Alternative Methods for Human Health Safety Assessment of Cosmetic Ingredients

Ian R. White
Cosmetics Directive

76/768/EEC

• Annexes
  • 3 restricted / conditions of use
  • 4 colorants
  • 6 preservatives
  • 7 UV filters

• 7th amendment
  • fragrance ingredient labelling
  • animal testing
The way forward.....?
Directives

Medicines -\textit{v}- Cosmetics

- risk to benefit

- no risk to benefit?
- must not cause damage to human health under normal or reasonably foreseeable conditions of use
SAFETY EVALUATION OF COSMETIC INGREDIENTS

INGREDIENTS IN ANNEXES (76/768/EEC)

II, III, IV, VI, VII

SCCS
IN DG SANCO

PUBLISHED OPINIONS

DG SANCO

RISK MANAGEMENT

FOR COMMISSION:
ADAPTATIONS TO
TECHNICAL PROGRESS

INGREDIENTS IN DOSSIER (93/35/EEC)

TIF, PIR

SAFETY ASSESSOR

WRITTEN SAFETY EVALUATION

MANUFACTURER
IMPORTER
MARKETER

RISK MANAGEMENT

INDUSTRIAL MEASURES FOR
CONSUMER PROTECTION
Risk assessment – general principles

- Hazard identification
  - *in vivo, in vitro* tests, QSAR, epidemiology

- Dose-response assessment
  - No observable adverse effect level (NOAEL)

- Exposure assessment
  - amount, frequency, specific groups

- Risk characterisation
  - Margin of safety (MOS)
Notes of Guidance for the Safety Evaluation of Cosmetic Ingredients - 7th revision

- Acute toxicity (oral / dermal / inhalation)
- Skin and eye irritation
- Skin sensitisation
- Dermal / percutaneous absorption
- Mutagenicity / genotoxicity
- Repeated dose toxicity
- Chronic toxicity
- Carcinogenicity
- Reproduction toxicity
- Toxicokinetics
- Photo-induced toxicity
- Human data
Animal testing in Europe

**Testing Ban**

- Prohibits animal tests in the EU to meet requirements of Cosmetics Directive

- Finished products:
  - September 2004

- Ingredients:
  - Gradual prohibition with validation/adoptions
  - March 2009

**Marketing Ban**

- Prohibits sale of cosmetics when product or ingredients tested on animals, within or out of the EU, to meet requirements of Cosmetics Directive

- Gradual prohibition with validation/adoptions
  - March 2009

- Tests exempted
  - Repeated dose toxicity, toxicokinetics, reprotoxicity
  - March 2013
The safety of cosmetic products and their ingredients may be ensured* through the use of alternative methods which are not necessarily applicable to all uses of chemical ingredients.

It will gradually become possible to ensure* the safety of ingredients used in cosmetic products by using non-animal alternative (validated) methods ......

*guaranteed, guarantee (Oxford English Dictionary)
Nanomaterials

- **Nanoparticle** is a particle with one or more dimensions at the nanoscale and is defined as a particle with at least one dimension <100nm.

- **Nanomaterial** is a material with one or more external dimensions, or an internal structure, on the nanoscale, which could exhibit novel characteristics compared to the same material without nanoscale features.

- Two principal factors cause the properties of nanomaterials to differ significantly from bulk materials:
  - increased relative surface area
  - quantum effects
JRC Evaluation

• Notwithstanding the substantial progress made over the past years, for five specific areas full replacement alternative testing methods will not be available by 2013.

• No specific timeline in the areas of
  – toxicokinetics
  – repeated dose toxicity
  – carcinogenicity
  – reproductive toxicity.

• Estimated for skin sensitisation point to 2017-2019, including the possibility to differentiate weaker from stronger sensitisers. Methods discriminating between skin sensitisers and non-sensitisers might become available earlier.
• The European Commission will now review the situation regarding the technical difficulties in complying with the 2013 ban and inform the European Parliament and the Council, proposing any measures to be taken.
## Status of available validated replacement alternative methods

<table>
<thead>
<tr>
<th>Validated replacement alternatives <strong>available</strong></th>
<th>Validated reduction / refinement alternatives <strong>available</strong></th>
<th>Validated alternatives <strong>not available</strong></th>
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<tbody>
<tr>
<td>→ endpoints not affected by EU testing or marketing ban</td>
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- skin corrosivity
- skin irritation
- dermal absorption
- mutagenicity/genotoxicity
- phototoxicity

- acute toxicity
- skin sensitisation

- repeated dose toxicity
  - subacute toxicity
  - subchronic toxicity
  - chronic toxicity
  - carcinogenicity
- reproductive toxicity
- toxicokinetics
Data available for risk assessment

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*animal test(s) performed outside the EU
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Bis(butylbenzoate) diaminotriazine aminopropyltrisiloxane

- Safe use as an UV-filter in cosmetic products in a concentration up to maximum 10.0% cannot be assessed based on the available data. As low oral bioavailability of the substance is anticipated, a quantitative risk assessment based on the oral NOAEL cannot be performed in the absence of adequate information on the extent of internal exposure.

- 90-day dermal toxicity study or sound data on oral bioavailability are required.

- SCCS is aware that such studies are no longer permitted in the European Union.
Faith in their models’ predictive powers led them to ignore what was happening in the real world....