G. Mildau [1], A. Burkhard [2], J. Daphi-Weber [3], J. Große-Damhues [4], J. Jung [5], B. Schuster [6], C. Walther [7]

Basic Requirements for Safety Assessments of Cosmetic Products

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Introduction

The safety assessment of cosmetic products has been anchored in European cosmetics legislation by Directive 93/35/EEC (6th amendment) to the Cosmetics Directive 76/768/EEC. The provisions of Article 7a of this Directive are an important instrument for protection from health impairments following the use of cosmetic products. In its most recent position paper entitled »Simplification of Cosmetics Directive 76/768/EEC« the European Commission emphasised that it intends to give high priority to safety assessment in future (1). It is, therefore, all the more important to elaborate EU-wide harmonised basic requirements so that manufacturers and competent authorities can proceed from the same prerequisites. The European Cosmetics Association COLIPA published its »Guidelines for the Safety Assessment of a Cosmetic Product« in 1997. These Guidelines dealt, more particularly, with alternative test methods to animal experiments (2). The Expert Group »Safety and Tolerance« of the German Society for Scientific and Applied Cosmetics (DGK) published »Key elements of a safety assessment« in 2005 which for the first time systematically defined minimum standards of safety assessment. This met with considerable interest in Germany (3). In the following publication German cosmetics experts from different state investigation agencies and laboratories have drawn together their experience from many safety assessments by German manufacturers and formulated some basic requirements.

In accordance with Article 7a of the EC Cosmetics Directive every cosmetic product must be subject to an assessment of its safety for human health by the manufacturer or the person responsible for placing the product on the market (4). For that purpose a qualified person responsible for the assessment must be appointed who is personally responsible for the safety of the cosmetic product. This means that the product must comply with all measures and conditions imposed by the EC Cosmetics Directive in terms of its safety for human health when applied under normal or reasonably foreseeable conditions of use.

When preparing a safety assessment the expert must first of all review all existing basic requirements of cosmetics legislation (substance regulations, labelling provisions etc.). A more extensive assessment must be undertaken in conformity with the basic requirements of Article 7a (1) d of the Cosmetics Directive. According to this provision, the general toxicological profile of the ingredients, their chemical structure and their level of exposure must be taken into account. Furthermore, the applicable Notes of Guidance of the SCCP (»Notes of Guidance for the Testing of Cosmetic Ingredients and Their Safety Evaluation«; currently valid version: 6th Revision of December 2006) must always be referred to in which the independent body instructed by the European Commission and the Member States makes recommendations on the safety of cosmetic ingredients and finished products (5).

As far as the qualification of the safety assessor is concerned, Article 7a (1) e of the Cosmetics Directive stipulates that the person must hold a diploma as defined in Article 1 of Directive 89/48/EEC in the field of pharmacy, toxicology, dermatology, medicine or a similar discipline. When instructing a safety assessor it must, however, be taken into account that the latter must not only fulfil the formal requirements regarding his completed course of study but should also have concrete experience, more particularly in the fields of experimental/clinical toxicology and/or dermatology, cosmetics chemistry and cosmetics legislation. At the same time, we believe that it is particularly important that the safety assessor keep pace with the latest scientific findings and technological developments by regularly attending further training. In this connection the industry associations and scientific societies are particularly required to stage appropriate further training courses at regular intervals.

Of course, a safety assessment can only refer to the concrete formulation of the product which means that every new formulation of the cosmetic product must undergo a further review and possible update of the safety assessment. This is also the case if the specifications of raw materials and data have changed for the substances used (taking into account the latest scientific findings).

This Guideline aims to explain in more detail the existing requirements to be met under cosmetics legislation in respect of safety assessment. It outlines the main basic criteria which must always be taken into account when preparing safety assessments in order to fulfil the statu-

tory requirements in an appropriate and sound manner. Nevertheless, it neither represents a conclusive list nor a checklist for the preparation of a safety assessment. At the end of the day, every safety assessment must be adjusted individually to the concrete product under review.
The safety assessment can be made by an internal or an external expert. In the case of an internal safety assessment, the process should ideally be designed to accompany the development of a new product from the outset. In the case of a safety assessment by an external expert, we believe it is indispensable for the conditions for the implementation and update of the safety assessment to be contractually defined between the manufacturer and the instructed safety assessor. The manufacturer must have structures in place that adequately integrate the external safety assessor into internal processes so that he has access to all the necessary information on the product (e.g. raw material specifications, product presentation and additional advertising).

Part A: Fundamental data on product characterisation

1 Information on product identity:

a. Product name

b. Product typ

c. Formulation number

d. Manufacturer and person placing the product on the market

2 General product description (unless covered by reference to separate documents)

a. Form of preparation, consistency, type of emulsion (if necessary)

b. Organoleptic properties

c. Characterisation of the intended use (function, e.g. according to declaration)

d. Information on qualitative and quantitative composition (see number 3)

Please note:

1. In the case of raw materials which are themselves preparations of several ingredients, a quantitative specification of all ingredients with their INCI designation is necessary; this must include all excipients such as water, solubiliser, perfumes, fragrances subject to labelling, preservatives or stabilisers.
2. For the correct preparation of the list of ingredients (order) as well as the toxicological assessment, the total concentration of all ingredients must be taken into account, i.e. even excipients or additives of raw materials.

