EUROPEAN COMMISSION

Brussels, XXX
[…](2012) XXX draft

COMMISSION IMPLEMENTING DECISION

of XXX

on Guidelines on Annex I to Regulation (EC) No. 1223/2009 on cosmetic products

(Text with EEA relevance)

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THE EUROPEAN COMMISSION,

Having regard to the Treaty on the Functioning of the European Union,

Having regard to Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products[1], and in particular the third subparagraph of Article 10(1) thereof,

Whereas:

(1) It is essential that cosmetic products made available on the Union market be safe for human health when used under normal and reasonably foreseeable conditions of use. To that end, Regulation (EC) No 1223/2009 requires that, in order to establish that a cosmetic product is safe under those conditions, cosmetic products undergo a safety assessment.

(2) The operator designated as the responsible person in accordance with Regulation (EC) No 1223/2009 is to ensure that, for each cosmetic product which is to be placed on the Union market, a cosmetic product safety report is drawn up on the basis of the relevant information and in accordance with the requirements laid down in Annex I to Regulation (EC) No 1223/2009.

(3) In order to facilitate the understanding of the requirements of Annex I to Regulation (EC) No 1223/2009 by all undertakings, and especially small and medium-size enterprises, the Regulation requires that the Commission adopts appropriate guidelines.

(4) This Decision sets out appropriate guidelines on Annex I to Regulation (EC) No 1223/2009. They were developed with the contribution of the relevant stakeholders, including representatives of small and medium-sized enterprises.

(5) The guidelines should assist responsible persons in complying with their regulatory obligations. However, they are not meant to replace the knowledge and expertise of the qualified safety assessor, as required by Article 10(2) of Regulation (EC) No

[1] OJ L 342, 22.12.2009, p. 59.

1223/2009, who should remain the only professional allowed to carry out the cosmetic product safety assessment as described in Part B of Annex I.

(6) The measures provided for in this Decision are in accordance with the opinion of the Standing Committee on Cosmetic Products,

HAS ADOPTED THIS DECISION:

Article 1

The guidelines to enable undertakings to comply with the requirements laid down in Annex I to Regulation (EC) No 1223/2009 on cosmetic products are set out in the Annex to this Decision.

Article 2

This Decision shall enter into force on the twentieth day following that of its publication in the *Official Journal of the European Union*.

Done at Brussels,

For the Commission
The President
José Manuel BARROSO

ANNEX

Guidelines on Annex I to Regulation (EC) No 1223/2009 on the Cosmetic Product Safety Report

1. INTRODUCTION

Article 11 of Regulation (EC) No 1223/2009 requires that a product information file is drawn up for each product before it is placed on the market. The product information file should be updated when necessary and kept readily accessible, in electronic or other format, at the address of the responsible person given on the label, to the competent authorities for market surveillance purposes for a period of ten years following the placing on the market of the last batch of the product.

The most important element of the product information file, from a safety point of view, is the cosmetic product safety report referred to in Article 10(1). The other elements are a clear description of the cosmetic product, a description of the method of manufacturing and a statement on compliance with good manufacturing practice, the proof of the effects claimed, and data on animal testing[2].

Where the responsible person drawing up the cosmetic product safety report is not the manufacturer of the product, they should ensure they have access to all the technical and scientific skills necessary to obtain reliable cosmetic product safety information and an appropriate safety assessment to demonstrate that the product they are responsible for is safe, in accordance with Article 3 of Regulation (EC) No 1223/2009. They may therefore need to involve not only the safety assessor, but also the manufacturer, the suppliers of raw materials, and other technical experts.

In any case, the responsible person is to ensure that the intended use of the cosmetic product and the anticipated systemic exposure to individual ingredients in a final formulation are taken into account in the safety assessment; an appropriate weight-of-evidence approach is used in the safety assessment for reviewing data from all existing sources; the cosmetic product safety report is kept up to date in view of additional relevant information generated subsequent to placing the product on the market[3].

The cosmetic product safety assessment, as set out in Part B of Annex I to Regulation (EC) No 1223/2009, is to be carried out by a qualified safety assessor. The responsible person and the safety assessor should work closely together to ensure that the safety of the product is properly assessed and documented and that the assessment is kept up to date. The responsible person and the safety assessor should gather all the necessary information as required by Part A of Annex I to Regulation (EC) No 1223/2009.

The cosmetic product safety report should be drawn up in a transparent way and should be well-argued and easily understood.

The Cosmetic Product Safety Report is an expert piece of work made up of different modules and where the information required under Part A may be stored in different databases. The report, which should contain, as a minimum, all the information indicated in Annex I to Regulation (EC) No 1223/2009, should appear under the same or similar headings for ease of reference of the competent authorities. However, it may be sufficient

[2] Article 11(2) of Regulation (EC) No 1223/2009.
[3] Article 10(1) of Regulation (EC) No 1223/2009.

to provide under each heading a clear reference to a document containing the information and readily available in electronic or printed format.

2. ANNEX I TO REGULATION (EC) NO 1223/2009 — COSMETIC PRODUCT SAFETY REPORT

In accordance with Annex I to Regulation (EC) No 1223/2009, the Cosmetic Product Safety Report is to contain, *'as a minimum'*, the information required under each of the headings of Part A and Part B.

Part A aims to gather all the data necessary for the safety assessment of the product, while Part B sets out the reasoning, starting from the data, for drawing conclusions as to the safety of the product.

The structure and content of the safety report should reflect the requirements of Annex I to Regulation (EC) No 1223/2009. However, if the report does not directly contain the required information, it should provide a reference to another readily available source.

The responsible person is to ensure that the Cosmetic Product Safety Report is kept up to date in the light of additional relevant information emerging after the product has been placed on the market.[4]

3. PART A — COSMETIC PRODUCT SAFETY INFORMATION

Part A of the cosmetic product safety report is intended to gather the data necessary to prove that the cosmetic product is safe. The information should enable the safety assessor to clearly identify and quantify, based on the identified hazards, the risks a cosmetic product may present to human health. A hazard may arise, for example, from the raw materials, the manufacturing process, the packaging, the conditions of use of the product, the microbiological specifications, the quantities used, the toxicological profile of the substances, etc.

As Part A of Annex I to Regulation (EC) No 1223/2009 requires that the data listed under its headings are provided as a minimum, any discrepancy with regards to the requirements of Part A should be justified.

Part A of Annex I to Regulation (EC) No 1223/2009 lists the data that is to be available, *'as a minimum'*, for the safety assessor to be able to carry out the safety assessment.

In addition to the minimum data listed in Part A of Annex I to Regulation (EC) No 1223/2009, the safety assessor can use any additional data, where relevant. On the other hand, they, or the responsible person, may consider that, depending on the type of product, some of the required data are not relevant or necessary to assess the safety of the product (e.g. preservation challenge test). In this case, the absence of specific data is to be clearly justified in Part A and the justification is to be repeated and validated by the safety assessor in their reasoning in Part B. The responsible person should check the presence of the required data or the justification for their absence.

The data required by Part A can be drawn from any reliable source. Examples include: data from suppliers, scientific literature, experience gained with similar or other product categories, results of studies on the

[4] Article 10(1)(c) of Regulation (EC) No 1223/2009.

product itself or on the substances it contains, available data on similar formulations, or computer models. The safety report should highlight the relevance of the data in relation to the product.

