Nam et ipsa scientia potestas est
For knowledge itself is power

Francis Bacon (1561- 1626) Essays

This document, the "***Notes of Guidance for Testing of Cosmetic Ingredients for Their Safety Evaluation***" represents a contribution of the members of the Scientific Committee on Cosmetology (SCC) of the Commission of the European Union dedicated to public authorities as well as to cosmetic industry within the scope of interest in the safety evaluation of cosmetic products and their ingredients, as requested by the Directive 76/768 EEC and especially by the Sixth Amendment (93/35/EEC - OJ L 151 of 23.6.93) to this Directive.

The background of the Third Revision 1999 of the "Notes of Guidance" has been the progress in scientific knowledge in general and especially the experiences developed by the former SCC and the present SCCNFP in the field of cosmetology and risk assessment.

In this context the contribution of valuable information which scientists from industry laboratories and the speaker of manufacturers, the European Cosmetic Toiletry and Perfumery Association (COLIPA), submitted, is gratefully acknowledged.

The "***Notes of Guidance***" should not be used as a check list but could be of assistance for those responsible for consumer health protection, in which position whatever.

This document was drawn up in general terms and will require amendments in the future as scientific knowledge and also technical innovation in the cosmetic sector will advance.

The Chairman

INDEX

1. INTRODUCTION

Council Directive 76/768/EEC of 27 July 1976, as amended by six Directives, imposes, the following rules related to the safety of cosmetic products:

Art 1: "A cosmetic product means any substance or preparation intended for placing into contact with the various parts of the human body (epidermis, hair system, nails, lips and external genital organs) or with the teeth and mucous membranes of the oral cavity with a view exclusively or principally to cleaning them, perfuming them or protecting them, in order to keep them in good condition, change their appearance or correct body odours".

Art. 2: "A cosmetic product put on the market within the Community must not cause damage to human health when applied under normal or reasonably foreseeable conditions of use".

Ingredients are defined as any substances used in cosmetic products. Examples of ingredients are provided by Annexes III, IV, VI, VII to Council Directive 76/768/EEC of 27 July 1976 and its amendments.

Cosmetic products have a history covering thousands of years with the use of many ingredients from plants, animals and mineral sources. Present technology has resulted in the use of many synthetic chemicals as ingredients in cosmetic products .
Present-day use, particularly as toiletries, is extensive and affects most population groups, although the degree and nature may vary within different countries of the European Union.

In practice, cosmetic products have rarely been associated with serious health hazards. However, this does not mean that cosmetics are always safe in use, especially with regard to possible long-term effects. Together with the fact that the products may be used extensively over a large part of the human lifespan, has created a need to ensure, as far as possible, their safety-in-use by controlling the ingredients content and the toxicity.

An original document on "Guidelines for the toxicity testing of cosmetic ingredients" was prepared by the Scientific Committee on Cosmetology in June 1982 (Report EUR 8794).
Two other documents (SPC/803-5/90; XXIV/1878/97) took into account both the experience gained by the SCC-SCCNFP in its past work in evaluating the toxicological profiles of many cosmetic ingredients, as well as the development of scientific knowledge in the field of specific areas of toxicology.

This document - the third revision - takes into account the concept incorporated in the Sixth Amendment (93/35/EEC Directive) to Directive 76/768/EEC and the Commission Directive 97/18/EC of 17th April 1997 (OJ L 114 of 1.5.97) which implies new approaches to improving consumer health protection.
The present notes of guidance (SCCNFP/0119/99) will apply to all cosmetic ingredients for which the producer must perform a safety evaluation to be included in the "*dossier*", as well as new cosmetic ingredients, for inclusion in Annexes IV, VI, and VII of the 76/768/EEC Directive, and to those cosmetic ingredients about which safety concerns have been expressed, bearing in mind their relevant toxicity data already available to the SCCNFP.
These notes of guidance will require further revision in future as scientific knowledge advances.

The relevance of this document also derives from the need to furnish scientific support to the development of the Council Directive 76/768/EEC, represented, at this stage, by its *"Sixth Amendment"* (Council Directive 93/35/EEC of 14 June 1993).