3 Specification of the starting materials (unless covered by reference to separate documents)

a. Chemical identification of each individual raw material (e.g. INCI designation, CAS No., EINECS No., trade name etc.);

b. If necessary, manufacturing description/origin (natural substances)

c. Information on the purity of the substance

d. Chemico-physical specifications

e. Microbiological specifications, if relevant

f. Specifications of any water used

Please note:
The safety assessor can only confirm the safety of the raw material with reference to the documentation of the raw material manufacturer and the specifications defined by the latter. The safety assessment must reflect the fact that no raw materials are used which are contaminated or adversely modified beyond the technically avoidable extent (e.g. 1,4-dioxane in ether sulphates, peroxides in essential oils). In this connection it may be necessary for the safety assessor to obtain sufficient information about the specifications of different raw material suppliers.

4 Specification of the finished product (unless reference is made to separate documents)

a. Chemico-physical specifications of the finished product

b. Microbiological specifications

c. Chemico-physical and microbiological stability of the product, e.g. results of storage tests, preservation challenge tests.

Please note:
Chemico-physical stability is not only relevant for quality but also for the safe use of certain products (e.g. efficacy of sunscreen products, peroxide content of tea tree oil).

d. Information on the packaging material (empirical values, theoretical considerations or experimental data on stability, tolerance with the fillings, microbiological purity etc.)

Please note:

- Microbiological stability also includes product data on minimum durability and/or duration of use after the first opening. Since there are no legal requirements (limit values, binding methods on microbiological stability), product related specifications of the manufacturer must be obtained on the basis of appropriate, if possible validated test procedures. In this connection manufacturers should orient themselves on the state of science and technology, e.g. the guidance of SCCP, microbiology guidelines of IKW and/or COLIPA, European Pharmacopoeia, PAO Guidelines of COLIPA or the European Commission (1).

Part B: Safety assessment

1 Toxicological profile of the ingredients

a. The taking into account of the toxicological profile of the individual components is a basic prerequisite to every safety assessment

b. Information on the toxicological characterisation of the ingredients can be obtained from technical literature as well as databases. Frequently, the necessary information is available from the raw material manufacturer. For fragrance preparations the respective raw material manufacturer normally makes a safety assessment available which is adjusted to the finished product.

c. The relevance of the available data varies depending on the product type and type of exposure (e.g. inhalation toxicity of sprays, phototoxicity of sunscreen products, oral toxicity of mouth care agents). The margin of safety must be calculated on the basis of the relevant data.

d. In cases where the ingredients influence each other, an additional analysis of the overall formulation is required (e.g. in the event of possible nitrosamine formation, neutralisation reaction).

e. When statutory limit values and restrictions on use for individual ingredients of the finished product must be complied with, no safety assessment of these ingredients is normally required. A new assessment may, however, be necessary if new findings of toxicological relevance about these ingredients become available for instance in SCCP opinions (6).

2 Description of the conditions of use

The safety assessment must be based on normal and reasonably foreseeable conditions of use of the product. The description of concrete conditions of use for the purposes of exposure analysis should take the following parameters into account:

a. Product typ (e.g. leave-on, rinse-off)

b. Target group for the use (e.g. babies, infants)

c. Area of application (e.g. whole body, eyes, mouth-cavity)

d. Possible (foreseeable) routes of exposure (e.g. oral for lipstick, toothpaste or products which may be mixed up with foodstuffs)

e. Amount per application in the case of normal and foreseeable use, e.g. when using a face lotion as body lotion

f. Duration and frequency of use

Concerning the conditions of use to be taken as a basis, all necessary warnings and use instructions must be considered as well. These result firstly from concrete legal provisions (Article 6 (1) d of the Cosmetics Directive). Furthermore, the safety assessor must check whether additional information may be necessary which is not explicitly regulated. Information about complementary warnings and conditions of use may result when considering the respective exposure more particularly from the data on the toxicological profile of the ingredients as well as possibly from existing tolerance tests with the finished product or the complaint statistics. Furthermore, recommendations of the relevant expert bodies, public authorities and associations must be taken into account.

Examples:

- »Use once a day only«
- »Not to be used for whole body care«
- »Avoid contact with eyes«

3 Exposure review of the finished product and its ingredients

a. Knowledge of the toxicological profile of the ingredients and the concrete conditions of use (exposure considerations) for the finished product is a prerequisite to the safety assessment of the finished product and its ingredients.

b. The scientific basis is to be found in the SCCP »Notes of Guidance«. They describe the state of science and may be supplemented by appropriate technical and scientific literature.

c. In the case of toxicologically relevant ingredients a sufficient margin of safety (MOS) must be required in accordance with the criteria of the »Notes of Guidance«.

d. In cases of insufficient toxicological data the application of the exposure threshold value determined according to the TTC principle (»Threshold of toxicological concern«) may be useful, e.g. if the concentration of the substance concerned in the finished product is below this value.