The guidance published by the EU scientific committees concerned with risk assessment,[5] as well as the recommendations of national competent authorities or professional organisations, may provide further helpful support.

3.1. Quantitative and qualitative composition of the cosmetic product

The aim of that section of the cosmetic product safety report is to provide the exact quantitative and qualitative composition of the finished product, starting from the raw materials. Raw materials are substances or mixtures used in the manufacturing of the cosmetic product. The intended function of each substance is to be indicated.

The complete product composition is to be specified, stating the name and identity (qualitative) of each raw material (including chemical name, INCI, CAS, EINECS/ELINCS, where possible), and the amount of each raw material, stating the weight percentage (quantitative). Ranges should not be used, unless this can be justified (e.g. viscosity or pH adjusters). If concentration ranges are unavoidable, toxicological considerations and calculations should be based on the highest concentration figure. It may also be useful to indicate the supplier(s) of the raw materials.

All substances entering into the composition of commercial mixtures supplied as raw materials (including directly added preservatives, antioxidants, chelators, buffering agents, solvents, other additives, etc.) are to be identified and quantified in the formula of the finished product. This also applies to all substances indirectly added to the product, such as preservatives used for preserving raw materials. The intended function of each substance is to be indicated.

When chemically well-defined substances are present, their quantity and molecular formula should be given together with their analytical specifications (degree of purity, identification of major impurities, criteria and test methods used).

When complex ingredients are present, their nature and quantity together with a clear definition of the mixture and the material(s) used should be given in order to identify the substances with regard to their composition and effects (manufacturing and purification processes, including physical, chemical, enzymatic, biotechnological and microbiological steps). The purity criteria and test methods used should be provided. Examples of complex ingredients include those of mineral, botanical, animal or biotechnological origin. The scope of the information needed on complex ingredients, depending on their nature and origin, is explicitly listed in the Scientific Committee for Consumer Safety (SCCS) Note of Guidance.[6]

When a mixture of both chemically well-defined substances and complex ingredients is present, the above guidance also applies.

Where any fragrance (or flavour) compound comprising a mixture of fragrance (or flavour) ingredients and functional components with olfactory, odour-enhancing, odour-protecting or blending properties is formulated and intentionally added to a cosmetic product to impart a scent (or flavour) or to cover a

5 The SCCS's Notes of Guidance for the Testing of Cosmetic Ingredients and their Safety Evaluation, 8th Revision, SCCS/1501/12, and its subsequent updates.

6 SCCS Notes of Guidance, para. 3-6.2, pp. 35-36.

malodour, its identification is to include the name and code number as well as the identity of the supplier. Qualitative and quantitative information about regulated substances in the fragrance (or flavour) compound and information relevant for a safety assessment should be disclosed to the responsible person and the safety assessor, and should be included in the safety report.

3.2. Physical/chemical characteristics and stability of the cosmetic product

The aim of that section of the cosmetic product safety report is to describe the relevant physical and chemical specifications of the substances or mixtures used and the cosmetic product itself. These specifications are crucial for an appropriate safety assessment, as they may influence the safety of a cosmetic product. For example, physico-chemical properties, in combination with other information, can help the safety assessor determine the need to investigate relevant toxicological parameters.

In addition, the physico-chemical characteristics of the substances or mixtures and finished products set the benchmark against which the products and the raw materials can be considered acceptable from a quality point of view.[7]

That section of the cosmetic product safety report also requires an assessment of the stability of the cosmetic product, under reasonably foreseeable storage conditions. The aim is to evaluate if the stability of the cosmetic product affects the safety and quality of the product, and to use the information to determine its minimum durability and period-after-opening (PAO).

3.2.1. Physical/chemical characteristics of substances or mixtures

This description is to include the most relevant physico-chemical properties of each substance and mixture contained in the product, for example: chemical identification, physical form, molecular weight, solubility, partition coefficient, substance purity, other parameters relevant for the characterisation of specific substances and mixtures, and, for polymers, the average molecular weight and range.

Where relevant, the particle-size distribution curve of substances should be included in the physico-chemical characteristics, especially for nanomaterials.

Cosmetics manufacturers should ensure that the specifications of raw materials are properly documented by their suppliers. Specifications should be available for each raw material actually used in the product. Based on function, additional specifications may be needed. For UV absorbers, for instance, the absorption spectra should be provided.

For each description of physico-chemical properties and specifications (for each substance and mixture contained in the product), the reference methods should be stated in the safety report.

[7] This point is relevant in the context of Good Manufacturing Practices, and is explicitly addressed by the relevant standard EN ISO 22716:2007. More specifically, it matches the requirements for the release of raw materials and the finished product.

3.2.2. Physical/chemical characteristics of the finished cosmetic product

This description is to contain the specifications of the finished product. Each specification should be given with relevant limits, e.g. pH between 5.5 and 6.5.

For each description of physico-chemical properties and specifications of the finished product, the reference methods should be stated in the cosmetic product safety report.

3.2.3. Stability of the cosmetic product

As the requirement is to assess the stability of the cosmetic product under reasonably foreseeable storage conditions, if stability is dependent on storage conditions, information about these conditions should be passed on throughout the supply chain, and, if relevant for the end user, it should be indicated on the labelling of the product.

The methodology used to determine the product's minimum durability should be described. Any specific preservation precautions should be mentioned.

All available data used to justify the indicated minimum durability should be listed in the safety report. In order to determine the coherence of the stability study conducted, and to check the relevance of the date of minimum durability chosen for the product, the description of the tests specific to the stability study and the results of those tests should be included in the cosmetic product safety report. In addition, the following should also be provided:

(1) Evidence that the composition of the product used for stability testing corresponds to the product actually placed on the market;

(2) The results of the preservative efficacy study, e.g. challenge test, if applicable;[8]

(3) When applicable, the period-after-opening (PAO)[9] and its justification.

The SCCS has recommended that '*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.*'[10]

3.3. Microbiological quality

The aim of that section of the cosmetic product safety report is to determine the acceptable microbiological specifications of the raw materials (substances or mixtures) and finished product from a microbiological point of view. In accordance with Annex I to Regulation (EC) No 1223/2009, particular attention is to be paid to the microbiological specifications of cosmetic products intended to be used on sensitive body parts and on specific populations. In

[8] See section 3.3 on Microbiological quality.

[9] See 'Practical implementation of Article 6(1)(c) of the Cosmetics Directive (76/768/EEC)1: LABELLING OF PRODUCT DURABILITY: 'PERIOD OF TIME AFTER OPENING' http://ec.europa.eu/consumers/sectors/cosmetics/files/doc/wd-04-entr-cos_28_rev_version_adoptee20040419_en.pdf.

[10] SCCS Notes of Guidance, para. 4-3.3, p. 74.

addition, information regarding microbiological quality is essential in order to justify the effectiveness of the preservation system and justify the indicated minimum durability of the cosmetic product stored under appropriate conditions and period-after-opening (PAO)[11] of the finished product in terms of safety.

The microbiological specifications of the raw materials (substances or mixtures) and cosmetic product are to form part of the safety assessment. Particular attention is to be paid to the microbiological specifications of cosmetic products intended to be used around the eyes, on mucous membranes in general, on damaged skin (e.g. skin care products suitable for atopic or irritated skin), on children under three years of age, on elderly people or on persons with compromised immune responses.