The purpose of this document is to provide guidance for testing cosmetic ingredients and for the safety assessment of the finished product, both to the competent monitoring authorities of the Member States, and to persons responsible for putting cosmetics on the market (manufacturers or importers within the European Union) pursuant to the Sixth Amendment.

These notes of guidance are not a checklist. This means that they can be adapted case by case, depending for instance on the ingredients used, the formulation of the finished product, and the degree and route of consumer application.

2. THE SCIENTIFIC COMMITTEE ON COSMETIC PRODUCTS AND NON-FOOD PRODUCTS INTENDED FOR CONSUMERS

A Scientific Committee on Cosmetology (SCC) was established on 19th December, 1977 by Commission Decision 78/45/EEC (1978): it has assisted the European Commission in examining the complex scientific and technical problems surrounding the drawing up and amendment of European Union rules governing the composition, manufacture, packaging, and labelling of cosmetic products marketed in EU countries.
In 1997 a new scientific Committee, named Scientific Committee on Cosmetic and Non-Food Products intended for consumers (SCCNFP) has been appointed by the Commission Decision of 23 July 1997 (OJ L 237 of 28-8-97); it is composed by 16 members, which are qualified scientists in the fields of medicine, toxicology, biology, chemistry, and other similar disciplines.

The SCCNFP is consulted by the Commission on any scientific or technical problems arising in the connection with cosmetic products, and, in particular, on substances used in the preparation of cosmetic products and the composition and the conditions of use of such products.

The SCCNFP has also been requested to make it possible to perform the safety evaluation of cosmetic ingredients by

1. **analysing the studies presented to the Commission and developed by the cosmetics industry on potentially hazardous cosmetic ingredients;**
2. **evaluating the most recent scientific literature on different toxicological aspects of relevance for the safety evaluation of the cosmetic ingredients;**
3. **requiring in same cases additional safety testing to examine any new potential hazard connected with a particular ingredient, thus making reassessment of its safety possible.**

The opinions adopted by the Scientific Committee at Commission's request were included in EC-Reports (EUR 7297, 8634, 8794, 10305, 11080, 11139, 11303, 14208). Starting from 1997 they are present in Internet*. They mainly refer to cosmetic ingredients included in Annexes II, III, IV, VI and VII of Council Directive 76/768/EEC.

One of the main actions undertaken by the SCC-SCCNFP has been to recommend a set of guidelines to be taken into consideration by the cosmetics industry in developing adequate studies to be used in the safety evaluation of cosmetic ingredients. The SCC has adopted the following opinions concerning the safety evaluation of cosmetic ingredients:

(a) **Notes of Guidance for the toxicity testing of cosmetic ingredients (28 June 1982; EU Report 8794);**

* (http://www.europa.eu.int/comm/dg24/health/sc/ncomm6/index_en.htm)

(b) **Notes of Guidance for testing of cosmetic ingredients for their safety evaluation (SPC/803/5/90);**

(c) **Notes of Guidance for testing of cosmetic ingredients for their safety evaluation (DGXXIV/1878/97).**

These guidelines recommend as test procedures for the toxicity studies needed to evaluate different toxicological endpoints those reported in Commission Directive 87/302/EEC of 18 November 1987(OJ L 133 of 30-5-88) and in Commission Directive 92/69/EEC of 31 July 1992 (OJ L 383 of 29-12-92) adapting to technical progress the Council Directive 67/548/EEC on the approximation of laws, regulations and administrative provisions relating to the classification, packaging and labelling of dangerous substances: they represent the basic toxicity testing procedures internationally accepted as being the result of long-term scientific agreement. These procedures include, at present, 27 studies based on *in vivo* animal models and 10 studies based on *in vitro* models (genotoxicity). Moreover, the SCC when evaluating the information dossiers on several cosmetic ingredients proposed for inclusion in Annexes IV, VI, and VII, has accepted all types of testing procedures based on a scientifically justified model and procedure (for instance, *in vitro* studies on percutaneous penetration), or in accordance with OECD Guidelines.

