



The Challenge of the Cosmetics Directive 2009 deadline: what do we have ?

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*9th Annual ecopa Workshop
November 29-30 , 2008, Brussels*

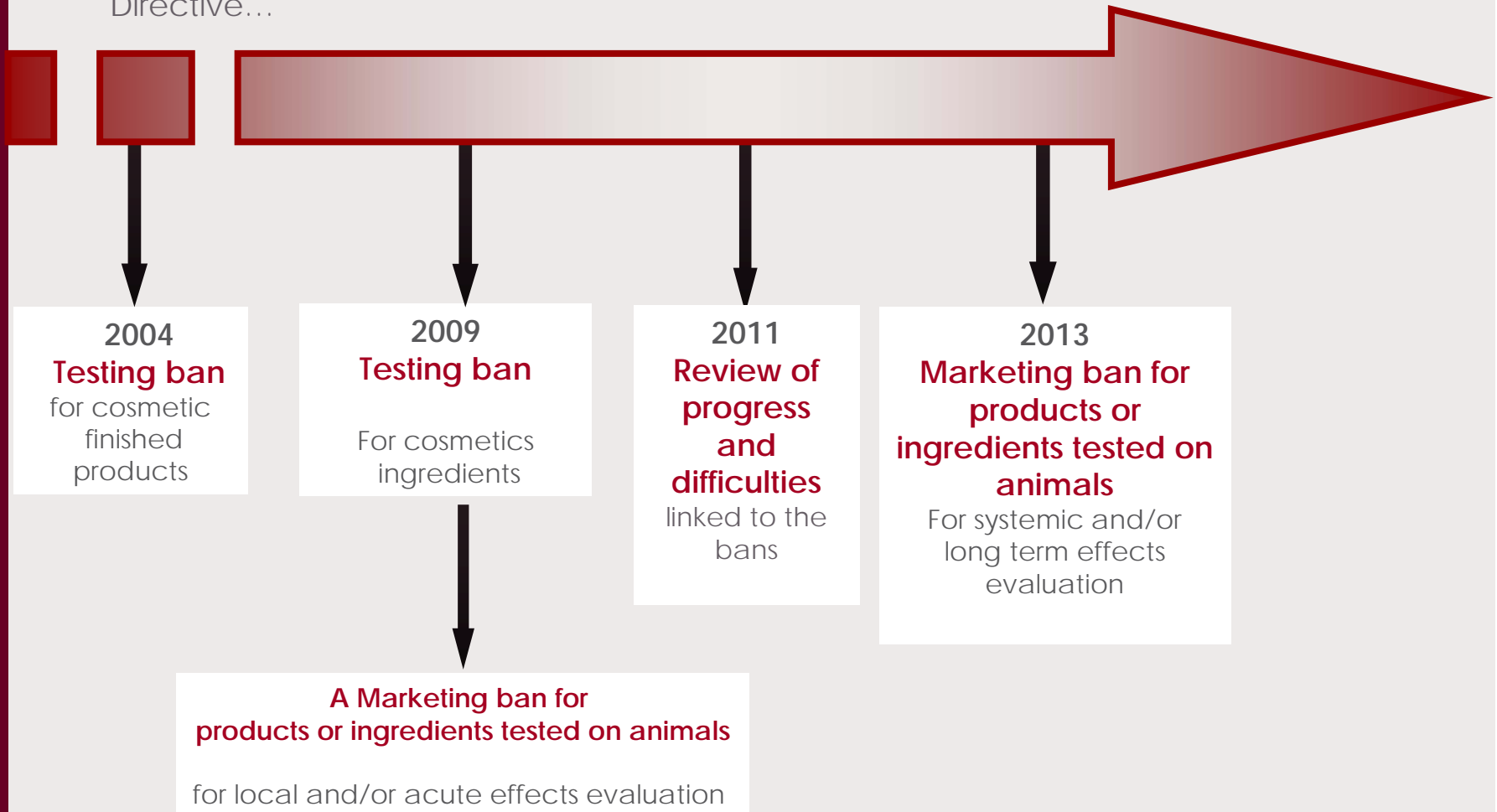


A new EU regulatory context

The EU 7th Amendment prohibits:

- the **performance of animal tests in the EU** to meet the requirements of the Cosmetics Directive...
- the **sale** of cosmetics products, when the **final formulation or ingredients** have been tested on animals to meet the requirements of the Cosmetics Directive...