3.3.1. Microbiological quality of substances and mixtures

The main parameters for microbiological quality are the original level of contamination and the possibility of microbial growth. Particular attention should be paid to the raw materials (substances and mixtures) most susceptible to microbial growth (e.g. water-based mixtures, protein-rich materials, plant or animal raw materials). On the other hand, there are raw materials which do not support microbial growth, e.g. organic solvents.

3.3.2. Microbiological quality of the finished cosmetic product

Concerning microbiological susceptibility, there is a difference between three product categories:

(1) Low microbiological risk products (e.g. products with an alcohol content >20%, products based on organic solvents, high/low-pH products), for which neither a preservation challenge test nor microbiological quality tests on the finished product are necessary. A scientific justification is to be provided, however;

(2) Single-use products, and products which cannot be opened (e.g. for which the packaging allows dosing the product without it coming in contact with the air), for which only microbiological quality tests on the finished product are necessary. A scientific justification is to be provided, however;

(3) All other products, for which both a preservation challenge test and microbiological quality tests on the finished product are necessary.

Specific 'Guidelines on Microbiological Quality of the Finished Product' are provided in the SCCS Notes of Guidance.[12]

[11] The 'date of minimum durability' is the date until which the cosmetic product, stored under appropriate conditions, will continue to fulfil its initial function and, in particular, will remain safe; the PAO is the period of time after opening for which the product can be used without any harm to the consumer. See 'Practical implementation of Article 6(1)(c) of the Cosmetics Directive (76/768/EEC)1: LABELLING OF PRODUCT DURABILITY: 'PERIOD OF TIME AFTER OPENING'.

[12] SCCS Notes of Guidance, para 4-4, pp. 75–76.

3.4. Impurities, traces, information about the packaging material

The aim of that section of the cosmetic product safety report is to assess whether the cosmetic product contains substances that have not been intentionally added to the formulation, and which may have an impact on its safety.

Impurities are unintended substances in raw materials.

A trace is a small quantity of an unintended substance in the finished product. Traces are to be evaluated with regard to safety of the finished product. When traces of prohibited substances are present, evidence of their technical unavoidability are also to be provided.

Traces can originate from the following sources: impurities in the raw materials/substances; the manufacturing process; potential chemical evolution/interaction and/or migration of substances in the product that could occur under normal storage conditions and/or through contact with the packaging material.

Because substances may migrate from the packaging to the formulation, the relevant characteristics of the packaging material are to be considered.

In accordance with point 4 of Annex I to Regulation (EC) No 1223/2009, the section on 'Impurities, traces, information about the packaging material' is to address three specific issues:

(a) The purity of substances and mixtures;

(b) In case of traces of prohibited substances, evidence of their technical unavoidability;

(c) The relevant characteristics of the packaging material, in particular purity and stability.

In practical terms, those elements may be interpreted as follows:

(a) Precise definition of impurities and traces (see 3.4.1);

(b) Evidence of technical unavoidability of prohibited substances (see 3.4.2);

(c) Potential release of substances from the packaging or possible deterioration of the product in contact with the packaging (see 3.4.3).

For the analysis of impurities and packaging material, data from suppliers are of crucial importance and should be preferred.

3.4.1. Purity of substances and mixtures

The presence of unintended substances, such as impurities and traces, can have an impact on the safety of the finished product. The cosmetic product safety report is to include data on the purity of raw materials (substances and mixtures) and the identification of the toxicologically relevant unintended substances. These substances should be taken into account in the safety assessment of the product.

Impurities are unintended substances in raw materials.

A trace is a small quantity of an unintended substance in the finished product.

The presence of traces in the finished product can be evaluated in two ways:

(d) through the specifications/technical data for each raw material, based on knowledge of the process for manufacturing the raw material (origin of substance, production process, synthesis route, extraction process, solvent used, etc.);

(e) through a physico-chemical analysis of possible impurities in raw materials and, if necessary, in the final product (e.g. nitrosamines which are potentially generated during or after the manufacturing process).

Traces of prohibited substances are dealt with in paragraph 3.4.2 of these Guidelines.

Some traces have regulatory concentration limits. For the presence of traces of substances that are not prohibited, and for which there are no regulatory concentration limits, but which could be expected to impact consumer safety, the safety assessment needs to be carried out by the safety assessor.

3.4.2. Evidence of the technical unavoidability of traces of prohibited substances

While the procedure outlined in paragraph 3.4.1 should be followed for all known impurities and traces to evaluate their toxicological impact, further investigation is required for prohibited substances present as traces in the finished product[13].

When such presence is technically unavoidable, the cosmetics manufacturers are required to provide evidence of the technical unavoidability. That means they have to justify the presence of those traces by all necessary means. The presence of traces of prohibited substances should be kept as low as is reasonably achievable under good manufacturing practices. In addition, the safety assessor has to decide whether their levels are toxicologically acceptable and whether the product is still safe.

Especially in the case of non-threshold genotoxic and carcinogenic substances[14], the cosmetic industry should keep improving its best practices in order to eliminate these substances (ALARA principle[15]) in the finished cosmetic product. The main concern is to ensure the protection of human health, as required by Article 3 of Regulation (EC) No 1223/2009.

Traces generated by the degradation of substances within the final product (stability issues), by preservation or transport problems, or by the interaction of raw materials should be avoided through good manufacturing practices, or possibly through re-formulation of the product.

3.4.3. The relevant characteristics of packaging material

Packaging material means the container (or primary packaging) that is in direct contact with the formulation. The relevant characteristics of packaging materials in direct contact with the final product are important for

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13 Article 17 of Regulation (EC) No 1223/2009 establishes that traces of prohibited substances are only permitted if they are technically unavoidable and if they have no impact on the safety of the cosmetic products.

14 The 'non-threshold genotoxic and carcinogenic substances' are the genotoxic and carcinogenic substances without a threshold for the carcinogenic-genotoxic effects.

15 *Opinion of the Scientific Committee on a request from EFSA related to A Harmonised Approach for Risk Assessment of Substances Which are both Genotoxic and Carcinogenic*, The EFSA Journal (2005) 282, pp. 1-31.

the safety of the cosmetic product. Reference to Regulation (EC) No 1935/2004 of the European Parliament and of the Council[16] could be useful.

Experience with similar formulation/packaging combinations already on the market provides useful indications. Materials that have been developed for food packaging have often already been tested, so relevant information on stability and migration may be available. Additional testing may not be required. However, more evaluation may be needed for new or novel packaging.

The combination of packaging material, formulation of the cosmetic product and contact with the external environment may have an impact on the safety of the finished product, due to the following factors:

(a) interaction between the product and the packaging material;

(b) barrier properties of the packaging material;

(c) substance migration from/to the packaging material.

The information on relevant characteristics of the packaging materials in direct contact with the product should allow an estimation of potential risks. Relevant characteristics could include, for example, the following:

(a) composition of the packaging material, including technical substances such as additives;

(b) technically unavoidable impurities;

(c) possible migration from the packaging.

This information only indicates the hazard. It is up to the safety assessor to evaluate the risk[17].

Studies on interactions/suitability between formulation and packaging allow testing of the potential migration of small amounts of substances from the primary packaging material to the product. These tests are performed under specific and relevant test conditions. There are, however, no standard procedures for cosmetic products. An appropriate assessment may be made based on knowledge of the formulation and primary packaging materials and experienced expert judgment.

If migration is dependent on storage conditions, the correct conditions should be indicated on the product labelling. If the formulation is sensitive to light or air, and would degrade in a way that impacts product safety or product efficacy, appropriate packaging should be used.