In response to DGXXIV's request to assess the possibility of replacing data obtained on the basis of animal tests with data obtained making use of alternative methods in the safety evaluation of cosmetic ingredients, the SCCFNP established a Working Group (Subcommittee "Guidelines: Alternative Methods") to follow up validation studies co-ordinated by ECVAM (European Centre for the Validation of Alternative Methods) and by other centres, and to study the applicability of validated alternative methods in toxicity testing to evaluating the safety of cosmetic ingredients.
Moreover a mandate for SCCFNP was defined by the Commission and adopted by the plenary section on 20th May 1998 (DGXXIV/1890/98).

1.1 The SCCNFP shall act as a resource of scientific expertise to the European Commission, with regards to the development of alternative methods. To that effect they will regularly meet with representatives from the concerned parties to :

- give pro-active advice on research proposals and on-going studies
- offer, as appropriate, peer reviews of study data.

However, such advice in no way prejudices the right of the SCCNFP to reject data previously discussed, if the scientific standard of the work is considered inappropriate.

- The SCCNFP shall serve as an expert resource, as appropriate, to those services of the Commission charged with the validation of alternative methods. Specifically, they should offer expert guidance in the design and applicability of test methods, the selection of test materials and communication of results as they apply to cosmetic products.
- The SCCNFP shall, on the request of the appropriate Commission services, review data submitted on in vitro methods that have been assessed and validated by the services of the European Commission, or could be considered appropriate for the replacement of methods using animal testing. The SCCNFP shall give an opinion,

and offer guidance as appropriate, on the applicability of such tests in the evaluation of the safety of cosmetic ingredients and products.

- The SCCNFP should encourage the use of appropriate in vitro methods for use in the safety evaluation of cosmetic ingredients and products. To this end, it shall consider data from in vitro tests that are submitted in support of safety dossiers from the Industry, if the scientific design, justification and data presentation of such studies are considered of an acceptable scientific standard.
- Upon request, the SCCNFP shall advice the European Commission on the status of alternatives to animal testing in cosmetics on an on-going basis and in particularly, in accordance with Article 4, 1(1) of the EU Cosmetic Directive 76/768/EEC.

Although this mandate has been developed in relation to cosmetic ingredients, it is envisaged that scientifically sound non-animal methods for safety assessment will have broad application.

1.2. The SCCNFP was requested moreover to continuously update the Notes of Guidance for Testing of Cosmetic Ingredients for their Safety Evaluation as stated on page 8 of the 2nd Revision, adopted by the former SCC (Scientific Committee on Cosmetology) on January 16th, 1997.

Due to the almost complete review of the former SCC, and the presence in the SCCNFP of experts on other disciplines, it was decided to include technical modifications to the content of the Notes, such as Guidelines for Human Testing, as it seems appropriate to give advice on this new aspects.

During 1998 SCCNFP received another request by the Commission to elaborate an opinion on Clinical Testing of Cosmetic Finished Products to assess Skin Compatibility, taking into consideration the following items:

- ethical and safety consideration of the cosmetic finished products testing on human volunteers when assessing skin compatibility;
- end-points for which such tests are appropriate and the most robust protocol for such studies.

3. THE SIXTH AMENDMENT (COUNCIL DIRECTIVE 93/35/EEC)

Council Directive 93/35/EEC of 14 June 1993 amended for the sixth time Council Directive 76/768/EEC on the approximation of laws of the Member States relating to cosmetic products. Among several amendments, the revised Article 4 banned the marketing of cosmetic ingredients or their combinations tested on animals after 1 January 1998. The Commission Decision 97/18/EC of 17th April 1997 has postponed the ban to the 30th of June 2000 (Table 1).

According to Council Directive 93/35/EEC, Article 2:

"A cosmetic product put on the market within the Community must not cause damage to human health when applied under normal or reasonably foreseeable conditions of use, taking into account, in particular, the product's presentation, its labelling, any instructions for its use and disposal as well as any other indication or information provided by the manufacturer or his authorised agent or by any other person responsible for placing the product on the Community market".