REGULATION





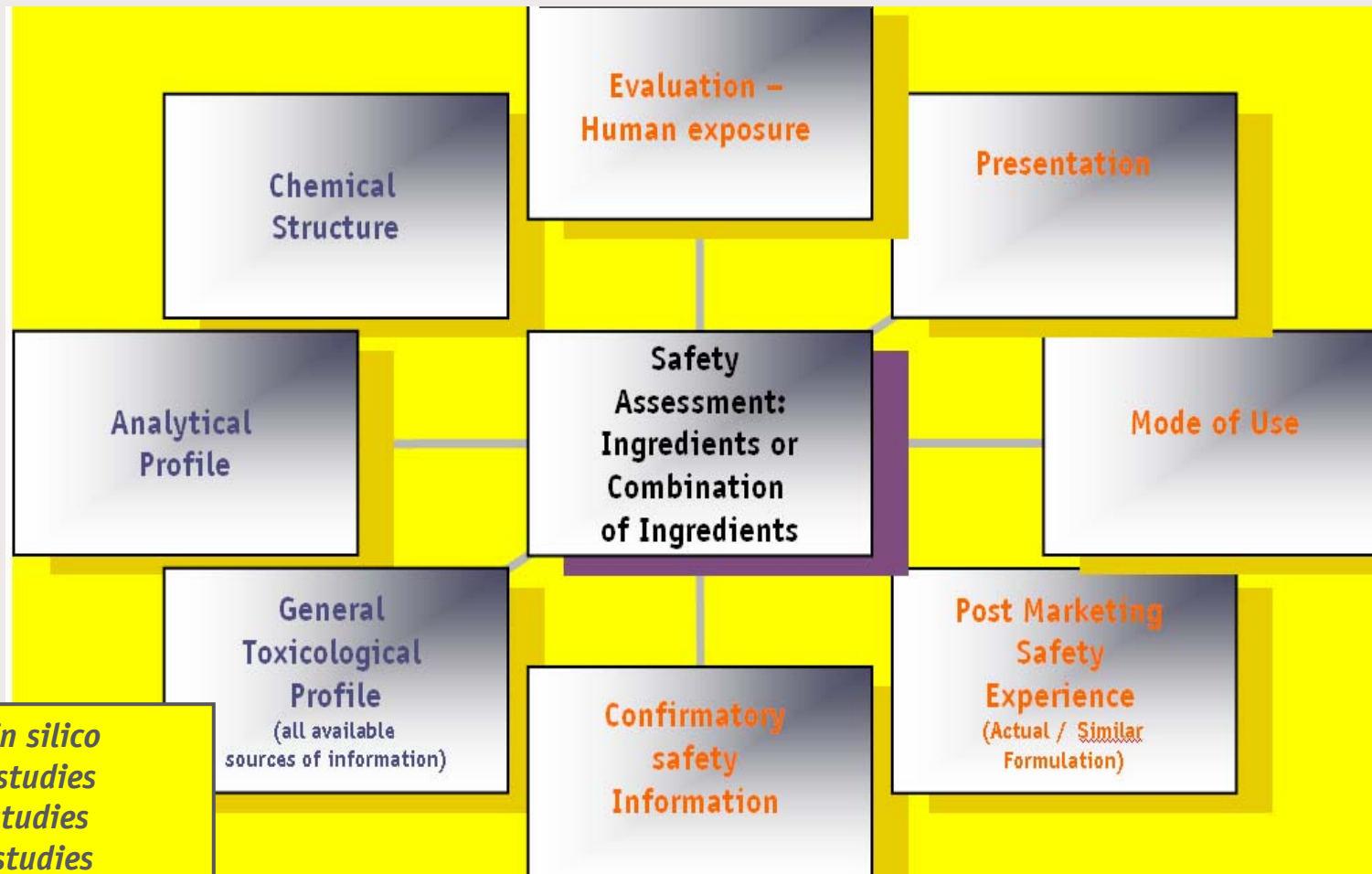
Science and cosmetics business

Products and safety assessment : responsibility with the manufacturer, open choice of data/methods consistent with the 7th Amendment

