
INTRODUCTION
On 11 March 2005 Directive 2003/15/EC (1), an amendment to Directive 76/768/EEC on Cosmetic Products (2) (hereinafter CP) entered into its application phase. The Directive introduces, *iter alia*, restrictions on the use of 24 fragrance ingredients and 2 natural materials in CP (3). The Directive requires, by way of derogation from the current exemption from the general labelling requirements, that the presence of these allergens in the final CP above a certain concentration level be indicated in the ingredient label there of.

There does not seem to be agreement among safety assessors on the effects and implications of the newly introduced restrictions on the safety assessment of CP, a prerequisite for the placing on the Community market of CP. The view has been expressed that the new restrictions require a reduction in the concentration of the fragrance ingredients concerned to a level considered to be safe for fragrance sensitive consumers (4) and CP with higher concentration levels have been rejected on safety grounds.

The use restrictions of Directive 2003/15/EC have to be interpreted in the light of the general principles governing the safety of CP laid down by Directive 76/768/EEC. After an analysis of the regime established by Directive 76/768/EEC, this article will discuss the effects and the practical implications of the restrictions introduced by Directive 2003/15/EC for the safety assessment of CP.

DIRECTIVE 76/768/EEC
Directive 76/768/EEC provides that, CP put on the market must not cause damage to human health when applied under normal or reasonably foreseeable conditions of use and places responsibility for the safety of CP on industry. The Directive mainly addresses “chemical risks” and requires that the safety assessment of the safety has to be conducted on the basis of the general toxicological profile of the ingredients, their chemical structure and their level of exposure.

The general safety requirement is complemented by specific prohibitions and restrictions on the use of certain substances in CP, which are listed in Annex I and III part I respectively and which address risks for one of more specific endpoints. Compliance thereof does not necessarily ensure that the product is safe with regard to unaddressed endpoints or risks highlighted by new available scientific evidence. In this regard, the general safety clause requires industry to continuously monitor the advances of scientific knowledge and the after market use of the CP, and to take risk management measures necessary to address new risks.

The safety assessment must be based on information on full product composition. A list of the ingredients in descending order must also be included in the label of the finished CP (5). This does not apply to perfume compositions and perfumes (fragrance compounds), which, for reasons related to protection of trade secret and intellectual property must be indicated by the name and code of the composition instead of listing the individual ingredients. This exemption does not nevertheless release the manufacturer and/or the safety assessor of the finished CP from the obligation to carry out a safety assessment, which means that appropriate information on the composition of the fragrance compound needs to be made available to him. In order to protect the confidentiality of commercially sensitive information, an assessment of the safety of perfume compositions in the finished products is carried out upstream by fragrance suppliers and a certificate of conformity with International Fragrance Association (IFRA) Guidelines (6) usually accompanies the fragrance compounds, along with safety information on problematic substances, when so recommended. The Directive does not specify whether this certificate and other IFRA safety information can be used as a basis for the safety
assessment of the finished cosmetic products. National implementing legislation and official guidance documents (7) seems to acknowledge the validity of this practice and so does to a certain extent the SCCP (8). It remains nevertheless the responsibility of the manufacturer of the finished CP and of the safety assessor to decide whether to rely on information supplied by fragrance suppliers (9).

The potential toxicity of cosmetic ingredients is commonly evaluated against the classification criteria laid down by Directive 67/548/EEC on dangerous substances. These cover a wide range of endpoints. However, for most of the CP, only skin sensitisation, irritancy and phototoxicity potential is relevant for the safety assessment.

Sensitising substances have the inherent capacity to induce long-lasting or permanent hypersensitivity in exposed individuals so that, following re-exposure, an adverse reaction (allergic contact dermatitis) may occur. The dose sufficient for induction is generally larger than the dose sufficient for elicitation (10). This is also reflected in the labelling requirements provided for by Directive 1999/45/EC (11, 12) for preparations containing substances classified as sensitisers.

Due to the absence of sufficiently reliable in-vitro and in-vivo (on animals) predictive methods, the identification of substances with allergic potential has been relying heavily on human data. Although it is generally recognised that a number certain fragrance ingredients of natural origin have a sensitising potential, identification thereof has been mainly based on experimental data rather than clinical data. A review of all relevant human data available was carried out by the SCCNFP in 1998 and a first list of fragrance ingredients identified as having a sensitising potential was finalised in 1999 (13). In view of the risk-based approach underlying Directive 76/768/EEC, the use of sensitising ingredients in CP is allowed to the extent that it is assessed as not being liable to induce sensitisation of healthy individuals. The safe use of the allergens is generally ensured by reducing their concentration in the finished product to a level assessed not to cause sensitisation (14). This approach is not followed with regard to the risks of elicitation of allergic reaction in sensitised individuals, which are either considered as not being relevant for the safety assessment (15) of a CP or as requiring far less stringent risk management measures.

Consumer information on CP composition is generally recognised to contribute to the protection of sensitive consumers in that it enables them to avoid the use of CP containing allergens to which they know they are allergic. The Directive requires that all ingredients be listed on the label of CP, with the exception of fragrance compounds.

