

We are pleased to be able to give the following comments on the proposed simplification of Cosmetics Directive 76/768 EEC.

Item 4 considered by the Commission and submitted for public consultation: Which terms would need to be included in a set of definitions in order to make the Cosmetics Directive clearer?

1. Definition of fragrance-free

Enhancing the transparency vis-à-vis consumers and professionals by ingredient labelling of fragrance allergens in cosmetics is an important move to increase consumer safety. The labelling will permit the consumer with a diagnosed fragrance allergy to avoid contact with a particular allergen.

However, confusion may arise for products which are developed to be fragrance-free but contain any one of the identified 26 fragrance materials (FM26). One obvious conflict is concerns benzyl alcohol, which is a commonly used preservative and also belongs to Annex III.

Current discussions in Denmark and Sweden between regulatory authorities and trade-organisations may result in a prohibition of labelling products as “fragrance-free” if they contain benzyl alcohol as preservative but otherwise contain no “parfum”. However, we found it misleading to label the product as fragranced, since the use of benzyl alcohol as preservative at a maximum concentration of 1% does not give a perfumery scent to the product. It is obvious that consumers would like to know whether a product is fragranced or not before they decide upon a potential purchase.

The two most apparent solutions to this inconvenient conflict are:

- Remove benzyl alcohol from the FM26 list, since this substance belongs to Annex III. This is further supported by its weak, or almost absent odour, when used alone in concentrations up to 1%. Furthermore, benzyl alcohol is used at higher concentrations in topical pharmaceuticals, without these products being considered as fragranced. A worst-case scenario from this pathway is that individuals with a known sensitivity to benzyl alcohol expose themselves to fragranced products containing benzyl alcohol in the added fragrance, but without benzyl alcohol being labelled due to its removal from the FM26-list. The likelihood that this may happen is unknown, but can be considered as very rare for two reasons: a) benzyl alcohol may not be able to elicit eczema in the concentrations found in fragrances, and b) individuals sensitized to benzyl alcohol may also have a concomitant allergy to fragrances and abstain from using cosmetics containing “parfum”.
- Acknowledge the possibility of using benzyl alcohol as preservative without considering it misleading to market such products as “fragrance-free”. This action would allow patients with a diagnosed allergy to benzyl alcohol to avoid fragranced products containing the preservative in the added “parfum”. However, the likelihood that this approach will serve as a prejudice for the other FM26 has to be considered; It is possible that several of the other listed ingredients are found in botanicals, which are used in cosmetics for other purpose than perfuming them. Therefore, from this perspective it

would make sense to prohibit labelling of cosmetics containing e.g. botanicals with the other known fragrance allergens as “fragrance-free”. (Furthermore, it could be argued that their content of any of the FM26 also should appear in the ingredient listing according to the same rules as for “parfum”-ingredients, but this is another discussion).

In summary, consumers should be able to make an informed choice in the selection of fragrance or fragrance-free products. Moreover, consumers with a known fragrance allergy should ideally know which fragrance-allergens to avoid and identify products containing these ingredients. Furthermore, it should be remembered that if the future definition of fragrances also will include substances which are used in cosmetics mainly for other purposes, then it may be impossible to provide consumers with “fragrance-free” cosmetics. Benzyl alcohol is one important substance which should be allowed in “fragrance-free” cosmetics. Other examples, which currently do not belong to the FM26 list, are solvents and solubilisers, which do not provide any particular odour to the product, but may indeed have resulted in case reports of contact allergy (e.g. isopropyl myristate, alcohol).

In conclusion, removal of the preservative benzyl alcohol from the FM26 list would be the most appropriate step to reduce misleading information to the consumers and at the same time facilitate the possibility for consumers to use “fragrance-free” products.

2. Definition of “Actives”

Product claims and ingredients in topical formulations result in different regulatory procedures. The category ‘cosmetic product’, as defined in the EU Cosmetics Directive (76/768/EEC) has borders with a range of product categories, including medicinal products, biocides and medical devices.

The new European medicinal legislation defines a medicinal product either by virtue of its “presentation” or its “function”.¹ Thus, any substance or combination of substances presented for treating or preventing disease in human beings are considered a medicinal product. Furthermore, products which are used in or administered to human beings with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action are also covered by the Medicinal Products Directive, (i.e. definition by virtue of function).¹ These terms can be defined according to the following:²

- **“Pharmacological action”**: interaction between the molecules of the substance in question and a cellular constituent usually referred to as a receptor, which either results in a direct response, or which blocks the response to another agent. Although not a completely reliable criterion, the presence of a dose-response correlation is indicative of a pharmacological effect.
- **“Immunological action”**: action in or on the body by stimulation and/or mobilisation of cells and/or products involved in a specific immune reaction.