Ingredients regulated by the Cosmetics Directive: **need for EU scientifically validated and accepted replacement methods by regulatory authorities or the Scientific Committee for Consumer Products (SCCP)**

Other ingredients : data/methods consistent with REACH & the 7th Amendment

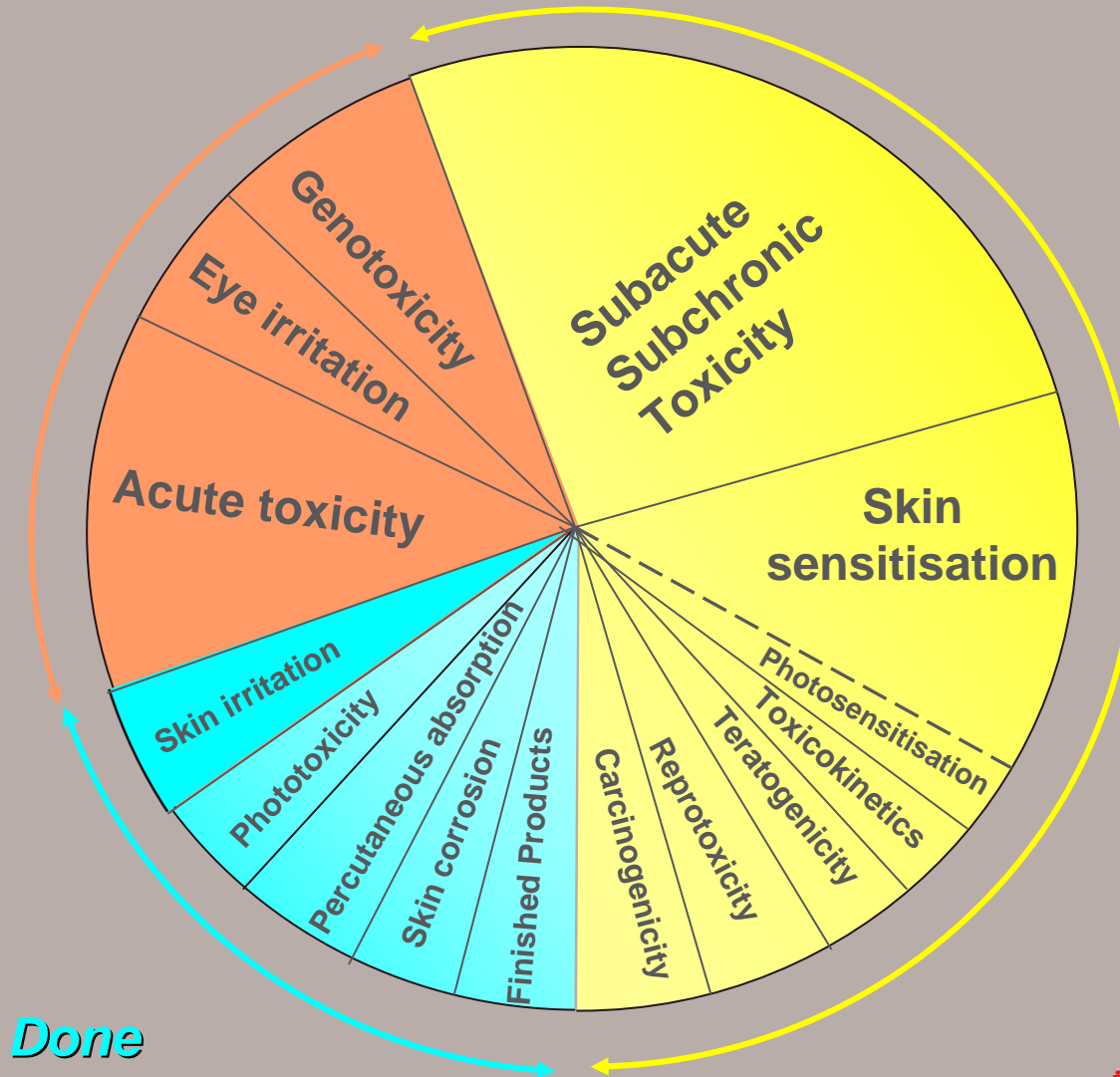
SAFETY ASSESSMENT



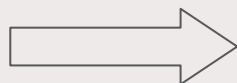
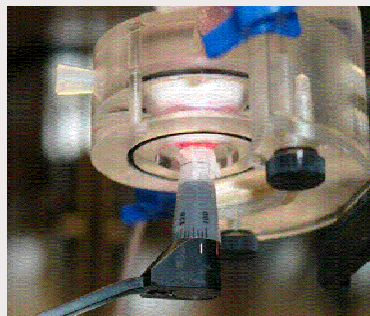
VALIDATION / REPLACEMENT - WHERE ARE WE ?

2009

2013



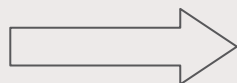
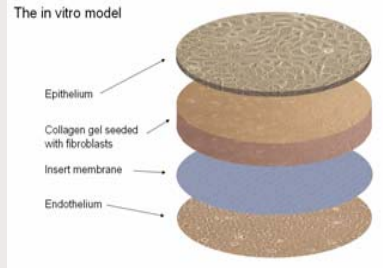
COLIPA Eye Irritation Programme



Integrated research projects

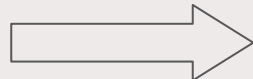
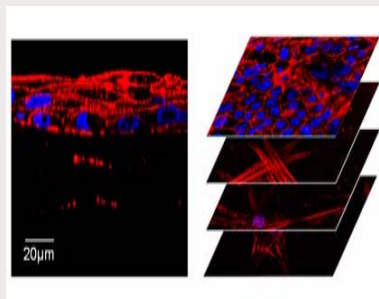
- *In vitro* corneal culture eye irritation assay
- Cell culture models for ocular toxicity studies
- Genomics project