It is our opinion that the risks of allergic reactions in fragrance sensitive consumers have to be considered in the safety assessment of CP and that specific risk management measures have to be implemented. As a result, if the concentration level of an allergen in a CP is liable to elicit an allergic reaction, the indication of its presence in the ingredient label constitutes a minimum requirement in a consumer protection perspective. This presupposes that appropriate information on the presence of the allergen in the fragrance compound is communicated by the suppliers to the manufacturer and/or the safety assessor of the finished cosmetic products. Such an approach appears to be in line with the general safety requirement of Directive 76/768. The Directive does not require that a product be intrinsically “chemically” safe and explicitly allows for risk management measures to be implemented in the form of risk communication, which includes information on product composition and instructions for use. A further reduction in the concentration of the allergens would therefore be required for products for which no information relevant is conveyed to the consumer. It has to be noted that the indication of the presence of the allergens in the label can ensure effective protection of individuals who are aware of the ingredients to which they are allergic and that it is not sufficient to avoid the risks of allergies in unaware sensitive individuals. These cannot make use of this information and may therefore be exposed to risks of allergic reaction from use of CP containing allergens. A further indication of the risks associated with the presence allergens, though allowing for a reduction of these risks, does not nevertheless seem to be required by the Directive. Like any act of the Community Institutions, the Directive has to be interpreted in the light of the proportionality principle, according to which measures necessary to protect a public interest, including human health, do not have to go beyond what is necessary to achieve the objective pursued. A further indication of risks of allergic reactions may considerably affect the perception of the product in terms of safety, whose effects are likely to go much beyond what it is necessary to protect sensitive consumers. The CP is safe for the large majority of the consumers and the risk of allergic reactions is not the direct effect of the CP but depends on a pre-existing condition of hypersensitivity to which the CP has not contributed. In addition, allergic reactions are reversible diseases which can be avoided if the conditions allowing for appropriate diagnosis exist. The indication of the allergens in the label, though not ensuring protection of unaware sensitive consumers, facilitates the identification of the allergens to which fragrance sensitive consumers are allergic thereby allowing them to avoid future use of the CP.

It has to be noted that the proportionality principle acts as a limit not only for safety assessors and national enforcement authorities but also for the Community Institutions. As a result, any Community legislative acts addressing the risk of allergic reaction in sensitive consumers cannot go beyond the requirement to include the allergens in the list of ingredients to be affixed in the labelling.

**DIRECTIVE 2003/15/EC**

Directive 2003/15 addresses the risk of elicitation of allergic reactions in sensitive consumers from use in CP of one or more of the 24 fragrance ingredients and 2 natural materials identified by the SCCNFP as having varying degrees of allergenic activity (16). The Directive does not prohibit their use, nor does it impose concentration limits but simply requires that...
their presence in the CP be indicated in the ingredient label if their concentration exceeds 10 ppm in leave-on and 100 ppm in rinse-off CP. The risk of sensitisation in healthy individuals is still subject to a safety evaluation under the general safety requirement, which in most of the cases take the form of a reduction of their concentration levels.

The use of the allergens concerned in concentrations above the threshold in question and below the concentration capable to cause sensitisation is therefore allowed if the labelling requirement is complied with. As a result, neither safety assessor nor enforcement authorities may require risk management measures going beyond indication of the presence of the allergens concerned in the ingredient label. In this regard the risk reduction measures introduced are line with the general regime of the Directive and the proportionality principle. Reducing the concentrations of the allergens therefore remains a simple option for those manufacturers who wish to enhance the safety profile of his CP and/or avail themselves of the possibility of claiming the hypoallergenic character of the CP.

CONCLUSIONS

The restrictions introduced by Directive 2003/15/EC have not resulted in a de facto ban on the use of one or more of the 26 listed allergens in CP. These allergens can still be used if their presence in the CP is indicated in the ingredient label. However, compliance with the above labelling requirement only ensures the safety of the CP with regard to the risk of elicitation of allergic reactions in sensitive consumers, leaving the requirement to take measures addressing the risks of sensitisation unaffected.

REFERENCES AND NOTES

4. Evelyne Prat, “Rhodan’s solutions to enhance performance of home and personal care formulations and better respect health and environment”, H&PC Today, p. 18 (2005). In this article, it is indicated that Directive 2003/15/EC requires the listed fragrance ingredients be incorporated at levels below the indicated thresholds in order to limit the risk of allergy and sensitisation (p. 20, last paragraph).
5. Article 6(g) of Directive 76/768/EEC.
6. The application of these Guidelines and Standards is considered to ensure International Fragrance Association, UK Department of Trade and Industry (Dti), Cosmetic Safety, Guidance on the implementation of the Cosmetic Products (Safety) Regulations 2004, paragraph 125, http://www.dti.gov.uk/ccp/topics1/safetyprods.html#cosmetic
7. SCCNFP, The SCCNFP’s notes of Guidance for the testing of cosmetic ingredients and their safety evaluation, 5th Revision, SCCNFP/0690/03 Final, Section 3-6.3, page 39.
8. There is no a consolidated practice in this sector. Companies and safety assessors either require disclosure of the full composition of the fragrance compounds or simply rely on the IFRA certificate.
11. Preparations must be classified as sensitising and assigned the risk phrase “R43 May cause sensitisation by skin contact” if a sensitising substance is present in the preparations in concentrations ≥ 1%, whereas preparations containing sensitising substances in concentrations >0,1 and ≤1% have to be labelled with the warning phrase “Contains xxx (name of the substance). May cause an allergic reaction”.
14. In certain cases, however, the risk of sensitisation is addressed by alternative risk management measures. For example, according to IFRA Standards, no use concentration limits are recommended for Citral, one of most known sensitisers and for which it is recommended that this ingredient is used in conjunction with substances preventing sensitisation.
15. This opinion seems to underlay the IFRA Standards, which only address the risk of sensitisation, without recommending complementary measures to address the risks for sensitive consumers.
16. See footnote 12