Council Directive 76/768/EEC, as amended by Council Directive 93/35/EEC is designed to protect consumer health from possible deleterious effects due to the presence of specific substances or preparations which harm humans because of their intrinsic unsafe properties.

Several mechanisms have been developed under this Directive in order to fulfil its main requirements regarding consumer health protection, namely:

- list of chemicals which must not be contained in finished products (Annex II);
- list of substances which cosmetic products must not contain except under the restrictions and conditions laid down in Annex III;
- lists of authorised substances, which may include colorants, preservatives and ultraviolet filters (Annexes IV, VI, VII).

The amendment of Art.4, subparagraph (I), is also based on the new recital of the Sixth Amendment which states that:
"...assessment of the safety of use of the ingredients employed in cosmetics and of the final product, should take into account the requirement of Directive 86/609/EEC which concerns the protection of animals used for experimental and other scientific purposes".

Table 1

COUNCIL Directive 76/768/EEC ART. 4
1. WITHOUT PREJUDICE TO THEIR GENERAL OBLIGATIONS DERIVING FROM ARTICLE 2, MEMBER STATES SHALL PROHIBIT THE MARKETING OF COSMETIC PRODUCTS CONTAINING:
a. substances Listed in Annex II;
b. substances listed in the first part of Annex III, beyond the limits and outside the conditions laid down;
c. colouring agents other than those listed in Annex IV, Part I. with the exception of cosmetic products containing colouring agents intended solely to colour hair:
d. colouring agents listed in Annex IV, Part 1, used outside the conditions laid down, with the exception of cosmetic products containing colouring agents intended solely to colour hair;
e. preservatives other than those listed in Annex VI, Part 1;
f. preservatives listed in Annex VI, Part 1, beyond the limits and outside the conditions laid down, unless other concentrations are used for specific purposes apparent from the presentation of the product;
g. UV filters other than those listed in Part 1 of Annex VII;
h. UV filters listed in Part 1 of Annex VII, beyond the limits and outside the conditions laid down therein.
i. ingredients or combinations of ingredients tested on animals after 30 June 2000 in order to meet the requirements of this Directive.

Clearly, the legislator wishes to ban animal trials of cosmetic ingredients or combinations of ingredients whose purpose is to identify the toxicity or evaluate the safety of these specific chemicals or their combinations, only when alternative methodologies are available.

The Sixth Amendment, however, states that "*if there has been insufficient progress in developing satisfactory methods to replace animal testing, and in particular in those cases where alternative methods of testing, despite all reasonable endeavours, have not been scientifically validated, the Commission shall, by 1st January 1997, submit draft measures to postpone the date of implementation of this provision*". This requirement is not in conflict with Art.7 of Council Directive 86/609/EEC on the protection of animals used for experimental and other scientific purposes (OJ L 358 of 18.12.86) which states that "*an experiment shall not be performed, if another scientifically satisfactory method of obtaining the result sought, not entailing the use of an animal, is reasonably and practically available*".

Should it prove impossible to adopt alternative methodologies as a substitute for animal toxicity testing procedures in the safety evaluation of cosmetic ingredients, the Commission, having consulted the Scientific Committee on Cosmetology, will seek to postpone the date of the implementation of such a ban.

Commission Directive 97/18/EC of 17th April 1997 has postponed the date of 1st January 1998 to 30th June 2000 (Art. 1). Article 2 states that " *if there has been insufficient progress in developing satisfactory methods to replace animal testing, and in particular in those cases where alternative methods of testing, despite all reasonable endeavours, have not been scientifically validated ...., the Commission shall, by 1st January 2000, submit draft measures to postpone the date*"

Alternative methodology means any modification to the present toxicity assay protocols, which are internationally and scientifically approved and based on animal models, so as to introduce a different method of conducting the toxicological studies necessary to assess the safety of ingredients used in the manufacture of finished cosmetic products.
Alternative Methods must offer a level of protection to consumers equivalent to that now offered by toxicological studies performed on animals: this means that the alternative methods must be scientifically validated.