3.5. Normal and reasonably foreseeable use

The section on normal and reasonably foreseeable use of the product is essential for the safety assessor to be able to determine a relevant exposure scenario. The intended use should be appropriately communicated to the consumer in order to avoid misuse of the product.

[16] OJ L 338, 13.11.2004, p. 4.

[17] To evaluate the risk, one needs to consider the hazard together with the exposure, and this is the duty of the safety assessor.

In addition, warnings and other explanations on the labelling should be consistent with the identified normal and reasonably foreseeable use, and the reasoning justifying their inclusion is to be given.

A clear explanation of the normal intended use and the reasonably foreseeable use should be provided. For instance, in the case of a shampoo, the normal intended use would be to use it on the scalp; an (unintended) reasonably foreseeable use would be for it to be used as a shower gel. Ingestion would be a clear misuse.

To this end, a practical approach may be useful. For example, one could include a photo of the packaging or the artwork in the cosmetic product safety report to show the presentation of the product and its intended use. It would also be useful to make the link with the warnings and labelling, as highlighted by Annex I to Regulation (EC) No 1223/2009 on this point.

3.6. Exposure to the cosmetic product

The exposure assessment is an essential element of risk assessment. The aim of this section is to quantify the amount of cosmetic product coming into contact with the external parts of the human body or the teeth and the mucous membranes of the oral cavity under normal or reasonably foreseeable use for each use and the frequency of use.

The assessment of exposure to the cosmetic product shall take into consideration the findings regarding 'normal and reasonably foreseeable use' under section 5 of Annex I to Regulation (EC) No 1223/2009 in relation to a set of elements that are explicitly listed in section 6. Secondary exposure routes should also be taken into consideration, where appropriate.

The description of concrete conditions of use for the purpose of exposure analysis should also take the following parameters into account:

(a) product type (e.g. leave-on, rinse-off);

(b) area of application (e.g. whole body, eyes, mouth cavity);

(c) amount per application in the case of normal and reasonably foreseeable use, e.g. including when a shampoo is used as shower gel;

(d) duration and frequency;

(e) possible (foreseeable) routes of exposure (e.g. oral for lipstick and toothpaste, or inhalation for aerosols and solvents);

(f) target group for use (e.g. children under the age of three years, adults);

(g) impact of particle size on exposure.

The SCCS Notes of Guidance provide useful information on exposure calculations and particularly relevant tables.[18]

[18] SCCS Notes of Guidance, para 4, p. 66 *et seq*.

However, as the tables may not contain the daily exposure values for specific cosmetic products, other ways of calculating exposure may be used. Several alternatives are possible. For instance, calculations could be performed based on either skin surface data or user experience data.

If the available data are considered insufficient, it is recommended to assume a worse-case exposure taking into account the foreseeable conditions of use.

The specific target population and the populations otherwise exposed to the product should be kept in mind. For example, in the case of products for professional use, there will be different exposure scenarios for the targeted consumers and the exposed professionals in terms of exposure frequency, exposure duration and size of exposed skin area, possible exposure through inhalation (for example, in the case of shampoos, when assessing the risk for consumers, exposure of the scalp with a frequency of approximately once a day should be considered, whereas for hair dressers exposure of the hands several times a day should be considered).

3.7. Exposure to the substances

The assessment of the exposure to each of the substances contained in the cosmetic product is necessary in order to assess the risk associated with each individual substance. The objective of that section of the cosmetic product safety report is to determine the amount of each substance coming into contact with the external parts of the human body or the teeth and the mucous membranes of the oral cavity under normal or reasonably foreseeable use, for each use.

Exposure to each of the substances in the cosmetic product is calculated from the exposure to the final product and the concentration of the individual substances in the final product. It is necessary to calculate this exposure in order to assess the potential risk from each substance.

Exposure to individual substances is calculated from the quantitative composition of the product. Where substances are generated or released during the use of the product, the exposure should be estimated and taken into account in the safety assessment.

The exposure conditions to each individual substance are determined by those for the finished cosmetic product under 3.6.

3.8. Toxicological profile of the substances

The aim of this section of the cosmetic product safety report is to describe the toxicological hazard of each of the substances in the finished product, determine the potential exposure, and draw up a risk characterisation. These aspects are of crucial importance in order to perform the risk assessment, as they are the three essential steps of the risk assessment process.[19]

The endpoints to be considered, as well as the necessary data, depend on a number of factors, including the routes of exposure, the conditions of use of the product, the physico/chemical

[19] M. Pauwels, V. Rogiers, *Human Health Safety Evaluation of Cosmetics in the EU: A Legally Imposed Challenge to Science*, Toxicology and Applied Pharmacology, 243 (2010), p. 261.

characteristics and the possible absorption of the substance. The choice of relevant endpoints should be the responsibility of the safety assessor, who should justify their decisions.

The safety assessor should ensure that the experimental data comply with the requirements of Article 18 of Regulation (EC) No 1223/2009 concerning animal testing. Such requirements are clarified in the Commission Communication on the animal testing and marketing ban and on the state of play in relation to alternative methods in the field of cosmetics[20].

Point 8 of Part A of Annex I to Regulation (EC) No 1223/2009 establishes the key requirements for the cosmetic product safety report as far as the toxicological profile of substances is concerned.

3.8.1. General considerations concerning the toxicological profile as part of the safety assessment

The relevant elements of the toxicological profile of each substance or mixture should be described in detail in the cosmetic product safety information (Part A) and assessed in the safety assessment (Part B), bearing in mind the exposure situation, the intrinsic toxicity (or hazard) of each substance, and the specific conditions of use of the product.

Human experiences, animal studies or alternative methods to animal testing are helpful in understanding the health risk for humans exposed to dangerous substances. For the toxicological profiles, toxicological studies are used to identify the hazards which could be associated with a risk to humans. It is essential to consider the quality and limitations of the studies that have been performed. The validity of a study should be taken into consideration in determining whether there is a need for new information to understand the risk to human health[21]. Studies conducted in accordance with international guidelines are the most useful, but unfortunately not all studies meet these standards. Thus, the limitations of such studies should be considered in assessing the toxicological profile for each substance.

The safety assessor should ensure that the experimental data comply with the requirements of Article 18 of Regulation (EC) No 1223/2009 concerning animal testing. The Communication from the Commission to the European Parliament and the Council on the animal testing and marketing ban and on the state of play in relation to alternative methods in the field of cosmetics outlines the Commission's interpretation of those requirements[22].

3.8.2. Toxicological profile of substances for all the relevant toxicological endpoints

The toxicological profile for each substance is determined by the hazard identification and the dose-response characterisation.

The first essential step in developing the toxicological profile is to gather all the relevant information about the intrinsic properties of the substance. Such information should include the following:

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20 Communication from the Commission to the European Parliament and the Council on the animal testing and marketing ban and on the state of play in relation to alternative methods in the field of cosmetics, COM(2013) 135 final.

21 H.J. Klimisch, E. Andreae and U. Tillmann (1997), *A systematic approach for evaluating the quality of experimental and ecotoxicological data*. Regul Toxicol Pharmacol 25:1-5.

