Issues and Challenges in Cosmetic Risk Assessment in Europe

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müsst man den amerikanern mal sagen, dass cosmetic products bei denen personal care products sind - oder wissen das alle, die da sitzen?
Rettinger, Klaus; 20.10.2015
Some examples

- Assessment of mixtures (aggregate exposure)
- CMR substances
- Endocrine disruptors
- Packaging
- ....
Risk assessment challenges for chemical mixtures and safety assessment
Cosmetic products have a history, covering thousands of years, in using a variety of substances derived from plants, animals and mineral sources. Modern technology has added an important number from synthetic and semi-synthetic origin. Present-day use of cosmetic products has become very extensive and is common in most population groups within the European Union, although the degree and nature may vary within the different Member States.*

*) quote SCCS-Guidelines 8th revision – Dok. SCCS/1501/12
Huge diversity of products

• Creams, emulsions, lotions, gels and oils for skin care (hands, face, feet)
• Perfumes, toilet waters and eau de Cologne
• Bath and shower preparations
• Deodorants and antiperspirants
• Hair care products
• Products for care of teeth and mouth
• Products for nail care and make-up
• Sunbathing products
• Anti-wrinkle products
• [ ... ]
Exposure is of key importance

- Consumers: babies, children, adults, pregnant women, professionals
- Application area (body, face, hand, axillae)
- Use conditions (leave on, rinse off)
- Contact with the eye (eye cream, mascara, eye make-up remover)
- Intended use (once per day, twice per day, once per month)
- Contact with mucosa (oral cavity, genital area)
Product composition

• More than 10,000 potential ingredients are available
• One product may contain from 1 up to 80 ingredients or even more
• One ingredient may be used in different product categories, e.g.
  – Alcohol in perfumes, face cream, hair tonic
  – Surfactants in shampoo, face cleansing, shower gel
Requirements on safety
Art. 3 EC Cosmetics Regulation*)

A cosmetic product made available on the market shall be safe for human health when used under normal or reasonably foreseeable conditions of use, taking account, in particular, of the following:

(a) presentation including conformity with Directive 87/357/EEC (Potential Health Risks posed by chemical consumer products resembling food and/or having child-appealing properties)

(b) labeling;

(c) instructions for use and disposal;

(d) any other indication or information provided by the responsible person defined in Article 4.

*) EC Cosmetics Regulation 1223/2009
How do companies fulfil this requirement?
Safety assessment for each cosmetic product

In order to demonstrate that a cosmetic product complies with Article 3, the responsible person shall, prior to placing a cosmetic product on the market, ensure that the cosmetic product has undergone a safety assessment on the basis of the relevant information and that a cosmetic product safety report is set up in accordance with Annex I*

*)EC Cosmetics Regulation 1223/2009
Safety assessment is mainly based on ingredients of the product

Annex I
EC Cosmetics Regulation

- PART A – Cosmetic product safety information
  1. Quantitative and qualitative composition of the product
  2. Physical/chemical characteristics and stability of the cosmetic product
  3. Microbiological quality
  4. Impurities, traces, information about the packaging material
  5. Normal and reasonably foreseeable use
  6. Exposure to the cosmetic product
  7. Exposure to the substances
  8. Toxicological profile of the substances
  9. Undesirable effects and serious undesirable effects
  10. Information on the cosmetic product

- PART B – Cosmetic product safety assessment
  1. Assessment conclusion
  2. Labeled warnings and instructions of use
  3. Reasoning
  4. Assessor’s credentials and approval of part B
Commission Guidelines


• Comments on legislation, particularly designed for SMEs, to fulfil the requirements of the Cosmetics Regulation
• Should not be regarded as
  – simplification;
  – guidance for two-class safety assessment;
  – schoolbook for safety assessment.
• Guidelines do not replace advanced training!
Tasks of Safety assessors

- Preparation of the safety assessment in accordance with legal requirements
- Examination of the raw material data
- Microbiological assessment
- Exposure assessment
- Examination of health claims
- Possible restrictions of concentration for individual substances
- Possible introduction of warnings
- Observation of the market and resulting measures if necessary
- Ensure general safety of the product
Safety assessor: Competence required

„... by a person in possession of a diploma or other evidence of formal qualifications awarded on completion of a university course of theoretical and practical study in pharmacy, toxicology, medicine or a similar discipline, or a course recognised as equivalent by a Member State.”*  

*) Art. 10 of the EC Cosmetics Regulation
The Safety Assessor Courses for Cosmetic Products in Germany
Background / Concept

- Practical experience is needed
- Course system developed in 1998
- Co-operation with the German Society for Scientific and Applied Cosmetics (DGK)
- 7 individual courses (now also in English!), lasting two days each
- 35 attendees max.
- No specific qualification required for participation in courses
- Costs about 800 €/course
Concept

• Examinations on the knowledge acquired at the end of each course.
  ✓ 18 out of 24 questions must be answered correctly

• Participants receive a certificate for the respective course.