A series of other improvements in the safeguarding of public health were introduced in EC cosmetics law with the adoption of the Sixth Amendment (Council Directive 93/35/EEC). These improvements comprise:

(A) the compilation by the Commission, of an inventory of ingredients used in products, in particular on the basis of information supplied by the industry concerned (Article 5a.1). The same article states that "cosmetic ingredient" shall mean any chemical substance or preparation of synthetic or natural origin, except for perfume and aromatic compositions, used in the composition of cosmetic products. The inventory shall contain information on:

(i) the identity of each ingredient, in particular its chemical name, the CTFA name, the European Pharmacopeia name, the international non-proprietary names recommended by the World Health Organisation, the IUPAC name, the EINECS, CAS and Color Index Numbers, and the common name;

(ii) the usual functions of the ingredient in the final product;

(iii) where appropriate, restrictions and conditions of use and warnings that must be printed on the label. This inventory shall be updated periodically. It is indicative and shall not constitute a list of substances authorised for use in cosmetic products.

(B1) The manufacturer or his agent or the person to whose order a cosmetic product is manufactured or the person responsible for placing an imported cosmetic product on the Community market shall for control purposes keep the following information readily accessible to the competent authorities of the Member State concerned at the address specified on the label in accordance with Article 6(1)(a):

(a) The qualitative and quantitative composition of the product; in the case of perfume compositions and perfumes, the name and code number of the composition and the identity of the supplier.

(b) The physico-chemical and microbiological specifications of the raw materials and the finished product and the purity and microbiological control criteria of the cosmetic product

(c) The method of manufacture complying with the good manufacturing practice laid down by Community law or, failing that, laid down by the law of the Member State concerned; the person responsible for manufacture or first importation into the Community must possess an appropriate levels of professional qualification or experience in accordance with the legislation and practice of the Member State which is the place of manufacture or first importation.

(d) Assessment of the safety for human health of the finished product. To that end the manufacturer shall take into consideration the general toxicological profile of the ingredients its chemical structure and its levels of exposure. Should the same product be manufactured at several places within Community territory, the manufacturer may choose a single place of manufacture where that information will be kept available. In this connection, and when so requested for monitoring purposes, he shall be obliged to indicate the place so chosen to the monitoring authority/authorities concerned.

(e) The name and address of the qualified person or persons responsible for the assessment referred to in (d). That person must hold a diploma as defined in Article I of Council Directive 89/48/EEC in the field of pharmacy, toxicology, dermatology, medicine or a similar discipline.

(f) Existing data on undesirable effects on human health resulting from use of the cosmetic product.

(g) Proof of the effect claimed for the cosmetic product, where justified by the nature of the effect or product.

(B2) The assessment of the safety for human health referred to in Paragraph 1(d) shall be carried out in accordance with the principles of good laboratory practice laid down in Council Directive 87/18/EEC of 18 December 1986 (OJ L 15 of 17.1.87) on the harmonisation of laws, regulations and administrative provisions relating to the application of the principles of good laboratory practice and the verification of their application for tests on chemical substances.

(B3) The information referred to in Paragraph 1 must be available in the national language or languages of the Member State concerned, or in a language readily understood by the competent authorities.

The authorities requirements for Product Information (I), as in the text cited, are clearly related to the requirement to have prompt access to all information that might be needed "for control purposes" on the technical characteristics and safety of every cosmetic product placed on the market. The (I) is in fact set out so that information is easily accessible for an overall assessment of the safety of the cosmetic product on the basis of all relevant knowledge.

4. TESTING OF INGREDIENTS AND SAFETY ASSESSMENT OF THE FINISHED PRODUCT

Although there are many thousands of different cosmetic products on the market within the EU, they are all derived from a far smaller number of ingredients. This is the rationale for concentrating toxicity testing on ingredients, and particularly those of most concern. This is the basis of the lists of authorised ingredients referred to in the preamble to Council Directive 76/768/EEC currently covering colouring agents, preservatives and UV filters. This approach avoids the costly duplication of studies and the unjustifiable use of animals that would result from the routine testing of products.