¹ Eudralex. <http://europeaeu/enterprise/pharmaceuticals/eudralex/homev1.htm#Regulations>

² EC. MEDEV guidance document 2. 1/3 rev 2 July 2001, page 3:.

http://europeauint/comm/enterprise/medical_devices/meddev/2_1_3_07-2001pdf

- **“Metabolic action”**: action which involves an alteration, including stopping, starting or changing the speed of the normal chemical processes participating in, and available for, normal body function. The fact that a product is metabolised *by* the human body does not necessarily mean that the substance contained in the product has a metabolic action *upon* the body.

Thus, making the wrong claims or including ingredients in topical products that significantly modify the physiological functions of the skin can result in a medical classification of cosmetics and hence the need to comply with the medicinal products regime, e.g. more rigorous safety documentation in order to protect public health. It is for the national competent authorities and national courts to assess on a case-by-case basis which regulatory framework that applies for a certain formulation, based upon the composition and the physiological properties of the product and the risk which its use may entail.

It is obvious that most of the adverse effects induced by cosmetics (e.g. contact allergy) arise from a physiological effect on the skin, for example immunological changes induced by contact allergens, such as preservatives and fragrances. However, it does not make sense to classify such preparations as medicines. However, when the effects from “actives” in the formulations are linked to physiological actions in the skin, then it would make sense to consider the formulations as medicines. Therefore, a clear definition of “actives” is required. Some examples from the marketing of botanicals as ingredients are given below.

Examples of botanicals marketed to be used in anti-wrinkle creams³.

International Nomenclature Cosmetic Ingredient (INCI) name	Claimed properties
<i>Aemella oleracea</i> extract	From tropical plants. Ideal in wrinkle care dedicated to expression line smoothing. The ingredient limits microcontraction that aggravates facial wrinkles.
<i>Argania spinosa</i> kernel extract	Proteic fraction of Argan seeds, recommended for the use in antiaging care for its antiwrinkle and tightening properties.
<i>Curcuma longa</i> (tumeric) root extract	Skin lightening via inhibition of tyrosinase for antiaging products.
Dihydromyricetin	Acts on lipid metabolism and differentiation processes of adipocytes. Promotes lipolysis by selective inhibition of tyrosine kinase activity of the β -receptor subunit.
<i>Euglena gracilis</i> extract	Cell energizer which helps skin to recover its firmness and tone by triggering cell metabolism and stimulating calcium release.
<i>Garcinia cambogia</i> fruit extract	Garcinol inhibits skin glycation that leads to reduced suppleness, inflammation and injury to the extracellular matrix.
Hydrolyzed <i>Cucurbita pepo</i> (pumpkin) seed cake	The ingredient smoothes the skin and evens skin tone by controlling the protease activity and stimulating the extracellular matrix constitutive fibers.
Hydrolyzed <i>Opuntia ficus indica</i> flower extract	Stimulates the activity of skin enzymes involved in the exfoliation process. It favours cell renewal and reduces lines and wrinkles.
<i>Magnolia officinalis</i> bark extract	Potent anti-inflammatory used to reduce dark areas around eyes.
<i>Melia azadirachta</i> leaf extract	Whitens/brightens skin by decreasing the rate of melanin production.
Palmitoyl hydrolyzed wheat protein	Quick mechanical action to smooth out expression lines and a long-term biological effect to re-densify skin and fill deep wrinkles.

³ Naturals encyclopedia. Cosmet Toilet. 2006;121(2):75-89.

3. Others

The expressions “organic”, “naturals”, “preservative-free” should benefit from an agreed definition.

Item 5 considered by the Commission and submitted for public consultation: Do you agree that objective criteria should apply for defining groups of substances, independent of the purpose for which a substance was added to a cosmetic product?

Objective criteria should possibly rely on biologic activity rather than function. I.e. the preservatives used today are active at low concentrations, whereas a re-definition of preservatives into any substance which prevent microbial growth would classify ingredients, such as alcohol, glycerol, acids, and at very high concentrations also fats etc, as preservatives. This does not make sense. Hence, the potency has to be taken into account.

Item 6 considered by the Commission and submitted for public consultation: An alternative approach could be to establish a single list of all regulated substances. With regard to positive lists, it could be specified that substances with specific properties (e.g. anti-microbial, colouring, UVabsorbing or UV-reflecting, etc.) have to be listed in the annex before they can be used as an ingredient in cosmetics.

Would this approach be preferable? Can you see any difficulties which this approach would pose? What would be the impact on the safety of the products containing these substances? What would be the socio-economic impacts of this envisaged change? Are there alternative approaches to consider?

A single list would be desirable. This list could possible be linked to the claimed “activity” and/or inherent toxicity of the ingredients.