Please note:
If a value remains below the TTC the probability of a health risk is very unlikely. The TTC concept can, however, only be used for low substance concentrations.

e. If data are missing about toxicologically relevant parameters for one or more raw materials and the TTC concept cannot be applied, a safety assessment of the finished product is not possible.

f. As a rule the experimental verification of skin tolerance for formulations with known ingredients or for minor deviations from standard market formulations is not necessary. The overall formulation, i.e. possible interactions of ingredients amongst themselves, may influence the local tolerance of a cosmetic product. In specific cases it may be necessary to confirm tolerance in experiments.

g. The Cosmetics Directive requires in Article 7a (2) that the tests be carried out in accordance with the principles of good laboratory practice (GLP) laid down in Council Directive 87/18/EEC. This must be verified, if necessary, by the safety assessor.

4 Consideration of proof of efficacy

Proof of efficacy must be taken into account within the framework of the safety assessment if its results are of

overall relevance for the safety assessment of the finished product.

Examples:

- Study to prove UV protection for sun protection agents
- Study to prove a caries prophylaxis effect of tooth care products.

5 Inclusion of the complaints statistics

a. Substantiated complaints (e.g. intolerance confirmed by rechallenging) provide important information on the actual tolerance of the product under market conditions, i.e. also in respect of incorrect uses which were possibly not foreseeable during the initial safety assessment.

b. For that reason it is important that the complaints statistics of the finished product be regularly processed and changes to the safety assessment possibly derived therefrom.

■ Part C: Documentation and validity of the safety assessment

a. The assessment result is summed up in a formal declaration on the safety of the product under normal and reasonably foreseeable conditions of use taking into account any necessary warnings and instructions for use. This can be done in written or electronic form. All documents and calculations which result in the declaration on safety must be kept accessible to the competent authorities.

b. The result of the safety assessment may be signed by the responsible person stating the date of preparation or based on an electronic release which establishes a clear relationship between the assessor, the formulation and the date of assessment. The electronic version must be protected from abuse by unauthorised persons.

c. The safety assessment prepared in this way must be verified and, if necessary updated, if

- new scientific findings and toxicological data on the active ingredients used are available which could modify the result of the existing safety assessment,
- relevant changes occur in terms of formulation and areas of use or specifications of raw materials
- legal requirements change or
- there is a significant number of consumer complaints (e.g. intolerances confirmed by rechallenging).

d. A valid safety assessment must be available as long as the product is on the market and used by consumers (foreseeable product life).

e. The manufacturer or importer responsible for the product must establish structures and processes in order to ensure that the safety assessor is aware of formulation changes.

f. A document should be attached to the product documentation which outlines the qualifications of the safety assessor in accordance with Article 7a (1) e of the Cosmetics Directive.

■ Summary

This Guideline formulates the essential basic criteria which, in the authors' opinion, must always be taken into account when preparing safety assessments in order to ensure proper and sound compliance with the statutory requirements. However, it is neither an exhaustive list nor a checklist for the preparation of a safety assessment. Every safety assessment must be adjusted individually to the concrete product under review.
For that reason the significance and relevance of an appropriately qualified safety assessor cannot be rated highly enough. Every safety assessor is obliged to fulfil his duties in accordance with objective criteria which reflect the technical state of the art. He is personally liable for the accuracy of the safety assessment signed by him. This special responsibility must be recognised within the company's organisational structure regardless of whether the safety assessor is an internal or external expert.

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Authors' addresses:
[1] Dr. Gerd Mildau
Chemisches und Veterinäruntersuchungsamt Karlsruhe
Weissenburger Str. 3
76187 Karlsruhe
Germany
Email: poststelle@cvuaka.bwl.de

[2] Dr. Annemarie Burkhard
Landesuntersuchungsamt Rheinland-Pfalz ILCA Mainz
Emy-Roeder-Str. 1
55129 Mainz
Germany

[3] Juliane Daphi-Weber
Chemisches- und Veterinäruntersuchungsamt Ostwestfalen/Lippe
Oststraße 55
33604 Bielefeld
Germany

[4] Dr. Josef Große-Damhues
Chemisches und Lebensmitteluntersuchungsamt Recklinghausen
Kurt-Schumacher-Allee 1
45655 Recklinghausen
Germany

[5] Jürgen Jung
BBGes - Institut für Lebensmittel, Arzneimittel und Tierseuchen (ILAT)
Invalidenstraße 60
10557 Berlin
Germany

[6] Dr. Bernhard Schuster
Chemisches und Veterinäruntersuchungsamt Freiburg
Bissierstraße 5
79114 Freiburg
Germany

[7] Dr. Cornelia Walther
Bayerisches Landesamt für Gesundheit und Lebensmittelsicherheit
Veterinärstraße 2
85764 Oberschleißheim
Germany