22 See in particular point 3.1 of the Communication.

(1) As the most valuable toxicity information, actual test data from *in vivo* or *in vitro* studies obtained in accordance with Council Regulation (EC) No 440/2008 (REACH)[23], recognised international guidelines, or standards (e.g. OECD Test Guidelines), and performed in accordance with good laboratory practice principles;

(2) Existing test data that have not been obtained in accordance with the latest adopted/accepted version of a test guideline or with good laboratory practice standards, but which are considered valid;

(3) *In vitro* data or alternative data from valid test systems, to be used as a screening study to predict toxicity;

(4) Human data and/or experience. It is in general not acceptable to perform human toxicology studies for hazard identification, but, if data or experience exist, they should be included in the final assessment;

(5) Human (clinical) data, including data from clinical trials and applications in other industries such as food and medicinal products;

(6) Data gathered from post-marketing surveillance;

(7) Human volunteer compatibility studies, which should only be used to confirm safe levels of use for a relevant target population;[24]

(8) Read-across[25] approaches, based on the chemical structure and properties of related substances in order to predict the toxicity of the ingredient, grouping of substances, and non-testing data from QSAR model outputs.

Based on data obtained from all available sources, and taking into account the quality of the data, the safety assessor can evaluate the likelihood of adverse effects in humans through the 'weight of evidence' approach[26].

A prerequisite for a proper risk assessment is the availability of adequate data. For additional support on this matter, one may consult the guidance for the preparation of safety dossiers for submission to the Scientific Committee for Consumers Safety (SCCS), set out by the Committee itself in its Notes of Guidance. Though these Notes of Guidance are provided for substances where an authorisation is needed, i.e. for colorants, preservatives and UV filters, or which otherwise raise concern, the requirements they set out may be helpful

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23 OJ L 142, 31.5.2008, p. 1.

24 SCCS Notes of Guidance, para. 3.4.11. Also cf. opinions SCCNFP/0068/98, an earlier version of the Notes of Guidance, and SCCNFP/0245/99 on Basic Criteria of the Protocols for the Skin Compatibility Testing of Potentially Cutaneous Irritant Cosmetic Ingredients or Mixtures of Ingredients on Human Volunteers.

25 Read-across is a technique for data gap filling in which information for one or more source chemicals is used to make a prediction for a target chemical, which is considered to be similar in some way. From ECHA, 'Guidance on information requirements and chemical safety assessment Chapter R.4: Evaluation of available information ', December 2011, p. 12. http://echa.europa.eu/documents/10162/17235/information_requirements_r4_en.pdf

26 One definition for weight of evidence is: 'the process of considering the strengths and weaknesses of various pieces of information in reaching and supporting a conclusion concerning a property of the substance.' From ECHA, 'Practical guide 2: How to report weight of evidence', 2010, p. 2, http://echa.europa.eu/documents/10162/13655/pg_report_weight_of_evidence_en.pdf

for the safety assessment of all substances used in cosmetic products. In addition, a section of the most recent Notes of Guidance focuses on the safety assessment of finished cosmetic products[27].

The toxicological profile may address a number of different endpoints. A final decision about which endpoints are relevant is made by the safety assessor on a case-by-case basis, taking into account exposure, use of the product, the physico-chemical characteristics of the substances, experience with the substances, etc[28]. Attention should also be paid to local effects (e.g. irritation and photo-toxicity), when relevant. Where a certain endpoint is considered to be not relevant, this should be justified.

Endpoints that may be relevant for the toxicological profile are:

(1) Acute toxicity via relevant routes of exposure;

(2) Irritation and corrosivity;

(3) Skin irritation and skin corrosivity;

(4) Mucous membrane irritation (eye irritation);

(5) Skin sensitisation;

(6) Dermal/percutaneous absorption;

(7) Repeated dose toxicity (normally 28- or 90-day studies);[29]

(8) Mutagenicity/genotoxicity;

(9) Carcinogenicity;

(10) Reproduction toxicity;

(11) Toxicokinetics (ADME studies);

(12) Photo-induced toxicity;

For the appropriate endpoints, the most relevant concentrations or No Observed Adverse Effect Levels (NOAEL) or Lowest Observed Adverse Effect Levels (LOAEL) should be identified for further use in the risk characterisation process.

Additional information regarding endpoint specific data and their interpretation can be found in the endpoint specific guidance[30] prepared by the European Chemical Agency (ECHA) for the implementation of

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27 Cfr. SCCS Notes of Guidance, Section 3-6 Basic Requirements for Cosmetic Substances Present in Finished Cosmetic Products (which are to be evaluated by individual safety assessors).

28 The SCCS Notes of Guidance clearly address this issue in para. 3-6.1 General toxicological requirements.

29 According to the SCCS's Notes of Guidance (para. 3-4.5), priority should be given to the NOAEL as regards sub-chronic toxicity (90 day study). Only if such values are not available should results relating to sub-acute toxicity (28-day study) be used.

30 ECHA, Guidance on information requirements and chemical safety assessment - Chapter R.7a: Endpoint specific guidance, May 2008.

Regulation (EC) No 1907/2006[31] on Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH).

For some cosmetic ingredients e.g. of mineral, animal, botanical and biotechnological origin (see also Substances of Unknown or Variable composition, Complex reaction products or Biological materials or 'UVCB substances' under REACH),[32] their identification should carefully address source, process, organisms involved, etc., in order to evaluate their toxicological profile.

If certain hazards cannot be sufficiently addressed, or if doubts remain regarding the robustness of the data, additional uncertainty factors may be introduced or additional data may need to be generated.

3.8.3. Consideration of all the significant routes of absorption

Dermal, oral and inhalation routes of exposure are potentially relevant for human exposure to cosmetic products. It is essential to calculate the systemic exposure in order to compare it with the relevant NOAEL. The ratio between these two is defined as the margin of safety, which is an indicator of whether the product can be considered safe or not (see also section 3.8.4 and following).

Absorption is linked to the bioavailability of a substance, and is essential for calculating the margin of safety. Systemic exposure can be calculated as:

Systemic exposure dose[33] (SED) = External exposure x absorption

Absorption can occur through several external routes: dermal, oral and inhalation.

If the intended exposure for the cosmetic product is not in line with the route of exposure in the safety data, route-to-route extrapolation should be considered.

(a) Absorption after dermal exposure

The dermal absorption[34] of a substance in a product is dependent on both intrinsic factors (e.g. LogPow, molecular weight) and its behaviour in the vehicle. Dermal *in vivo* human absorption of a substance can be estimated using the data from existing *in vivo* animal studies and *in vitro* studies on animal and human skin. When no measurement data are available and no absorption rate can be determined using a scientifically valid *in silico* method or default absorption rates, a worst case value of 100 % should be used for calculation of the systemic exposure.[35] In case MW > 500 Da and log Pow is smaller than -1 or higher than 4, a value of 10 % dermal absorption can be considered.

(b) Absorption after oral exposure

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31 OJ L 396, 30.12.2006, p. 1.

32 Cfr. ECHA, Guidance for identification and naming of substances under REACH and CLP, November 2011, p. 29. http://echa.europa.eu/documents/10162/17235/substance_id_en.pdf

33 *I.e.* 'the systemically available dose that passes the relevant physical barriers (gastro-intestinal, skin or lung structures) and becomes available in the blood stream for subsequent distribution to tissues and organs', ref. M. Pauwels, V. Rogiers, p. 262.

34 Basic criteria for the in vitro assessment of dermal absorption of cosmetic ingredients (SCCS/1358/10).

35 SCCS Notes of Guidance, para 3-7.2, p. 49.

When a reasonably foreseeable use can entail ingestion, the oral route should be included in the exposure scenarios.