Item 9 considered by the Commission and submitted for public consultation: The Cosmetics Directive could specify more clearly the information to be made available in the product information file requested via in-market controls to prove the safety of the product. The extent and content of the information required could be based on:

- the SCCP guidelines for safety evaluation of cosmetic ingredients; and/or
- the “technical dossier” and “chemical safety report” requirements in the REACH Regulation 1907/2006 as far as human health risks are concerned.¹⁶

Which concrete information (including safety data) would the product information file need to contain to allow for more efficient in-market controls of the safety of the products/their substances? How does this information compare with what is usually available in product information files today? Would this mean an increase in information as compared to today? What would be the socio-economic impacts of these envisaged changes?

The forthcoming REACH regulation aims at ensuring a high level of chemicals safety to protect human health and the environment. However, REACH is considered to have limited impact on the availability of toxicological data for substances used in cosmetics, since animal testing will be phased out and, perhaps more importantly, less toxicological data are needed on low-volume chemicals in Europe. The limited data requirements on low-volume chemicals may influence the toxicological data on “actives” in cosmetics, since no tests at all are required for production volumes below 1 ton, which is actually a change for the worse as the previous limit was 100 kg. This change in limit is aims at facilitate the innovation and competitiveness of the EU chemical

industry. Toxicological test programs may be too resource demanding for small and medium sized enterprises. Furthermore, for production volumes of 1-10 tons, the only test required that may give some indication of a potential of carcinogenic, mutagenic or reproductive effect (CMR) is a mutagenicity test in bacteria. Mutagenicity test is insufficient for a proper toxicological evaluation of the potential for substances to be classified as CMR-compounds. CMR-compounds is prohibited in cosmetics, but this does not trigger any additional toxicological studies, not even for substances to be included in the annexes to the Cosmetics Directive. Hence, it remains the responsibility of the safety assessor at the cosmetic company to justify whether enough information on the ingredients, the finished product and the exposure is available for the safety evaluation. This is a rather difficult situation, as in most cases it can be argued that more information is needed to be able to make a reliable evaluation. Particularly the evaluation of complex mixtures such as botanicals is very difficult, as they often contain numerous of more or less defined substances, and as the content may vary with the production method, the part of the plant used, growing conditions, time of harvest etc.

Item 11 considered by the Commission and submitted for public consultation:

The Cosmetics Directive could include a mandate for the Commission to assist in coordinating cooperation between the Member States in the field of “cosmetovigilance”.

What is your view on this? How would this information flow need to be organized to ensure an efficient surveillance of the safety of the products? What would be the socio-economic impact?

Pharmacovigilance has been in place for long, whereas cosmetovigilance still is in its infancy. An efficient post-marketing system is therefore timely, where the consumers and professionals’ awareness of potential disadvantages of cosmetic products are elicited. Most of the adverse reactions are not reported and recorded in a standardised way. Currently, the quality of collected data is poor, due to insufficient involvement of the industry, dermatologists and the affected consumer. As the cosmetic industry is global, the multinational companies have the possibility to collect data from a very large number of exposed persons, giving the basis for extensive epidemiological studies and/or early indications of potential side effects. The industry are also obliged to collect complaints and inform customers upon their request on undesirable effects that have been reported to them by other customers. Furthermore, consumer associations should encourage, by any appropriate means, those consumers who notice an undesired reaction to consult a health professional or to report to the competent authorities or at least to the person responsible for placing the product on the market. The establishment of national networks of health professionals which test and report to health authorities in a standardised procedure should also be encouraged. Harmonisation in handling of undesirable effects and proper aggregation of data would significantly enhance the quality of the collected information.

For some biological endpoints reflecting acute problems, this seems a simple strategy. A more challenging problem would be the time gap from exposure to appearance of adverse effect for some endpoints, such as cancer, which would require more complicated but nevertheless important follow-up analyses. Risk management might prioritise cosmetics marketed for their stimulating and cell-renewal activities.

Making such information along with the quantitative composition publicly available should allow a more efficient assessment of the substances with insufficient toxicological data.

Evidence regarding the claimed effects, as well as of the safety assessment of the cosmetics, could be published at the company website, or being administered by some other independent organisation or regulatory authority. . Efficient post-marketing surveillance activities focusing on undesirable effects, their analyses, evaluation and dissemination of the conclusions and follow-up measures would be an essential move for the cosmetic industry and its stakeholders.

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ACO Hud Nordic AB is a small dermatological company with its main business within cosmetics and topical pharmaceuticals. Geographical area is the Nordic countries, i.e. Sweden, Norway, Finland and Denmark. The number of employees is about 90, with an approximate turnover of Euro 50 million,