The in vitro model



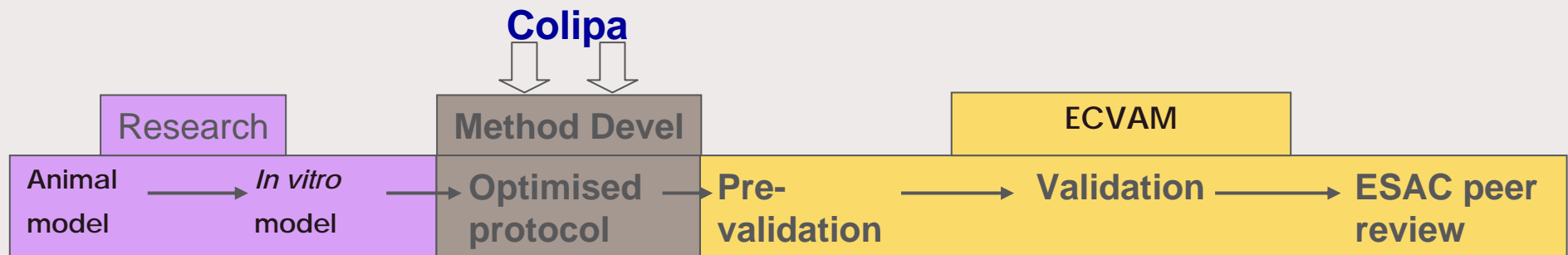
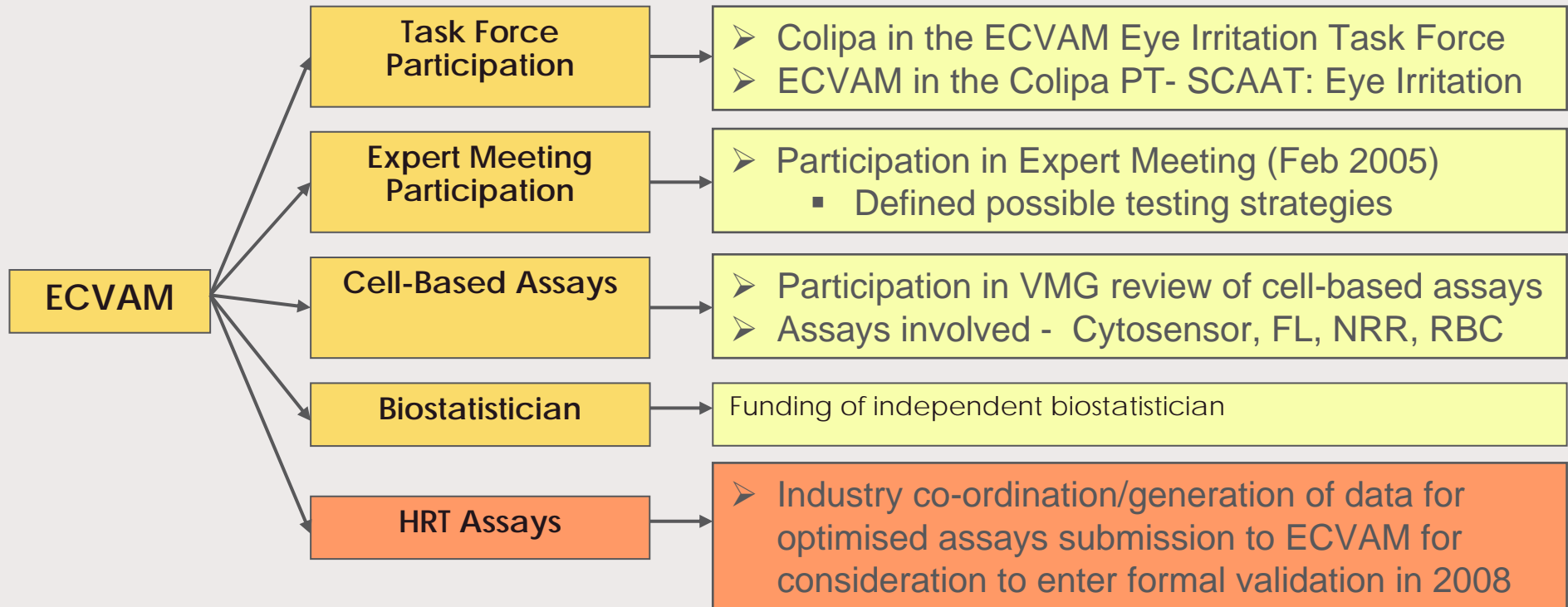
Method development/optimisation of existing models

- Focus on Human Reconstructed Tissue (HRT) Models



Collaborative activities with external partners e.g. ECVAM, Academia

External Collaborative Activities



2009 EYE

Safety assessment :

Many in vitro methods are available and **COLIPA** has prepared a scientific review

however

Eye irritation is complex and there will be a need for several methods to achieve full replacement expected by 2010

EU Validation under way (ECVAM)

- > 2008/2009 : 2 Human corneal models submitted by **COLIPA** will start validation in December after optimisation and development of an extensive data base
- > 2009/2010 : evaluation of 8 existing methods with industry data

Research

- > **COLIPA** is sponsoring research to include mechanistic endpoints which could improve predictivity of existing methods



2009 SKIN

Safety assessment : methods are available and **COLIPA** has prepared a scientific review

EU Validation (ECVAM) :

For skin irritation we have been successful and validated replacement methods developed in part by **COLIPA** companies are already available

Regulatory acceptance :

The validated methods are now under discussion at SCCP and OECD levels.