• Participants successfully completing all seven courses receive a certificate for the whole series.

• Speakers: Members from the Advisory Committee on Cosmetic Products of the Federal Institute for Risk Assessment (BfR), SCCS, University, Industry, DGK
The Courses

1. Exposure to Cosmetic Products / Percutaneous Penetration
2. Skin Compatibility and Sensitization
3. Metabolism, Kinetics and Structure-Activity Relationships
4. Carcinogenesis and Mutagenesis
5. General and Systemic Toxicology
6. Reproduction Toxicology
7. Microbiological Safety of Cosmetic Products

(Regular exchange of persons responsible for courses once per year)
Before marketing the finished product

- Safety assessment of the ingredients
- In-vitro studies to determine the irritation and sensitization potential of the formula

If the a.m. bullet points indicate safety, on case-by-case basis:

- Skin compatibility studies in humans (e.g. patch-test)
- In-use-tests under medical control with human volunteers (to confirm local tolerance)
- Consumer tests (case by case)
Safety assessment has to be completed by market surveillance
Three columns of market surveillance

1 – Industry

• Complaint management of undesirable adverse events (cosmetovigilance)

• Statistics: IKW follows the market since 1976: 1.3 incompatibilities per million units sold
Three columns of market surveillance

2 – In-market control

- Controlling authorities:
  - Through in-market control or control of imported products harmful products can be identified and taken from the market.
In-market control in Germany

Consumer protection

Market surveillance products

In-market control
Three columns of market surveillance

3 – RAPEX

If correctly applied

• System allows to identify harmful products
• Information of Member States is assured
• Warning of consumers is possible
• The RAPEX classification scheme has weaknesses for cosmetics

* RAPEX: EU rapid alert system that facilitates the rapid exchange of information between Member States and the Commission on measures taken to prevent or restrict the marketing or use of products posing a serious risk to the health and safety of consumers
Is there a need to test potential combination effects?

Exposure to a combination of substances that possess individual potentials of adversity could theoretically produce the following outcomes:

a. attenuation of effects
b. same toxicity as displayed by individual substances
c. additive or synergetic effects
d. inhibition of certain effects
The facts

- Additive or synergetic adverse effects from exposure to combinations of substances are rarely reported outside of pharmacologically active drugs.

- Absence of relevant combination effects at low exposure was experimentally demonstrated in numerous studies.

- Typical cosmetic ingredients have a low level of systemic exposure. Therefore relevant health risk by “not identified mixture effects” is extremely unlikely as sufficient safety factors for the individual ingredients do exist.

- Risk assessment and risk management approaches under the current cosmetics legislation are sufficiently conservative to protect consumers and the environment.
Conclusion

• The following elements ensure the marketing of safe products
  – Safety of ingredients
  – Safety of the finished product
  – Cosmetovigilance
  – In-market control

• This strategy followed by the European regulators and industry is an appropriate and successful tool to demonstrate the safety of cosmetic products

• This system must be secured in the future
Position Paper on mixtures of Cosmetics Europe

Will be published in the near future on www.cosmeticseurope.eu
CMR substances –
the current regulation and interpretation
of the European Commission
What is a „CMR ingredient“

• Carcinogen (C)
• Mutagen (M)
• Toxic for Reproduction (R)

GHS (CLP) Regulation 1272/2008 and safety data sheet classified as

Carc, Muta, Repr (1A, 1B, 2)

[CLP: Regulation on classification, labelling and packaging of substances and mixtures. It aligns existing EU legislation to the United Nations Globally Harmonised System (GHS)]
Categories of CMR substances (simplified according to GHS criteria)

- CAT 1A: classification according to effect on humans (epidemiological data)
- CAT 1B: classification according to effects on animals (two species or other strict criteria)
- CAT 2: classification based on information from animal tests. Either unclear data, which cannot be improved through other studies or unsufficient data which need further clarification
How does an ingredient become a CMR substance?

