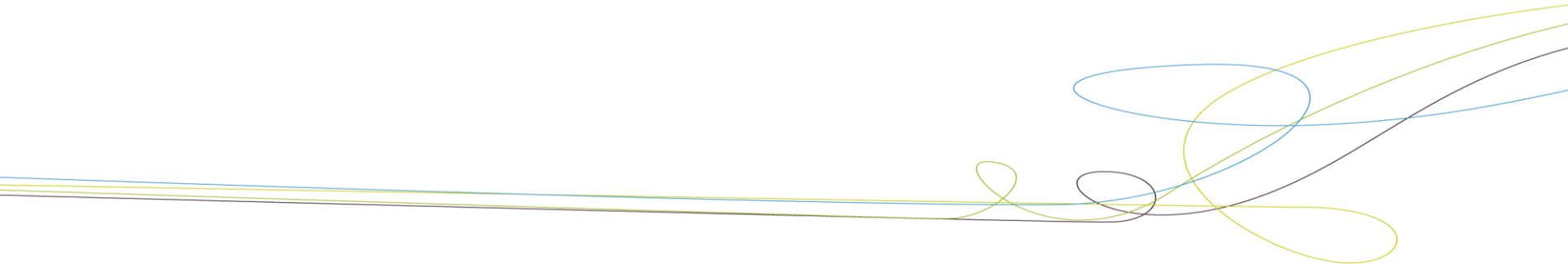
- Consider the breakdown of hydrolysable precursors of potential sensitizers in the consumer products for risk assessment, e.g. Cinnamal diethylacetal which may be hydrolyzed to Cinnamicaldehyde
- Considerations
 - Product base and pH
 - Structure of the hydrolysable precursor (e.g. formates hydrolyze faster than acetates)
 - in the absence of information as worst case scenario assume 100% dissociation



Pro-haptens (what happens on/in the skin)



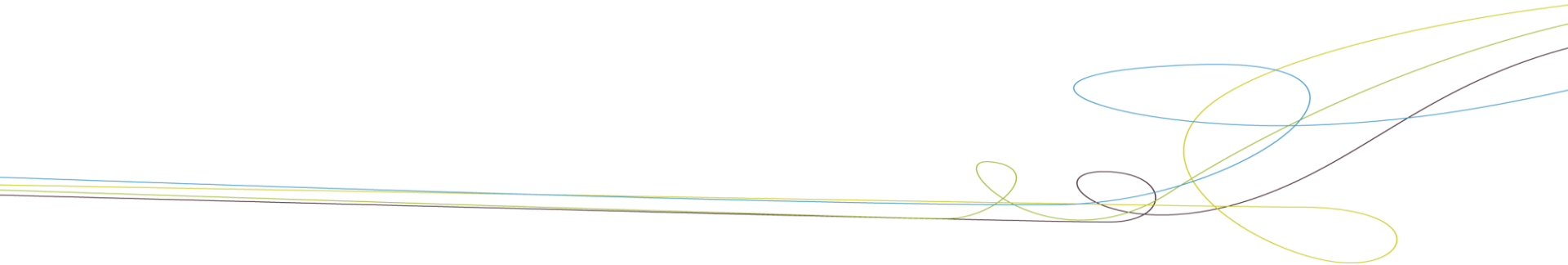
- Consider active formation of reactive species through metabolic pathways
 - Is this sufficiently considered in the current QRA approach
 - Understand if activation in the skin may contribute to hapten formation
 - Understand the balance of activation / deactivation
 - Further explore appropriate in-vitro test systems (e.g. metabolic activating systems such as S9)

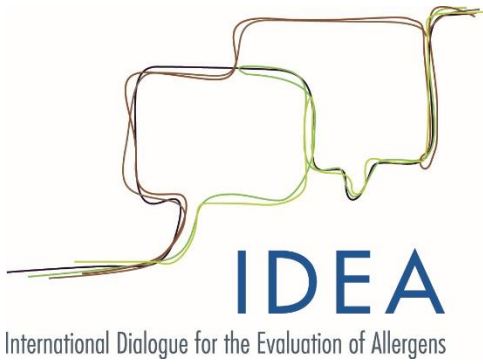


General comment



- There is a need for a clear understanding of the contribution of the consumer products (under the scope of the QRA) to the clinical picture.





**Thank you for
your attention**