2009 ACUTE SYSTEMIC TOXICITY

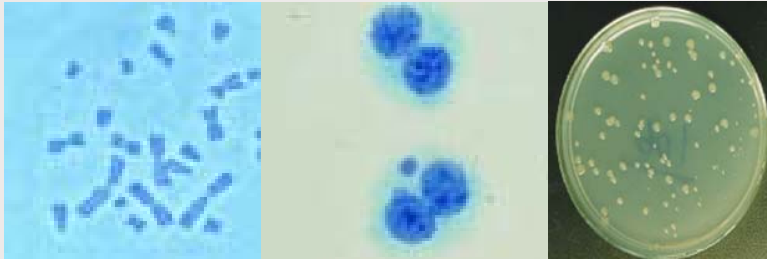
Acute toxicity is a very complex test to replace. More research is needed.

EU Validation (ECVAM) :

Methods aiming at reduction are under pre-validation, results will become available from 2010 onwards

PT-SCAAT Genotoxicity, portfolio of work

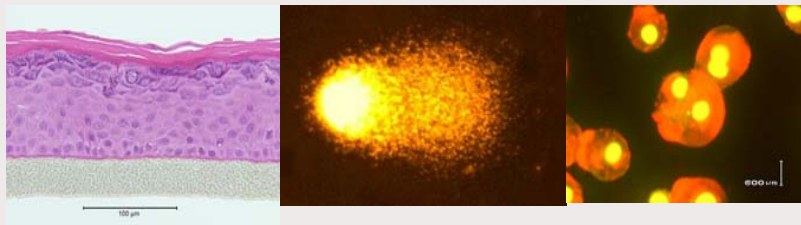
A. Research to identify and resolve problems with current assays



Understand causes for false positive results

Evaluate recent assays and currently used standard cell lines, improving test conditions and selection of cells

B. Develop new in vitro methods



Develop / optimize genotoxicity assays in human 3D skin models

Understand epidermal bioavailability of cosmetic ingredients

Understand skin metabolism of cosmetic ingredients

Delivery during last 12 months

- A**
 - Established 3 year **COLIPA** “false-positives” project
 - > Co-funded by ECVAM and UK NC3Rs
 - > Project performance at Covance, UK
 - > Selection of a validation set of Chemicals (D Kirkland, G Speit, P Kasper, L Mueller), Publication accepted
 - > Project work started Summer 07 (4 collaborators hired)
 - > First comparison of performance of 4 different cell types shows Promising results
 - > Extensive literature review (ECVAM sponsored)
 - Contract extended to incorporate work with liver cells, additional funds added
 - Presentation of **COLIPA** genotox program at several scientific meetings, interaction with other activities



Delivery during last 12 months

- B**
 - 2.5 year **COLIPA** “3D skin project” (evaluation of genotoxicity in 3D human skin models) running since April 07
 - > Collaboration between TNO (paid via ECVAM), IIVS, P&G, L’Oreal, Wella/Cosmital and Phenion/Henkel
 - Successfully finished phase I of the project (protocol optimization and transferability)
 - Phase II (Reproducibility between labs) has started in May 08
 - Supportive data generated by **COLIPA** skin metabolism project
 - > Co-worked with PT-SCAAT Skin Tolerance; characterises the metabolic capacity of human skin & 3D skin models

2009 GENOTOXICITY

Safety assessment : Methods are available and **COLIPA** has prepared a scientific review

For genotoxicity , non animal tests exist and we are working to improve their predictive capacity.

The **COLIPA research programme** is already making significant improvements to existing assays, that will result in fewer chemicals being rejected. These improvements are anticipated to continue up to the deadline and beyond.