- Defined criteria for the classification of an ingredient as carcinogen, mutagen oder toxic for reproduction (design of the study, gender of animals etc.) according to the chemical legislation
- Discussion and decision by ECHA (European Chemical Agency under REACH) based on preparations by national governments
- Publication of the classification in the chemical legislation (Official Journal in the EU)

→ One single article with a suspicion is not enough to classify a substance as CMR legally
CMR ingredients in the Cosmetics Regulation (1223/2009)

Art. 15 (1)

1. The use in cosmetic products of substances classified as CMR substances, of category 2, under Part 3 of Annex VI to Regulation (EC) No 1272/2008 shall be prohibited. However, a substance classified in category 2 may be used in cosmetic products where the substance has been evaluated by the SCCS and found safe for use in cosmetic products.
CMR ingredients in the Cosmetics Regulation (1223/2009)

Art. 15 (2)

2. The use in cosmetic products of substances classified as CMR substances, of category 1A or 1B under Part 3 of Annex VI to Regulation (EC) No 1272/2008 shall be prohibited. However, such substances may be used in cosmetic products by way of exception where, subsequent to their classification as CMR substances of category 1A or 1B under Part 3 of Annex VI to Regulation (EC) No 1272/2008, all of the following conditions are fulfilled:
Cosmetics Regulation – Categories 1A and 1B

Such substances may be used in cosmetic products by way of exception where all of the following conditions are fulfilled:

• comply with the food safety requirements
• no suitable alternative substances available
• application is made for a particular use of the product category with a known exposure
• evaluated and found safe by the SCCS for use in cosmetic products
  – Specific labelling?
  – Reevaluation by SCCS every 5 years
Regulation 790/2009 to GHS Regulation

- Some hundred pages; only some new CMR ingredients
- NEW from December 2010:
  Commission does only see the need for a listing of an ingredient in the cosmetic Regulation if the ingredients has been approved by the SCCS; the ban is directly linked to the chemicals legislation. Consequence: The deadlines set in the chemicals legislation are applicable

→ Industry position: the interpretation of the Commission is not consistent with the Cosmetics Regulation.
Summary for CMR

- The new bans for CMR substances are relevant from 1.12.2010 – except for those ingredients which have been evaluated by the SCCS. According to the European Commission the deadlines from the Chemical legislation are relevant.

Therefore:

- It is important to know as early as possible if an ingredient will be banned.
- If such an upcoming classification becomes obvious it is important to inform the industry associations.
- If there is an interest it is of importance to set up a Consortium for the ingredient defense asap.
Endocrine Effects –
do many cosmetic ingredients have an active hormone effect?
EC Cosmetics Regulation, Article 15 (4)

When Community or internationally agreed criteria for identifying substances with endocrine-disrupting properties are available, or at the latest on 11 January 2015, the Commission shall review this Regulation with regard to substances with endocrine-disrupting properties.
What are endocrine active substances?

- An endocrine active substance is a chemical or natural substance which triggers a reaction of the hormone system (endocrine effect).

And an endocrine disruptor?

- A hormone active substance which causes harm in an intact organism is called an endocrine disruptor (adverse effect; WHO/IPCS definition 2002).
Basic question

• Do we have a new, up to now not identified problem which is caused by natural or chemical ingredients?

OR

• Are the effects which we can see today or we think we are seeing (reduced sperma quality, premature puberty, premature menopause, obesity of the population) a lifestyle problem (wrong nutrition, less or too much sport...)?
Legal requirements


• Clear criteria are necessary when an (even weak) endocrine active substance becomes an endocrine disruptor and therefore falling under the legislation.

• Cosmetics legislation: 2015 check of the criteria was planned according to the criteria in other legislations.
Current discussions and development of criteria on EU level

- Main discussion points: one category (substances of regulatory concern), or 2 – 3 categories („suspected“)
- Roadmap impact assessment; public consultation
- Problem for cosmetics, if 2 or 3 categories are identified: If an ingredient is listed as probable endocrine disruptor it will not be possible to relieve – only with animal tests which are forbidden
- Important issues: Potency and threshold
- Difficult: evaluation of environment – complex compared to evaluation of human health.
- Sources
Cosmetics legislation

- Substances with certain endocrine effects are forbidden since 1976 (androgen, gestagen, antiandrogen, estrogen) – potent active ingredients.
- Several priorisation programmes on EU level exist: Some cosmetic ingredients are mentioned as potential candidate ingredients. Most of them are classified as safe for the conditions used in cosmetics by the SCCS (or its predecessors SCCNFP or SCCP).
- No cosmetic ingredient has been classified on EU level according to clear criteria as endocrine active ingredient with a need for regulation.
Cosmetic Packaging
Cosmetic packaging has many roles

• Basics
  – Packaging should not cause any interactions with the product or deterioration of the product ...

• Protection
  – Packaging should protect the consumer against the product ...
  – Packaging should protect the product against the environment and the consumer ...