Article 2 of Council Directive 76/768/EEC requires that cosmetic products put on the Community market must not cause damage to human health when they are applied under normal and reasonably foreseeable conditions of use. Adequate information should therefore be provided in order to evaluate the safety of the final product. In general this can be derived from knowledge of the toxicity of the ingredients, with no need to test the final product. However, in a few cases, testing of the final product may be necessary (Annex 6). Examples are when the vehicle used results in considerably greater skin penetration than that observed in the toxicity studies on the ingredients or if interaction between ingredients is likely to result in the formation of a new, potentially toxic substance, or when there is a claim of reduced skin penetration or toxicity resulting from the formulation. It is up to the suppliers of new products placed on the Community market to ensure that adequate information can be provided for a safety assessment of the finished product.

5. LISTS OF INGREDIENTS

Through progressive amendments to the Council Directive 76/768/EEC, several lists of ingredients have been established on the basis of the results of the latest scientific and technical research.
These lists include cosmetic ingredients for which already existing and new toxicological data have been evaluated and for which conclusions have been drawn concerning their risk for human health when used in cosmetic products.
For some ingredients only concentrations below certain limits are allowed and the field of application is limited for safety reasons.
All cosmetic ingredients so far analysed by the SCC-SCCNFP have been included in a series of Annexes to Council Directive 76/768/EEC. Annexes IV, VI and VII represent the existing "positive lists" respectively for Colouring agents, Preservatives and UV Filters.
Annex II of Council Directive 76/768/EEC lists all the cosmetic ingredients which may not be used cosmetic products, due to their toxicological properties. Annex III lists substances which cosmetic products must not contain except subject to restrictions and conditions laid down.
The Sixth Amendment provides that the Commission shall compile an inventory of cosmetic ingredients on the basis in particular of information supplied by the industry concerned. Also, the Commission must adopt a common ingredient nomenclature which will be integrated into the inventory. The Inventory must be indicative, updated periodically and must not constitute a list of substances authorised for use in cosmetic products.

On 8th May 1996, the European Commission established an Inventory and a common nomenclature of the ingredients employed in cosmetic products (Commission Decision 96/335/EC - OJ L 132 of 1.6.96).
The Inventory contains information concerning a series of details need to identify correctly each ingredient.

The ingredients included in Section 1 (more than 6.000 entries) are listed in the alphabetical order of their INCI names, and the information provided covers all particulars concerning identity, usual functions and restrictions. The abbreviation INCI stands for International Nomenclature of Cosmetic Ingredients and was adopted by COLIPA (European Cosmetic, Toiletry and Perfumery Association) as a truly international approach.
The following technical identification is also included, where applicable:

* INN (International Non-proprietary Name) name

* Ph. Eur. (European Pharmacopoeia) name
* CAS (Chemical Abstract Service) number
* EINECS (European Inventory of Existing Commercial Chemical Substances) number
* ELINCS (European List of Notified Chemical Substances) number
* Chemical/IUPAC (International Union of Pure and Applied Chemistry) name

Section II, on perfume and aromatic raw materials, includes more than 2.400 entities with the information necessary to describe a chemical substance, i.e., a chemical name, a CAS number and an EINECS number. The function of all ingredients is to perfume and the restrictions on the use of a given ingredient are identified wherever relevant with asterisks.

Progress is being made to improve the Inventory.

The SCCNFP has adopted in its Plenary Meeting of 17 February 1999, the following Status Report on the Inventory of Cosmetic Ingredients (SCCNFP/0098/99 Final):

1) During the 59th Plenary Meeting (19th April 1995) of the former Scientific Committee (SCC), the Committee approved the Inventory of ingredients employed in cosmetic products which was proposed, in spite of its problems, in order to comply with the provisions of the 6th Amendment of the "Cosmetics" Directive 76/768/EEC. Nevertheless the SCC gave its approval under two conditions:
   a) Swiftly improve the inventory on the lines proposed by the Working Party (see Annex I).
   b) Clearly state in the introduction to the Inventory that it would be regularly updated.
2) The objective of the Inventory is to ensure consumer protection and information by an appropriate labelling of the ingredients using a common nomenclature, and to serve as a tool in the Commission's efforts for the protection of the consumer's health.