New **COLIPA** tests, using reconstructed 3D human skin models, are shaping up to be effective tools

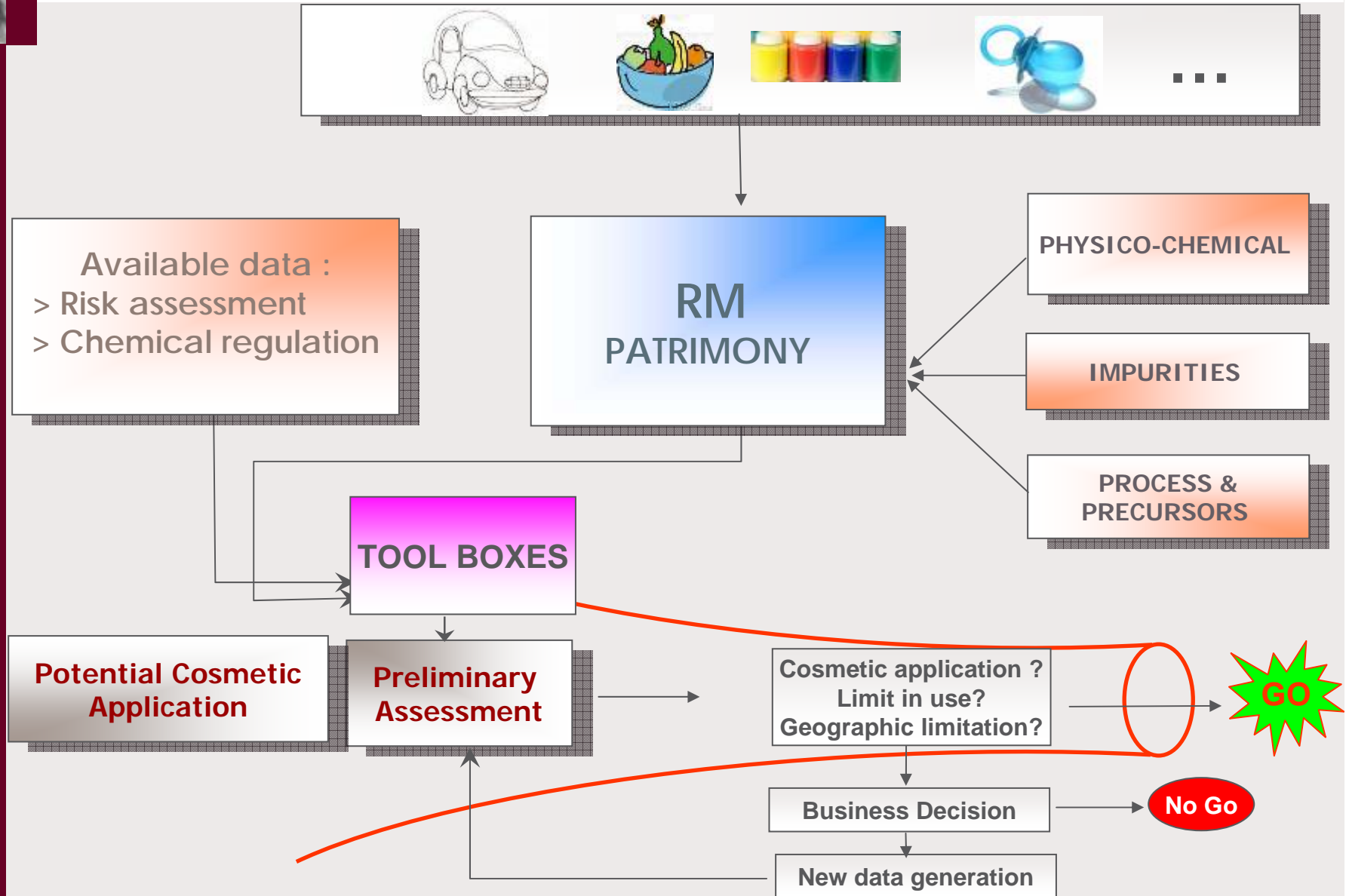
COLIPA efforts are shared with scientists and regulators (SCCP)





The future predictive approaches for safety assessment

PREDICTIVE APPROACHES



2009 : in some rare cases

when non animal tests are lacking and data cannot be generated in vivo :