(c) Absorption after inhalation

For all substances used in spray applications and some powders, the inhalation route is to be taken into consideration in determining the systemic exposure.

In addition, there may also be a possibility of secondary inhalation exposure where cosmetic products contain volatile substances which can be inhaled unintentionally in the case of direct use, e.g. toluene in nail polish, various substances contained in nail modelling gels, etc.

3.8.4. Consideration of systemic effects and calculation of the margin of safety

The safety assessment of a product for systemic toxicity is highly dependent on data on each substance, since there will be no data on systemic toxicity for the finished cosmetic product.

Risk characterisation usually involves an expert evaluation of the potential non-quantifiable adverse effects, followed by calculation of an uncertainty factor or margin of safety.[36] This calculation depends on the systemic exposure to the substance and its toxicological parameters.

In accordance with Point 8 part A of Annex I to Regulation (EC) No 1223/2009, systemic effects and margin of safety are to be considered in Part A of the safety report. As they are mandatory, the omission of these steps is to be duly justified. An example where this could apply would be the presence of a substance in the cosmetic product at a low level, with the expected (worst case) exposure levels being below the appropriate threshold of toxicological concern (TTC) values[37]. Another example could be the inclusion of food materials for which a much higher innocuous ingestion level is known.

When the requirement to calculate the margin of safety cannot be met, a different way of expressing the safe dose for each substance may be appropriate, where justified. When a NOAEL is not available, other reference toxicology values such as No Observed Effect Level (NOEL), LOAEL, Lowest Observed Effect Level (LOEL), can be used to calculate the margin of safety; Benchmark Dose (BMD) or Virtually Safe Dose (VSD), used to qualify and quantify a risk in other fields, may be used in the context of cosmetic products safety assessment, provided a relationship with exposure is established, by comparing the exposure from cosmetics and these reference doses.

Otherwise, the safety of a particular substance in a particular product cannot be demonstrated.

According to the procedures described in the SCCS Notes of Guidance,[38] the margin of safety (MoS) for a specific route of exposure can be calculated using the following formula:

MoS = Systemic No-Observed-Adverse-Effect Level (NOAEL) / Systemic Exposure Dose (SED)

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36 M. Pauwels, V. Rogiers, p. 262.

37 SCCS, SCHER and SCENIHR, Opinion on Use of the Threshold of Toxicological Concern (TTC) Approach for Human Safety Assessment of Chemical Substances with focus on Cosmetics and Consumer Products, SCCP/1171/08.

38 SCCS Note of Guidance, para 3-7, p. 46.

where the Systemic Exposure Dose (SED) is obtained by combining the external exposure (mg/kg bw/day) with the absorption rate (typically expressed in % or µg/cm^2), frequency and retention factors.

It is generally accepted that the margin of safety should be at least 100 to declare a substance safe for use in a finished product.

In the case of route-to-route extrapolation, the respective bioavailability via each route should ideally be taken into consideration. The assumption of 100 % oral bioavailability might overestimate the systemic exposure in a toxicity study via the oral route. Therefore, in the absence of data, it should be assumed that not more than 50 % of an orally administered dose is systemically available. If there is evidence to suggest poor oral bioavailability, for example if the substance is a poorly soluble particulate, it may be more appropriate to assume that only 10 % of the administered dose is systemically available[39]. Whenever oral absorption data are available, these should be included in the calculations.

The NOAEL chosen for calculating the margin of safety is taken from long-term repeated dose toxicity studies (sub-acute, sub-chronic, and/or chronic toxicity tests, carcinogenesis tests, teratogenesis tests, reproduction toxicity, etc.).

The value used will be the lowest NOAEL obtained by the most pertinent study with respect to the conditions of use of the substance, to species sensitivity, etc.

From the complete toxicological profile, a NOAEL should be determined for the systemic effects. In general, the lowest relevant NOAEL of the most relevant endpoint is selected for calculating the margin of safety.

The calculation of the margin of safety based only on Median Lethal Dose (LD50) data derived from single dose tests (instead of a NOAEL from at least sub-acute tests) cannot be used to justify safe use.

When the absence of bioavailability can be clearly demonstrated, the calculation of the margin of safety is not necessary. In these cases the possible local effects on skin or mucous membranes should still be considered.

3.8.5. Impact on the toxicological profile of certain characteristics of the substances or the product

(a) Particle size

The particle size and its distribution curve can have an influence on the toxicity of a substance. When it cannot be excluded that they have an impact on the safety of the finished product, they should be included among its physico-chemical characteristics, and be taken into account during the safety assessment. The most recent scientific opinions on the subject should be followed (SCENIHR, SCCS)[40].

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39 IGHRC, Guidelines on route-to-route extrapolation of toxicity data when assessing health risks of chemicals. The Interdepartmental Group on Health Risks from Chemicals (2006), http://www.silsoe.cranfield.ac.uk/ieh/ighrc/ighrc.html

40 See for example: SCCS (Scientific Committee on Consumer Safety), Guidance on safety assessment of nanomaterials in cosmetics, SCCS/1484/12; SCENIHR (Scientific Committee on Emerging and Newly

(b) Impurities in the substances and raw materials

Impurities can have a major impact on the overall toxicity of any substance. It is important to check the impurities profile of a substance to avoid, or at least assess, any additional risk from the impurities. In the absence of safety data from toxicological studies, the threshold of toxicological concern (TTC)[41] might be a useful tool for assessing the safety of certain impurities.

When toxicological studies are used to characterise the toxicological profile of a substance, the purity and impurities profile of the substance used in the toxicological studies should be described. If the batches actually used in the formulation of the cosmetic product do not have a comparable impurity profile, the differences need to be assessed.

3.8.6. Use of read-across should be substantiated and justified

Several approaches exist for the read-across technique. The use of this technique should be substantiated and justified.

3.8.7. Identification of the sources of information

The determination of the toxicological profile requires a minimum of information on the substance to be evaluated.

This information can be collected from toxicological studies. If data from human experience exist, they should be taken into account.

Other tools such as quantitative structure-activity relationship (QSAR) or bridging approaches are only estimations of toxicity, and the weight of evidence should be substantiated and justified.

The following sources of data should be taken into consideration:

(a) Safety and quality data which may be on file with the respective suppliers of the raw materials in the formulation, and which the supplier should share with the manufacturer of the cosmetic product. This is an important element in considering the availability of relevant data to demonstrate the safety of each cosmetic ingredient in the final product formulation;

(b) If an opinion of the SCCS exists, the NOAEL used in the opinion should be used. The safety assessor should take into account the most up-to-date scientific opinion;

(c) If an opinion of another authoritative scientific committee exists, the NOAEL used in the opinion could be used, provided that the conclusions and limitations are applicable to the expected use (the use taken into account for calculating the margin of safety can be different). The safety assessor should take into account the most up-to-date scientific opinion;

Identified Health Risks), Opinion on the scientific basis for the definition of the term “nanomaterial”, 8 December 2010.

[41] R. Kroes, A. G. Renwick, V. Feron, C. L. Galli, M. Gibney, H. Greim, R. H. Guy, J. C. Lhuguenot, J. J. M. van de Sandt, *Application of the threshold of toxicological concern (TTC) to the safety evaluation of cosmetic ingredients*, Food and Chemical Toxicology 45 (2007), pp. 2533–2562.