The following comments on the relevance of the Inventory of cosmetic ingredients may be emphasized:

a) First of all, the word "Inventory" is rather poor to express its role and function, mentioned above, because the Article 5a does not intend to establish just a catalogue of ingredients; on the contrary, each entry must contain information of a given ingredient able to permit a correct chemical identification as well as the ingredient's functions and, where appropriate, any restrictions and conditions of use and warnings. This information is necessary because it is useful for the Health Authorities of the Member States to solve medical problems potentially associated with the use of a cosmetic product. It is impossible for an individual to know the toxicological profile of all possible ingredients which may be included in a cosmetic formulation; in this context, the Inventory of Cosmetic Ingredients should be the essential tool to more easily obtain the information needed to determine a medical decision.
b) Each entry of the Inventory should include a precise identification of the cosmetic ingredient using the following parameters: its chemical name, the CTFA (Cosmetic, Toiletry and Fragrance Association) name, the European Pharmacopoeia name, the international non-proprietary names recommended by the World Health Organisation, the IUPAC name, the EINECS, CAS and Colour Index Numbers, and the Common Name. As a consequence, each entry must

identify only one ingredient and one ingredient must be identified by only one entry.

c) The Commission has adopted as Common Names the former CTFA Names, which were re-named INCI (International Nomenclature Cosmetic Ingredient) Names to indicate their official acceptance at international level. Objective exceptions to this rule were the substitution of the English botanical names by their systematic (Linné) latin names, and the substitution of the US FDA names for certified colors by the names adopted in the Annexes of the Cosmetic Directive (CI Numbers, codified HC hair dyes etc).

3) A Commission's expert has proposed corrections and amendments to the Inventory and has reviewed the information regarding the new ingredients to be incorporated in the Update. Industry has introduced new functions and amended the Inventory accordingly.
4) A draft update concerning existing ingredients was presented by Industry in November 1998. A final Update of the Inventory should include the new ingredients and the modifications proposed for existing ingredients.
5) The Specific Working Party (SWP) "Inventory" has presented working documents on specific issues such as "INCI names of Ethyl Hexyl derivatives", "INCI names of Amphoderivatives", "Nomenclature of ingredients of botanical origin", "Section II of the Inventory on Fragrances" and has discussed these issues with the concerned bodies.

At present the information given for many entries in the Inventory is not adequate and needs to be corrected. In particular, the following six priorities must be incorporated into the 1st update of the Inventory.

- To accomplish the principle: each INCI name should refer to only one specific ingredient.
- To correct the INCI names of Ethyl Hexyl derivatives and to adopt a final decision about Amphoderivatives.
- To solve problems of nomenclature of ingredients of plant and animal origin with more transparency, as approved, particularly by indicating: the part of the plant used and the type of preparation or derivative. In addition the main chemical components and, if appropriate, specific components of potential concern must be included under Chem/IUPAC name.
- To solve problems on chemical identification associated with polymers.
- To solve the problem of hair dyes/cosmetic colorants concerning C.I. identification and restrictions.
- To improve the functions of the ingredient. Examples: Additive, Biological additive, Oral care.

The adoption of these 6 recommendations by the Industry requires:

- To change the statement in the preamble of the Section I: "An INCI name may cover several chemical entities" by "one ingredient one INCI name and one INCI name one ingredient".
- To revise and to modify accordingly the nomenclature conventions referring to the proposed 6 recommendations.

6) The Committee considers that it is indispensable to take into account the suggested modifications of the entries of the Inventory published in 1995, before the adoption of the 1st update of the Inventory.

Annex

INVENTORY SUB-GROUP MEETING
Brussels, 12th December 1996

SCC RECOMMENDATIONS FOR UPDATING THE INVENTORY OF COSMETIC INGREDIENTS

1) Include INCI nomenclature conventions to explain abbreviations and generic names.