• Function
  – Packaging should provide a proper way for a directed and safe application of the product ...
  – Packaging should display all necessary information of the product ...
  – Packaging should enable safe transport and storage of the product ...

• Marketing
  – Packaging should make the product appealing to the consumer ...
Regulatory requirements

Packaging (safety) evaluation has to take into account the following directives and regulations*:

- (EC) No. 1223/2009 (Cosmetics regulation)
- (EC) No. 1907/2006 (REACH)
- (EC) No. 1935/2004 (European regulation on materials to come on contact with food)
- (EC) No. 10/2011 (European regulation on plastic materials and articles)
- Framework resolution ResAP (2004)1 on coatings intended to come in into contact with foodstuffs
- (EC) No. 1272/2008 (CLP)
- (EC) No. 94/62 (Directive on packaging and packaging waste)
- (EC) No. 2001/95 (Directive on general product safety)
- (EC) No. 75/324 (Directive on aerosol dispensers)

* List probably not exhaustive, as others may also be or become relevant
Regulatory requirements
European Cosmetics Regulation EC 1223/2009:

**Article 3** of Regulation EC 1223/2009 requires that:
* A cosmetic product made available on the market shall be safe for human health when used under normal or reasonably foreseeable conditions of use.

- The packaging has to be part of the cosmetic safety evaluation, but no concrete requirements are given (Art. 17, + Annex I, Part A, No. 4, Cosmetics safety report).

**Article 17 – Traces of prohibited substances**
*The non-intended presence of a small quantity of a prohibited substance, stemming from impurities of natural or synthetic ingredients, the manufacturing process, storage, migration from packaging, which is technically unavoidable in good manufacturing practice, shall be permitted provided that such presence is in conformity with Article 3.*
Regulatory requirements
European Cosmetics Regulation EC 1223/2009:

- The packaging safety evaluation has to be part of the *product information file (PIF)*. Information about the material, impurities and traces have to be given.
- The product has to be stable after manufacturing (i.e. in its packaging).

- See IKW publications on [www.safetyassessor.info](http://www.safetyassessor.info)
Regulatory requirements

SCCS Notes of Guidance for the testing of cosmetic substances and their safety evaluation (SCCS/1501/12) 8th Revision, Dec. 2012

- Relevant stability tests, adapted to the type of cosmetic product and its intended use, should be carried out.

- To make sure that no stability problems are induced by the type of container and packaging used, physical stability tests are currently carried out with inert containers and those intended to be used on the market.

- Also potential leaching of substances of the packaging into the product should be investigated.
Regulatory requirements

Are these new legal requirements?

No, they are not!

- The safety evaluation requirements of the 6th Amendment (1993) to the Cosmetic Directive (76/768/EEC) already included the packaging
- This included the aforementioned stability and safe use requirement of the product in its packaging
- However, more details may be needed for documentation
Packaging safety evaluation

There is no standard procedure available for the safety evaluation of cosmetic packaging.

Every product has to be evaluated based on its own specific characteristics and peculiarities.

The evaluation is mainly based on:
• The experience with existing products and packaging in the market
• Tests and measurements
• Visual judgment
• The judgment and experience of the safety assessor

Good news: In-market control reports by competent authorities have not been indicating that packaging had caused significant safety issues in the past!
Packaging safety evaluation

Information to be provided by the supplier

- IKW and Cosmetics Europe are working together on standardized supplier questionnaire
- Close cooperation with packaging suppliers
  → Very complex supply chain situation
- A publication of the final document is expected in the near future
Consumer safety is of highest priority for cosmetic products. This includes their packaging, of course.

- The packaging is an elementary part of the product and must be considered in combination with the formulation.
- The product stability test plays the central role. Wealth of experience shows that even subtle changes are detected.
- Packaging evaluation cannot be done by a general standard protocol. It needs to be adapted and modified according to the needs of each individual product, i.e. not a schematic approach.
- The safety of the packaging is already routinely and successfully assessed at various stages of the regular product development process, as evidenced by a long history of safe packaging use in the market.
- This is also confirmed by the low numbers of incidences reported by competent authorities through in-market control.
Conclusions 2

- Most elements of the required information and documentation will be already available, but may be “hidden” at various places in your organization.

- The key role of the safety assessor is to collect the information and put all the pieces together for a weight-of-evidence assessment (WOE) and for a proper documentation in the PIF.

- Involve experts from other areas (e.g. packaging engineers, PD, QAU, S&R, Microbiology) on order to obtain the information required for your WOE and the PIF documentation.

- Look for smart and practicable solutions rather than for new, sophisticated testing requirements.
Many other “hot” issues?

Of course! May be next time?
Thank you for your attention