(d) If no scientific opinion exists, it will be necessary to provide information to characterise the toxicological profile of each substance. The data can be obtained from several databases or literature (see Appendix I);[42]

(e) Classification under Regulation (EC) No 1272/2008 of the European Parliament and of the Council;[43]

(f) Studies performed or obtained by the manufacturer of the product;

(g) *In silico* prediction (QSAR);

(h) Bridging approach;

(i) Assessments of non-cosmetic uses of the substance (foodstuffs, food additive, food contact materials, biocides, Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH)…) may also be used in order to complete information on the toxicological profile of the substance.

(j) When available, the CSR (Chemical Safety Report) or the robust study summaries submitted pursuant to Regulation (EC) No 1907/2006 (REACH).

A number of substances and/or mixtures have not been studied sufficiently to determine all the pertinent toxicological parameters. For these missing parameters, or where the risk characterisation is based on an approach using toxicological data acquired for other substances (for example similar structures) or for uses other than cosmetics (food, biocides, pharmaceutical products, *etc.*), justifications should be included in the report.

3.9. Undesirable effects and serious undesirable effects

The aim of that section of the cosmetic product safety report is to monitor the safety of the product after it has been placed on the market and to take corrective action, where necessary. To this end, the responsible person (in collaboration with the distributors) is required to set up a system to collect, document, establish the causality of and manage the undesirable effects caused by the product after its use in the Union[44]. When the undesirable effects are serious, the responsible person (and the distributors) are to notify the competent authority of the Member State where the effects occurred[45].

Information on undesirable effects and serious undesirable effects is to be included in the cosmetic product safety report, kept up-to-date and made available to the safety assessor, who may revise their assessment or take the information into account when assessing similar products.

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42 Several publicly available databases containing toxicological data on substances used in cosmetics exist, and are listed in Appendix I to this Guideline.

43 OJ L 353, 31.12.2008, p. 1, and ECHA's registration website: http://apps.echa.europa.eu/registered/registered-sub.aspx.

44 This is a consequence of the requirement of Article 23 of Regulation (EC) No 1223/2009, which establishes the obligation for responsible persons to notify serious undesirable effects to competent authorities in the EU Member States.

45 Article 23 of Regulation (EC) No 1223/2009.

The cosmetic product safety report is to include all the available data, including statistical data, on the undesirable effects and serious undesirable effects of the cosmetic product or, where relevant, other cosmetic products.

In particular, information on **undesirable effects** which, according to the causality assessment, are found to be very likely, likely, not clearly attributable or unlikely to be attributable[46] to the cosmetic product in question are to be included in the safety report.

Data on undesirable effects may be included in this part of the safety report in the form of statistical data such as the number and type of undesirable effects per year.

Information on **serious undesirable effects** which, according to the causality assessment, are found to be very likely, likely, not clearly attributable or unlikely to be attributable to the cosmetic product in question are to be included in the safety report in accordance with section 9 of Part A of Annex I to Regulation (EC) No 1223/2009, and notified to the national competent authorities, in accordance with Article 23 of the same Regulation[47]. The notification forms sent to the competent authorities are therefore to be attached to the cosmetic product safety report.

The responsible person's reaction to and handling of the reported serious undesirable effects is to be stated. The corrective and preventive measures taken, if any, should be described.

The information on undesirable effects is to be kept up-to-date and regularly made available to the safety assessor[48], who may consider it necessary to revise the safety assessment, suggest improvements to the formulation or use the information to establish the safety assessment for similar products.

Additional cosmetovigilance data, such as serious undesirable effects of a non-intended use may also provide helpful information that the safety assessor should consider.

3.10. Information on the cosmetic product

That section of the cosmetic product safety report allows the inclusion of any additional information which is not covered under the other headings of Part A of Annex I to Regulation (EC) No 1223/2009, but is considered relevant in order to carry out the safety assessment of the product.

This section of the cosmetic product safety report should contain other relevant information, either relating to the product or similar formulations, such as existing studies on human volunteers, or relating to specific substances, such as the duly confirmed and substantiated findings of risk assessments carried out in other relevant areas.

This section could be used to refer to information on substances or mixtures also used in other kinds of products, such as food and pharmaceuticals.

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46 For undesirable effects that are very likely or likely to be attributable to the cosmetic product, Article 21 of Regulation (EC) No 1223/2009, 'Access to information for the public', applies.

47 European Commission, Serious Undesirable Effects (SUE) Reporting Guidelines, http://ec.europa.eu/consumers/sectors/cosmetics/files/pdf/sue_reporting_guidelines_en.pdf

48 This is an obligation of the responsible person according to article 10(1)(c) of Regulation (EC) No 1223/2009.

4. PART B OF ANNEX I TO REGULATION (EC) NO 1223/2009 — COSMETIC PRODUCT SAFETY ASSESSMENT

Part B of the report is the actual assessment of the safety of the product. In their reasoning, the safety assessor is required to take into account all the hazards identified for the product and the exposure to it.

Part B of the cosmetic product safety report comprises:

(1) The assessment conclusion;

(2) The labelled warnings and instructions of use;

(3) The reasoning;

(4) The credentials of the safety assessor and their final approval.

4.1. Assessment conclusion

The assessment conclusion is a statement on the safety of the cosmetic product in relation to the safety requirement of Article 3 of Regulation (EC) No 1223/2009.

The conclusion should state whether the product is safe, safe with restrictions or not safe for human health when used under normal or reasonably foreseeable conditions of use.

The legal framework for the assessment should be explicitly mentioned, in particular Regulation (EC) No 1223/2009 on cosmetic products (Official Journal L 342, 22 December 2009, pp. 59–209).

If the product has been assessed as not safe, it cannot be considered to comply with Regulation (EC) No 1223/2009 and therefore is not to be placed on the market.

4.2. Labelled warnings and instructions of use

The aim of that section of the cosmetic product safety report is to explicitly list the particular precautions to be observed in use, including at least those listed in Annexes III to VI to Regulation (EC) No 1223/2009 and any special precautionary information on cosmetic products for professional use, which should appear on the labelling.

In accordance with Annex I to Regulation (EC) No 1223/2009, this section is to be a statement regarding the need to label any particular warnings and instructions of use in accordance with Article 19(1)(d) of Regulation (EC) No 1223/2009.

It is the task of the safety assessor to determine which warnings or instructions of use, in addition to those listed in Annexes III to VI, need to be labelled to ensure the safe use of the product.

The safety assessor should decide what is to appear on the labelling on a case-by-case basis, taking into account the legal obligations deriving from Article 19 and the Annexes to Regulation (EC) No

1223/2009 and, where relevant, instruments such as Commission Recommendation 2006/647/EC[49] and other guidelines published by the Commission such as those on the 'period of time after opening' labelling[50] and the labelling of ingredients under Directive 76/768/EEC[51].

4.3. Reasoning

The reasoning is the core of the safety assessment, as its aim is to clearly and accurately explain how the safety assessor reaches his or her conclusions on the safety of the cosmetic product from the data gathered under Part A of Annex I to Regulation (EC) No 1223/2009.

The safety assessment is to be performed on a case-by-case basis for each individual cosmetic product and be the result of an expert evaluation of the available data. The safety assessor should ensure that all the information (s)he needs to carry out a safety assessment is available; (s)he should check the relevance of the data provided on the product to be assessed; and (s)he should justify the absence of data required under Part A, when (s)he considers they are not relevant or necessary.