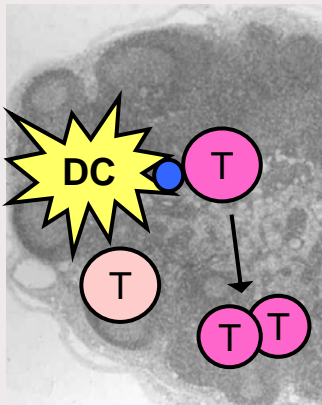
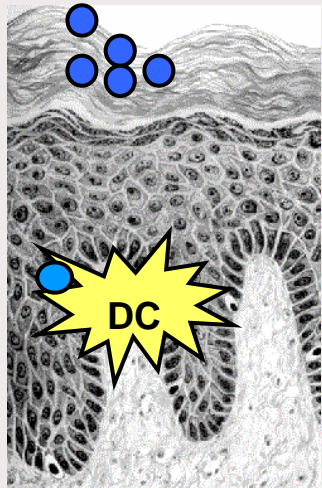
- no information which could permit the introduction of a novel ingredient.
- no possibility to defend an existing ingredient

2011

The Commission will

- > assess the progress made and the difficulties to meet the bans.**
- > make a legislative proposal to the Council and the Parliament**

COLIPA PT-SCAAT Skin Tolerance



Research/Method Development

Competitive Tender I
 Increased understanding of keratinocyte: DC & sensitiser: DC interactions

Skin Metabolism project

DC intracellular signalling pathways as markers for DC activation

Development of *in vitro* T cell proliferation assay

Toxicokinetic model for prediction of epidermal bioavailability

Next Generation Peptide Binding Assay + Alternative Metabolic System

High Throughput (HT) DC activation method: gene changes

Competitive Tender II
 Increased understanding of sensitiser-specific T and B cell responses

Method Evaluation (i.e. ECVAM prevalidation)

Direct Peptide Reactivity assay

hCLAT assay

MUSST test

?????

Key

- = work continues
- = funding renewed
- = new area of research

2013 SKIN ALLERGY

COLIPA aims to provide :

- > a first generation integrated testing strategy capable of providing skin allergy information, based on validated in vitro tests developed by **COLIPA** companies
- > Cutting-edge research aimed at delivering second generation methods more predictive and more applicable by 2013
- > The **COLIPA** Programme goal is to progress the most scientifically advanced and comprehensive research in the field of replacement



2011 REPEAT DOSE SYSTEMIC TOXICITY

With the support of the International Cosmetics Companies CEOs , **COLIPA** has proposed a joint collaboration with the European Commission for the co-funding of systemic toxicity research for a total of 50Mios€

This new initiative has been officially announced by Commissioner Potocnik at the opening of the Annual Conference of the **European Partnership for Alternative Approaches (EPAA)**

Contracts are currently being finalized, the Joint Expert Group set up by the Commission with the help of **Colipa** has started its work ie preparing the specific call for tender which will be launched in 2009.

This will contribute to move forward effectively in this area of science.





Conclusion

- 1. The Cosmetics & Personal Care Industry is involved in the development of alternatives to animal testing since the early 80s. We have boosted our efforts in alternative strategies to achieve the best possible results vs. the specific goals set by the March 2009 deadline.**

Innovation of cosmetics & personal care products will continue and, at the same time, their safety will be ensured and the 2009 European deadline will be adhered to by our industry.



Conclusion

- 2. Science is a continuous process. We will face very significant challenges to meet the 2013 goals. At this stage it is recognized by the scientific community and the regulatory authorities as well that some important toxicological end points will not be met.**

Some research projects are already well under way whilst others are about to start. A progress review is set by the 7th amendment in 2011.



Conclusion

- 3. The cosmetics and personal care products industry will not lower their efforts in researching alternatives in spite of deadlines and difficulties encountered. We are fully committed to answer in the best possible way the societal and ethical demands.**
- 4. We are and we will continue to be proactive ambassadors of these moral values at the international level.**