2) Include structural formula for well defined chemicals.

3) Specify in the complex extracts (from plants or animal sources) the principal component(s) and other component(s) with specific functions.

4) Apply special case by case consideration for those natural extracts recognised as possibly containing substances known to have toxic potential. Placing into Annex III should be considered.

5) Correct the errors in common names.

6) Include well known ingredients not present in the Inventory but currently in use by the Cosmetic industry.

7) Consider ELINCS as a useful source of new ingredients for updating the Inventory.

8) Delete ingredients not presently used by the Cosmetic industry.

9) Describe more accurately the actual functions of Cosmetic ingredients.

10) If several synonyms exist for a given ingredient, make cross reference to the most widely used (e.g. "Matricaria chamomilla", See "Chamomilla recutita"; "Acid blue 1", See "C.I. 42045").

ADDENDUM

In the light of the revision of the Inventory, some particular problems concerning (1) UV filters and UV absorbers, (2) Preservatives and Antimicrobials, have to be taken into consideration.
According to their use, both categories are submitted to restrictions (positive list Annexes) or not.

Whatever their actual regulatory status, regarding their toxicological profile they must be considered on the same basis.

6. CATEGORIES OF COSMETIC PRODUCTS AND EXPOSURE LEVELS IN USE

The assessment of the safety of a cosmetic product clearly depends on how it used. This is important, since it determines the amount of substance which may be ingested, inhaled or absorbed through the skin or mucous membranes. Consideration of the quantity of ingredients used in the different products is also important, as the following examples may illustrate.

For example, soaps are applied in dilute form and although the area of application may be extensive, the product is rapidly washed off.

Products used on the lips and mouth will be ingested to some extent.

Cosmetics used around the eyes and genital regions may come into contact with the conjunctiva or mucosa respectively, resulting in reactions due to the thin epithelial lining of these areas.

Sunscreens, body lotions or body creams may be applied over a large surface of the body and the ingredients, often at appreciable concentrations, may remain in contact with the skin over several hours. Sunscreens, due to their extensive skin contact, combined with direct exposure to UV radiation for prolonged periods, require a distinct type of safety evaluation (see Annex 2)

Thus before any safety evaluation and risk assessment of a finished product is made, the degree and route of consumer exposure must be ascertained. This has to be done on a case-by-case basis but the following may provide guidance.
In calculating the exposure the following factors at least must be considered.

1. *Class of cosmetic product(s) in which the ingredient may be used.*
2. *Method of application: rubbed-on, sprayed, applied and washed off, etc.*
3. *Concentration of ingredients in product.*
4. *Quantity of product used at each application.*
5. *Frequency of application.*
6. *Total area of skin contact.*
7. *Site of contact (e.g., mucous membrane, sunburnt skin).*
8. *Duration of contact (e.g., rinse-off products)*
9. *Foreseeable misuse which may increase exposure.*
10. *Nature of consumers (e.g., children, people with sensitive skin).*

11. *Quantity likely to enter the body.*
12. *Projected number of consumers.*
13. *Application on skin areas exposed to sunlight.*

The relevant exposure depends upon the toxicological effects under consideration. For example, for skin irritation or phototoxicity the exposure per unit area of skin is important, while for systemic toxicity the exposure per unit of body weight is of more significance.

The exposure route or routes (skin, mucous membranes, ingestion, inhalation, skin exposed to sunlight) must be considered in designing any test programme and in risk analysis. The possibility of secondary exposure by routes other than those resulting from direct application also should be considered, e.g.. inhalation of hairsprays, ingestion of lip products.

Usage of cosmetics products depends on several factors, some of which will vary over time, such as age group, seasonal variations, local habits, fashion trends, disposable income, product innovation.

Because of these changing conditions, it is not possible to indicate in this document specific use levels of cosmetics. They should be defined in a case-by-case approach in the safety evaluation, once the results of testing, as recommended in the guidelines have become available.

In Annexes 4, 5, and 6 some data concerning the level of consumer exposure for specific categories of cosmetic ingredients, are however included.