In order to draw conclusions on the safety of a cosmetic product, the safety assessor is required to evaluate the safety of the individual substances or mixtures present in the formulation and the safety of the finished product. His/her conclusions are to be based on a body of evidence showing that, for all the hazards identified, the product can be considered safe in terms of human health.

The safety assessor may accept, reject, or accept under specific conditions the formulation under consideration. A product that does not comply with Regulation 1223/2009 is to be rejected and not marketed.

The reasoning for the safety assessment sets out the considerations that lead the safety assessor, based on all available safety-related information, to an overall conclusion on the safety of a product.

In their reasoning, the safety assessor is required to take into account all the hazards identified, the intended and reasonably foreseeable exposure conditions of the individual substances or mixtures present in the formulation and of the finished cosmetic product.

Analysis and evaluation of the validity/reliability of all existing information is the task of the safety assessor. By conducting this analysis, the safety assessor is able to decide whether the available data are sufficient to perform a safety assessment or whether additional data need to be obtained on an individual substance or the finished cosmetic product.

The reasoning is based on the data compiled in Part A of the cosmetic product safety report and takes into account the safety evaluation of substances and mixtures, carried out by the Scientific Committee for Consumer Safety when the substances appear in the Annexes to Regulation (EC) No

[49] OJ L 265, 26.09.2006, p. 39.

[50] Available on http://ec.europa.eu/consumers/sectors/cosmetics/documents/guidelines/labelling/index_en.htm.

[51] Available on http://ec.europa.eu/consumers/sectors/cosmetics/files/doc/guide_labelling200802_en.pdf.

1223/2009, by other competent scientific committees or panels, or by the safety assessor him/herself, and the safety evaluation of the cosmetic product.

4.3.1. Safety Evaluation of Substances and /or Mixtures

The safety evaluation of substances and/or mixtures consists of three main steps:

(1) hazard characterisation of substances and mixtures;

(2) assessment of the local and systemic exposure (considering absorption data);

(3) risk assessment of systemic effects (calculation of margin of safety) and risk assessment of local effects (such as skin allergy, skin irritation).

For fragrance and flavour compounds, where information on their composition is confidential, a safety assessment may be provided to the responsible person for the finished cosmetic product by the manufacturer of that mixture. Taking into account the concentration in the final cosmetic product and its exposure pattern, the safety assessment of the fragrance and flavour compound should be prepared following the principles described in Annex I to Regulation (EC) No 1223/2009 and these guidelines. An appropriate document demonstrating the safety of the fragrance or flavour compound should be provided by the supplier to the responsible person for the finished cosmetic product.

4.3.2. Safety Evaluation of the Cosmetic Product

The safety evaluation of the cosmetic product covers three main aspects:

(1) Summary of the risk assessment based on the local and systemic effects of all individual substances/mixtures[52];

(2) Additional assessment of the safety of the formulated product, which cannot be assessed by assessing the substances/mixtures separately. This could for instance be the formulation's skin compatibility, assessment of possible combination effects, such as one ingredient that can increase the absorption rate of another ingredient, possible effects that could arise from interaction with packaging material, or possible effects due to chemical reactions between the individual substances/mixtures in the formulated product[53];

(3) Other factors that influence the safety assessment, such as stability, microbiological quality, packaging, and labelling, including use instructions and precautions for use.

The specific assessment for cosmetic products intended for use on children under the age of three which is required in accordance with Regulation (EC) No 1223/2009 should take into account the specific recommendations in the SCCS Notes of Guidance.[54]

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52 For products in the same range, where the only difference among different products is the colouring agent, and that has no impact on safety, e.g. for lipsticks or other colour make-up, a combined product safety report may be considered (so-called omnibus procedure), but is to be justified.

53 SCCS, SCHER, SCENIHR, Toxicity and Assessment of Chemical Mixtures, 2012 http://ec.europa.eu/health/scientific_committees/environmental_risks/docs/scher_o_155.pdf

54 SCCS Notes of Guidance, para 3-7.3, p. 51.

In the specific assessment required in accordance with Regulation (EC) No 1223/2009 for cosmetic products intended exclusively for use in external intimate hygiene, the particular characteristics of the application site also are to be taken into account.

The safety assessor may accept, reject, or accept under specific conditions the formulation under consideration. A product that does not comply with Regulation (EC) No 1223/2009 is to be rejected and is not be marketed. Recommendations by the safety assessor regarding the safe use of the product should be followed.

In order to ensure that the cosmetic product safety report is kept up to date as required by Article 10(1)(c) of Regulation (EC) No 1223/2009, the safety of the finished product should be reassessed regularly.

When changes in the legal requirements occur (e.g. restrictions of one of the substances included in the formulation), it should be checked, amongst others (e.g. labelling), whether the formulation still complies with the law, and the safety assessment should be reviewed and, if necessary, updated.

The safety assessment should also be reviewed and, if necessary, updated, where one or more of the following circumstances apply:

(a) new scientific findings and toxicological data on the substances are available which could modify the result of the existing safety assessment;

(b) changes occurring in the formulation or specifications of raw materials;

(c) changes occurring in the conditions of use;

(d) a rising trend in terms of the nature, severity and frequency of undesirable effects, both under reasonably foreseeable conditions of use and in the case of misuse[55]

Structures and processes should be established to ensure that the information relevant for the update of the cosmetic product safety report is efficiently exchanged between the responsible person and the safety assessor, and that the safety assessor is in a position to intervene where an update is necessary.

4.4. Assessor's credentials and approval of Part B

The safety assessor is to be a professional with the necessary knowledge and expertise to draw up an accurate safety assessment, as indicated by the qualification requirements in Article 10(2) of Regulation (EC) No 1223/2009. That section of the cosmetic product safety report aims at ensuring that this requirement is met and that the necessary evidence is provided.

That section of the safety report is required to list the name and address of the safety assessor and to be dated and signed.

[55] European Commission, Serious Undesirable Effects (SUE) Reporting Guidelines, http://ec.europa.eu/consumers/sectors/cosmetics/files/pdf/sue_reporting_guidelines_en.pdf.

The result of the safety assessment is to be signed stating the date of preparation or be issued based on an electronic release establishing a clear relationship between the assessor, the formulation and the date of assessment. The electronic version should be protected from abuse by unauthorised persons.

In accordance with Article 10(2) of Regulation (EC) No 1223/2009, the safety assessor is required to be *'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'*.

A person who has obtained qualifications in a third country may act as a safety assessor if they have completed *'a course recognised as equivalent [to a university course of theoretical and practical study in pharmacy, toxicology, medicine or a similar discipline] by a Member State'*.

Proof is to be provided of the safety assessor's qualification (i.e. copy of the diploma and, where needed, proof of equivalence) laid down in Article 10 of Regulation (EC) No 1223/2009.

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Appendix I – Known Databases Containing Toxicological Data on Substances Used in Cosmetics

ChemIDPlus Light — http://chem.sis.nlm.nih.gov/chemidplus/chemidlite.jsp

ChemIDPlus Advanced — http://chem.sis.nlm.nih.gov/chemidplus/

COLIPA Recommendations — http://www.colipa.eu/publications-colipa-the-european-cosmetic-cosmetics-association/recommendations.html

IPCS Inchem — http://www.inchem.org/pages/jecfa.html

PubMed — http://www.ncbi.nlm.nih.gov/pubmed

ToxNet — http://toxnet.nlm.nih.gov/